ORIGINAL ARTICLE

A study of blood product use in patients with major trauma in Scotland: analysis of a major trauma database

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Objectives: (1) To define blood product requirements in patients with trauma whose underlying injuries are consistent with major blood loss; (2) to use these data to estimate the annual number of patients in Scotland who sustain significant trauma and require substantial blood product replacement; and (3) to place these data in the context of recent findings concerning the efficacy of recombinant factor VIIa in patients with major trauma.

Methods: A retrospective casenote review study was conducted for patients who presented with trauma at each of four Scottish hospitals. The four sites were selected from the 26 hospitals that were the source of data for the Scottish Trauma Audit Group (STAG) database. Collected between 1991 and 2002, STAG encompasses approximately 53 000 patients. 129 patients whose trauma codes were likely to be linked to injuries associated with major blood loss were selected. Data on the use of blood products for each patient were collected and analysed for three periods: (1) time spent in the emergency department (ED); (2) time from leaving the ED to the end of the first 24 h; and (3) time from the end of the first 24 h to 7 days. Blood product use for each period and for the entire first week of care was described for all patients and for blunt and penetrating injury subgroups. Using national population data estimates, the incidence of major trauma requiring blood transfusion was calculated for Scotland.

Results: Among the patients with trauma codes predicting significant blood loss, the proportion of patients requiring any blood transfusion within the first 7 days was 53.9%. 27.4% of patients received ≥ 8 units of red cell concentrate (RCC) within the first 24 h of hospitalisation. By direct extrapolation, we estimated that the annual number of Scotland's patients (aged >13 years) with a significant blood transfusion requirement secondary to traumatic injury was 67. Of these, 35 patients would require ≥ 8 units of RCC within the first 24 h.

Conclusion: In summary, this study estimates that approximately 67 patients annually in Scotland, above the age of 13 years, require blood transfusion as a direct result of significant traumatic injury. Of these 67 patients, an estimated 35 patients (28 of whom had a blunt form of trauma) require ≥ 8 units of RCC during the first 24 h in hospital. On the basis of the current limited trial evidence, the potential benefit in using recombinant factor VIIa in such patients, in Scotland, is small—approximately seven patients per million population aged >13 years, per year.

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Trauma remains the leading cause of death in the UK in young adults.^{1,2} Haemorrhage is a major cause of death in such patients with trauma. In recent years there has been a move towards hypotensive/normotensive resuscitation and, in general, time to theatre and surgery by a senior surgeon (particularly out of hours) has improved. These two factors may have reduced the number of blood units given to patients with trauma, but despite this, haemorrhage remains a major cause of death in such patients. The burden placed on blood services by patients with trauma has not previously been defined at a national level, but is of interest in terms of both blood supply and the cost of blood products. In addition, major haemorrhage and massive blood transfusion are associated with potentially life-threatening complications such as coagulopathy. Exposure to massive blood transfusion increases the risk of well-documented adverse blood reactions, such as transfusion-associated lung injury, and also uncertain adverse effects such as those associated with the red cell storage lesion. Cohort studies of patients with acute trauma have found independent associations between blood transfusions and mortality, intensive care unit (ICU) admission, length of stay and total length of stay at hospital.^{3,4} For these reasons, the volume and consequences of blood transfusions may contribute to the illness costs associated with major trauma.⁵

Potential new treatments for haemorrhage associated with trauma have been investigated recently.⁶ Recombinant factor

VIIa (rFactor VIIa) may decrease blood product requirements in major blunt trauma, and has been effective in many case reports. To assess the potential impact of this expensive treatment, it is relevant to understand the epidemiology of such haemorrhage. rFactor VIIa already has a role in some forms of non-traumatic haemorrhage, and its use in these areas may expand in the future.

The objectives of this study were: first, to define the blood product requirements, over time, in a group of patients with trauma whose underlying injuries would be consistent with major blood loss; second, to use these data to estimate the annual number of patients in Scotland who sustain trauma associated with substantial blood product requirement; and third, to place this in the context of recent findings⁶ on the efficacy of rFactor VIIa in such patients.

METHODS

This was a retrospective casenote review study of patients who had been cared for at four Scottish hospitals after a presentation of trauma.

Abbreviations: ED, emergency department; FFP, fresh frozen plasma; ICU, intensive care unit; RCC, red cell concentrate; rFactor VIIa, recombinant factor VIIa; STAG, Scottish Trauma Audit Group

Figure 1 Overall selection of patients. STAG, Scottish Trauma Audit Group.

