Title: A new prognostic model for predicting 30-day mortality in acute oncology patients.

ABSTRACT:

Introduction: Acute oncology services (AOS) provide rapid review and expedited pathways for referral to specialist care for cancer patients presenting in the emergency setting. Routine blood tests may support AOS in providing reliable estimates of prognosis. Thus, we aimed to develop a validated prognostic model of 30-day mortality based on routine blood markers, for predicting an AOS decision to actively treat or palliate patients.

Methods and Materials: Using clinical data from 752 AOS admissions between January 2015 and July 2017, multivariable logistic regression analysis was conducted to develop the 30-day mortality prognostic model. Internal validation and then internal-external cross-validation were used to examine overfitting and generalisability of the model's predictive performance.

Results: Urea, alkaline phosphatase, albumin and neutrophils were the strongest predictors of the outcome. The model was able to separate patients into distinct prognostic groups from the cross-validation (C Statistic: 0.70; 95% CI: 0.64-0.76). The calibration of observed and predicted risks of the model varied by calendar time and therefore admission year was included as a predictor in the model to improve the model calibration, with the final model using the most recent calendar year (2017) to estimate predicted risk.

Conclusion: The developed prediction model, based on routinely available clinical variables, was able to classify patients into distinct prognostic risk groups, which is clinically useful for delivering an evidence based Acute Oncology Service. Collation of data from other AOS centres would allow for the development of a more generalisable prognostic model.

Keywords: Prognosis; Urea; Alkaline Phosphatase; Albumin; Neutrophil; Emergency Service, Hospital; Neoplasms

INTRODUCTION

A large and increasing proportion (24%) of cancer cases in the UK are diagnosed in an acute setting [1, 2]. Following the 2008 *National Confidential Inquiry into Patient Outcomes and Death*, concerns were raised about the quality of care and mortality rate of cancer patients, with only 35% of patients receiving 'good' care [1]. In response, the National Chemotherapy Advisory Group recommended the formation of an acute oncology service (AOS) in all hospitals with an emergency department, providing rapid reviews and expedited pathways for referral to specialist care [3]. AOS teams currently rely on clinical experience, imaging and multidisciplinary discussion. Insight from routine blood tests may support AOS teams in providing faster and more reliable estimates of prognosis, thus accelerating subsequent investigations and referrals.

Whilst an association between blood-based markers and prognosis has been established in specific cancer types [4, 5] established prognostic factors include age, stage, number of metastatic sites, and performance status. However, the use of routine blood tests to predict short-term mortality has not yet been considered within the acute oncology context. The aim of our study was to develop and validate a prognostic model from blood-based markers that is predictive of 30-day mortality in acute cancer patients.

MATERIAL AND METHODS

Data sources and study population

The model was derived from all adult referrals to the acute oncology service of a large tertiary academic hospital, between 1st January 2015 and 31st July 2017 (N=752). For each patient, we extracted information on age, sex, cancer type and dates relating to admission and discharge/death. Electronic patient records were used to obtain blood results from the day of

admission. If blood test results were not available from the day of admission, the next available result within 48 hours was used. Patients were included whether they were referred to the AOS based on a suspected new diagnosis or following complications from a previously diagnosed cancer. However, re-referrals of the same patient were excluded.

Outcome, candidate predictors, missing data and power calculations

The primary outcome of interest was patient mortality within 30-days of hospital admission. The following blood markers, previously shown to be associated with an increased risk of mortality in acute cancer patients were obtained from; urea, creatinine, alanine aminotransaminase (ALT), alkaline phosphatase (ALP), gamma-glytamyl transpeptidase (GGT), albumin, adjusted calcium, C-reactive protein (CRP), white blood cells (WBC), neutrophil–lymphocyte ratio (NLR) and platelet–lymphocyte ratio (PLR) [6].

A multiple imputation model was implemented to replace missing values, using a chained equations approach, containing all remaining 13 candidate predictors as covariates and the outcome of interest (30-day post admission mortality). Imputation was conducted separately by year of admission. We created 25 imputed datasets and combined the estimates using Rubin's rules [7].

