Med Clin (Barc). 2016;146(6):254–257

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Brief report

Identifying clinical risk factors in recurrent idiopathic deep venous thrombosis☆

M. Lourdes del Río Solá*, José Antonio González Fajardo, Carlos Vaquero Puerta

Servicio de Angiología y Cirugía Vascular, Hospital Clínico Universitario de Valladolid, Valladolid, Spain

ARTICLE INFO

Article history:
Received 21 April 2015
Accepted 15 October 2015
Available online 16 June 2016

Keywords:
Thromboembolism
Idiopathic deep venous thrombosis
Risk factors

ABSTRACT

Background and objective: Oral anticoagulant therapy for more than 6 months in patients with an episode of idiopathic thromboembolic disease is controversial. The objective was to determine predictive clinical signs that identify patients at increased risk of thromboembolic recurrence after stopping anticoagulant therapy for 6 months after an episode of idiopathic deep vein thrombosis (DVT).
Patients and methods: A prospective study which included 306 consecutive patients with a first episode of idiopathic DVT from June 2012 to June 2014. Predictor variables of recurrent thromboembolic disease and episodes of recurrence during follow-up of the patients (28.42 months) were collected. We performed a multivariate analysis to analyse possible predictors ($p < 0.20$) and an analysis of Kaplan–Meier to establish mean recurrence-free survival.
Results: We identified 91 episodes of residual vein thrombosis on follow-up of the patients (37.5% men and 20.3% women) (OR 1.84; 95% CI 1.25–2.71). In the Cox regression analysis stratified by gender, variables showed significant presence of hyperechoic thrombus ($p = 0.001$) in males, and persistence of residual thrombus in women ($p = 0.046$). The mean recurrence-free survival was shorter in both groups.
Conclusions: The presence of echogenic thrombus in men and the existence of residual DVT in women were 2 clinical signs associated with increased risk of thromboembolic recurrence after stopping anticoagulant therapy for 6 months after an episode of idiopathic DVT in our study.

Identificación de factores de riesgo clínicos en la trombosis venosa profunda idiopática recurrente

Palabras clave:
Enfermedad tromboembólica
Trombosis venosa profunda idiopática
Factores de riesgo

RESUMEN

Fundamento y objetivo: El tratamiento anticoagulante oral durante más de 6 meses en pacientes con un episodio de enfermedad tromboembólica idiopática es controvertido. El objetivo fue determinar los signos clínicos predictores que permiten identificar a los pacientes con mayor riesgo de recurrencia tromboembólica después de suspender el tratamiento anticoagulante de 6 meses, tras un episodio de trombosis venosa profunda (TVP) idiopática.
Pacientes y métodos: Es un estudio prospectivo en el que se incluyeron 306 pacientes consecutivos diagnosticados de un primer episodio de TVP idiopática desde junio de 2012 a junio de 2014. Se recogieron los datos de variables predictoras de enfermedad tromboembólica recurrente y los episodios de recurrencia durante el seguimiento de los pacientes (28,42 meses). Realizamos un análisis multivariable para analizar las posibles variables predictoras ($p < 0,20$) y un análisis de supervivencia de Kaplan-Meier para establecer el tiempo medio libre de recidiva.

☆ Please cite this article as: del Río Solá ML, González Fajardo JA, Vaquero Puerta C. Identificación de factores de riesgo clínicos en la trombosis venosa profunda idiopática recurrente. Med Clin (Barc). 2016;146:254–257.

* Corresponding author.
E-mail address: mlriosol@yahoo.es (M.L. del Río Solá).

Resultados: Identificamos 91 episodios de enfermedad tromboembólica recurrente durante el seguimiento de los pacientes (37,5% varones y 20,3% mujeres) (OR 1,84; IC al 95% 1,25-2,71). En el análisis de regresión de Cox estratificado por sexo se mostraron significativas las variables presencia de trombo hiperecogénico (p = 0,001) en varones y persistencia de trombo residual en mujeres (p = 0,046). El tiempo medio libre de recidiva fue más corto en ambos grupos.
Conclusiones: La presencia de trombo hiperecogénico en los varones y la existencia de TVP residual en las mujeres fueron 2 signos clínicos predictores asociados a un mayor riesgo de recurrencia tromboembólica después de suspender el tratamiento anticoagulante de 6 meses, tras un episodio de TVP idiopática en nuestro estudio.

