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Cost of screening strategies for kidney disease before intravenous contrast administration

S.I. Moos*, R.S. de Weijert, G. Nagan, J. Stoker, S. Bipat

Department of Radiology, Academic Medical Center, Amsterdam, the Netherlands,
*corresponding author: tel.: +31 (0)20-5662630, fax: +31 (0)20-5669119, e-mail: s.i.moos@amc.uva.nl

ABSTRACT

Purpose: To assess whether selective use of estimated glomerular filtration rate (eGFR) in patients with risk factors for kidney disease is more cost-effective than measuring eGFR in all patients undergoing contrast-enhanced computed tomography (CECT).

Methods: Risk factors and costs were assessed in consecutive patients. eGFR was evaluated in all patients, considering a tenability of 12 months. For the three-month tenability and the pre-selection strategy based on risk factors for kidney disease, we extrapolated data by assuming equal distribution of patient characteristics.

Results: We included 1001 patients, mean age 59.9±13.6 years.

Strategy with eGFR in all patients: eGFR measurements specifically performed for CECT in 645/1001 (in 356 patients the eGFR was already known). The total cost including costs of an extra visit to the hospital (49 patients) and absence from work (11 patients) were € 6037.20. Considering a tenability of 3 months, eGFR had to be measured in 786 patients, 60 would have paid an extra visit and 14 would have been absent from work: total cost € 7443.54. Pre-selection strategy: 807 patients had risk factors, necessitating eGFR measurement and an extra visit would be paid by 61. Fourteen patients would have been absent from work: total cost € 7585.16. Of the patients with an eGFR <60 ml/min/1.73m², 94.8% were identified including all with an eGFR <45 ml/min/1.73m².

Conclusion: Determining eGFR based on risk factors for kidney disease is not more cost-effective than eGFR testing in all patients if the eGFR is tenable for 12 months or for 3 months.

KEYWORDS

Computed tomography, contrast-induced nephropathy, cost-effective, kidney disease, prevention

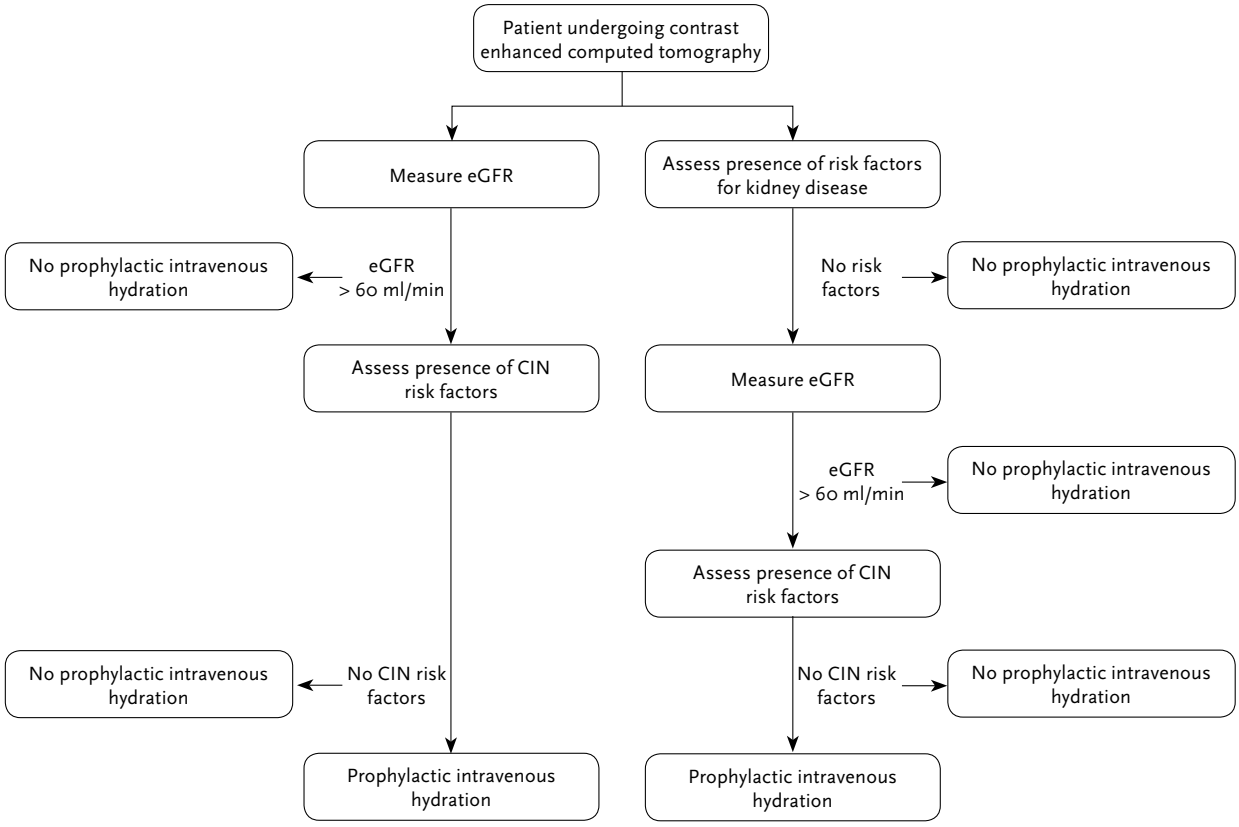
INTRODUCTION

The number of computed tomography examinations increases every year due to the improvement of availability and progress in clinical application.[1] The majority of computed tomography examinations are intravenously contrast-enhanced with iodinated contrast medium. Unfortunately the use of iodinated contrast medium can lead to acute nephropathy, also known as contrast-induced nephropathy (CIN).[2]

