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Comparison of the Sensitivity of a Pre-MRI Questionnaire and Point of Care eGFR Testing for Detection of Impaired Renal Function

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Abstract

Rationale and Objectives—The Food and Drug Administration recommends renal function estimation using laboratory testing for patients at risk for chronically reduced kidney function before the administration of gadolinium-based contrast agents (GBCAs). Point-of-care (POC) estimated glomerular filtration rate (eGFR) testing was added to the pre-magnetic resonance (MR) questionnaire at our institution in June 2008 for all patients undergoing a contrast-enhanced MR exam. This study was done to evaluate the effectiveness of a pre-MR screening questionnaire about kidney disease and to assess POC eGFR detection of additional patients at risk for nephrogenic systemic fibrosis.

Materials and Methods—This retrospective study was approved by our institutional review board and determined to be Health Insurance Portability and Accountability Act compliant. Medical records, laboratory data, and pre-MR questionnaires of all patients who presented for contrast-enhanced MR scans during October 2008 were reviewed. The National Kidney Disease Education Program isotope-dilution mass spectrometry-traceable Modification of Diet in Renal Disease equation was used to calculate eGFRs using the POC creatinine laboratory value, age, race, and gender. Sensitivity and specificity were calculated using 2×2 tables, and 95% confidence intervals were calculated with exact binomial confidence intervals.

Results—A total of 1167 individuals presented for contrast-enhanced MR scans. Of 13 individuals on dialysis, 2 did not report renal disease. Of 1154 individuals not on dialysis, 25 had an eGFR <30 mL/min/1.73 m² (95% CI 1.41%–3.18%). Of these 25, 13 did and 12 did not report renal disease. The sensitivity of the questionnaire for identifying patients with an eGFR <30 mL/min/1.73 m² was 63.2%. POC eGFR estimations identified a prevalence of 2.17% (95% CI: 1.41%–3.18%) of the total individuals not on dialysis, with an eGFR <30 mL/min/1.73 m². Patients who denied kidney dysfunction had a 1.08% (95% CI: 0.56%–1.88%) posttest probability of having an eGFR <30 mL/min/1.73 m².

Conclusions—POC eGFR testing identified a significant number of individuals with renal dysfunction not found by the pre-MR imaging questionnaire alone.

Keywords

Estimated glomerular filtration rate (eGFR); gadolinium-based contrast agents (GBCAs); point-of-care (POC); nephrogenic systemic fibrosis (NSF); screening questionnaires

Nephrogenic systemic fibrosis (NSF) was first recognized in 1997 and first reported in the literature in 2000 (1). NSF is a systemic-fibrosing disorder that may occur days to months following a magnetic resonance (MR) examination with contrast in those with renal dysfunction (1). Clinically, patients describe swelling and tightening of the skin, which contributes to pain and loss of mobility (2). Although originally thought to be limited to the skin, the fibrosing process also occurs systemically (3). Consequently, scarring of internal organs may impair vital function and lead to death (4). In 2006, its association with gadolinium-based contrast agents (GBCAs) was suggested in the literature (1,5,6). In 2007, the Food and Drug Administration (FDA) requested a boxed warning for GBCAs to include the risk of developing NSF in those with severe kidney insufficiency who receive a GBCA (7). NSF occurs in patients with end-stage renal disease (ESRD), on dialysis, or with acute kidney injury. The risk associated with an estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m² has been variably reported as 1%–7% after GBCA administration (2,8,9). However, one study by Rydahl and colleagues have shown that the incidence of NSF can be as high as 18% in patients with stage 5 chronic kidney disease in which eGFR <15 mL/min/1.73 m² (10).

In an attempt to avoid new cases of NSF in June 2008, point-of-care (POC) estimated glomerular filtration rate (eGFR) testing was routinely performed at our institution in addition to the existing screening questionnaire for all patients before anticipated contrast-enhanced MRI. Because many hospitals use questionnaires to assess NSF risk (11,12), the purpose of this study was to evaluate the effectiveness of our pre-MR imaging screening questionnaire with respect to kidney disease and to determine if POC eGFR testing detects additional patients at risk for NSF. Our hypothesis was that POC eGFR testing will be more sensitive in the detection of renal disease than our pre-MR imaging questionnaire.

