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# Factors affecting change in renal function after contrast-enhanced computed tomography in cancer patients

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## ABSTRACT

**Objectives.** Contrast-enhanced computed tomography (CECT) is the most common form of assessing the effectiveness of cancer patient treatment. However, an injection of an iodine-based contrast agent can cause acute kidney damage (AKI). To determine the frequency and factors affecting post-contrast kidney function deterioration during oncological treatment.

**Material and methods.** Kidney function in cancer patients with solid tumors undergoing a total of 206 CECTs was retrospectively analyzed.

**Results.** Two hundred and six CECT procedures in 79 patients (age 68.4 ± 10.6 years) were included in the study. The median eGFR before CECT according to the MDRD was 81 mL/min/1.73m$^2$ (IQR 26). The median time between CECT and kidney function examination was 8 (IQR 8) days. In the whole group, the median eGFR change defined as the difference between eGFR after and before CECT was 0.0 (9.0) mL/min/1.73m$^2$ and was not significant. eGFR decreased in 100/206 (48.5%) CECT procedures with the median difference = –5.0 (6.0) mL/min/1.73m$^2$. However, clinically significant deterioration of renal function (an increase in SCr of > 0.3 mg/dL) was found only in two cases (0.9%). The change in eGFR associated with CECT correlated significantly ($p < 0.05$) with initial creatinine ($r = 0.117$) and urea ($r = 0.158$), but not with age and comorbidities. After dividing the analyzed population according to the median GFR, it turned out that in the group of patients with eGFR < 81 mL/min/1.73m$^2$, the median difference in GFR level was 1 (IQR 10), and in the group with a higher eGFR level the median was –1 (IQR 8.5), which was statistically significant ($p = 0.03$). The multivariate logistic regression analysis in subsequent reduced models confirmed that SCr, uric acid level, and the use of antimetabolites were the factors independently reducing the risk of deterioration of renal function after CECT.

**Conclusions.** CECT can be responsible for kidney function deterioration; however, it has no impact on oncological treatment.

**Key words:** contrast-enhanced computed tomography, CECT, post-contrast kidney function, cancer, oncological treatment

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## Introduction

Cancer treatment in advanced stages of the disease can prolong survival; however, it is connected with toxic side effects. The basic form of monitoring response to anticancer treatments is contrast-enhanced computed tomography (CECT); however, administration of iodinated contrast media (CM) can be complicated by a decrease in renal function. The kidney function deterioration is usually mild, and renal function usually

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returns to baseline values within 3 weeks; unfortunately, post-contrast acute kidney injury (PC-AKI) is responsible for increased short- and long-term morbidity and mortality [1]. It is estimated that up to 2% of all CECT examinations are connected with acute kidney injury (AKI), and administration of iodinated CM can be responsible for almost 11% of all cases of AKI [2]. However, recent meta-analyses showed PC-AKI incidences of 5–6.4%, and in 1 % of all patients, kidney function deterioration persisted for 2 months [3, 4]. AKI and chronic kidney disease are common in cancer patients [5–9].

This study aimed to assess real risk of kidney function deterioration in cancer patients treated at the Oncology Department after iodinated CECT measuring the serum creatinine (SCr) and the estimated glomerular filtration rate (eGFR). The data collected in this study allowed for evaluation if CECT gives clinically significant renal function deterioration and contributes to interruptions in oncology treatment.

## Materials and methods

### Study design

This was a single-center retrospective analysis of all consecutive patients who were treated at the Oncology Department at the Medical University of Warsaw from October 2020 to January 2021. If the patient started the treatment before October 2020, the data about earlier CECT scans were also included. Data were collected on designed proformas by the study team.

### Study population

We included adult patients (≥ 18 years) with active solid tumors who underwent CECT. All patients have SCr and eGFR measured according to modification of diet in renal disease (MDRD) before the CT scan and in subsequent follow-up. CECT were performed between chemotherapy (CHTH) courses, usually a few days after a CHTH administration. Patient demographics, underlying cancer diagnoses, medical conditions, concurrent nephrotoxic medication, and laboratory variables were obtained. Available follow-up creatinine results were collected for the next chemotherapeutic course after CECT. The primary endpoint of this study was the frequency of post-contrast kidney function deterioration during oncological treatment defined by an absolute increase of SCr to at least 0.3 mg/dL or at least a 1.5-fold increase over baseline SCr.

