Original Articles

Using the MDRD value as an outcome predictor in emergency medical admissions

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Abstract

Background. Both physiological- and laboratory-derived variables, alone or in combination, have been used to predict mortality among acute medical admissions. Using the Modification of Diet in Renal Disease (MDRD) formula not as an estimate of glomerular filtration rate but as an outcome predictor for hospital mortality, we examined the relationship between the MDRD value and in-hospital death during an emergency medical admission.

Methods. An analysis was performed on all emergency medical patients admitted between 1 January 2002 and 31 December 2008, using the hospital in-patient enquiry system, linked to the patient administration system and laboratory datasets. Hospital mortality (any in-patient death within 30 days) was obtained from a database of deaths occurring during the same period under physicians participating in the ‘on-call’ roster. Logistic regression was used to calculate unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (CI) for MDRD value.

Results. Univariate analysis identified those with MDRD value of <60 as possessing increased mortality risk. Their 30-day mortality rate was 21.63 versus 4.35% for patients without an abnormal value (P < 0.0001) with an OR of 6.07 (95% CI's 5.49, 6.73: P < 0.001). After adjustment for 12 other outcome predictors including comorbidity, the OR was 4.63 (4.08, 5.25: P < 0.0001). Using the Kidney Disease Outcomes Quality Initiative (KDOQI) class, the respective mortality rates by 30 days increased with a lower MDRD value, from 2.8% in KDOQI Class 1 to 48.6% in KDOQI Class 5. Outcome prediction of in-hospital death, at 5 and 30 days with the MDRD, yielded areas under the receiver operator curves of 0.84 (0.83, 0.84) and 0.77 (0.77, 0.78).

Conclusions. Many factors predict survival following an emergency medical admission. The MDRD value offers a novel readily available and reliable estimate of mortality risk.

Keywords: GFR; MDRD; MDRD value; mortality risk; outcome predictor

Introduction

The prediction of mortality among acute medical admissions is something of a ‘holy grail’ in modern medical practice. Much work had been completed in this field, focussing on both physiological- and laboratory-derived variables, alone or in combination [1–6].

The clinical parameters utilized encompass the level of consciousness, blood pressure reading, heart rate, respiratory rate, temperature, oxygen saturation and urine output, while laboratory investigations include full blood count, renal profile, liver profile and other biochemical series. There has been increasing interest in utilizing laboratory data as predictors of hospital mortality. One prospective study has shown that the risk of hospital death could be predicted using routinely available laboratory data during admission to hospital, for unselected general medical patients [4]. A further study of common admission laboratory variables revealed a strong association between deranged laboratory data and subsequent in-patient death. High mortality was associated with severe hyponatraemia, hyperkalaemia, uraemia, leucocytosis and lymphopaenia [5]. These data were further supported by the observation that serum sodium at time of an emergency hospital admission was a powerful predictor of in-hospital mortality [7].

Virtually all patients admitted with an acute medical issue undergo testing of their renal function. In 1999, the Modification of Diet in Renal Disease (MDRD) formula was devised in an attempt to estimate glomerular filtration rate (GFR) [8]. While initially employed in the setting of relatively young patients with stable chronic kidney disease, it has since been validated in a variety of patient cohorts [9–12]. The MDRD formula utilizes six variables—age, race, gender, serum creatinine, urea and albumin levels (Figure 1). Standing alone, some of the variables used in these equations have been independently shown to predict mortality in the acute setting [13–15].
The MDRD formula to estimate GFR has not been validated in acute kidney injury. We proposed using the MDRD value as an outcome predictor following emergency admission to hospital. Hence, the aim of this study was to examine the relationship between MDRD value and short-term (5 and 30 days) in-hospital mortality in a complete set of all unselected acute medical emergencies admitted to a large university teaching hospital over a 7-year period between January 2002 and December 2008.

Methods

Background

St. James’ Hospital (SJH) is a tertiary referral centre for various specialities but is on continuous call for emergency medical admissions in its local Dublin catchment area. All such patients requiring hospitalization, apart from cases admitted directly to the coronary care or intensive care unit, are admitted to the acute medical admissions unit (AMAU), essentially a medical receiving unit dedicated to acute care. The 59-bed capacity of the AMAU is sufficient that with an average of 20 admissions each day, up to 70% of all admissions receive their entire hospital care within this environment.

A patient database, dating from 2002, linked the patient administration system to the Hospital In-Patient Enquiry Scheme (HIPE). HIPE is a national database of coded discharge summaries from acute public hospitals in Ireland. Ireland uses the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; ICD-10 from 2005) for both diagnosis and procedure coding since 1990, with updates every 5 years. Sixty hospitals nationally participate in the system and it is an important information source for research and health service planning activities [16, 17]. Data collected include hospital number, patient’s name, dates of admission and discharge, date of birth, patient gender, area of residence by county, diagnosis—principal and up to nine additional secondary diagnoses; procedures—principal and up to nine additional secondary procedures and consultant responsible for care. The HIPE dataset lists all coded diseases at time of discharge or death, together with procedures and investigations undertaken during the hospital episode. Additional biochemical and haematological data were downloaded from other hospital systems.

