New way of predicting kidney function could improve chemotherapy dosing

July 7 2017

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Scientists at the University of Cambridge have developed a new statistical model which estimates kidney function in patients with cancer. This is the most accurate model for estimating kidney function yet developed and should help cancer specialists treat their patients more safely and improve the accuracy of chemotherapy dosing. The model is now available free online.

Kidneys perform a number of vital functions, including filtering waste and toxins out of the blood, producing vitamin D, and regulating blood pressure. The filtration function of the kidneys is measured by the glomerular filtration rate (GFR), the rate at which blood is passed through the glomeruli, the small blood vessel filters in the kidneys.

Determination of the GFR is important because the assessment of kidney function can indicate how a disease is progressing, whether a drug treatment is having adverse side-effects on key bodily functions, and if it is safe to prescribe a drug at a certain dose, a question of particular importance to cancer doctors when prescribing chemotherapy drugs. However, measuring GFR is technically difficult. Doctors therefore often rely on ways to estimate GFR, which can be relatively inaccurate.

"Almost every patient with cancer gets a measurement of their kidney function, reported as estimated GFR, and this value influences many treatment decisions, but until now, we did not know the best way to provide this value for patients with cancer," says Dr Tobias Janowitz from the Cancer Research UK (CRUK) Cambridge Institute at the University of Cambridge, joint first author. "Given how important this measure is in day-to-day clinical practice, we felt that we should provide an evidence-based model for its calculation in this context."

Now, in a study published today in the *Journal of Clinical Oncology*, the authors describe a new and better way to estimate the GFR, which has

been developed using data from a large dataset of over 2,500 patients. They used accurate measurements of GFR to provide a gold standard and then statistical modelling methods to find the best mathematical model to estimate GFR. The new model also provides a measure of the uncertainty for this estimate.

To test the use of this revised method of estimating GFR, the researchers focused on the precision of chemotherapy dosing, specifically dosing of carboplatin, which is used to treat multiple cancers, such as lung cancer, germ cell tumours, ovarian cancer, and breast cancer. The new model reduced the probability of incorrect dosing for carboplatin substantially compared to the current models used in clinical practice, from more than 20% for the currently published models to 11.7% with the new model.

"Accuracy in chemotherapy dosing is very important," says Edward Williams, joint first author, also from the CRUK Cambridge Institute. "Too much chemotherapy can be toxic and can even be life threatening, but too little chemotherapy may be ineffective against the cancer. Our model should help doctors calculate chemotherapy doses more accurately and thereby reduce the risk of toxicity or treatment failure."

The model has been made available for clinicians to access online free of charge.

"We believe this tool, which is based on stringent methodology, could have a positive impact on the care for a great many patients with cancer," says senior author Professor Helena Earl from the Department of Oncology at Cambridge. "This is why we have made it free and easily accessible."

"The limitation of our work that we are most aware of is that due to the patient demographics in our data set, our model does not provide guidance on the impact of race on the estimated GFR, though it is well

known that race can be a key variable," explains Dr Janowitz. "This will be addressed in future work. We are also keen to explore how well the new model performs for patients with diseases other than cancers.

"The work is a very good example of scientists from different specialties coming together to provide an advance for the care that we offer to patients with cancer."

The study was supported by Cancer Research UK, the Wellcome Trust, and the National Institute of Health Research Cambridge Biomedical Research Centre.

Professor Peter Johnson, Cancer Research UK's chief clinician, said: "Chemotherapy drugs are very powerful, so having the correct dose makes an enormous difference to how effective they are and how we can avoid unnecessary side effects. This way of measuring how well a patient's kidneys are working and how quickly chemotherapy drugs like carboplatin leave the body helps to make our treatments more accurate and better suited to each individual."

More information: Janowitz, J et al. A new model for estimating glomerular filtration rate in patients with cancer. *Journal of Clinical Oncology*; 7 July 2017; DOI: 10.1200/JCO.2017.72.7578

Provided by University of Cambridge