Derivation and Validation of a Simple, Accurate & Robust Prediction Rule for Risk of Mortality in Patients with *Clostridium difficile* Infection.

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Introduction

Clostridium difficile **is a Gram positive, anaerobic, spore forming, rod shaped bacterium, associated with nosocomial infection. Symptoms of infection range from asymptomatic carriage, mild diarrhoea and from moderate to fulminant pseudomembranous colitis (PMC). According to the National Office of Statistics, *C. difficile* related deaths accounted for 1.1% of all deaths in England and Wales between 2006 and 2010 with patients over 65 years having a particularly high incidence of mortality**

Study Aim and Method

Aim -

This study aimed to identify a prediction rule to stratify hospital inpatients at initial diagnosis of infection according to risk of all-cause mortality.

Method-

Univariate, multivariate and decision tree analysis was used to deduce a prediction rule from over 186 variables; retrospectively collated from clinical data for 213 patients

Statistical Inferences

• Independent K-Median, Chi-Square and Means Tests were used to find variables independently associated with all-cause mortality.

Variables were combined in a multinomial logistical regression model and the following variables were seen to significantly contribute to the model -

• Serum albumin levels (g/L) (P= 0.000),

• Respiratory rate (resps /min) (P=0.002)

• C-reactive protein (mg/L) (P=0.034)

• White cell count (mcL) (P=0.049)

• Variable contribution to both CDI and non-CDI related mortality was also assessed (Table 1)

Table 1

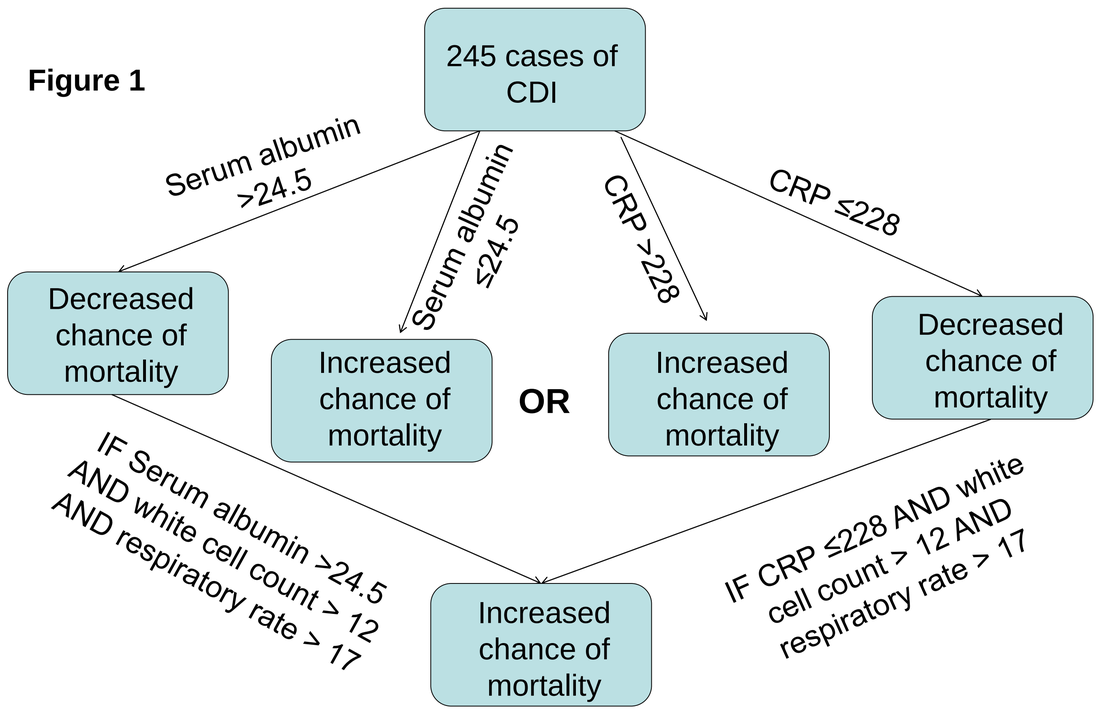
All cause Mortality		Sig.	Exp(B)	95% Confidence Interval for Exp(B)	
				Lower Bound	Upper Bound
CDI related mortality	Intercept	0.566			
	Respiratory Rate	0.003	1.222	1.070	1.395
	Albumin	0.001	.801	.703	.914
	White Blood Cell Count	0.025	1.046	1.006	1.088
	C-Reactive Protein	0.020	1.009	1.001	1.017
Non-CDI related mortality	Intercept	0.618			
	Respiratory Rate	0.007	1.186	1.048	1.342
	Albumin	0.004	.844	.751	.948
	White Blood Cell Count	0.877	1.005	.947	1.066
	C-Reactive Protein	0.074	1.007	.999	1.015