Data related to all emergency medical patients admitted to SJH between 1 January 2002 and 31 December 2008 were recorded. Where patients had multiple admissions, to maintain the independence of observations, we based calculations on the last clinical episode; consequently, numbers refer to unique patients rather than total hospital episodes. Mortality was defined as any death recorded within 30 days of the index acute hospital admission.

Statistical methods

Descriptive statistics for baseline demographic data included, as appropriate, means/SD, medians/interquartile ranges (IQR) or percentages. Comparisons between categorical variables and mortality were with chi-square tests. The admission MDRD value was categorized into five groups, based on the Kidney Disease Outcomes Quality Initiative (KDOQI). A stepwise logistic regression analysis examined the association between 30-day mortality and the following predictor variables: age, gender, Major Disease Category (MDC) classification, a prior admission, the triage category at presentation in the Emergency Department, an intensive care unit (ICU) admission, any blood transfusion, the Charlson comorbidity index [18], the impact of the AMAU and MDRD renal calculation. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated for those predictors that significantly entered the model. Statistical significance was at $P < 0.05$ throughout. The analysis software was JMP® (version 7: SAS Institute Inc.).

Results

Patient characteristics

These data related to 20 035 consecutive patients with an emergency acute medical admission in the 7 years between 1 January 2002 and 31 December 2008 and whose hospital episode had been completed or who had died within 30 days (Table 1). Between 2002 and 2008, there was an overall increase of 75.3% (2501 to 4385) in patients admitted annually. There were 1956 such in-hospital patient deaths between 2002 and 2008; the annual mortality decreased from 10.7% in 2002 to 5.3% in 2008, representing a 50.2% relative reduction over 6 years ($P < 0.0001$). The fully adjusted OR for death at 30 days showed a highly significant reduction over that time period [OR 0.42 (95% CI 0.34, 0.52): $P < 0.0001$].

The median length of stay for all patients was 5.4 days (IQR 2.4, 10.3); the 99.5% limit of the length of stay was 29.0 days for this cohort. The median age was 59.9 years (IQR 39.2, 76.1) with the upper 10% boundary at 83.9 years; 48.5% were male. The median GFR estimated by MDRD was 76.4 mL/min/1.73m² (56.4, 95.3). The median values for males ($n = 9719$) and females ($n = 10 316$) were 81.9 mL/min/1.73m² (62.1, 100.9) and 71.0 mL/min/1.73m² (52.1, 89.4), respectively.

AMAU activity and outcomes

Following establishment of the AMAU, there was an overall increase of 75% (2501 to 4385) in patients admitted annually between 2002 and 2008. The 30-day mortality decreased from 10.7% in 2002 to 5.3% in 2008, representing a 50% relative reduction over 7 years ($P < 0.0001$) with a calculated number needed to treat of 18.6.

Mortality for MDRD subsets (unadjusted OR)

We analysed the MDRD value by the KDOQI classification; the respective mortality rates by 30 days increased with declining function (Table 2), from 2.8% in KDOQI Class 1 ($> 90$ mL/min/1.73m²) to 48.6% in KDOQI Class 5 ($< 15$ mL/min/1.73m²). The unadjusted OR for 30-day death were KDOQI Class 1: 0.21 (95% CI 0.18, 0.24), KDOQI Class 2: 0.43 (0.39, 0.49), KDOQI Class 3a: 1.44 (1.27, 1.63), KDOQI Class 3b: 3.21 (2.83, 3.64), KDOQI Class 4: 7.77 (6.75, 8.94) and KDOQI Class 5: 9.88 (7.87, 12.4), respectively.
We adjusted for other known predictors of 30-day hospital mortality (Table 3). All the following significantly predicted death; a previous admission, MDC, a readmission, the triage category in the Emergency Department at presentation, an ICU admission, any blood transfusion, the Charlson comorbidity score and the introduction of the AMAU. After adjustment for 12 outcome predictors, including gender, age, albumin, creatinine and urea in the MDRD (Table 3), the adjusted OR of 30-day death for the highest risk group of emergency admissions (MDRD value < 60) was 4.63 (4.08, 5.25; P < 0.0001). The relationship between the MDRD value and predicted 30-day mortality is shown in Figure 2; the areas under the receiver operator curves to predict 30-day mortality were 0.84 (0.83, 0.84) at 5 days and 0.77 (0.77, 0.78) at 30 days (Figure 3).

