Coagulopathy and transfusion product usage in relation to ruptured abdominal aortic aneurysm scoring systems in a tertiary care centre in Japan

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Dear Sir,

Ruptured abdominal aortic aneurysm (rAAA) is a frequently fatal condition, with a mortality of approximately 67% in Japan[1]. Recently, two studies on the outcome of rAAA were reported from the viewpoint of blood transfusion for haemostasis. Johansson *et al.* reported on the application of platelet concentrates in rAAA patients undergoing surgery[2]. In the intervention group, platelet concentrates were transfused at the time rAAA was suspected and before clamping the aorta, and blood transfusion with a ratio of fresh-frozen plasma to red cell concentrate (FFP:RCC) of 1:1 was given. The 30-day survival rates were higher in the intervention group than in the control group. Mell *et al.* reported the effect of early plasma transfusion on mortality in patients with rAAA; in their study the FFP:RCC ratio was1:2[3]. These reports suggested that prevention of coagulopathy in patients with rAAA improves the outcome.

Pre-operative scoring systems for rAAA are widespread in Europe. The outcome of patients with rAAA undergoing vascular surgery has been evaluated using rAAA scoring systems[4-5]. In this study, we retrospectively scored the pre-operative status of patients undergoing vascular surgery and examined the relationship between the rAAA score and coagulopathy in a single tertiary care centre in the metropolitan Tokyo area in Japan. To our knowledge, our study is the first to suggest that severe coagulopathy is a predictor of rAAA in patients with a high rAAA score.

Tokyo Metropolitan Bokutoh Hospital has 729 acute-care beds and is located in eastern Tokyo. We reviewed the cases of 64 patients with rAAA who underwent vascular surgery from April 2000 to March 2010. The clinical data of the 64 patients with rAAA were reviewed for parameters such as age, gender, clinical manifestations (blood pressure and Glasgow coma scale [GCS]), laboratory test results (haematology, clotting tests and biochemistry), use of transfusion, and rAAA score (Glasgow aneurysm score [GAS], Edinburgh ruptured aneurysm score [ERAS], and Hardman Index [HI]). A rAAA was diagnosed on the basis of computed tomography, open surgery, or post-mortem findings. We evaluated three previously reported rAAA scoring systems[4-5]. According to their scores, the patients were divided into subgroups from the viewpoint of outcome: (i) GAS: low-score subgroup, <88 points; middle-score subgroup, 88-99 points; and high-score subgroup, >99 points. (ii) ERAS: low-score subgroup, 0-1; high-score subgroup, 2-3. (3) HI: low-score subgroup, 0-1; high-score subgroup, 2-5. This study was performed in accordance with the principles of the Declaration of Helsinki. We noted that the ERAS gave the most striking results among the three rAAA scoring systems. In the ERAS group, we compared the differences between the low-score and high-score groups in terms of clinical manifestations, pre-operative and post-operative laboratory data, and use of blood transfusions. Post-operative laboratory samples were obtained immediately after the patients had been transferred from the operating theatre to the intensive care unit. As shown in Table I, patients with rAAA were mainly elderly and predominantly male. Of the 64 patients undergoing vascular surgery, 42 died in the hospital (in-hospital mortality, 65%). Causes of in-hospital death were mainly haemorrhage and related complications (27 patients, 65%), multiple organ failure (14 patients, 33%), and acute myocardial infarction (1 patient, 2%).

We first compared the differences between the low-score group (n=43) and high-score (n=21) groups of ERAS in terms of clinical manifestations such as age, gender, blood pressure, GCS at presentation, and rAAA score. There was no significant difference in age between the low-score and high-score groups of ERAS. Systolic blood pressure and GCS scores at presentation were significantly lower in the high-score group than in low-score group. We calculated rAAA scores using three rAAA scoring systems, as shown in Table I. The HI score of the high-score group of ERAS was significantly higher than that of the low-score group, but the GAS score did not differ significantly between the two groups. The

*Blood Transfus 2012; **10**: 393-5* DOI 10.2450/2012.0071-11

Table I - A comparison between low-score and high-score groups of ERAS based on clinical characteristics, laboratory findings, and transfusion product usage from admission to the peri-operative stage in rAAA patients undergoing vascular surgery.

