Comorbidity and intensive care outcome – a multivariable analysis 2C01, 3C00

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Decisions regarding admission to intensive care are made considering both the physiological state of the patient and the burden of comorbidity. Despite many retrospective cohort studies looking at isolated comorbidities, there has been little work to study multiple comorbidities and their effect upon intensive care outcome. In this retrospective cohort analysis, detailed comorbidity and demographic data were gathered on 1,029 patients from the West of Scotland and matched to both unit and hospital mortality at 30 days. Logistic regression was performed to investigate the factors associated with death within 30 days at both hospital and unit level. Variables with a p-value <0.25 at the univariable level were considered in a multivariable model. Variable selection for the multivariable modelling was carried out using backward selection and then replicated using forward selection to check for model stability. A modelling tool was constructed for both unit and hospital mortality at 30 days. This modelling has shown significant odds ratios for hospital death for alcoholic liver disease (OR 4.83), age (1.03), rheumatological diseases (1.93) and functional exercise tolerance prior to admission (3.08). Results from this work may inform a national prospective study to validate the modelling tool on a wider population.

Keywords: *comorbidities; intensive care; outcomes; modelling; prognostication*

Introduction

Comorbidity is a significant factor as a consideration when assessing patient suitability for admission to the intensive care unit (ICU), due to its impact on survival from critical illness. Since the inception of modern intensive care as a specialty, there has been interest in the ability of clinicians to predict outcome at the time of admission. The knowledge could be used to appropriately allocate expensive resources and accurately communicate risks to patients and relatives. The last thirty years has seen numerous models emerge, from 'snapshot' methods such as the APACHE (Acute Physiology and Chronic Health Evaluation) series,[1] to evolving scores such as SOFA (Sepsis-related Organ Failure Assessment)[2] that can be used to follow physiological deterioration. There has been much debate over how much weight should be given to the acute physiological state of patients admitted to ICU, and how important the pre-existing comorbid conditions of a patient are. The APACHE score has gone through four iterations and has included points for chronic health to reflect pre-existing comorbidity, but those represent severe forms of disease such as New York Heart Association (NYHA) Class 4 heart failure. The APACHE series are only validated following 24 hours of intensive care admission, and as such have limited utility for prognosticating prior to admission. More modern scoring systems such as APACHE-IV and SAPS 3 (Simplified Acute Physiology Score)[3] give a greater weighting to comorbidity, in recognition of the shortcomings of older scoring systems, but we continue to use APACHE-II in Scotland to provide information for predicted mortality.

Scoring systems or predictive models based purely on comorbidities are rarely used, an example being the Charlson Comorbidity Index (CCI), which is almost 25 years old.[4] This performs well against physiological scores when using receiver operating characteristic (ROC curve) analysis, despite having been derived from non-ICU populations.[5]

Scotland has areas of major socio-economic deprivation. Deprivation is associated with poorer health and life expectancy.[6] This is evident in Scotland, with a lower life expectancy and higher rates of heart disease, cancer, alcohol addiction and suicide.[7] Even within Scotland, there is wide variation in socio-economic deprivation and its effect on health. For example, between the most affluent and most deprived areas of Glasgow there is a difference in life expectancy of 28 years.[8]

In this study we investigated whether multiple comorbidities not severe enough to be counted in scoring systems such as APACHE-II, have an effect upon intensive care outcome. The utility of a predictive model that eschews APACHE-II is that it could be used at the time of referral, without requiring physiological data gathered after intensive care admission.