Worldwide several CIN prevention guidelines have been introduced.[2-8] Most guidelines describe risk profiles by which potential CIN patients can be recognised in order to determine whether CIN prevention measures are necessary.[2-8] This usually involves the recognition of patients with the most important risk factor for CIN: pre-existent (chronic) kidney disease, which is usually defined as an estimated glomerular filtration rate (eGFR) <60 ml/min/1.73m².[2-8] Kidney disease in combination with other risk factors related to CIN, for example diabetes mellitus or cardiovascular disease, outlines the patients who need CIN prevention.[2-8] CIN prevention usually entails volume expansion through oral or intravenous hydration and discontinuation of diuretics or nephrotoxic medication.[2-8]

To screen for the presence of kidney disease, eGFR measurement is inevitable. Some CIN prevention guidelines indicate that the eGFR should be known in all patients before administration of iodinated contrast medium.[4,6,7,9] To reduce the number of eGFR measurements these guidelines usually recommend a tenability period for eGFR of 3-12 months with the exception of patients with a history of kidney disease, or a relevant medical event that might have influenced the eGFR (kidney function).[4,6,7,9] Other CIN prevention guidelines indicate that risk factors associated with kidney disease should be assessed first and if these risk factors are present, the eGFR should be measured in these patients only.[2,3,5,8] See *figure 1* for an overview of these screening strategies.

Figure 1. *Flow chart for different screening strategies*



CIN = contrast-induced nephropathy; eGFR = estimated glomerular filtration rate

The literature shows that there is a preference among radiologists to routinely measure eGFR or serum creatinine in all patients before administering iodinated contrast medium instead of measuring eGFR or serum creatinine in patients with risk factors for kidney disease.[10-12]

It is not clear which screening strategy is more cost-effective. Measuring eGFR or serum creatinine in all patients seems costly. On the other hand, if eGFR or serum creatinine is measured in a select group of patients, patients without risk factors for kidney disease but with unknown severe kidney disease (eGFR <45 ml/min/1.73m^2) would be missed. Furthermore, most CIN prevention guidelines are based on articles where iodinated contrast medium is administered intra-arterially, mostly during (emergency) cardiac intervention.[4-6,8] This patient population differs from the patient population undergoing intravenous iodinated contrast-enhanced computed tomography (CECT).[13]

We therefore wanted to compare the cost-effectiveness of the different screening strategies in patients undergoing intravenous iodinated CECT. The first screening strategy considers that eGFR is known in all patients undergoing intravenous iodinated CECT. This means that eGFR is available in all patients with a tenability of 12 months. The second strategy considers that eGFR is available in all patients with a tenability of three months. Finally, the third strategy considers a pre-selection strategy, where eGFR would have been measured after assessment of risk factors for kidney disease in patients undergoing intravenous iodinated CECT.

We will compare the costs and the number of patients with severe kidney disease (eGFR <45 ml/min/1.73m^2) who would be missed by the pre-selection strategy (effectiveness). This concerns patients without any risk factors, but with severe kidney disease.

MATERIALS AND METHODS

Design

This study was internally funded as 'Quality assessment project' in the Academic Medical Center, University of Amsterdam. The funding body was not involved in the design or the execution of this study, did not have access to the data, and was not involved in data analysis or preparation of this article.

The standard procedure at our institution is that eGFR is available in all patients prior to intravenous iodinated

CECT. A tenability of 12 months is maintained with the exception of patients with known kidney disease or a clinical event, which could affect eGFR, in these cases eGFR measurement is indicated. Estimated GFR was calculated using the four-point Modification of Diet in Renal Disease (MDRD) formula which takes into account age, sex and race and is expressed as ml/min/1.73m^2. This is in accordance with the national CIN prevention guideline that is used in our hospital.[4]

According to this guideline, in patients with pre-existent (chronic) kidney disease, defined as an eGFR <60 ml/min/1.73m^2, risk factors related to CIN should be checked.[4] This means that in patients with an eGFR >60 ml/min/1.73m^2, CIN risk factors are not checked or registered. These CIN risk factors are very similar to risk factors for kidney disease. For research purposes, we checked and registered all risk factors for CIN and kidney disease in all patients, in order to be able to simulate the screening strategy in which pre-selection by risk factor assessment for kidney disease preceding the eGFR measurement is performed.