The Scottish Trauma Audit Group database

The source of data was the Scottish Trauma Audit Group (STAG) database, which was collected between 1991 and 2002. During this period, data on some 53 000 patients were collected. The overall national capture rate was 95% from 26 major Scottish hospitals. From this database, by consensus, we selected patients whose trauma codes were likely to be linked to injuries associated with major blood loss. The trauma codes selected identified those patients with

- (1) listed chest, abdominal or extremity injury, who had documented blood loss >20% of the total blood volume, and/or
- (2) penetrating injuries, who either died in the emergency department (ED) and/or had chest and abdominal injuries with Abbreviated Injury Score ≥ 4 .

A full list of the trauma codes used to extract cases is shown in appendix A (available online at <http://emj.bmj.com/supplemental>).

All patients with trauma who were managed in the resuscitation room and who either died or were hospitalised for at least 3 days as a result of their injuries were alone

included. Patients aged <13 years were excluded, as were patients who had an isolated fracture of the neck of femur or pubic ramus.

Data extraction from casenote review

We designed a data extraction form for all blood products from each patient for three time periods:

- during the time spent in the ED;
- from leaving the ED to the end of the first 24 h; and
- from the end of the first 24 h to the end of the first 7 days.

Data extraction from casenotes was undertaken by audit personnel trained specifically for trauma data.

Analysis

Patients were grouped according to their transfusion status (transfused vs non-transfused). We calculated the mean transfusion rates for red cells, fresh frozen plasma (FFP), platelets and cryoprecipitate for each of the three time periods considered, and for the total period, as estimates of blood product usage for this patient group. As data were not normally distributed, we also calculated the median (quartiles; range) to describe the distribution of blood product use.

We considered separately those patients who required ≥ 8 units of red cell concentrate (RCC), because (1) this is a marker of significant haemorrhage, and (2) it was used as the threshold for randomisation in a recent trial looking at the effect of rFactor VIIa on blood requirements in patients sustaining trauma.⁶ We also specifically examined the numbers of patients with blunt versus penetrating trauma.

Using estimates of the population catchment areas for the four hospitals considered, together with national population statistics, we extrapolated estimates for the likely rates of significant haemorrhage associated with trauma in Scotland.

RESULTS

We identified 434 patients who fulfilled the study criteria from the 26 hospitals. From these, casenotes on 129 patients were requested from the four selected hospitals on three occasions. Of these, 113 casenotes were reviewed (casenote review rate 88%). Of the 113 patients examined, transfusion status could not be determined accurately in 19 patients. Figure 1 summarises the selection of patients from the national dataset.

Among the 94 patients analysed, 59 (63%) were transfused RCC during the first 7 days after injury. A total of 31 patients received ≥ 8 units of RCC during the first 24 h following injury

Table 1 Demographics of dataset

	Transfused		Non-transfused	Not known	Total
	≥ 8 units of RCC in the first 24 h	<8 units of RCC in the first 24 h			
Male	26	24	22	14	86
Female	5	4	13	5	27
Median age, years (1st, 3rd quartile; range)			34 (21, 53; 15–96)		
Mechanism of injury					
RTA	18	16	16	6	56
Assault	6	7	2	5	20
Fall	6	5	14	6	31
Other	1	0	3	2	6
Median hospital LoS, days (1st, 3rd quartile; range)	17 (2, 45; 1–90)	17.5 (3, 34; 1–92)	11 (6, 29; 1–59)	6 (1, 12; 1–42)	11 (2, 29; 1–92)
Median ICU LoS, days (1st, 3rd quartile; range)	1 (0, 6; 0–18)	0 (0, 1; 0–11)	0 (0, 0; 0–2)	0 (0, 1; 0–13)	0 (0, 1; 0–18)
Mortality (%)	32.2	26.6	14.3	58.0	28.3

ICU, intensive care unit; LoS, length of stay; RTA, road traffic accident.

Table 2 Summary figures for blood product usage in the transfused patients group (n = 59)