Methods

A prospective case note review was conducted for 1,073 patients admitted to the Glasgow Royal Infirmary (GRI) ICU between October 2008 and November 2010. The ICU admission dataset collected for all admissions includes all comorbidities present at the time of admission. Only index

	n(%)	Median (IQR) length of stay	% hospital death within 30 days	% unit death within 30 days
Age group	1,029 (100%)	1 (2-7)	30.2	24.3
<30	107 (10.4%)	1 (1-5)	14.0	12.1
30-39	123 (12.0%)	1 (2-5)	16.3	13.0
40-49	170 (16.5%)	1 (3-9)	22.4	18.2
50-59	177 (17.2%)	1 (2-6)	33.3	29.4
60-69	214 (20.8%)	1 (3-8)	35.5	29.0
70+	235 (22.8%)	1 (2-6)	43.0	31.5
missing	*3 (0.3%)*	*1 (1-14)*	*66.7*	*66.7*
Sex	1,029 (100%)	1 (2-7)	30.2	24.3
Female	410 (39.8%)	1 (2-6)	29.3	24.4
Male	619 (60.2%)	1 (3-7)	30.9	24.2
SIMD decile*	1,029 (100%)	1 (2-7)	30.2	24.3
1	397 (38.6%)	1 (2-6)	31.7	25.9
2	185 (18.0%)	1 (3-8)	29.7	25.4
3	98 (10%)	1 (2-9)	27.6	26.5
4	62 (6%)	1 (2-4)	32.3	21.0
5	79 (7.7%)	2 (4-7)	29.1	21.5
6	44 (4.3%)	1 (3-7)	20.5	11.4
7	36 (3%)	2 (2-7)	33.3	25.0
8	34 (3%)	1 (2-5)	26.5	14.7
9	61 (5.9%)	1 (2-7)	36.1	29.5
10	27 (2.6%)	1 (3-7)	25.9	22.2
missing	*6 (0.6%)*	*1 (3-7)*	*16.7*	*16.7*
Smoking	1,029 (100.0%)	1 (2-7)	30.2	24.3
No	453 (44.0%)	1 (2-7)	28.7	23.0
Yes	576 (56%)	1 (3-6)	31.4	25.3
Drugs	1,029 (100.0%)	1 (2-7)	30.2	24.3
No	881 (85.6%)	1 (2-7)	31.2	24.6
Yes	148 (14%)	1 (3-7)	24.3	22.3
Employment	1,029 (100.0%)	1 (2-7)	30.2	24.3
No	622 (60.4%)	1 (2-6)	30.7	24.6
Yes	407 (40%)	1 (2-7)	29.5	23.8
ET NYHA†	1,029 (100.0%)	1 (2-7)	30.2	24.3
1	589 (57.2%)	1 (2-6)	19.7	16.5
2	269 (26%)	1 (3-7)	40.1	31.6
3	149 (14%)	1 (2-8)	52.3	40.9
4	21 (2.0%)	1 (2-4)	42.9	33.3
missing	*1 (0.1%)*	*2*	*0.0*	*0.0*
No. of meds	1,029 (100%)	1 (2-7)	30.2	24.3
0	202 (20%)	1 (2-6)	18.8	15.8
1-3	316 (30.7%)	1 (2-5)	27.5	22.5
4+	509 (49.5%)	1 (3-7)	36.3	28.7
missing	*2 (0%)*	-	*50.0*	*50.0*

Table 1 Categorical demographic data as related to hospital and unit 30-day outcome. Values are number (proportion).
*SIMD – Scottish Index of Multiple Deprivation
†ET NYHA – Exercise tolerance, New York Heart Association

admissions were used for this study, with 44 readmissions during the study period excluded. Paper notes, admission letters, primary care summaries and information on the electronic patient record were all checked as part of this process. This project received Caldicott Guardian approval. It was also discussed with the Local Research Ethics Service (West of Scotland) who agreed that Research Ethics Committee review was not required.

GRI is a university teaching hospital, serving an inner-city area with significant socio-economic deprivation. At the time of this study the GRI ICU was a nine-bedded mixed unit, receiving tertiary referrals from the region including acute severe pancreatitis, burns and major trauma. Historically 66% of admissions to the ICU at Glasgow Royal come from areas considered to be among the most deprived in Scotland. The ICU is equipped with electronic data recording and all outcome data are collected and entered on record by a dedicated member of staff.

