Evaluation of renal function in elderly cancer patients

This issue of Annals of Oncology sees the publication of an Australian–British retrospective study on the evaluation of renal function in elderly cancer patients [1]. Unexpected toxicity as a result of cancer chemotherapy is a frequent occurrence in elderly cancer patients, but as more data is acquired on the association of reduced physical activity, depression and mental deterioration with toxicity, the more we come to understand that in those cases with age-associated conditions, the chance of observing grade 3–4 toxicities is increased [2, 3]. In addition, by paying more attention to the possibility of renal function deficit, among other underlying comorbidities, in patients where it has not yet been detected clinically, it may be possible to gain a better understanding of the reasons for other unpredictable toxicities in some older cancer patients with borderline kidney function tests. Therefore, an article dedicated to the identification of the best method for studying renal function in elderly patients with cancer is important, especially if it helps us to refine our abilities to best detect even small variations in kidney function.

As people age, the renal mass shrinks; in addition, an associated reduction in glomerular number, number of nephrons and cortical volume is also observed [4]. Renal blood flow is also reduced, probably due to glomerular sclerosis, and consequently a progressive decline in the glomerular filtration rate (GFR) occurs with advancing age [5, 6]. This reduction in GFR may lead to enhanced toxicity of drugs, such as methotrexate, bleomycin, carboplatin, cyclophosphamide, ifosfamide and fludarabine, excreted by the kidneys [7]. As a consequence, in patients >70 years of age, the dosage of these agents should be adjusted relative to the measured creatinine clearance levels in order to avoid excessive toxicity.

The Calvert formula is currently used to calculate the reduction in dosage of carboplatin in relation to renal function [8]. While guidelines on dose adjustment for other renally excreted drugs, based on levels of creatinine clearance, are not provided by the majority of oncology textbooks, the most valuable reference can be found in the first manual of geriatric oncology [9]. Here indications are given for creatinine levels of ≤60 ml/min (drug reduction ranging from 20% to 35%), ≤45 ml/min (reduction from 25% to 50%) and ≤30 ml/min (information only available for certain drugs). Another method of dose reduction according to creatinine levels is given by the Kintzel–Dorr formula [10], although how many medical oncologists use this, or any other formulae, to adjust dosing during routine clinical practice is questionable. Nevertheless, adjustment of dosage in relation to creatinine clearance levels is believed to be a necessary part of treating patients with renally excreted drugs. Its measurement, with 24 h of urine collection, is cumbersome and unreliable; therefore, a number of formulae have been proposed for the estimation of renal function, but not all have the same degree of precision when compared with the EDTA method of GFR measurement, a method considered to be the gold standard.

All three formulae (Cockroft–Gault, Jelliffe and Wright) retrospectively tested by Marx et al. [1] have a correction factor linked to age. In principle, the correction factor should also be applicable in healthy elderly patients, as well as for patients in whom cancer, or the comorbidities associated with them, have played a negative impact on renal function.

Renal insufficiency as a result of cancer is mainly due to urethral obstruction, complications from multiple myeloma, hyperuricemia, ascites and probably cachexia, while the most frequent comorbidities causing kidney damage in elderly cancer patients are diabetes, hypertension with renal artherosclerosis, undetected nephritis, interstitial nephritis secondary to infection, and exposure to a wide range of drugs (polypharmacy).

In this study, it is not known whether the type of tumor, extension (stage) or course of disease and its complications may induce a lowering of creatinine clearance levels, nor do we have information on which comorbidities influence creatinine clearance; although it is probable that the majority of patients in the study of Marx et al. [1] had normal creatinine clearance levels. Median creatinine clearance was 76 ml/min; only 42 patients (18.6%) had creatinine clearance levels <50 ml/min. Let us then assume that this was a population mainly composed of healthy elderly people. At this point, we cannot really determine whether cancer and/or a possible renal comorbidity were better assessed by one of the three different formulae, but only that a measurement of a creatinine level normal or slightly inferior to normal values in this population could be better evaluated with the Wright formula rather than the Cockroft–Gault or Jelliffe formulae.

Previous reports have already shown that measurements using the Cockroft–Gault and Jelliffe formulae are imprecise in patients with advanced metastatic carcinomas [11–13]. The value of this retrospective report then is to give further support in favor of a better method—the Wright formula—in estimating creatinine clearance ‘in general’ in cancer patients. However, in order to accumulate more information on the evaluation of renal function in elderly cancer patients requires the planning of prospective studies in selected populations of elderly patients with, or at risk of having, renal insufficiency. Future prospective studies should then be addressed specifically to the study of GFR in those tumors in which the natural history of the disease and the drugs used in the treatment of that disease may cause kidney damage, as, for example, in the case of ovarian carcinoma (ascites, urethral compression and use of platinum or carboplatin) and plasmacytoma (renal failure and treatment with cyclophosphamide).
The second group that may benefit from these findings is those elderly cancer patients who have comorbidities, such as diabetes, hypertension and cardiac problems, that may possibly affect kidney function. In these patients, with median creatinine clearance levels that are certainly lower than that observed in the population covered by this study, it is important to reach the conclusion that the Wright formula is more precise than that of the Jelliffe and Cockcroft–Gault formulae. This would then facilitate more accurate dosing of some antineoplastic agents used in this population of elderly, vulnerable patients.

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