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DEEP VENOUS THROMBOSIS IN LOWER LIMBS, USING CRITERIA WELLS ET AL. (2003), D-DIMER, DUPLEX AND EVALUATION OF C-REACTIVE PROTEIN

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ABSTRACT

Deep vein thrombosis (DVT) is common and important cause of morbidity- mortality, presenting Potentially fatal complications such as pulmonary thromboembolism. Diagnosis is one of the most problematic aspects. The disease signs and Symptoms are non-specific, complementary exams must be Performed to confirm diagnosis and start of anticoagulant treatment. To evaluate the efficacy of the Wells et al. Protocol (2003) and D Dimer test (DD) the diagnostic methods for DVT Compared to Duplex Mapping (DM) and analyze changes in C-reactive protein (CRP) Compared to DD. We selected 203 Patients with signs and Symptoms suggesting DVT. After being Submitted to anamnesis and general physical examination to fill out the Wells et al. evaluation protocol card and collection of material is DD and CRP measurements, pacientes Were submit test to DM to confirm or exclude DVT. There Were the significant differences between gender and age in the groups. The Wells protocol is a good predictive exam. DD presented high efficacy of the diagnosis method, useful for excluding DVT and CRP levels did not present any relationship with DD levels.

KEYWORDS: Venous thrombosis; Lower extremity; Diagnosis; Ultrasound; Doppler; Duplex Mapping.

1. INTRODUCTION

Deep vein thrombosis (DVT) is a disease characterized by acute thrombus formation in the deep venous system and the lower limbs the most affected sites. The clinical picture is quite varied, depending on the extent of thrombosis and the affected veins and may have local or systemic manifestations. Symptoms can range from a small local discomfort to serious complications such as pulmonary embolism (PE), with dyspnea and acute respiratory failure, chronic venous insufficiency (CVI) and chronic respiratory failure.[1,2]

DVT is a common cause of morbidity and mortality in both bedridden or hospitalized patients, as in previously healthy patients. Its exact incidence is unknown, as most studies are limited by the difficulty in clinical diagnosis.

The data likely underestimate the true incidence of DVT suggest about 80 cases per 100,000 inhabitants each year just in the United Unidos.[3] About one person in 20 develops DVT throughout his life, totaling about 600,000 hospitalizations per year. Of these, 50,000 are complicated with PE and possibly DVT is the main cause 90% of deaths by acute PE.[4]

In Brazil, the estimate is 0.6 occurring DVT cases per 1000 inhabitants to year.[5] In 2012, the National Health System, 35,120 admissions were made by DVT, developing 4,892 to EP. Of this total, 1,157 patients died, indicating a mortality rate of 23%.[6]

DVT in the lower extremities may be divided, according to their location, proximal and distal. It is considered proximal when it affects iliac vein and / or femoral and / or popliteal with or without thrombosis in the veins of the leg and distal when only affects the leg veins. The correct location of DVT is important for assessing the risk of complications, since the risk of PE and severity of

CVI are greater in the cases of proximal DVT. Despite the lower risk of complications at the distal DVT, it is known that up to 20% of cases may have progression of thrombosis distal proximal segments.[7]

One of the biggest problems is the diagnosis DVT. The signs and symptoms of DVT and PE are nonspecific and, consequently, many patients with pain and swelling in the lower limbs or chest pain and dyspnea can be investigated, but not having DVT or EP.[8] The opposite can also occur, as in early stages, only 30 to 50% of patients present with signs and symptoms typical of DVT.[9,10] in addition, patients with subtle symptoms of lower limb DVT can be extended because the recent thrombus, when it reaches the larger veins, can be floating in the bloodstream without causing significant obstruction and so the clinical manifestations are small and intense.[2]

The main symptoms reported by patients with DVT are: calf pain, swelling, muscle tenderness, dilated superficial veins, painful palpable cord in path of the deep venous system and increased temperature in the affected limb. The sensitivity and specificity of these symptoms are too low to be considered in isolation in the diagnosis of DVT and moreover, only 46% of patients with a clinical diagnosis of DVT have their diagnosis confirmed by venography.[2]

Pain in the calf and is the most common symptom is also the most sensitive, with values ranging from 62 to 90%. The presence of a palpable cord painful path in the deep venous system is the most specific sign of DVT (98%), but with a sensitivity of only 10%.[11] Local inflammatory signs may also be present in cases of DVT. Pain, swelling and temperature rise have 86, 97 and 72% sensitivity, respectively, but with lower specificity.[12]

Thus, patients with suspected DVT have become subjected routinely to further examination which may confirm, directly or indirectly, the presence of thrombus.

MD enables the assessment of venous flow quickly and easily, with good visualization of veins, including allowing the identification of non-occlusive thrombi and the smaller caliber vein. characteristics are evaluated as the vessel compressibility phasic flow variations with respiration or Valsalva maneuver and the presence of echogenic material within the vein. Currently, the most widely used method for the diagnosis of DVT and its main limitations the high cost of the device and the fact that the examiner dependent.[16,17]

To better define patients with suspected DVT of the possibility of actually presenting the disease, some authors have proposed the use of clinical models as a pre-test to determine the probability of DVT in symptomatic patients.[19,20,21]

In these clinical models, the signs and symptoms of the

The ideal method for DVT diagnosis would be one with high accuracy, high sensitivity and specificity, and high predictive value. Furthermore, it should be safe, low cost, with minimal discomfort to the patient, easily applicable and interpretable. None of the methods currently used can fulfill these criteria completely. However, each test has its peculiarities, advantages and disadvantages.

To date, venography is the technique considered the gold standard in the diagnosis of DVT. When done well, it has high specificity and sensitivity. When performed under appropriate conditions and by a qualified examiner, it provides an excellent assessment of the deep venous system, demonstrating the absence of DVT through uniform distribution of contrast in the veins. The occurrence of failures in the vessel filling by contrast confirms the diagnosis of DVT, determining the location and extent of thrombus.[13]

Despite the effectiveness venography is an invasive diagnostic method of implementing uncomfortable and painful for patients. In addition to the contrast hypersensitivity reaction and the risk of renal injury nephrotoxicity, 7% of patients may have thromboembolic complications after the examination, including the risk of EP.[14]

Among the survey's limitations we can also cite the risks of performing during pregnancy and the impossibility of performing it in seriously ill patients, hospitalized in intensive care unit.[15]

Care unit because of these limitations, venography has been gradually replaced by non-invasive methods, especially by ultrasound (US). In current equipment, the US is associated with Doppler and duplex scanning call (MD) or eco-doppler, which allows a simultaneous evaluation of the vessel image and blood flow characteristics in Doppler spectral analysis.

disease are combined with known data on the incidences and DVT risk factors. Among the developed models, the Wells[19] protocol was the only tested in practice for DVT as its reliability and accuracy.

