Comparison of prevalence of metabolic syndrome between idiopathic and secondary deep vein thrombosis

Ata Firouzi MD, Shahab Tohidnia M, Farshad Shakerian MD, Hamidreza Sanaati MD, Arash Hashem MD, R. Vagheei Tabar MD

Abstract

Background- The association of the metabolic syndrome with idiopathic or secondary deep vein thrombosis (DVT) remains uncertain. In addition, the relevance of the different features of the metabolic syndrome as an independent or pivotal risk factor for DVT is controversial. We aimed to evaluate the prevalence of the metabolic syndrome in patients with idiopathic or secondary DVT and also compare the prevalence of the different components of this syndrome in the two clinical etiological conditions of DVT.

Methods- In a cross-sectional study, 115 consecutive patients with a recent objective diagnosis of DVT (idiopathic in 87 patients and secondary to a known risk factor in 28 patients) who were referred to Rajaei Heart Center between April 2009 and January 2010 were enrolled in the study. In all the patients, DVT was diagnosed by means of compression Doppler ultrasonography. The metabolic syndrome was defined according to the ATP III recommendations.

Results- Overall prevalence of the metabolic syndrome in the study participants was 9.6%, and the prevalence of the metabolic syndrome in patients with idiopathic or secondary DVT was 9.2% and 10.7%, respectively, which was not different between them. Relative to the presence of the different numbers of the metabolic syndrome features, no difference was found between the groups with idiopathic or secondary DVT. The presence of no feature was found in 6.9% and 7.1%, the presence of one feature was seen in 51.7% and 42.9%, and the presence of two features was found in 32.2% and 39.3%, respectively.

Conclusion- Regardless of the etiology of DVT, the overall prevalence of the metabolic syndrome in our DVT subjects ranged from 9.2% to 10.7%, and this prevalence was independent of the etiology (idiopathic or secondary) of DVT ***(Iranian Heart Journal 2012; 13 (1):23 -28*).**

Keywords: Deep vein thrombosis■ Metabolic syndrome

Deep vein thrombosis (DVT) is one of the most prevalent medical problems worldwide and can lead to important life-threatening events and serious co-morbidities such as pulmonary emboli. Early recognition and appropriate treatment of DVT and its complications can effectively increase survival and, therefore, the main goals of therapy for this complication are to reduce morbidity, prevent post-thrombotic syndrome, and prevent pulmonary emboli.[1,2]

It has been now suggested that atherosclerosis has the potential to promote the development of thrombotic disorders, including DVT, in the venous system. The two clinical conditions of idiopathic or secondary DVT can be simultaneously triggered by biological stimuli responsible for activating coagulation and inflammatory pathways in both the arterial and the venous system and thus might have a strong link with atherosclerosis.[3]

Received Mar. 26, 2012; Accepted for publication May. 2, 2012

*Corresponding Author, Rajaie Cardiovascular, Medical and Research Center - Tehran University of medical science, Tehran Iran

The results of recent studies have suggested that patients with idiopathic or secondary DVT can be at increased risk of asymptomatic atherosclerosis and cardiovascular events. The metabolic syndrome is a cluster of risk factors for atherosclerosis and, therefore, may play a role in the pathogenesis of idiopathic or secondary DVT and may act as a link between venous thrombosis and atherosclerosis.[4,5] In fact, the metabolic syndrome might increase DVT risk, and different components of this syndrome seem to be the pivotal factors.[6] Thus, recent hospital protocols developed for prophylactic anticoagulation have given special consideration to patients with the metabolic syndrome.[7] However, the relevance of the different components of the metabolic syndrome as an independent or related risk factor for VTE in the metabolic syndrome cluster has remained controversial. We aimed to evaluate the prevalence of the metabolic syndrome in patients with idiopathic or secondary DVT and also compare the prevalence of the different components of this syndrome in the two clinical etiological conditions of DVT.