The recording of multiple comorbidities mandated a pragmatic approach. With the exception of more defined subgroups, such as NYHA class, to fulfil most subgroups required a diagnosis to be mentioned within the medical record or clear supporting evidence (such as obstructive pulmonary function tests without bronchodilator effect for example), which has led to the comorbidity groups including a wide spectrum of disease states.

The patient's Scottish Index of Multiple Deprivation (SIMD) data zone was derived using the SIMD 2009 report, which also allocated the data zone into deciles.[9] The report identifies small area concentrations of deprivation across Scotland. The population in each data zone is similar in number but each is assessed in seven domains: income, employment, health, education, skills and training, housing, and geographical access and crime.

ICU and hospital survival data were collected from WardWatcher (Critical Care Audit Ltd, Ilkley, UK) the national Scottish intensive care audit database. This collects demographic and outcome data on every ICU admission in Scotland. This database also calculates APACHE-II scores for all appropriate admissions.

Statistical methods

The 1,029 patients suitable for APACHE II scoring from a database of 1,073 patients were considered for analysis. Furthermore, patients without a suitable value recorded for each covariate considered in the modelling were excluded from all modelling. The covariates for which there were missing values, together with the number of patients involved were as follows: age (3), number of medications (2), SIMD decile (6), NYHA performance status (1). This involved a total of 12 patients leaving 1,017 available for modelling.

Logistic regression was performed to investigate the factors associated with death within 30 days at both hospital and unit level. Variables with a p-value <0.25 at the univariable level were considered in a multivariable model. Variable selection for the multivariable modelling was carried out using backward selection and then replicated using forward selection to check for model stability. Asthma was not considered in any

