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Incidence of Renal Insufficiency in Cancer Patients

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ABSTRACT

The frequency of chronic renal insufficiency among cancer patients is unclear. The aim of this study was to determine the frequency of impaired renal function within a population of cancer patients. One thousand two hundred seventeen patients (563 women, 654 men) with cancer underwent serum creatinine concentration and glomerular filtration rate (GFR) evaluations. The Cockcroft-Gault formula was used to estimate the GFR from the creatinine clearance (Cl_{cr}). Renal insufficiency was defined as a GFR ≤90 mL/min. Among this population, 72 (5.9%) demonstrated an abnormal serum creatinine concentration (>1.2 mg/dL). According to the Cockcroft-Gault formula evaluations, however, 330 (27.1%) of the patients had an estimated GFR <90 mL/min. Among these, the Cl_{cr} was between 60 and 89 mL/min in 241 patients (19.8%); 30 and 59 mL/min in 75 patients (6.2%); and 15 and 29 mL/min in 7 patients (0.6%); 7 patients (6%) had a Cl_{cr} <15 mL/min. As a result, 21.2% of patients demonstrating a normal serum creatinine level had abnormal renal function. Renal function should be evaluated in all cancer patients, regardless of their serum creatinine level, before any drug regimen is administered. The Cockcroft-Gault formula appears to be more accurate than serum creatinine concentration for diagnosing renal insufficiency in patients with cancer, but more prospective studies in this population will be necessary to confirm this finding.

Keywords: cancer; GFR; Cockroft-Gault

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INTRODUCTION

The frequency of chronic renal insufficiency among cancer patients is unclear. Because the mechanisms of renal failure vary significantly in patients with different types of cancer, detection of the disorder is possible only through a careful assessment of the pathophysiologic abnormalities, symptoms, and antineoplastic therapy involved in each case. This task often requires a collective effort from an internist, oncologist, nephrologist, and urologist.[1-3]

Some evidence suggests that early detection of renal involvement and treatment may improve the prognosis. A number of methods for evaluating renal function have been proposed, although they have not been specifically evaluated in patients with cancer. The serum creatinine concentration is an unreliable measure in the evaluation of renal function, owing to the influence of a number of nonrenal factors.[4] The determination of 24-hour urine creatinine clearance (Cl_{cr}) provides a more accurate estimation of the glomerular filtration rate (GFR) than does the serum creatinine concentration alone, but this test is often inconvenient for patients and can be inaccurate in those who don't have cancer. The Cockcroft-Gault formula,[5] which estimates the GFR from serum creatinine concentration, is used to detect the onset of renal insufficiency and has been shown to correlate with the 24-hour urine Cl_{cr} test. True GFR can also be measured by the renal clearance of an exogenous marker that is filtered freely by the kidney rather than being secreted or absorbed.

The clinical importance of reduced renal function associated with drug therapy among patients undergoing treatment for cancer has been widely stressed in the medical literature, yet the assessment of GFR is still not commonly implemented in general practice or hospitals. The aim of this study was to determine the frequency of impaired renal function within a population of patients undergoing treatment of cancer.

PATIENTS AND METHODS

Between 2003 and 2004, cancer patients from various regions in Turkey underwent serum creatinine and Cl_{cr} testing at Yuzuncu Yil University in Van, Turkey, to determine the status of their renal function. Before testing, each patient's sex, age, weight, body mass index (BMI), body surface area, and cancer type and stage were recorded and routine hematologic and biochemical tests were performed.

For each patient, the Cl_{cr} was estimated from the serum creatinine concentration, age, and body weight according to the Cockcroft-Gault formula. In each case, the predicted GFR was categorized in the ranges of <15, 15–29, 30–59, 60–89, and ≥90 mL/min, according to the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines. Renal insufficiency was defined as a GFR ≤90 mL/min. Within each GFR category, patients were stratified by sex and age.

