

The non-compressibility ratio for accurate diagnosis of lower extremity deep vein thrombosis

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ABSTRACT

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BACKGROUND

Accurate identification of patients with deep vein thrombosis (DVT) is critical, as untreated cases can be fatal. It is well established that the specificity of the clinical signs and symptoms of DVT is low. Therefore, clinicians rely on additional tests to make this diagnosis. There are three modalities for DVT diagnosis; clinical scoring, laboratory investigations, and radiology. The objective of this study was to determine the correlation of plasma D-dimer concentration with the ultrasonographic non-compressibility ratio in patients with DVT in the lower extremities.

METHODS

This research was a cross-sectional observational study. The sample comprised 25 subjects over 30 years of age with clinically diagnosed DVT in the lower extremities. In all subjects, D-dimer determination using latex enhanced turbidimetric test was performed, as well as ultrasonographic non-compressibility ratio assessment of the lower extremities. Data were analyzed using Pearson's correlation at significance level of 0.05.

RESULTS

Mean plasma D-dimer concentration was 2953.00 ± 2054.44 $\mu\text{g/L}$. The highest mean non-compressibility ratio ($59.96 \pm 35.98\%$) was found in the superficial femoral vein and the lowest mean non-compressibility ratio ($42.68 \pm 33.71\%$) in the common femoral vein. There was a moderately significant correlation between plasma D-dimer level and non-compressibility ratio in the popliteal vein ($r=0.582$; $p=0.037$). In the other veins of the lower extremities, no significant correlation was found.

CONCLUSION

The sonographic non-compressibility ratio is an objective test for quick and accurate diagnosis of lower extremity DVT and for evaluation of DVT severity.

Key words: Deep vein thrombosis, D-dimer, non-compressibility ratio, age >30 years

Non-compressibility ratio untuk keakuratan diagnosis trombosis vena dalam pada tungkai bawah

ABSTRAK

LATAR BELAKANG

Identifikasi yang akurat pada pasien dengan trombosis vena dalam (TVD) sangat penting, karena bila tidak ditangani dengan baik bisa berakibat fatal. Diagnosis TVD secara klinis sangat sulit, sebab itu klinisi membutuhkan pemeriksaan tambahan untuk menegakkan diagnosis. Terdapat tiga modalitas yang digunakan untuk diagnosis adanya TVD, skor prognosis klinis, pemeriksaan laboratorium dan pemeriksaan radiologi. Penelitian ini bertujuan untuk menentukan adanya korelasi kadar d-dimer dengan non-compressibility ratio pada sonografi TVD tungkai bawah.

METODE

Penelitian observasional dengan desain belah lintang mengikutsertakan 25 orang penderita TVD secara klinis, berusia 30 tahun keatas. Pemeriksaan kadar d-dimer dalam plasma menggunakan metode Latex enhanced turbidimetric test. Ultrasonografi pada tungkai bawah dilakukan untuk mengukur non-compressibility ratio vena tungkai bawah. Analisis data dengan uji korelasi Pearson pada tingkat kemaknaan 0.05.

HASIL

Rata-rata kadar D-dimer plasma besarnya $2953,00 \pm 2054,44$ $\mu\text{g/L}$. Nilai rata-rata non-compressibility ratio tertinggi ditunjukkan pada vena femoralis superficial sebesar $59,96 \pm 35,98\%$ dan terendah pada vena femoralis komunis sebesar $42,68 \pm 33,71\%$. Didapatkan korelasi moderat yang bermakna antara kadar D-dimer plasma dengan non-compressibility ratio pada vena poplitea ($r=0,582$; $p=0,037$). Pada vena-vena tungkai bawah lainnya tidak terdapat hubungan yang bermakna.

KESIMPULAN

Non-compressibility ratio secara sonografi merupakan pemeriksaan obyektif yang dapat digunakan untuk menghasilkan diagnosis secara cepat dan akurat adanya TVD tungkai bawah dan untuk evaluasi berat-ringannya TVD.

