Point-of-care creatinine tests to assess kidney function for outpatients requiring contrast-enhanced CT imaging: systematic reviews and economic evaluation

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Scientific summary

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Background

Intravenously administered contrast agents are thought to occasionally cause acute kidney injury, particularly in patients with existing kidney disease. There is debate about whether or not low-osmolar and iso-osmolar contrast agents pose any meaningful risk of acute kidney injury. Some guidelines recommend that patients with abnormal estimated glomerular filtration rates (derived from serum creatinine measurements) may need prophylactic intravenous hydration to reduce the risk of post-contrast acute kidney injury or that alternative imaging strategies may be used without the use of a contrast agent. The risk of post-contrast acute kidney injury can be assessed in most hospital patients awaiting a computed tomography scan or procedure. All inpatients should have a recent estimated glomerular filtration rate measurement available as part of other hospital tests, as should many outpatients. However, some outpatients present at their computed tomography scan appointment without a recent estimated glomerular filtration rate measurement. Although a blood sample could be processed by the hospital laboratory, results typically require at least 1 hour to be available. Consequently, rather than being subject to an uncertain risk of post-contrast acute kidney injury, the patient's computed tomography scan appointment may be rescheduled or performed without a contrast agent. Point-of-care devices allow rapid blood sampling and measurement of estimated glomerular filtration rate, enabling post-contrast acute kidney injury risk to be assessed and, if the risk is low, the computed tomography scan appointment to go ahead as planned.

Objectives

To evaluate the clinical effectiveness and cost-effectiveness of point-of-care creatinine tests to estimate kidney function for people who need contrast-enhanced computed tomography imaging in a non-emergency setting and who do not have a recent serum creatinine measurement.

Methods

Assessment of clinical effectiveness

Two systematic reviews were conducted to evaluate the test accuracy of point-of-care creatinine tests and to assess their implementation outcomes and clinical impact. Numerous bibliographic sources, including MEDLINE and EMBASE, were searched from inception to November 2018 for published and unpublished literature. Pragmatic reviews of the risk of acute kidney injury from contrast agents and on prophylactic interventions for post-contrast acute kidney injury were also undertaken.

For test accuracy outcomes, observational studies that compared the results of point-of-care creatinine tests with laboratory-based tests to assess kidney function in a non-emergency setting were included. Studies reporting sufficient data to allow the calculation of diagnostic accuracy estimates (expressed as or allowing calculation of sensitivity and specificity), correlation or measurement bias were included. For clinical and implementation outcomes, any studies of point-of-care creatinine tests to assess kidney function in adults before computed tomography imaging in a non-emergency outpatient setting were included.

Eligible point-of-care devices included StatSensor® devices (Nova Biomedical, Runcorn, UK), i-STAT (Abbott Point of Care, Inc., Princeton, NJ, USA), ABL800 FLEX (Radiometer Ltd, Crawley, UK), ABL90 FLEX (Radiometer Ltd), epoc® (Siemens Healthineers AG, Erlangen, Germany), Piccolo Xpress® (Abaxis, Inc., Union City, CA, USA) and DRI-CHEM NX 500 (Fujifilm Corporation, Tokyo, Japan).

Two researchers independently screened titles and abstracts and full texts. Data extraction and quality assessment were performed by at least one researcher and checked by a second. The quality of diagnostic accuracy studies was assessed using a modified version of the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool. Where sufficient data were available, probabilities of individuals being correctly classified by the point-of-care device according to estimated glomerular filtration rate laboratory reference test measurement categories were estimated within a Bayesian framework using Markov chain Monte Carlo methods. Data were pooled using a fixed-effects model. Results were reported as posterior medians with 95% credible intervals and plotted as density strips.

Economic assessment

A review of full economic evaluations was conducted. Two researchers independently screened the titles and abstracts of all reports identified by the bibliographic searches and all full-text papers subsequently obtained. The main findings were narratively summarised.

A de novo decision model was developed to evaluate the cost-effectiveness of point-of-care testing to assess kidney function, for people who need contrast-enhanced computed tomography imaging in a non-emergency outpatient setting and who present without a recent estimated glomerular filtration rate measurement. The model provides a quantitative framework to link the diagnostic accuracy of point-of-care creatinine tests to short-term costs and consequences (e.g. the impact on cancelled or delayed appointments, use of contrast media with and without intravenous hydration and associated risks such as post-contrast acute kidney injury) and final health outcomes expressed in terms of quality-adjusted life-years. Costs were estimated from the perspective of the NHS and Personal Social Services.

A decision tree cohort approach was used to estimate the costs and health outcomes of alternative testing and treatment strategies, based on:

- an individual's true estimated glomerular filtration rate status
- how these individuals are classified by different testing strategies
- clinical decisions aimed at reducing post-contrast acute kidney injury risk
- the subsequent risk and consequences of post-contrast acute kidney injury.