MATERIALS AND METHODS

A total of 1168 individuals, 628 females (mean age 53.1) and 540 males (mean age 55.1) presented for contrast-enhanced MR scans. There was a wide age distribution; 87.0% were between 30 and 80 years old and 11 children younger than age 18 were scanned. One thousand and eighty-six patients went on to receive a GBCA, whereas 81 did not as a consequence of low renal function. The demographics and contrast agents administered are in Table 1. The electronic medical records (Powerchart, Cerner Corporation, Kansas City, MO) of all patients who presented to our institution for contrast-enhanced MR examinations during October 2008 were reviewed. Each patient had completed a pre-MR imaging questionnaire that asked the patient, “Do you have history of kidney disease” as well as “Are you currently on kidney dialysis?” Data collected included age, sex, self-reported weight, ethnicity, MR scan performed and GBCA used, most recent eGFR, dialysis status, and self-reported kidney disease. POC eGFR calculations were obtained using an iSTAT instrument (Abbott Point of Care, Inc., Princeton, NJ) immediately before the exam. Testing for correlation with conventional laboratory examinations had been completed before the study period to confirm the accuracy of the iSTAT measurements. The National Kidney Disease Education Program isotope-dilution mass spectrometry-traceable Modification of Diet in Renal Disease equation was used to calculate eGFRs using the POC creatinine laboratory

value, age, race, and gender. Because calculations are imprecise above an eGFR of 60 (13), any values above 60 were marked as >60 mL/min/1.73 m². Sensitivity and specificity were calculated using 2×2 tables, and 95% confidence intervals were calculated with exact binomial confidence intervals.

This retrospective study was institutional review board approved and Health Insurance Portability and Accountability Act compliant.

RESULTS

On the pre-MR questionnaire, only 11 of 13 (84.6%) patients on dialysis reported having kidney disease, whereas 2/13 (15.4%) did not. Of 25 patients with eGFR <30 mL/min/1.73 m², 13 (52.0%) reported having kidney disease, whereas 12 (48.0%) specifically denied CKD (Fig 1). Of 237 individuals with eGFR 30–60 mL/min/1.73 m², 25 (10.5%) reported having CKD, whereas 212 (89.5%) did not. Of the 892 patients with eGFR >60 mL/min/1.73 m², 5 (0.56%) reported having CKD (Table 2).

The questionnaire had low sensitivity at all eGFR levels observed (Tables 3 and 4). The sensitivity was highest at low eGFRs but remained low at 81%, 95% CI (0.544–0.960), for eGFR <15 mL/min/1.73 m² (Table 3). For eGFR <30 mL/min/1.73 m², the sensitivity was 63% with a 95% CI 0.460–0.782. When dialysis patients were stratified out of the calculation, the sensitivity dropped to 60%, 52%, and 15% for eGFR <15 , 30, and 60 mL/min/1.73 m², respectively.

Regardless of what was reported on the questionnaire, all patients with an eGFR below 30 mL/min/m² did not get contrast, and patients with eGFR 30–60 mL/min/m² received half-dose gadobenate dimeglumine. All patients who reported chronic kidney disease despite a normal eGFR received contrast material. There were no false-positive or false-negative results of the point of care testing to our knowledge. The laboratory does routine and rigorous quality control checks to make sure that the iSTAT device stays in range with the lab analysis.

DISCUSSION

In 2006, the FDA issued the first public health advisory regarding the use of GBCAs in those with advanced renal failure (14), but it was only in 2010 that an updated safety communication required that, for patients at risk for chronically reduced kidney function (such as those older than age 60 years, with high blood pressure, or diabetes), an eGFR be measured through laboratory testing (15). Questionnaires or, at times receptionists, continue to be used to screen for compromised renal function. The reliability of these techniques is not known. Many institutions and radiology practices neither have the time nor resources to perform screening prior to each examination. In 2008, in addition to a pre-MR imaging questionnaire universal POC testing was initiated at our institution.

It is apparent from this data collection that our renal status questionnaire is inadequate for reducing the risk of NSF development in patients undergoing contrast-enhanced MR examinations. First, the low negative predictive value of the pre-MR questionnaire did not significantly change the risk of having an eGFR <30 mL/min/m² from the population prevalence. At the same time, the questionnaire was not sensitive because patients with a low eGFR did not report their renal status and thus could potentially be given gadolinium if this were the only screening mechanism used.

Specificity for the questionnaire was high at all eGFR levels ($P > .965$), suggesting that the self-report questionnaire does not falsely identify cases of kidney disease for whom patients

may not be given GBCA because of suspected renal disease (Table 4). POC eGFR estimations identified a prevalence of 2.17% of the total individuals not on dialysis who presented for MR scans with contrast with an eGFR <30 mL/min/1.73 m² (Fig 1). Individuals with no self-report of kidney dysfunction had a 1.08% posttest probability of having an eGFR <30 mL/min/1.73 m². Although these are small percentages, our institution performs more than 20,000 MR exams with contrast each year, potentially missing more than 200 patients at increased risk for NSF per year.