The clinical utility of Wells protocol was further demonstrated in practice in other studies using the MD to confirm the diagnosis of DVT, resulting in a reduction of the need for the use of venography or MD repeat the diagnostic strategy DVT.[22, 23]

Laboratory diagnosis is based on the search of coagulation and fibrinolysis markers. Although activated enzymes of the coagulation and fibrinolysis are transient, by-products of activation can be measured. Other products that can be titrated are prothrombin fragment 1 + 2, fibrinopeptide A and the thrombin-antithrombin complex. These tests reflect the activation of thrombin activity, despite, are not routinely used in clinical

practice, because they are complex and determining slow.[24]

The D-dimer (DD) is a specific product of the degradation of fibrin by plasmin. The measurement of plasma levels and fibrinolytic activity reflects the presence of thrombi within the vessels, with good sensitivity for the diagnosis of DVT.[25] However, since the DD is present in any situation in which no fibrin formation and degradation he is not a specific marker for DVT and can generate false positives in various situations, such as recent surgery, trauma, cancer, and sepsis. Thus, DD acts as an important test, especially in the diagnosis of exclusion, since almost normal levels exclude the presence of DVT.[26,27]

Brotman et al (2003)[28] observed that, in hospitalized patients with venous thromboembolism, there are factors that influence the specificity of the DD, and the increased levels of C-reactive protein (CRP) reduces the specificity to 28% of the method.[29] Despite, the influence of CRP in the dosage of DD in patients with DVT, not hospitalized, has not been evaluated.

Moreover, Bucek et al (2002)[30] evaluated the CRP and DD test and found that the CRP does not have improved sensitivity and negative predictive value but has demonstrated better specificity and positive predictive value. However, this test does not provide information about the etiology of this increase or the differential diagnosis of DVT.

The latest strategy for the diagnosis of DVT is based on the application of a clinical model already recognized and validated[31] in association with a specific test and goal for the diagnosis of DVT, such as MD and measurement of DD, seeking a rational algorithm, safe and lower cost.

Studies according to this new strategy have shown similar results. However, the number of tests performed in the algorithm is different between studies, should be the particularity of each algorithm, making it difficult consensus on which one is the best to evaluate patients with suspected DVT lower members.[32, 33 34]

In this paper, we evaluate the diagnostic efficacy of Wells and DD protocol compared to MD and analyzing the increase in CRP levels compared to DD.

2. GOALS

2.1. General objective

To evaluate the tests used in the diagnosis of DVT of the lower limbs: Criteria Wells et al (2003) and DD with respect to the MD. Also check the role of C-reactive protein in the diagnosis of DVT.

2.2. Specific objectives

a) Evaluate the effectiveness of the clinical model of Wells (2003) for the diagnosis of DVT compared to MD.
b) Evaluate the effectiveness of DD dosage for the diagnosis of DVT compared to MD.
c) To assess possible changes in CRP levels compared to DD levels and no influence on the diagnosis.

3. LITERATURE REVIEW

3.1 Mapping Duplex

The US is a mechanical wave whose frequency is greater than 20kHz, maximum frequency of human hearing. For image acquisition purposes, the frequency used ranges from 1 to 10 MHz. As for the acquisition of 2D images of peripheral vessels, the frequency typically used in US equipment revolves around 7MHz, allowing reduced penetration loss signal penetration and better spatial resolution because the higher the frequency, the higher the resolution.[35]

The US showed considerable technological progress in the last 30 years. The simplest technique is ultrasound B mode, which provides the image to grayscale and allows direct visualization of the vessel lumen. More recently, US have been complemented by a set of Doppler ultrasound techniques that contribute to the analysis of the blood flow image to grayscale using techniques such as flow image in color and power Doppler.[36]

The Doppler technique relies on the difference between the frequencies of a transmitted signal and a received signal when there is a relative movement between the source and receiver signals. On examination of us, the Doppler effect can be observed in two stages: first, the signal source (transducer) is stationary in relation to the propagation and receivers (blood cells), which reflect and scatter the signal, are in motion. In the second stage, considering the reflected signal sources (blood cells) are moving and the receiver (transducer) is stationary relative to the middler.[18,37]

The velocity information is contained in an image generated by the Doppler technique, which has a blood speed versus time graph. Once blood flow is formed by a set of cells, with different speeds, that reflect and scatter the signal in a different frequency, the graph can be represented by a simple and well-defined line. The end result is a speed versus time graph comprises the range of frequencies corresponding to the different speeds of cells to each unit of time.[38]

Doppler allows you to check the presence of venous flow through the spontaneous sound signal detection and phasic with respiration in the projection of the veins to be assessed and an increase of the signal in response to distal or proximal compression sudden decompression. Based on the changes in these parameters, the examiner can diagnose DVT.

The MD is the combination of US image or real time techniques associated with the Doppler speedometer, allowing simultaneous evaluation of the image of the vessel and blood flow characteristics in spectral analysis

or color Doppler. Thus, a better evaluation of venous flow and better visualization of the veins is possible, facilitating the identification of non-occlusive thrombi and the veins of lower caliber.[5]

The advantage of the color flow image is mainly to help identify the deep veins, especially in the calf. The techniques used for diagnosis of DVT include venous compressibility assessment (normal veins can be fully compressed) to viewing clots directly on the generated image and the presence of flow in the vessel. Despite the good acceptance among patients, the MD requires an experienced examiner and prolonged time to complete evaluation of the veins of lower members.[36]

Currently, MD is the non-invasive procedure considered the gold standard for the diagnosis of DVT. It has a sensitivity of 100% and specificity of 98% for cases of proximal DVT, and sensitivity of 94% and specificity of 75% for cases of distal DVT, with a positive predictive value (PPV) of 94% and negative predictive value (NPV) 99.3%.[39,40] The compressibility test can be performed both in MD and in the US mode B. Its effectiveness in MD is high, with 95% sensitivity and 96% specificity, in addition to PPV 97% and NPV of 98% in symptomatic patients with DVT proximal.[41]

In patients with distal DVT, the accuracy of MD drops significantly, with sensitivity and specificity around 70%.[7] Although a generally self-limiting condition and low risk for PE, about 20 to 30% of patients with DVT distal can present great length and involve larger proximal veins, potentially increasing the risk of EP.[42] for this reason, patients with initially negative US usually undergo a further examination in seven or 10 days to exclude proximal extension of thrombosis.

