Cancer Age: Can We Reliably Estimate and Apply This Knowledge?

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In their article, Patrone et al utilize a modified version of Collins’ law to estimate the age of breast, lung, and colorectal cancers. Collins’ law, which states that the period of risk for recurrence of a tumor is equal to the age of the patient at diagnosis plus 9 months, has been applied primarily to pediatric tumors, in particular embryonal tumors.[1,2] The results from the application of Collins’ law to these tumors have been reasonable, although exceptions have been reported and the law is not applicable to all cancers.[3,4] Its utilization in adults in the manner used in this paper is therefore unique.

The current study is predicated on the assumption of a constant rate of cancer growth after surgery, which the authors concede is a potential limitation. Bias may also have been introduced in the selection of “surgery only” patients, especially those from retrospective studies, although the impact of this is possibly lessened by the fact that the studies used were older in most cases (likely from a time when there was less utilization of multimodal therapy than there is at present). Finally, there is admitted heterogeneity in the time to recurrence based on residual tumor burden following resection and the intensity of follow-up. Some of these concerns are addressed by the authors’ use of primarily prospective studies and the finding of no difference between the pace of recurrence in the retrospective studies and that seen in the prospective studies, despite differences in absolute numbers.

Despite these limitations, the study concept is novel and extremely interesting. Still, the application of the results remains unclear. From the perspective of the treating physician, knowing the “age” of a tumor is unlikely to change management. From the perspective of the patient receiving a new diagnosis of cancer, while this knowledge may alleviate anxiety around treatment urgency, it might exacerbate anxiety of the “what if” variety. For example, a patient who has just been told that her cancer is probably 5 to 6 years old might berate herself with thoughts along the lines of “if only I had or hadn’t done X then, I wouldn’t be in this situation now.”

One potential application of the study results from the physician’s perspective lies in the possibility of performing a retrospective review of a patient’s contact with the healthcare system during the period of the estimated age of his/her tumor. Were there subtle physical examination or imaging findings that could be reliably attributed to the patient’s tumor and applied to future patients to facilitate an earlier diagnosis and hopefully a more favorable outcome? However, a less positive side of this potential application in our current medicolegal environment is the possibility of increased litigation risk because of perceived negligence (eg, “Doctor X missed my cancer 3 years ago”).

As stated previously, the conclusions of the article rely on the assumption of a constant tumor growth rate after surgery, and as a result, patients treated with chemotherapy, radiation, or hormonal therapy were excluded because of the potential of these therapies to alter growth kinetics. While necessary for the internal validity of the study in estimating the age of a given cancer, this limitation of the patient population makes it difficult to use the findings to determine the prognosis or duration of postoperative follow-up after resection except in patients treated with surgery only. For all three cancers chosen for this study (breast, lung, and colorectal), a substantial number of patients today are treated with neoadjuvant or adjuvant chemotherapy, radiation, or hormone therapy. It would be interesting to know growth rates in these settings and to be able to predict a
reasonable interval after which recurrence is extremely unlikely. We could then tailor the intensity of our follow-up accordingly. However, I imagine that these would prove difficult to estimate given the varied responses of tumors to multimodal therapy.

Patrone et al conclude that the typical “age” of a breast cancer at diagnosis is about 5 to 6 years, while that for lung and rectal cancer is 3 to 4 years, based on time to recurrence in most patients. For these and many other cancers, the current clinical standard is to perform fairly intensive follow-up for the first 5 years after the first round of treatment. Thereafter, if there is no evidence of recurrent disease, we cautiously consider the patient cured and decrease the intensity of our surveillance. This 5-year period aligns neatly with the timeframe observed in this study. While this is reassuring, it does not change the current paradigm.

Finally, the authors mention possibly conducting a similar analysis of resected metastatic lesions and making inferences about their “age” relative to the primary tumor. This knowledge would be extremely valuable for guiding clinical decision making, especially now when increasingly aggressive metastasectomies are being performed. Once again, however, this analysis would be difficult to interpret given our current multimodal treatment regimens and their somewhat unpredictable effects on tumor growth kinetics.

Overall, this paper presents an intriguing, thought-provoking concept, but it is uncertain how the authors’ findings can best be exploited.

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