	In ED	Exit ED to 24 h	Exit 24 h to 7 days	Total for a period of 7 days
RCC units				
Mean (SD)	3.72 (4.35)	9.24 (14.32)	1.69 (3.49)	14.59 (15.49)
Median (1st, 3rd quartile; range)	2 (0, 6; 0–12)	3 (0, 13; 0–73)	0 (0, 2; 0–16)	9 (4, 19; 0–81)
Platelet pools				
Mean (SD)	0 (0)	0.61 (1.07)	0.24 (1.06)	0.85 (1.52)
Median (1st, 3rd quartile; range)	0 (0, 0; 0–0)	0 (0, 1; 0–4)	0 (0, 0; 0–7)	0 (0, 1; 0–8)
Cryoprecipitate pools				
Mean (SD)	0 (0)	1.97 (5.68)	0 (0)	1.97 (5.68)
Median (1st, 3rd quartile; range)	0 (0, 0; 0–0)	0 (0, 1; 0–30)	0 (0, 0; 0–0)	0 (0, 1; 0–30)
FFP units				
Mean (SD)	0 (0)	2.51 (3.71)	0.17 (0.75)	2.68 (3.84)
Median (1st, 3rd quartile; range)	0 (0, 0; 0–0)	0 (0, 4; 0–15)	0 (0, 0; 0–4)	0 (0, 4; 0–15)

ED, emergency department; FFP, fresh frozen plasma; RCC, red cell concentrate.

(27.4% of the total; 53% of transfused patients). Table 1 shows the characteristics of the reviewed patients, and of transfused and non-transfused subsets of patients.

Transfused patients

Use of blood products during each time period for the 59 transfused patients, together with the total use of each product over the first 7 days of treatment, are shown in table 2.

Patients who received ≥ 8 units of RCC during the first 24 h

Table 3 shows the use of blood products for the subgroup of patients who received ≥ 8 units of RCC during the first 24 h.

Blunt versus penetrating trauma

Table 4 shows a comparison of RCC use for patients with blunt versus penetrating trauma.

Extrapolation to the Scottish population

The current estimation of Scotland's human adult population aged >13 years is 4.3 million.² We estimate the total population served by the hospitals from which this cohort was drawn as 1.9 million.^{7–9} Using our selected trauma codes, we estimate that annually 35 patients in Scotland have haemorrhage, due to trauma, requiring transfusion of ≥ 8 units of RCC within 24 h of hospitalisation. For blunt trauma, we estimate that approximately 28 patients per year require ≥ 8 units of RCC

in the first 24 h in hospital (seven patients per million population per year).

DISCUSSION

The patients who fulfilled the above criteria were extracted from the STAG database for the two full calendar years that yielded the highest percentage data capture rate (1998 and 2000). From the 26 admitting Scottish hospitals that constituted STAG data sources, we chose four representative hospitals for a casenote review (two district general hospitals; two teaching hospital-based trauma centres). Casenotes were requested on up to three occasions, after which no further attempt was made.

Using this dataset, we have shown that, among patients with trauma codes likely to predict significant blood loss, the proportion of patients requiring blood transfusion within the first 7 days is 53.9%. Among the total cohort, 27.4% received ≥ 8 units of RCC within the first 24 h. Men clearly dominated in numbers within the dataset by a ratio of 3:1 (table 1). They also outnumbered women by 5:1 in those who required a transfusion of ≥ 8 units. Those within the total cohort of 113 patients whose casenotes were reviewed had a median age of 34 years, indicating that this is generally a young group of patients with potentially significant number of years of life lost/number of years of earning lost. They therefore potentially have a large benefit to gain by timely and successful intervention. The group receiving ≥ 8 units of RCC had a similar median ICU

Table 3 Total extended blood product use for the group of patients who received ≥ 8 units of red cell concentrate in the first 24 h (n = 31)

	Within the first 24 h	Exit 24 h to 7 days	Total for a period of 7 days
RCC units			
Mean (SD)	21.9 (16.33)	1.52 (2.74)	23.4 (16.74)
Median (1st, 3rd quartile; range)	16 (10, 28; 8–81)	0 (0, 3; 0–11)	18 (10, 31; 8–81)
Platelet pools			
Mean (SD)	1.1 (1.25)	0.3 (1.27)	1.4 (1.78)
Median (1st, 3rd quartile; range)	1 (0, 2; 0–4)	0 (0, 0; 0–7)	0 (0, 2; 0–7)
Cryoprecipitate pools			
Mean (SD)	3.7 (7.44)	0 (0)	3.7 (7.44)
Median (1st, 3rd quartile; range)	0 (0, 2; 0–30)	0 (0, 0; 0–0)	0 (0, 2; 0–30)
FFP units			
Mean (SD)	4.4 (4.23)	0.2 (0.88)	4.6 (4.39)
Median (1st, 3rd quartile; range)	4 (0, 7; 0–15)	0 (0, 0; 0–4)	0 (0, 8; 0–15)

FFP, fresh frozen plasma; RCC, red cell concentrate.