	n(%)	Median (IQR) length of stay	% hospital death within 30 days	% unit death within 30 days
APACHE II score	1,029 (100%)	1 (2-7)	30.2	24.3
<10	111 (10.8%)	1 (1-3)	4.5	2.7
10-14	246 (23.9%)	1 (2-6)	11.8	7.3
15-19	220 (21.4%)	1 (2-6)	23.2	16.8
20-24	192 (18.7%)	1 (3-8)	42.2	33.9
25-29	146 (14.2%)	1 (4-11)	46.6	39.0
>30	114 (11.1%)	1 (3-8)	67.5	61.4
Ischaemic heart disease	1,029 (100%)	1 (2-7)	30.2	24.3
No	764 (74.2%)	1 (2-6)	27.1	21.5
Yes	265 (25.8%)	1 (3-7)	39.2	32.5
Peripheral vascular disease	1,029 (100%)	1 (2-7)	30.2	24.3
No	943 (91.6%)	1 (2-7)	29.0	23.5
Yes	86 (8.4%)	1 (3-6)	44.2	32.6
Cerebrovascular disease	1,029 (100%)	1 (2-7)	30.2	24.3
No	963 (93.6%)	1 (2-7)	29.9	24.2
Yes	66 (6.4%)	1 (3-6)	34.8	25.8
Hypertension	1,029 (100%)	1 (2-7)	30.2	24.3
No	760 (73.9%)	1 (2-7)	27.5	22.5
Yes	269 (26.1%)	1 (2-7)	37.9	29.4
Atrial fibrillation	1,029 (100%)	1 (2-7)	30.2	24.3
No	966 (93.9%)	1 (2-7)	30.1	24.2
Yes	63 (6.1%)	1 (2-7)	31.7	25.4
COPD*	1,029 (100%)	1 (2-7)	30.2	24.3
No	862 (83.8%)	1 (2-6)	27.1	21.7
Yes	167 (16.2%)	2 (3-7)	46.1	37.7
Thromboembolic disease	1,029 (100%)	1 (2-7)	30.2	24.3
No	1,004 (97.6%)	1 (2-6)	30.1	24.0
Yes	25 (2.4%)	1 (3-9)	36.0	36.0
Alcoholic liver disease	1,029 (100%)	1 (2-7)	30.2	24.3
No	935 (90.9%)	1 (2-7)	27.2	21.3
Yes	94 (9.1%)	1 (3-8)	60.6	54.3
Pancreatitis	1,029 (100%)	1 (2-7)	30.2	24.3
No	939 (91.3%)	1 (2-6)	30.4	24.3
Yes	90 (8.7%)	1 (3-10)	28.9	24.4
Inflammatory bowel disease	1,029 (100%)	1 (2-7)	30.2	24.3
No	1,003 (97.5%)	1 (2-7)	30.1	24.3
Yes	26 (2.5%)	1 (3-8)	34.6	23.1
Diabetes	1,029 (100%)	1 (2-7)	30.2	24.3
No	881 (85.6%)	1 (2-6)	28.5	23.2
Yes	148 (14.4%)	1 (3-8)	40.5	31.1
Obesity	1,029 (100%)	1 (2-7)	30.2	24.3
No	931 (90.5%)	1 (2-6)	29.6	23.3
Yes	98 (9.5%)	1 (3-9)	35.7	33.7
Rheumatological and dermatological disorders	1,029 (100%)	1 (2-7)	30.2	24.3
No	964 (93.7%)	1 (2-7)	28.8	23.1
Yes	65 (6.3%)	1 (3-7)	50.8	41.5
Malignancy	1,029 (100%)	1 (2-7)	30.2	24.3
No	872 (84.7%)	1 (2-7)	29.1	23.5
Yes	157 (15.3%)	1 (2-5)	36.3	28.7
Hepatitis C	1,029 (100%)	1 (2-7)	30.2	24.3
No	981 (95.3%)	1 (2-6)	29.9	24.1
Yes	48 (4.7%)	1 (4-9)	37.5	29.2
Asthma	1,029 (100%)	1 (2-7)	30.2	24.3
No	937 (91.1%)	1 (2-7)	31.8	25.8
Yes	92 (8.9%)	1 (2-7)	14.1	8.7
Congestive cardiac failure	1,029 (100%)	1 (2-7)	30.2	24.3
No	1,009 (98%)	1 (2-7)	30.1	24.3
Yes	20 (2%)	1 (2-6)	35.0	25.0
Interstitial lung disease	1,029 (100%)	1 (2-7)	30.2	24.3
No	1,019 (99%)	1 (2-7)	29.6	23.8
Yes	10 (1%)	3 (5-9)	90.0	70.0
Hepatitis B	1,029 (100%)	1 (2-7)	30.2	24.3
No	1,021 (99%)	1 (2-7)	30.0	24.1
Yes	8 (1%)	1 (4-8)	62.5	50.0
HIV status†	1,029 (100%)	1 (2-7)	30.2	24.3
No	1,026 (100%)	1 (2-7)	30.2	24.3
Yes	3 (0%)	3 (5-5)	33.3	33.3

Table 2 Categorical comorbidity data as related to hospital and unit outcome. Values are number (proportion).
*COPD – chronic obstructive pulmonary disease; †HIV – human immunodeficiency virus

modelling due to the relatively small number of unit deaths within 30 days in asthma sufferers. In addition the effects of congestive cardiac failure, interstitial lung disease, hepatitis B and HIV status were not considered in the modelling due to the small number of patients with those comorbidities. Patients were followed up to discharge and it was assumed that those discharged from hospital before 30 days were alive at 30 days.

The linearity of continuous variables on the log odds scale for each of the two death outcomes was checked using the user-defined program 'nlcheck' in Stata. The calibration and

discrimination of the models was evaluated using Hosmer-Lemeshow tests and areas under ROC curves respectively.

All analysis was performed using Stata v.11 (2009, Statacorp, College Station, Texas). The 5% level was used to determine statistical significance.

Results

In total, 1,073 patients were included in data collection, with 1,029 patients put forward for logistic regression (only patients with APACHE-II scoring were eligible) using the selected comorbidity and demographic data. This gave figures of 24.3% and 30.2% respectively for unselected unit and hospital mortality. **Tables 1 and 2** detail the raw data of each demographic and comorbidity variable collected by unit and hospital outcome; totals not equalling 1,029 are due to incomplete data sets.