Kata kunci: Trombosis vena dalam, D-dimer, non-compressibility ratio, usia >30 tahun

INTRODUCTION

For the last 25 years the annual incidence of venous thromboembolism (VTE) in the USA has remained stable at approximately 900,000 cases, with 300,000 deaths from pulmonary embolism.^(1,2) First-time VTE incidence is around 1 per 1000 per year in the adult population, and after 45 years of age VTE increases sharply to 5-6 cases per 1000 persons 80 years of age.⁽³⁾ There is no significant difference in its incidence in males and females.⁽⁴⁾ According to more recent prospective studies, sex has no significant impact on VTE prevalence.^(5,6)

Studies on deep vein thrombosis (DVT), one of the manifestations of VTE, have been focused only on one to a few variables in their cohort such as the distribution and extent of thrombosis, and their association with risk factors. In DVT of the lower extremities, thrombi are formed in veins of the femoral and/or crural regions. Accurate identification of patients with DVT is essential, since if DVT is not well managed, it may have fatal results. The condition is very serious because it can result in permanent damage and can cause pulmonary embolism.⁽³⁾

There are three modalities used in the diagnosis of DVT, i.e. the clinical prognostic

score, laboratory investigations, and radiological examination.⁽⁷⁾ In the clinical prognostic score, the following features are taken into account: presence or absence of lower extremity paralysis, orthopedic surgical history, swelling of the lower extremity, pitting edema, superficial venous collaterals, and presence of cancer.⁽⁸⁻¹⁰⁾ The D-dimer test for the presence of cross-linked D fragments of fibrin, indicative of ongoing thrombus formation, has been applied in an algorithm for evaluation of suspected VTE.⁽¹¹⁾ According to several case reports, negative results for D-dimer eliminate the need for further examinations, such as ultrasonography (USG).^(12,13) Kurklinsky et al.⁽¹³⁾ sought to find an association between the D-dimer value and sonographic thrombus volume, and concluded that in spite of the many clinical prognostic scores in existence, determination of D-dimer fibrin is a sensitive test for venous thrombosis and is correlated with thrombus volume.

The most common radiological examination performed for the diagnosis of DVT is B-mode USG, which can rapidly give information on the presence or absence of a thrombus.⁽¹⁴⁾ Tsao et al.⁽¹⁵⁾ studied the non-compressibility ratio in DVT in relation to the clinical prognostic score, and found that USG with compression is a rapid and objective examination to evaluate the severity of the formed thrombus. The non-compressibility ratio is found from the diameter of the lower extremity veins before and after compression.⁽¹⁴⁻¹⁵⁾

There are 3 types of DVT results on sonographic compression, i.e. patent, partial occlusion, and total occlusion. The patent type is easily diagnosed if there is total collapse of the vascular lumen. Total occlusion is also easily seen from the persistent dilation of the venous lumen upon compression. The only type of venous thrombosis, the severity of which is difficult to determine, is the partially occlusive type.⁽¹⁴⁾ In measuring the venous diameter, the transducer should be gently pressed on the region to be examined, making sure to avoid

accidental compression of the adjacent arterial structure.⁽¹⁶⁻¹⁷⁾

In view of the above background, the purpose of the present study was to determine the relationships between D-dimer concentration and USG non-compressibility ratio in thrombi of the lower extremities.

METHODS

Design of the study

This study used a cross-sectional observational design and was carried out at Dr. Kariadi Central General Hospital, Semarang, from January to May 2014.

Study subjects

The subjects of this study were patients with DVT of the lower extremities, undergoing D-dimer determination at the Clinical Pathology Department and USG at the Radiology Department of Dr. Kariadi Central General Hospital, Semarang, and meeting the following inclusion criteria: being >30 years of age, having a high clinical prognostic score, and being a new case. The exclusion criteria were: being on anticoagulant therapy, having severe hemorrhage, infection, or edema of upper extremities, and history of previous DVT. The sample size was calculated from the correlation test formula with a minimum sample size of 25. The subjects were selected by consecutive sampling, which is based on the patients' presentation at Dr. Kariadi Hospital, Semarang.

Data collection

Patients referred from the internal medicine clinic of Dr. Kariadi Central General Hospital, Semarang, with signs and symptoms of DVT of the lower extremities, were interviewed using a questionnaire containing items on age, sex, and history of the present disease. These patients were subjected to determination of D-dimer concentration and USG of the lower extremity veins.