On the basis of 141 deaths within 30-days of hospital admission and the minimum of 10 events-per-variable rule of thumb [8], we had an effective sample to consider a maximum of 14 candidate predictors. We therefore considered 11 blood markers, along with sex and age as candidate predictors, and excluded cancer type due to the number of categories and limited sample size. Data pertaining to the reason for referral (i.e. if due to a new suspected case or a complication of a previous case) was of poor quality in the dataset and therefore was not included as a predictor variable.

Statistical analysis for model development

Stata v14 was used for all analyses. The TRIPOD guidance for development and reporting of multivariable prediction models was followed [9]. All data was used for model development, to avoid data splitting [10]. Mortality within 30-days of admission was treated as a binary outcome measure. For derivation of the prediction model, we used a stepwise approach through backwards elimination, beginning with a model that included all predictors, where candidate predictors were excluded from the saturated model based on their statistical significance ($p_{wald}>0.05$). Non-linear relationships between outcome and continuous predictors were considered by identifying, at each iterative step of the stepwise process, the best-fitting fractional polynomial terms [11-13]. The 'risk score' was then formed for predicting the log odds of death within 30-days of admission by using the estimated regression coefficients multiplied by the corresponding predictors included in the final model along with the intercept term. The predicted risk of 30-day mortality was then estimated via the equation: predicted risk = $1/(1+e^{\text{risk score}})$.

Model performance and adjusting for overfitting

The predictive performance of the final model was assessed in terms of the calibration slope, calibration-in-the-large (CIL) and the C statistic. The calibration slope and CIL are an assessment of the relationship between the observed and predicted risks for individuals where ideal values are 0 and 1 respectively. The C statistic represents the probability that for any randomly selected pair of patients of which only one died within 30-days following hospital admission, the patient who died had a higher predicted 30-day mortality risk from the derived model [14]. A C statistic of 0.5 represents no discriminative ability and 1 represents perfect discrimination. The performance of the model was assessed, in terms of these three statistics, within each of the 25 multiply imputed datasets and subsequently pooled using Rubin's rules as suggested by Wood et al. [15] We also assessed the overall calibration of the model using

the Brier score (which can range between 0 and 0.25; lower indicating better model calibration) and graphically by plotting agreement between predicted and observed risks across tenths of predicted risk. To adjust for model overfitting during the development stage, an estimate of a uniform shrinkage factor was obtained (using the method proposed by Van Houwelingen et al. [16]) and multiplied by the original beta coefficients to obtain coefficients adjusted for overfitting [9, 16]. At this stage, the intercept of the model was re-estimated based on the adjusted coefficients to maintain overall model calibration, producing a final model [9].

Internal–External Cross Validation

The generalisability of the developed prediction model beyond the dataset used for its development is extremely important. The optimal method to examine this would be to apply the derived model to an independent external dataset and assess its predictive performance. However, due to the limited availability of an appropriate independent dataset, internal–external cross validation was conducted to further assess the model performance [17, 18]. This internal−external approach involved cross-validation, omitting data from one of each of the three calendar years in turn and re-developing the model, using the same approach as outlined above, within the data from the two remaining calendar years. The following steps were taken; 1) Using the same model development strategy, a model was developed on data from two of the three calendar years and the beta coefficients from the model predicting 30-day mortality were obtained, 2) The predictive performance of the model from step 1. was assessed within the third 'external validation' calendar year data in terms of accuracy of predicted risk by means of the calibration slope, CIL and the C statistic measures and finally 3) Steps 1-2 were repeated until 'external validation' was assessed for each of the three calendar years' datasets. Overfitting was assessed in each round of the cross-validation, a

uniform shrinkage factor was obtained [9, 16] and applied to the beta coefficients from step 1. Calibration slope, CIL and C statistic measures derived from this procedure for each of the studies were then pooled and estimated via a random effects meta-analysis to assess the heterogeneity across studies (using with the τ^2 statistic estimated using the Mantel-Haenszel method). The pooled estimates of the calibration slope, CIL and C statistic measures provide insight into whether there appears to be a time-trend in the performance of the model across the three calendar years. Should there be evidence of a time-trend in the performance statistics (i.e., the performance of the model varies within each round of cross validation and the pooled estimates indicate poor predictive performance), the final model developed in the entire dataset will be re-fitted including calendar year as a continuous covariate. The 'risk score' (equation for predicting the 30-day risk mortality) will then be based on the coefficients of this re-fitted model using the most recent calendar year, 2017, to derive predictions. As described above, a uniform shrinkage factor will be used (using the method proposed by Van Houwelingen et al. [16]) to adjust the beta coefficients from this re-fitted model, providing a final prediction model.