The renal status questionnaire lacked sensitivity (63%) to determine patients with eGFR <30 mL/min/1.73 m², dropping further to 52% when those on hemodialysis were discounted. Of the 38 patients with an eGFR <30 mL/min/1.73 m², 13 patients were on hemodialysis. It is disconcerting that two of them (15%) did not report this renal disease on the questionnaire. Excluding those on hemodialysis did not drastically affect the specificity of the test, but it revealed low sensitivities for all eGFR levels tested (Table 3). With a sensitivity of 52% at an eGFR <30 mL/min/1.73 m², it is interesting that patients were not aware of their renal dysfunction. However, while the sensitivity is low, patients who do report to have kidney disease had a 30.23% (13/43), 95%CI (17.18%–46.13%) risk of having an eGFR <30 mL/min/1.73 m². A patient admitting to kidney disease merits a POC eGFR test or laboratory exam if universal testing is not used to determine the GFR before gadolinium-enhanced MR as not all patients had a GFR of less than 30.

The amount of GBCA administered during MRI has been reduced at our institution since the association between GBCA and NSF was made. With the onset of POC testing, eGFR is an important component of the algorithm for GBCA dosing in addition to weight. With the onset of POC testing, we also have developed algorithms to evaluate patients based on their eGFR. The radiologist must be notified for those patients that have an eGFR <30 mL/min/1.73 m², or patients on hemodialysis, peritoneal dialysis, or with acute kidney injury. The radiologist then contacts the ordering physician and they discuss if the benefit of the contrast-enhanced MR exam outweighs the risk of the procedure. If the exam is performed then the patient is given half-dose gadobenate dimeglumine and informed consent is obtained from the patient. If the patient is already on dialysis and a contrast-enhanced exam is warranted, then hemodialysis is administered shortly after and again at 24 hours after the examination. If the patient is not on dialysis, then the risks and benefits of initiating hemodialysis are weighed. The ordering physician and radiologist may also opt for the exam without contrast, cancel the exam, or request an alternative imaging study. At our institution during the study period, patients with an eGFR of 30–60 mL/min/1.73 m² received a half-dose of gadobenate dimeglumine. Gadobenate dimeglumine is used as similar diagnostic images are obtained with a lower dose compared to other GBCAs because of its higher relaxivity (16).

Since the first FDA alert, several articles have evaluated screening techniques to prevent high-risk patients receiving GBCAs. In 2008, Weinreb published a report of Yale's evolving policy as the concern for NSF mounted. After describing ways the at-risk patients were identified, including a message in the computerized information system, schedulers asking screening questions, and providing safety forms before administering GBCA, Weinreb states that they were more recently using POC testing on outpatients. This change correlated with a change in thinking from limiting the risk to eliminating the risk of NSF development (17).

Martin et al and Wang et al reported a decreased incidence of NSF at their respective institutions after change of GBCA MR protocols (18,19). Martin reported a drop in NSF incidence in those with ESRD from 2.6% to 0.0% after switching from gadodiamide at routine doses to gadobenate dimeglumine at half-dose (18). Subsequently, Wang similarly reported no new cases of clinicopathologically confirmed NSF cases after adopting new,

more restrictive GBCA guidelines. These guidelines included recent serum creatinine level measurements in those >60 years of age or at risk for renal disease, limiting the maximum weight-based GBCA dose administered to those with eGFR <60 mL/min/1.73 m², and prohibiting GBCA administration in those with eGFR <30 mL/min/1.73 m² or on dialysis (19).

As institutions struggle to find the best way to administer GBCAs safely, a cost–benefit analysis would be helpful to demonstrate the utility of new POC testing devices (20). At our institution, each cartridge for the iSTAT costs the hospital less than \$10. This estimate does not take into account the cost of the device itself or associated staff time to administer the test; it merely represents the equipment cost per patient. Likewise, it is difficult to evaluate the cost of a practice that may delay patients being scanned and affect the MR schedule, and, at times, require ordering physician contact to discuss an eGFR value, although we have been able to accommodate this process with little difficulty. Since we have instituted POC testing, we have not had new cases of NSF, although other institutions have instituted other policies with success. Irrespective of monetary cost, POC causes some strain not felt before these concerns and we recognize this is merely one way to decrease or eliminate the risk of NSF. Although other risk factors may contribute to its development, until we know more about what these other factors may be, decreasing those with low eGFR who receive GBCA or changing dosing practices in this population seems appropriate. However even with POC testing, practitioners still face dilemmas with certain populations, including those with acute kidney injury and those with liver disease where eGFR measurements are less reliable (21).

