Prediction of Hospital Mortality by Changes in the Estimated Glomerular Filtration Rate (eGFR)

Abstract:
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Deterioration of physiological or laboratory variables may provide important prognostic information. We have studied whether a change in estimated glomerular filtration rate (eGFR) value calculated using the Modification of Diet in Renal Disease (MDRD) formula over the hospital admission, would have predictive value. An analysis was performed on all emergency medical hospital episodes (N=61964) admitted between 1 January 2002 and 31 December 2011. A stepwise logistic regression model examined the relationship between mortality and change in renal function from admission to discharge. The fully adjusted Odds Ratios (OR) for 5 classes of GFR deterioration showed a stepwise increased risk of 30-day death with ORs of 1.42 (95% CI: 1.20, 1.68), 1.59 (1.27, 1.99), 2.71 (2.24, 3.27), 5.56 (4.54, 6.81) and 11.9 (9.0, 15.6) respectively. The change in eGFR during a clinical episode, following an emergency medical admission, powerfully predicts the outcome.

Introduction
St James’ Hospital (SJH) is a tertiary referral centre for various specialties, but is on continuous call for emergency medical admissions. In 2002 there was a major reorganisation of acute care with the establishment of an Acute Medical Admissions Unit (AMAU). Following this system change, key quality markers included hospital length of stay, hospital emergency department wait-times, in-hospital mortality and readmissions were improved. Further improvement in the outcomes for unselected emergency medical admissions may be achieved by closer monitoring and early detection of deteriorating patient. Previous studies have shown that deterioration in the clinical status of patients can be anticipated by changes in physiological parameters and laboratory variables. Much work had been completed in this field, focusing on both physiological- and laboratory-derived variables, alone or in combination. This has led to the development of Early Warning Systems tools for ward based patients to identify patients at risk and prevent further deterioration.

Emergency medical patients have frequent blood and biochemistry analyses; on our electronic patient record, there is an automated calculation of the GFR value following each creatinine determination. A more robust estimate of the glomerular function can be made using the Modification of Diet in Renal Disease (MDRD) formula, which was devised in 1999. It uses six variables (age, race, gender, serum creatinine, urea and albumin levels). The MDRD formula to estimate GFR has not been validated in acute kidney injury, however, standing alone; some of the variables used in these equations have been independently shown to predict mortality in an acute setting. We have previously demonstrated that admission eGFR can predict the in-hospital mortality in emergency medical admissions. The aim of this study therefore, was to explore how the eGFR value might change during an acute hospital admission, and whether it could be used to predict in-hospital mortality. The setting was a study of all unselected acute medical emergencies admitted to a large university teaching hospital over a 10-year period between January 2002 and December 2011.

Methods
An anonymous dedicated patient database was created in 2002 to characterise emergency admitted patients, using components from the administration system (PAS), the emergency department database, and the hospital biochemical, haematology and microbiological databases; some discharge and procedural codes were derived from the hospital in-patient enquiry (HIPE) scheme (Table 1). The admission and discharge eGFR values were used to calculate the change in the hospital episode. The extended MDRD equation (MDRD Value = 170 x Sr. Creatinine-0.999 x Age-0.176 x [0.742 if Female] x [1.210 if Black] x BUN-0.176 x Albumin+0.318) was utilized. We categorised patients by any improvement in delta GFR (Group I) or of this variable over the clinical episode: deteriorations were of <= 5 (Group II), > 5 <=10 (Group III), 10 <=20 (Group IV), > 20 <=40 (Group V) and > 40 ml/min/1.73m2 (Group VI). Mortality rate in any in-hospital death at a designated cut-offs; we examined the association of change in eGFR from admission, at designated cut-offs of 24 hr, 72 hr, 7 day, 14 and 30 days on mortality by that point. Descriptive statistics for baseline demographic data included, as appropriate, means / standard deviations (normal distribution) or medians / inter-quartile ranges (IQR) or percentages. Comparisons between categorical variables and mortality were with Chi-square tests. We examined the association between mortality at cut-offs (24 hr, 72 hr, 7 day, 14 day and 30 day) and the following predictor variables: age, change in eGFR over the hospital episode, the O2 saturation and troponin status (all at time of presentation in the Emergency Department).

Results
Renal function over time
The median GFR at admission was 75.3 ml/min/1.73m2 (IQR: 53.8, 97.7); the grouped data suggested an increase following admission being at 24 hr 87.4 ml/min/1.73m2 (IQR: 67.2, 107.6), at 72 hr 85.7 ml/min/1.73m2 (IQR: 64.7, 106.8), at 7 day 80.8 ml/min/1.73m2 (IQR: 59.9, 101.8) and at 30 days 72.5 ml/min/1.73m2 (IQR: 52.9, 93.2). However, within patients different lengths of hospital stay: direct comparisons must be done to establish whether an on a paired basis patients dropped their MDRD value over time. Most patients showed small improvements in MDRD value; the change from baseline to discharge or death value were respectively +1.3, +2.6, +2.8 and +2.2 ml/min/1.73m2 at the sample points of 24, 72 hr, 7 day and 30 days. Patients who died had a much lower GFR at admission 48.9 ml/min/1.73m2 (IQR: 35.4, 69.7) but showed a crucial difference with a substantial fall by day 2 33.5 ml/min/1.73m2 (IQR: 19.9, 59.4) with little further change thereafter. 3 day 36.3 ml/min/1.73m2 (IQR: 26.0, 64.7) - 7 day 38.4 ml/min/1.73m2 (IQR: 28.1, 64.5) and 30 days 40.2 ml/min/1.73m2 (IQR: 21.1, 64.1). For patients who died, the change from baseline to discharge or death value were respectively -3.9, -3.7, -4.2 and -7.5 ml/min/1.73m2 at the sample points of 24, 72 hr, 7 day and 30 days.