Introduction

Venous thromboembolism (VTE) is a common disease with a sometimes fatal evolution. The risk of a recurrent thromboembolism (RTE) after stopping 3–6 month anticoagulant therapy varies. In some groups of patients, such as those with an idiopathic VTE episode, the risk is 5–27%[1] in the first year. Anticoagulant therapy is an effective tool to reduce the risk of recurrence while undergoing therapy, but this benefit disappears when treatment is suspended.[2] In addition, oral anticoagulation involves a significant major haemorrhage risk (0.9–3%/year).[3] Therefore, there are doubts about whether to discontinue anticoagulation after 6 months in patients with an idiopathic episode of thromboembolic disease.[4,5]

The aim of our study was to determine predictors of clinical signs identifying patients with an increased risk of thromboembolic recurrence after stopping a 6-month anticoagulant therapy after an episode of idiopathic deep vein thrombosis (DVT).

Materials and methods

Study design

It was a prospective study that included patients from our service who were consecutively diagnosed with a first episode of idiopathic DVT, from June 2012 to June 2014.

Patients were treated as outpatients, with low molecular weight heparin (LMWH) (enoxaparin) at therapeutic doses (1 μg/kg, 2 times daily) for 10 days, and subsequent to that prophylactic doses (1 μg/kg, once daily) until treatment was complete at 6 months. They were instructed to walk soon after and to use a strong compression stocking.

The diagnosis of DVT was made by physical examination and Doppler ultrasound. There was a clinical suspicion of pulmonary embolism (PE) so a computed tomographic angiography was requested.

Clinical patient characteristics were collected and a blood test was conducted to obtain plasma levels of homocysteine, factor V Leiden, gene mutation prothrombin, factor VIII, D-dimer,[6] anti lupus anticoagulant and anticardiolipin antibodies IgG and IgM.

We define idiopathic DVT episodes as those which occur in the absence of a fracture or a period of immobilisation of more than 3 days or surgery under general anaesthesia 3 months before the episode or absence of neoplastic disease 5 years earlier.

Bleeding was defined as severe if it was situated in the retroperitoneal or intracranial area, or if there was a decrease in haemoglobin of at least 2.0 g/dl. Bleeding was considered minor if the above criteria were not met.

We excluded patients who: did not sign the consent form, were under 18 years-old, had prior or concomitant anticoagulation, might not have access to hospital tests, had had a previous episode of idiopathic DVT and had known thrombophilia.

The study was presented at our hospital's Research Committee, which gave its approval for it to be done.

Monitoring

Patients were monitored at 3, 6 and 12 months and thereafter every 6 months to determine the existence of RTE and/or bleeding episodes. The criteria for RTE were clinical and ultrasound.

Statistical analysis

Comparisons between groups were carried out using the Chi-square test for qualitative variables and Student's *t*-test for quantitative variables.

A univariate statistical analysis was performed to determine the strength of association between each potentially predictor variable and the RTE. Subsequent to that, a multivariate Cox regression analysis with potentially significant variables ($p < 0.20$) was performed. To study the time without a relapse a Kaplan–Meier survival analysis and log-rank test were performed. The level of statistical significance was considered attained when $p < 0.05$. Statistical analysis was performed using SPSS® 18.0 (IBM, Chicago, Illinois, USA).

Results

Between June 2012 and June 2014, 380 patients with proximal DVT without associated EP were included in a study. Of these, 331 were idiopathic DVT, and of those, 306 completed the study (Fig. 1).

The mean age of patients was 54.57 years (range 25–92), and 45.1% were women (Table 1). During the average follow-up time of 28.42 months (range 6–47), 91 of 306 patients (29.73%) had at least one episode of recurrent DVT, representing an annual risk of 14.86%. No bleeding episodes were described during monitoring and there was no mortality.

Out of the males, 37.5% developed RTE during an average follow-up time of 18 months, compared with 20.3% of women, with an average follow-up time of 21 months (OR 1.84; CI 95%, 1.25–2.71).

The variables included in the Cox regression analysis for males were: erythema, history of chronic bronchitis, family history of VTE, presence of hyperechogenic thrombus at the time of diagnosis and the presence of residual thrombus after 6 months of anticoagulation. The only variable that showed significance was the presence of hyperechogenic thrombus at the time of diagnosis ($p = 0.001$), where the model was able to adjust 62.5% of patients.

In the case of women, the variables included were: factor V Leiden, presence of hyperpigmentation, oedema and erythema, family history of VTE, existence of hyperechogenic thrombus at the time of diagnosis and existence of residual thrombus after 6 months of anticoagulation. After analysis, the only variable that showed significance was the presence of residual thrombus ($p = 0.001$), where the model was able to adjust 79.7% of patients.

The average risk of recurrence showed no statistically significant difference between the sexes (log-rank, $p = 0.42$). When the thrombus was hyperechogenic at the time of diagnosis, the time without a relapse was 6.43 months compared to 11.35 months when the thrombus was hypoechoic ($p = 0.001$). The average recurrence time