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Intraoperative Platelet and Plasma Improves Survival in Patients Operated for a rAAA: A Follow-up Evaluation

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Abstract *Objectives:* Continued haemorrhage remains a significant contributor to mortality in massively transfused patients. We found that early administration of platelets and plasma reduced mortality from 54% to 36% in rAAA patients. The aim of the present evaluation was to evaluate whether reduced mortality in rAAA patients related to a pro-active transfusion therapy is maintained.
Design: Single-centre observational study.
Methods: Mortality of patients operated for rAAA 2006–07 was compared to that of patients operated 2004–05 (intervention group; $n = 50$) and 2002–04 (control group, $n = 82$).
Results: 64 consecutive patients with rAAA received, similar to the intervention group, more platelets (5 and 4 vs. 0 units, $P < 0.05$) and plasma (12 and 11 vs. 7 units, $P < 0.05$) intraoperatively and had a higher platelet count (158 and 155 vs. 69×10^9/L, $P < 0.0001$) upon arrival at the intensive care unit and the 30-day mortality remained reduced (24% and 36% vs. 56%, $P < 0.01$ and $P = 0.02$, respectively) as compared to the control patients.
Conclusions: Early administration of platelets and plasma, together with red blood cells maintained reduced mortality in patients operated for rAAAin a 18 month period.
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Introduction

Continued haemorrhage remains a significant contributor to mortality in massively transfused patients and many patients develop coagulopathy.[1] Patients surviving massive transfusion have a higher platelet count[2] and a shorter prothrombin (PT) and activated partial thrombin time (APTT)[3]

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than non-survivors and maintained coagulation competence appears to be of importance for haemostasis and, thereby, survival.[4,5]

Current transfusion recommendations appear to be extrapolated from elective surgery and may not be applicable to patients with massive bleeding who are likely to be hypocoagulable because of hypothermia, acidosis, and haemorrhagic shock.[6] The recommended resuscitation regimen advocates early administration of crystalloids and colloids supplemented by administration of fresh frozen plasma (FFP) and platelets only when one whole blood volume is replaced and this may further impair haemostatic competence.[7] Thus, administration of FFP and platelet concentrates (PC), in addition to red blood cells (RBC), as a part of a transfusion package, immediately when the patient with a ruptured abdominal aortic aneurysm (rAAA) arrives at the hospital and throughout surgery, appears to reduce mortality in these patients.[8] Survival was related to maintenance of haemostatic competence, resulting in reduction in postoperative transfusion requirements. However, survivals in these rAAA patients vary from year to year and it may be that the reduced mortality following introduction of a balanced blood transfusion strategy resulted from such random variation in mortality following rAAA surgery.[9]

We hypothetizised that administration of transfusion packages would maintain a reduced mortality in rAAA patients and, hence, the aim of this observational follow-up study was to evaluate whether the reduced mortality in rAAA patients was maintained in patients undergoing rAAA surgery in the 18-months following the end of the first evaluation of the change in transfusion strategy.

Material and Methods

The background of the study was an observational study of all patients operated for a rAAA from January 1st 2006 to June 30th 2007. Data were collected and entered into a study database according to a unique personal identity number after approval from the Danish Data Protection Agency. Consent was not obtained as Danish legislation allows database studies without approval from the ethics committee system and the local ethics committee did not endorse a randomized trial. In Denmark, treatment of acute AAA takes place in six centers and this hospital cover 70% of the Eastern part of the country. Throughout the period of the study (2002–2007) there were no deliberate changes in referral practice or surgical procedures and specifically there were no identified change from the period before implementation of the revised transfusion strategy to the present follow-up study. The diagnosis of rAAA was established by an ultrasound image at the local hospital and that was confirmed at the hospital the patient was referred to for surgery. The surgical procedure employed laparotomy and no endovascular repair was performed. The transfusion strategy included administration of platelets and FFP together with RBC as a part of a transfusion package immediately the patient arrived at the hospital and continued throughout surgery. In addition, two PC were administered before reperfusion of the aorta and for the patients included in this follow-up study also tranexamic acid 2 g i.v., considering that this may further improve haemostatic competence, was administered at induction of anaesthesia and further 1 g was administered at reperfusion of the aorta.

Transfusion requirements and mortality of these patients were compared to those of patients operated for a rAAA from 2002–2005. Patients operated for a rAAA between January 1st 2002 and April 30th 2004 constituted a control group that had been transfused according to existing guidelines as outlined above. Patients operated for an acute AAA was identified from the national vascular database and those presenting with intra –or retroperitoneal haematoma during dissection of the aorta as stated in the surgical record were included. The national vascular database also identified those patients transferred directly to the referral hospital and those who were transferred through another hospital. The intervention group, identified as described above was treated with transfusion packages, from May 1st 2004 until 2006.

