Prevalence of ischaemic heart disease at admission to intensive care and its influence on red cell transfusion thresholds: multicentre Scottish Study†

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Background. Restrictive transfusion triggers are safe for most critically ill patients, but doubts exist for patients with ischaemic heart disease (IHD). We investigated the prevalence of reported IHD at admission to the intensive care unit (ICU) and investigated how this influenced red cell transfusion triggers. We also compared observed practice with the clinicians’ responses to clinical scenarios.

Methods. We studied 1023 sequential ICU admissions over 100 days to 10 Scottish ICUs. Daily haemoglobin, red cell transfusion, and haemorrhage data were available for 99.4% of 5638 ICU patient days. We recorded if IHD was recorded in clinical records at ICU admission. We grouped admissions as having a non-cardiac primary ICU diagnosis and no documentary evidence of IHD (Group 1, n=697), a non-cardiac primary ICU diagnosis with evidence of IHD (Group 2, n=213), or a cardiac primary ICU admission diagnosis (Group 3, n=113). We examined pre-transfusion haemoglobin concentration (Hb) for transfusion episodes not associated with haemorrhage. Clinical transfusion scenarios were sent to intensivists in the ICUs after data collection, which were designed to explore the clinicians’ attitude to transfusion triggers in patients with IHD.

Results. Previous myocardial infarction was documented in 159 (16%), cardiac failure in 142 (14%), and angina in 167 (16%). Overall, 28.8% of admissions had ≥1 of these documented. The adjusted mean (±SE) pre-transfusion Hb concentrations varied across the groups. These were 74 (2.2) g litre⁻¹ in Group 1, 77 (2.3) g litre⁻¹ in Group 2, and 79 (3.1) g litre⁻¹ in Group 3 (P=0.003 across the groups). There was concordance between observed practice and responses to the scenario similar to Group 1, but discordance for patients with IHD (Groups 2 and 3). In scenario responses, intensivists stated these patients should have significantly higher transfusion triggers than were actually observed (median [IQR] response for both groups: 90 [80–100] g litre⁻¹).

Conclusions. About 29% of patients admitted to Scottish ICUs had documented IHD, which was associated with small adjustments to Hb transfusion triggers. In response to scenarios, clinicians believe that patients with IHD require higher transfusion triggers than are observed in practice.

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Anaemia is well tolerated by most critically ill patients. The best evidence for this was the Transfusion Requirements in Critical Care (TRICC) study, which compared a transfusion trigger of less than 70 g litre\(^{-1}\) with a trigger of less than 100 g litre\(^{-1}\) and found similar overall 30 and 60 days mortality. Recent transfusion guidelines recommend the use of conservative transfusion triggers for most critically ill patients. Most state that red blood cell (RBC) transfusion is indicated when the haemoglobin concentration (Hb) is less than 70 g litre\(^{-1}\) and should be avoided when the Hb is more than 100 g litre\(^{-1}\). Despite these guidelines, recent studies show that many clinicians administer RBCs at values significantly higher than 70 g litre\(^{-1}\). The reasons for this are poorly understood.

No large studies have specifically addressed what transfusion practice is appropriate for critically ill patients with ischaemic heart disease (IHD), but systematic reviews of the available evidence and expert opinion acknowledge that these patients may require a higher Hb. The prevalence of IHD among patients admitted to general ICUs has not been investigated, and it is not known how these patients are currently managed in comparison with those without known IHD. Equally, there is little information about what ICU clinicians currently believe are appropriate transfusion thresholds for these patients or how beliefs compare with actual practice.

We carried out a large multi-centre audit of transfusion practice in 10 Scottish ICUs. We present data on the prevalence of documented IHD among the patients admitted during the study period and describe the Hb transfusion thresholds that were observed with respect to whether documentary evidence of IHD was present at the time of ICU admission. We also present data from a scenario-based questionnaire concerning transfusion thresholds among critically ill patients with or without IHD that was sent to the same group of consultants responsible for patients in the ICUs after completion of the transfusion audit.

Methods

The Audit of Transfusion in Intensive Care in Scotland (ATICS) study

The ATICS study was a prospective benchmarking study of transfusion practice in Scottish ICUs. The aim was to collect a prospectively defined dataset, using a standard daily case record form (CRF) for 1000 sequential admissions to 10 Scottish adult ICUs. These comprised 10 of the 26 general ICUs in Scotland, and included all the large teaching hospital ICUs in Scotland (n=7) and three smaller ICUs in large regional hospitals (see Acknowledgements for details of the exact units). All the participating units were mixed general surgical, medical, and trauma ICUs. We did not study patients admitted to cardiac ICUs or specialist paediatric ICUs. Data from all Scottish ICUs were collected prospectively by medical and nursing staff using a ward-based audit system (Wardwatcher, Critical Care Audit Ltd, Yorkshire, UK), and subsequently exported to the Scottish Intensive Care Society Audit Group (SICSAG) database. We used this as the reference standard for documenting ICU admissions and to collect demographic and outcome data. The ethics committee did not consider informed consent necessary to carry out the audit.