RESULTS

Study population

Data on 752 (48% female) adult referrals to our AOS between January 2015 and July 2017 was analysed. A summary of the key participant characteristics is presented, by sex and overall, in Table 1. Blood marker levels were similar amongst both sexes, with the exception of creatinine and GGT, for which levels were higher in males compared to females. The type of cancer did not markedly differ by sex, with the exception of Brain/CNS and Lung which had greater representation amongst males (Table 1). Our derivation data had missing information for some blood markers (Table 1), particularly for GGT (58% missing), which

was therefore excluded as a candidate predictor. Table 2 presents the patient characteristics by outcome (i.e. 30-day mortality). Those who died within 30-days were on average, 6 years older, and had elevated average levels of the majority of blood markers compared to those who survived this period (Table 2).

Model development, performance measures, and internal-external cross validation

Within the study timeframe, there were 141 deaths (18.8%) within 30-days from admission. Of the thirteen candidate predictors considered, four were included in the model selected by the development process, namely; urea, ALP, albumin and neutrophils. Non-linear terms were required for each of these predictors with the exception of albumin (Table 3). Table 4 shows the apparent predictive performance of the model from the internal validation and the performance under the internal–external cross validation process. The model, demonstrated good apparent predictive performance for 30-day mortality (C statistic = 0.77; 95% confidence interval = 0.73 to 0.81) and was, as expected, perfectly calibrated in the development data (apparent slope =1, apparent CIL = 0). The Brier score from the model was 0.13, indicating good apparent model calibration. This is confirmed by the calibration plot, assessing agreement between observed and predicted risk (Figure 1). A uniform shrinkage factor of 0.9558 was required to adjust predictor coefficients in the developed model for overfitting after which the constant term was re-estimated to ensure overall model calibration (Table 4). The internal–external cross validation procedure suggested good generalisability in terms of the models discriminative ability (Table 5), but poor in terms of the calibration (slope and CIL) where there was evidence of a clear time-trend in the model's calibration performance (Table 5, Supplementary Table 1). The developed model was therefore re-fitted in the complete dataset to include admission year as a continuous covariate before a uniform shrinkage factor was estimated and applied to the model coefficients. The most recent

calendar year of 2017 was used to obtain the "risk score" and the corresponding 30-day mortality risk prediction equation (Figure 2).

Sensitivity analyses were conducted to assess the predictive performance of the developed model within sub-groups of sex (Supplementary Table 2, Supplementary Figure 1) and cancer type (Supplementary Table 3). These results demonstrated that the predictive performance of the model was largely similar across both sexes and also by cancer type, albeit with less precision for cancers with fewer cases in this study.

DISCUSSION

We found that levels of urea, ALP, albumin and neutrophils on admission can be combined in a model to predict 30-day mortality of acute oncology patients (Figure 2) with good discriminative ability. Calibration of observed and predicted risks varied by calendar year, and thus the development of the "risk score" and the corresponding 30-day mortality risk prediction equation included admission year as a predictor. To our knowledge, this is the first time a prognostic model has been developed in this way to quantify absolute risk of 30-day mortality in a heterogenous acute oncology population presenting in an emergency setting.

Knowing the likelihood of survival may help medical teams expedite further investigations or palliative care referrals [3]. Coping with either the complications of cancer or a new diagnosis is a trying time for patients, with many often asking for estimates of their mortality or whether any treatment can be given. Alongside clinical expertise, histopathological, and radiological input, a score to predict 30-day mortality would support clinicians in discussions with patients about their prognosis. The developed model could be used to estimate risk of

30-day mortality very rapidly, in order to aid these conversations and support the decision-making process related to intervention or palliation.

