Venous thromboembolism (VTE) is a frequent event in the clinical course of patients with exocrine pancreatic cancer; studies have been designed to evaluate the role of prophylactic anticoagulation in this ominous disease. Searches for the molecular basis of thrombosis in cancer Bozkurt et al. present in the abstract #e22049 the result of their investigation on the frequency of inherited and carcinogenesis-acquired proteins in oncologic patients with and without venous thromboembolism. From the bedside, Muñoz Martin et al. present in the abstract number #e15817 their work on the incidence of venous thromboembolism in patients with exocrine pancreatic cancer and the role of the established Khorana score in predicting symptomatic and incidental venous thromboembolism. At last, Cella et al. in the Abstract #e20625 expand the predictor landscape from the Khorana score to other risk factors for venous thromboembolism, refining the selection of oncologic patients who can benefit from prophylactic anticoagulation.

**What Did We Learn at 2014 ASCO Annual Meeting?**

Bozkurt et al. evaluated the frequency of inherited (Factor V of Leiden, prothrombin G20210A mutations and PSLG-1 VNRT polymorphisms) and carcinogenesis-acquired (Tissue Factor and soluble P-Selectin) protein genotypes and levels respectively in patients with adenocarcinoma [15]. From a screened population of 1,838 patients with adenocarcinoma, 63 patients with venous thromboembolism and 38 controls had their blood tested for the above mutations and levels. In the population with venous thromboembolism, tissue factor levels were higher in patients with adenocarcinoma than those with other tumors (p=0.02). Also, the PSLG-1 VNRT
Table 1. Khorana and Vienna assessment scores for prediction of venous thromboembolism.

<table>
<thead>
<tr>
<th>Site of cancer</th>
<th>Very high risk</th>
<th>Pancreas, stomach *</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count</td>
<td>&gt;350,000/dL</td>
<td>Lung, lymphoma, gynecologic, bladder, testicular</td>
<td>1</td>
</tr>
<tr>
<td>Hemoglobin or ESA use</td>
<td>&lt; 10 g/dL</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Leukocyte count</td>
<td>&gt;1,100,000/dL</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Body mass index</td>
<td>&gt;35 kg/m²</td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

Vienna VTE risk assessment score

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<tbody>
<tr>
<td>D-dimer</td>
<td>&gt;1.44 µg/mL</td>
</tr>
<tr>
<td>Soluble P-selectin</td>
<td>&gt;53.1 mg/mL</td>
</tr>
</tbody>
</table>

*In the Vienna score, high-grade gliomas are considered very high risk sites of cancer.

polymorphisms AB and AC were more frequent in central venous catheter related, subclavian, jugular and pelvic venous thromboembolism.

Incidence of Incidental and Symptomatic Venous Thromboembolism (VTE) and Khorana’s Score in Ambulatory Pancreatic Cancer Patients Receiving Chemotherapy

Muñoz Martin et al. designed a multicentric retrospective cross-sectional study involving a population of ambulatory patients with exocrine pancreatic cancer (EPC) treated with chemotherapy, where the investigators followed 517 patients from January 2008 to December 2011 [16]. Venous thromboembolism was identified in 22.6 % of the patients with a median time to diagnosis of 3 months and 67% of cases occurring within 6 months of diagnosis. Around 50% of the patients had incidental venous thromboembolism. Interestingly visceral thromboembolism was an incidental finding in 91% of the identified cases, representing 38% of all cases of venous thromboembolism in the study. The Khorana score consolidated its clinical usefulness when it predicted symptomatic venous thromboembolism while having no predictive value for incidental venous thromboembolism.

Risk Factors for Cancer-Related Venous Thromboembolism in Ambulatory Patients

Cella et al. validated the Khorana score and identified additional predictor factors for venous thromboembolism in their ambulatory oncologic population on antineoplastic therapy [17]. They followed up 544 ambulatory patients with various cancers, 8% of them with pancreatic cancer. Among the confirmed risk factors were previous venous thromboembolism, metastatic disease, vascular or lymphatic compression by the tumor, extremity edema of extremities, surgical procedure in the last 6 months, and central venous catheter. Venous thromboembolism associated with cancer surgery has been increasing frequency although mortality associated with surgery has been decreasing [18]. This new risk factors help to define which population of oncologic patients would benefit most from prophylactic anticoagulation.

Discussion

Venous thromboembolism is a frequent event in ductal adenocarcinoma. Scores carrying predictive value will support the indication of prophylactic anticoagulation for patients at low bleeding risk and high risk for venous thromboembolism. Biomarkers, especially acquired circulating factors and inherited gene polymorphisms, will redefine venous thromboembolism care in the genomic era. It is now known that Asian patients with ductal adenocarcinoma of the pancreas have lower incidence of venous thromboembolism. It remains to be described if this effect is a consequence of genetics or behaviors (i.e. smoking, metabolic syndrome and diet) affecting epigenetic silencing or activation of cancer pathways. The ESA therapy is one of the components of predicting scores and International Guidelines clearly recommend prophylactic anticoagulation for chemotherapy combinations of thalidomide or lenalidomide and steroids; redefining risks for newly developed monoclonal antibodies and combination chemotherapy for pancreatic cancer and confirming in phase III trials the role of anticoagulation in clinical outcomes will further refine the role of prophylactic anticoagulation in ductal adenocarcinoma.

Conflict of Interest

The authors hereby state that there is no conflict of interest to disclose during the time of submission of this manuscript.

References


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