We collected data for 100 days, because we predicted this would generate a cohort of 1000 admissions. Additional data concerning RBC transfusions, Hb, haemorrhage, and organ failures were collected on a daily basis throughout ICU stay. This was done by chart review and discussion with ICU staff. The ICU stay was described in 24 h periods (with part periods at the start and end of ICU stay). For each 24 h period the daily morning Hb was recorded, together with the number of RBC units transfused during the 24 h. Any additional Hb concentrations that may have influenced transfusion decisions were also documented. Any RBC transfusions during a 24-h period were termed a ‘transfusion episode’. We used a consensus definition of ‘clinically significant haemorrhage’ as ‘the loss of \(\geq 300\) ml (1 RBC unit) during the 24-h period from any sites’, and documented this on a daily basis independently from RBC transfusions. To describe illness severity we used the APACHE II score and the daily Sequential Organ Failure Assessment (SOFA) score.

After admission to ICU, the patient charts, hospital notes, and referral letter were examined. Using these, we recorded if the patient had a documented previous history of myocardial infarction, angina, or cardiac failure at any time. We defined the presence of any combination of these in the history as ‘documented pre-existing ischaemic heart disease’. We did not attempt to grade the severity of IHD because pilot studies showed that it was not feasible to report this consistently.

All data were made anonymous using a unique SICSAG reference number. All CRFs were checked manually by one of the authors (C.R.M.), and queries resolved with individual units. Forms were scanned to database and a series of automated consistency and coherency checks were performed to detect data entry and transcription errors. Demographic and outcome data for all admissions during the study period were exported from the SICSAG database and merged with the study database. Further consistency checks were performed to compare recorded admission rates and duration of stay. The checked merged dataset formed the ATICS study database.

We categorized all transfusion episodes as either associated with clinically significant haemorrhage (where RBCs were administered primarily to replace lost blood) or not associated with haemorrhage (where RBCs were administered primarily to increase the Hb when there was no evidence of active or recent bleeding). We used the convention that a RBC transfusion episode was associated with clinically significant haemorrhage if it occurred on the day before, the same day, or the day after a day on which...
clinically significant haemorrhage was recorded. We measured the ‘trigger’ Hb used by clinicians when no clinically significant haemorrhage was present using the closest recorded pre-transfusion Hb concentrations.

We classified patients into the following three groups based on the presence of documented IHD and the primary ICU admission diagnosis (using the primary ICU admission diagnosis category). Group 1: patients with a non-cardiac primary ICU admission diagnosis and no documented pre-existing IHD. Group 2: patients with a non-cardiac primary ICU admission diagnosis, but with documented pre-existing IHD. Group 3: patients with a cardiac primary ICU admission diagnosis.

For each of these groups we calculated the pre-transfusion Hb concentrations for transfusion episodes that were not associated with haemorrhage.

To investigate the beliefs about Hb transfusion thresholds of the intensivists in charge of patients during the study, we sent each of them three clinical scenarios. These were designed to explore attitudes towards transfusion triggers for critically ill patients with stable or unstable ischaemic heart disease and were intended to represent patients similar to those in each of the three groups (see Appendix). The first scenario was designed to represent a critically ill patient with sepsis who was not bleeding and had no evidence of IHD. The second was identical, except that the patient had documented IHD at the time of admission. The third patient had evidence of acute myocardial ischaemia. We asked each consultant to document the Hb concentration below which they would definitely give RBC transfusion and also the Hb concentration above which they would definitely not give RBC transfusion. Scenarios were sent independently to all consultants in the ICUs that participated in the audit and managed the patients during the study period after completion of the audit.

We assumed a null hypothesis that there were no differences in pre-transfusion Hb values between the three groups. We compared the pre-transfusion Hb concentrations using a mixed model, with admission fitted as random to account for the repeated measurements at the admission level. This approach was used to adjust for the possible confounding effect of repeated transfusions in some patients. We calculated mean differences between the groups with 95% confidence intervals. The F-test was used to assess the statistical significance of the differences between the adjusted group means. We reported responses to scenarios in the form of histograms.