The serum creatinine was measured by routine colorimetric methods on a modular autoanalyzer. A χ^2 test was used to compare categorical data and a one-way analysis of variance was used to determine the influence of cancer type on GFR.

RESULTS

A total of 1217 patients (mean age, 57.3 y; range, 26–80 years were tested. The most common types of cancer were gastrointestinal system cancers (55% of patients), breast cancer (10%) and lung cancer (7%) (Table, Figure).

In 1145 patients (94.1%), the serum creatinine concentration was normal (<1.2mg/dL in women, <1.4mg/dL in men), and in 72 patients (5.9%), the concentration was higher than normal. When renal function was estimated with the Cockcroft-Gault formula, however, 27.1% of the patients had an estimated GFR <90 mL/min. Among these, the Cl_{cr} ranged from 60 to 90 mL/min in 19.8%, from 30 to 60 mL/min in 6.2%, and from 15 to 30 L/min in 0.6%; 0.6% of the patients had a Cl_{cr} <15 mL/min.

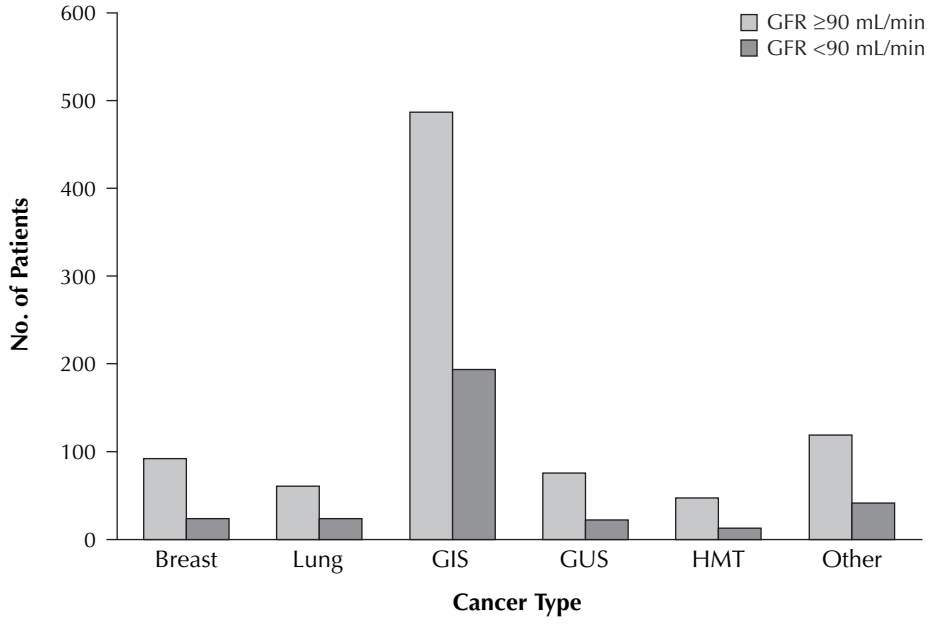
When all GFR results were compared according to age, sex, cancer type, BMI, and body surface area, no significant difference was observed. Similarly, none of these variables had a significant effect on the prevalence of renal insufficiency (*P*=.517).

Main Clinical Characteristics and Laboratory Findings of Patients

		GFR, mL/min				
	Totals	**≥90**	**60–89**	**30–59**	**15–29**	**<15**
No. of patients	1217	887	241	75	7	7
Sex, no.						
Male	654	456	136	53	5	4
Female	563	431	105	22	2	3
Age	52±12	52±14	53±13	53±14	52±20	53±18
Weight, kg	60.0±24	60.4±27	60.8±14.1	59.0±14	64.2±7.5	69.0±4.1
Serum creatinine concentration, mg/dL	0.9±1.3	0.9±0.3	1.7±0.4	2.3±0.5	2.9±0.2	3.5±1.9
Serum albumin concentration, g/dL	3.4±0.6	3.5±0.6	3.4±0.6	3.5±0.5	3.2±0.5	2.8±0.7
Hemoglobin, g/dL	11.9±2.1	11.9±2.1	11.8±2.2	11.2±2.1	11.0±2.3	10.0±2.6
Body mass index	23.1±5.1	3.1±4.1	22.8±5.1	21.9±5.1	21±2.1	21.1±41
Body surface area, m^2	1.6±0.2	1.6±0.2	1.6±0.4	1.4±0.5	1.4±0.2	1.4±0.6

All values expressed as mean±SD except as indicated.

