Quality of Life After a Venous Thrombosis in Elderly Patients: Results From a Prospective Spanish Cohort

Calidad de vida tras una trombosis venosa en pacientes mayores: resultados de una cohorte prospecpectiva española

Dear Editor:

Venous thromboembolism (VTE) can have long-term consequences, such as post-thrombotic syndrome (PTS) or chronic thromboembolic pulmonary hypertension (CTPH). Recurrent thrombosis or bleeding can occur during follow-up. These post-VTE complications can have adverse effects on quality of life (QoL). Previous research on QoL after VTE included only middle-aged subjects.[1] Although the elderly are more prone to VTE[2] and the proportion of aged individuals is increasing worldwide,[3] there are no data on QoL in this population. We investigated the QoL of a cohort of patients older than 75 y after VTE and analyzed the determinants 18 mo post-VTE.

This was a prospective observational study of consecutive patients older than 75 y with acute VTE (pulmonary embolism [PE] and/or deep vein thrombosis [DVT]) who presented to Hospital Universitario 12 de Octubre, Spain between 2015 and 2017. Comorbidity was measured using the non-age-adjusted Charlson index,[4] and the functional status of the patients in terms of basic activities of daily living was assessed using the Barthel index (BI) (score range: 0-100).[5] Depression was established based on a review of the patient's history.

Clinical practitioners registered VTE recurrence and major bleeding. A diagnosis of CTPH required documented pulmonary hypertension (echocardiography or right catheterization) and evidence of chronic thrombosis on ventilation-perfusion scintigraphy or computed tomography at least 3 mo post-PE. The Ginsberg clinical scale was used to diagnose PTS 18 mo after DVT.[6] To assess QoL, we administered the Short Form 36 (SF-36) survey 18 mo after VTE and calculated the mean and its 95% confidence interval (95%CI) for each SF-36 subscale and two summary measures (physical summary measure [PSM] and mental summary measure [MSM]).[7,8] The subscale values ranged from 0 to 100, with higher scores corresponding to better health status. The summary measures were "norm-based." Thus, scores above or below 50 were considered above or below the mean of the reference population. We compared the results with those previously published in a Spanish population of the same age.[9] A difference of 5 points or more in any subscale was accepted as clinically and socially relevant,[7] and a *p*-value lower than 0.0005 was considered statistically significant, according to a Bonferroni correction for multiple comparisons. Finally, we pre-selected variables related to QoL in older and VTE patients.[1,10–12] We analyzed their impact on the summary measures using multivariable linear regression. The variables included in the multivariable models for PSM were age, sex, Charlson index, BI, recurrent VTE, bleeding, CTPH, and PTS. Depression was included in the multivariable models for MSM.

The local ethics committee approved this study. Prior to enrollment, the subjects were informed about the study, and provided written or verbal informed consent.

In total, 101 of 151 (67%) patients completed the SF-36 questionnaire 18 mo post-VTE. The median age was 81 y (interquartile range [IQR]: 79, 86), 61% were females, and 19% had cancer. The median BI was 100 (IQR: 85, 100), and the Charlson index was 1 (IQR: 0, 2). Eighty-two% of patients had experienced a PE, with or without DVT. VTE recurrence, major bleeding, CPTH, and PTS occurred in 8%, 5%, 3%, and 10% of patients, respectively. The means for the two summary measures were lower than the values for the Spanish population older than 60 y (PSM, 45.51 [95%CI: 43.68, 47.35]; MSM, 47.30 [95%CI: 44.95, 49.65]) (Table 1). After the multivariable analysis, the BI was the only determinant related, clinically and statistically, to PSM at the 18-mo follow-up (*B*-coefficient: 0.119 [95%CI: 0.043, 0.195], $p = 0.002$). Neither the Charlson index nor VTE-related factors were related to PSM (Charlson *B*-coefficient: −0.126 [95%CI: −1.238, 0.986], recurrence *B*-coefficient: −3.650 [95%CI: −11.051, 3.751]; bleeding *B*-coefficient: 1.846 [95%CI: −2.934, 6.625]; CTPH *B*-coefficient: 2.182 [95CI%: −6.659, 11.022]; PTS *B*-coefficient: −5.212 [95%CI: −10.980, 0.557]). No factors were related to MSM after the multivariable analysis.

This study showed that older VTE patients reported worse QoL than that of older patients in the general Spanish population, with mainly physical function affected. Although several studies concluded that VTE had a negative impact on the QoL of middle-aged people,[1] a recent study[13] reported that QoL 1 y after VTE improved to a level similar to that of a healthy population. This finding differs from that found in our study, in which both summary measures were below the population norms after 18 mo. We ascribe this disparity to the age difference of the study populations. The disability prevalence increases among the aged,[14] and it have been linked to a reduced QoL in several disorders.[12,14,15] In the present study, the BI was the only independent determinant of a low PSM score.

Our study had some limitations. First, the small sample size limited the power to detect an association between QoL and long-term complications. Thus, no conclusions can be drawn about the impact of recurrence, bleeding, CTPH or PTS on QoL. In addition, this was a monocentric study, which limits its external validity. Finally, we did not use a disease-specific QoL questionnaire, which could have been more sensitive than the SF-36 survey in detecting differences in QoL. However, previous studies on VTE and QoL employed the SF-36 survey and demonstrated good reliability and validity.[1,13]

Despite the aforementioned limitations, to our knowledge, this is the first study to examine QoL in aged VTE patients. The response rate in the present study was similar to that of earlier research[1]

Table 1
Results of SF-36 questionnaire: comparison with Spanish population.