This study has a number of strengths. The cohort contained a sufficient number of individuals over a three-year period for the testing of 13 candidate predictors of short-term mortality adhering to the 10 events-per-variable rule of thumb [8]. Backwards selection is not always the preferred method for variable selection due to the likelihood of overfitting; however, the assessment of overfitting in this case appears to be minimal. Furthermore, backwards selection was used in the selection process to try and account for all correlations between candidate predictors in the modelling procedure. The blood markers used in the predictive model are readily tested as part of the admissions pathway and will incur no additional costs. The data was collected recently and therefore holds continued relevance. The discriminative ability of the model is good across each of the calendar years' with no suggestion of a time trend from the cross-validation. Although, the calibration of individual predicted risk from the model with observed risks was poor and suggested a clear trend over time in performance. However, admission year was included as a predictor in the final risk score equation and the most recent year of 2017 used for predictions to account for this trend. To represent the breadth of referrals made to AOS teams, the study population includes both new diagnoses, as well as referrals due to treatment-related and cancer-related complications. While we were unable to ascertain the proportions of the new suspected cases in the study population, as the specific referral details was of poor quality (missing or not recorded accurately), this information was available from a sub-sample of the study population (N=466), where 69% were referred based on a new suspected case. Therefore, generalisability of this model to those with complications from a previous cancer diagnosis should be done with caution. A lack of sufficient data lead to the exclusion of GGT as a candidate predictor.

A further limitation is that the study population only includes patients at a single London hospital and thus may not represent the wider population. This sample includes both solid and liquid cancers, which behave differently, with haematological malignancies representing just 6.4% of the sample. While this proportion is lower than the average proportion of haematological cases estimated in the UK of 9.1% [19], it is reflective of the existence of a dedicated referral pathway for haematological patients within this trust. Studies in a larger haematological sample would provide further insight. Amongst male patients the most common cancers in male patients were lung, urological and gastric cancers with breast, lung, gastric and gynaecological cancers being the most common amongst females. These rankings generally are in line with the national statistics for the UK, where prostate, lung and bowel cancers as most prevalent in men and breast, lung and bowel cancer most prevalent in women, but suggests that the study population is under-representative of bowel cancer [19]. The prevalence of CNS malignancies (6.4%) in the sample is proportionally higher than expected when comparing to national incidence statistics (3%) [19].

A previously developed prognostic model assessing patient survival in an oncology setting based upon blood markers, the mGPS scoring system, contained just CRP and albumin as significant predictors of survival [20]. However, this study used a scoring system approach which assigns a value of 0 or 1 to the patient based on whether they had abnormal or normal blood marker levels for CRP and albumin; individuals with a total score of 2 are considered to be at the highest risk and those with a score of 0 considered to have the lowest risk [20]. This approach, whilst providing a simple bed-side method for clinicians to assess survival, is generally not recommended as a large amount of information is lost when simply grouping individuals based on a cut-off of the mentioned blood markers [9]. When this scoring method

was applied to our dataset and compared with the predicted risks from our developed model, the median predicted risk of 30-day mortality was 7% amongst those with an mGPS score of 0, 11% with an mGPS score of 1 and 26% for those with an mGPS score of 2. However, 53% of all individuals in our study population were assigned a score of 2 from the mGPS, indicating poor discriminative ability of the mGPS scoring approach.

Urea has previously been shown to be an independent predictor of 30-day mortality post-oesophagectomy [21] and post-colectomy for colon cancer [22]. Underlying theories include treatment-related nephrotoxicity [23], and an association between glomerular disease and malignancy. Furthermore, a meta-analysis of 242,953 all-cause mortality outcomes concluded that ALP and GGT may screen for individuals at high risk of dying from all-causes [24]. Raised ALP has been associated with cancer recurrence and overall survival [25].

Serum albumin is well established as a marker of poor outcome in the critically ill and an independent prognosticator in cancer [26]. A large prospective study of 21,118 patients showed that the 30-day mortality of emergency patients with hypoalbuminaemia was three-times higher than that of patients with normal levels [27], with serum albumin predicting a patient's ability to tolerate aggressive anticancer therapy [28].

The mechanism of cancer-related neutrophilia includes extrinsic factors such as infection, bone marrow infiltration, and corticosteroids [29], as well as direct causes such as the production of hematopoietic colony-stimulating factors and inflammatory cytokines by tumours [30]. In our study, indices such as NLR and PLR did not feature in the prognostic model of mortality but have previously been associated with survival [6].

