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Original

Cost-effectiveness study of deep venous thrombosis diagnosis at the hospital setting

Estudio coste-efectividad del diagnóstico de trombosis venosa profunda en el medio hospitalario

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Abstract

Introduction and objective: deep venous thrombosis (DVT) is a significant economic burden. The study primary endpoint is to compare two diagnostic strategies in terms of cost and effectiveness: D-dimer to all patients with suspected DVT vs conditioning it to the pre-test clinical probability; the secondary endpoint is to analyze the cost of DVT diagnosis in our center and the factors associated with its presentation.

Material and methods: this was a prospective study of patients with suspected DVT of lower extremities conducted between May and October 2019. The variables of the Wells scale, associated PTE, D-dimer levels, Doppler echocardiography and costs (emergency care, D-dimer and Doppler echocardiography obtained from the region Official Bulletin and the hospital billing unit) were analyzed. The statistical analysis was performed with SPSS, the chi-square test, and Fisher's exact test.

Results: a total of 249 patients were studied, 116 of whom (46.59 %) presented with DVT. The mean age was 70 years (21-95). Those with DVT were predominantly men (52.6 % vs 39.8 %; $p = .04$), had cancer (29.3 % vs 16.5 %, $p = 0.016$), pain (80.2 % vs 45.1 %; $p < .001$), edema (93.1 % vs 57.1 %, $p < .001$), slurring (72.4 % vs 14.3 %; $p < .001$), PTE (25.9 % vs 13.5 %, $p = .014$), less alternative diagnosis (0.9 % vs 62.4 %; $p = .001$) and less obesity (7.8 % vs 18.8 %; $p = .011$). The cost generated was € 192.49 per patient. Regarding the primary endpoint, 144 patients (those with D-dimer) were analyzed. Strategy #1 resulted in a cost of €190.41 per patient with 100 % sensitivity and 7.1 % specificity; strategy # 2, resulted in a cost of €188.51/patient, with 88.3 % and 78.5 % sensitivity and specificity rates, respectively. Both strategies are 1 % and 2 % cheaper than the cost generated.

Conclusion: the application of diagnostic algorithms for suspected DVT is cost-effective, so its use should be generalized.

Keywords:
Deep venous thrombosis. Diagnosis. Cost. Effectiveness.

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Resumen

Introducción y objetivos: la trombosis venosa profunda (TVP) supone una importante carga económica. Nuestro objetivo primario es comparar dos estrategias diagnósticas en cuanto a costes y a efectividad: la prueba del dímero D a todos los pacientes con sospecha con condicionarla a la probabilidad clínica pretest. El secundario, analizar el coste del diagnóstico en nuestro centro y los factores asociados a su presentación.

Material y métodos: estudio prospectivo de los pacientes atendidos con sospecha de TVP de extremidad inferior entre mayo y octubre de 2019. Se analizaron las variables de la escala de Wells, el TEP asociado, el dímero D, el resultado del eco Doppler y los costes (atención en Urgencias, el reactivo del dímero D y la realización de un eco Doppler, obtenidos del Boletín Oficial de la comunidad y de la unidad de cobros del hospital). El análisis estadístico se realizó con SPSS, pruebas de χ^2 y el test exacto de Fisher.

Resultados: se estudiaron 249 pacientes. 116 (46,59 %) presentaron TVP. La edad media fue de 70 años (21-95). Aquellos con TVP presentaron con más frecuencia: sexo masculino (52,6 % frente a 39,8 %, $p = 0,04$), cáncer (29,3 % frente a 16,5 %, $p = 0,016$), dolor (80,2 % frente a 45,1 %, $p < 0,001$), edema (93,1 % frente a 57,1 %, $p < 0,001$), empastamiento (72,4 % frente a 14,3 %, $p < 0,001$), TEP (25,9 % frente a 13,5 %, $p = 0,014$), menor diagnóstico alternativo (0,9 % frente a 62,4 %, $p < 0,001$) y menor obesidad (7,8 % frente a 18,8 %, $p = 0,011$). El gasto generado fue de 192,49 euros por paciente. Para el objetivo primario se analizaron a 144 pacientes (aquellos con dímero D). La estrategia 1 generó un gasto de 190,41 euros por paciente, con una sensibilidad del 100 % y una especificidad del 7,1 %; la estrategia 2, 188,51 euros por paciente, con una sensibilidad del 88,3 % y una especificidad del 78,5 %. Ambas estrategias son un 1 % y un 2 % más económicas que el gasto generado, respectivamente.

