

Safe time interval for screening estimated glomerular filtration rate prior to gadolinium-enhanced MRI scan

Dear Editor,

Magnetic resonance imaging (MRI) contrast media are commonly used in medical imaging and are usually gadolinium-based contrast agents (GBCAs). They can be divided into 3 groups. Group I consists of compounds with linear molecular structures. Group II consists of compounds with macrocyclic molecular structures. Group III currently includes only gadoxetate disodium, which is a new generation GBCA with a linear molecular structure and partial biliary excretion.¹

Nephrogenic systemic fibrosis (NSF) is associated with the use of GBCAs. NSF is a systemic fibrosing condition involving various organs, particularly the skin. It is potentially fatal, particularly in patients with significant renal impairment.² Screening for impaired renal function in patients prior to performing a contrast-enhanced MRI scan is therefore important to guide and determine suitability for contrast administration. This is usually done using the estimated glomerular filtration rate (eGFR). While eGFR as a surrogate measure for renal function has limitations, its use as a rapid point-of-care test (POCT) is adequate in most clinical settings, including for contrast administration.^{3,4}

There are several established international guidelines on timing of eGFR for patients requiring GBCA administration. In Singapore, the American College of Radiology (ACR) guidelines are used and appear to be the most stringent in terms of the recommended time of eGFR testing.⁵ For example, for outpatients with chronic kidney disease (CKD) stage 3a renal impairment based on the Kidney Disease: Improving Global Outcomes criteria (eGFR 45–59 mL/min/1.73 m²), ACR recommends an eGFR measured within 6 weeks of the MRI study. For outpatients with stage 3b renal impairment (eGFR 30–44 mL/min/1.73 m²), ACR recommends eGFR obtained within 2 days of the MRI study. For patients with eGFR <30 mL/min/1.73 m², contrast is to be avoided.

However, group I GBCAs, associated with the highest risk of NSF, are virtually not used in clinical practice in Singapore. There is evidence that risk of unconfounded NSF in groups II and III GBCAs is almost negligible in patients with eGFR ≥30 mL/min/1.73 m².^{3,6} Based on this, the latest available ACR guidelines at the time of our study may potentially result in repeated eGFR

testing in the interval between eGFR screening and GBCA administration.

We sought to establish if a longer time interval between eGFR screening and GBCA administration than that proposed by the ACR guidelines would be safe in clinical routine, in an outpatient setting. We also sought to identify risk factors that may lead to worsening of eGFR. These factors can help to identify patients who would likely still require eGFR testing on the day of the MRI scan.

We reviewed all outpatients who presented to the radiology department from 1 November 2019 to 31 June 2020 for a contrast-enhanced MRI scan and underwent POCT for eGFR (eGFR_{POCT}) based on the ACR guidelines. Prior eGFR result (eGFR_{prior}) and same-day eGFR_{POCT} were compared. The time interval between eGFR_{prior} and eGFR_{POCT} was divided into <3 months, 3–6 months and >6 months. Patients were grouped according to eGFR_{prior} into Group A (eGFR ≥60 mL/min/1.73 m²), Group B (eGFR 45–59 mL/min/1.73 m²) and Group C (eGFR <45 mL/min/1.73 m²), reflecting the criteria for eGFR testing based on the ACR guidelines.

A total of 472 patients were reviewed. There were 394 patients in Group A, 45 patients in Group B and 33 patients in Group C. Prior to POCT for contrast administration, there were 33 patients with at least one eGFR_{prior} result within <3 months, 210 patients with at least one eGFR_{prior} result 3–6 months, and 442 patients with at least one eGFR_{prior} result ≥6 months. We compared the median eGFR_{POCT} and eGFR_{prior} based on CKD stage recorded prior to MRI scan. There were no significant differences between median eGFR_{POCT} and eGFR_{prior} at all time intervals prior to POCT for all 3 groups of patients (Table 1). No patient had documented NSF.

However, there were 42 patients with a significant drop in eGFR (decrease from most recent eGFR_{prior} to eGFR_{POCT}) of at least one CKD stage to that of CKD stage 3a or worse (<60 mL/min/1.73 m²) prior to MRI scan. The drop in eGFR did not appear to be significantly associated with established risk factors based on the Choyke questionnaire: diabetes ($P=0.75$), pre-existing renal impairment ($P=0.07$), hypertension ($P=0.76$) and gout ($P=0.36$).

Out of these 42 patients, 38 had a significant drop in eGFR up to that of CKD stage 3b. However, as their eGFR remained $\geq 30\text{mL/min/1.73m}^2$, these patients still proceeded with GBCA administration for MRI scan, and the impact on workflow was minimal. Four patients had a drop in eGFR resulting in CKD stage 4 or 5 ($\text{eGFR} < 30\text{mL/min/1.73m}^2$) and were unable to proceed with GBCA administration. Review of medical records for these 4 patients revealed that 1 had recent prolonged hospitalisation for urosepsis, 2 already had a borderline baseline eGFR of 30mL/min/1.73m^2 (hence a drop of a single unit in eGFR resulted in a worse CKD stage), while 1 was on hydroxyurea, which is known to cause falsely elevated serum creatinine due to interference with the POCT cartridge system. Repeat eGFR testing performed 2 days after POCT did not show significant change from $\text{eGFR}_{\text{prior}}$. Therefore, we conclude that in our study population, only 1 out of 472 patients had a significant drop in eGFR to a level where contrast could not be administered.

