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A conservative screening approach to kidney disease before contrast-enhanced computed tomography in outpatient population

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Abstract. – OBJECTIVE: To determine the incidence of abnormal renal function in an outpatient population referred for contrast-enhanced computed tomography (CECT) and assess the risk factors that could be used to eliminate superfluous estimated glomerular filtration rate (eGFR) testing.

PATIENTS AND METHODS: The following risk factors were assessed in random patients referred for outpatient CECT: age >60 years, diabetes mellitus, hypertension, anemia, congestive heart failure, and a history of kidney/urological disease or renal surgery. The patients' serum creatinine and eGFR levels, gender, and the type of CECT were recorded.

RESULTS: The study included 500 patients (mean age 50±16 years). Among them, 36 (7.2%) patients had an eGFR <60 ml/min/1.73 m² of which 31 (6.2%) had an eGFR of 59-45 ml/min/1.73 m² and 5 (1%) patients an eGFR <45 ml/min/1.73 m². No patients had an eGFR <30 ml/min/1.73 m². There was a statistically significant association between an abnormal eGFR and age >60 years, diabetes mellitus, hypertension, and chronic kidney disease ($p<0.05$). By selecting only, the patients with one of the identified risk factors for eGFR assessment before CECT, all the patients with an abnormal eGFR (<60 ml/min/1.73 m²) were detected with sensitivity and a negative predictive value of 100%.

CONCLUSIONS: Patients with an abnormal eGFR can be detected with sensitivity and a negative predictive value of 100% using our screening approach before CECT, and superfluous eGFR testing can thus be reduced by approximately 50% with concomitant cost savings. Outpatients without any risk factors should be excluded from routine renal function assessment before CECT.

Key Words:

Post-contrast acute kidney injury, Contrast-enhanced computed tomography, Contrast medium, Risk factors, Acute kidney injury.

Introduction

Post-contrast acute kidney injury (PC-AKI) or contrast-induced nephropathy (CIN) is a significant complication of intravenous (IV) contrast medium. The potential impact of CIN ranges from a slight increase in serum creatinine to severe acute renal failure with anuria[1,2]. The clinical impact of CIN is a major patient safety challenge in health care and a significant economic burden. Screening for CIN using renal function assessments before contrast-enhanced computed tomography (CECT) is highly recommended for all patients undergoing routine computed tomography (CT) imaging[3,4]. However, the practice of performing a renal function test before CT for outpatients attending radiology departments without a recent blood test can be challenging. This problem has been reported to occur in 5.3% of patients[5], and patients without recent blood tests are sent for a blood test. This causes increased patient waiting times, wasted scanner capacity, and longer waiting times in radiology departments.

A recent survey demonstrated that renal function testing is only required for patients at high risk for CIN. The practice has a significant impact on staff workloads, waiting times for scanners, and the streamlining of CT services[6]. In the absence of evidence, the question remains: should blood tests be performed on everyone or only on patients at high risk of CIN? The true risk of CIN from the intravenous administration of a contrast medium is not and may never be precisely known. Recently published evidence suggests that the risk of CIN in outpatients is much smaller than previously thought[7]. In an analysis of six prospective studies[8], which included more than 1000 patients who underwent CECT, the overall

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prevalence of PC-AKI was 5.1%, and there were no cases of death or dialysis as a result of PC-AKI[8]. Furthermore, a recent meta-analysis of 13 controlled studies found a similar or lower rate of CECT use compared to non-contrast enhanced CT use, suggesting that contrast medium is not the causative agent in the majority of PC-AKI cases[9].

Some evidence[10,11] suggests that the risk of CIN is greatest in patients with acute renal failure or established chronic renal disease (CKD). Although the pathogenesis of PC-AKI is not entirely clear, it is directly related to a number of preexisting conditions, including diabetes, advanced age, hypertension, dehydration, heart failure, and anemia, and the concomitant use of nephrotoxic drugs[12]. The estimated glomerular filtration rate (eGFR) is the standard test to measure renal function in a stable outpatient population. Davenport et al[13] showed that the use of eGFR thresholds (instead of serum creatinine-based thresholds) can more appropriately identify patients who may be at risk of CIN. Currently, there is no definitive eGFR threshold below which the risk of CIN increases, and there are wide variations in the risk thresholds, prophylactic strategies, and absolute contraindication levels being applied at a clinical level. Data on the true incidence and the screening approach or models of outpatients with an abnormal renal function referred for CECT are lacking and conflicting in the current literature[14-16]. Therefore, the main objective of this study was to document the incidence of abnormal eGFR (<60 ml/min/1.73 m^2 and <45 ml/min/1.73 m^2) and to determine which combination of risk factors mentioned in CIN prevention guidelines most accurately detect decreased eGFR in patients referred for CECT in outpatient settings. Based on our study findings and the evidence in the literature, we then developed a simplified screening method to accurately detect patients with an abnormal renal function who may benefit from renal assessments to eliminate superfluous eGFR testing before CECT and thus potentially reduce costs and decrease the waiting times in radiology departments.