**Discussion**

With over 20,000 patients, this is the largest single study to date to evaluate the relationship between the admission MDRD value and mortality in hospitalized general medical patients. The population in this study is unbiased, being composed of consecutive acute emergency medical admissions to a large university teaching hospital over a 7-year period. The data suggested that an admission MDRD value of <60 independently estimated between a 12.3 and 48.6% increased risk of a 30-day death. This level of increased risk of death persisted after adjustment for multiple outcome predictive covariates including MDC, a hospital readmission, the triage category in the emergency room, an ICU admission, any blood transfusion, the burden of comorbidity and the impact of the establishment of an acute admission unit. In our study, ICU admission appeared to be the most important predictor of 30-day mortality with an OR of 7.34 (6.05, 8.91; P < 0.0001). Although not directly comparable, the admission MDRD value of <60 had an OR of 4.63 (4.08, 5.25; P < 0.0001). There appears to be an almost 2-fold increased risk of mortality in patients with KDOQI Class 3b (22.2%) compared to patients with KDOQI Class 3a (12.3%). This highlights that in addition to KDOQI Classes 4 and 5, with OR of 7.77 (6.75, 8.94) and 9.88 (7.87, 12.4), respectively, patients with KDOQI Class 3b should be deemed moderately high risk and monitored closely.

The MDRD equation had been used in a number of different studies with various subsets of patients for prognostication. In patients with cardiovascular disease, there...
have been numerous studies demonstrating that worsening of renal parameters, including estimated GFR, predicts mortality, both in the acute setting and over longer term follow-up [19–21]. In predicting cardiovascular outcomes after myocardial infarction, the risk of death or composite end point of death from cardiovascular causes, congestive cardiac failure, reinfarction, stroke or resuscitation after cardiac arrest increased with declining estimates of GFR. Anavekar et al. [22] had shown that there is a 10% increased risk of death and non-fatal cardiovascular outcomes, for every 10 mL/min decrease of GFR estimated by MDRD, <81.0 mL/min/1.73m². In a population of patients with acute ischaemic stroke, a decreased GFR was associated with higher inpatient mortality, even when adjusted for other predictors of death [23]. Equally, renal dysfunction is a prognostic marker in outcome of patients with peripheral vascular disease [24].

GFR as estimated by MDRD has its limitations. According to pooled databases evaluating the performance of GFR with MDRD, the MDRD study equation displayed little bias for GFR estimates <60 mL/min/1.73m². This holds true in subgroups defined by demographic and clinical characteristics. By contrast, GFR estimates ≥60 mL/min/1.73m² showed greater bias and this varies substantially among subgroups [11]. This prompted Smith et al. [25] to further analysis, concluding that MDRD had failed to recognize increased mortality risks in patients with normal to near-normal GFR (>60 mL/min/1.73m²) as a result of the J-shaped association between MDRD estimated GFR with mortality. These deficiencies have led to the development of a more refined equation to estimate GFR, the Chronic Kidney Disease–Epidemiology Collaboration equation, which addresses in particular the underestimation of GFR at higher values [26].

Our observation has several limitations. As the MDRD equation was not initially designed for outcome prediction, the weighting of the individual variables in the formula may present with some degree of bias. Similarly, it is acknowledged that the estimation of MDRD value on the basis of a solitary set of laboratory data in the acute setting has certain inherent flaws. Nevertheless, one can argue that the MDRD value at a point in time reflects the underlying physiological milieu. Depleted intravascular volume, sepsis and organ-specific toxicity are some of the insults that have a deleterious effect on renal function and which is duly reflected in the MDRD value.

Given that various components of these equations have been shown to be useful in risk estimation [13–15, 25], it is reasonable to posit that a composite parameter would have value in this domain. Our data clearly show that mortality in acute medical patients is closely related to the reciprocal of the MDRD value, that is patients with the lowest MDRD have the highest risk and the relationship is not linear.

The MDRD value can be readily calculated by many laboratory data programmes and we propose that it has significant merit as an easily available tool in risk stratification of medical patients in the acute setting. We would caution that predictions at 30 days, using any combination of physiological or biochemical variables, are less reliable compared with predictions over 5–7 days. With this caveat, we could recommend the MDRD value as risk predictors when estimates of risk are required, and hospital systems could be engineered for specific predictions of outcome for medical patients on admission. This represents a novel use of the MDRD equation not merely an estimate of GFR but rather a predictor of mortality. The generalization of our observations to other groups of ill patients warrants investigation.

Acknowledgements. We wish to recognize the contribution of our consultant medical colleagues and the non-consultant members of the ‘on-call’ teams without which the AMAU initiative could not have progressed. The dedicated contribution of Sr S. Donnelly, her Clinical Nurse Managers and the ancillary professions related to medicine (SCOPE) is gratefully acknowledged.

Conflict of interest statement. None declared.

References

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*Received for publication: 31.3.10; Accepted in revised form: 13.1.11*