Based on our findings, we propose that the time interval between contrast-enhanced MRI and eGFR can be lengthened up to 6 months regardless of the degree of renal impairment, as we found no significant difference between median $\text{eGFR}_{\text{POCT}}$ and $\text{eGFR}_{\text{prior}}$ across all time points. Furthermore, we suggest that in deciding

whether POCT of eGFR is required, additional factors that may contribute to acute-on-chronic renal injury—such as infection; cancer; or trauma and surgery related to the kidneys and urinary tract—should be considered, as these factors are more likely to be associated with progression of renal impairment.^{5,7-9}

While we recognise that findings based on our study population may not be generalised to all patients with varying degrees of renal impairment, our proposal would simplify clinical workflows and save healthcare costs by reducing the need for POCT. Larger studies to determine the precise safe time interval between eGFR screening and MRI scan are needed.

REFERENCES

1. Rodby RA. Group II GBCM Can Be Used Safely for Imaging in Stage 4/5 CKD Patients: PRO. *Kidney360* 2020;2:10-2.
2. Mathur M, Jones JR, Weinreb JC. Gadolinium deposition and nephrogenic systemic fibrosis: A radiologist's primer. *Radiographics* 2020;40:153-62.
3. Satchidanand N, Withiam-Leitch M, Dickinson M, et al. Positive Predictive Value of a Single Assessment of Estimated GFR in the Diagnosis of Chronic Kidney Disease. *South Med J* 2016; 109:351-5.
4. Levey AS, Coresh J, Tighiouart H, et al. Strengths and limitations of estimated and measured GFR. *Nat Rev Nephrol* 2019;15:784.
5. ACR Committee on Drugs and Contrast Media. ACR Manual on Contrast Media (2022). Available at: <http://www.acr.org/-/media/ACR/>

Table 1. Patients classified into 3 groups (A, B and C) based on $\text{eGFR}_{\text{prior}}$. Median $\text{eGFR}_{\text{POCT}}$ and $\text{eGFR}_{\text{prior}}$ were compared for each group stratified by time interval between the 2 readings. In all 3 groups, differences in median eGFR values did not present any significant difference, regardless of time interval from point-of-care test.

Group	Time interval between $\text{eGFR}_{\text{POCT}}$ and $\text{eGFR}_{\text{prior}}$	No. of patients in group	No. of patients with progression in CKD stage (%)	Median $\text{eGFR}_{\text{prior}}$ mL/min/1.73m ² (IQR)	Median $\text{eGFR}_{\text{POCT}}$ mL/min/1.73m ² (IQR)	P value
Group A ($\text{eGFR}_{\text{prior}} > 60\text{mL/min/1.73m}^2$)	<3 months	4	0	100 (92–119)	117 (92–157)	0.144
	3–6 months	167	12 (3.0)	85 (75–102)	85 (71–101)	0.350
	>6 months	223	12 (3.0)	87 (76–100)	88 (76–102)	0.327
Group B ($\text{eGFR}_{\text{prior}} 45\text{--}59\text{mL/min/1.73m}^2$)	<3 months	8	4 (8.9)	50 (45–59)	45 (39–55)	0.067
	3–6 months	21	6 (13.3)	52 (49–57)	51 (44–61)	0.658
	>6 months	16	4 (8.9)	54 (48–57)	51 (43–55)	0.379
Group C ($\text{eGFR}_{\text{prior}} < 45\text{mL/min/1.73m}^2$)	<3 months	23	4 (12.1)	38 (34–41)	38 (31–42)	0.671
	3–6 months	6	0	43 (38–43)	40 (36–46)	0.750
	>6 months	4	0	42 (40–43)	36 (31–43)	0.144

CKD: chronic kidney disease; eGFR: estimated glomerular filtration; IQR: interquartile range; POCT: point-of-care test; prior: prior eGFR result

files/clinical-resources/contrast_media.pdf. Accessed on 30 January 2022. Reston, VA: American College of Radiology.

6. Weinreb JC, Rodby RA, Yee J, et al. Use of intravenous gadolinium-based contrast media in patients with kidney disease: Consensus statements from the American College of Radiology and the National Kidney Foundation. *Radiology* 2021;298:28-35.
7. Choyke PL, Cady J, DePollar SL, et al. Determination of serum creatinine prior to iodinated contrast media: is it necessary in all patients? *Tech Urol* 1998;4:65-9.
8. Chawla LS, Eggers PW, Star RA, et al. Acute kidney injury and chronic kidney disease as interconnected syndromes. *N Engl J Med* 2014;371:58-66.
9. Tippins RB, Torres WE, Baumgartner BR, et al. Are screening serum creatinine levels necessary prior to outpatient CT examinations? *Radiology* 2000;216:481-4.

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