Patients and Methods

We enrolled 500 random patients (232 females, 268 males) in this retrospective study in our tertiary care hospital between October and November 2020. All the patients were outpatients who were scheduled for CECT and had undergone serum creatinine and eGFR testing less than 30 days prior to CECT. Patients younger than 18 years, emergency room patients, in-patients, patients in intensive care, and patients with missing data were excluded from the study. The types of CECT included head and neck, vascular, cardiac and chest, and abdomen and pelvis CT. The standard departmental CT protocol was utilized. This included iodinated non-ionic contrast media such as iohexol (Omnipaque) and iodixanol (Visipaque) (GE Health Care Inc., Boston, MA, USA) with an osmolality of 300-350 mOsm/kg/H_2O. The dose is usually weight-dependent and ranges from 100 to 150 cc. The flow rate of the contrast is 2-5 ml/s, and the needle size is 18-22 gauge depending on the phase of the study (i.e., arterial *vs.* porto-venous).

We screened for the presence of the risk factors associated with abnormal kidney function (i.e., an abnormal eGFR) that had been considered in the recent literature and most CIN prevention guidelines[13,17]. This was done by reviewing the patients' electronic medical records. Patients with incomplete data were excluded from the study. The risk factors included the presence of diabetes mellitus, hypertension, anemia, congestive heart failure, peripheral vascular disease, a history of kidney or urological disease, prior kidney surgery, or a single kidney. We considered these risk factors regardless of whether the patients were currently receiving therapy or not. We also did not classify these risk factors according to severity or duration. Certain medications with potential nephrotoxicities, such as metformin-containing drug combinations, non-steroidal anti-inflammatory drugs, and chemotherapy, were reported.

The patients' kidney function was obtained from their electronic records (serum creatinine and eGFR) before CECT. eGFR was determined using the four-inputs modification of diet in renal disease (MDRD-4) formula, which takes into account serum creatinine levels, age, race, and sex, although the MDRD equation derives from a study where only patients under 70 years of age were included; therefore, the eGFR results should be interpreted cautiously for patients older than 70 years. We also recorded the time between the eGFR measurement and CECT. Notably, eGFR was not measured after CECT to determine CIN. The requirement for informed consent was waived by the hospital ethics committee as the study was retrospective, did not interfere with the patients' management, and did not compromise the patients' expectations of confidentiality. The study was approved by our internal Review Board.

Statistical Analysis

The descriptive statistics detailing the patients' age characteristics were analyzed using frequencies and relative frequencies (percentage) for the categorical variables and means and standard variations for the numeric variables. The difference between the patients' characteristics in the two eGFR groups was compared. A chi-squared test or Fisher's exact test was used for the categorical variables and an independent *t*-test for the numeric variables. The proposed screening method was assessed using sensitivity, specificity, and positive and negative predictive values. SPSS software version 26 (IBM, Armonk, NY, USA) was used for the statistical analyses, and a *p*-value less than 0.05 was considered significant.

Results

Patients Characteristics

We included 500 patients in our study, of which 268 (53.6%) were male and 232 (46.4%) were female. The mean age of the cohort was 50±16 years. Among the patients, 345 (69%) were <60 years of age, and 155 (31%) were aged >60 years. The mean body mass index was 28.5±6.7 kg/m^2. The types of CECT included head and neck, cardiac and chest, vascular, and abdomen and pelvis (Table I).

Risk Factors

Diabetes was present in 131 (26%) patients, 141 (28%) had hypertension,15 (3%) had congestive heart failure, 73 (14.6%) had anemia,13 (2.6%) had peripheral vascular disease, and 37 (7.4%) had chronic liver disease. Table I lists the nephrotoxic medications in use and the type of CECT.

