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Association of Age and Packed Red Blood Cell Transfusion to One-Year Survival- an Observational Study of ICU Patients

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Abstract

Objectives—To compare the 1-year survival for different age strata of intensive care unit (ICU) patients after receipt of packed red blood cell (PRBC) transfusions.

Background—Despite guidelines documenting risks of PRBC transfusion and data showing that increasing age is associated with ICU mortality, little data exist on whether age alters the transfusion-related risk of decreased survival.

Methods—We retrospectively examined data on 2393 consecutive *male* ICU patients admitted to a tertiary-care hospital from 2003 to 2009 in age strata: 21–50, 51–60, 61–70, 71–80, and >80 years. We calculated Cox regression models to determine the modifying effect of age on the impact of PRBC transfusion on 1-year survival by using interaction terms between receipt of

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transfusion and age strata, controlling for type of admission and Charlson co-morbidity indices. We also examined the distribution of admission haematocrit and whether transfusion rates differed by age strata.

Results—All age strata experienced statistically similar risks of decreased 1-year survival after receipt of PRBC transfusions. However, patients age >80 were more likely than younger cohorts to have hematocrits of 25–30% at admission and were transfused at approximately twice the rate of each of the younger age strata.

Discussion—We found no significant interaction between receipt of red cell transfusion and age, as variables, and survival at 1 year as an outcome.

Introduction

Ageing leads to a progressive derangement of normal homeostatic molecular and tissue functions that can cause individuals to become frail and critically ill (Marik, 2006). The elderly (age >65) often present to the intensive care unit (ICU) with anaemia that is, in turn, associated with an increased risk of death, independent of other co-morbidities. (Penninx *et al.*, 2006; Napolitano *et al.*, 2009) The elderly also have a disproportionately high rate of packed red blood cell (PRBC) transfusions. (Anderson *et al.*, 2007). Despite consensus guidelines documenting risks of PRBC transfusion and data showing that increasing age is associated with ICU mortality, little data exist on whether older age exacerbates the decreased survival noted with PRBC transfusions. (Marik, 2006; Napolitano *et al.*, 2009)

We hypothesised that for ICU patients, after accounting for other patient factors, age would modify the impact of PRBC transfusion on 1-year survival i.e. the very old (age>80) would have the worst survival relative to younger cohorts. Data came from our institution, which is a university-affiliated, 900-bed, tertiary care United States Veterans Affairs (VA) hospital providing care in all major diagnostic and treatment specialties. Our ICU comprises 14 Level-1 beds and 14 intermediate care unit beds with occupancy rates approaching 100%. Many patients are post-operative having undergone major surgeries including vascular, abdominal, neurosurgical, or cardiothoracic surgeries.

Materials and Methods

Our primary analytic goal was to compare the 1-year survival for ICU patients for different age strata after receipt of PRBC transfusions. We developed a study sample, compared patient, treatment and clinical characteristics in various age strata, and built Cox regression models with fully specified interaction terms. Data were collected from the VA Analytics Data Warehouse (“VA Analytics”) and VISTA, the VA centralised electronic medical record. (Goldstein *et al.*, 2003; Mudumbai *et al.*, 2011) VA Analytics aggregates clinical and administrative data for patients from ICU admission to discharge. VISTA contains administrative data on hospital and ICU stay, diagnoses and procedures, and mortality. Our affiliated university Institutional Review Board approved this study.

Study Population

All patients (n=2491) admitted to the ICU from 2003 to 2009 one or more times were included in the initial sample. We excluded females because of their low percentage (2.9 %; n=72). For patients admitted more than once (16.3%; n=391), only data from first admissions were included. We excluded patients with missing data on admission hematocrit (Hct) (1.1%; n=26 patients) or co-morbidities (1%; n= 23). Our final sample consisted of 2393 male patients.

Patient characteristics

We stratified patients by age strata: 21–50, 51–60, 61–70, 71–80 and >80 years. We had 340 patients (14.2% of the sample) over age 80 years (median = 83.4 years). An admission type variable was created to differentiate surgical (43.4%; n= 1,039) and medical (56.6%; n=1,354) admissions.