Patient population and recruitment

Because our study did not influence standard care, participation in our study was considered a minor burden for patients (scripted interview). Informed consent was waived by the medical ethics committee of our institute.

We prospectively included consecutive patients who underwent intravenous iodinated CECT in our institute, from October 2012 until May 2013. The contrast medium used in all procedures was iopromide (Ultravist 300, Bayer, Leverkusen Germany), or iomeprol (Iomeron 400, Bracco, Milan Italy), which both have low osmolality and are nonionic.

Patients were excluded if they were <18 years of age, unresponsive due to severe illness and could not be interviewed, unwilling to participate, if they did not speak Dutch or English or if it was logistically impossible to interview the patient (e.g. if there was more than one patient at the same time, if there was no space available to interview the patient or if the patient had no time due to commitments elsewhere). Patients admitted to the intensive care or emergency department were also excluded, as most prevention guidelines are not applicable for these patients.

Data collection

Data were collected from the digital patient record as well as through scripted interviews. The data collected from the digital patient record were: age, gender, type of intravenous iodinated CECT procedure, indication for the intravenous iodinated CECT, serum creatinine and eGFR before the procedure, whether they were inpatients or outpatients and whether they were on diuretics/ nephrotoxic medication (e.g. non-steroidal anti-inflammatory drugs (NSAIDs) as well as any other medication indicated as nephrotoxic in a national database (Farmacotherapeutisch Kompas) containing information on all (human) registered drugs in the Netherlands and Europe.[14] We also assessed if multiple myeloma or Waldenström's disease was present.

To assess the presence of other risk factors we performed scripted face-to-face interviews on the day of the intravenous iodinated CECT to obtain data to supplement the findings in the digital patient record. In the interview we asked if patients suffered from diabetes mellitus, cardiovascular disease, hypertension or history of urological or nephrological disease. The interviews were conducted by four researchers (SM, RW, GN, DVV) who received interview instructions from a senior researcher (SM) to guarantee uniform data collection.

We defined the following risk factors as associated with kidney disease in patients receiving iodinated contrast medium: age >60 years, hypertension, use of nephrotoxic medication, cardiovascular disease, a history of urological or nephrological disease, diabetes mellitus, use of metformin, multiple myeloma or Waldenström's disease. These risk factors were chosen based on CIN prevention guidelines indicating that risk for kidney disease should be assessed preceding eGFR measurement.[2,3,5,8] We collected these data in all patients.

Cost-analysis

We used the costs associated with eGFR measurement to calculate direct medical costs (eGFR tests), direct non-medical costs (travel costs) and indirect non-medical costs (productivity loss) due to a visit to the hospital for eGFR measurement. We did this for all screening strategies.[15,16]

eGFR in all patients with a tenability of 12 months

To assess the costs of this screening strategy, we looked at the number of patients in whom the eGFR was measured for the sole purpose of intravenous iodinated CECT. This was done as follows.

Costs associated with eGFR measurement: As we were unable to ascertain if eGFR measurements were performed for the sole purpose of intravenous iodinated CECT in our patient population, we assumed that all eGFR measurements within one month before the intravenous iodinated CECT were for this purpose. This included the patients who stated during the interview that they paid an extra visit to the hospital for the sole purpose of eGFR measurement. For patients who stated during the interview that they paid an extra visit to the hospital for the sole purpose of eGFR measurement >1 month before intravenous iodinated CECT, costs for these eGFR measurement were added to the costs made for eGFR measurements within one month before intravenous

iodinated CECT. We considered these to be direct medical costs. For all other patients with an eGFR value >1 month before intravenous iodinated CECT, we assumed that the eGFR was already known.

Travel costs: As we had asked patients if they had to pay an extra visit to the hospital for the sole purpose of eGFR measurements in preparation for the intravenous iodinated CECT, we were able to calculate travel costs. For travel costs, we also asked them about their means of transportation to and from the hospital. All extra visits (both <1 month and after 1 month) were used for calculation of the travel costs. For the remaining patients, no travel costs were taken into account. We assumed that in these patients eGFR measurement was combined with a visit to the hospital with another purpose than eGFR measurement.

Costs associated with productivity loss: For the loss of productivity, we asked patients who had to pay an extra visit to the hospital for eGFR measurement if they had to take time off from work and if so how long.

eGFR in all patients with a tenability of three months

We also calculated costs related to an eGFR tenability of three months. We than considered that all eGFR values measured within one month were for the sole purpose of intravenous contrast-enhanced computed tomography and that eGFR should have been measured if the eGFR value was older than three months and costs associated with eGFR measurement were calculated.

To enable data extrapolation for calculation of the indirect costs (travel costs and loss of productivity), we assumed that the same percentage of patients would have paid an extra visit to the hospital and had to take time off from work, using the same means of transportation.

eGFR in patients with risk factors for kidney disease

For this screening strategy we determined the number of patients in whom eGFR would have been measured because of the presence of one or more of the above-mentioned risk factors for kidney disease. This number was used to calculate the direct costs (eGFR evaluation). We also extrapolated data for calculation of travel costs and costs associated with productivity loss.