We chose to quantify absolute risk of 30-day mortality; however, investigation into 60-day and 90-day mortality may be warranted. As more data is collected, a long-term aim would be to predict overall survival, as achieved by models developed in renal cell carcinoma and laryngeal cancer [31-32]. Futher work is needed to derive cut-offs based on predicted risks from this developed model. Due to the lack of an available external dataset and to avoid data splitting, the full dataset was used to develop the model which was then validated using an internal-external cross-validation method. Collaboration with other AOS teams would provide more data to develop a more accurate model and allow for further validation.

CONCLUSION

A new prediction model has been developed to quantify absolute risk of 30-day mortality in acute cancer patients presenting in an emergency setting. It comprises of routine blood markers: urea, albumin, ALP and neutrophils, which can be taken at initial presentation. This model could serve as the basis for real-time decisions on whether intervention or palliation is most appropriate. Collating data from other UK AOS centres would allow for the extension of such a modelling approach to develop a more accurate model which may be more generalisable to a wider UK setting.

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Table 1: Descriptive statistics of the key participant characteristics and blood markers, by sex and overall

Variable	Male (N=391)		Female (N=361)		Overall (N=752)	
	N	Median (LQ-UQ)	N	Median (LQ-UQ)	N	Median (LQ-UQ)
Death within 30days	67	-	74	-	141	-
Age (yrs)	391	70.0 (59.0-79.0)	361	72.0 (61.4-81.1)	752	71.0 (60.6-80.1)
Urea (mmoll)	391	7.0 (4.8-10.0)	359	6.0 (4.5-9.0)	750	6.5 (4.6-9.5)
Creatinine (umol/L)	390	84.0 (68.0-112.0)	361	66.0 (54.0-94.0)	751	76.0 (59.0-107.0)
ALT (IU/L)	330	24.0 (16.0-49.0)	326	21.0 (13.0-35.0)	656	23.0 (15.0-43.0)
ALP (IU/L)	361	106.0 (78.0-204.0)	347	104.0 (79.0-163.0)	708	106.0 (78.0-177.0)
Albumin (g/L)	362	31.0 (26.0-36.0)	349	32.0 (27.0-36.0)	711	32.0 (27.0-36.0)
Calcium (adjusted) (mmol/L)	297	2.5 (2.4-2.6)	293	2.5 (2.4-2.6)	590	2.5 (2.4-2.6)
CRP (mg/dL)	362	38.1 (8.1-102.5)	334	33.0 (7.1-90.4)	696	35.0 (7.7-96.0)
WBC (x 10^9/L)	388	10.4 (7.5-13.2)	359	9.5 (6.8-12.9)	747	10.0 (7.2-13.1)
Neutrophils (x 10^9/L)	387	7.3 (5.3-10.8)	359	7.5 (4.7-10.4)	746	7.3 (5.0-10.6)
NLR	388	6.6 (3.9-12.0)	360	5.6 (3.5-9.6)	748	6.0 (3.7-10.9)
PLR	387	221.7 (152.9-406.7)	360	230.7 (149.2-362.8)	747	224.6 (152.4-381.4)
GGT (IU/L)	166	113.5 (36.0-365.0)	148	80.5 (30.0-241.0)	314	92.5 (34.0-319.0)
Cancer Type (N,%)						
Brain/CNS	33 (8.4)		15 (4.2)		48 (6.4)	
Breast	-		53 (14.7)		53 (7.1)	
Colorectal	26 (6.7)		25 (6.9)		51 (6.8)	
Gynaecological	-		35 (9.7)		35 (4.7)	
HPB	28 (7.2)		22 (6.1)		50 (6.7)	
Haematological/Lymphoma	25 (6.4)		28 (7.8)		53 (7.1)	
Head/Neck	6 (1.5)		5 (1.4)		11 (1.5)	
Lung	92 (23.5)		61 (16.9)		153 (20.4)	
Melanoma	7 (1.8)		4 (1.1)		11 (1.5)	
Oesophago-gastric	47 (12.0)		35 (9.7)		82 (10.9)	
Urological	61 (15.6)		66 (18.3)		127 (16.9)	
Other	66 (16.9)		12 (3.3)		78 (10.4)	

Footnote: CNS = Central Nervous System, HPB = Hepato Pancreatic Biliary. Other group consists of cancers of unknown primary, and referrals that resulted in no malignancy being identified

Table 2: Descriptive statistics of the key participant characteristics and blood markers, by 30-day mortality

