of VT in UC patients was comparable among males and females. The highest odds ratio for VT was observed among patients under 40 years of age [adjusted OR of 4.60 (3.78–5.52)], but did not differ regarding localization and disease duration. Flare-ups of the UC increased this risk further, up to 8.3-fold (95% CI, 5.6–11.4). The risk of VT was even higher when the flare-up was experienced being ambulatory (HR 15.8; 95% CI 7.2–24.5). In the end, patients in remission kept an elevated risk of VT compared to non-UC controls (HR 2.2; 95% CI 1.6–2.9). Medication at first VT included corticosteroids (53.7%), thiopurines (31.8%) and infliximab (14.5%). No significant association between classical risk factors such as the use of contraceptives, pregnancy, coagulation disorders or smoking and the risk of VT were found.
Conclusions: UC is an independent risk factor for VT. DVT and PE are the most usual sites of thrombosis in UC patients. The risk factors for these events were young age and flare-ups of the UC.

C0463
A CLINICAL SCORE TO RULE OUT THE CONCOMITANT PRESENCE OF DEEP VEIN THROMBOSIS IN PATIENTS PRESENTING WITH SUPERFICIAL VEIN THROMBOSIS: THE ICARO STUDY

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Background: Superficial vein thrombosis (SVT) is commonly encountered in clinical practice. Recent studies have suggested that the concomitant presence of deep vein thrombosis (DVT) or pulmonary embolism (PE) at the time of SVT diagnosis is not uncommon, thus increasing the interest on this disease. Whether this coexistence is predicted by specific risk factors remains unknown. Thus, to evaluate potential risk factors for DVT coexistence in patients presenting with acute objectively diagnosed SVT of the lower limbs and to develop a simple score entirely based on clinical variables to define the pre-test probability of DVT in these patients.
Methods: A multicenter, retrospective cohort study of SVT patients was conducted. Information was collected on clinical signs and on risk factors for venous thrombosis.
Results: 494 patients (mean age 56.3±17.9 years, 64.2% women) were included. Concomitant DVT was found in 16.0% of patients. After multivariate analysis, we identified 5 independent variables that were used to develop the ICARO score: active malignancy (1.5 points), limb oedema (1.5 points), rope-like sign (−1 point), age ≥50 years (1 point), unprovoked SVT (−1 point). The prevalence of concomitant DVT was 1.1% in the low-probability category (<0 points), 12.0% in the intermediate-probability category (0 to 1 points), and 32.3% in the high probability category (>1.5 points).
Conclusions: The concomitant presence of major DVT is not negligible in patients with SVT. Our prediction score entirely based on simple clinical variables may be useful in assessing the risk of concomitant DVT in these patients.

C0525
LONG-TERM RECURRENCE OF VENOUS THROMBOEMBOLISM AFTER TREATED SYMPTOMATIC DISTAL VEIN THROMBOSIS: A RETROSPECTIVE COHORT STUDY

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Background: Distal deep vein thrombosis (dDVT) is a common clinical manifestation of venous thromboembolism (VTE). However, it is still a matter of debate whether or not to treat all cases of dDVT. Moreover, only few and heterogenous data are available on the long-term risk of recurrent VTE after dDVT.
Methods: A retrospective cohort study was conducted on consecutive patients diagnosed with symptomatic isolated dDVT between 2004 and 2011 at the Thrombosis Center of Varese, Italy. All patients were given anticoagulant therapy. Patients were followed-up for at least 2 years.
Results: 321 patients were enrolled. dDVT was associated with a transient risk factor or with cancer in 52.6% and 17.4% of patients, respectively. 89% of patients received low molecular weight heparin for at least 4 to 6 weeks, 6% received warfarin for at least 3 months, 4% received a shorter course of anticoagulant therapy. Overall, during a mean follow-up of 45 months, 61 patients (19%) developed recurrent VTE, which was represented by a major event in 42.6% of cases. According to index dDVT association with a transient risk factor, with cancer or with no risk factors (unprovoked), recurrence rate was 2.7, 8.4 or 9.7 per 100 patient-years, respectively ($p < 0.001$). Six patients (1.9%) experienced major bleeding during follow-up.
Conclusions: The long-term risk of recurrent VTE after treated symptomatic dDVT is not negligible. Cancer patients and those with unprovoked dDVT show a significantly higher risk of recurrent VTE. Further studies are needed to identify those patients who may deserve an extended course of anticoagulant treatment.

GENETICS OF THROMBOSIS AND HEMOSTASIS

C0047
CYTOPROTECTIVE SELECTIVE HUMAN 3K3A-ACTIVATED PROTEIN C VARIANT DETOXIFIES HISTONE H1 AND STABILIZES ENDOTHELIUM FROM PRO-INFLAMMATORY CYTOKINES

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Background: Activated Protein C (APC) exerts anticoagulant and cytoprotective activities. The major adverse effect observed after administration of APC to adult severe sepsis patients was an increased risk of serious bleeding. The pharmacologic utility of APC may be enhanced by APC variants with reduced anticoagulant but preserved or enhanced cytoprotective actions. Here we report some new studies of the cytoprotective selective 3K3A-APC.
Methods: Human wild type (wt) and the variant "3K3A-APC" bearing 3 mutations (Lys191–193 to Ala) were characterized in multiple *in vitro* assays: Anticoagulant activity using APTT assays, clot lysis assays in presence of tPA, prevention of histone H1 toxicity on epithelial and endothelial cells (monitored using LDH release assays), and protection of *EAy926* human endothelial cells from a mixture of pro-inflammatory cytokines (TNF-α and IFN-γ) determined using trans-endothelial resistance assays (real time monitoring with iCelligence).
Results: The relative anticoagulant activity for 3K3A was <10% wt-APC. The results from the plasma turbidimetric clot lysis assays show that 3K3A-APC did not influence tPA-induced clot lysis in vitro when compared with wt-APC using pharmacologic APC concentrations. In studies of APC-dependent loss of histone H1 cellular toxicity over 16 hrs incubation, we observed that the 3K3A-APC was 2-fold more active than wt-APC for protecting cells from H1's toxicity. 3K3A-APC variant showed a dose dependent (0.5–4.0 μg/ml) beneficial protection similar to that of plasma-derived APC for endothelial cells from toxicity caused by a mixture of TNF-α and IFN-γ measured over 75 hrs. Retention of some other cytoprotective actions in 3K3A-APC was previously reported.
Conclusions: Mutations of APC residues 191–193 decreases anticoagulant activity by >90% while retaining excellent cytoprotective activities. These mutations in 3K3A-APC improved