Statistical analysis of the results was performed using the Statistica software (StatSoft Inc.), version 12.

## Results

A total of 206 CECT examinations in 78 oncology patients with a solid tumor were retrospectively identified by a database search (Tab. 1). Medications that were received by the patients are presented in Table 2.

**Table 1. General characteristics of patients in the study (n = 78)**

| Variable | Value | Percentage (%) |
|---|---|---|
| **Age (years)** | | |
| Mean | 67.6 (32–89) | – |
| Median | 68 | – |
| ≥ 70 | 34 | – |
| 70–60 | 28 | – |
| <60 | 16 | |
| **Sex** | | |
| Male | 43 | 55 |
| Female | 35 | 45 |
| **Mean eGFR before IV contrast (mL/min)** | 80.53 | |
| **Comorbidities** | | |
| Yes | 56 | 72 |
| No | 22 | 28 |
| **Diabetes** | | |
| Yes | 26 | 33.3 |
| No | 44 | 56.7 |
| **Hypertension** | | |
| Yes | 51 | 65.4 |
| No | 27 | 34.6 |
| **Heart disease** | | |
| Yes | 16 | 20.5 |
| No | 62 | 79.5 |
| **Hemoglobin ≤ 9.5 g/dL** | | |
| Yes | 11 | 14 |
| No | 67 | 86 |
| **Tumor type** | | |
| Digestive tract cancer | 31 | 40 |
| Pancreatic cancer | 15 | 19 |
| Cholangiocarcinoma | 8 | 10 |
| Liver cancer | 7 | 9 |
| Other | 17 | 22 |
| **Chemotherapy** | | |
| No | 10 | 13 |
| Yes | 68 | 87 |

IC — intravenous contrast; eGFR — estimated glomerular filtration rate

The median eGFR according to the MDRD was 81 mL/min/1.73m$^2$ (IQR 26). The median time between CECT and kidney function examination was 8 (IQR 8) days. An increase (SCr > 0.3mg/dL) was found in two cases (0.9%). There was no statistically significant difference in the SCr and eGFR before and after CECT [0.875 (0.250) *vs.* 8.70 (0.260) mg/dL; p = 0.962 and 80.0 (26.0) *vs.* 81.0 (27.0) mL/min/1.73m$^2$; p = 0.851]. However, after dividing the analyzed population according to the median eGFR, it turned out that in the group of patients with initial eGFR < 81 mL/min/1.73m$^2$, mean GFR rose after CECT [the median eGFR difference =1 (IQR 10) mL/min/1.73m$^2$], but in the group with a higher initial eGFR, the median eGFR decreased after CECT [median difference = –1 (IQR 8.5) mL/min/1.73m$^2$], which was statistically significant (p = 0.03) However, it was not clinically substantial as it had no impact on chemotherapy administration. A statistically significant negative correlation was found between the baseline eGFR value and the eGFR difference before and after CECT (r= –0.143; p < 0.05) and between baseline Scr and urea and the eGFR difference before and after CECT (respectively r = 0.171 and r = 0.158; p < 0.05). No correlation was found between the CECT number or comorbidity and the eGFR difference.

The univariate logistic regression analysis is presented in Table 3. The multivariate logistic regression analysis in subsequent reduced models confirmed that SCr, uric acid level, and the use of antimetabolites were the factors independently reducing the risk of deterioration of renal function after CECT (Tab. 4).