Primary Discharge Diagnosis and Illness Severity

Using the Clinical Classifications Software (CCS; Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project; Rockville, Maryland, USA) 2008 classification system (Elixhauser *et al.*, 2008), we grouped patients' primary discharge diagnosis (ICD-9 codes) into six disease categories: (i) respiratory system, (ii) neoplasms, (iii) injury and poisoning, (iv) digestive system, (v) circulatory system, and (vi) other, for all other diseases.

To adjust for differences in distribution of co-morbidities and events during an ICU or hospital stay (e.g., acute myocardial infarction) potentially contributing to 1-year survival, using the Charlson-Deyo-Quan method, we constructed Charlson illness severity indices using both primary and up to seven, secondary discharge diagnosis codes (Quan *et al.*, 2005). We aggregated patients' scores into levels (0 to 3+) on the basis of sample distribution: 0 (17.7%; n=423); 1(24.7%;n=591); 2(24.4%;n=584); and 3+ (33.2%;n=795).

Admission Hematocrit

We calculated the median value of up to five haematocrit readings for each ICU patient during first 24 h. While anaemia can be defined as Hct < 39.0%, this definition may not necessarily correspond to decreased survival or be useful for transfusion decision-making (Wu *et al.*, 2007). To create Hct groupings useful for analysis, we examined unadjusted and adjusted (for age, admission type, and Charlson score) hazard ratios for 1-year mortality for each one-unit increment of haematocrit from 22.0% to 38.9%. Patients with Hct levels 39.0% (i.e., normal) were the reference group that included two patients (0.08%) with haematocrit values 54.0% or higher. We noted increases in hazard ratios for 1-year mortality at haematocrits of 25%, 30%, and 39%. Our overall analyses yielded four haematocrit groups: Hct< 25 (4.0%; n=95); 25 ≤ HCT<30 (27.3%;n=653); 30 ≤ HCT < 39 (57.1%; n=1367); and HCT ≥ 39 (11.6%;n=278).

Treatment factors

We created two, dichotomous variables: (i) hospital length of stay (LOS), defined by whether the number of days from hospital admission to discharge exceeded 10 days and (ii) receipt of one or more PBRC transfusions during ICU stay.

Mortality measures

We created two variables: a dichotomous variable indicating whether a patient had died within 365 days and a second variable indicating exact number of days until death from ICU admission up to 365 days (including those who died in the hospital). For all patients, date of last follow-up was either date of death or date of last known follow-up. Patients who survived longer than 365 days were given a value of 365, i.e., censored at 365 days. Patients not followed for a full year but alive at last follow-up were censored at the time of their last follow-up (days from ICU admission until follow-up).

Statistical Analysis

After determining distributions, we used a Kruskal-Wallis test for admission haematocrit and hospital LOS variables and χ^2 tests to compare the outcomes of interest for categorical variables. For comparisons of proportions, when expected cell size fell to less than five, we replaced a χ^2 test with a Fisher's exact test. We performed Dunn's *post hoc* multiple comparisons for admission haematocrit and hospital LOS variables and Tukey-type *post hoc* comparisons for categorical variables (Elliott & Reisch, 2006; Elliott & Hynan, 2007).

To compare long-term survival associated with receipt of transfusions, we calculated crude survival rates within each age stratum's transfused and non-transfused sub-groups. We then evaluated full Cox proportional hazard regression models (adjusting for admission type and Charlson index score) to determine hazard ratios associated with receipt of one or more transfusions. We excluded patients whose baseline hematocrit was <25% for two reasons: (i) there were too few patients with an admission haematocrit <25% (n=95) within the various age stratum to generate adequate statistical power for this lowest Hct group and (ii) our prior research with the same cohorts showed a mortality benefit for transfused patients with an admission hematocrit <25% (Mudumbai *et al.*, 2011). We therefore included patients whose admission haematocrit were Hct=25%–30%, 30%–39%, and >39%. Within each age stratum, those who did not receive a transfusion served as the reference group. We then constructed a second Cox model that included interaction terms between transfusion status and age strata.

Secondary outcomes: hematocrit levels upon admission and rates of transfusion

After calculating descriptive statistics for admission haematocrit values, we calculated a linear regression between admission haematocrit and age in years. We also evaluated the risk of various levels of haematocrit for 1-year survival using log-rank tests.