Conclusión: la aplicación de algoritmos diagnósticos en las sospechas de TVP es coste-efectiva, por lo que su empleo debería ser generalizado.

Palabras clave: Trombosis venosa profunda. Diagnóstico. Coste. Efectividad.

INTRODUCTION

Deep vein thrombosis (DVT) often shows as edema and limb pain leading to pulmonary thromboembolism (PTE). Additionally, DVT has significant associated morbidity and mortality rates.

Its annual incidence is 50 to 100 cases per 100 000 inhabitants (1). DVT is more common among women aged 20 to 40 years, though in the 54 to 60 age group, it is more common in men (1).

Its pathophysiology is explained by Virchow's triad: hypercoagulability, venous stasis, and endothelial damage. DVT main risk factors include cancer, acute illness, surgery, trauma, immobility, obesity, infectious or inflammatory diseases, hormonal therapy, pregnancy, and thrombophilia (1).

OBJECTIVES

This study endpoint is to compare two diagnostic strategies in terms of costs and effectiveness:

Strategy #1: perform D-dimer analysis on all patients with suspected DVT and conduct a Doppler echocardiography on patients testing positive.

Strategy #2: use Wells' criteria on all patients with suspected DVT and perform D-dimer analysis on those with low probability, and a Doppler echocardiography on those with moderate or high probability, and on those with a positive D-dimer test.

The study secondary endpoint is to analyze spending at our center regarding the diagnosis of DVT, and identify factors associated with its presentation.

MATERIALS AND METHODS

This was a prospective study of patients with a 6-month history of suspected DVT in the lower extremities from May through October 2019 treated in our unit. The following variables were analyzed: bed rest, paralysis or paresis, recent surgery, active cancer, thrombophilia, history of DVT/PTE, pregnancy, clinical signs of edema, slurring, increased collateral circulation, alternative diagnosis, results of Wells' criteria, presence of associated PTE, D-dimer results, venous Doppler echocardiography results, and generated costs.

Costs were calculated based on spending and categorized into emergency care, D-dimer test reagent, and venous Doppler echocardiography, obtained from the of the community Official Bulletin (BOCYL) and the hospital billing unit.

The statistical analysis was performed using the SPSS program. The chi-square test was used to compare two dichotomous qualitative variables, and Fisher's exact test was used to analyze a dichotomous qualitative variable against another quantitative variable. Sensitivity, specificity, positive and negative predictive values were calculated to analyze the effectiveness of the two strategies. The costs incurred per patient and the costs that would have been generated with the two proposed strategies were analyzed too.

RESULTS

A total of 249 patients were included in the study, with a mean age of 70 years (ranging from 21 to 95), 46.59 % of whom (116) had DVT.

Compared with those without DVT, patients with DVT showed a statistically significant presence of the following factors: male gender, cancer, pain, edema, slurring, PTE, obesity, and fewer alternative diagnoses (Table I).

Table I. Characteristics of the patients (overall suspected DVT) with DVT vs those without it

	TVP	No DVT	*p*
Men	52.6 %	39.8 %	0.04
Cancer	29.3 %	16.5 %	0.016
Pain	80.2 %	45.1 %	< 0.001
Edema	93.1 %	57.1 %	< 0.001
Slurring	72.4 %	14.3 %	< 0.001
PTE	25.9 %	13.5 %	0.014
Alternative diagnosis	0.9 %	62.4 %	< 0.001
Obesity	7.8 %	18.8 %	0.011
Palsy	10.3 %	8.3 %	0.57
Recent surgery	6 %	11.3 %	0.14
Bed rest	22.4 %	15.8 %	0.18
Thrombophilia	1.7 %	1.5 %	0.89
History of TED	22.4 %	15.8 %	0.18
Collateral circulation	6 %	6 %	0.99
Pregnancy	0.9 %	0 %	0.28 %

The overall costs generated by the diagnosis or exclusion of DVT amounted to €47,934.63 (Table II), which resulted in €192.5 per patient among the 249 individuals from the sample.

Table II. Cost derived from diagnosing/ruling out DVT in our center across a 6-month period

	Cost (€)	Source	*n*	Total (€)
ER care	101.41	BOCYL	249	25,254.09
D-dimer test	3.85	Hospital billing unit	144	554.4
Doppler echocardiography	88.86	BOCYL	249	22,126.14
Total				47,934.63

After applying Wells' criteria, 116 patients (46.58 %) had low chances of developing DVT, while 133 (53.41 %) had moderate-to-high chances. Among the former with low clinical pretest probabilities of DVT, only 11 (9.4 %) actually had DVT compared with 105 (78.94 %) of those with moderate-to-high pretest probabilities.