The mean age at admission was 54.4 years (standard deviation (SD) 17.4) and 62.3% of the sample were male. The average median length of stay was two days (interquartile range (IQR) 1-7), with a median APACHE-II score of 21 (IQR 13-25) at 24 hours.

Table 3 details the univariable modelling of unit and hospital 30-day outcome. **Tables 4 and 5** contain the results of multivariable logistic regression modelling for hospital and unit outcome respectively. On initial testing, the models of unit death were found to be a poor fit to the data. Therefore they were each fitted again without the variable with the least significant effect on the outcome. In the model with APACHE II score, this was obesity, and in the model without APACHE II score, this was rheumatological and dermatological disorders. **Table 5** displays only the revised models.

For both models the strongest associated variable was alcoholic liver disease (ALD), with mortality odds ratios (ORs) of 5.12 for unit outcome, and 4.83 for hospital outcome. Exercise tolerance as represented by NYHA classification was represented in both models, as was age, with a year increase in age carrying an OR of 1.02 for unit outcome and 1.03 for hospital outcome. The unit model includes chronic obstructive pulmonary disease (COPD) with an OR of 1.60, while the hospital model includes the category of rheumatological and dermatological disorders, with an OR of 1.93.

Table 6 details the results of calibration and discrimination tests for each of the models. Each model discriminated well, with the models including APACHE II score unsurprisingly being able to discriminate better than the corresponding models without APACHE II scores. Possible reasons for the lack of fit evident in the previous two unit death models are multiple co-linearity between variables and sensitivity to the choice of groupings used for the goodness of fit test.

Discussion

As far as we can establish, this is the most complete published comorbidity dataset in the modern ICU setting, with complete follow-up to hospital discharge or death. Data were collected on serial admissions to minimise selection bias, and therefore there were no admission/exclusion criteria.

Assuming that survival to hospital discharge is the primary outcome variable of interest, these results reveal an insight into the role of comorbidity. APACHE-II score was statistically associated with outcome, despite being an outcome score that is only recorded at 24 hours, which therefore can be heavily affected by short-term physiological derangement amenable to modulation by treatment. Another hypothesis would be that the use of a more frequently measured scoring system like SOFA might show a stronger association with outcome. As described above, APACHE-II is only validated for use after 24 hours in intensive care, and as such is unavailable to help prognostication prior to admission.

ALD has the strongest statistical association in the entire dataset, both in terms of unit death and hospital death with a multivariable OR of 5.12 for unit death and 4.83 for hospital death. We used a necessarily pragmatic definition, which encompasses a broad spectrum of disease. Despite this, the regression association is very strong, and reflects the wide-ranging physical effects of alcohol damage. Due to the nature of the communities served by our hospital, there is a strong prevalence of alcohol abuse and this is reflected by the development of the Glasgow Alcoholic Hepatitis Score.[10] Unit outcomes have been looked at using smaller cohorts, and generally patients with underlying Child's-Pugh stage 3 disease are not admitted to intensive care due to their poor prognosis. This allied with the data above would suggest that even mild forms of ALD carry a significant burden both within the ICU and beyond.

Age is a non-modifiable factor that is easy both to measure and to compare when looking at intensive care outcomes. The UK is no different from other developed nations in having an ageing population that has benefited from improvements in public health and preventative medicine, which as a result will make more demands upon health care as a whole. A previous multivariable analysis looked at patients admitted to intensive care following surgery, and found no significant effect on mortality with increasing age, although the presence of multi-organ failure carried a poor prognosis.[11] This may be explained by the selection process of elderly patients for emergency surgery, which applies physiological and comorbid triage prior to operation. The hospital model may underestimate mortality in the elderly, as longer admissions are seen in the elderly who may survive a brief stay in ICU but then have a further deterioration while still in hospital due to impaired physiological reserve, and are either declined for readmission to ICU or not considered for re-referral by parent teams.