Unit prices and costs

Costs associated with eGFR measurement: 1) Costs related to determining eGFR measurement. In our hospital these costs were € 6.03 per eGFR measurement 2) Travel costs were categorised in number of kilometres (km) using a car (€ 0.20/km + € 3.00 for parking), using public transport (€ 0.20/km) or a taxi (€ 2.00/km + € 3.50 start rate). For patients travelling by bicycle or on foot no additional costs were added. 3) Productivity related costs were calculated by the number of hours absent from work multiplied by € 32.49 for men and € 25.94 for women (this was based on information gathered by Central Bureau for Statistics the Netherlands (CBS) and represents the mean contribution value per person per hour of labour).[15] Using these costs, the total costs per strategy were calculated and also the average per patient was calculated for each strategy. This was done by dividing the total costs by the number of patients screened.

Statistical analyses

We used descriptive statistical analysis to summarise the results. We expressed the continuous data as means and standard deviation (SD) and categorical data as numbers and percentages. We organised our data using Microsoft Office Access® 2003, Microsoft Corp. Redmond, WA and analysed the data using IBM® SPSS® statistic data editor version 20 SPSS® Inc. Chicago, Il.

RESULTS

Baseline patient characteristics

Between October 2012 and May 2013 there were 1191 eligible patients. Of these patients 176 could not be included due to a language barrier, or patients did not want to participate, there was no time to interview the patient or the patients did not show up for the examination. We were finally able to interview 1015 patients. Seven patients did not receive intravenous iodinated contrast medium during their computed tomography; for another six patients the data could not be used for analysis due to incomplete data and one patient was <18 years. In total 1001 patients were included for analyses. See *figure 2*.

The mean age was 59.9 years (SD: 13.6), there were 548 males (54.7%) in the patient population and 74 patients

Figure 2. *Patient inclusion flow chart*

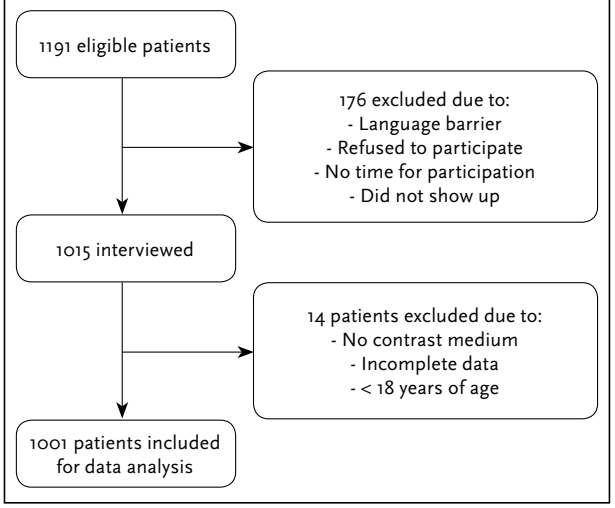


Table 1. *Baseline characteristics in patients undergoing intravenous contrast enhanced computed tomography*