Methods

In a cross-sectional study, one hundred fifty consecutive patients with a recent objective diagnosis of DVT who were referred to Rajaei Heart Center between April 2009 and January 2010 were enrolled. In all the patients, DVT was diagnosed by means of compression Doppler ultrasonography. Patients were excluded if they had renal dysfunction, abnormal liver function tests, or autoimmune diseases. The following data were collected from hospital recorded files or face-to -ace interviewing from all the patients: demographic characteristics, general risk factors for coronary artery disease, history of surgery, pregnancy, different types of malignancies, history of recent trauma, oral contraceptive therapies, chemotherapy, and recent hormonal replacement therapies. The patients were then categorized into two groups with idiopathic or secondary DVT. DVT was defined as idiopathic in the absence of any of the following risk factors: recent (< 3 months) surgery, trauma, fracture, acute medical disease or pregnancy, concomitant immobilization, use of oral contraceptives, and known active malignancy. In the presence of at least one of the previous risk factors, DVT was defined as secondary.[8] On admission, the study participants underwent a comprehensive baseline examination for cardiovascular disease risk factors. Seated blood pressure was measured using a random-zero sphygmomanometer. The body mass index (BMI) was calculated as weight in kilograms divided by the square of standing height in meters. Waist circumference was measured at the umbilicus. Fasting blood specimens were collected centrifuged at 4°C, and plasma and serum frozen at −70°C until analysis in central laboratories. Lipids, glucose, and C-reactive protein were measured. The metabolic syndrome was defined according to the ATP III recommendations as 3 or more risk factors, including, abdominal obesity: waist circumference ≥ 102 cm for men and ≥ 88 cm for women; triglycerides ≥ 150 mg/dL; HDL-cholesterol levels for men < 40 mg/dL and for women < 50 mg/dL; glucose ≥ 110 mg/dL, on drug treatment for elevated glucose, or a diagnosis of diabetes; systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg; or on antihypertensive therapy.[9]

Results are presented as mean ± standard deviation (SD) for the quantitative variables and are summarized by absolute frequencies and percentages for the categorical variables. The categorical variables were compared using the chi-square test or the Fisher exact test when more than 20% of cells with expected counts of less than 5 were observed. The quantitative variables were compared using the *t*-test. For the statistical analysis, the statistical software SPSS version 19.0 for Windows (SPSS Inc., Chicago, IL) was used.

P values of 0.05 or less were considered statistically significant.

Results

A total of 115 patients with a first episode of DVT were enrolled in the study. DVT was idiopathic in 87 patients and secondary to a known risk factor in 28 patients. In the idiopathic and secondary DVT groups, 62.8% and 77.8% were women, respectively. Also, 41.4% and 39.3% were older than 60 years, respectively. Mean age and sex ratio of patients with idiopathic and secondary DVT were statistically comparable (Fig. 1).

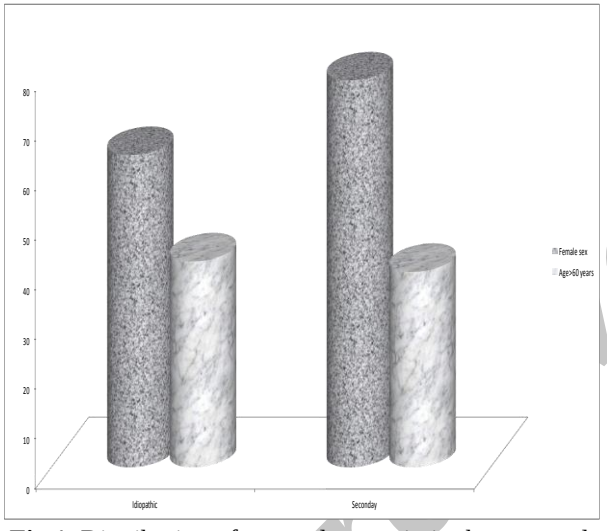

Fig.1. Distribution of age and sex ratio in the two study groups

The most common individual component of the metabolic syndrome in both groups was HDL < 40 mg/dL, followed by triglyceride > 150 mg/dL (Table I). Positive CRP was also similarly observed in the two groups with idiopathic or secondary DVT (33.3% versus 35.7%). Overall prevalence of the metabolic syndrome in the study participants was 9.6%; the prevalence of the metabolic syndrome in the patients with idiopathic or secondary DVT was 9.2% and 10.7%, respectively, which was not different between them (p = 0.728).

Table I. Individual components of metabolic syndrome in the two groups with idiopathic or secondary DVT

Component	Idiopathic DVT	Secondary DVT	P-value
Hypertension	13 (14.9)	4 (14.3)	0.999
FBS > 110 g/dL	27 (31.6)	11 (39.9)	0.419
TG > 150 mg/dL	29 (33.3)	11 (39.3)	0.565
HDL < 40 mg/dL	31 (35.6)	11 (39.3)	0.727
Positive CRP	29 (33.3)	10 (35.7)	0.817

Relative to the presence of the different numbers of the metabolic syndrome features (Table II), no difference was found between the groups with idiopathic or secondary DVT; the presence of no feature was found in 6.9% and 7.1%, the presence of one feature was seen in 51.7% and 42.9%, and the presence of two features was found in 32.2% and 39.3%, respectively.

