CORRESPONDENCE

Renal Failure—Measuring the Glomerular Filtration Rate

by Dr. med. Christian Thomas, Prof. Dr. med. Lothar Thomas
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Nephrotoxic Chemotherapy

Thomas et al. report on the value of early detecting impaired renal function. This excellent article clarifies how often chronic renal failure is underestimated and that early diagnosis of renal function by measuring serum creatinine alone is low in sensitivity, but is none the less important to recognize in an early, easily treatable stage. The authors refer to the most important causes of renal function impairment, such as hypertension and diabetes. We wish to emphasize the value of recognizing renal impairment also in tumor patients, in whom it is necessary to diagnose this condition as early as possible due to our administration of nephrotoxic chemotherapy agents. Owing to our increasing life expectancy, tumor patients constitute an important and increasing larger growing patient cohort.

We examined renal function in 167 hematology and oncology patients by measuring serum creatinine, Cystatin-C, and estimated glomerular filtration rate (eGFR according to the Cockcroft-Gault [CG] equation and the MDRD [modification of diet in renal disease] equation). We found mild renal failure (eGFR $<90\text{ mL/min/1.73m}^2$) in 52% and chronic kidney disease (CKD) stages 3–5 in 22% of patients. The MDRD equation had higher accuracy than the CG equation, which confirms that the MDRD formula has advantages also in cancer patients with often impaired renal function. Measuring Cystatin-C did not add much to our sensitive assessment of renal function measurement provided by the eGFR. In patients with impaired renal function, additional comorbidities and cardiovascular risks were identified (1). These results were verified in 198 patients with multiple myeloma in whom mild, moderate (eGFR $<60\text{ mL/min/1.73m}^2$), and severe renal failure (CKD stages 4 and 5) was present in 58%, 29%, and 12%, respectively. A deterioration in renal function was also clearly associated with impaired progression free survival and overall survival (OS). Multivariate analysis confirmed the eGFR as an important risk factor, this allowing to create a new risk stratification model with broad availability and cost efficacy: combination of eGFR – as the most essential multivariate risk factor – and β_2 -microglobulin (β_2 -MG) permitted to define three groups: with 0, 1 or 2 risk factors, median OS was largely different with 71, 48 and 24 months, respectively. This suggests that this new MM-score may be useful to improve risk prediction in MM which was tested in another data set of 127 and

subsequently 466 consecutively treated myeloma patients, again confirming the relevance of assessing the eGFR and eGFR- β_2 -MG score (3).

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Only Sparse Data Are Available for Elderly Patients

In our opinion, the article contains a few imprecisions. The authors describe methods of determining the measured and estimated glomerular filtration rates (mGFR and eGFR). With regard to the measurement approach we miss a more detailed explanation of the different approaches, or, at least, a citation of a recent review (1). With regard to the eGFR, the authors did not mention the so called CKD-Epi equation, which was published in May 2009 (2). This formula is more precise than the MDRD equation, and many laboratories are now providing this test.

Further, we do not agree with the reference ranges for the GFR listed in table 2. Especially in estimating renal function in patients older than 60 years, the data are scarce, and not a single eGFR formula has been validated. The Cockcroft-Gault equation as well as the MDRD equation underestimate renal function in this age group; when the CKD-Epi formula was developed the number of older people was too low to reach a definite conclusion. Giving an “age specific” GFR in elderly people is therefore difficult if not downright impossible. In view of current demographic trends, this is an important topic. Renal function in patients of an advanced age is being investigated in the context of the

Berlin initiative study, a population based age exploration of renal failure in patients aged 70 or older.
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In Reply:

We agree with Engelhardt and Kleber. Using the MDRD equation has proved useful in routine diagnostic evaluation. Measuring Cystatin-C to measure the glomerular filtration rate (GFR) is a method that we use in clinical routine diagnostic evaluation in tumor patients who receive cisplatin in order to assess the development of renal function, since in our experience, the Cystatin-C based eGFR detects impaired GFR in such patients at an earlier stage. We should not forget that for the individuals and groups of patients in our *Table 3*, only the mGFR is reliable if impaired renal function is suspected.

We read Schäffner and Schindler's comments with interest and wish to comment as follows.

- The suggested recent review was published in November 2009. We were therefore not able to include it as our article was about to be published. We cited a current overview from 2009, which explains the differences between the mGFR and eGFR, in our reference 13.
- We did not include the CKD-Epi equation because—in contrast to the MDRD equation that we listed—only few experiences have been reported in Germany so far as this equation is currently not widely used.
- We are aware of the scarce data on age related reference ranges of the GFR. Unfortunately, it would have exceeded the scope of our article to list all publications from which the GFR reference ranges were taken. We think the reported ranges are valid and would have appreciated reading alternative suggestions in the readers' letter. It deserves praise that Schäffner and Schindler are about to start such a study; however, this is of little use to the readers of *Deutsches Ärzteblatt* at this precise point in time.

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Conflict of interest statement

The authors of all contributions declare that no conflict of interest exists according to the guidelines of the International Committee of Medical Journal Editors.