Classifying Risk in Patients With Chronic Kidney Disease

TO THE EDITOR: Tonelli and colleagues’ excellent study (1) demonstrates that a classification system for chronic kidney disease (CKD) that includes proteinuria in addition to estimated glomerular filtration rate (eGFR) reduces the misclassification of patients compared with the National Kidney Foundation’s Kidney Disease Outcomes Quality Initiative (KDOQI) classification system. Although the proposed system seems to be more reliable than the KDOQI system, the comparison suffers on 2 counts.

First, Tonelli and colleagues used the Modification of Diet in Renal Disease (MDRD) Study (2) equation to estimate glomerular filtration rate (GFR). This equation tends to underestimate GFR among patients with early stage 3 disease. The KDOQI system recommends use of the MDRD Study equation to estimate GFR but does not require it. Newer equations are available (3) that reduce the number of patients with stage 3 disease who are identified and decrease misclassification.

Second, Tonelli and colleagues’ study does not require the GFR to remain within a particular range for 3 months before staging patients, as the KDOQI system does (4). Requiring the calculation of at least 2 eGFRs more than 3 months apart reduces the number of patients with CKD and only modestly reduces the number of patients who ultimately progress to end-stage renal disease (5).

It is unclear from Tonelli and colleagues’ study whether adding proteinuria to a single eGFR by using the MDRD Study equation would improve the ability to predict whether a patient will develop end-stage renal disease compared with the KDOQI system, which includes both the best available equation and a decreased eGFR of 3 months’ duration. The addition of proteinuria to any system may add significant predictive value. Determining how a system similar to that described by Tonelli and colleagues that includes proteinuria in addition to estimated glomerular filtration rate (eGFR), and longer period of renal disease would improve prediction of end-stage renal disease.

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Potential Conflicts of Interest: None disclosed.

References

Racial and Ethnic Differences in Blood Pressure

TO THE EDITOR: I found Houston and colleagues’ article (1) to be quite interesting. I feel certain that the use of storytellers from the patient population was critical to the success of their intervention. What the article lacked, and what I think that the success of the intervention can be attributed to, was the role of positive deviance. The concept of positive deviance has been defined as follows:

[In every community there are certain individuals or groups [the positive deviants] whose uncommon behaviors and strategies enable them to find better solutions to problems than their peers, while having access to the same resources and facing similar or worse challenges (2).]

In other words, we don’t need to discover new approaches to help patients deal with their chronic diseases. Somewhere out there are other patients with the same diseases and life conditions who have somehow already figured things out for themselves and are...
Addressing Missing Data in Clinical Trials

TO THE EDITOR: We read with interest Fleming’s excellent article (1), which calls attention to the problem of missing data in clinical research. In the past, patient withdrawal from clinical trials has not received the attention that it deserves as a potential source of bias.

In many trials, insufficient attempts have been made to retain patient participation in clinical trials after study treatment has been discontinued, compromising the integrity of an unbiased intention-to-treat efficacy analysis. As Fleming notes, there is a need to distinguish between nonadherence, when patients have discontinued the study treatment, and nonretention, when patients decline to participate further in the observation schedule. The latter scenario should be decreased as much as possible to allow an unbiased intention-to-treat analysis under minimal assumptions.

However, the phenomenon of missing data will remain an issue even if Fleming’s advice is strictly implemented. Clinical situations always will occur in which patients change their minds about adherence to study procedures. For example, patients with cancer may become discouraged if their disease seems to progress and may no longer wish to endure the extra time and effort needed to remain a study participant. Other traditional clinical indications for high withdrawal rates from studies include psychiatric disease and obesity.

Methods are being developed that improve statisticians’ ability to account for biases introduced by missing data that avoid the simplifications assumed by traditional regression methods. Techniques using causal inference and semiparametric targeted estimation have been shown to provide unbiased and efficient estimators of the desired treatment effect under much less stringent assumptions than those on which current methods rely (2–6). Finally, investigators may actively encourage study participants to complete the trial in which they are enrolled; however, this encouragement may raise ethical issues in that the study investigators may be perceived as being coercive.

The problem of missing data is likely to remain an issue in clinical investigation that should be addressed with all of the tools available to the clinical research community.

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Potential Conflicts of Interest: None disclosed.

References

Medical Management of the Acute Radiation Syndrome

TO THE EDITOR: The nuclear accident at the Fukushima power station in Japan, which reminded us of the nightmare of Hiroshima and Nagasaki, raised serious international concerns about radiation exposure. Stable iodine (for example, potassium iodide) is indicated only as a thyroid-blocking agent to prevent the uptake of radioactive iodine; however, persons living within 1000 miles of Fukushima frantically tried to obtain potassium iodide (1) because they believed that it was a general radioprotective agent and a “magic bullet” in the event of a nuclear accident.

Current recommendations from guidelines on potassium iodide therapy derive almost exclusively from observational studies on the incidence of thyroid cancer in children after the accident at Chernobyl (2, 3). These data are the best evidence currently available, and the recommendations state that the risk for thyroid cancer in adults exposed to radioactive iodine is minimal. This conclusion seems appropriate, because many adult patients with hyperthyroidism have...
received radioactive iodine therapy to treat their condition. Persons older than 20 years who are exposed to radioactive iodine are at little risk for thyroid cancer, whereas persons older than 40 years are at virtually no risk (4).

Moreover, the use of potassium iodide for prophylaxis of thyroid cancer is a legitimate concern for children and pregnant and lactating women but not for other adults. After the Chernobyl disaster, 7 million adults in Poland took potassium iodide against the recommendations of the government (5). Because the window for prophylactic administration of potassium iodide is limited, health care officials should ensure that this agent is promptly available to persons who would most benefit from it during nuclear accidents and should avoid its overuse.

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Potential Conflicts of Interest: None disclosed.

References

CORRECTIONS

Correction: Acute Hepatitis A Virus Infection Without IgM Antibodies

The authors of a recent letter (1) should be listed in the following order:

Catherine Chakvetadze, MD; Laure Gaussec, MD; Vincent Mallet, MD, PhD; Laurent Hannoun, MD; and Stanislas Pol, MD, PhD.

This has been corrected in the online version.

Reference

Correction: Age at Cancer Diagnosis Among Persons With AIDS

In a recent letter (1) on age at cancer diagnosis among persons with AIDS, the labels in the figure contained 2 errors. The solid line is the “Observed [cases] in the AIDS population using hypothesis 2” (not hypothesis B), and the dotted line is the “Observed [cases] in the AIDS population using hypothesis 1” (not hypothesis A). This has been corrected in the online version.

Reference

Correction: Clinical Trials: Discerning Hype From Substance

An error appears in the 21 September 2010 article “Clinical Trials: Discerning Hype From Substance” (1). For the GIPF-001 trial, the data cutoff date for the primary analysis of the “progression-free survival” for the primary end point was 26 June 2002, not 15 June 2002 as stated in the article. This has been corrected in the online version.

Reference