For the follow-up group, data were collected on patients undergoing rAAA surgery during the study period and a review of their records was conducted with respect to presence of intra –or retroperitoneal haematoma during dissection of the aorta, gender, age, weight, co-morbidities defined as diabetes type I, cerebrovascular disease including stroke, TCI, intracranial bleeding, hypertension, cardiovascular disease including myocardial infarction, angina pectoris, and pulmonary disease including chronic obstructive pulmonary disease and asthma. Furthermore, the peri operative blood loss, supra/infra renal aortic clamping position and clamping time, duration of surgery, re-do surgery, length of stay (LOS) in the intensive care unit (ICU), LOS in hospital, and 30-day mortality were noted. Time and amount of transfused RBC, FFP, and PC were obtained from the database in the blood bank. Haemoglobin, platelet count, activate partial thromboplastin time (APTT), international normal ratio (INR), and serum creatinine at admission to the ICU following the operation were obtained from the laboratory database.

All patients received the same anaesthetic regimen including preoxygenation followed by rapid sequence induction and relaxation with suxamethonium follwed by endo tracheal intubation and mechanical ventilation. Anaestheisa was maintained by inhalation of sevoflurane. Volume replacement was individually goal- directed to maintain maximal venous oxygen saturation.[10] Lactated Ringers solution and RBC were administered to maintain a haematocrit of 30%. No cell saver was used to maintain coagulation competence and all blood products and fluids administered were pre-warmed to maintain patientś temperature at $\sim 37\,^{\circ}C$ with use of external heating. Data analysis was performed using SAS 9.1 (Cary, NC, USA) and are presented as median and range. Results were compared using the two-sample Wilcoxon rank sum test or Fisher's exact test as appropriate with a p-value < 0.05 considered as statistically significant.

Results

Records of 64 consecutive patients operated for rAAA were identified from 2006 to 2007 (18 months) and there were no significant differences between the follow-up and the

control or intervention groups of patients in regard to baseline characteristics (Table 1).

The 30-day mortality in the follow-up group was 25%, not being significantly different from the intervention group (34%, $P = 0.29$), whereas both of these groups presented with a lower mortality when compared to that of the control group (56%; $P < 0.01$ and $P = 0.02$, respectively). No significant differences in RBC requirements were found between groups, whereas both the follow-up and intervention group received more FFP (12 and 11 vs. 7 units, $P < 0.05$), and platelets (5 and 4 vs. 0 units, $P < 0.05$) as compared to the control group (Table 2). In the ICU, however, the control group received more RBC (6 vs. 3 and 2 units respectively, $P < 0.05$), FFP (4 vs. 2 and 2 units, $P < 0.05$), and PC (1 vs. 0 and 0 units, $P < 0.05$) as compared to patients receiving transfusion packages intraoperatively. The follow-up as well as the intervention groups had a higher platelet count (158 and 155 vs. 69×10^9/L., $P < 0.0001$) and shorter APTT upon arrival at the ICU (38 and 39 vs. 44 s, $P < 0.05$).

Table 1 Descriptive data for patients operated for a ruptured abdominal aortic aneurysm

	Follow-up group	Intervention group	Control group
Year	2006–2007	2004–2005	2002–2004
Number	64	50	82
Patient Characteristics			
Male/Female	55/9	43/7	72/10
Age, Median (range) years.	77 (62–90)	71 (48–89)	73 (51–84)
Weight (kg)	83 (53–124)	77 (55–100)	80 (35–115)
Medical history No. (%)			
Co-morbidity	75%	73%	74%
Diabetes	12%	11%	10%
Cerebrovascular	12%	11%	9%
Hypertension	45%	41%	37%
Cardiac disease	24%	25%	27%
Pulmonary disease	22%	20%	18%
Surgery			
Tube graft	40	35	60
Bifurcated graft	24	15	22
Clamping position (S/I)	3/61	4/46	4/78
Clamping time (min) Median (range)	94 (35–224)	96 (50–140)	97 (40–205)
Surgery (min)	191 (105–320)	183 (120–300)	194 (120–400)
Bleeding (L)	5,8 (1,5–15)	6.1 (0.6–20.0)	6.3 (1.0–27.0)
Re-do surgery (No).	4	5	11
Re-do survival (No).	2	2	3

Suprarenal/Infrarenal clamping position (S/I).