We compared age strata on (i) proportions of patients transfused during ICU stay using χ^2 tests and (ii) a multivariate logistic regression predicting receipt of transfusion. Our predictor variables were age and haematocrit stratum, type of admission and Charlson co-morbidity index. We evaluated an alternate model that incorporated LOS, which could help

adjust for unobserved risk and potentially drive the choice to transfuse. Using a conversion factor of 250mL equal to 1 unit of PRBC, we calculated volumes of transfused PRBC for each age stratum and used ANOVA to compare the volumes.

All reported p-values are two-sided; a P-value ≤ 0.05 is considered statistically significant. We used SAS software, version 9.2 (SAS Institute Inc, Cary, NC, USA) and IBM SPSS Statistics software, version 18.0 (SPSS, Chicago, IL, USA) for the statistical analyses and R software, version 2.9.2 to prepare the graphics.

Results

Table 1 provides a description of patient and treatment characteristics for the entire sample and within each age stratum. All age strata were comparable on percentage of surgical admissions, hospital LOS, but not on receipt of transfusion. The age > 80 cohort ($n=340$) contained few individuals with an admission Hct less than 25% ($n=9$); this cohort was more likely than others to receive a transfusion and present with a circulatory system-based primary discharge diagnosis. Otherwise, the age > 80 cohort's co-morbidity burden was comparable to that in other age strata.

Primary Outcome

All age strata had decreased survival at all time points associated with PRBC transfusion (Table 2). Table 3 displays results of the crude and adjusted Cox regression models for 1-year survival for each age stratum based on receipt of transfusion. Adjusted survival rates showed transfusions were associated with decreased survival for all age groups. Our Cox regression interaction model (Table 4) showed a lack of statistical significance for the interaction terms: age $\times$ transfusion. In other words, all age groups experienced a statistically similar survival risk from PRBC transfusions.

Secondary Outcomes

Haematocrit levels upon admission and rates of transfusion—Although the median admission haematocrit was clinically comparable across the entire sample and for each age stratum (Fig 1), patients age > 80 were less likely than younger ones to have normal haematocrit levels (e.g., 39% and higher) and more likely to have sub-normal levels (e.g., 25%–30%). Haematocrit levels trended downward for older patients ($\beta = -0.59$ Hct 10-years-1; 95% CI $[-0.37, -0.8]$, $P < 0.001$). Lower haematocrits were also associated with decreased 1-year survival as seen in the overall logrank test ($\chi^2 = 22.1$, d.f.=3, $p < .001$) and pair-wise logrank tests between Hct $< 25\%$ vs. Hct $\geq 39.0\%$ ($\chi^2 = 8.2$, d.f.=1, $p = .004$) and Hct 25–30% vs. Hct $\geq 39.0\%$ ($\chi^2 = 6.1$, d.f. = 1, $P = 0.014$).

Rates and volumes of PRBC transfusion for different age strata—Patients age > 80 were transfused at about twice the rate of the three lowest age groups (21–50, 51–60, and 61–70) even after we controlled for haematocrit levels (Table 5). Lower haematocrit values and surgery were associated with increasing odds of transfusion. Including LOS (e.g., a marker for LOS > 10) in the model did not change the odds ratio for receipt of transfusion for the younger age strata.

There was no significant difference among age groups in median blood volume administered or number of units transfused. Although patients age>80 were transfused more often than younger ones, they were not given greater volumes of blood. Among transfused patients, the average number of PRBC units for each age group was as follows: for age 21–50, 3.73(95%CI [2.32,5.14]); for age 51–60, 3.52 (95%CI [2.12,4.92]); for age 61–70, 3.43(95%CI [2.06,4.77]); for age 71–80, 3.43(95%CI [2.11,4.75]); and for age >80, 3.52(95%CI [2.11,4.91]); p-value: 0.99.

Discussion

We found no significant interaction between receipt of red cell transfusion and age, as variables, and survival at 1 year as an outcome. Because increasing age and PRBC transfusions were each associated with reduced survival, however, the higher transfusion rates in the elderly suggest that transfusion decisions may be especially important in older patients. These observational data in no way imply a causal relationship between age, transfusion and survival, but our study does explore potential associations between age and survival after PRBC transfusion. Over the past decade, the trend has been to limit PRBC transfusion because of evidence from investigations like the TRICC and FOCUS studies showing that PRBC transfusion does not reduce mortality (Herbert *et al.*, 1999; Herbert *et al.*, 2007; Carson *et al.*, 2011). On the other hand, PRBC transfusions have been reported to be beneficial for certain subgroups: surgical patients with low haematocrit thresholds (e.g., Hct<24%), patients with acute myocardial infarction or sepsis (e.g., SOAP study), and high-risk ICU patients as seen in our case-mix (Wu *et al.*, 2001, 2007, 2010; Marik & Corwin, 2008; Vincet *et al.*, 2008; Sakr *et al.*, 2010).