**Table 2. Administered drugs**

| Medication | Number | Percentage (%) |
|---|---|---|
| **Chemotherapy** | 69 | |
| Platin compound | 13 | 32 |
| Antimetabolite* | 38 | 55 |
| TKI | 6 | 8 |
| Monoclonal antibodies | 9 | 13 |
| Others chemotherapeutic agents | 23 | 33 |
| **Nephrotoxic drugs** | 36 | |
| Zoledronic acid | 6 | 17 |
| NSAID | 6 | 17 |
| Diuretics | 8 | 22 |
| ACI/ARB | 28 | 77 |

*Antimetabolite = gemcitabine, capecitabine, 5-fluorouracil; TKI — tyrosine-kinase inhibitors; NSAID — non-steroidal anti-inflammatory drug; ACI/ARB — angiotensin-converting-enzyme inhibitors/angiotensin receptor blockers

## Discussion

Cancer patients are in the high-risk group for kidney injury, and its consequences and the frequency of AKI was highest in patients with renal cell cancer, liver cancer, pancreatic cancer, and hematological malignancies [5, 6]. Clinicians are afraid of kidney injury connected with iodinated CM, make an effort to avoid additional risk factors, and try to assess the effectiveness of CT treatment without contrast administration or by

**Table 3. Univariate analyses of variables for possible association with estimated glomerular filtration rate deterioration**

| Variable | OR | 95% CI | p |
|---|---|---|---|
| SCr before CECT | 0.163 | 0.038–0.693 | 0.0140 |
| Uric acid before CECT | 0.590 | 0.361–0.963 | 0.0349 |
| CHTH | 0.367 | 0.169–0.796 | 0.0111 |
| Platin compound | 0.453 | 0.223–0.923 | 0.0293 |
| Antimetabolite* | 0.450 | 0.254–0.796 | 0.0061 |
| TKI | 1.571 | 0.574–4.302 | 0.3791 |
| Monoclonal antibodies | 0.490 | 0.235–1.022 | 0.0572 |
| Bisphosphonates | 2.490 | 0.908–6.832 | 0.0764 |
| ACE-I | 1.091 | 0.610–1.950 | 0.7691 |
| Diuretics | 0.751 | 0,289–1.951 | 0.5566 |
| NSAID | 1.571 | 0.574–4.302 | 0.3791 |
| Three concomitant nephrotoxic drugs | 1.061 | 0.065–17.189 | 0.9670 |
| Hemoglobin level | 0.941 | 0.809–1.094 | 0.4301 |

*Antimetabolite = gemcitabine, capecitabine, 5-fluorouracil; SCr — serum creatinine; CECT — contrast-enhancement computed tomography; CHTH — chemotherapy; OR — odds ratio; CI — confidence interval; TKI — tyrosine-kinase inhibitors ; ACE-I — angiotensin-converting-enzyme inhibitors; NSAID — non-steroidal anti-inflammatory drug

**Table 4. Subsequent reduced multivariate logistic regression models, with factors independently reducing the risk of worsening renal function after contrast-enhancement computed tomography**

| Variables | Model 1 | Model 2 | Model 3 |
|---|---|---|---|
| | CHTH | CHTH | CHTH |
| | Platin compound | Platin compound | Platin compound |
| | Antimetabolite* | Antimetabolite* | Antimetabolite* |
| | Uric acid before CECT | Uric acid before CECT | |
| | SCr before CECT | | |
| Results | **SCr before CECT** | **Uric acid before CECT** | **Antimetabolite*** |
| OR ± 95% CI | 0.0003 (0.0000–0.0933) | 0.590 (0.361–0.963) | 0.45 (0.254–0.796) |
| Significance — p | 0.005 | 0.035 | p = 0.006 |

*Antimetabolite = gemcitabine, capecitabine, 5-fluorouracil; SCr — serum creatinine; CHTH — chemotherapy; CECT — contrast-enhancement computed tomography; OR — odds ratio; CI — confidence interval

ultrasonography. This strategy does not allow for an accurate assessment of the effectiveness of the treatment and thus unnecessarily exposes the patient to suboptimal treatment because, in our study, clinically relevant deterioration in renal function after administration of iodinated contrast in cancer patients was detected in 0.9% of analyzed cases. The frequency in our study is lower than in previous studies [2]. Moreover, the performed analyzes allow us to state that the short interval between the administration of chemotherapy and CECT did not result in the deterioration of kidney function, even though such a relationship has been reported [7, 8]. Similarly, oncological treatment, use of other potentially nephrotoxic drugs, age, and comorbidities were not connected with the risk of renal injury. Moreover, in the examined population, patients during active oncological treatment (mainly patients that received antimetabolites) were in the group with a lower risk of eGFR deterioration after CECT than patients during follow-up or patients before the start of the therapy. It seems that this association is connected with ensuring adequate hydration as part of premedication; however, more research is needed in this area.