SF-36 subscales	Cohort results (mean (95%CI))	Comparison with Spanish population over 60-year-old			Comparison with Spanish population from 80 to 85-year-old		
		Reference values (mean)[a]	Mean difference (95%CI)	*p*	Reference values (mean)[a]	Mean difference (95%CI)	*p*
Physical functioning	44.66 (38.30, 51.02)	65.7	−21.04 (−27.40, −14.68)	<0.001	68.93	−24.27 (−30.63, −17.91)	<0.001
Physical role	60.19 (50.15, 70.24)	73.3	−13.11 (−23.15, 3.06)	0.100	63.18	−2.99 (−13.03, 7.06)	0.100
Bodily pain	57.40 (50.51, 64.28)	68.4	−11.00 (−17.89, −4.12)	0.011	64.44	−7.04 (−13.92, −0.16)	0.096
General health	48.27 (43.91, 52.63)	55.9	−7.63 (−11.99, −3.27)	0.004	52.51	−4.24 (−8.60, 0.12)	0.063
Vitality	52.14 (46.12, 58.15)	60.5	−8.36 (−14.38, −2.35)	0.007	54.39	−2.25 (−8.27, 3.76)	0.705
Social functioning	75.24 (69.05, 81.44)	79.2	−3.96 (−10.15, 2.24)	0.645	72.79	2.45 (−3.74, 8.65)	0.110
Emotional role	66.34 (56.54, 76.15)	84.8	−18.46 (−28.26, −8.65)	0.172	82.10	−15.76 (−25.56, −5.95)	0.652
Mental health	61.32 (56.17, 66.47)	68.3	−6.98 (−12.13, −1.83)	0.019	62.70	−3.79 (−8.94, 1.36)	0.401

[a] Estimated from data published by López-García et al.[9]

and can be attributed to the challenging nature of follow-ups of elderly populations. Given that VTE-related complications usually occur within the first 2 y,[1] we estimate that an average follow-up of 1.5 y should be sufficient to identify the impact of most of these complications on QoL.

In our cohort, older VTE patients reported worse QoL than that of the general population of the same age, and the BI was the only independent determinant of QoL. Although our study cannot lead to firm conclusions, the results may be relevant for future research on the influence of VTE-related complications or treatment on the QoL of patients.

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Acute Chest Syndrome in Sickle Cell Disease

Síndrome torácico agudo en la anemia de células falciformes

Dear Editor:

A 24-year-old man with sickle cell disease was admitted to our emergency department due to high fever (39.4 °C) and bilateral pleuritic chest pain that had started 5 days previously. He had been admitted two times in the previous month due to pain crisis and respiratory symptoms. At that time, a chest X-ray showed a consolidation in the left lower lobe, and bacterial pneumonia was diagnosed. Pulmonary auscultation revealed decreased breath sounds over the lower lung fields. Laboratory tests showed mild leukocytosis (white cell count, 14,100/cm^3) with 64% neutrophils, anemia (hemoglobin level, 7 g/dl), thrombocytosis (790,000 platelets), and elevated C-reactive protein (98 mg/L) and lactate dehydrogenase levels (482 U/L). The patient underwent chest computed tomography (CT) angiography, which demonstrated bilateral pulmonary opacities associated with ground-glass attenuation over the lower lung fields (Fig. 1A) and mild pleural effusion on the right side. Pulmonary thromboembolism was ruled out (Fig. 1B). Two blood culture sets were negative and bronchoscopy was performed; cultures (bacterial and fungal) and GeneXpert results from bronchoalveolar lavage were negative. The patient was diagnosed with acute chest syndrome (ACS) and was treated successfully with blood transfusion, aggressive crystalloid hydration, analgesia, and antibiotic therapy with ampicillin plus sulbactam. His laboratory test values improved to normal and he was discharged from the hospital 7 days after initial treatment with an oral hydroxyurea prescription. One month after discharge, the patient underwent chest CT, which showed complete resolution of the pulmonary opacities (Fig. 1C). CT also showed characteristic findings of sickle cell disease, such as a small and calcified spleen and H-shaped vertebral bodies secondary to bone infarction of the central endplates (Fig. 1D). The final diagnosis of the condition leading to the patient's hospitalization was ACS.

ACS in patients with sickle cell disease is defined as an acute illness characterized by fever and/or respiratory symptoms (chest pain, dyspnea, or tachypnea), accompanied by the appearance of new pulmonary opacities on imaging examinations.[1,2] This condition is most commonly associated with homozygous sickle cell disease and rarely with heterozygous sickle cell disease.[2] ACS is the leading cause of hospitalization and death among patients with sickle cell disease.[3–5] An exceedingly rare, yet often fatal, complication of ACS is rapid progression to acute respiratory distress syndrome.[2] Three major underlying mechanisms of ACS have been proposed. Infection with an excessive inflammatory response to lung injury is the most frequent cause.[3–5] Infectious agents associated with ACS in children, in decreasing order of frequency, include viruses, mycoplasma, chlamydia, and bacteria (*Staphylococcus aureus, Streptococcus pneumoniae*, and others). Fungal infections are uncommon.[4] Another proposed mechanism is that the sickled cells cause vascular occlusion and pulmonary infarction. Lastly, fat embolism syndrome may occur as a result of contents released during