Results

The study period was the 100 days from 08:00 on June 4, 2001 to 08:00 on September 12, 2001.

The 10 ICUs that took part in the study admitted patients with a high illness severity (Table 1). None of the ICUs were designed as units providing combined intensive and high dependency care throughout the patients’ illness. In most centres patients were discharged either to separate high dependency areas or to the ward when their condition permitted. This accounted for the short median duration of stay, which is typical for many UK ICUs.

There were 1042 admissions to the ICUs during the study period. Fourteen patients were excluded from analysis based on prospectively defined criteria (two ‘dead on arrival’; one palliative care; 11 ‘patients admitted for postoperative recovery, but not requiring intensive care’). For the remaining 1028 admissions data were available for 1023 (99.5%). The total ICU stay for the 1028 admissions was 5638 days; data were available for 99.4% of these days. There were 2367 admissions to Scottish ICUs during the 100 days study period; our sample therefore represented 43% of all Scottish general ICU admissions. Overall characteristics for the cohort are shown in Table 1. There was a documented past history of myocardial infarction in 159 (16%), of cardiac failure in 142 (14%), and of angina in 167 (16%). Taking any combination of these as evidence of pre-existing IHD (n=295), the prevalence of IHD in our sample at admission to ICU was 28.8% (95% CI: 26.1–31.7%).

Overall 404 (39.5%) of patients received ≥1 RBC transfusion for any reason. The numbers of admissions in each of the groups considered together with the proportion of patients transfused in the absence of haemorrhage are shown in Figure 1 and Table 2. The diagnostic subgroups for patients with a cardiac primary ICU diagnosis were: acute myocardial infarction (five), cardiac arrest (50), cardiac failure (39), cardiogenic shock (12), mitral regurgitation (one), poor left ventricular function (two), supraventricular tachycardia (two), and other arrhythmia (three).

The numbers of transfusion episodes for patients in each of the groups, and the mean (SE) pre-transfusion Hb values after adjusting for repeated measures, are shown in Table 2. The mean difference between admissions with a non-cardiac primary ICU diagnosis with documented IHD (Group 2)
compared with those without documented IHD (Group 1) was 3 g litre$^{-1}$ (95% CI between 1.1 and 5.6, $P=0.004$). The mean difference between admissions with a cardiac primary ICU diagnosis (Group 3) and those with a non-cardiac primary ICU diagnosis and no documented IHD (Group 1) was 5 g litre$^{-1}$ (95% CI between 0.5 and 9.8, $P=0.03$).

The difference between admissions with a cardiac primary ICU diagnosis (Group 3) and those with a non-cardiac primary diagnosis, but documented IHD (Group 2) was 2 g litre$^{-1}$ (95% CI between 3.1 and 6.7, $P=0.46$).

For the clinical scenarios, there were 63 consultants in the 10 ICUs during the study period. We obtained completed returns from 52 of these (83% response rate). Responses to the clinical scenarios are shown in Figure 2.

### Table 2

<table>
<thead>
<tr>
<th></th>
<th>Group 1: non-cardiac ICU admission diagnosis, no documented IHD (n=697)</th>
<th>Group 2: non-cardiac ICU admission diagnosis, with documented IHD (n=213)</th>
<th>Group 3: cardiac ICU admission diagnosis (n=113)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%) transfused in the absence of haemorrhage</td>
<td>173 (25)</td>
<td>79 (37)</td>
<td>18 (16)</td>
</tr>
<tr>
<td>Mean number of transfusion episodes not associated with haemorrhage for transfused admissions</td>
<td>1.9</td>
<td>1.7</td>
<td>1.2</td>
</tr>
<tr>
<td>Number (%) who received one transfusion episode</td>
<td>104 (60)</td>
<td>56 (71)</td>
<td>15 (83)</td>
</tr>
<tr>
<td>Number (%) who received two transfusion episodes</td>
<td>32 (18)</td>
<td>10 (13)</td>
<td>2 (11)</td>
</tr>
<tr>
<td>Number (%) who received three transfusion episodes</td>
<td>21 (12)</td>
<td>6 (8)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Number (%) who received more than/equal to four transfusion episodes</td>
<td>16 (9)</td>
<td>7 (9)</td>
<td>0</td>
</tr>
<tr>
<td>Adjusted mean (SE) pre-transfusion haemoglobin concentration</td>
<td>74 (2.2)</td>
<td>77 (2.3)</td>
<td>79 (3.1)*</td>
</tr>
</tbody>
</table>