Baseline characteristics	**Total study population (*n*= 1001)**	**eGFR ≥ 60 ml/ min/1.73m² (*n*=886)*****	**eGFR 45-59 ml/ min/1.73m² (*n*=82)**	**eGFR 30-44 ml/ min/1.73m² (*n*= 26)**	**eGFR 15-29 ml/ min/1.73m² (*n*= 4)**
Demographics					
Age (yrs) mean ± SD	59.9 ± 13.6	59.2 ± 13.5	65.3 ± 12.6	68.3 ± 11.9	62.8 ± 20.2
Male: female *n* (%)	548 (54.7) : 453 (45.3)	487(55.1) : 399(44.9)	41 (47.6) : 41 (52.4)	16 (61.5) :10 (38.5)	1 (25.0) : 3 (75.0)
Height (cm) mean ± SD*	172.8 ± 10.2	173.0 ± 10.3	170.9 ± 9.3	171.9 ± 8.6	172.5 ± 13.1
Weight (kg) mean ± SD	75.9 ± 16.5	75.5 ± 16.0	80.4 ± 18.3	78.0 ± 20.3	71.5 ± 7.9
BMI (kg/m²) mean ± SD*	25.4 ± 4.8	25.2 ± 4.7	27.5 ± 5.0	26.3 ± 6.3	24.1 ± 2.7
Kidney function					
Serum creatinine (µmol/l) mean ± SD**	79.0 ± 23.0	73.9 ± 15.6	105.6 ± 15.8	142.7 ± 17.9	224.5 ± 48.8
eGFR (ml/min/) mean ± SD***	-	-	53.8 ± 4.1	38.7 ± 4.0	21.5 ± 4.2
Type of CT scan					
Chest/ Abdomen *n* (%)	388 (38.8)	339 (38.3)	37 (45.1)	11 (42.3)	-
Abdomen *n* (%)	146 (14.6)	131 (14.8)	11 (13.4)	3 (11.5)	1 (25.0)
Kidney *n* (%)	107 (10.7)	89 (10.0)	12 (14.6)	5 (19.2)	1 (25.0)
Pancreas *n* (%)	95 (9.5)	90 (10.2)	4 (4.9)	1 (3.8)	-
Cardiac *n* (%)	56 (5.6)	49 (5.5)	4 (4.9)	2 (7.7)	1 (25.0)
Chest *n* (%)	53 (5.3)	51 (5.8)	2 (2.4)	-	-
Aorta *n* (%)	45 (4.5)	39 (4.4)	3 (3.7)	2 (7.7)	1 (25.0)
Liver *n* (%)	41 (4.1)	33 (3.7)	4 (4.9)	2 (7.7)	-
Cerebrum *n* (%)	12 (1.2)	12 (1.4)	-	-	-
Other *n* (%)	58 (5.8)	53 (6.0)	5 (6.1)	-	-
Indication CT scan					
Malignancy *n* (%)	451 (45.1)	393 (44.4)	43 (52.4)	12 (46.2)	-
Suspected malignancy *n* (%)	260 (26.0)	233 (26.3)	20 (24.4)	7 (26.9)	-
Vascular deformation *n* (%)	79 (7.9)	70 (7.9)	6 (7.3)	2 (7.7)	1 (25.0)
Nephrological disease *n* (%)	34 (3.4)	29 (3.3)	3 (3.7)	2 (7.7)	-
Infection *n* (%)	51 (5.1)	51 (5.8)	-	-	-
Kidney donation *n* (%)	15 (1.5)	15 (1.7)	-	-	-
Family history of cardiac disease	13 (1.3)	12 (1.4)	1 (1.2)	-	-
Pulmonary embolism	7 (0.7)	5 (0.6)	2 (2.4)	-	-
Macroscopic haematuria	6 (0.6)	3 (0.3)	1 (1.2)	1 (3.8)	1 (25.0)
Cysts (liver, kidney, pancreas)	7 (0.7)	7 (0.8)	-	-	-
Angina pectoris	9 (0.9)	8 (0.9)	1 (1.2)	-	-
Other *n* (%)	69 (6.9)	60 (6.8)	5 (6.2)	2 (7.7)	2 (50.0)
Patient status					
Inpatient *n* (%)	74 (7.4)	55 (6.2)	9 (11.0)	8 (30.8)	1 (25.0)
Outpatient *n* (%)	927 (92.6)	831 (93.8)	73 (89.0)	18 (69.2)	3 (75.0)

***One patient did not know their height; **serum creatinine values were missing in 25 patients; ***eGFR was missing in 3 patients: these patients could not be categorised; other information was available.**

(7.4%) were inpatients, 5.7% of the patient population were Afro-European (n=57).
Most patients underwent intravenous iodinated CECT because of a malignancy (n=451, 45.1%) or because a malignancy was suspected (n=260, 26.0%). CECT of the chest and abdominal region was the most common examination (n=388, 38.8%).
The mean serum creatinine at baseline was 79.0 μmol/l (SD: 23.0). The eGFR was ≥60 ml/min/1.73m² in 882 (88.1%) patients, 82 (8.2%) patients had an eGFR between 45-59 ml/min/1.73m², 26 (2.6%) between 30-44 ml/min/1.73m² and 4 (0.4%) patients had an eGFR <30 ml/min/1.73m². In three patients eGFR was unknown but we had complete information on risk factors and indirect cost. We therefore included these patients in our analysis. See *table 1* for detailed information.

Risk factors for kidney disease

In total 576 (57.5%) of the patients were aged >60 years at the time of the examination. Hypertension was present in 370 (37.0%) patients, 301 (30.1%) used nephrotoxic medication, 295 (29.5%) suffered from cardiovascular disease, 232 (23.2%) patients had a history of urological or kidney disease, 137 (13.7%) patients suffered from diabetes mellitus and 89 (8.9%) patients used metformin at the time of the intravenous iodinated CECT. Of the 1001 patients, 807 (80.6%) had ≥1 risk factor for chronic kidney disease.
Of the 886 patients with an eGFR ≥60 ml/min/1.73m², 694 (78.3%) patients had ≥1 risk factors for kidney disease. There were 78 patients (95.1%) with an eGFR between 45-59 ml/min/1.73m², 26 (100%) with an eGFR between 30-44 ml/min/1.73m² and 4 (100%) with an eGFR <30 ml/min/1.73m² who had ≥1 risk factors for kidney disease. All three patients with an unknown eGFR had ≥1 risk factors for kidney disease. In total 112 patients had an eGFR <60 ml/min/1.73m² and 108 (98.4%) had risk factors for kidney disease. Two patients had no risk factors and would not be identified by risk factor assessment. Of the 30 patients with an eGFR <45 ml/min/1.73m², all were identified through risk factor assessment. No patients who would be classified as being at risk for CIN were missed by either strategy because these patients with an eGFR <60 ml/min/1.73m² had no risk factors. See *table 2* for more details on risk factors for kidney disease.

