Development of risk models for the prediction of new or worsening Acute Kidney Injury (AKI) on or during hospital admission

Michael Bedford,[1*] Paul Stevens,[1] Simon Coulton,[2] Jenny Billings,[2] Marc Farr,[3] Toby Wheeler,[1] Maria Kalli,[4] Tim Mottishaw,[5] Chris Farmer[1]

[1]Kent Kidney Research Group (KKRG), East Kent Hospitals University NHS Foundation Trust, Kent and Canterbury Hospital (EKHUFT), Ethelbert Road, Canterbury, Kent. CT1 3NG.

[2]Centre for Health Services Studies (CHSS), University of Kent, Canterbury, Kent. CT2 7NF.

[3]Department of Information, East Kent Hospitals University NHS Foundation Trust, Kent and Canterbury Hospital (EKHUFT), Ethelbert Road, Canterbury, Kent. CT1 3NG.

[4]CCCU Business School, Canterbury Christ Church University (CCCU), North Holmes Campus, North Holmes Road, Canterbury, Kent. CT1 1QU.

[5]Strategic Development, East Kent Hospitals University NHS Foundation Trust (EKHUFT), Royal Victoria Hospital, Radnor Park Avenue, Folkestone, Kent. CT19 5BN.

[*]Corresponding author Michael.bedford@nhs.net

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Scientific Summary

Background

Acute kidney injury (AKI) is a global health issue and is a common clinical problem characterised by an acute decline in renal function, the result of which ranges from small changes in serum creatinine to anuric renal failure requiring renal replacement therapy (RRT). Its prevalence (5-7% amongst inpatients) is increasing, associated with an aging population, and increasing co- morbidity. Patients with AKI have significantly increased in-hospital and 12 month mortality, length of stay, admission to ITU, 30 day re-admission, increase in care on discharge. All hospitalised patients are at risk of AKI, resulting from their presenting disease or subsequent iatrogenic injury. It is often preventable and reversible, however the 2009 National Confidential Enquiry into Patient Outcome and Death (NCEPOD) highlighted systematic failings of identification and management, and recommended risk assessment of all emergency admissions. NICE Guideline 169 suggests research to assess risk of AKI to drive prevention and early recognition.

Aims

1. **Identification of AKI:** Accurately identify and report patients with AKI.
2. **Develop Predictive Models:** Based on factors identified in primary and secondary care records and the admission characteristics of each patient, develop three predictive models to stratify the risk of: **(1)** AKI on arrival in hospital. **(2)** Developing AKI during the admission. **(3)** Worsening AKI if it is already present.
3. **Produce a Clinical Algorithm:** Use the predictive model to develop an algorithm for all patients admitted to hospital to stratify them according to risk of developing AKI.
4. **Integration into Clinical Practice:** Define the most effective way to incorporate the risk model into a clinical decision support system (CDSS) that can be integrated into everyday clinical practice. This will inform the follow on study from this project.

Study Design

This study involved both quantitative and qualitative methodology; Quantitative methodology to: (1) formulate the predictive risk models. (2) validate the risk model in the East Kent population and a second population and NHS Trust (Medway NHS Foundation Trust).

Qualitative methodology was employed to: plan the clinical intervention and clinical decision support system (CDSS) development, and effective integration of the CDSS into everyday clinical care.

Settings

The study population included all patients presenting to the three acute hospitals of East Kent Hospitals University NHS Foundation Trust (EKHUFT); Kent and Canterbury Hospital in Canterbury, William Harvey Hospital in Ashford, and Queen Elizabeth the Queen Mother Hospital in Margate, in the calendar year of 2011. The renal tertiary referral centre is based at Kent and Canterbury Hospital. The secondary validation population included all patients presenting to Medway NHS Foundation Trust.

Participants

Quantitative Analysis: For risk model development and validation in the first population the study included hospital admissions to EKHUFT over the year of 2011, excluding maternity admissions, and elective admissions. For validation in the second population the study included hospital admission to Medway over the same time period and with the same exclusions.

Qualitative Analysis: The sample consisted of six renal consultants for the individual interviews and six outreach nurses who attended the focus group. All consultants worked across the three hospitals within the Trust, and there was representation from all hospitals from the outreach nurses.

Data Collection

Data was extracted from five primary databases at EKHUFT. The hospital episode database (age, sex, co-morbidities, hospital admission and outpatient history), pathology database (relevant pathology tests for example c-reactive protein, white blood cells, microbiology tests, proteinuria testing and including creatinine testing to define AKI and CKD stage), electronic discharge notification database (drug history),and operation database (operative procedures).