Variable	Death within 30-days (N=141)		Survived past 30-days (N=611)	
	N	**Median (LQ-UQ)**	**N**	**Median (LQ-UQ)**
Age (yrs)	141	76.0 (66.1-84.0)	611	70.0 (59.9-79.6)
Urea (mmoll)	140	8.4 (5.8-13.7)	610	6.1 (4.5-8.6)
Creatinine (umol/L)	141	85.0 (58.0-123.0)	610	74.5 (59.0-101.0)
ALT (IU/L)	126	30.0 (16.0-74.0)	530	21.0 (14.0-37.0)
ALP (IU/L)	134	147.0 (96.0-337.0)	574	101.0 (74.0-153.0)
Albumin (g/L)	134	27.0 (23.0-33.0)	577	32.0 (28.0-37.0)
Calcium (adjusted) (mmol/L)	112	2.5 (2.4-2.6)	478	2.5 (2.4-2.6)
CRP (mg/dL)	135	76.0 (27.7-150.0)	561	28.0 (5.8-79.4)
WBC (x 10^9/L)	140	11.8 (8.6-15.8)	607	9.5 (7.0-12.6)
Neutrophils (x 10^9/L)	140	9.0 (5.3-11.9)	606	7.1 (5.0-10.3)
NLR	140	7.5 (4.4-13.4)	608	5.9 (3.6-10.5)
PLR	140	226.3 (148.3-430.4)	607	223.8 (152.9-365.4)
GGT (IU/L)	73	243.0 (80.0-667.0)	241	75.0 (26.0-239.0)
Cancer Type (N,%)				
Brain/CNS	3 (2.1)		45 (7.4)	
Breast	8 (5.7)		45 (7.4)	
Colorectal	10 (7.1)		41 (6.7)	
Gynaecological	7 (5.0)		28 (4.6)	
HPB	10 (7.1)		40 (6.6)	
Haematological/Lymphoma	3 (2.1)		50 (8.2)	
Head/Neck	2 (1.4)		9 (1.5)	
Lung	44 (31.2)		109 (17.8)	
Melanoma	1 (0.7)		10 (1.6)	
Oesophago-gastric	18 (12.8)		64 (10.5)	
Urological	11 (7.8)		103 (16.9)	
Other	24 (17.0)		67 (11.0)	

Footnote: Other group consists of cancers of unknown primary, and referrals that resulted in no malignancy being identified

Figure 1: Calibration plot assessing agreement between observed and predicted risk across tenths of predicted risk before adjusting model for overfitting