Direct medical costs

eGFR in all patients with a tenability of 12 months

In 631 (63.0%) patients the eGFR was measured within one month of the intravenous iodinated CECT and we considered these eGFR measurements to be related to the intravenous iodinated CECT.
When we asked patients if they had paid an extra visit to the hospital for the eGFR measurement only, 49 (4.9%) patients answered affirmatively. Of these 49 patients, 35 reported that eGFR measurement took place within one month of the intravenous iodinated CECT, 11 patients reported that they had to pay an extra visit for the sole purpose of eGFR measurement between 1-3 months and 3 (0.3%) between 3-12 months before the intravenous iodinated CECT. In total 645 (631+11+3) eGFR measurements were performed for intravenous iodinated CECT. To calculate direct medical costs we multiplied this by the cost of the eGFR

Table 2. *Risk factors for kidney disease*

Risk factors for kidney disease *n* (%)	**Total study population (*n*= 1001)***	**eGFR ≥ 60 ml/min/1.73m² (*n*= 886)**	**eGFR 45-59 ml/min/1.73m² (*n*=82)**	**eGFR 30-44 ml/min/1.73m² (*n*= 26)**	**eGFR 15-29 ml/min/1.73m² (*n*= 4)**
Age >60 years	576 (57.5)	492 (55.1)	60 (73.2)	20 (76.9)	2 (50.0)
Hypertension	370 (37.0)	302 (34.0)	51 (62.2)	15 (46.2)	2 (50.0)
Use of nephrotoxic medication	301 (30.1)	254 (28.7)	33 (40.2)	12 (46.2)	2 (50.0)
Cardiovascular disease	295 (29.5)	252 (28.4)	29 (35.4)	13 (50.0)	1 (25.0)
Urological/ nephrological history	232 (23.2)	167 (18.8)	39 (47.6)	22 (84.6)	3 (75.0)
Diabetes mellitus	137 (13.7)	112 (12.6)	15 (18.3)	10 (38.5)	-
Use of metformin	89 (8.9)	76 (8.6)	7 (8.5)	6 (23.1)	-
Multiple myeloma/ Waldenström's disease	3 (0.3)	2 (0.2)	1 (1.2)	-	-
Total number of patients with risk factor(s) *n* (%)	807 (80.6)	694 (78.3)	78 (95.1)	26 (100)	4 (100)

***eGFR was missing in 3 patients: these patients could not be categorised; other information was available.**

measurement (€ 6.03); the costs for eGFR measurement were € 3889.35. See *tables 3* and *4* for more details.

eGFR in all patients with a tenability of three months
As mentioned above, in 631 (63.0%) patients the eGFR was measured within one month of the intravenous iodinated CECT. Another 11 patients had to pay an extra visit for the sole purpose of eGFR measurement between 1-3 months. In 144 patients the eGFR was measured >3 months before the intravenous iodinated CECT. With a tenability of three months eGFR would have been measured in another 144 patients.
For this strategy eGFR would have been measured in 786 (78.5%, 631+144+11) patients, multiplied by € 6.03, the cost for eGFR testing would have been: € 4739.58. See *tables 3* and *4* for details.

eGFR in patients with risk factors for kidney disease
When risk factors for kidney disease were assessed, 807 (80.6%) patients had ≥1 risk factors indicating eGFR measurement, multiplied by € 6.03, the costs for eGFR measurement would have been € 4866.21. See *tables 3* and *4*.

Indirect medical costs (travel costs)
eGFR in all patients with a tenability of 12 months
Forty-nine patients (7.6%) paid an extra visit to the hospital for the sole purpose of measuring the eGFR. Thirty-two patients travelled by car over a total distance of 1172.9 km (one way), multiplied by € 0.20, making the cost of the trip € 469.16 (to and from hospital); with the addition of € 3.00 parking costs per visit, the travelling costs were € 565.16. Seven patients used public transportation covering a total distance of 390.1 km (one way), multiplied by € 0.20, costing € 156.04 (to and from hospital). One patient used a taxi over a distance of 13.9 km (one way), multiplied by € 2.00, making the costs (to and from hospital) € 55.60; with the addition of twice € 3.50 starting rate (to and from hospital), the taxi costs were € 62.60. The other ten patients travelled by bicycle or foot (59.9 km one way). The total travelling costs for eGFR measurement were: € 783.80. See *table 5* for more details.

eGFR in all patients with a tenability of three months
If we had maintained a tenability of three months, 60 patients (7.6% of 786) would have travelled to have eGFR measured. At an average of € 783.80/49 per patient (see previous paragraph) this would cost € 959.76. See *table 5* for more details.

eGFR in patients with risk factors for kidney disease
When we extrapolated data for the 807 patients with risk factors for kidney disease (hence an indication for eGFR measurement) we found that 61 (7.6% of 807) patients would have travelled for eGFR testing. At an average of € 783.80/49, multiplied by 61, this would cost € 975.75. See *table 5* for more details.