In the analyzed population, the median difference in GFR level after CECT was 1 in the group of patients with eGFR < 81mL/min/1.73m$^2$ which means that in this group, CM administration was connected with kidney function improvement. Similarly, patients with higher SCr or higher urea levels have a lower risk of worsening renal function after CECT. This phenomenon occurs in patients with lowered eGFR values in which the ability to remove excessive amounts of water from the body is impaired because of CKD (chronic kidney disease). It could be connected with higher hydratation before examination compared to a cohort of patients with normal eGFR values due to stop diuretics taking 48 h before ICM administration. Proper hydration enables a reduction in the tubular concentration of ICM and its viscosity, a less marked stimulation of the renin-angiotensin-aldosterone system, inhibition of antidiuretic hormone synthesis, and minimization of the reduction of nitric oxide (NO) and prostacyclin synthesis [8]. Each patient before ICM administration had an intravenous fluid infusion or is pretreated by oral water intake. Oral water intake, by suppressing vasopressin release, leads to a rapid increase in diuresis and provides rapid short-term renal protection. Conversely, the renal response to intravenous administration of isotonic saline is delayed — as saline loading suppresses the renin-angiotensin-aldosterone system — but offers long-lasting renal protection [2].

As a result of a higher amount of water in the body than in healthy individuals, in those patients, the osmolality and cytotoxicity properties of ICM decrease. Additionally, the serum creatine concentration decreases, and as a consequence, eGFR value calculated within CKD-EPI equilibrium could be greater than in the case of less hydrated patients.

According to previous reports one of the most significant risk factors for AKI is pre-existing CKD [9], and in our population, eGFR < 60 mL/min/m$^2$ was detected only in 32 cases (15.4%). Patients with kidney, liver, and pancreatic cancers, which are also connected with a high risk of AKI, constituted only 36.7% of our study population. We assessed kidney function within a few days after CECT so it cannot be ruled out that the frequency of deterioration of renal function after CECT could be higher if the control test was performed earlier. It should also not be forgotten that kidney injury can be caused by many reasons, including fluid restriction or taking non-steroidal anti-inflammatory drug (NSAID), so the deterioration in renal function observed in these cases may be related to CM administration only temporarily. However, the low percentage of patients with a significant increase in SCr allows us to conclude that the possible CECT-related kidney injury was not clinically significant, as the renal function spontane-

ously returned to the baseline. Besides, AKI did not affect the oncological treatment, was not a reason for treatment interruption or dose reduction and was not associated with increased toxicity.

Our study has some limitations. It is retrospective in character, and there is no comparison with different contrast agent volumes or concentrations. Besides, due to the retrospective character of the study, not all potential coexisting pathologies could be excluded as direct causes of kidney function deterioration. However, we found a relatively low incidence of PC-AKI during oncological treatment. In addition, there was no statistically significant difference in SCr before and after CECT. Hence, the use of the contrast medium seems to be safe in oncology patients.

## Conclusions

In patients with cancer kidney function deterioration is common and it causes interruptions in therapy and decrease the treatment effectiveness. One of the possible reasons for this is CECT. However, clinically significant kidney injury was detected in 0.9% of analyzed cases which is relatively lower as compared to previous studies done on cancer patients. Moreover, the interval between the administration of chemotherapy and CECT did not influence on kidney function. Besides, the identified disorder had no influence on the oncological treatment - it was not a reason for treatment interruption, dose reduction and was not associated with an increase in toxicity so we can conclude that the use of the contrast medium is safe in oncology patients.

## Conflict of interest

Authors declare no conflict of interest.

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