The NYHA functional classification is a simple way of grading the effect of heart failure, ranging from the absence of symptoms while engaged in normal activity up to those who experience cardiac symptoms while at rest.[12] We originally collected both NYHA class and metabolic equivalent of tasks performed (METs). We defaulted to NYHA alone when it became clear that the subjective variance in gauging METs was too high to supply meaningful results. This in itself carries the problem that the NYHA status was originally specific to chronic heart failure, but in practice its utility as a simple measure of cardio-respiratory insufficiency outweighed these considerations. Previous studies have shown conflicting results when correlating functional status with outcome, with several only identifying severe dependence with poor outcome. Our

	Univariable			
	Hospital death within 30 days		Unit death within 30 days	
	OR (95%CI)	p-value	OR (95%CI)	p-value
APACHE II score	1.14 (1.12-1.17)	<0.001	1.15 (1.12-1.17)	<0.001
Ischaemic heart disease	1.75 (1.30-2.35)	<0.001	1.78 (1.30-2.43)	<0.001
Peripheral vascular disease	1.83 (1.16-2.89)	0.009	1.45 (0.89-2.36)	0.133
Cerebrovascular disease	1.29 (0.76-2.18)	0.347	1.12 (0.63-1.98)	0.702
Hypertension	1.61 (1.20-2.16)	0.002	1.43 (1.04-1.96)	0.026
Atrial fibrillation	1.11 (0.64-1.92)	0.714	1.10 (0.61-1.97)	0.759
Chronic obstructive pulmonary disease	2.31 (1.64-3.24)	<0.001	2.21 (1.55-3.14)	<0.001
Thromboembolic disease	1.40 (0.61-3.23)	0.432	1.91 (0.83-4.43)	0.129
Alcoholic liver disease	4.06 (2.61-6.30)	<0.001	4.32 (2.79-6.69)	<0.001
Pancreatitis	0.89 (0.55-1.45)	0.652	0.96 (0.58-1.61)	0.891
Inflammatory bowel disease	1.09 (0.47-2.55)	0.842	0.78 (0.29-2.10)	0.621
Diabetes	1.65 (1.15-2.37)	0.007	1.43 (0.97-2.10)	0.071
Obesity	1.30 (0.84-2.02)	0.242	1.65 (1.05-2.59)	0.029
Rheumatological and dermatological disorders	2.55 (1.54-4.23)	<0.001	2.38 (1.42-3.98)	0.001
Malignancy	1.41 (0.98-2.02)	0.062	1.32 (0.90-1.94)	0.153
Hepatitis C	1.41 (0.77-2.57)	0.260	1.31 (0.69-2.48)	0.411
Age	1.03 (1.02-1.04)	<0.001	1.03 (1.02-1.03)	<0.001
Male gender	1.11 (0.85-1.47)	0.438	1.03 (0.77-1.38)	0.857
SIMD decile		0.852		0.454
SIMD decile 2 *vs* decile 1	0.91 (0.62-1.34)	0.642	0.98 (0.66-1.46)	0.915
SIMD decile 3 *vs* decile 1	0.79 (0.48-1.30)	0.355	1.00 (0.60-1.66)	0.992
SIMD decile 4 *vs* decile 1	1.03 (0.58-1.82)	0.923	0.76 (0.40-1.46)	0.414
SIMD decile 5 *vs* decile 1	0.85 (0.50-1.45)	0.549	0.74 (0.41-1.34)	0.323
SIMD decile 6 *vs* decile 1	0.56 (0.26-1.19)	0.131	0.37 (0.14-0.96)	0.041
SIMD decile 7 *vs* decile 1	1.08 (0.52-2.23)	0.835	0.96 (0.44-2.10)	0.914
SIMD decile 8 *vs* decile 1	0.85 (0.38-1.88)	0.680	0.53 (0.20-1.42)	0.207
SIMD decile 9 *vs* decile 1	1.22 (0.69-2.14)	0.492	1.20 (0.66-2.18)	0.543
SIMD decile 10 *vs* decile 1	0.76 (0.31-1.83)	0.536	0.82 (0.32-2.09)	0.679
Smoking	1.14 (0.87-1.50)	0.340	1.14 (0.85-1.53)	0.366
Drugs	0.71 (0.47-1.06)	0.094	0.88 (0.58-1.34)	0.561
Employment	0.96 (0.73-1.26)	0.753	0.98 (0.73-1.31)	0.885
ET NYHA score		<0.001		<0.001
ET NYHA 2 *vs* 1	2.72 (1.98-3.75)	<0.001	2.32 (1.65-3.26)	<0.001
ET NYHA 3 *vs* 1	4.56 (3.11-6.69)	<0.001	3.55 (2.39-5.28)	<0.001
ET NYHA 4 *vs* 1	3.07 (1.26-7.45)	0.013	2.55 (1.00-6.48)	0.050
Number of regular medications		<0.001		<0.001
1-3 regular medications *vs* none	1.64 (1.06-2.54)	0.025	1.55 (0.97-2.47)	0.064
>3 regular medications *vs* none	2.47 (1.65-3.68)	<0.001	2.14 (1.39-3.29)	0.001