Table 3. *eGFR measurement*

eGFR available for all patients tenability 12 months		**eGFR available for all patients tenability 3 months***		**eGFR determination after risk assessment****	
eGFR within one month of examination *n* (%)	631 (62.1)*	**eGFR within one month of examination *n* (%)**	631 (62.1)	**Patients with pre-selection risk factors *n* (%)**	807 (80.6)*
eGFR > 1 month *n* (%)	370 (36.9)	**eGFR > 3 month *n* (%)**	144 (14.4)	***NA***	-
Extra visit *n* (after one month)	14*	**Extra visit *n* (%) (between 1-3 months)**	11* (1.1)	***NA***	-
Total eGFR for CT n (%)*	645 (64.4)	***Total eGFR for CT n* (%)***	786 (78.5)	***Total eGFR for CT n* (%)***	807 (80.6%)
Total extra visits n (%)**	49 (7.6% of 645)	***Total extra visits n* (%)****	60 (±7.6% of 786)***	***Total extra visits n* (%)****	61 (±7.6% of 807)***

*** Used for calculation of total eGFR for CT direct costs; ** Used for calculation of indirect costs (see table 4); *** Extrapolated (same percentage as in the first model)**

Table 4. *Direct costs associated with eGFR determination*

eGFR available for all patients tenability 12 months		**eGFR available for all patients tenability 3 months***		**eGFR determination after risk assessment****	
Total eGFR for CT *n* (%)*	645	**Total eGFR for CT *n* (%)**	786	**Total eGFR for CT *n* (%)**	807
Costs €	3,889.35	**Costs €**	4,739.58	**Costs €**	4,866.21

*** Within 1 months and extra visit in > 1 months; ** These numbers were extrapolated from the total patient population**

Table 5. *Travel costs associated with eGFR measurement*

eGFR available for all patients tenability 12 months ***n*** **= 49**			**eGFR available for all patients tenability 3 months*** ***n*** **= 60**	**eGFR test after risk assessment*** ***n*** **= 61**
Means of transportation	**Distance** Km**	**Costs €**	**Costs €**	**Costs €**
Car (*n*=32)	1172.9	565.16	Average travel cost per patient €15.99 *(783.80/49)*	Average travel cost per patient €15.99 *(783.80/49)*
Public transportation (*n*=7)	390.1	156.04		
Taxi (*n*=1)	13.9	62.60		
Bicycle/ by foot (*n*=9)	59.9	0		
Total	1636.8	783.80	959.76	975.75

*** These numbers were extrapolated from the total patient population; **distance was given for one way.**

Indirect non-medical costs (productivity loss)

eGFR in all patients with a tenability of 12 months

We also calculated loss of productivity. Of the 49 patients who had to pay an extra visit to the hospital for the sole purpose of the eGFR measurement 11 (22.4%) patients had to take a leave of absence from work. Eight men were absent for 31 hours in total and 3 women for 14 hours in total. Costs: 31 multiplied by € 32.49 plus 14 multiplied by € 25.49 resulted in a total of € 1364.05. See *table 5*.

eGFR in all patients with a tenability of three months

If we had maintained a tenability of 3 months, we would find that 14 (22.4% of 60) patients would have taken leave of absence. Of these 14 patients there would have been 10 men and 4 women (based on same distribution). This would result in 38 hours and 45 minutes of absence from work for the men and 18 hours and 40 minutes for the women. This would lead to a productivity loss of € 1258.99 for the men and € 482.48 for the women, in total € 1743.20. See *table 6*.

eGFR in patients with risk factors for kidney disease

Extrapolation for the group of patients with risk factors for kidney disease also resulted in 14 patients (22.4% of 61 patients) who would have taken leave of absence, resulting in the same amount of € 1743.20. See *table 6*.

Total costs per strategy

We added all the costs for the population of 1001 patients in whom eGFR was made available either in all patients with tenability of eGFR of 12 months, 3 months or in all patients with risk factors for kidney disease. Total costs if eGFR had been known in all patients with a tenability of 12 months were: € 6037.20 (average € 6.03/patient). If tenability had been three months, the total cost would be € 7442.54 (average of € 7.43/patient).

For the strategy of patient population with risk factors for kidney disease, the total costs were: € 7585.16 (average of € 7.58/patient).

DISCUSSION

Our results suggest that measuring eGFR based on risk factors for kidney disease (pre-selection strategy) is not more cost-effective than eGFR measurement in all patients if the eGFR is tenable for 12 months. Because the patients with an eGFR <60 ml/min/1.73m^2 who were missed by the pre-selection strategy had no risk factors, the risk for CIN can be considered to be comparable with patients with an eGFR ≥60 ml/min/1.73m^2.[2-8] If tenability of eGFR is set at three months, the costs are comparable with the pre-selection strategy.