A limitation of this study is the relatively small sample size for patients with low eGFR. There were only 25 patients with an eGFR <30 mL/min/1.73 m². Additionally, this study only includes a single institution's experience using an institution-specific questionnaire. Perhaps other institutions have more successful questionnaires or other procedures to screen for renal disease. In the future, we would recommend that our institution's questionnaires be modified to ask specific questions that more directly query causes of renal disease although have switched to using point of care testing routinely. We also would attempt a prospective assessment rather than a retrospective assessment to maximize accuracy.

In conclusion, these results demonstrate the inadequacy of the pre-MR questionnaire used at this institution to identify patients at greatest risk for NSF. To avoid scanning patients at risk for NSF, we elected to use POC testing and changed our gadolinium chelate selection pattern. These actions appear to have been effective because we have not had additional cases of NSF. Considering the potential of developing an incurable disease relies on knowing renal status before GBCA administration, it is important to continue to examine ways to gather this information. Our institution found POC testing to be useful in identifying those at risk; however, other institutions may have found alternative solutions.

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Figure 1.

Point-of-care estimated glomerular filtration rate (eGFR) estimations identified a prevalence of 2.17% (25/1154), 95% CI (1.41%–3.18%) of the total individuals not on dialysis who presented for magnetic resonance scans with contrast with an eGFR <30 mL/min/1.73 m². Statistical analysis showed that individuals who denied kidney disease on questionnaire had a 1.08% (12/1111) 95% CI (0.56%–1.88%) of having an eGFR <30 mL/min/1.73 m².

TABLE 1

Demographic Characteristics of Study Population

Data Element	Number (n = 1168)	Percentage (n = 1168)
Gender		
Females	628	53.77
Male	540	46.23
Age (y)		
0–19	13	1.11
20–29	76	6.51
30–39	146	12.50
40–49	216	18.49
50–59	248	21.23
60–69	247	21.15
70–79	157	13.44
80–89	56	4.79
90–99	8	0.68
Ethnicity		
Asian	21	1.80
Black or African American	187	16.01
Declined to answer	68	5.82
Hispanic or Latino	76	6.51
Unable to answer	99	8.48
White or Caucasian	716	61.30
Gadolinium-based contrast agent administered		
Gadopentetate dimeglumine (Magnevist)	866	74.14
Gadobenate dimeglumine (Multihance)	210	17.98
No contrast agent given	81	6.93

TABLE 2

Estimated Glomerular Filtration Rate (eGFR) and Patient Self-report of Kidney Disease Demographics

Variable	Number	Percentage
Point-of-care eGFR results (mL/min)		
0–9	10	0.9
10–19	11	0.9
20–29	17	1.5
30–39	30	2.6
40–49	83	7.1
50–59	124	10.6
>60	892	76.4
Patients with no self-report of kidney disease	1113	95.4
eGFR		
0–9	0	0.0
10–19	6	0.5
20–29	8	0.7
30–39	24	2.2
40–49	70	6.3
50–59	118	10.6
>60	887	79.7
Patients with a self-report of kidney disease	54	4.6
eGFR		
0–9	10	18.5
10–19	5	9.3
20–29	9	16.7
30–39	6	11.1
40–49	13	24.1
50–59	6	11.1
>60	5	9.3

TABLE 3

Dialysis, Estimated Glomerular Filtration Rate (eGFR), and Patient Self-report of Kidney Disease Demographics

Variable	Number	Percentage
On dialysis	13	1.1
Self-reported kidney disease	11	84.6
eGFR values		
0–15	11	100.0
15–30	0	0.0
No self-reported kidney disease	2	15.4
eGFR values		
0–15	0	0.0
15–30	2	100.0
Not on dialysis	1154	98.9
Self-reported kidney disease	43	3.7
eGFR values		
0–14	3	7.0
15–29	10	23.3
30–59	25	58.1
60+	5	11.6
No self-reported kidney disease	1111	96.3
eGFR values		
0–14	2	0.2
15–29	10	0.9
30–59	212	19.1
60+	887	79.8

TABLE 4

Effectiveness of Patient Self-report of Renal Function Compared to Estimated Glomerular Filtration Rate (eGFR) Values after Excluding Hemodialysis Patients

Calculation	eGFR <60	eGFR <30	eGFR <15
Sensitivity	0.145	0.520	0.600
95% confidence interval	0.105–0.194	0.313–0.722	0.147–0.947
Specificity	0.994	0.973	0.965
95% confidence interval	0.987–0.998	0.962–0.982	0.953–0.975
Positive predictive value	0.884	0.302	0.070
95% confidence interval	0.749–0.961	0.172–0.461	0.015–0.191
Negative predictive value	0.798	0.989	0.998
95% confidence interval	0.774–0.822	0.981–0.994	0.994–0.999

95% confidence intervals calculated at <http://statpages.org/confint.html> using the exact binomial confidence interval.