The lower a0ccuracy of MD in cases of distal DVT has been overcome with the technological advances of the last decade. The use of equipment with better acquisition of image and color flow improves the diagnostic accuracy of the DS for DVT distal.[15] The combination of MD in color and power Doppler use increases the sensitivity of the test to 100% and the specificity to 79%, with PPV of 71% and NPV of 100%.[43]

Another limitation of the MD is in the evaluation of asymptomatic patients because, similarly to what happens in cases of distal DVT, the accuracy of the MD for asymptomatic DVT diagnosis is also lower compared to symptomatic DVT. This difference has been linked to the fact that the newly formed thrombus present decreased consistency and not fully occlude the venous lumen, which impairs the compressibility test. In addition, the recent thrombus has the same echogenicity of the blood and hinders your visibility in the US. In these patients, the MD has a sensitivity around 55% and specificity of 98%. Thus, the method can be safely used to confirm the diagnosis of DVT when positive, but can not delete it when negative.[44]

Recent studies have sought to overcome the limitations of MD for the diagnosis of distal DVT and asymptomatic cases. When done fully, in all the deep veins of the leg from the ankle to the groin of patients with symptoms suggestive of DVT, the test has improved reliability, since 99% of test patients with initially normal not present thromboembolic events in the following three months.[45]

Another possibility is to perform serial examinations to assess the progression of distal DVT initially undiagnosed and adoption of clinical pre-test or combination with laboratory tests in conjunction with the MD.[41.43]

Despite its limitations, the role in the MD in the diagnosis of DVT is well established. The MD remains the best non-invasive method to replace venography. It presents the main advantages are lower cost, the absence of the use of radiation and contrast and a high accuracy, in addition to good acceptance and tolerability by the patient.[5]

3.2 Pre-Clinical Testing of Wells

In order to overcome the limitations of the US, Wells et al (1995)[46] developed a clinical model for evaluating symptomatic patients and indicate the actual probability of DVT in association with the US. For this, we elaborated criteria divided into three categories: signs and symptoms, risk factors and likely differential diagnosis (Table 1).

The criteria were divided into major and minor, according to its relevance and the final analysis was classified as follows:

a) A high probability of presenting DVT: 3 or more major criteria and no differential diagnosis or two or more major criteria, added to 2 minor criteria and no differential diagnosis.

b) Low probability of having DVT: 1 major criterion plus 2 or more minor criteria and 1 differential diagnosis; 1 major criterion plus 1 or more minor criteria and no differential diagnosis; No major criterion with 3 or more minor criteria 1 and differential diagnosis; or no greater criterion with 2 or more minor criteria and no differential diagnosis.

c) Moderate probability of presenting DVT: all other combinations.

Table 1 - Clinical model to determine the probability of having DVT proposed by Wells et al. (1995)

Major criteria
Neoplasia activity Paralysis, paresis or recent immobilization with plaster of the lower limbs Recent bed rest for more than 3 days and / or major surgery in the last 4 weeks Increased sensitivity along the deep venous system veins Edema around the member Calf swelling (> 3 cm) from the normal leg Family history of DVT (two or more first-degree relatives)
Minor criteria
Recent history of trauma in the symptomatic leg Pitting edema (locker) higher in the affected leg (unilateral) Superficial collateral veins Previous hospitalization in the last 6 months Erythema

The authors demonstrated a high positive predictive value of US in patients with clinical moderate and high probability of DVT and a high negative predictive value of US in patients with low probability. Thus, the use of clinical model combined with the US reduce the number of positive and false negative results, thus simplifying the diagnostic process by excluding the test series those patients with a low probability of DVT and negative US.

To facilitate its practical application, the model was modified using logistic regression analysis. The revised model took into account risk factors for DVT, such as cancer activity, immobilization with plaster, paralysis and major surgery and clinical characteristics such as edema in every member, difference between the diameters of calf presence of movement visible superficial vein and pain in the path of the deep veins. Each criterion was given one point and when the patient had a more likely differential diagnosis, such as cellulitis, lymphedema, Baker's cysts or muscle bruising, were subtracted from colon, as shown in.[19]

In this model, the patients were classified into three groups: low probability, when the score equals 0 or less; moderate probability when the score is equal to 1 or 2; and high probability when the score is equal to or greater than 3. The follow-up of patients was performed according to the algorithm described in (Figure 1).

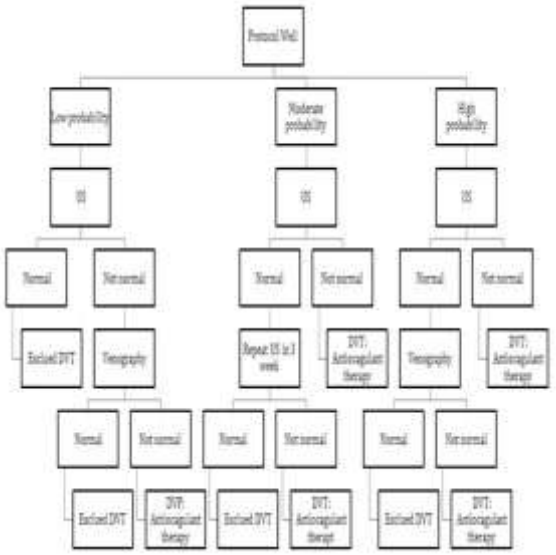

Figure 1 - Algorithm for clinical application of the model proposed by Wells et al. (1997) table list.

Patients with low probability were subjected to a single US. If the US was negative, the diagnosis of DVT was deleted and the US is positive, the diagnosis was confirmed by venography. Patients with moderate probability and positive US were treated for DVT, while those with negative US underwent a new US in a week. Patients with high probability and positive US were treated for DVT, while those with negative US underwent venography.

The new version of the clinical model proved the reduction in the number of positive and false negative results as well as reduce the need for US series.

The clinical trial was reproduced by other authors proved to be effective in all studies.[22,26,47]

In Brazil, the second version of the Wells model was applied to 489 patients, found 147 patients with low probability of DVT, 171 and 171 with an average probability with high probability. Those with initially negative MD, the second examination after seven days

DVT found in only 2.4% of patients with low probability. These results prove the efficiency of the Wells model and allow patients with low to moderate probability of DVT are discharged from the second scan.[23]

A study in the ER has also demonstrated that the application of pre- clinical testing is effective in the evaluation of patients with suspected DVT treated at the emergency sector. In this study, we found 9.6% of cases of DVT in patients high probability. The sensitivity and NPV for the DD associated with pre-clinical testing were 100%, however for the DD alone were 80 and 95%, respectively. These results corroborate earlier, suggesting that patients with low to moderate probability of DVT with negative DD need not perform MD.[48]

Despite ample evidence of the effectiveness of the Wells model, a study in Switzerland pointed as the main test disadvantages the fact of not taking into account the family history of DVT and the exclusion of patients with previous DVT.[21]

From this study, the third change was made in the predictive model of Wells, which has included among the risk factors to DVT antecedent proven by objective examination.

The final classification was simplified again and the patients divided into only two groups:
a) Possibly without DVT when the score was less than 2.
b) Possibly with DVT when the score was equal to or greater than 2.

A new follow-up protocol was tested in which the patients were subjected to dosage DD before performing the US (Figure 2).

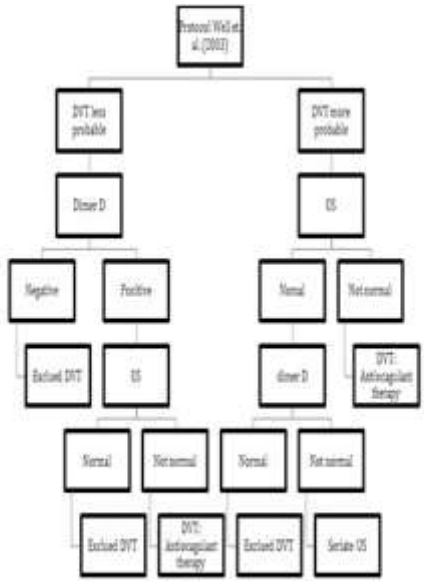

Figure 2 - Algorithm for application to the clinical model reviewed by Wells et al. (2003).