Correlation between cancer type and GFR.



GIS=gastrointestinal system tumor
GUS=genitouronary system tumor
HMT=hematologic cancer

DISCUSSION

When the renal excretion of drugs and their metabolites is impaired in patients undergoing pharmacologic therapy, the dosing regimen must be adjusted to prevent the accumulation of active compounds, which can lead to adverse effects and reactions and other sequelae. Cancer patients, who usually receive multiple drug regimens, are particularly at an increased risk of potentially harmful drug interactions.[6,7]

Renal failure in cancer patients has several pathophysiologic manifestations, including obstructive nephropathy, tubular necrosis, metastatic infiltration, and glomerulonephritis. Treatment-related nephropathies include radiation nephropathy and drug-induced nephrotoxicity. Other manifestations include amyloidosis, disseminated intravascular coagulation, and electrolyte abnormalities such as dysphosphoremia, hypercalcemia, and inappropriate secretion of antidiuretic hormone.[1,7]

In adults, the serum creatinine level is considered an acceptable measure of renal function. Because this level remains fairly stable throughout life, however, even as the renal excretory capacity declines gradually, serum creatinine does not serve as a sufficient guide for physicians who must administer anticancer drugs to patients who have cancer. Instead, it is used to define the dosage limits of some of those regimens.[8]

Some sophisticated methods used to measure renal function, such as technetium-99m diethyl triamine penta-acetic acid clearance, are not feasible in everyday practice, particularly in cancer patients. Hence, the Cockcroft-Gault formula and other formulae have been developed to estimate the GFR.[5,9] Levey et al found that the 24-hour urine Cl_{cr} test overestimated true GFR by 19% and that the Cl_{cr} predicted by the Cockcroft and Gault formula overestimated the GFR by 16%.[10] Other researchers claim the Wright formula is superior for assessing renal function in cancer patients.[4,11] Some studies suggest that in the Cockcroft-Gault formula, the true GFR is underestimated when the calculated GFR is >60 mL/min, owing to an inappropriately strong effect of age in the formula.[12,13] Pool et al also suggested that both younger and older age biases the results of the Cockcroft-Gault formula when it is applied to cancer patients.[14] Because the mean age in the present study was 57.3 years, however, the Cockcroft-Gault formula was a valid method for evaluating renal function and revealed a dramatically higher frequency of renal insufficiency than the estimation based on serum creatinine levels: 27.1% of patients demonstrated a Cl_{cr} <90 mL/min, whereas only 5.9% had a and abnormally high serum creatinine level. As a result, 21.2% of patients demonstrating a normal serum creatinine level had abnormal renal function.

The GFR results in this study were slightly higher than those observed in a previous study of cancer patients.[6,15,16] The GFR data also did not reveal any correlation between cancer type and GFR, nor was the GFR (or the risk of renal insufficiency) affected any differently by metastatic or nonmetastatic cancer. In this study, the calculation of GFR was not adjusted for each patient's body surface area, which does not have a significant effect on the Cockcroft-Gault formula calculation.[13] This approach is also recommended by the K/DOQI guidelines.[9]

CONCLUSION

Renal function should be evaluated in all cancer patients, regardless of their serum creatinine level, before any drug regimen is administered. The Cockcroft-Gault formula can give a reliable estimate of Cl_{cr} when it is applied to middle-aged cancer patients, but more prospective studies are necessary to confirm the value of the test in this population.

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