Do Anticoagulants (Blood Thinners) Improve Survival in Cancer?

Blood clots are a common problem in cancer, including lung cancer, and several studies have shown that this contributes to diminished survival in cancer patients (abstract here):

![Diminished Survival in Canadian Patients with Blood Clot (Venous Thrombosis, VTE)](click to enlarge)

Once a blood clot has been detected, most typically a deep vein thrombosis (DVT) that is commonly detected in the leg, or a pulmonary embolus (PE) (clot in the lung), the standard treatment is blood thinners, usually starting with either “unfractionated” heparin, the older form that is given through an ongoing IV and requires frequent checks of the level of blood thinning and adjustment, or “low-molecular weight heparin” (LMWH), which includes just active pieces of the heparin protein, for which there are several brands that are given once or twice daily as a subcutaneous (under the skin) injection and have a more reliable level of blood thinning, so constant monitoring of the level of blood thinning is not required. Patients commonly transition to the oral blood thinner warfarin/coumadin after several days, largely due to the convenience of maintaining a prolonged blood thinning effect with an oral treatment instead of daily injections (and keeping an IV drip of unfractionated heparin going indefinitely, requiring constant checks of the blood, isn’t feasible). LMWH is also very expensive, while coumadin is quite inexpensive.

The American College of Cancer Physicians (ACCP) actually recommends that patients stay on subcutaneous LMWH (an agent known as dalteparin/Fragmin, based on some trial results we’ll review) for 3-6 months for the majority of cancer patients who develop a blood clot (ACCP reference here). While there isn’t an established optimal duration of keeping blood thinners going after a blood clot in a patient, it is generally felt that the underlying cancer continues to put a patient at greater risk for future blood clots, so blood thinners are often recommended to continue as long as a person has active cancer (so if someone has been treated and has no evidence of disease, it’s considered appropriate to discontinue blood thinners (anticoagulation).

So there’s no question that blood thinners are an appropriate treatment for blood clots, which are common in patients with cancer. But there have also been several studies that have suggested a potential survival benefit from blood thinners in patients with cancer, in some cases focusing on patients treated for blood clots, and in other trials in patients given blood thinners without any evidence of a blood clot yet. We’ll review some of the evidence to support a survival benefit, but one key take home point is that there have been reports of studies that don’t support this idea, and there are not guidelines at this point that incorporate blood
thinners as a standard therapy to improve survival in cancer patients.

So why might blood thinners actually improve survival in patients with cancer? While people with cancer can die from clot-related complications (especially more serious, dangerous ones like pulmonary emboli) that may be prevented by treatment with blood thinners, there are actually reasons to think that heparins may have direct antitumor effects. For instance, one of the most important founders of the field of angiogenesis, Dr. Judah Folkman at Harvard, found that unfractionated heparin (old standard, through IV) with steroids had anti-angiogenic (blocking tumor blood supply) effects in animal models (abstract here). Tumors produce large amounts of an enzyme known as heparinase, which can break down the “extracellular matrix”, the tissue that is a barrier for tumors invading into the bloodstream (abstract here), and administering heparin reverses that effect. Heparins may also block the ability of cancer cells to metastasize (reviewed here). Finally, some forms of heparin can potentially lead to tumor apoptosis, or programmed cell death, which is a mechanism thriving cancers can circumvent. This work is still early and in animal models, but it helps offer another plausible explanation for how anticoagulation can contribute to improved survival in patients with cancer, independent of the effects on blood clots. Next, we'll explore the actual evidence for and against this concept.