Table 3 Univariable logistic regression modelling of unit and hospital death.

	Hospital death within 30 days			
	with APACHE II score		without APACHE II score	
	OR (95%CI)	p-value	OR (95%CI)	p-value
APACHE II score	1.12 (1.10-1.15)	<0.001		
ET NYHA score		<0.001		<0.001
ET NYHA 2 *vs* 1	1.95 (1.35-2.81)	<0.001	1.84 (1.31-2.59)	<0.001
ET NYHA 3 *vs* 1	3.05 (1.98-4.69)	<0.001	3.08 (2.05-4.63)	<0.001
ET NYHA 4 *vs* 1	1.88 (0.69-5.14)	0.216	2.32 (0.92-5.86)	0.075
Alcoholic liver disease	3.50 (2.10-5.81)	<0.001	4.83 (3.00-7.78)	0.001
Age	1.02 (1.00-1.03)	0.006	1.03 (1.02-1.04)	<0.001
Rheumatological/dermatological disorders			1.93 (1.12-3.34)	0.018

Table 4 Hospital death after multivariable logistic regression, with and without APACHE II.

	Unit death within 30 days			
	with APACHE II score		without APACHE II score	
	OR (95%CI)	p-value	OR (95%CI)	p-value
APACHE II score	1.14 (1.11-1.17)	<0.001		
ET NYHA score		0.003		0.002
ET NYHA 2 *vs* 1	1.64 (1.11-2.42)	0.014	1.50 (1.04-2.17)	0.032
ET NYHA 3 *vs* 1	2.25 (1.43-3.55)	<0.001	2.31 (1.50-3.54)	<0.001
ET NYHA 4 *vs* 1	1.53 (0.53-4.40)	0.430	1.86 (0.70-4.93)	0.211
Alcoholic liver disease	3.49 (2.12-5.76)	<0.001	5.12 (3.19-8.19)	<0.001
COPD	1.54 (1.02-2.33)	0.040	1.60 (1.09-2.34)	0.017
Age			1.02 (1.01-1.04)	<0.001

Table 5 Unit death after multivariable logistic regression, with and without APACHE II.

results show that a poor functional exercise performance prior to admission was associated with a poorer outcome with incremental increases in mortality. The lack of significance of NYHA IV versus NYHA I is most likely a spurious result created by the small (<2%) prevalence in the sample of class IV patients.

Obese patients are prone to multiple chronic health conditions including an increase in prevalence of diabetes mellitus and these patients consume more primary and secondary healthcare resources than their normal weight counterparts, and incur difficulties in the delivery of care.[13,14] Previous work in the area of intensive care has remarked upon the potential 'paradoxical epidemiology' where obese patients with chronic disease states did better than their lighter counterparts, and some advocate the idea of a U-shaped curve with both extremes of BMI faring poorly in the intensive care setting.[15] Our study showed a weak association with unit mortality but not in-hospital mortality, which was removed on removing obesity as one of the weakest variables; this may be due to the way obesity was classified, as a binary variable rather than using objectively measured BMI with multiple groups. This may have led to missing an underlying signal where, as in previous studies, the higher extreme of BMI was associated with increased mortality.