Regarding the primary endpoint, only patients who had undergone D-dimer testing (n = 144) were included to guarantee a homogeneous sample in both strategies (Fig. 1). The costs for each strategy were:

In strategy #1:

144 × €101.41 (emergency care for suspected DVT) + 144 × €3.85 (D-dimer for all suspicions) + 138 × €88.86 (Doppler echocardiography only for positive D-dimer suspicions) = €14,603.04 + €554.4 + €12,262.68 = €27,420.12 → €190.41 per patient.

In strategy #2:

144 × €101.41 (emergency care for suspected DVT) + 71 × €88.86 (Doppler echocardiography only for moderate-to-high chances) + 73 × €3.85 (D-dimer for low probability) + 67 × €88.86 (Doppler echocardiography for low probabilities with positive D-dimer testing) = €14,603.04 + €6,309.06 + €281.05 + €5,953.62 = €27,146.77 → €188.51 per patient.

Regarding the effectiveness study of both strategies, strategy #1 (Table III), based on the direct use

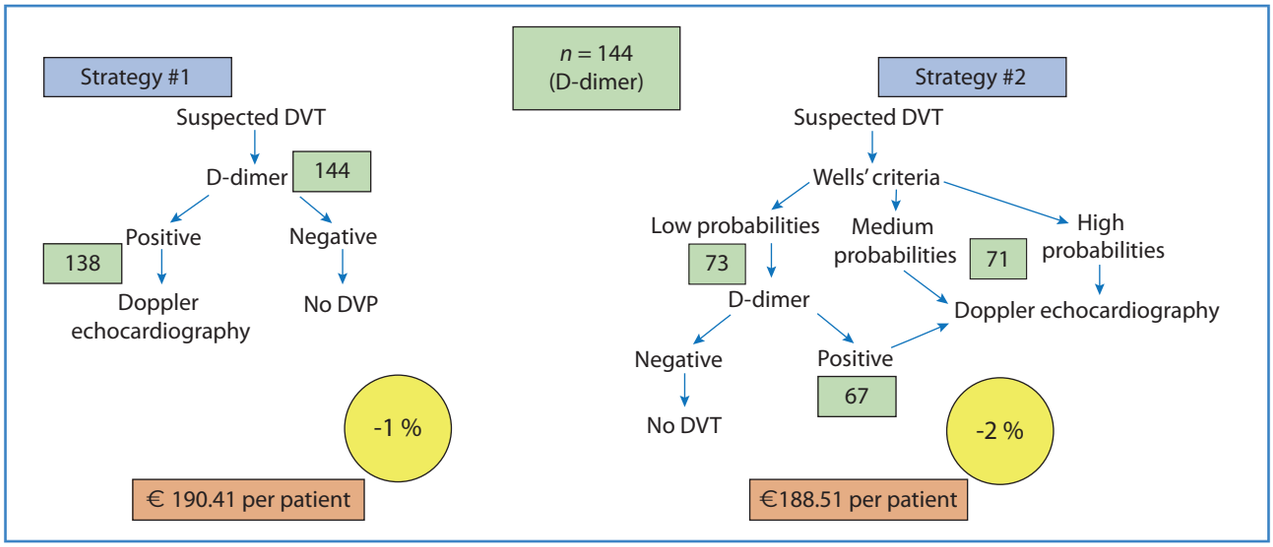

Figure 1. *Distribution of both strategies to assess their corresponding costs.*

Table III. Contingency table of strategy #1

	Doppler echocardiography + (DVT)	Doppler echocardiography - (without DVT)	Total
D-dimer test +	60 (41.67 %)	78 (54.17 %)	138 (95.83 %)
D-dimer test -	0 (0 %)	6 (4.17 %)	6 (4.17 %)
Total	60 (41.67 %)	84 (58.33 %)	144 (100 %)

Table IV. Contingency table of strategy #2

	Doppler echocardiography + (DVT)	Doppler echocardiography - (without DVT)	Total
Medium-high probability	53 (36.81 %)	18 (12.50 %)	71 (49.31 %)
Low probability	7 (4.86 %)	66 (45.83 %)	73 (50.69 %)
	60 (41.62 %)	84 (58.33)	144 (100 %)

of D-dimer, achieved sensitivity rates of 100 % (all 60 patients with DVT had a positive D-dimer tests), specificity rates of 7.1 % (6 out of the 84 patients without DVT, had a negative D-dimer test), positive predictive values of 43 % (60 out of the 138 patients with positive D-dimer tests had DVT), and negative predictive values of 100 % (none of the 6 patients with negative D-dimer tests had DVT).