Incidence of Normal and Abnormal eGFR

The total number of patients with a normal eGFR (≥60 ml/min/1.73 m^2) was 464 (92.8%), and the number with an eGFR <60 ml/min/1.73 m^2 was 36 (7.2%). The number of patients with an eGFR of 59-45 ml/min/1.73 m^2 was 31 (6.2%). The mean eGFR was 54±4 ml/min/1.73 m^2. Only 5 patients had an eGFR <45 ml/min/1.73 m^2 (mean eGFR 42.6±1.5 ml/min/1.73 m^2).

Table I. Patient characteristics (N = 500).

		Frequency	Percent
Gender	Male	268	53.6
	Female	232	46.4
Age, years mean ±SD		50.32 ± 16.42	
Age ≤ 60		345	69
Age >60		155	31
Body mass Index (BMI), mean ±SD		28.56 ± 6.76	
Creatinine, mean ±SD		72.07 ± 20.63	
eGFR	< 45	5	1.0
	45-59	31	6.2
	60 and above	464	92.8
Risk Factors			
DM		131	26.2
HTN		141	28.2
CKD		18	3.6
CHF		15	3.0
Anaemia		73	14.6
Liver disease		37	7.4
PVD		13	2.6
Medications			
NSAIDs		124	24.8
Chemotherapy		120	24.0
Metformin		49	9.8
Type of CECT	Head and neck CT	122	24.4
	Vascular CT	125	25.0
	CT chest and cardiac	125	25.0
	CT abdomen and pelvis	128	25.6

Abbreviations: eGFR; estimated glomerular filtration rate, CECT=contrast enhanced computed tomography, DM; diabetes mellitus, CKD; chronic kidney disease, CHF; congestive heart failure, PVD; peripheral vascular disease, NSAID; non-steroidal anti-inflammatory drugs.

Association Between Risk Factors and eGFR <60 ml/min/1.73 m²

The total number of patients with an eGFR <60 ml/min/1.73 m^2 was 36 (7.2%). This included the patients with a GFR of 59-45 ml/min/1.73 m^2 and those with an eGFR of <45 ml/min/1.73 m^2. There were statistically significant associations between the normal eGFR and abnormal eGFR groups for multiple risk factors, namely, age >60 years (p<0.0010), diabetes (p<0.001), hypertension (p<0.001), CKD (p<0.001), and chronic liver disease (p<0.012). Otherwise, there were no statistically significant associations between the two groups (Table II).

Table II. Patient characteristics compared between eGFR groups.

		eGFR condition		
		Normal eGFR ≥ 60 (N = 464)	Low eGFR < 60 (N = 36)	*p*-value*
Gender				
Male	N	245	23	0.199
	%	52.8%	63.9%	
Female	N	219	13	
	%	47.2%	36.1%	
Age				
Age ≤ 60	N	330	15	0.001
	%	71.1%	41.7%	
Age >60	N	134	21	
	%	28.9%	58.3%	
BMI, mean±SD	28.5±6.9	29.2±5.4	0.542	
Risk Factors				
DM	N	110	21	<0.001
	%	23.7%	58.3%	
HTN	N	121	20	<0.001
	%	26.1%	55.6%	
	%	0.4%	0.0%	
CKD	N	12	6	0.001
	%	2.6%	16.7%	
CHF	N	14	1	>0.999
	%	3.0%	2.8%	
	%	8.8%	25.0%	
Anaemia	N	65	8	0.179
	%	14.0%	22.2%	
Liver disease	N	30	7	0.012
	%	6.5%	19.4%	
PVD	N	11	2	0.240
	%	2.4%	5.6%	
Nephrotoxic Medications				
NSAIDs	N	118	6	0.238
	%	25.5%	16.7%	
Chemotherapy	N	112	8	0.5795
	%	24.1%	22.2%	
Metformin	N	46	3	0.792
	%	9.9%	8.3%	
Type of CECT				
Head and neck CT	N	117	5	0.064
	%	25.2%	13.9%	
Vascular CT	N	120	5	
	%	25.9%	13.9%	
CT chest and cardiac	N	112	13	
	%	24.1%	36.1%	
CT abdomen and pelvis	N	115	13	
	%	24.8%	36.1%	

Abbreviations: eGFR; estimated glomerular filtration rate, CECT=contrast enhanced computed tomography, DM; diabetes mellitus, CKD; chronic kidney disease, CHF; congestive heart failure, PVD; peripheral vascular disease, NSAID; non-steroidal anti-inflammatory drugs.

