

THROMBOSIS IN THE CANCER PATIENT

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The link between malignancy and thromboembolism has long been recognized. Cancers possess the ability to activate the coagulation cascade by elaborating prothrombotic factors. Two prominent prothrombotic factors include tissue factor and cancer procoagulant. Tissue factor is known to participate in the activation of the extrinsic pathway. Cancer procoagulant is found in cancer cells but not in normal cells. Cancer procoagulant activates factor x directly. The prothrombotic factors of cancer lead to a general state of disseminated intravascular coagulation (DIC). DIC results in the consumption of coagulation factors and platelets and the generation of fibrin. This process may result in either bleeding or thrombosis depending on the relative activation or inactivation of the coagulation cascade as dictated by the cancer.

Several solid tumors are highly associated with DIC and include tumors of the pancreas, prostate and lungs. Acute promyelocytic leukemia is well known to cause an aggressive form of DIC. Other factors confronting the cancer patient also can serve to promote thrombosis including immobility due to weakness, compression of vessels by the cancer, central venous catheters and chemotherapeutic agents.

Treating VTE (venous thromboembolic events) in cancer patients is similar to the management of VTE in the noncancer patient. Unique issues of VTE in cancer patients relate to duration of therapy and failure of therapy. Initial treatment of VTE in cancer patients involves the use of heparin either unfractionated or fractionated simultaneously with the institution of coumadin. Depending on the success of the treatment of the cancer the coumadin can be maintained indefinitely. Recent studies have suggested low molecular weight heparin is more effective than warfarin in avoiding recurrent DVT. Vena Cava filters are indicated in patients who either have a contraindication to anticoagulation such as bleeding or have failed prior anticoagulant therapy. However, studies have shown the initial benefit of vena caval filters for prevention of pulmonary embolus is counterbalanced by an excess of recurrent DVT without a survival benefit. The recurrent DVT can result in massive edema of the legs.

Patients who develop recurrent DVT while on warfarin present a challenge. These patients can be managed by either increasing the INR though running the risk of bleeding or using unfractionated heparin or fractionated heparin. Studies have shown fractionated low molecular weight heparin is as effective and possibly safer than warfarin for the treatment of venous thromboembolism in the cancer patient.

Direct thrombin inhibitors may prove to be superior in treating cancer associated venous thromboembolism. Ximelagatran (Exanta) is an orally administered direct thrombin inhibitor still in experimental development though with exciting potential.

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