The third version of the pre-test was used in association with the MD and DD in 566 patients and associated only with the MD in 530 patients. The result was less need for MD, since this test may be omitted safely in patients allocated to group possibly without DVT and negative DD.[31]

3.3 D-dimer

DD is a specific product generated from the degradation of the fibrin matrix in cases of endogenous fibrinolysis. It is typically high in cases of DVT, however, it is a bit specific method and may present high levels in the event of major surgery, hemorrhage, sepsis, trauma and malignancy. DD levels may also be increased during pregnancy and at advanced ages.[49,50,51]

Many studies have shown that DD has high NPV and good sensitivity in the diagnosis of DVT, but low specificity. For this reason, the DD dosage has been not used for the diagnosis of DVT, but for its exclusion.[46,52,53,54]

There are several ways to measure the DD, the most prominent methods, qualitative latex test, the quantitative ELISA *(enzyme linked immunosorbent assay)* and derivatives ELISA methods, these, the ELFA method *(enzyme linked fluorescent assay)* is the most used today. Each technique provides different sensitivity and specificity for the DD.

Conventional ELISA has a sensitivity ranging 95-99% and specificity 37- 45%.[47] Since the ELISA, the ELFA method, the VIDAS® equipment *(immunofluorescent Vitro Diagnosis Assay)*, which is a technique of simple and rapid implementation the conventional ELISA has a sensitivity of 96% and specificity of 39%, with NPV of 99%, a figure that confirms its importance as a diagnostic method of exclusion.[32]

The qualitative latex method is little used due to its low sensitivity (78 to 87%) and low (VPN 84 to 91%).[34, 54]

In a comparative study between different DD measurement techniques, the conventional ELISA and rapid techniques showed similar sensitivity, with values of 98 and 96%, respectively.[55] Since the agglutination test for latex showed much lower results than the other tests, preventing his technique, even as diagnostic exclusion method.

Brotman et al. (2003)[27] evaluated the utility and limitations of DD in the diagnosis of DVT in patients hospitalized with four different dosing methods and found that the test has little or no utility in distinguishing patients with and without DVT in cases of more hospitalization than three days, the age of 60 years old and elevated CRP levels. On the other hand, the use of DD in emergency rooms may be useful because often you can not perform a definitive test for the diagnosis of DVT.[56]

It is believed that DD specificity is strongly associated with clinical probability of DVT, so that patients with low probability of DVT generates less false positives than expected when compared to tests carried out in an unselected population. Thus, there is a promising role of DA as adjunctive test in the diagnosis of DVT, especially when used in conjunction with US or MD and examinations clinical prediction as the template Wells. Patients with low clinical probability of DVT and negative DD test associated with MD also negative, need not undergo serial examinations, simplifying the management of patients with suspected DVT.[5]

3.4 C-Reactive Protein

CRP is an acute phase protein, synthesized by the liver in response to cytokines, are important systemic inflammation marker. Clinically, patients with DVT may present the four cardinal signs of inflammation: pain, heat, redness and swelling, particularly when associated with other diseases such as erysipelas. Once the inflammatory response can play an important role in the development of DVT, it has suggested that the dose CRP could be used as a diagnostic method.[57]

It is known that thrombin, a known pro-coagulant factor, is able to stimulate multiple inflammatory pathways and the specific cytokines, such as interleukin-6 (IL-6), IL-8 and monocyte chemoattractant protein-1 (MCP-1), all capable of activating the coagulation cascade.[58,59]

Laboratory studies have shown that peripheral blood monocytes when incubated with highly purified human CRP (> 90%) for six hours, exhibit significant increase in the procoagulant activity due to increased expression of tissue factor responsible for activating the extrinsic coagulation pathway.[60]

Studies in animals have shown that thrombosis induces a direct inflammatory response in the affected vein wall, which involves the activation of neutrophils and expression of selectins, cytokines and cellular adhesion molecules.[61,62] In addition, a study of human saphenous vein, showed that endothelial cells increased the secretion of IL-6 and MCP-1, when incubated with human recombinant CRP.[63]

In a case-control, it was observed that increased levels of inflammatory cytokines IL-6, IL-8 and MCP-1 were associated with DVT however, no significant differences were observed in the levels of inflammatory markers in patients with past DVT and DVT recent. Although the authors postulated that the inflammatory state possibly precede DVT, this relationship was not directly established.[64,65]

In another study, it was observed that during the acute phase of DVT, the levels of IL-6, IL-8 and CRP are significantly higher than in the other patients. CRP levels show an initial increase in the second and third days of development, remaining elevated for up to five days after the onset. The progressive decline in CRP levels during the first five days, could indicate that the inflammatory process is a consequence and not the cause of DVT. This reduction can be attributed to the beginning of anticoagulant treatment.[66]

Different studies were conducted to evaluate the importance of CRP also as a predictive factor for DVT, but none of them was able to prove the association between CRP levels and the subsequent development of DVT.[67,68]

On the other hand, since the main limitation of DD is the high number of false positives in patients with inflammatory diseases and cancer, CRP could also be used as an auxiliary in the differential diagnosis and explain a positive DD in the absence of DVT fact opposed to theories that seek a positive association between DVT and systemic inflammatory response.[29]

- **High-sensitivity C-reactive protein (hs-CRP)**

C-reactive protein, the acute phase protein is known since the beginning of the last century, however, its use as a cardiovascular risk score, consolidated only in recent years with the discovery that atherosclerosis has a strong component inflammatory in its etiology, therefore, the determination of hs-CRP, has become an important diagnostic tool for predicting heart attack and stroke in healthy subjects with no history of cardiovascular disease and recurrent events in people with these diseases.

The hs-CRP is considered high when it is above 3 mg/l, in the absence of other inflammatory diseases. To avoid falsely elevated results in the presence of infectious and acute inflammatory processes, hs-CRP dosage should be avoided.

The population distribution of hs-CRP levels was observed that there is no ethnic and gender differences. It is used to evaluate the hs-CRP, the following values: Low risk, less than 1 mg/l, medium risk, from 1 to 3 mg/l and high risk above 3 mg/l.[96]

Despite the developments and benefit, in the sense of an early approach to cardiovascular pathologies regarding deep vein thrombosis, evaluation of hs-CRP as a specific method for the diagnosis has not been used.

4. METHODS

4.1. Type Study Location

This is a prospective, cross-sectional study conducted in the two largest public emergency rooms of Manaus, Amazonas.

The Hospital and Municipal Emergency Room August 28 has 369 ward beds and 238 surgical beds and 125 beds for clinical treatment beyond 40 ICU beds and five operating rooms.

Hospital and Emergency Room Dr. João Lúcio Pereira

Machado has 204 beds, with 174 beds and 30 wards ICU beds and four operating rooms. annually are recorded an average of 207 thousand people in this institution.

Besides being referral hospitals in the state of Amazonas, they are the ones who have medical experts in the field of vascular surgery, 24 hours a day in the service of emergency care.