Fourteen strategies were evaluated, grouped into six general types:

1. laboratory testing only
2. risk factor screening combined with point-of-care testing
3. risk factor screening combined with laboratory testing
4. risk factor screening combined with point-of-care testing and laboratory testing
5. point-of-care testing only
6. point-of-care testing combined with laboratory testing.

Only those point-of-care devices that reported diagnostic accuracy data using estimated glomerular filtration rate thresholds were included (i.e. i-STAT Alinity, ABL800 FLEX and StatSensor).

Results

Diagnostic accuracy

Fifty-four studies were included. The systematic review of test accuracy included 12 studies that reported data for estimated glomerular filtration rates, seven that reported diagnostic accuracy data only for creatinine, and 50 studies that presented data on correlation and/or measurement bias between a point-of-care device and a laboratory reference test.

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Only studies of i-STAT, StatSensor and ABL reported data on diagnostic accuracy. Few studies were available on the epoc and Piccolo Xpress devices, which reported data only on measurement bias or correlation. There were no studies of DRI-CHEM NX 500.

Half of the diagnostic accuracy studies of estimated glomerular filtration rates were considered to be at low risk of bias, although there were some concerns about the applicability of results to the outpatient computed tomography setting in all but two studies.

Results of the estimated glomerular filtration rate data synthesis showed that i-STAT and ABL800/827 devices are more accurate than StatSensor devices at correctly detecting individuals with an estimated glomerular filtration rate of < 30 ml/minute/1.73 m^2 (i.e. better sensitivity). i-STAT and ABL devices also have higher probabilities than StatSensor devices of correctly classifying individuals in the same estimated glomerular filtration rate categories as the reference laboratory test. Additional analyses carried out using adjusted StatSensor data and including only studies that used the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation confirmed these findings.

Of the studies reporting data on creatinine/estimated glomerular filtration rate measurement bias, results from the StatSensor studies demonstrated wide variation in the size and direction of measurement bias. Although potentially important measurement bias was also identified in some studies of i-STAT and ABL devices, in most of these studies the concordance of results was generally better than in most of the StatSensor studies. Owing to limited data, conclusions cannot be drawn about measurement biases for the epoc and Piccolo Xpress devices.

Implementation and clinical outcomes

This review included six studies. The results illustrated variation in practice both in terms of the proportions of patients who do not have a recent estimated glomerular filtration rate result and the management decisions taken when a point-of-care device indicates an abnormal estimated glomerular filtration rate. Evidence from large studies of inpatients suggests no association between contrast and the risk of acute kidney injury in patients with an estimated glomerular filtration rate of ≥ 45 ml/minute/1.73 m^2, although uncertainty exists about whether or not contrast is associated with a small risk in patients with an estimated glomerular filtration rate of < 45 ml/minute/1.73 m^2. There was no evidence to suggest that intravenous hydration is more effective than oral hydration for preventing post-contrast acute kidney injury or the need for renal replacement therapy or reducing mortality.

Economic assessment

No previously published studies met the inclusion criteria for the cost-effectiveness review. One unpublished economic study was provided in academic confidence. (Confidential information has been removed.)

The base-case cost-effectiveness results showed that the strategy with highest net benefit (i.e. appearing to be cost-effective) was a three-step testing sequence that involves initially screening all individuals for risk factors using a questionnaire, then testing those with at least one risk factor with a point-of-care device and using a confirmatory laboratory test for those individuals who screen and test positive with point-of-care testing. Within this testing approach, the point-of-care device with the highest net benefit was i-STAT. However, the differences in the net benefit between the i-STAT and StatSensor devices were found to be extremely small.

Differences in the cost and diagnostic specificity of the individual testing strategies appeared more important drivers than diagnostic sensitivity. The reduction in post-contrast acute kidney injury risk and associated consequences were not major drivers in the model because of the low risk of post-contrast acute kidney injury estimated for this population, the lack of evidence of an increased risk of post-contrast acute kidney injury associated with the use of contrast media and the lack of evidence on the impact of intravenous hydration in reducing the risk of post-contrast acute kidney injury.

The base-case findings on the optimal type of testing strategy appeared robust to a number of alternative assumptions explored using scenario analysis. The key exception to this was when an additional 'no-testing and manage all with contrast-enhanced computed tomography strategy' was included. This strategy was not assessed in the base-case analysis as it was not considered clinically appropriate given current clinical guidelines that advocate testing or risk stratification prior to contrast-enhanced computed tomography scans. The model was also sensitive to the assumption that cancelled or delayed computed tomography would result in the loss of the imaging slot.