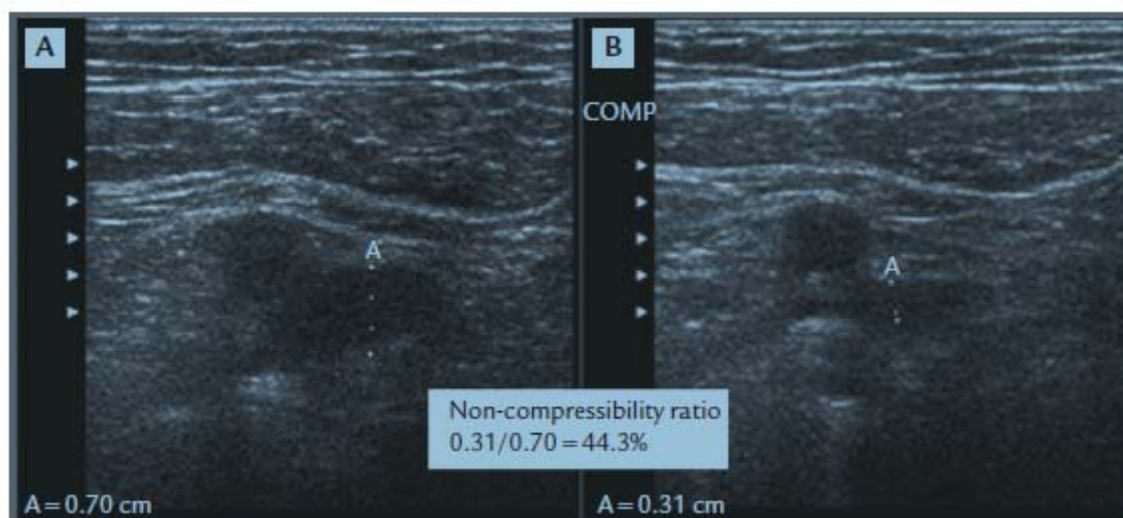


Figure 1. Non-compressibility ratio of venous thrombosis using sonographic transverse sectioning. A. Diameter of vein before compression. B. Diameter of vein after compression.⁽²⁾

Determination of D-dimer concentration

Plasma D-dimer concentration in the venous blood samples was determined in the Clinical Pathology Department of Dr Kariadi Hospital, by means of the latex enhanced turbidimetric test, using the Sysmex CA-1500 coagulometer, with a cut-off value of 500 ng/mL.

Measurement of non-compressibility ratio

The veins of the lower extremities of the subjects were examined by B-mode USG with a transducer linear frequency of 7.5 MHz. The lower extremity veins examined were the common femoral vein, superficial femoral vein, popliteal vein, and anterior and posterior tibial veins. In measuring the venous diameter, the transducer was pressed gently on the region to be examined, taking care to avoid compression of the adjacent arterial structure. The diameter of the vein was recorded before and after compression. The non-compressibility ratio was obtained from the formula (Figure 1):⁽²⁾ (diameter of vein after compression/diameter of vein before compression) x 100.

Data analysis

Data analysis was descriptive and bivariate analytic using the Pearson correlation test at a significance level of 0.05.

Ethical clearance

This study obtained ethical clearance from the Commission on Health Research Ethics, Faculty of Medicine, Diponegoro University/Dr. Kariadi Central General Hospital, Semarang.

RESULTS

Total sample size was 25, with the youngest subject 38 years of age and the oldest 86 years. Most of the subjects (11 or 44.0%) were found in the age group of >61 years, and 20 (80.0%)

Table 1. Distribution of demographic characteristics and accompanying clinical features in DVT subjects (n=25)

Variable	n (%)
Demographic characteristic	
Age (years)	
≤ 50	6 (24.0)
51- 60	8 (32.0)
≥ 61	11 (44.0)
Sex	
Male	5 (20.0)
Female	20 (80.0)
Accompanying clinical features	
Hypertension	14 (46.6)
Diabetes mellitus	2 (6.7)
Malignancy	10 (33.2)
Obesity	2 (6.7)
Hormonal contraception	1 (3.4)
History of surgery	1 (3.4)