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documented IHD compared with those given to admissions without documented IHD (adjusted mean values 77 and 74 g litre$^{-1}$, respectively). This difference was statistically significant and probably indicated a real, but clinically small, adjustment to transfusion decisions. The responses to clinical scenarios suggested some differences from the observed practice. The lowest tolerated Hb was similar for the patient with no pre-existing IHD (median Hb value 70 g litre$^{-1}$), but was higher to a clinically relevant extent for the patient with evidence of pre-existing stable IHD (median Hb value 90 g litre$^{-1}$). A similar difference existed between observed practice for admissions with a cardiac primary ICU diagnosis and the patient scenario with active myocardial ischaemia (observed adjusted mean pre-transfusion Hb 79 g litre$^{-1}$; median lowest tolerated Hb value in scenario 90 g litre$^{-1}$). Our data suggest that the clinicians’ attitude to transfusion triggers in scenarios was to use less restrictive triggers for patients with documented IHD, whether a stable underlying condition or the acute problem, than was observed in practice.

We studied a large number of patients and data were very complete, so it is unlikely that there was any selection bias in our findings. There were a large number of transfusion episodes, which we classified using their association with separately recorded episodes of clinically significant haemorrhage. In our pilot work we found that the rationale for RBC transfusions was rarely documented clearly in patient records, which is a recognized problem in many clinical settings. Other studies have attempted to categorize transfusion decisions in intensive care, but other than haemorrhage the reasons that clinicians choose to increase the Hb value are often unclear, making categorization subjective. We wanted to exclude transfusions associated with bleeding, because in these situations many rapidly changing factors may influence the decision to give blood, such as hypotension or the rate of haemorrhage. By comparing pre-transfusion Hb values only for transfusions not associated with bleeding we believe the best possible assessment of the clinicians’ Hb transfusion triggers in euvolaemic patients was obtained. We also adjusted for the potentially confounding effect of repeated transfusions within patients in the analysis, so differences in the numbers of transfusion episodes per admission across the groups were unlikely to have affected our findings.

![Fig 2 Histograms showing the responses to each of the three clinical scenarios sent to clinicians after collection of the clinical data. The lower threshold indicates the haemoglobin value below which clinicians stated they would definitely give red cell transfusion to patients and the upper threshold indicates the haemoglobin value above which they would definitely not transfuse. Median (IQR) values for each response are shown for each histogram.](https://academic.oup.com/bja/article-abstract/94/4/445/292466/449)
Using documented previous myocardial infarction, cardiac failure, or angina we found that 29% of admissions to the ICUs had IHD. Our approach could have under or over-estimated the true prevalence, but in practice obtaining a more detailed assessment is not feasible in this type of population. The Scottish Health Survey (1995) found 6.0% of males and 3.4% of females aged 45–54 yr and 17.0% of males and 11.4% of females aged 55–64 yr reported having IHD. Our data suggest that patients admitted to general ICUs in Scotland have a higher prevalence of IHD than the general population. It is known that the Scottish population has a higher prevalence of IHD than is typical of other European and North American populations. However, our data suggest that IHD is a common co-morbidity among patients admitted to ICUs. It is clearly important to understand how, if at all, this should modify intensive care treatment.

Overall, the observed transfusion thresholds for 70 g litre⁻¹ used in the TRICC study than have been reported in other recent epidemiological studies in Europe and North America.₃₀₄ For patients with no documented IHD, there was concordance between the observed practice and the scenario responses. There was discordance between the observed practice and responses to the scenarios when IHD was a documented co-morbidity or when a cardiac problem was the main reason for ICU admission. In responding to these clinical scenarios, 50% of clinicians stated they would definitely give a RBC transfusion when Hb was ≥90 g litre⁻¹, but the observed practice was a mean pre-transfusion Hb of less than 80 g litre⁻¹ for both groups. It is unlikely that this discordance was explained by rapid decreases in Hb values among the admissions studied, because we only examined transfusions not associated with bleeding. In this situation Hb values decrease on average by 5.2 g litre⁻¹ per ICU day overall, and after a third day in ICU by only 1.2 g litre⁻¹ per ICU day.₁₃ Using clinical scenarios to explore clinicians’ practices can be problematic. Only limited physiological data can be included and the cases cannot represent all the variability that was present in the three clinical patient groups. It is also not certain that responses to scenarios will be the same as clinical decisions. Despite this, the only difference between the scenarios we used related to IHD, and we only sent scenarios to clinicians responsible for the patients who were studied. Faced with the scenarios, clinicians said they would transfuse at higher Hb values than those observed in practice. Our study was not designed to explain why this occurs; it could be because clinicians were not aware of documentary evidence in the patient record or that this information was overlooked in the presence of other acute clinical problems. Alternatively, other unmeasured factors may have modified transfusion decisions.