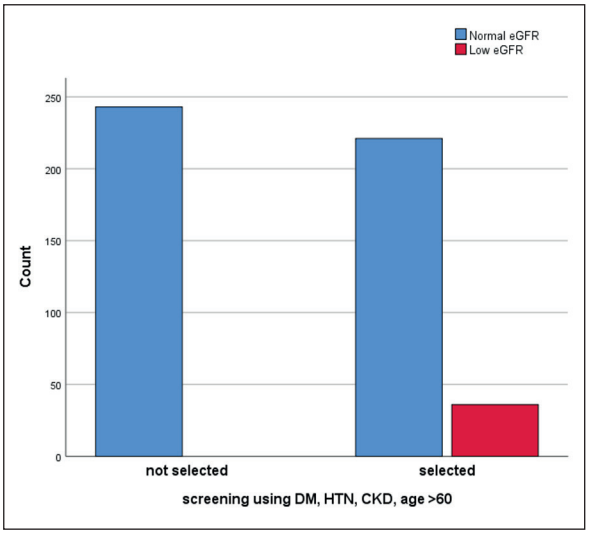

Figure 1. Screening for eGFR condition using DM, HTN, CKD, or age > 60.

Proposed Screening Method for Abnormal Kidney Disease

The proposed screening approach involved screening all the patients with diabetes, hypertension, CKD, or age >60 years. Based on this screening method, 257 patients were selected, which represented 51.4% of the total sample. All the patients with a low eGFR <60 were successfully selected (Figure 1). This indicated that the screening method had a high sensitivity of 100% (95% confidence interval: 90.26%-100.00%) and a negative predictive value of 100%, as presented in Tables III and IV.

Discussion

Our study data showed that the incidence of an abnormal eGFR <60 ml/min/1.73 m^2 in the outpatient population referred for CECT was 7.2% (6.2% <60 ml/min/1.73 m^2 and 1% eGFR <45 ml/min/1.73 m^2), and the mean eGFR of the patients with an eGFR <45 was 42.6±1.5 /min/1.73 m^2. Most importantly, there were no patients with an eGFR less than 30 ml/min/1.73 m^2. These data strongly suggest that routine renal function measurement in outpatient populations referred for CECT is not indicated as a significant risk for CIN from IV iodinated contrast material in all outpatients if we use an eGFR <30 ml/min/1.73 m^2 threshold. The patients with an eGFR of 30-44 ml/min/1.73 m^2 were borderline but not at a statistically significant risk[13]. In fact, one study showed that there is no risk for CIN from IV iodinated contrast media regardless of the baseline eGFR[11].

Table III. Screening for eGFR using DM, HTN, CKD, or age > 60.

			eGFR condition		
			Normal eGFR ≥ 60 (N = 464)	Low eGFR < 60 (N = 36)	Total
Screening using DM, HTN, CKD, or age > 60	Not selected for for eGFR measurement	N	243	0	243
		%	52.4%	0.0%	48.6%
	Selected for	N	221	36	257
		%	47.6%	100.0%	51.4%
Total		N	464	36	500
		%	100.0%	100.0%	100.0%

Abbreviations: eGFR; estimated glomerular filtration rate, DM; diabetes mellitus, CKD; chronic kidney disease.

Table IV. Characteristics of the proposed screening methodology.

Statistic	Value	95% CI
Sensitivity	100.00%	90.26% to 100.00%
Specificity	52.37%	47.72% to 57.00%
Disease prevalence	7.20%	5.09% to 9.83%
Positive predictive value	14.01%	12.90% to 15.20%
Negative predictive value	100.00%	

Our proposed approach was very conservative as we selected only patients with one risk factor, namely, diabetes, CKD, hypertension, or age >60 years. In our study, there was a reduction of 49% in the eGFR measurements (from a possible 500 to 257) when utilizing this very conservative approach. All the patients with an eGFR <60 ml/min/1.73 m^2 were detected with sensitivity and a negative predictive value of 100%. This simplified conservative approach can eliminate the need for pre-contrast renal function assessments in approximately 50% of patients. Schreuder et al[15] showed a 46% reduction in eGFR measurements (from a possible 1001 to 543) using a screening model that included diabetes, CKD, hypertension, and cardiovascular disease (as well as congestive heart failure); however, although this model had excellent sensitivity in detecting eGFR <45 ml/min/1.73 m^2, 11 (1%) patients with an eGFR <60 ml/min/1.73 m^2 were missed. A similar finding was reported by Moos et al[18].