	All subjects n=64	Low score n=43	High score n=21
Age #	74 (65-80)	74 (65-80)*	73 (65-79)
Gender (male/female)	50/14	33/10	17/4
Systolic blood pressure at presentation (mmHg)	87±6	108±5*	45±8
GCS at presentation #	15	15	7
% mortality	(13.3-15)	(15-15)*	(3-4)
rAAA score	42/64 (67%)	24/43 (56%)*	18/21 (86%)
Glasgow aneurysm score (GAS)	89±2	87±2	92±3
Edinburgh ruptured aneurysm score (ERAS)	±0.1	0.5±0.1*	2.3± 0.1
Hardman index (HI)	1.5±0.1	1.2±0.2*	2.1±0.2
Pre-operative data			
Haemoglobin (g/dL)	10.1±0.3	10.7±0.3*	8.9±0.5
Haematocrit (%)	30.2±0.8	31.8±0.9*	27.1±1.4
Red blood cells ($x10^9$/L)	3,200±90	3,390 ±100*	2,820±150
Platelets ($x10^9$/L)	173±8	181±9	156±17
PT (%)	85.5±3	88.3±3.6	79.3±5.8
aPTT (s)	34.8±2.1	30.7±0.9*	43.7±6.2
Fibrinogen (mg/dL)	269±16	291±19*	223±26
FDP (µg/dL)	88.4±33.7	47.5±10.8	134.9±92.4
D-dimers (µg/dL)	41±19	23±8	72±51
Albumin (g/dL)	3.2±0.1	3.3±0.1	3.0±0.1
Post-operative data			
Haemoglobin (g/dL)	8.9±0.3	9.2±0.3*	7.9±0.5
Haematocrit (%)	25.7±0.8	26.8±0.9	23.2±1.4
Red blood cells ($x10^9$/L)	2,860±80	2,970±100*	2,540±160
Platelets ($x10^9$/L)	68±6	70±7	61±13
PT (%)$	47.6±0.6	53±3*	33±8
aPTT (s)$	75.8±5.3	66.5±5.3*	99.2±10.6
Fibrinogen (mg/dL)$	119±14	140±17*	64±20
FDP (µg/dL)$	65±11	50±11*	110±26
D-dimers (µg/dL)$	33±8	20±4*	74±23
Albumin (g/dL)	2.4±0.1	2.6±0.1*	1.8±0.3
Transfusion product usage			
Red cell concentrate (mL)	4,389±403	3,193±300*	5,327±587
Fresh-frozen plasma (mL)	2,216±203	1,808±195*	3,051±426
Plasma to red cell transfusion (FFP:RCC) ratio	0.57±0.03	0.58±0.05	0.55±0.05
Platelet concentrates (n)	46 (72%)	33 (77%)	13 (62%)
Albumin (n)	49 (77%)	34 (79%)	15 (71%)
Amount of bleeding (g)	6,714±547	5,459±503*	9,283±1135

We compared the differences between the low-score and high-score groups by Wilcoxon's analysis. Data are expressed as group mean ± standard error of the mean, or medians with inter-quartile ranges. The comparisons of the mortality rates were analysed by the chi-square test with Yates' correction. All statistical procedures were conducted using JMP version 8.0 software (SAS Institute, Inc., Cary, NC, USA), and significance was defined as $p < 0.05$.# Data are expressed as group medians with inter-quartile ranges.*$p < 0.05$ versus non-survivors; $: n=52; data from 12 patients were lacking because of the patients' death.

pre-operative laboratory results showed that patients in the high-score group of ERAS were significantly more anaemic than those in the low-score group. Furthermore, we noted a significantly stronger association between coagulopathy and low plasma fibrinogen levels in the high-score group of ERAS than in the low-score group (Table I). The platelet count did not differ significantly between the two groups.