We also observed two key secondary results. First, patients age>80 were more likely than younger cohorts to have Hct levels between 25% and 30%, a finding consistent with other findings about the epidemiology of anaemia in the elderly. (Corwin *et al.*, 2004; Patel, 2008; Beyer *et al.*, 2010). Our results imply that as the population ages, more individuals age>80 will present to the ICU with low haematocrit values. Our other secondary finding that patients age>80 were transfused at higher rates (but not with greater blood volumes) has implications for blood bank utilization (Anderson *et al.*, 2007). As the number of ICU patients >80 increases relative to younger age patients, our transfusion data suggest that the number of PRBC transfusions for the very old will also increase. Our findings are consistent with Ding, et al. who examined transfusion practices among VA ICU patients and found that increased age was independently associated with PRBC transfusion.(Ding *et al.*, 2011)

Our study has several strengths; prior research on elderly ICU patients have been criticised for failure to assess gradations of age in those over 65 yrs and selection bias limiting ICU admission to few and largely healthier age>80 patients (Wood & Ely, 2003; Hennessy *et al.*, 2005; Boumendil *et al.*, 2004; Boumendil *et al.*, 2007). Our study addresses these concerns by stratifying our population by decade and including a substantial population age> 80. Stratifying by age in decades allowed for mortality comparisons to younger cohorts consistent with the SUPPORT group recommendations. (Hamel *et al.*, 2000) A substantial proportion (14.2%) of our total study population was age>80; Fifty-eight percent of our patients age>80 had a Charlson index of two or higher indicating significant diseases with a

substantial distribution of primary diagnoses of neoplasm, circulatory, and respiratory diseases (Table 1). Our study has potential limitations as well; a retrospective, observational, cohort study may be prone to selection bias, and we report associations that are not necessarily causal. In addition, because ours was a single center study, and focused entirely on male veteran patients, the results may not necessarily generalize to other sites or be applicable to women or non-veterans. We did not have enough patients over age 80 whose haematocrit was < 25% to examine effects for this haematocrit level. Lastly, we examined transfusions that occurred throughout a patient's entire ICU stay, not just during the first 24 h; initial haematocrit levels upon ICU admission are a major factor in deciding how to manage patients, but decisions on whether to transfuse may still occur over several days after admission. Future researchers should assess haematocrit levels before each transfusion and account for timing.

In summary, older age is not associated with worsened 1 year survival after PRBC transfusions in ICU patients. Our exploratory study indicates that older age in a patient should not deter PRBC transfusions. Rather, clinicians' decisions to transfuse should be based on the patient's clinical status, haematocrit level and expected response to transfusion.

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Figure 1.
Admission Hematocrit Levels for Intensive Care Unit Patients by Age Strata.
HCT=hematocrit