Model	Hosmer-Lemeshow test p-value	Area under ROC curve
Hospital deaths within 30 days with APACHE II	0.747	0.809
Hospital deaths within 30 days without APACHE II	0.564	0.739
Initial unit deaths within 30 days with APACHE II	0.023	0.817
Initial unit deaths within 30 days without APACHE II	0.042	0.724
Revised unit deaths within 30 days with APACHE II	0.197	0.815
Revised unit deaths within 30 days without APACHE II	0.752	0.714

Table 6 Hosmer-Lemeshow values and ROC curve analysis for unit and hospital models.

COPD was associated with unit but not hospital mortality on multivariable analysis, even after removing APACHE-II scoring. Previous studies have highlighted the 'prognostic pessimism' shown by intensive care clinicians to patients with COPD,[16] and suggested these patients be admitted for non-invasive and invasive ventilation. Follow-up articles have compared the poor outcomes seen in UK hospitals to international study populations, and have queried whether this is due in part to low rates of intensive care admission.[17] Our findings examined COPD as a comorbidity alone, and not specifically as the reason for admission. COPD is associated with poor five-year survival rates and is often seen in combination with other chronic diseases caused or exacerbated by smoking.

An unexpected finding was the effect of rheumatological and dermatological disorders on outcome. Multivariable analysis showed both an effect on hospital and unit outcome, but the effect on unit outcome was removed from the initial unit model when poor fit and calibration was shown. This category was used to describe patients with multi-system disorders requiring long-term pharmacological therapy for their disease. Previous work has identified similar patients as having markedly increased unit mortality, under-represented by their scores in models such as APACHE-II or SAPS.[18] Putative reasons include lack of physiological reserve as well as the multi-system iatrogenic effects of immunosuppressive and immunologically active therapy. Interestingly, this study only identified patients with such disorders in their medical history, rather than as the cause of their admission.

Scotland has many areas of major socioeconomic deprivation and this has been clearly linked to worsened life expectancy. One may assume that those living in deprived areas will have poorer access to health care, be less culturally inclined to seek the health care there is, and have greater exposure to alcohol and drug misuse. It may also be the case that an 'iceberg effect' of undiagnosed illnesses may contribute to poor outcomes when critical illness supervenes. An examination of the English ICNARC database showed a stepwise worsening in outcome with increasing levels of deprivation, not lost when corrected for severity of illness.[19] This differs from the results shown here, of no significant difference seen when comparing the most deprived decile to the most affluent reference decile. However, several key differences are seen when comparing our dataset to the larger ICNARC series. We have a markedly skewed population in comparison, with 60% of our patients coming from the two most deprived deciles. Our severity of illness, mortality and length of stay are all significantly higher, and this is true across the socioeconomic spectrum. A further national study would be useful in order to see whether this is true for the entire Scottish population, rather than simply a local effect, and also to look at propensity of ICU resource usage dependent on socioeconomic deprivation.

Conclusions

In summary, this study gives a detailed account of multiple comorbidities and their effects on intensive care and hospital outcome. It has shown that even with pragmatic classification of comorbidity, a significant effect can be seen on hospital outcome from age, ALD, functional exercise tolerance, rheumatological disorders and, in terms of unit outcome, from COPD. An interesting finding has been the lack of association with social deprivation, potentially for reasons explained above. The limitations of this work include its purely descriptive nature with the potential for observer bias, the pragmatic definitions used for comorbidity inclusion, and the fact that it may only represent the effect of the chosen comorbidities on the local population. The use of consecutive admissions should have mitigated this to some extent. The pragmatic nature was essential to ensure completeness of the dataset. The completeness of this series is a significant strength of the study. Future development of this work may include liaising with other ICUs, either regionally or nationally, to accumulate a wider picture. Another potential development would be to use the comorbidities identified to develop an intensive care-specific comorbidity score, and then validate it prospectively.

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