The post-operative laboratory results showed more severe anaemia in patients in the high-score group than in those in the low-score group. Patients in the high-score group of ERAS had more severe coagulopathy and elevated fibrinolysis than those in the low-score group, as shown in Table I. RCC (volume; mL) and FFP (volume; mL) were transfused significantly more often in the high-score group than in the low-score group (Table I). However, there were no significant differences between the two groups in terms of FFP:RCC ratio (volume; mL: volume; mL), administration of platelet concentrates, and albumin products. The amount of blood lost was significantly greater in the high-score group than in the low-score

group. The reason for the higher mortality in the high-score group than in the low-score group might be low plasma transfusion against bleeding mass. As for ERAS, lower plasma transfusion in the high-score groups of HI (FFP:RCC ratio: 0.54) and GAS (FFP:RCC ratio of middle-score group, 0.62, and of high-score group, 0.51) might have resulted in a poor outcome (mortality rates of the low-score groups of HI and GAS were 58% and 53%, respectively, while those of the high-score group of HI and the middle- and high-score groups of GAS were 75%, 76%, and 80%, respectively), in comparison with the outcome in the low-score groups of HI (FFP:RCC: 0.60) and GAS (FFP:RCC: 0.57).

Because there was no difference in post-operative haematological data on anaemia between survivors and non-survivors, transfusion with RCC was sufficient in both groups (pre- and post-operative Hb of survivors [n=22]: 11.5±0.5 g/dL and 9.2±0.4 g/dL, respectively; pre- and post-operative Hb of non-survivors [n=42]: 9.6±0.3 g/dL and 8.6±0.4 g/dL, respectively). However, there was a significant difference in the post-operative results of clotting tests between the survivors and non-survivors (post-operative percent prothrombin time [%PT], activated partial thromboplastin time [aPTT], and plasma fibrinogen levels of survivors (n=22): 59%±4%, 58.5±5.8 s, and 167±23 mg/dL, respectively; post-operative %PT, aPTT, and plasma fibrinogen levels of non-survivors [n=30, data from 12 patients lacking because of the patients' death]: 37%±4%, 91.6±7.2 s, and 79±12 mg/dL, respectively). These data suggest that plasma transfusions is not sufficient for non-survivors. Thus, severe coagulopathy in the high-score groups of ERAS as well as HI and GAS might cause more bleeding, and failure to control the bleeding may result in death due to haemorrhage.

In patients with rAAA, massive haemorrhage has already occurred in the abdomen. We, therefore, consider that the strategy of transfusion for rAAA differs from that for general surgery. Because hypofibrinogenaemia was noted in the high-score group of ERAS, early plasma transfusion was necessary to correct the coagulopathy, as Mell *et al.* suggested[3]. Moreover, health insurance limitations in the Japanese Medical Service prevent the use of fibrinogen concentrates and cryoprecipitates in patients with severe, secondary hypofibrinogenaemia. While the FFP:RCC ratio for rAAA was 0.5 as described by Mell *et al.*, it might be over 0.5-1.0 in the metropolitan Tokyo area in Japan, similar to that in Johansson's report (FFP:RCC=1). The difference between the results obtained by Mell *et al.* and the results of our clinical interventions might be due to the severity of rAAA or the medical system in Japan, in which no fibrinogen products such as fibrinogen concentrates or cryoprecipitates can be used.

Our study has some limitations: it was a retrospective, long-term study (10 years), with a small number of patients (n=64). Over the 10-year study period, various surgeons performed vascular surgery for rAAA, and the drugs and instruments used during the admissions and the operations were different. We, therefore, consider that a prospective, large sample, multi-centre study within a short-term time frame should be performed in order to further clarify the relationship between various rAAA scoring systems and transfusion ratio.

This study suggests that patients with high rAAA scores had severe coagulopathy due to rAAA, and that the strategy to improve outcome in patients with a high rAAA score would be sufficient plasma transfusion. In the future, we will consider a transfusion protocol for rAAA using a strategy based on FFP:RCC ratios and rAAA scores. In conclusion, our data suggest that the transfusion strategy for rAAA might be based on an adequate transfusion ratio and evaluation by rAAA scoring.

The Authors declare no conflicts of interest.

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Arrived: 12 July 2011 - Revision accepted: 30 January 2012
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