Table 1

Patient and treatment characteristics by age strata

	Overall Sample Median (IQR) or Number (%) (n = 2393)	Age strata (Median (IQR) or Number (%))				p-Value ^a	
		Age > 80 (n = 340, 14.2%)	71 <= Age <= 80 (n = 540, 22.6%)	61 <= Age <= 70 (n = 742, 31.0%)	51 <= Age <= 60 (n = 628, 26.2%)		21 <= Age <= 50 (n = 143, 6.0%)
Patient Characteristics							
Hematocrit (HCT) on admission (%)	32.1 (29.1–36.0)	31.1 (28.6–34.5)	31.6 (29.3–35.0)	32.7(29.2–36.4) ^b	32.7 (29.2–36.4) ^b	33.5 (28.7–39.7) ^b	<0.001
HCT < 25	95 (4.0%)	9 (2.6%)	15 (2.8%)	32 (4.3%)	28 (4.5%)	11 (7.7%)	0.052
25<=HCT<30	653 (27.3%)	123 (36.2%)	150 (27.8%)	187 (25.2%) ^b	162 (25.8%) ^b	31 (21.7%) ^b	0.001
30<=HCT<39	1367 (57.1%)	189 (55.6%)	335 (62.0%)	429 (57.8%)	354 (56.4%)	60 (42.0%)	0.001
HCT>=39	278 (11.6%)	19 (5.6%)	40 (7.4%)	94 (12.7%) ^b	84 (13.4%) ^b	41 (28.7%) ^b	<0.001
Surgical admission	1039 (43.4%)	124 (36.5%)	240 (44.4%)	319 (43.0%)	291 (46.3%)	65 (45.5%)	0.052
Treatment Factors							
Hosp length of stay (days)	10.1 (5.2–18.0)	10.1 (5.2–17.6)	10.0 (5.1–19.9)	10.1 (5.2–18.1)	10.1 (5.2–16.8)	9.7 (5.4–18.0)	0.986
Hosp length of stay >10 days	1212 (50.6%)	171 (50.3%)	270 (50.0%)	384 (51.8%)	318 (50.6%)	69 (48.3%)	0.939
Received transfusion	707 (29.5%)	136 (40.0%)	173 (32.0%)	204 (27.5%) ^b	159 (25.3%) ^b	35 (24.5%) ^b	<0.001
Primary discharge diagnosis							
Respiratory disease	178 (7.4%)	38 (11.2%)	42 (7.8%)	55 (7.4%)	34 (5.4%) ^b	9 (6.3%)	0.027
Neoplasm	408 (17.0%)	35 (10.3%)	92 (17.0%) ^b	149 (20.1%) ^b	113 (18.0%) ^b	19 (13.3%)	0.002
Injury or poisoning	177 (7.4%)	38 (11.2%)	42 (7.8%)	43 (5.8%) ^b	43 (6.8%)	11 (7.7%)	0.036
Digestive disease	151 (6.3%)	37 (10.9%)	29 (5.4%) ^b	36 (4.9%) ^b	41 (6.5%)	8 (5.6%)	0.004
Circulatory disease	1057 (44.2%)	132 (38.8%)	264 (48.9%) ^b	351 (47.3%)	274 (43.6%)	36 (25.2%) ^b	<0.001
Other disease	422 (17.6%)	60 (17.6%)	71 (13.1%)	108 (14.6%)	123 (19.6%)	60 (42.0%) ^b	<0.001
Illness severity							
Charlson score 0	423 (17.7%)	60 (17.6%)	76 (14.1%)	117 (15.8%)	114 (18.2%)	56 (39.2%) ^b	<0.001
Charlson score 1	591 (24.7%)	81 (23.8%)	135 (25.0%)	182 (24.5%)	160 (25.5%)	33 (23.1%)	0.965
Charlson score 2	584 (24.4%)	81 (23.8%)	122 (22.6%)	196 (26.4%)	157 (25.0%)	28 (19.6%)	0.334

Overall Sample Median (IQR) or Number (%) (n = 2393)	Age strata (Median (IQR) or Number (%))				p-Value ^a
	Age > 80 (n = 340, 14.2%)	71 <= Age <= 80 (n = 540, 22.6%)	61 <= Age <= 70 (n = 742, 31.0%)	51 <= Age <= 60 (n = 628, 26.2%)	21 <= Age <= 50 (n = 143, 6.0%)
Charlson score 3+	118 (34.7%)	207 (38.3%)	247 (33.3%)	197 (31.4%)	26 (18.2%) ^b
	795 (33.2%)				

^a p-Value of Kruskal-Wallis test for admission hematocrit (%) and hospital length of stay (days) and chi-square for categorical variables.

^b Differs from Age > 80 Strata at the p <0.05 level.

IQR=inter-quartile ratio; HCT=hematocrit

Table 2

Patient survival by age strata

	Overall Sample (Number (%)) (n = 2393)	Age strata (Number (%))					p-Value ^a
		Age > 80 (n = 340, 14.2%)	71 <= Age <= 80 (n = 540, 22.6%)	61 <= Age <= 70 (n = 742, 31.0%)	51 <= Age <= 60 (n = 628, 26.2%)	21 <= Age <= 50 (n = 143, 6.0%)	
<i>Survival</i>							
90-day	2075 (86.7%)	236(69.4%)	467 (86.5%) ^a	666 (89.8%) ^a	569 (90.6%) ^a	137 (95.8%) ^a	<0.001
180-day	1987 (83.0%)	222(65.3%)	446 (82.6%) ^a	634 (85.4%) ^a	550 (87.6%) ^a	135 (94.4%) ^a	<0.001
1-year	1892 (79.1%)	201(59.1%)	426 (78.9%) ^a	613 (82.6%) ^a	521(83.0%) ^a	131 (91.6%) ^a	<0.001

^a Differs from Age > 80 Strata at the p <0.05 level.