Table 4 Injury type by transfusion status

	Transfused		Non-transfused	Not known	Total
	≥8 units of RCC in the first 24 h	<8 units of RCC in the first 24 h			
Blunt	25	21	33	13	92
Penetrating	6	7	2	6	21
Total	31	28	35	19	113

RCC, red cell concentrate.

length of stay (17 vs 17.5 days) and greater mortality (32.2% vs 26.6%) when compared with the lesser-transfused group. Various previous studies have found that the number of RCC transfusions a patient receives is independently associated with longer ICU and lengths of stay at hospital and an increase in mortality.^{3,4}

The main strengths of this study lie in its foundation of a widely recognised national database that has a high completeness rate and high-quality data. We completed a detailed casenote review performed by trained data extractors. We attained a high proportion of casenote reviews for the patients selected by trauma code.

A possible weakness of this study lies in the limited numbers of patients with trauma, although this is inherent in the study of such patients. We identified the selected trauma codes by consensus, and hence some cases of trauma could have been missed, although this is unlikely. We limited our dataset to four hospitals owing to restriction of resources for casenote review that may create selection bias. This might be mitigated by the facts that (1) the known demographics of trauma in Scotland suggest that patterns of trauma in other centres were unlikely to be significantly different (this has been borne out in a recent Scottish-wide study by Sukumaran *et al*¹⁰), and (2) the hospitals deliberately chosen were two district general hospitals and two teaching hospitals.

We used the same threshold that in the template study by Boffard *et al*, of 8 units of RCC for potential administration to rFactor VIIa. In the future, rFactor VIIa may be given after fewer units of RCC. Therefore, the prediction in this paper may underestimate the number of patients meeting the criteria for administration. Overall, however, we believe that the potential requirements for rFactor VIIa in this patient group are still likely to be very small.

Existing papers on this subject are set in major US trauma centres and are therefore not readily transposable to the UK setting. Statistics available from the US have highlighted the difference in the pattern of injury between the US and the UK, in particular the violence-related injury death rate associated with firearms (National Vital Statistics System, National Center for Health Statistics, CDC, USA). There were no papers found estimating the use and timing of blood products in Scotland in the setting of trauma.

As expected, most of the RCC transfusion occurred in the ED, and within the first 24 h (table 2). This finding is in keeping with previous work from the US.¹¹ Other blood products including FFP, cryoprecipitate and platelets were never transfused in this group of patients during the time spent in the ED. Most FFP was used within the time frame from leaving the ED to the end of the first 24 h of the patient's hospital stay. Platelets were transfused infrequently beyond the same time period and never cryoprecipitated (table 2). Our data for the transfused group of patients are consistent with those reported by Como *et al*,¹¹ who found that a minority of patients use the greatest volume of blood product.

These estimated figures have cost and organisational implications for hospitals in Scotland. Our extrapolated figures

suggest that trauma requiring significant blood product replacement is an infrequent event in Scotland. As such, when it does occur, it demands a flexible and rapidly responsive blood transfusion service. Major centres may be able to cope with such acute demand for large volumes of blood products through the use of "major haemorrhage" protocols. For smaller, peripheral hospitals, this may be more difficult and such a demand further warrants for rapid transport to a trauma centre. rFactor VIIa may have a role not only for these smaller centres but also for major hospitals. The use of rFactor VIIa is therefore likely to be a relatively rare occurrence, in this patient group, and as such the experience in using the drug will be slow to accumulate. Its safety profile has been reassuring from many small case series,¹²⁻¹⁴ but there is still a paucity of experience and an ongoing need for a large multi-centre randomised controlled trial of its use in this particular group of patients. If rFactor VIIa is eventually to receive a licence for use in the UK in this setting, such use will need to be guided by clear protocols, given its cost and infrequency of usage.

Although the extent of blood transfusion has been shown to be an independent predictor of mortality,³ these results show a 67.8% survival of patients who received transfusion of ≥8 units of RCC. This reflects the findings of previous large retrospective studies by Como *et al*,¹¹ Vaslef *et al*¹⁵ and Velmahos *et al*¹⁶ who do not view a requirement for massive blood product replacement, a marker of the futility of resuscitation. Indeed, these Scottish figures support this stance to an even greater extent.

In summary, this study estimates that approximately 67 patients annually in Scotland, aged >13 years, require blood transfusion as a direct result of significant traumatic injury. Of these 67 patients, an estimated 35 patients (28 of whom have a blunt form of trauma) require ≥8 units of RCC within the first 24 h in hospital. On the basis of the current limited trial evidence, it can be concluded that the potential benefit in using rFactor VIIa in such patients, in Scotland, is small.

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Appendix A is available online at <http://emj.bmj.com/supplemental>.

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