Thrombosis Research (2008) **123**, 194–199

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THROMBOSIS RESEARCH

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REGULAR ARTICLE

Superficial venous thrombosis: Prevalence of common genetic risk factors and their role on spreading to deep veins

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Received 17 September 2007; received in revised form 9 January 2008; accepted 15 January 2008
Available online 2 April 2008

KEYWORDS
Color duplex scanning;
Genetic risk factors;
Inherited thrombophilic states;
Superficial venous thrombosis;
Venous thromboembolism

Abstract

Introduction: Superficial venous thrombosis (SVT) has been considered for a long time a limited clinical condition with a low importance, but this approach has changed in recent years, when several studies demonstrated spreading to deep veins occurring from 7.3 to 44%, with high prevalence of pulmonary embolism.
Materials and methods: To evaluate the prevalence of genetic risk factors for VTE in patients suffering from SVT on both normal and varicose vein, and to understand their role on spreading to deep veins, we studied 107 patients with SVT, without other risk factors. Ultrasound examination was performed, and the presence of FV Leiden, Prothrombin G20210A mutation, and MTHFR C677T mutation was researched.
Results: In the patients where SVT occurred in normal veins, the presence of FV Leiden was 26.3% of the non-spreading and 60% of the spreading to deep veins SVT; Prothrombin mutation was found in 7.9% of the former case and in 20% of the latter; MTHFR C677T mutation was found respectively in 23.7% and 40%. In the patients with SVT on varicose veins, the presence of these factors was less evident (6.7%, 4.4% and 6.7% respectively), but their prevalence was considerably higher (35.7%, 7.4% and 21.4% respectively) in SVT spreading to deep veins than in non-spreading.
Conclusions: Our data demonstrate the high prevalence of these mutations, especially FV Leiden and associations, in patients with SVT on normal veins and their role in the progression to deep vein system.

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doi:10.1016/j.thromres.2008.01.013

Introduction

The term superficial vein thrombosis (SVT) has replaced the former term thrombophebitis which was used in the past to indicate a pathological condition of superficial veins, especially of the lower limbs, and it's characterized by signs and symptoms related to inflammation and thrombosis. In fact, in the last few years, data about mechanism of thrombosis, capillaries permeability and endothelial function, have reduced the importance of the pathophysiological aspects creating a new classification based on the localization of the occlusion which brings to the identification of two different groups of thrombosis: superficial vein thrombosis (SVT) and deep vein thrombosis (DVT) [1].

In the past, SVT and especially varicophlebitis were considered pathological conditions with a low clinical relevance despite their frequency because of their rapid resolution and favourable outcome [2]. Instead, thrombosis on a "healthy" vein, that represents only 1/4 of all SVT, was considered more important because of its association with cancer ("neoplastic" thrombophlebitis) or other pathological conditions. Thus, they can occur in patients with an haemostasis disorder (hypercoagulable states, fibrinolysis disfunction), and can be associated with pregnancy [3], use of oral contraceptives [4], malignancy [5] and can be found in patients with endothelium alterations, as in Behçet, Burger and Mondor's diseases [6,7].

The progression of SVT into deep venous system

While SVT of collateral veins has a favourable course, SVT involving the main trunk may not be always benign. Progression of the thrombosis into deep venous system has been revealed in previous studies, and it caused an increment for pulmonary embolism (PE) risk [8]: this is true especially for varicophlebitis, and can occur according to three possible ways: from the collateral to the perforating vein (centripetal varicophlebitis), or from the saphena to the "crosse" (ascending varicophlebitis), or from the "crosse" to the deep vein (crosse varicophlebitis).

The frequency of the thrombotic process progression is controversial [9–17]. Whereas the first case of DVT and lethal PE subsequent to SVT was described in 1905 by Ritcher, only the diffusion of US examination [18,19] has allowed to detect many unsuspected cases of extension of the thrombotic process.

The data about the frequency do not agree. Propagation to deep veins ranged to 2.6–15% and the differences can be due to the different method used (phlebography or ultrasounds) or to the different ways to evaluate the extension of the process in various papers (some researchers consider only contiguous thrombosis, others also concomitant ones) or, as some authors do but not others [20–22], make a distinction between SVT on a healthy vein and SVT on a varicose vein.

SVT and hypercoagulable states

Previous studies showed a high prevalence of hypercoagulable states in patients with SVT [23–28]. De Morloose, i.e., demonstrated that Factor V Leiden is predisposing to SVT [25] and Godoy showed an association with protein S deficiency in repetitive superficial thrombophlebitis [27]. Furthermore, a high concentration of factor VIII has been demonstrated to be an independent risk factor for SVT in Schonauer's studies [28].

Aim of the study

With this research we are investigating the prevalence of the common genetic risk factors for thrombosis (gene mutation of Factor V Leiden, G20210A allele of the prothrombin gene) and also the prevalence of C677T mutation in the MTHFR gene associated to iperhomocysteinemia (Hcy), in patients suffering from SVT, both on normal and on varicose veins, and the extension of the thrombotic process into the deep venous system. The objective was to evaluate their possible role on spreading to deep veins.

Materials and methods

Patients and study design

We studied 107 patients referred to our center and aged between 17 and 62 years old, who had a first episode of SVT of the lower limbs. Thrombosis both on healthy vein and on varicose vein were included.

Patients with previous episodes of venous thromboembolism (DVT or PE), SVT of the upper limbs, malignancy, autoimmune diseases and suffering from SVT due to circumstantial factors (recent surgery or trauma, prolonged immobilization, use of oral contraceptives, pregnancy or puerperium, sepsi) were excluded.

The research was approved by the appropriate ethical Committee of the University Hospital P. Giaccone of Palermo, and was in accordance with the Helsinki Declaration.

All patients were informed about the nature and aim of the study and provided their consent to the participation. They were treated with low weight heparin and/or non steroid inflammatory drugs [29–31].

Procedures and measurements

Diagnosis of SVT was based on clinical assessment, and confirmed by color duplex scanning (DUS). Clinical features include the presence of a warm, tender, palpable cord or nodule-like structure that follows the course of a superficial vein. Such features really do not reveal the true extent of SVT, because the