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Prevalence, management and outcomes associated with anaemia in ICU survivors

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Prevalence, management and outcomes associated with anaemia in ICU survivors: a retrospective study

Survivors of critical illness experience poor health-related quality of life, especially during the first year following discharge from ICU [1]. Identification of modifiable risk factors and enhancing recovery from critical illness is now a recognised clinical and research priority.

Recent observational studies have demonstrated that anaemia in this cohort is associated with increased mortality, poor physical recovery, increased dependency and high levels of fatigue in the post-ICU recovery period [2–4]. Intensive care unit survivors display the hallmarks of anaemia of inflammation, which may be treatable with interventions such as intravenous iron but there is no literature describing how clinicians caring for ICU survivors manage anaemia. The aims of this study were to determine the prevalence, characteristics and management of anaemia in a large cohort of ICU survivors prior to hospital discharge.

We undertook a retrospective cohort study of general ICU survivors in two large health regions in the UK (Oxford University Hospitals NHS Foundation Trust, 1 December 2014–31 May 2015; Royal Infirmary of Edinburgh, 1 January 2015–31 December 2015) aiming to benchmark how many patients had anaemia-specific treatment (excluding blood transfusion) initiated prior to hospital discharge.

Data on patient demographics, acute physiology and chronic health evaluation 2 scores, admission categories and ICU and hospital length of stay were extracted along with haemoglobin (Hb) at ICU admission, ICU discharge and hospital discharge. We reviewed discharge summaries and prescription charts of all survivors for any documentation regarding management of anaemia. We also conducted exploratory multivariable analyses to investigate the associations between anaemia at ICU discharge and clinical outcomes, and any factors associated with Hb at hospital discharge. Anaemia was categorised as Hb < 100 $g.l^{-1}$ based on research, in critically and non-critically ill patients, which has found associations between this threshold and persisting anaemia [5] together with poor outcomes [2].

Complete data were available for 1174 ICU patients who survived to hospital discharge. Demographic and clinical characteristics are displayed in Table 1. In total, 626 patients were discharged from ICU with Hb < 100 g.l^{-1} (53.3%). Of these, 289 (46%) patients still had Hb < 100 g.l^{-1} at hospital discharge compared with 149 (27.2%) of patients who were discharged from ICU with Hb > 100 g.l^{-1}. Fifty-two (4.4%) patients received oral iron prior to hospital discharge. One patient received intravenous iron and two received vitamin B12 and folate. There was no mention of anaemia treatment and/or follow-up in any of the other discharge letters reviewed.

Patients discharged from ICU with Hb < 100 g.l^{-1} experienced a longer median (IQR [range]) post-ICU hospital length of stay when compared with those discharged with Hb > 100 g.l^{-1} (8 (4–15 [1–153]) vs. 3 (7–13 [1–106]) days, p = 0.0017) (Table 1). Following adjustment for covariates, Hb < 100 g.l^{-1} was associated with prolonged hospitalisation, defined as post-ICU length of stay > 7 days (relative risk (95%CI): 1.36 (1.10–1.68)). Factors associated with Hb at hospital discharge were acute physiology and chronic health evaluation 2 score, ICU discharge Hb and ICU length of stay (Table 2).

The key findings of this study were a high prevalence of anaemia at ICU discharge and subsequently hospital discharge; there is little active management of anaemia during this important time period; and Hb of <100 g.l^{-1} was associated with prolonged hospitalisation following ICU discharge. The latter finding may identify a group of patients who may benefit from closer follow-up.

The high prevalence of anaemia persisting at ICU and hospital discharge may, in part, be explained by increased adherence to restrictive transfusion thresholds recommended by guidelines [4]. However, our findings showed little change from over a decade ago [4, 5]. Although our data cannot establish causality, our findings support a causal pathway in which anaemia, as a driver of functional impairment, results in an increased requirement for hospitalisation following ICU discharge. Correcting anaemia may improve clinical outcomes, which have been shown in recent observational studies where a higher Hb at discharge was associated with improvements in functional activities, physical performance and lower mortality [6, 7].

Our study cohort was an unselected population from two large general ICUs with a case-mix typical of admissions to other ICUs and therefore our data are externally generalisable. Our study is subject to the usual limitations of observational studies such as unmeasured confounding. We did not collect data on factors that may influence recovery from anaemia such as red blood cell transfusion, inflammation and pre-existing comorbidities.

Early stage randomised controlled trials are currently ongoing to determine whether treating anaemia in the post-ICU period, with interventions such as iron [8] and red blood cell transfusion, improves clinical outcomes. Given the heterogeneous nature of the population of ICU survivors, there is also a need to further define the aetiology and trajectories of post-ICU anaemia in order to identify which patients may benefit the most from anaemia management.

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Table 1. Clinical characteristics of hospital survivors stratified by anaemia severity at ICU discharge. Values are median (IQR [range]), mean (SD) and number (proportion)

Characteristic	All patients n = 1174	Hb <100 g.l^{-1} n = 626	Hb ≥100 g.l^{-1} n = 548	p value
Age	58 (42–69 [17–114]	57 (41–68 [16–94])	58 (42–70 [18–114])	
Sex				
Male	692 (58.9)	360 (57.5)	332 (60.6)	
Female	482 (41.4)	266 (42.5)	216 (39.4)	
APACHE 2	15.4 (7.0)	15.7 (7.2)	15.0 (6.7)	
Admission category				
Emergency/urgent surgery	312 (26.6)	147 (23.5)	165 (30.1)	
Elective surgery	457 (38.9)	223 (35.6)	234 (42.7)	
Medical	405 (34.5)	256 (40.9)	149 (27.2)	
Haemoglobin, g.l^{-1}				
ICU admission	120 (102–135 [63–172])	113 (97–131 [61–169]	124 (108–137 [66–174])	
ICU discharge	96 (91–116 [57–171]	91 (89–91 [57–99])	116 (104–126 [100–171]	
Hospital discharge	105 (93–119 [61–177])	101 (90–115 [61–177])	110 (98–125 [62–171])	
Proportion discharged from hospital with Hb <100 g.l^{-1}	438/1174 (37.3%)	289/626 (46.2%)	149/548 (27.2%)	<0.0001
ICU length of stay, days	2 (1–5 [0–73])	3 (2–5 [0–54])	2 (1–4 [0–73])	
Post-ICU length of stay in hospital, days	7 (3–14 [1–153])	8 (4–15 [1–153])	3 (7–13 [1–106])	0.0017

APACHE, acute physiology and chronic health evaluation; Hb, haemoglobin.

Table 2. Multivariable analysis of factors associated with haemoglobin at hospital discharge

Variable	Regression coefficient (95% CI)	p value
APACHE 2*	-0.14 (-0.25 to -0.04)	0.006
ICU discharge Hb, g.l^{-1}	0.11 (0.07 to 0.16)	<0.001
Sex (female)	-0.75 (-2.48 to 0.97)	0.393
ICU length of stay	-0.48 (-0.62 to -0.35)	<0.001
Post-ICU length of stay	0.01 (-0.07 to 0.04)	0.626

*APACHEII score includes other important variables such as age, severe comorbidity and emergency admission.

APACHE, acute physiology and chronic health evaluation; Hb, haemoglobin.