The only randomized controlled trial data on mortality in relation to anaemia and transfusion practice in a general ICU population with IHD come from a retrospective subgroup analysis of the data from the TRICC study.¹⁴ The authors identified 257 patients who they classified from admission data as having IHD at admission to ICU, although they state ‘... it (IHD) was not the primary reason for ICU admission in a significant proportion of (this subgroup of) patients’.¹⁴ Mean daily Hb in the restrictive transfusion group was 85 g litre⁻¹, compared with 103 g litre⁻¹ in the liberal group. Among patients with IHD there was a non-significant trend towards higher mortality rates for patients managed with a transfusion trigger less than 70 g litre⁻¹ compared with less than 100 g litre⁻¹ (difference in 60 days mortality + 4% [95% confidence intervals between +14.9% and −6.9%]). This trend was consistent with the association between a Hb concentration less than 95 g litre⁻¹ and increased mortality among ICU patients with IHD that was observed in a Canadian cohort study that preceded the TRICC study.₁₅ Although the data are inconclusive, they illustrate the uncertainty that remains concerning optimum transfusion strategy among critically ill patients with IHD who do not have acute cardiac problems.₉₁₀₁₆ In patients with chronic cardiac failure, there is an association between anaemia and mortality, although it is unproven whether this is causal.₁₇ A small randomized study showed that treating mild anaemia in this setting with exogenous human erythropoietin can improve morbidity.₁₈ There are no similar published studies in critically ill patients with IHD either during ICU care or the recovery period.

There is particular uncertainty in the literature for patients with acute coronary syndromes, in whom there are physiological reasons why anaemia may be poorly tolerated.₁₀ The recent literature contains conflicting data from two large retrospective cohort studies. Wu and colleagues found an association between anaemia at hospital admission (Hb below 95–100 g litre⁻¹) and higher mortality for patients aged more than 65 yr admitted with acute myocardial infarction, and an association between receiving transfusion and lower mortality for anaemic patients.₁₉ In contrast, Rao and colleagues found an association between blood transfusions and higher mortality in the setting of acute coronary syndromes, which persisted after statistical adjustments for co-morbidity and timing of events.₂₀ Our study shows that uncertainty impacts on a high proportion of patients treated in ICUs and illustrates the urgent need for high quality evidence in this area.

In conclusion, we have shown that 29% of admissions to 10 Scottish general ICUs had documentary evidence of IHD at admission. Eighteen per cent of admissions had documented IHD, but an admission diagnosis that was not primarily cardiac in nature; 11% of admissions had a cardiac primary ICU diagnosis. These patients were managed with transfusion triggers that were restrictive and on average only slightly higher than patients without documentary evidence of IHD, despite responses to scenarios suggesting that clinicians believed that higher transfusion triggers should be used when IHD is present. This discordant practice emphasizes the need for more high quality evidence to guide the optimum management of anaemia in critically ill patients with IHD.
operative pneumonia following an emergency laparotomy

A 65-yr-old male is ventilated in your ICU. He has postoperative pneumonia following an emergency laparotomy for perforated diverticulum and requires ventilation for respiratory failure/hypoxia. He has a $P_{A Toledo}$ of 14 kPa on an $F_{O2}$ of 0.6. He is cardiovascularly stable and is not receiving inotropic therapy. There are no signs of clinical bleeding. His creatinine level is 250 μmol litre$^{-1}$; however, his urine output is 50–80 ml h$^{-1}$. The patient suffered an anterior myocardial infarction 3 yr ago but is normally fit and active. He experiences mild exertional angina 2–3 times per month and this is relieved by GTN. He normally takes aspirin and a beta-blocker.

Clinical scenario 3

A 65-yr-old man is admitted to your ICU 3 days after undergoing an emergency laparotomy for perforated diverticulum. He has developed severe left ventricular failure and requires mechanical ventilation. A 12 lead ECG shows antero-lateral ST segment depression. He has a $P_{A Toledo}$ of 14 kPa on an $F_{O2}$ of 0.6. He is not receiving inotropic therapy. There are no signs of clinical bleeding. His creatinine level is 250 μmol litre$^{-1}$, however, his urine output is 50–80 ml h$^{-1}$. The patient suffered an anterior myocardial infarction 3 yr ago but is normally fit and active. He experiences mild exertional angina 2–3 times per month and this is relieved by GTN. He normally takes aspirin and a beta-blocker.

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