Table 2. Mean D-dimer concentration and non-compressibility ratio in DVT subjects (n=25)

	DVT
D-dimer concentration ($\mu\text{g/L}$)	2953.00 \pm 2054.44
Non-compressibility ratio (%)	
Superficial femoral vein	59.96 \pm 35.98
Common femoral vein	42.68 \pm 33.71
Popliteal vein	47.84 \pm 38.21
Anterior tibial vein	47.91 \pm 33.78
Posterior tibial vein	51.20 \pm 36.53

Values are mean \pm SD

of the subjects were female. The majority of the subjects (14 or 46.6%) had hypertension (Table 1).

Mean D-dimer concentration was 2953.00 \pm 2054.44 $\mu\text{g/L}$. The highest mean non-compressibility ratio of 59.96 \pm 35.98% was found for the superficial femoral vein and the lowest ratio of 42.68 \pm 33.71% was for the common femoral vein (Table 2).

There was a moderately significant association between D-dimer concentration and non-compressibility ratio in the popliteal vein ($r=0.582$; $p=0.037$) (Table 3). The other veins of the lower extremities did not show a significant association.

DISCUSSION

In this study, the highest proportion of patients with lower extremity DVT (44.0%) was in the ≥ 61 year age group. Essentially similar results were obtained in several studies showing

that the mean age of patients with DVT was 62 years.^(18,19) The majority of DVT patients in the present study (80%) were female, which differs from studies reporting no difference in DVT prevalence in males and females up to 45 years of age.⁽¹⁹⁾ This topic is however still subject to controversy. Risk factors presumably accounting for sex differences are oral contraceptive use, pregnancy, and history of abortion or premature births. More recent prospective studies did not find differences in prevalence of venous thromboembolism (VTE) between sexes, although VTE may be more prevalent in premenopausal women.^(6,20) The higher prevalence of VTE in premenopausal women may be caused by the fact that women are particularly affected by hormones that may increase the levels of blood clotting factors and facilitate venous thrombus formation.

Our study results showed that the non-compressibility ratio was significantly but moderately correlated with plasma D-dimer levels in the popliteal veins of DVT patients. Plasma D-dimer determination appears to be a simple method with high clinical utility for excluding suspect acute recurrent DVT.⁽²¹⁾ A negative D-dimer test result in a patient who is clinically not suspected of having DVT, can be used to exclude the diagnosis of DVT, without having to resort to USG testing.

In an emergency situation requiring a quick and available diagnostic test for DVT, the non-compressibility ratio may be used, as it is significantly correlated with plasma D-dimer concentration. On account of its high high sensitivity (95%), specificity (99%), and

Table 3. Relationship between non-compressibility ratio and D-dimer concentration in DVT subjects

	D-dimer concentration	p value
Non-compressibility ratio		
Superficial femoral vein	0.232	0.387
Common femoral vein	0.451	0.141
Popliteal vein	0.582	0.037*
Anterior tibial vein	0.299	0.261
Posterior tibial vein	0.353	0.260

Values are Pearson correlation coefficients (r); *Significant at $p<0.05$

accuracy (98%), venous Doppler sonography is now the initial test used to determine the possibility of DVT.⁽¹⁵⁾

Determination of the non-compressibility ratio of thrombosed veins constitutes an objective test for assessing DVT severity and admitting patients for evaluation of potential adverse outcomes. Although D-dimer testing and several algorithms based on clinical criteria can be used for the diagnosis of DVT, there are increasing numbers of duplex ultrasonography (DUS) tests being performed annually. This may be a reflection of the importance of avoiding medicolegal issues and of time constraints for conducting physical examinations. However, DUS has a reduced accuracy in diagnosing distal thrombosis and is mainly available during regular clinic or hospital radiology department hours. A limitation of the present study was the restricted area of the USG scans for determination of the non-compressibility ratio, with an exclusive focus on thrombi in the superficial femoral, common femoral, popliteal, anterior tibial, and posterior tibial veins, thus being incapable of excluding the presence of thrombi in veins outside the scan area.

CONCLUSION

Plasma D-dimer level is correlated with the sonographic non-compressibility ratio of the popliteal vein in DVT of the lower extremities.



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