Table II. Number of Individual features of metabolic syndrome in the two groups with idiopathic or secondary DVT

Component	Idiopathic DVT	Secondary DVT	P-value
None	6 (6.9)	2 (7.1)	
One	45 (51.7)	12 (42.9)	0.872
Two	28 (32.2)	11 (39.3)	
Three or more	8 (9.2)	3 (10.7)	

Comparing the demographics between the patients with and without the metabolic syndrome showed no differences in these parameters between the two groups (Table III). No significant difference was also revealed between the groups with and without the metabolic syndrome in terms of a positive rate of serum CRP.

Table III. Comparing baseline data between the patients with and without metabolic syndrome

Component	With Met.S	Without Met.S	P-value
Idiopathic DVT			
Female gender	4 (50.0)	50 (64.1)	0.432
Age. Year	5 (62.5)	31 (39.2)	0.203
Positive CRP	3 (37.5)	26 (32.9)	0.999
Secondary DVT			
Female gender	2 (66.7)	19 (79.2)	0.545
Age. Year	1 (33.3)	10 (40.0)	0.999
Positive CRP	1 (33.3)	9 (36.0)	0.999

Discussion

The present study aimed to determine the prevalence of the metabolic syndrome in patients who suffered from DVT among Iranian patients. This study was the first study in Iran to evaluate and compare the prevalence of the metabolic syndrome between two subgroups of patients with idiopathic or secondary DVT. First, we revealed that the overall prevalence of DVT in our study population was 9.6%, which was not comparable in the patients with idiopathic DVT and those with secondary features of this event (9.2% versus 10.7%). Also, we managed to show that the rate of positive CRP was similar in the idiopathic and secondary DVT groups as well as in those with or without the metabolic syndrome. On the other hand, CRP measurement was not a sensitive tool for predicting the two types of DVT and also for differentiating the metabolic syndrome from the normal condition.

Regarding the prevalence of the metabolic syndrome in DVT patients, a wide spectrum of prevalence was reported in the previous studies. Ageno et al. found a prevalence of 50.5% of the metabolic syndrome in DVT subjects and 34.6% in normal individuals, which was considerably higher than that in our finding.[8] In the Ray et al. study and on admission time, 35% of the DVT patients had 0 to 1 features of the metabolic syndrome, 30% had 2 features, 24% had 3 features, and 11% had 4 features of this syndrome. On the other hand, the overall prevalence of the metabolic syndrome in their population was estimated to be 35%.[10] In another study by Ay et al, the prevalence of the metabolic syndrome in DVT and normal subjects was 35% and 20%, respectively. Besides, some authors reported similar or even a lower range of the metabolic syndrome in DVT patients. In the Steffen et al. study, the prevalence of the metabolic syndrome among women who did or did not develop incident DVT was similar (both 34%); however, the prevalence of the metabolic syndrome was greater among men who developed incident DVT than among those who did not (44% vs. 30%).[11] Moreover, Vayá showed that the metabolic syndrome was present in 19% of cases and only 8% of controls.[6] The differences in the reported prevalence of the metabolic syndrome in DVT patients group might be due to considering different criteria for the definition of the metabolic syndrome, differences in the patients' selection criteria, as well as to presence or absence of underlying factors related to the appearance of the metabolic syndrome. Furthermore, progressing diagnostic techniques for the diagnosis of DVT in recent years has resulted in more accurate estimations of DVT and also its-related metabolic syndrome. Also, designation of recent guidelines for managing the complications and co-morbidities of DVT has resulted in more appropriate controlling underlying risk factors such as diabetes mellitus, hypertension, and central obesity and thus the prevalence of this syndrome has been considerably presented lower compared to previous reports.

We also found that the prevalence of the metabolic syndrome was absolutely independent of the causes of DVT. Secondary DVT is usually related to the presence of some underlying etiological factors such as

recent surgery, trauma, fracture, acute medical disease or pregnancy, concomitant immobilization, use of oral contraceptives, and known active malignancy.[12-17] In our study, none of the patients had these underlying predisposing factors, except for valvular surgery.[18], which was the underlying in our factor for defining secondary DVT study patients. According to our finding, it seems that the underlying triggering factors of DVT were not associated with the appearance of the metabolic syndrome in the DVT patients; this should be evaluated further in future studies.

