

ADVANCES IN HEMATOLOGY

Current Developments in the Management of Hematologic Disorders

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Treatment of Incidental Thromboses in Cancer Patients

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H&O What is incidental thrombosis?

GG Incidental thrombosis refers to a blood clot that is detected by some test in a patient without any symptoms—no related shortness of breath, chest or limb pain, limb swelling or erythema. Blood clots most commonly occur in systemic veins, usually in the larger veins in the legs or pelvis. These clots can then break free and travel, or embolize, to the lungs. Cancer patients routinely undergo imaging to assess the extent of malignancy, assess the response to therapy, or to screen for metastases. This imaging often includes computed tomography (CT) of the chest, abdomen and/or pelvis, frequently including the use of intravenous contrast media. Although not specifically tailored for vascular evaluation, these CT scans are often performed with techniques sufficient to evaluate the vascular system. Thrombi are most often identified as filling defects in systemic veins, whereas emboli are usually filling defects in the pulmonary arteries. On examinations performed for evaluation of the patient's cancer, these thrombi and emboli are considered incidental. However, close questioning and review of medical records can often identify symptoms that might be attributable to thrombi or pulmonary emboli.

H&O With what types of cancer are incidental thromboses commonly associated?

GG A number of cancers are known to be associated with thromboses. The highest frequencies of thrombotic disease

are seen in pancreatic cancer, ovarian cancer, and brain cancer. We analyzed 403 patients who had chest CT scans performed for reasons other than evaluation for pulmonary embolism and discovered that incidental pulmonary embolism was most frequent in patients with gynecologic cancer and malignant melanoma. Those results were in accord with other published literature regarding the frequency of thromboses in patients with these diseases, but because the previously published literature was concerned with symptomatic conditions, we anticipated that there might be differences in prevalence among our patients. Incidental pulmonary emboli are most often encountered in patients with lung cancer or lymphoma because chest CT is routinely used in these diseases, and because of the higher prevalence of these diseases. Overall, we saw thrombi in a wide variety of malignancies, so it would be prudent to note that their presentation is not strictly confined to any one malignancy.

H&O Does the treatment approach for an incidental thrombosis differ from that for a symptomatic thrombosis?

GG At this time, there is some controversy regarding how to treat patients with incidental pulmonary embolism, especially if the embolism is small. Incidental emboli can vary in size considerably, and yet remain without appreciable symptoms. For large emboli, there is a general consensus to treat the patient as if he or she were symptomatic. For small asymptomatic embolisms—and sometimes small symptomatic emboli—some questions persist regarding their importance. For patients with massive symptomatic emboli, thrombolytic therapy or mechanical fragmentation may be used to rapidly eliminate the clot. However, for smaller emboli where the risk of thrombolytic therapy is not justified, treatment with anticoagulation therapy or vena cava filter placement is not directed at the clots present at the time of treatment. In particular, anticoagulation does not speed the resolution of pulmonary emboli significantly. The therapy is aimed at preventing future embolization, which might

produce or aggravate symptoms and potentially be fatal. As a result, many clinicians believe that because even a small clot indicates a greater likelihood of future clots, patients should receive treatment. Therefore, at my institution, nearly any reported pulmonary embolism, whether it is incidental or symptomatic, receives treatment. Furthermore, if an embolus is noted in the chest, an ultrasound of the legs is generally indicated in order to check for large clots that could migrate to the lungs. If such a clot is found, aggressive anticoagulation therapy is used. If only a small embolism is found in the chest, and none is found in the legs, a minority of physicians today choose to give no therapy.

There is some evidence that small emboli are not as predictive of future events as larger or symptomatic embolisms. Early outcomes trials on the use of CT for evaluation for pulmonary emboli showed a low frequency of future occurrence of pulmonary emboli in patients with a negative CT examination despite techniques that would likely have missed some small emboli. An article by Engelke and colleagues in *Radiology* in 2006 reported results from a study of patients who had pulmonary emboli demonstrated on multidetector CT. The trial included a mix of patients with and without prior clinical suspicion of pulmonary emboli. Some of the patients had emboli that were unsuspected and unreported at the time of the CT and were therefore not treated. It was found that there were more complications among those patients who were treated with thrombolytic therapy or therapeutic anticoagulation than among those who were not. It is difficult to compare these two groups because the size of the embolism varied between them. The early complications and deaths were due to either cardiorespiratory or renal failure, likely related to the embolism, or to hemorrhage related to the treatment. The smaller emboli that were not detected resulted in no deaths and few recurrent emboli. The authors therefore concluded that thrombolytic and therapeutic anticoagulation therapy confers more risk than recurrent pulmonary embolisms. In our study, which included a smaller cohort in which no patients had prior clinical suspicion of pulmonary emboli, there were no deaths attributable to anticoagulation therapy but two deaths attributable to thrombosis and emboli in patients who were being treated. Deep vein thrombosis was often present and recurrent thromboses and emboli occurred despite the lack of clinical suspicion. We concluded that even small asymptomatic emboli suggest the presence of other or future thromboembolic disease. Both trials demonstrated some recurrent emboli in asymptomatic patients, but no late deaths. It is unclear how aggressive anticoagulation therapy is appropriate in these patients or how long it should continue.

H&O Could you describe the use of vena cava filters in this setting?

GG Vena cava filters can be used in patients who have recurrent embolisms despite anticoagulation therapy, or in whom anticoagulation therapy is contraindicated. For example, a patient who has had recent surgery or with brain metastases is unlikely to be an appropriate candidate for anticoagulation. Interestingly, these patients can have bleeding and clotting problems concomitantly. In such patients, a wire mesh device, or filter, is placed into the inferior vena cava, because most large clots originate from the pelvis and lower extremities. The filter functions to catch the clots and allows them to dissolve through the normal coagulation system before it can reach the lungs and impair blood oxygenation. The filter thus can prevent symptoms or death associated with pulmonary embolism.

There are patients for whom both anticoagulation and filter placement are not appropriate. These patients can be difficult to manage and should have optimization of risk factors for thrombosis and hemorrhage.

H&O What are other important concerns regarding incidental thromboses?

GG Much of the imaging done for cancer evaluation is adequate for the evaluation of thromboses and pulmonary embolism, but it is not optimal for that purpose. Small emboli are missed either due to their size or because not enough attention is paid to the vessels themselves. It is very important, in routine evaluation of chest CT scans, to carefully evaluate the pulmonary vessels and all clots must be reported. Since the relative risk of anticoagulation is related to the therapy used, the use of low molecular weight heparin and other newer therapies should be evaluated in the setting of small and asymptomatic thromboses and emboli where the risk of future embolic disease and death is less well defined.

Suggested Readings

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