4.2. Ethical aspects
The study protocol was approved by the Ethics Committee of the Federal University of Amazonas.

The patients selected were contacted by the lead author and informed in clear and simple language on the realization of this research, which aims, risks and benefits and the procedures used. All were asked about their interest in participating in the study and if so, the patients were asked to sign the Informed Consent and Informed (IC).

4.3. Inclusion criteria
a) Patient of both sexes aged over 18 years old;
b) Patients with clinically suspected DVT, with or without the signs suggestive of EP;
c) Complaints lasting a maximum of 30 days.

4.4. Exclusion criteria
a) Patients under the age of 18 years old;
b) duration of complaints over 30 days;
c) present signs or symptoms of PE alone;
d) Patients on prophylactic heparin or therapy for more than 24 hours.

4.5. Sample
In the period 1º November 2011 to 30 November 2012 were selected prospectively and consecutively, the total of 203 patients who sought medical care in referral hospitals for this study with symptoms and signs suggestive of DVT.

4.6. Study Protocol
Patients who agreed to participate in the study and signed the informed consent were submitted to anamnesis containing an interrogation on the various devices of the human body, personal and family history, in addition to physical examination, as described in the clinical evaluation form of DVT. After that, the Wells Protocol was applied before conducting any laboratory tests, in order to estimate the likelihood of the patient having DVT. Only after the second questionnaire, patients proceeded to the collection of blood for DD and CRP.

4.7. Pre-Clinical Testing: Wells Protocol
The protocol consists of interrogating the patient and / or escort on the risk factors for the development of venous thromboembolic disease (cancer, immobilization, postoperative major surgery or orthopedic and paralyzes surgery) and to perform vascular physical examination (swelling, pain, measure the diameter of the calves, collateral venous circulation superficial view). a score in which the patient receives a point for the presence of each of the factors above was adopted. Furthermore, we investigated the presence of other conditions which justify clinical picture. If the patient presented a more likely differential diagnosis (superficial thrombophlebitis, cellulitis, muscle or tendon rupture, cramps, knee or ankle changes, Baker cyst, lymphatic changes) were deducted two points from their score.

According to the scores obtained in this protocol, patients were classified into two groups:
a) Patients with DVT less likely: lower score than 2 points.
b) Patients with DVT more likely: scores greater than or equal to 2 points.

4.8. D-Dimer dosage - ELFA method / equipment VIDAS®
The quantification of plasma DD levels was carried out in Analysis Laboratories Clinical hospitals Municipal Emergency Hospital on August 28 and João Lúcio Pereira Machado, the equipment BioMérieux brand, VIDAS® model with fluorescence detection at imunoanalisador. As fluorescence is the result of a series of reactions is proportional to the amount of antigens present in the sample.

4.8.1. Goal
The quantification of plasma DD levels, the ELFA method, was established as a useful tool for the exclusion of DVT and / or PE. A negative result defined as equal to or less than 500 mg / ml has a high sensitivity and NPV (100%) for DVT exclusion of the lower limbs.[69]

4.8.2. Principle of the method
Fibrin degradation products of (FbDP) are soluble fragments of heterogeneous composition and result in two simuntâneos phenomena, clotting of fibrinogen in stabilized fibrin after the action of thrombin and factor XIIIa and lysis of the fibrin clot by plasmin soluble fragments , released into the bloodstream. The final products of clot lysis, are D-dimers.

4.8.3. Collection and treatment of the sample
The collection was carried out in accordance with the recommendations on the homeostasis tests:
a) Collection: 9 volumes blood: 1 volume trisodium citrate (0.109 M);
b) centrifuging 15 minutes at 3000 revolutions per minute (rpm) to obtain platelet poor plasma (PPP);
c) Conservation in plasma: 8 am to 20 +/- 5°C or 1 month at -20°C (thawing at 37°C for 15 minutes before use).

4.8.4. usual values
The plasma level DD in adults is usually less than 0.500 g/ml. DD rates are calculated as initial fibrinogen (FEU). The amount of DD obtained from a lysate clot represents approximately 50% of the initially present fibrinogen

rate. For example, a value of 0.50 g/mL FEU corresponds to approximately 0.25 mg/ml DD.

Additional research on the clinical utility of DD test in suspected recurrent DVT patients recommend that it is safe to suspend the examination of venous MD in patients with low clinical probability for DVT and negative DD result.[70,71]

4.9. C-reactive protein

The determination in serum CRP levels was performed in clinical laboratories of hospitals where the study was conducted, following the same criteria for collection and analysis. The value found was considered in the interpretation of DD, being made a parameter in the evaluation of patients in this study.

4.9.1. Goal

Qualitative and semiquantitative CRP in serum.

4.9.2. Test principle

CRP TEST is a suspension of coated polystyrene latex particles with anti-CRP antibodies. This suspension, into contact with samples containing CRP produces agglutination of latex particles, macroscopically visible. The presentation of PRCTEST, comprises a kit containing tests 100 CRP-latex, positive control (1x0,5ml), negative control (1x0,7ml), blade (5) and rods for homogeineização (10).

4.9.3. Collection and Treatment of the sample

The collection was carried out in accordance with the recommendations on the homeostasis tests:

1) Harvest of 3ml blood from the patient;

2) centrifuging the blood, separating plasma (serum) blood from other elements for analysis.

4.9.4. Technical procedure

Qualitative -Test

1) The reagents and samples should be acclimatised before testing. The sensitivity of the reagent decreases at low temperatures. The CRP-latex must be previously stored at 2 to 8°C;

2) Add the first round blade 25 ul serum, 25 ul of the second positive control and 25 ul of the third negative control;

3) Homogeineizar CRP-latex and add 25 ul of the same in each circle;

4) Homogeineizar the drops with a plastic rod;

5) Print movements rotatory 80-100 r.p.m.à blade for 2 minutes to read the following interpretation:

● Positive test: Sharper agglutination

● negative test: Homogeneous suspension

- Interpretation of qualitative test serum with CRP tests than 6mg/l leads to latex agglutination, which is evidenced by the formation of fine or coarse lumps.

- Semiquantitative test

1) Label 5 tubes (12x75mm) from 1 to 5 and place from the tube 1, 200 ul of saline solution;

2) Transfer 200 ul serum into the tube 1, mix and transfer to the tube 2 and so on until the pipe 5. It will be considered positive, the highest dilution of the sample that presents agglutination. We then dilutions which follow, with their equivalents in CRP mg/l:

4.10. mapping Duplex

The MD was carried out in the Diagnostic Service Flow Laboratory Noninvasive in cardiovascular area of the University Hospital Getulio Vargas (UHGV) in imaging ultrasound equipment, Philips - En Display C HD multifrequency linear transducer, from 3 to 12 Mhz, obeying the examination protocol for DVT lab as compressibility and increase the caliber of the vein or committed segment of the intraluminal thrombus presence and absence of flow Doppler.