Table 3

1-year crude and adjusted survival rates by age strata and transfusion status

Age Strata	No. of Patients (row percent)		Crude Survival Rate		Adjusted ^a Survival Rate		Hazard Ratio ^b Receipt of transfusion	95% CI
	Did not receive transfusion	Received transfusion	Did not receive transfusion	Received transfusion	Did not receive transfusion	Received transfusion		
Age >80 (n=331)	202 (61%)	129 (39%)	0.62	0.50	0.66	0.51	1.73**	1.23–2.44
Age 71–80 (n=525)	365 (70%)	160 (30%)	0.81	0.71	0.82	0.72	1.69**	1.15–2.47
Age 61–70 (n=710)	532 (75%)	178 (25%)	0.85	0.72	0.86	0.71	2.33***	1.62–3.37
Age 51–60 (n=600)	463 (77%)	137 (23%)	0.87	0.73	0.87	0.71	2.50***	1.64–3.80
Age 21–50 (n=132)	105 (80%)	27 (20%)	0.94	0.84	0.93	0.78	3.29	0.93–11.67

^aBased on a Cox regression model adjusted for admission type (surgical vs. medical) and Charlson score among patients with hematoctrit>=25.

^bHazard ratio of receiving a transfusion within each age group (i.e. those who did not receive a transfusion within that age strata serve as the reference group) in the full Cox regression model adjusted for admission type (surgical v. medical) and Charlson score

**
p<.01

p<.001

Table 4

One- Year Mortality Risk with Age by Transfusion Interaction Model

Parameter	HR	95%CI	P-Value
<i>Age by Transfusion Interactions</i>			
Age >80 × trans	Ref.	Ref.	
Age 71–80 × trans	0.97	0.58–1.62	0.919
Age 61–70 × trans	1.35	0.82–2.22	0.245
Age 51–60 × trans	1.44	0.84–2.47	0.186
Age 21–50 × trans	1.90	0.51–7.04	0.338
<i>Age Strata</i>			
Age >80	Ref.	Ref.	
Age 71–80	0.47	0.33–0.65	<0.001
Age 61–70	0.35	0.25–0.48	<0.001
Age 51–60	0.32	0.23–0.46	<0.001
Age 21–50	0.17	0.08–0.40	<0.001
Transfusion	1.73	1.23–2.44	0.002
Surgery	0.40	0.33–0.50	<0.001
<i>Comorbidity Measures</i>			
Charlson index 0	Ref.	Ref.	
Charlson index 1	1.02	0.71–1.48	0.911
Charlson index 2	1.75	1.25–2.46	0.001
Charlson index 3+	2.72	1.99–3.72	<0.001

Ref.= Reference group; HR= Hazard Ratio; CI=Confidence Interval; Trans=transfusion.

Table 5

Odds ratios from multivariate logistic regression predicting receipt of transfusion

	Odds Ratio	95% CI	P-value
<i>Age Strata</i>			
Age>80	Ref.	Ref.	
Age 71–80	0.76	0.56–1.04	0.091
Age 61–70	0.61	0.45–0.83	0.001
Age 51–60	0.51	0.37–0.70	<0.001
Age 21–50	0.49	0.29–0.82	0.006
<i>Hematocrit Strata</i>			
Hematocrit <25	88.97	41.80–189.39	<0.001
25<=Hematocrit<30	22.60	12.63–40.41	<0.001
30<=Hematocrit<39	4.21	2.37–7.50	<0.001
Hematocrit >=39	Ref.	Ref.	
Surgical admission	1.58	1.29–1.93	<0.001
<i>Illness severity</i>			
Charlson score 0	Ref.	Ref.	
Charlson score 1	0.72	0.53–0.98	0.039
Charlson score 2	0.65	0.48–0.89	0.007
Charlson score 3+	0.76	0.57–1.01	0.057

Ref.= Reference group; CI= Confidence interval