Data Analysis

Quantitative: We investigated the use of both Bayesian and traditional regression methods to develop the risk models. In the Bayesian methods we worked out the likelihood function of the data, placed a prior distribution over all the unknown parameters, and used the Bayes theorem to calculate the posterior distribution over all parameters. We selected a normal distribution prior for the unknown coefficients, and within that incorporated the Stochastic Search Variable Selection (SSVS) approach described in George and McCullogh (1993). To proceed to the calculation of the posterior and to inference we used Monte Carlo Markov Chain (MCMC) methods and coded/constructed a Gibbs sampler. We ran the sampler for 200000 iterations with the first 10000 as burn-in.

The traditional methods were performed using ordinal logistic regression and employed robust standard error to account for multiple admissions for some patients. Initially the individual association between each factor and AKI stage was examined individually in a series of univariable analyses. Subsequently the joint association between the factors and AKI stage was examined in a multivariable analysis. A backwards selection procedure was used to retain only the statistically significant variables in the final models.

The developed models were validated in both the EKHUFT dataset and a second population data set at Medway NHS Foundation Trust. The first approach split the validation dataset into risk groups based on the predicted probabilities. Within each risk category, the actual occurrence of AKI was assessed, and compared to the predictions. This assesses both the discrimination and calibration of the model. Secondly the discrimination between high and low risk cases was assessed by calculating the area under the ROC curve. A final set of analyses examined the difference in the observed outcome and that predicted by the model using the Hosmer-Lemeshow test.

Qualitative: The analytical approach taken for the focus group and interviews was that of Flick's (1998) content analysis, whereby themes and subthemes are categorised within a pre-existing template (usually the instrumentation).

Findings

Quantitative: We have defined a clear clinical practice algorithm for risk assessment within the first 24 hours of hospital admission. Quantitative analysis has identified key variables from a large dataset which would be useful to predict acute kidney injury in patients admitted

to hospital. Bayesian methodology enabled prediction of those at low risk of AKI on admission but could not reliably identify high risk patients. Traditional methods to assess risk at admission (model 1) and at 24 hours (model 2) identified a number of key variables which predict AKI both at 24 hours and 72 hours post admission. Subsequent validation demonstrated area under ROC of 0.75 and 0.68 respectively. However, modelling was unable to reliably predict those with worsening AKI, (ROC of 0.53).

The predictive variables included in the first model for the prediction of AKI at the point of admission to hospital were age, previous hospital admissions, primary diagnosis, Charlson co-morbidity score, laboratory variables including CRP, Hb, HbA1c, troponin, proteinuria and baseline eGFR. Other variables included medications and microbiology including blood culture and MSU or CSU. For the second model predicting new AKI at 72 hours the results were similar, however Hb was not a significant predictor, but potassium, magnesium and WBC were. In the second model microbiology and medications were not significant.

Qualitative: The qualitative analysis gave valuable insights into the use of a clinical alerting system for AKI already in operation in clinical practice at the hospitals. The analysis suggested that initial responses to the system appeared encouraging, however there were some issues highlighted with regard to the user-friendliness of the system and the advantages and disadvantages of the timing of access to clinical alerts. The users also voiced concerns with regard to clinical communication and clinical responsibility. This work although of small scale, which may limit its generalizability, has informed the development of a new alerting system and pathway of care at the Trust for AKI which will be employed to deliver the risk modelling from this study into clinical practice.

Conclusion

In our studies we have been able to demonstrate that routinely available data can be used to highlight patients at risk of acute kidney injury both at the point of admission to hospital and following admission. However the methodology used has its limitations and further analysis and testing, including continuous modelling, non-linear modelling and interaction exploration may refine the model further. This study provides valuable evidence of the relationships between key variables available from hospital electronic records, and acute kidney injury. Some of the models may be refined further once physiological data becomes more commonly available across the NHS. We have provided a clear clinical algorithm for risk assessment within the first 24 hours of hospital admission and subsequently. The clinical

algorithm includes a decision matrix and the application of the multivariable analysis to patient data. The qualitative element of this study has also highlighted the complexity regarding the implementation and delivery of alerting systems to the clinical front line.

Recommendations for future research

The next stage of this work is to test these risk models in terms of their clinical, logistic and economic impact in routine clinical practice in a clinical intervention pilot study.

There should also be further work to investigate the development of clinical risk models in different settings (for example elective surgery, or radio-contrast investigations) within clinical practice as we believe a number of risk models we need to employed across the different settings within the secondary care environment. There should also be work to investigate the development of risk models to predict the presence of AKI in patients presenting to their general practitioner in primary care, to guide testing in this setting.

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