Strategy #2 (Table IV), based on pretest clinical probabilities (Wells' criteria), achieved sensitivity rates of 88.3 % (53 out of 60 patients with DVT had moderate-to-high chances), specificity rates of 78.57 % (66 out of 84 patients without DVT had a low probabilities), positive predictive values of 74 % (53 out of 71 patients with moderate-to-high probability had DVT), and negative predictive values of 90 % (66 out of 73 patients with low probability did not have DVT).

DISCUSSION

The total annual cost of thromboembolic disease is estimated to be 1.5 to 12.2 trillion euros in Europe and 7 to 10 trillion dollars in the United States (1-3). This represents a significant economic burden for all health care systems.

The use of diagnostic algorithms, specifically the combination of clinical probabilities and D-dimer testing before performing Doppler echocardiography, has proven cost-effective (4).

In our country, Fuentes et al. (5) conducted a cost-effectiveness study of the diagnostic process regarding DVT, with characteristics that are less comparable to ours, such as having been conducted in the primary care instead of the hospital set-

ting, different exclusion criteria, and varying costs associated with diagnostic tests and emergency care, since the study was conducted in two different health care systems. Nonetheless, they also concluded that the use of diagnostic algorithms regarding DVT is cost-effective.

The sensitivity of D-dimer testing is approximately 95 %, with negative predictive values of 99 % to 100 %, and specificity rates of 35 % to 55 % (6). In our sample, we obtained a sensitivity rate and negative predictive value of 100 %. However, the specificity rate < 7.1 % was probably due to the characteristics of the sample and its inclusion criteria, with a low number of patients and negative D-dimer results treated by our unit. Although the specificity rate is the result of initial screening in other units, if the algorithm recommended had been followed, it would have been cero. Specificity is expected to be higher in the overall population.

The sensitivity of Doppler echocardiography has been reported to be 97 % for proximal DVT and 73 % for calf veins (4,7). In our sample, we assumed a sensitivity rate of 100 % because a positive result on the Doppler echocardiography was considered indicative of the presence of DVT.

The presence of false negatives in the Wells' criteria (for low probabilities) has been described to be around 5 % (8). In our sample, it was slightly higher, and 9.4 % of the patients with low probabilities developed DVT.

Table V illustrates a comparison between the two strategies analyzed:

The specific weight of strategy #1, identified by the D-dimer result, is its high sensitivity and negative predictive value. However, its low specificity and positive predictive value mean that its indiscriminate use leads to more diagnostic tests (Doppler echocardiography) being performed on patients without DVT, resulting in more health care spending.

Strategy #2 uses pretest clinical probability (Wells' criteria) initially, which marks the result of the D-dimer testing, is consistent with the diagnostic algorithm recommended by the current clinical practice guidelines (1,9). This explains why it showed better results in our study, with higher effectiveness and lower costs.

Table V. Comparison between effectiveness and cost between the two strategies

	Strategy #1	Strategy #2	Overall sample (*n* = 249)
Sensitivity	100 %	88 %	
Specificity	7.1 %	78 %	
Positive predictive value	43 %	74 %	
Negative predictive value	100 %	90 %	
Cost per patient	190.41 €	188.51 €	192.49 €

Strategy #2 turned out to be 2 % more cost-effective than the spending generated at our center. Even the erroneous strategy #1 also turned out to be more cost-effective (1 %), maybe because analysis and Doppler echocardiography testing of 6 patients with negative D-dimer results were requested.

Despite the existence of these algorithms, the routine clinical practice does not always abide to them, leading to additional costs and burdens on the health care system, primarily due to unnecessary diagnostic tests being performed, due to either a certain lack of awareness of such algorithms or the use of defensive medicine. In our sample, we could have achieved a 2 % reduction in health care expenses per patient.

CONCLUSIONS

The use of diagnostic algorithms (in the case of DVT, the initial clinical probability stratification [Wells' criteria] combined with D-dimer analysis in cases of low probability) is a cost-effective strategy to select patients eligible for Doppler echocardiography.

Greater awareness is needed on the importance of abiding by the diagnostic process of DVT among the various health professionals involved, among whom vascular surgeons are often only the final step.

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