Our study evaluated and compared the metabolic syndrome condition in both types of DVT as idiopathic and secondary; it, however, has some major limitations, including a relatively small sample size, cross-sectional pattern of the study, absence of a control group to estimate the relative risk of the metabolic syndrome in DVT condition, and absence of a long-term follow-up approach for determining late prevalence of the metabolic syndrome in the DVT patients.

In summary, the current study showed that the metabolic syndrome could be observed in 9.2% to 10.7% of the DVT patients and the prevalence of this syndrome might be independent of the type of the etiology of DVT.

References

1. Silverstein MD, Heit JA, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ 3rd. Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25-year population-based study. Arch Intern Med. Mar 23 1998;158(6):585-93.

2. Tapson VF. Acute pulmonary embolism. N Engl J Med. Mar 6 2008;358(10):1037-52. ushman M, Tsai AW, White RH, Heckbert SR, Rosamond WD, Enright P, et al. Deep vein thrombosis and pulmonary embolism in two cohorts: the longitudinal investigation of thromboembolism etiology. Am J Med. Jul 1 2004;117(1):19-25.

3. Prandoni P. Venous thromboembolism and atherosclerosis: is there a link? J Thromb Haemost. 2007 Jul;5 Suppl 1:270-5.

4. Wakefield TW, Strieter RM, Schaub R, Myers DD, Prince MR, Wrobleski SK, et al. Venous thrombosis prophylaxis by inflammatory inhibition without anticoagulation therapy. J Vasc Surg. Feb 2000;31(2):309-24.

5. Elliott G. Thrombolytic therapy for venous thromboembolism. *Curr Opin Hematol*. Sep 1999;6(5):304-8.

6. Vayá A, Martínez-Triguero ML, España F, Todolí JA, Bonet E, Corella D. The metabolic syndrome and its individual components: its association with venous thromboembolism in a Mediterranean population. Metab Syndr Relat Disord. 2011 Jun;9(3):197-201.

7. Gandhi R, Razak F, Tso P, Davey JR, Mahomed NN. Metabolic syndrome and the incidence of symptomatic deep vein thrombosis following total knee arthroplasty. J Rheumatol. 2009 Oct;36(10):2298-301. Epub 2009 Aug 14.

8. Ageno W, Prandoni P, Romualdi E, Ghirarduzzi A, Dentali F, Pesavento R, et al. The metabolic syndrome and the risk of venous thrombosis: a case-control study. J Thromb Haemost 2006;4:1914-8.

9. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC, Spetus JA, Costa F. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Circulation 2005;112: 2735–52.

10. Ray JG, Lonn E, Yi Q, Rathe A, Sheridan P, Kearon C; HOPE-2 investigators, Yusuf S, Arnold MJ, McQueen MJ, Pogue J, Probstfield J, Fodor G, Held C, Micks M, Genest J Jr. Venous thromboembolism in association with features of the metabolic syndrome. QJM. 2007 Nov; 100(11): 679-84. Epub 2007 Sep 10.

11. Steffen LM, Cushman M, Peacock JM, Heckbert SR, Jacobs DR Jr, Rosamond WD, Folsom AR. Metabolic syndrome and risk of

venous thromboembolism: Longitudinal Investigation of Thromboembolism Etiology. J Thromb Haemost. 2009 May;7(5): 746-51.

12. Bovill EG, van der Vliet A (2011). "Venous valvular stasis-associated hypoxia and thrombosis: what is the link?". Annu Rev Physiol 73: 527–45.

13. Rosendall FR (2005). "Venous Thrombosis: the role of genes, environment, and behavior". Hematology Am Soc Hematol Educ Program 2005: 1–12.

14. Lijfering WM, Rosendaal FR, Cannegieter SC (2010). "Risk factors for venous thrombosis – current understanding from an epidemiological point of view". Br J Haematol 149 (6): 824–33.

15. Palareti G, Schellong S (2012). "Isolated distal deep vein thrombosis: what we know and what we are doing". J Thromb Haemost 10 (1): 11–9.

16. Rosendaal FR, Reitsma PH (July 2009). "Genetics of venous thrombosis". J. Thromb. Haemost. 7 (suppl 1): 301–4.

17. Stein PD, Beemath A, Meyers FA. (2006). "Incidence of venous thromboembolism in patients hospitalized with cancer". Am J Med 119 (1): 60–8.

18. Meissner MH, Gloviczki P, Comerota AJ, Dalsing MC, Eklof BG, Gillespie DL, Lohr JM, McLafferty RB, Murad MH, Padberg F, Pappas P, Raffetto JD, Wakefield TW. Early thrombus removal strategies for acute deep venous thrombosis: Clinical Practice Guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg. 2012 Mar 31.