Venous MD was performed in all patients with suspected DVT, with the patient in the supine position with the stretcher in proclive. a mapping of the deep veins was carried out throughout its length in cross section, observing their morphology, anatomical distribution, its compressibility, the presence of venous flow or thrombus. To carry out the MD of the popliteal and fibular veins was adopted horizontal prone position or lateral, with slight knee flexion.

4.11. Statistical analysis

The data were presented in graphs and tables, which were calculated in the simple absolute and relative frequencies of each variable and in the case of laboratory markers, the confidence intervals at 95% (95%). In the age analysis, we calculated the mean and standard deviation (SD), because the data had normal distribution at 5% by the Shapiro-Wilk test. When comparing the means of quantitative data in relation to categorical data was applied Student's t test or analysis of variance (ANOVA). In the analysis of categorical data we applied the chi-square test of Pearson, when possible.[72,73]

The software used in the analysis was the Epi-Info Version 7 for Windows, which is developed and freely distributed by the CDC (www.cdc.org/epiinfo) and the significance level for the tests was 5%.

5. RESULTS

5.1 Characterization of Patients

Of the 203 patients evaluated with a clinical diagnosis of DVT and included in the study, 111 (54.7%) were female and 92 (45.3%) were male. This initial sample, 133 (65.5%) patients were diagnosed with DVT confirmed by MD, the cases being considered and the other 70 (34.5%) patients whose MD was not compatible with DVT, the controls were considered.

Among the 133 patients who were diagnosed with DVT confirmed by MD 75 (56.4%) were female and 58 (43.6%) were male. The mean age of patients with DVT was 51.7 (± 17.5) years (Table 2).

Table 2 - Distribution by gender and age of the sampled patients with DVT and control.

Variables		Groups						
		TVP		Control				
		f_i	%	f_i	%	Total	%	P
Genre								0,500*
Female		75	56,4	36	51,4	111	54,7	
Male		58	43,6	34	48,6	92	45,3	
Age (years)								0,987**
1	– 29	13	9,8	7	10,0	20	9,9	
30	– 39	27	20,3	12	17,1	39	19,2	
40	– 49	19	14,3	10	14,3	29	14,3	
50	– 59	25	18,8	21	30,0	46	22,7	
60	– 69	22	16,5	9	12,9	31	15,3	
70	– 79	20	15,0	6	8,6	26	12,8	
> 80		7	5,3	5	7,1	12	5,9	
Média ± DP		51,7 ± 17,5		51,8 ± 16,2				

* Pearson's chi-square test; ** Student's t test to compare means; fi = simple absolute frequency; SD = standard deviation.

Among the 70 patients diagnosed with DVT excluded by MD, 36 (51.4%) were female and 34 (48.6%) were male. The mean age of the controls was 51.8 (± 16.2) years (Table 2). No significant differences were observed in gender distribution between cases and controls (p = 0.500) nor between the mean age (p = 0.987), as shown in (Figure 3).

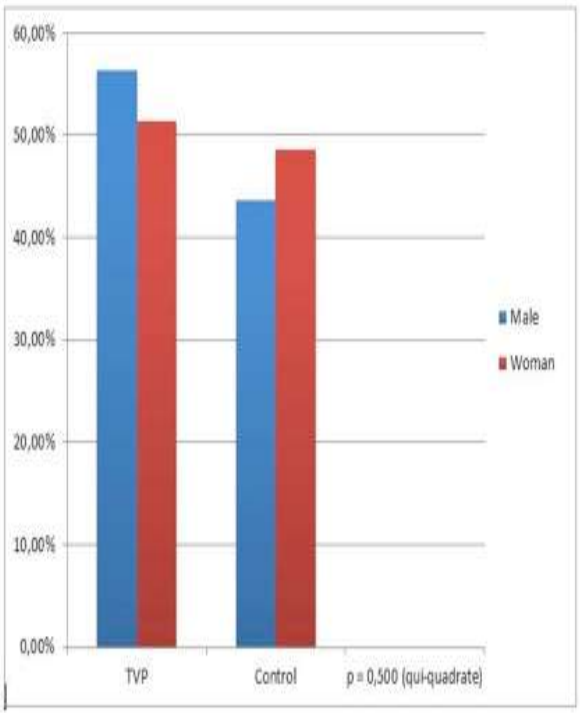

Figure 3 - Distribution according to the frequency of the gender of the sampled patients with DVT and control, Manaus – AM

The breakdown by age group between cases and controls is shown in (Table 2). The site most affected by DVT was the left lower limb. In the control group, the right lower limb was the most affected (Table 3).

Table 3 - Distribution according to a member of the affected frequency in relation to DVT and control groups

		Groups				
The affected limb		**TVP**	**Control**			
	f_i	**%**	**f_i**	**%**	**Total**	**%**
Bottom right	54	40,6	38	54,3	92	45,3
Lower left	79	59,4	32	45,7	111	54,7
Total	133	65,5	70	34,5	203	100,0

P = 0,332 (chi-square test); fi = simple absolute frequency; SD = standard deviation

The main differential diagnoses found in the control group are shown in (Table 4).

Table 4 - Distribution according to the frequency of the result of the differential diagnosis in relation to the gender of the sampled patients

Differential diagnosis		**Genre**				
	Female			**Male**		
	f_{i*}	**%**	**f_i**	**%**	**Total**	**%**
Erysipelas	8	22,2	14	41,2	22	31,4
Varicose veins CEAP** 3	11	30,6	5	14,7	16	22,9
Pedrada Syndrome	5	13,9	7	20,6	12	17,1
Thrombophlebitis of the great	4	11,1	2	5,9	6	8,6
Lymphedema	2	5,6	3	8,8	5	7,1
Edema	3	8,3	1	2,9	4	5,7
Cyst Baker	2	5,6	-	-	2	2,9
Trauma knee	1	2,8	-	-	1	1,4
Snakebite	-	-	1	2,9	1	1,4
Cellulitis	-	-	1	2,9	1	1,4
Total	36	51,4	34	48,6	70	100,0

*fi = simple absolute frequency. You can not apply the chi-square test due to restrictions Cochran (VIEIRA, 2004).
**CEAP = varices Classification (Clinical/Etiology / Anatomy / Pathophysiology) CEAP 3 = Varicose veins with edema.

5.2 Wells Protocol Assessment

In evaluating the clinical efficacy of predictive model of Wells, 152 patients were classified as likely DVT group and of these, 133 (87.5%) had the diagnosis confirmed by MD. On the other hand, in the group classified as DVT unlikely, all they had negative results in the MD, as shown in (Table 5).

Table 5 - Distribution according to the protocol of Wells et al. (2003) about the outcome of the Duplex mapping of the sampled patients.

		Mapping Duplex				
Wells 2003	**Positive**		**Negative**			
	f_i	**%**	**f_i**	**%**	**Total**	**%**
Likely	133	100,0	19	27,1	152	74,9
Not likely	-	-	51	72,9	51	25,1
Total	133	65,5	70	34,5	203	100,0

Sensitivity: 100.0%, 95% CI (99.6, 100.0); Specificity: 72.9%, 95% CI (61.7, 84.0) VPP: 87.5%, 95% CI (81.9, 93.1); VPN: 100.0%, 95% CI (99.0, 100.0).

