A math model may predict time to relapse after prostate cancer surgery

2 September 2016

A mathematical model that uses four consecutive prostate-specific antigen (PSA) test results from a patient who had prostate cancer surgery can predict the time it might take for the disease to relapse, and this can help clinicians optimize patients' follow-up visits and develop a treatment plan best suited for each individual patient, according to a study published in *Cancer Research*, a journal of the American Association for Cancer Research.

"One in four patients who undergo prostate cancer surgery experiences a relapse. Predicting, and possibly preventing a relapse with adjuvant therapies is a major goal; however, overtreatment is a risk as well, because Androgen Deprivation Therapy (ADT) given after surgery, for instance, may promote the occurrence of new hormone-resistant tumor clones," said Ilaria Stura, a mathematician and a doctoral candidate in the Complex Systems for Life Sciences program at University of Turin, Italy. "Algorithms that use easily obtainable biological data to accurately predict prognosis can help clinicians and patients make more informed choices."

Stura explained that the mathematical model her team developed can potentially improve patient quality of life, because it can give valuable information to the urologist, for example, by reporting that the growth velocity of a patient's tumor is increasing and that a relapse is expected within a certain number of months. With this information, the clinician could choose the best therapy for the patient (e.g., hormone therapy or radiotherapy) in order to stop the spread of the disease or, conversely, delay therapy if relapse is not indicated, she noted.

"Obviously, clinicians already try to do this based on their experience, but our method provides further confidence in their 'investigational' work, since the algorithm is validated based on data coming from a database much larger than his/her personal experience," she said.

Stura and colleagues collected data from 3,538 patients who underwent surgery to remove prostate cancer. Of them, 707 received ADT after surgery, and 728 had a relapse.

Using multiple PSA values from each patient and data on survival outcomes, the researchers used a formula to estimate the parameter alpha (?), for 211 patients who did not receive ADT and 40 patients who did. Stura explained that ? is defined as the ratio between the energy required by the cancer cell to survive and the energy it needs to replicate in order to create a new cell. The higher the rate of replication of a cancer cell, the greater its production of PSA; therefore, ? represents the aggressiveness of the tumor cells, she said.

The mathematicians found that four consecutive PSA values collected after surgery, ?4, were enough to consistently predict the time to relapse. The higher the value of ?4 was, the greater the probability of relapse.

For example, for a patient who underwent prostate surgery and had not received any adjuvant ADT, an ?4 value below 0.01 means there is an 82 percent probability that his cancer will not relapse within three years, and a 54 percent probability that his cancer will not relapse in four years. Conversely, an ?4 value between 0.02 and 0.04 means there is a 71 percent probability that his cancer will relapse in two years, and a 95 percent probability that his cancer will relapse in four years. An ?4 value greater than 0.04 means that there is an 87 percent probability that his cancer will relapse in a year and 93 percent probability that his cancer will relapse in two years.

The team further developed the algorithm for patients who receive ADT after prostate cancer surgery, in order to account for the fact that the treatment would cause the left-over cancer cells to

die, or not replicate rapidly and produce PSA. The researchers also developed the algorithm to account for the development of resistance to ADT, at which point the cancer cells start to replicate rapidly leading to a high probability of relapse.

"Our work is another small step towards personalized medicine, and shows how mathematics can be important to better understand tumor evolution," Stura said. "We are working to improve the reliability of the model by testing it on data from new patients and making the algorithm available for clinicians and patients for free."

A limitation of the study is that the model was developed using retrospective data and has not yet been tested in patients newly diagnosed and treated with surgery. Also, in building the model, the researchers did not have detailed information about the dose and duration of ADT in patients who received it.

More information: I. Stura et al. A Simple PSA-Based Computational Approach Predicts the Timing of Cancer Relapse in Prostatectomized Patients, *Cancer Research* (2016). DOI: 10.1158/0008-5472.CAN-16-0460

Provided by American Association for Cancer Research