Arguments for the strategy in which eGFR is available to all patients prior to intravenous iodinated CECT are that it is safer and implementation is fairly easy.[4] However tenability for eGFR of 12 months is rather long and a tenability of three months does not seem as cost-effective. Our results also suggest that when risk factors for kidney disease are assessed preceding eGFR measurement almost all patients with kidney disease (eGFR <60 ml/min/1.73m^2) including all patients with rather severe kidney disease (eGFR <45 ml/min/1.73m^2) are identified, thus this strategy seems equally safe/effective. On the other hand, with an incidence of kidney disease of 11.2% (eGFR <60 ml/min/1.73m^2) and eGFR measurement in 63%, 78% and 80% of the patients, respectively, none of the strategies seem cost-effective. There again, the difference in screening costs per patient of 1-2 euros seems relatively small, but with the increasing number of iodinated CECT examinations annually the cost reduction achieved by more cost-effective screening strategies could be substantial.[1]

Table 6. *Productivity loss associated with eGFR measurement*

eGFR available for all patients tenability 12 months		**eGFR available for all patients tenability 3 months***		**eGFR test after risk assessment***	
Absence from work (m : f = 8 : 3)	***n* =11 (22.4% of 49)**	**Absence from work (m : f = 10 : 4)**	***n* =14 (± 22.4% of 60)**	**Absence from work (m : f = 10 : 4)**	***n* =14 (± 22.4% of 61)**
Men hours	31	Men hours	38.75	Men hours	38.75
Women hours	14	Women hours	18.66	Women hours	18.66
Costs productivity loss		Costs productivity loss		Costs productivity loss	
Men €	1007.19	Men €	1258.99	Men €	1258.99
Women €	356,86	Women €	484.21	Women €	484.21
***Total* €**	1364.05	***Total* €**	1743.20	***Total* €**	1743.20
***These numbers were extrapolated from the total patient population; **distance was given for one way.**					

Since the risk factors mentioned in most guidelines were based on expert opinion or studies describing the relationship with risk factors and serum creatinine instead of eGFR a way to improve cost-effectiveness could be to reduce the number of risk factors in screening for kidney disease in CIN prevention guidelines. This will reduce the number of eGFR measurements and costs. Recent literature suggests that other risk factors are related to kidney disease in patients undergoing intravenous iodinated CECT.[17-19] Utsunomia *et al.* showed that risk factors associated with kidney disease were cardiovascular disease, advanced age (>70 years) and diabetes mellitus in patients undergoing intravenous iodinated CECT without oncological disease.[17] A recent meta-analysis suggests that kidney disease, advanced age (>65 years), use of NSAIDs, malignancy and diabetes are associated with CIN in patients undergoing intravenous iodinated CECT.[18] This could mean that a combination of these risk factors could provide a more specific and thus cost-effective screening tool for patients at risk for CIN and could reduce the number of eGFR measurements.

LIMITATIONS

Our study has some limitations. One limitation was that we had to extrapolate data to enable cost analyses. Hence we do not know in all patients with risk factors for kidney disease if eGFR was measured for the sole purpose of intravenous iodinated CECT.

Another limitation was that we did not know the actual number of patients in whom eGFR was measured for the sole purpose of intravenous iodinated CECT in the strategy in which eGFR should be available in all patients. Because our time frame was rather wide (within one month) it is possible that eGFR was measured for other purposes. The time gap between the interview and eGFR measurement could have introduced a recollection bias, leading to underestimation of the number of extra visits for eGFR measurement.

Our study was performed in an academic medical centre in the Netherlands and costs cannot be directly translated to other (peripheral) hospitals and other countries.

Furthermore we were not able to take into account the labour intensity of the screening strategies. Nonetheless, we do feel that our results give an indication of the potential proportional difference in cost-effectiveness between strategies.

Besides the additional costs of strategy in which eGFR is measured based on risk factors, patients also had to travel more often to the hospital for eGFR measurement. Patients could experience physical and emotional inconvenience. On the other hand, patients could interpret the eGFR measurement as a safety measure and therefore feel safer, this could translate into more convenience. Unfortunately we could not quantify the potential (in)convenience suffered by patients undergoing iodinated CECT, as we used data of one strategy (used in our institute), to extrapolate data for the other two strategies. The (in) convenience would therefore be directly related to the number of visits instead of potential difference in patient population between strategies. We do think that in daily practice clinicians try to take this into account by trying to combine the eGFR measurement with other visits to the hospital.

CONCLUSION

Measuring eGFR in a selected group of patients based on assessment of risk factors for kidney disease seems to cost more but is equally effective/safe compared with a strategy in which eGFR is available for all patients when undergoing intravenous iodinated CECT.

To reduce the cost of either strategy, a more tailored model for patients undergoing intravenous iodinated CECT is needed in order to simplify prevention strategies, thereby reducing the number of eGFR measurements. The recent insights gained with respect to CIN risk factors for intravenous contrast medium for CECT can be instrumental. Perhaps a combination of reducing the number of risk factors in the screening for kidney disease and a tenability period for the eGFR value would achieve a more cost-effective CIN prevention strategy.

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