The test sensitivity was 100% (95% CI 99.6 to 100.0) and the specificity was 72.9% (95% CI: 61.7 to 84.0).

The VPP was 87.5% (95% CI: 81.9 to 93.1) and the NPV was 100% (95% CI 99.0 to 100.0). They found 19 false-positive results (27.1%) and no false negative result. Among the false-positive results, 12 (63.2%) patients Syndrome Pedrada and three (15.8%) had edema.

5.3 Dimer-D evaluation

Regarding the effectiveness of DD, 134 (66%) patients had changed DD and, among these, 133 (99.2%) were diagnosed with DVT confirmed by MD. Of the 69 patients with normal DD, none had DVT in the MD.

The sensitivity was found for DD in relation to MD was 100% (95% CI: 99.6 to 100.0), while specificity was found to be 98.6% (95% CI: 95.1 to 100, 0).

The VPP found was 99.3% (95% CI 97.4 to 100.0) and NPV was 100.0% (95% CI 99.3 to 100.0).

It was only found a false-positive result, which correct diagnosis was erysipelas.

5.4 Evaluation of C-Reactive Protein

CRP dosage results are reported in (Table 6).

Table 6 - Distribution by gender and age of the patients regarding the outcome of the average CRP.

Variables		CRP						
		Positive (n = 74)		Negative (n = 129)				
		f_i	%	f_i	%	Total	%	P
Group DVT (n = 133)								
Genre								0,127*
Female		33	64,7	42	51,2	75	56,4	
Male		18	35,3	40	48,8	58	43,6	
Age (years)								0,157**
1	– 29	6	11,8	7	8,5	13	9,8	
30	– 39	13	25,5	14	17,1	27	20,3	
40	– 49	7	13,7	12	14,6	19	14,3	
50	– 59	9	17,6	16	19,5	25	18,8	
60	– 69	9	17,6	13	15,9	22	16,5	
70	– 79	6	11,8	14	17,1	20	15,0	
> 80		1	2,0	6	7,3	7	5,3	
Média ± DP		49,0 ± 17,3		53,4 ± 17,5				
Group Control (n = 70)								
Genre								0,150*
Female		9	39,1	27	57,4	36	51,4	
Male		14	60,9	20	42,6	34	48,6	
Age (years)								0,151**
1	– 29	2	8,7	5	10,6	7	10,0	
30	– 39	-	-	12	25,5	12	17,1	
40	– 49	5	21,7	5	10,6	10	14,3	
50	– 59	9	39,1	12	25,5	21	30,0	
60	– 69	3	13,0	6	12,8	9	12,9	
70	– 79	2	8,7	4	8,5	6	8,6	
> 80		2	8,7	3	6,4	5	7,1	
Mean ± DP		55,8 ± 14,9		49,8 ± 16,6				

* Pearson's chi-square test; ** Student's t test to compare means; fi = simple absolute frequency; SD = standard deviation.

High CRP levels were observed in 74 (36.4%) patients. Of these, 51 (69%) were diagnosed with confirmed DVT, 33 (64.7%) were female and 18 (35.3%) were male.

In the control group, 23 (32.9%) patients had elevated CRP levels, nine women (39.1%) and 14 (60.9%) were male. There were no statistically significant differences in CRP levels in relation to gender and age in both groups (Table 6).

No statistically significant differences were observed between the CRP level and extent of thrombosis (P = 0.151), as described in Table 7.

Table 7 – Distribution according to the frequency of the result of the extension of thrombosis in relation to the result of the CRP of the sampled patients

			CRP			
Thrombosis extension	**Positive**		**Negative**			
	f_i	**%**	**f_i**	**%**	**Total**	**%**
Distal	2	3,9	9	11,0	11	8,3
Proximal	49	96,1	73	89,0	122	91,7
Total	51	38,3	82	61,7	133	133

P = 0,151 (chi-square test); fi = simple absolute frequency.

Among the cases of DVT, 51 were found positive CRP results (38.3%) DD changed. In contrast, 22 patients had positive CRP even with MD and negative DD (Table 8).

Table 8 – Distribution according to the frequency of the D-dimer result for the outcome of the CRP of the sampled patients for DVT and Control.

		CRP				
Group/D-Dimer	Positive		Negative			
	f_i	%	f_i	%	Total	%
Duplex scan positive (n = 133)						
D-Dimer						
Not normal	51	38,3	82	61,7	133	100,0
Normal	-	-	-	-	-	-
Duplex scan negative (n = 70)						
D-Dimer						
Not normal	1	100,0	-	-	1	1,4
Normal	22	31,9	47	68,1	69	98,6

f_i = Simple absolute frequency

6. DISCUSSION

The prevalence of DVT in several published studies vary considerably depending on the population studied. Fortes et al. (2007) 23 found a total of 191 (39.1%) cases of DVT confirmed among the 489 patients. In the same study, the prevalence of DVT observed between ambulatory and hospitalized patients was 38.1% and 40.7%, respectively.

A study of patients seen in the emergency department found a considerably smaller number of DVT, with confirmed only 45 (13%) of the 344 patients evaluated. Of these, 20 (44.5%) were men and 25 (55.5%) were mulheres. 22 this study, whose population also involved only patients seen in the emergency department, the total incidence of DVT was significantly higher, and found 133 (65.5%) cases of DVT among 203 evaluated patients and 70 (34.5%) without DVT.

This difference can be explained by the fact that in hospitals where the study was conducted, the service was conducted by specialists in vascular surgery and it is referral hospitals, where they receive patients from nearby towns. Similarly to the aforementioned study, the number of female cases (56.4%) was higher than that of males (43.6%), but no statistical value.

Our study coincides with the one conducted by Rollo et al., At the Hospital of the Botucatu Medical School and Hospital Botucatuense Mercy, which evaluated 424 patients using venography as a diagnostic means, of these, 291 (68.63%) had DVT and 133 (31.77%), phlebography showed the presence of DVT.[95]

The etiology of DVT, in our study is similar to that presented by Heit et al (2000) 74, in which they found the detention, as most common cause (59%), followed by idiopathic (26%), where there is no risk factor, cancer (18%) and trauma (12%). In our study, we found more frequently also the immobilization (40.6%), then idiopathic (27.8%), cancer and other risk factors (16.5%), trauma (9.7%) and still other medical procedures (5.2%).

According to Richard (2003) 75, about 25% to 50% of patients experiencing a first episode of DVT, do not have associated risk factors being considered idiopathic.[76]

Among the 203 patients evaluated in this study, 152 (75%) were classified as having a high probability of presenting DVT and 51 (25%) were classified with low probability of DVT, according to the protocol Wells et al. (2003). In the group with DVT, 100% of patients were classified as high probability of DVT. In the control group, 27.1% of patients were classified as high probability of DVT and 72.9% were classified as low probability of DVT. These results differ from the original study presented by Wells et al. (2003) 30, in which the study group showed 45.7% of patients with high probability of DVT and 54.3% with low probability.