-2Log Likelihood =166.3 (χ^2= 58.6, df=8, P=0.000), Nagelkerke R^2=40.5, Pearson Chi-square Test; P=0.996.

Classification and Regression Tree Analysis

Classification and Regression decision tree analysis (figure 1) was used to determine the threshold of the variables which best classified test data into the mortality outcome

Figure 1



• A points score was devised (figure 2) and tested on all cases in the derivation cohort and an independent (validation) cohort (Bhangu *et al*. (2010)[1] (table 2)-

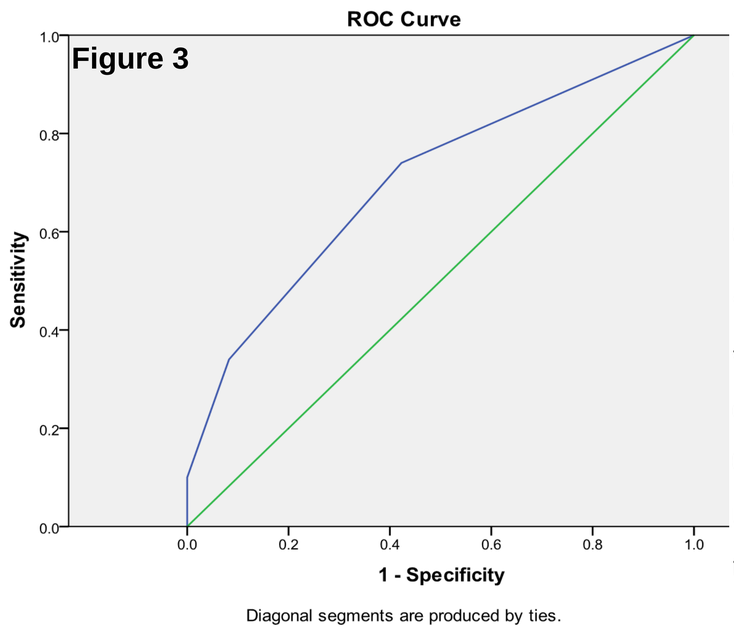
Figure 2

- 1 point for a Serum Albumin level ≤ 24.5 (g/L),
- 1 point for a CRP level >228 (mg/L)
- 1 point for a combination of WCC >12 (mcL) and respiratory rate >17 (resps/min).

Table 2

	Prediction rule Risk Score on Derivation Cohort (N=244)		Prediction rule Risk Score on Validation Cohort (N=154).	
Score	Mortality Risk	Count (number of cases)	Mortality Risk	Count (number of cases)
0	10.4 %	13/125	20.9 %	9/43
1	23.3 %	20/86	37.1 %	23/62
2	42.9%	12/38	54.3%	25/46
3	100 %	5/5	66.7 %	2/3

Figure 3



• ROC analysis of the rule in the derivation cohort revealed an AUC of 0.754 (P=0.00; 95% CI: 0.670-0.837) (figure 3)

• ROC analysis of the rule in the validation cohort revealed an AUC of 0.653 (P=0.001 95% CI: 0.565-0.741), *However the prediction rule used to obtain this score was missing the variable respiratory rate

Conclusion

The use of the prediction rule in a clinical setting could facilitate the way in which clinicians are able to effectively manage a patient with CDI, perhaps prompting a more aggressive treatment regime if a high risk of mortality is identified. The prediction rule is simple and could be used by non-specialists to consider mortality risk.

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References

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