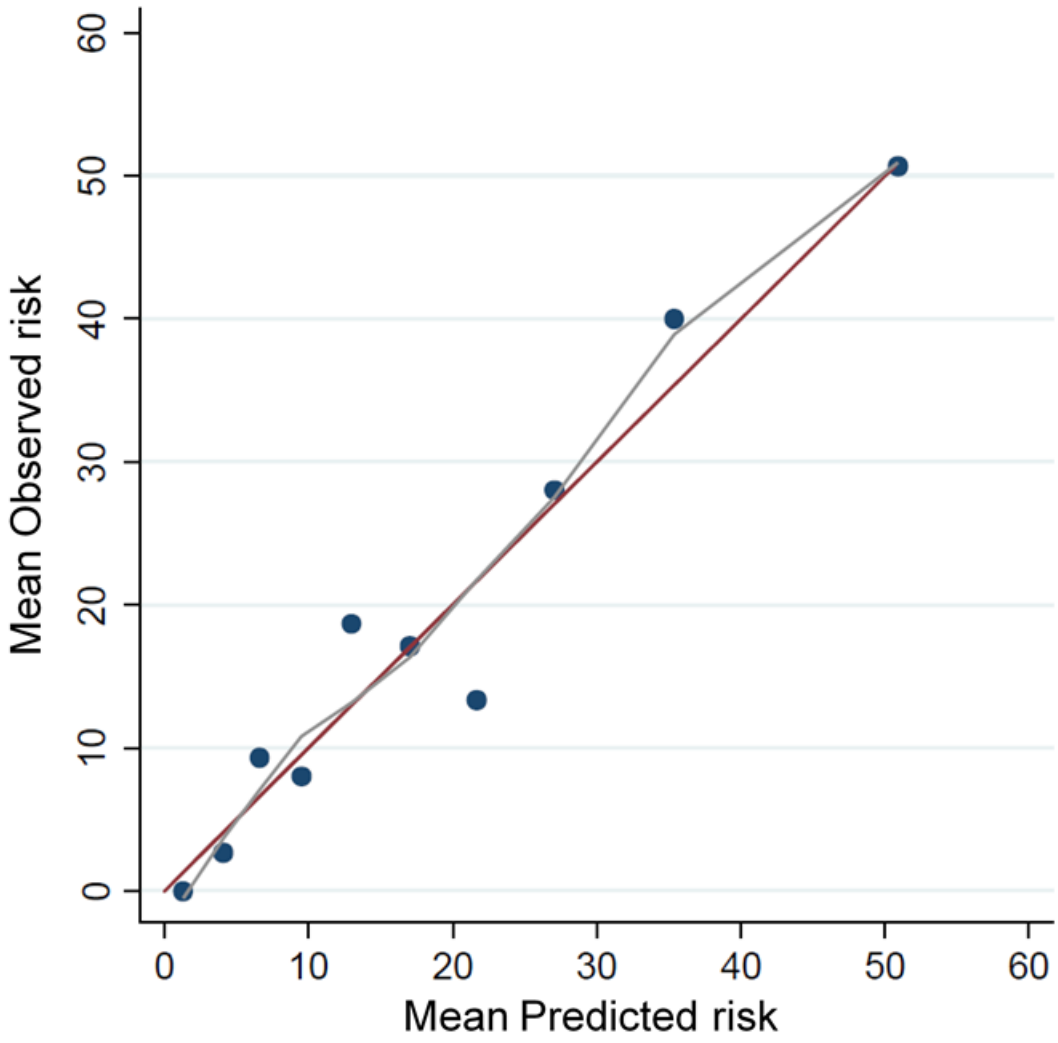

Figure 2: Final developed risk score from a logistic regression model to predict 30-day mortality

Risk Score:

$= -0.051*(\text{Urea}/100)^{-1} - 0.006*(\text{ALP}/1000)^{-2} - 0.068*\text{Albumin} + 0.486*(\text{Neutrophils}/10)^{3}$

$-0.610*((\text{Neutrophils}/10)^{3} * \ln(\text{Neutrophils}/10)) + 0.135 *\text{Admission Year} - 271.457$

$= -0.051*(\text{Urea}/100)^{-1} - 0.006*(\text{ALP}/1000)^{-2} - 0.068*\text{Albumin} + 0.486*(\text{Neutrophils}/10)^{3}$

$-0.610*((\text{Neutrophils}/10)^{3} * \ln(\text{Neutrophils}/10)) + 0.135 *(2017) - 271.457$

$= -0.051*(\text{Urea}/100)^{-1} - 0.006*(\text{ALP}/1000)^{-2} - 0.068*\text{Albumin} + 0.486*(\text{Neutrophils}/10)^{3}$

$-0.610*((\text{Neutrophils}/10)^{3} * \ln(\text{Neutrophils}/10)) + 1.8731415$

Predicted 30-day mortality = $(1/1+e^{-\text{Risk Score}}) * 100$

Units are: mmol/L for urea, IU/L for ALP, g/L for albumin, 10^9/L for neutrophils

Example:

For a patient presenting with: Urea = 4mmol/L, ALP = 80IU/L, Albumin = 30g/L, Neutrophils = $5x10^9$/L

Risk score = $-0.051*(4/100)^{-1} - 0.006*(80/1000)^{-2} - 0.068*30 + 0.486*(5/10)^{3} -0.610*((5/10)^{3} * \ln(5/10)) + 1.8731415$

$= -0.051*(0.04)^{-1} - 0.006*(0.080)^{-2} - 2.04 + 0.486*(0.5)^{3} - 0.610*((0.5)^{3} * \ln(0.5)) + 1.8731415$

$= -1.275 - 0.9375 - 2.04 + 0.0608 + 0.0529 + 1.8731415$

$= -2.2656585$

Therefore predicted 30-day mortality = $(1 / 1 + e^{-\text{Risk Score}}) * 100 = 1 / (1 + e^{2.2656585}) *100 = 9.40\%$