Discussion

The principal finding of this 18 month follow-up study is that administration of a balanced transfusion strategy through provisions of ''transfusion packages'', encompassing PC and FFP together with RBC, provided from the start of surgery and repeated during surgery as needed, maintained a reduced mortality rate in patients operated for a rAAA, as compared to a historical control group of patients treated in accordance to recommendations from existing transfusion guidelines.[7] Following the local change in transfusion practice,patients received more PC and FFP intraoperatively and they had a higher platelet count and a shorter APTT when entering the ICU than was the case for the historic control group of patients. Administration of tranexamic acid to the rAAA patients may have contributed to enhance the survival of the patients although this finding was not statistically significant when compared to when the change in blood component usage was introduced.

Implementation of a transfusion protocol for massively bleeding patients to provide timely and balanced delivery of blood components aimed at preventing, rather than to ''catch up'' with coagulopathy as it develops, and that appeared to maintain a low mortality rate for patients operated for a rAAA.[11] Both the follow-up and the intervention groups of patients operated for rAAA presented with a platelet count well above 100×10^9/L upon arrival at the ICU, while the control group was thrombocytopenic, although the value was above the presently recommended level of 50×10^9/L. The control group received more transfusions in the ICU, suggesting improved haemostatic ability in the groups of patients receiving transfusion packages. This apparent increased coagulation competence concurred with findings in patients presenting with uncontrolled haemorrhage receiving transfusion packages and monitored by thrombelastography (TEG) before and after each package, who demonstrate normal haemostatic competence even when up to 7 packages are administered.[12] Accordingly, experience from the Iraqi war supports that patients having a high FFP to RBC ratio and receiving more platelets demonstrate a lower mortality rate than those receiving less plasma and platelets following trauma.[13]

Mortality of patients operated for a rAAA ranged from 40% to 70% with a mean of ~50% in the years before the introduction of a balanced blood component therapy by predefined packages of blood products. Thus, with introduction of the transfusion packages mortality decreased to 36% and, as demonstrated in this follow-up study, stabilized below 30%.

Transfusion medicine is a young speciality and its members are largely drawn from among clinical pathologists or haematologists and its concerns are focused on how to keep blood banks and transfusion services staffed, licensed, accredited and supplied.[6] Those in charge of organising and maintaining a transfusion service have, in general, little clinical experience and focus is on standard operating procedures and evidence based guidelines. The majority of the evidence and, accordingly, the guidelines released during the past two decades suggest that

Table 2 Outcome data for patients operated for a ruptured abdominal aortic aneurysm

	Follow-up group	Intervention group	Control group
Year	2006–2007	2004–2005	2002–2004
Transfusions intraoperatively (No)			
RBC	10 (3–24)	12 (2–40)	10 (4–65)
FFP	12 (4–24)	11 (2–42)	*7 (0–46)
PC	5 (3–11)	4 (2–16)	*0 (0–3)
Transfusions postoperatively (No.)			
RBC	2 (0–20)	3 (0–31)	*6 (0–54)
FFP	2 (0–10)	2 (0–12)	*4 (0–32)
PC	0 (0–5)	0 (0–4)	*1 (0–6)
Laboratory values at admission to ICU			
Haemoglobin (g/L) Median (range)	122 (78–150)	123 (72–171)	121 (105–134)
Platelet count ($\times 10^9$/L)	158 (77–286)	155 (31–557)	*69 (29–236)
APTT (s)	36 (20–124)	39 (22–130)	*44 (28–145)
INR (arbitrary units)	1.2 (0.8–3.9)	1.3 (0.9–4.2)	1.3 (1.0–2.1)
S-Creatinine (mg/dL)	1.3 (0.65–7.3)	1.3 (0.52–9.2)	*1.7 (0.91–5.2)
Length of stay (LOS)			
ICU (d)	5.5 (0–22)	6.3 (0–26)	4.2 (0–33)
Hospital (d)	11.1 (1–47)	12.0 (1–42)	10.0 (1–86)

Activated partial thromboplastintime (APTT); prothrombintime (PT); all values for arrival at the intensive care unit (ICU) after surgery. Data are median and range. *difference between the follow-up and intervention vs. control group ($p < 0.05$).

administration of less blood is better, but the caveat is that these guidelines apply to haemodynamically stable patients.[6] The data presented here adds to the body of reports[14–17] corroborating that early administration of platelets and FFP, together with RBC appear to be associated with improved survival in massively bleeding patients and suggest that maintained coagulation competence is important for patients operated for a rAAA

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