Among the group with DVT, 54% had a low probability of DVT and 46% had a high probability of DVT.[31] The difference in results can be explained by the division adopted by the authors among the groups.

In this study, cases were defined from the DVT diagnosis confirmed by MD and controls those who were diagnosed excluded by MD. In the study by Wells et al. (2003), the division of the groups was done randomly and only after allocated to the groups, patients had confirmed or excluded DVT diagnosis. Since we consider only those cases proven patients with DVT, it is expected that most of them has high clinical probability.

The use of clinical tests probability is intended to stratify patients according to risk of developing DVT and thus identify those requiring anticoagulant therapy (moderate or high probability) while awaiting the performance of diagnostic tests. In addition, objective select patients in whom the diagnosis of PE can be discarded (patients with low probability of DVT) when additional tests present negative results.[77]

Based on this concept, few studies have examined the effectiveness of Wells protocol as a single diagnostic method. According Hildner and Ormond (1967)[78], the diagnosis of DVT can not be done based only on clinical suspicion, due to lack of sensitivity and specificity of signs and isolated symptoms, in addition to the low predictive value.

When considering the efficiency of the Wells protocol isolated as a diagnostic method in comparison with MD, we find values that support the concepts described in the literature. The sensitivity of Wells protocol in this study was 100% and specificity was 72.9%. The PPV was 87.5% and NPV was 100%.

Despite high sensitivity, low VPP and low specificity limit its use in clinical practice due to the high number of false-positive results in this study was 27.1%. Still, our results showed higher accuracy than those described by Oudega et al. (2005)[79], who found a sensitivity of 78.9% and specificity of 44.3%, with NPV of 88%.

DD is a well-known test for their high sensitivity and low specificity and, therefore, used as a diagnostic method of exclusion.[52,53]

Although the VPN DD increases proportionally with increased sensitivity, as well as all diagnostic tests, DD VPN is inversely related to the incidence of DVT in the study population. Some studies suggest that most of the techniques used for the DD dosage is presented under the same ROC curve (Receiver Operating Characteristic), demonstrating similar efficacy.[80,81,82] However, a meta-analysis suggested that three techniques performed worse in compared to the ELFA method with VIDAS® equipment, which was the test considered as standard, suggests that it is better to consider the DD tests with moderate sensitivity and specificity, or those with high sensitivity and low especificidade.[83,84]

Using a cutoff level of 400 ng/ml Escoffre Barbe et al. (1998)[87] found a sensitivity of 94.6% and specificity of 35% for LIATEST® D-dimer, which is analyzed by immunoturbidimetric test using latex microparticles coated with anti-D-dimer antibodies. The reported accuracy was higher for cases of proximal DVT, with sensitivity of 98.5% and NPV of 95.6%, while in cases of distal DVT found the sensitivity was 83.8% and NPV 84.6%. The lower accuracy of LIATEST® found by Escoffre Barbe et al. (1998) regarding this study reflects the difference in shear values adopted by both. In our study, using the ELFA method, the adopted cutoff value was 500 ng/ml, a level higher than the previous study. Thus, the test specificity is increased and hence the number of false-positive results in this study was only 1.4%.

A systematic review article made by Goodacre et al. (2005)[88], evaluated changes in DD performance according to the technique used. The studies using LIATEST® had a mean sensitivity of 94% and mean specificity of 46%, inferior results to those found in this study, we used the ELISA, the ELFA method, the VIDAS ® equipment.

The role of CRP in the diagnosis of DVT is not well established. Thomas et al. (1989)[89] evaluated 47 patients with suspected DVT and found 18 (38%) with high CRP levels and diagnosis of DVT confirmed by phlebography. Although the study by Thomas et al., When considering CRP levels as a diagnostic examination isolated compared to phlebography, sensitivity was 100% and specificity of 52%, with PPV of 56% and NPV of 100%, suggesting that low CRP levels could exclude DVT in patients under clinical suspicion. The small number of patients was a limiting factor to the cited work.

larger and more recent studies have shown opposite results to those presented by Thomas et al. (1989), indicating that CRP levels have no value in the diagnosis of DVT. For treating a disease adopted in isolation, or in combination with other tests should be as close as possible to 100%.

In a review article, the sensitivity and specificity found averages for CRP as a diagnostic method for DVT were 77 and 66%, respectively, with an average of 85% NPV, indexes well below expectations for a test diagnóstico.[57]

Wong et al. (1996) 90 evaluated 150 patients, 56 with DVT confirmed. The sensitivity and specificity found for CRP compared to venography were 84 and 62%, respectively, PPV 57% and NPV of 87%. The results presented by Maskell et al. (2001)[91] Were even less promising, with sensitivity and specificity of 60 and 70%, respectively and NPV of only 80%.

In our study, we found 74 (36.4%) patients with elevated CRP levels and of these, 51 (69%) were diagnosed with confirmed DVT, superior numbers to those described by Thomas et al. (1989). In contrast, 82 (40%) patients with DVT confirmed by MD had normal CRP levels, suggesting the low diagnostic value of CRP for DVT cases, although the sensitivity and specificity of the examination have not been calculated.

Regarding the extent of thrombosis, previously published studies suggested a positive correlation with CRP levels. Patients with distal thrombosis had significantly lower CRP levels compared to patients with proximal thrombosis.[66,92] In contrast, our results showed no statistically significant correlation between proximal or distal DVT and CRP levels, suggesting that the extent of thrombosis does not exert any influence on the intensity of the inflammatory response.

Bucek et al. (2002)[29] evaluated 233 suspected cases of DVT and found a positive correlation between CRP levels and DD in patients diagnosed with DVT confirmed by venography or MD. Among the 140 patients with positive DD, 91 also showed high levels of CRP, while among the 93 patients with negative DD, only 14 had elevated CRP levels and 79 had negative CRP.

In our study, of 133 patients with DVT proven by MD, only 51 (38.3%) had elevated CRP and DD, while 82 (61.7%) had high DD with negative CRP.

MD, is considered today, the examination more cost-effective among the imaging methods for evaluation of a patient with suspected deep venous thrombosis.[93]

In our study, the MD, was highly effective, of the 203 patients studied, 133 patients had DVT confirmed by MD. As previously mentioned, the MD has its limitations, especially when it comes to asymptomatic patients and distal DVT. Regarding asymptomatic DVT, the less accurate the MD, with respect to symptomatic DVT, can be explained due to venous thrombus, newly formed, can not be occlusive and have decreased consistency, damaging the test compressibility as well as the thrombus recent have the same echogenicity of the blood, making it difficult to visibility.[44]

7. CONCLUSION

Wells protocol showed good sensitivity and high negative predictive value, but with low specificity. Because it is a predictive test should not be used as isolation, but in combination with more specific diagnostic tests.

The D-dimer proved to be a good diagnostic test with high levels of sensitivity, positive predictive value and negative predictive value, but low specificity and is useful for exclusion of deep vein thrombosis.

With the method, the determination of C-reactive Protein in this study and taking into account the fact that they are not hospitalized patients, did not influence the diagnosis and no correlation was observed between the levels of C-reactive Protein and D-dimer.

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