Our data also showed a statistically significant difference in the risk factors in the patients with both normal and abnormal eGFRs. As expected, these factors (i.e., age >60 years, diabetes mellitus, hypertension, CKD, liver disease) were more prevalent in patients with abnormal eGFRs. The most prevalent risk factor in our population was diabetes (26%). The majority of previous studies have reported that diabetes is an independent predictor of CIN[19]. In a large study[20] of patients with normal renal function, diabetes was an independent predictor of CIN (odds ratio, 1.19; 95% confidence interval, 1.38-2.61). The most appropriate characterization of diabetes with respect to CIN is that, in the setting of an eGFR <60 ml/min/1.73 m^2, diabetes amplifies the risk of CIN[21].

There are several risk factors for decreased kidney function described in CIN prevention guidelines, but these may be cumbersome to apply in daily practice. A survey among European radiologists showed that they had highly variable insights into the definition, impacts, and risk factors for CIN[22]. Several risk factors for predicting CIN are not typically present in outpatient populations, such as hypotension (systolic blood pressure <80 mmHg for 1 hour requiring inotropic support), intra-aortic balloon pumps (within 24 hours periprocedurally), and the administration of high-dose contrast media. The overall incidence of PC-AKI in a study of coronary angiography was higher than in studies of patients who received IV iodinated contrast media. The data from cardiac angiography studies are therefore likely to overestimate the risk of CIN in patients undergoing CECT[23]. Although multiple risk factors have been proposed as risk factors for CIN, these factors have not been rigorously observed. For example, we did not find a significant association between an abnormal eGFR and risk factors such as anemia, congestive heart failure, peripheral vascular disease, nephrotoxic medications such as non-steroidal anti-inflammatories, or chemotherapy. Notwithstanding, a positive association between these risk factors and abnormal renal function and CIN has previously been reported[24-27].

Our simplified conservative screening approach for renal function before IV contrast medium administration is highly concordant with previously published expert opinions suggesting that a renal assessment is required before CECT if a patient has one of the following risk factors: age >60 years, history of CKD (e.g., dialysis, kidney transplantation, single kidney, renal cancer, or prior renal surgery), a history of hypertension requiring medical therapy, or diabetes mellitus, or if the patient is on a metformin-containing combination therapy[28,29].

Limitations

As with any retrospective study, our investigation had some limitations. Our study analyses include eGFR and CIN risk factors in a single-center hospital. We did not include all outpatients referred for IV CECT during the study period, and patients with incomplete risk factors were excluded. Therefore, selection bias cannot be excluded, and our findings cannot be generalized without further validation. A large multicenter prospective study is needed to better define the true incidence of abnormal renal function before IV CECT and to better predict the patients with risk factors who may benefit from a renal assessment before CECT, if there are any. We did not perform repeat serum creatinine and eGFR tests in our patients; however, the objective of our paper was not to determine the rate of CIN, which is a diagnosis with inconsistent definitions based purely on laboratory values. Accordingly, this is not to be considered a limitation of the present study. We also did not include in-patients or emergency room patients as these patients may have other indications requiring renal function testing and may have different risk factors.

Conclusions

Based on our study findings of a very low incidence of abnormal eGFR (1% eGFR <60 ml/min/1.73 m^2) and a review of literature, we arrived at the following conclusions and recommendations:

- Routine renal function assessment before IV CECT in outpatients could be reasonably eliminated for all patients since there were no patients with an eGFR <30 ml/min/1.73 m^2 in our study, and there is very little evidence that IV iodinated contrast materials are an independent risk factor for PC-AKI in patients with an eGFR >30 ml/min/1.73 m^2.
- All the outpatients in our study without risk factors for CIN, namely, age >60 years, diabetes, a history of CKD, or hypertension, had a normal renal function.
- Renal function assessment before IV CECT may be justified in high-risk patients, such as patients with any of the identified risk factors. By selecting these patients for eGFR measurements, the number of superfluous eGFR tests can be reduced by approximately 50%, with significant cost savings, reduced waiting times in the radiology department, and reduced scanner use.
- Large multicenter or nationwide prospective studies are needed to better define the true incidence of abnormal eGFRs and accurately detect patients who will benefit from renal assessment before IV CECT in outpatient settings.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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