Discussion

The systematic reviews used transparent, reproducible and robust methods, and sought to identify all relevant published and unpublished studies. Key review processes were performed in duplicate, which minimised the possibility of reviewer errors and biases. Previously unpublished data from two important studies of diagnostic accuracy based on estimated glomerular filtration rate thresholds were obtained. Studies reporting measurement bias and clinical or workflow outcomes were included. Study quality was evaluated in studies reporting estimated glomerular filtration rate diagnostic accuracy data using a modified version of the QUADAS-2 tool. Appropriate synthesis methods were used to evaluate the accuracy of the devices and provide the inputs needed for the economic evaluation in the form of probabilities. Uncertainty was accounted for, although it was not possible to fully account for between-study differences in results.

Most of the 54 studies that were eligible for inclusion in the systematic review reported only measurement bias or correlation outcomes and so were of limited relevance to the economic modelling part of the assessment. Correlation results data are limited because results that might appear impressive can sometimes hide imperfect agreement between methods.

Some studies were limited by small sample sizes and most studies had few patients with estimated glomerular filtration rates below < 30 ml/minute/1.73 m^2. Although this is reflective of outpatient populations, it limits the data available for analyses based on the more clinically relevant estimated glomerular filtration rate threshold of < 30 ml/minute/1.73 m^2. Few studies directly compared different point-of-care creatinine devices, and estimated glomerular filtration rate diagnostic accuracy data were not available for the ABL90 FLEX PLUS, DRI-CHEM NX 500, epoc and Piccolo Xpress point-of-care devices.

There were few studies that reported data on the impact of point-of-care devices in computed tomography scanning departments on the use (or rates of non-use) of contrast agents for diagnostic procedures nor were there many data on the use of prophylactic treatments or workflow outcomes, such as cancelled appointments. No data were available on clinical outcomes such as need for renal replacement therapy or hospital admissions. The impact of point-of-care testing on these important outcomes is therefore uncertain.

The de novo decision model is the first formal evaluation of the potential clinical benefits, risks and costs of incorporating point-of-care testing to assess kidney function in people who need contrast-enhanced computed tomography imaging in a non-emergency outpatient setting and who present without a recent estimated glomerular filtration rate measurement. The findings suggest that the use of point-of-care devices may reduce costs to the health system arising from unnecessary delays in computed tomography scanning appointments for the majority of individuals. Any savings also need to be considered against the potential risks arising from misclassification. Although the use of point-of-care devices results in a marginal reduction in outcomes compared with a strategy of obtaining a laboratory test measurement for all individuals, the loss in outcomes appears more than offset by the estimated cost savings.

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A potential limitation of the study's findings is the assumption made in the base-case analysis that all individuals will eventually undergo contrast-enhanced computed tomography. This simplification was considered necessary given the limited data available, the heterogeneity in the overall population, including underlying reasons for imaging, and challenges in linking these parameters to individualised clinical decision-making and associated outcomes. The model was also sensitive to assumptions on the proportion of cancelled and rescheduled computed tomography scans. However, an extensive series of scenario analyses were undertaken to explore the potential impact of alternative assumptions on both these parameters.

The finding that a 'no-testing and use of intravenous contrast for all' strategy had the highest net benefit suggests that additional testing costs of either a laboratory reference test or a point-of-care test result may not provide sufficient improvements in patient outcomes to warrant routine testing. Such a strategy is, however, unlikely to be considered clinically acceptable. These findings also need to be considered alongside the limitations of the model assumptions and the uncertainties that remain regarding the effect of contrast media on the risk of post-contrast acute kidney injury, and the benefits of prophylactic management to reduce the risk of post-contrast acute kidney injury.

Conclusions

A three-step testing sequence that involves combining a risk factor questionnaire, point-of-care testing and confirmatory laboratory testing could potentially reduce unnecessary delays or rescheduling of computed tomography scans. This testing approach appears more cost-effective than the current approach that involves obtaining a recent laboratory-based measurement prior to administering contrast media. However, the contribution of intravenous contrast media to the development of acute kidney injury, particularly in patients with an estimated glomerular filtration rate of < 30 ml/minute/1.73 m^2, and the benefits and risks of intravenous hydration prophylaxis in this population remain uncertain. Although uncertainties remain, the study's findings suggest that these risks appear very low and that delaying contrast-enhanced computed tomography scans appears unnecessary for the vast majority of patients.

Studies evaluating the impact of risk stratifying questionnaires on workflow outcomes in computed tomography scanning patients attending without recent estimated glomerular filtration rate results are needed. Further research on the risk of contrast and benefits and harms of intravenous hydration in patients with an estimated glomerular filtration rate of < 30 ml/minute/1.73 m^2 may also be warranted.

Study registration

This study is registered as PROSPERO CRD42018115818.

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This report

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