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Changes in GFR by group and mortality risk (Figure 1)

We analysed the GFR value by change over the clinical episode. We categorised patients based on the variation of GFR from admission in 6 groups: as any improvement in delta GFR (Group I) or a deterioration of one of five categories: <= 5 (Group II), > 5 <= 10 (Group III), 10 <= 20 (Group IV), 20 <= 40 (Group V) and > 40 ml/min/1.73m^2 (Group VI). These groups respectively contained 53.6%, 23.7%, 8.2%, 7.7%, 5.0% and 1.8% of the patients with mortalities of 4.4%, 4.2%, 6.6%, 9.4%, 15.7 and 24.5%. The unadjusted OR for a 30-day death for the five groups with declines of <=5, >5 < 10, >10 < 20, >20 < 40 and >40 ml/min/1.73m^2, compared with the baseline of an improved GFR, were 0.96 (0.87, 1.06), 1.54 (1.35, 1.74), 2.74 (2.0, 3.52), 4.06 (3.64, 4.54) and 4.06 (3.64, 4.54) respectively.

Risk prediction based on lab data and change in GFR (Figure 2)

We identified an efficient model using only four predictors of 30-day outcome: these were age, change in GFR between admission and end of the hospital episode, troponin status (negative or positive) and O2 saturation level at time of admission. The fully adjusted Odds Ratios for each of the classes of GFR deterioration showed a stepwise increase in risk of 30-day death, compared with those showing no change or an improvement. The prediction was of a high order at each of the time points assessed at 24 hr, 72 hr, 7 days, 14 days and 30 days. The Area under the Receiver Operator Curve at each of these prediction time points were 24 hr 0.94 (0.92, 0.96), 72 hr 0.93 (0.91, 0.94), 7 days 0.91 (0.90, 0.92), 14 days 0.90 (0.89, 0.90) and 30 days 0.88 (0.87, 0.89). The fully adjusted odds ratio vs. improvers at 30 days were OR's of (Group II) 1.42 (95% CI: 1.20, 1.68), (Group III) 1.59 (1.27, 1.99), (Group IV) 2.71 (2.24, 3.27), (Group V) 5.56 (4.54, 6.81), and (Group VI) 11.9 (9.0, 15.6) The model fit across each of the deciles assessed was good, as evidenced by the Hosmer-Lemeshow chi statistic = 8.5 and a non-significant p value of 0.58 indicating no significant deviation between the predicted and observed observations within each of the deciles (Figure 2).

Discussion

Acute kidney injury is not uncommon in emergency medical admission; what our data emphasises is that, for emergency medical admissions, homeostasis of the internal environment is the norm. Blood tests are routinely collected (often daily) in emergency hospitalised medical patients; therefore there is an opportunity to deploy these as a monitoring and an early warning system. A combination of markers, when formalized, then constitute an aggregate score system. Hucker et al suggested that a combination of clinical and biochemical measurements in the accident and emergency department proved the best predictors of hospital mortality based on the logistic regression analyses rather than each of them taken individually. These results were supported by Prytherch et al and Asadollahi et al, both confirming the relationship between admission abnormal laboratory data and a predicted worse outcome in general medical patients. The difficulty is that these studies could require specific knowledge of different scoring system, complex calculation or additional adjustments for age of clinical variables in order to predict the outcome.

Others agree that there are major ramifications for changes in renal function in specific contexts and that even small alteration can have important consequences. Grigorian Shamagian et al demonstrated that renal dysfunction was a powerful predictor of mortality and morbidity in patients hospitalized for CHF, irrespective of left ventricular systolic function. Similarly, Gottlieb et al and Smith et al demonstrated increase in mortality and length of stay with even very small increases in creatinine in patients admitted with congestive heart failure. The limitation of these studies is that they were performed on selected groups of patients, representing all emergency medical admissions over a 10 yr period. Therefore the findings can be applied to all medical patient groups. Nearly 80% of patients, the eGFR will either show no change or improve over the course of the admission. For the remaining 20% of patients, the drop in renal function is exponentially related to the risk of an in-hospital death. It is important to note that we are not considering patients with advanced or deteriorating renal function; as the average eGFR value on admission was 74 ml/min/1.73m^2 (IQR 54 – 98), a threshold cut-off of 5 ml/min/1.73m^2 (Group I) represents a change of 8.7% from baseline. This variation would be at the level that might be considered important in a clinical context.

There has been debate about whether absolute decline in renal function or relative decrease (for example 25%) would provide a better discriminator. This in our view would be a high threshold as only 5.8% of our patients encountered such a deficit, but with a mortality of 50.7% and an OR of 15.5 (95% CI: 13.5 - 17.3) for a 30-day in-hospital death. Thus any significant deterioration in GFR, following an emergency medical hospital admission, must be considered a high-risk event and mandate closer monitoring.
We have previously shown that admission eGFR is a reliable tool to predict mortality following acute medical admission. This study expands on this work by demonstrating any deterioration in the admission eGFR value is an indicator of increased risk of death during that admission. The hope is that a move to standardise of National Early Warning Systems will provide a basis to detect early deterioration in perturbed physiology, initiate corrective action and further improve clinical outcomes. As patients frequently have biochemistry determinations during such an admission, algorithms could be devised to track and trigger with such deterioration. The impact of an automatic laboratory based alerting system, providing feedback to the clinical care process, would be of great interest.

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References