Intraoperative blood product resuscitation and mortality in ruptured abdominal aortic aneurysm

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Objectives: The resuscitation of patients with ruptured abdominal aortic aneurysms (RAAA) has not been well studied, and the potential benefit of autotransfusion (AT) is unknown. The increased use of fresh-frozen plasma (FFP) has been associated with decreased mortality rates in trauma patients and may also improve RAAA survival. We explored the influence of intraoperative AT and FFP resuscitation on mortality rates in massively transfused RAAA patients.

Methods: A single-center review of RAAA patient records from April 1989 to October 2009 was undertaken. Clinical data and outcomes were studied. Operative and anesthesia records were queried for intraoperative transfusion totals. Massive transfusion was defined as ≥10 units of red blood cells (RBCs) inclusive of AT units.

Results: We identified 151 RAAA patients, of which 89 (60%) received a massive transfusion and comprised the study population. These 89 patients had an in-hospital mortality rate of 44%. Univariate predictors of mortality included increased age, preoperative hypotension, operative blood loss, and crystalloid, RBCs, and FFP volume. AT was used in 85 patients, with an increased ratio of AT:RBC units associated with survival. Mortality was 34% with AT:packed RBCs (PRBC) ≥1 (high AT) and 55% with AT:PRBC of <1 (low AT; P = .04). On multivariate analysis, age >74 years (P = .03), lowest preoperative systolic blood pressure (SBP) <90 mm Hg (P = .06), blood loss >6 liters (P = .06), and low AT (P = .02) independently predicted mortality. The mean RBC:FFP ratio was similar in those that died (2.7) and in those that lived (2.9; P = .66). RBC:FFP ≤2 (high FFP) was present in 38 (43%) patients, with mortality of 49%. RBC:FFP >2 (low FFP) had 40% mortality (P = .39). RBC:FFP ratios decreased over time from 3.6 (years 1989 to 1999) to 2.2 (years 2000 to 2009; P < .001), but more liberal use of FFP was not associated with decreased mortality (47% vs 41%; P = .56). AT:PRBC ratios were stable over time (range, 1.4–1.2; P = .18).

Conclusions: Greater use of AT but not of FFP was associated with survival in massively transfused RAAA patients. No mortality benefit was seen with increased FFP, but few patients had high FFP transfusion ratios. Further study to identify RAAA patients at risk for massive transfusion should be undertaken and a potentially greater role for AT in RAAA resuscitation investigated. (J Vasc Surg 2012;55:688-92.)

Ruptured abdominal aortic aneurysm (RAAA) continues to have a high mortality rate despite recent advances in critical care.1,2 The mortality risk factors that have been identified have been reported with an eye toward the triage of patients in the attempt to determine the feasibility and justification of repair in certain populations.3 Most of the identified predictors of death are pre-existing patient factors such as shock and renal failure and cannot be altered during treatment, limiting their usefulness in planning a strategy for preventing death.1

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METHODS

This study was approved by the Institutional Review Board at the University of Utah. A retrospective review of patient records from April 1989 to November 2009 was undertaken. Surgeons’ operative notes were examined for operative details. All patients who underwent attempted open repair of a ruptured abdominal aortic, isolated iliac, or aortoiliac aneurysm were included. The study excluded patients who had undergone previous open or endovascular AAA repair or who had no evidence of rupture at the time of operation.

Estimated operative blood loss and intraoperative transfusion and resuscitation totals were obtained from anesthetic records. No resuscitation guidelines for RAAA patients were in place at our institution during the study period. Resuscitation fluids of interest included crystalloid (0.9% sodium chloride or Ringer’s lactate, or both) and colloid (5% human albumin) volumes. Transfusions recorded included PRBC and FFP units.

AT is currently prepared using the Sorin BRAT 2 system (Sorin Group, Arvada, Colo) and performed at the discretion of the attending anesthesiologist. Standard practice at our institution is to set up the AT system for urgent and elective AAA cases. The amount of AT infused was recorded as a total volume, then divided by 250 mL (the infusion volume/unit at our institution) to arrive at a number of AT units. To generalize our results to compare with those where AT is not used or reported, we generated AT:PRBC calculations are based on the 85 patients who acquired specific treatment. Colon ischemia was suspected with clinical deterioration (fever, leukocytosis, acidemia) and confirmed with endoscopy or during laparotomy.

Statistical analysis was performed using Stata 11.1 software (StataCorp LP, College Station, Tex). Univariate comparisons were performed using the t test, \( \chi^2 \) test, or Fisher exact test as appropriate. Multivariate logistic regression was performed to test for independent contributions of dichotomous univariate variables to death. Data are reported as mean ± standard deviation, with median as appropriate. Statistical significance was defined at \( P \leq .05 \).

RESULTS

During the study period, 151 patients were operated on for RAAAs, with 89 (59%) undergoing massive transfusion and comprising the study cohort. Their average age was 74 years (range, 41-93 years), and 72 (81%) were men. Seventy-seven patients (87%) were transferred from another institution. The mean lowest preinduction systolic blood pressure (SBP) among the 89 patients was 99 mm Hg.

All 89 patients received PRBC, and 87 received FFP. Colloid was used in 37 patients. The TRBC:FFP calculations are based on the 87 patients who received FFP. The AT:PRBC calculations are based on the 85 patients who received AT.

There were 39 in-hospital deaths for an overall mortality rate of 44%, with 18 deaths (46%) occurring ≤24 hours of operation. A univariate analysis of mortality among massively transfused patients with ruptured abdominal aortic aneurysm

<table>
<thead>
<tr>
<th>Variable*</th>
<th>Lived (n = 50)</th>
<th>Died (n = 39)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>71 ± 9</td>
<td>77 ± 9</td>
<td>.0002</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>104 ± 24</td>
<td>92 ± 36</td>
<td>.06</td>
</tr>
<tr>
<td>Suprarenal clamp</td>
<td>32 (64)</td>
<td>28 (72)</td>
<td>.40</td>
</tr>
<tr>
<td>EBL, mL</td>
<td>6570 ± 3406</td>
<td>9062 ± 6152</td>
<td>.03</td>
</tr>
<tr>
<td>Crystalloid, mL</td>
<td>7737 ± 3817</td>
<td>10,208 ± 4633</td>
<td>.007</td>
</tr>
<tr>
<td>Colloid, mL</td>
<td>1500 ± 1021</td>
<td>1462 ± 1561</td>
<td>.93</td>
</tr>
<tr>
<td>PRBC, units</td>
<td>9 ± 13</td>
<td>13 ± 9</td>
<td>.004</td>
</tr>
<tr>
<td>FFP, units</td>
<td>7 ± 4</td>
<td>11 ± 10</td>
<td>.06</td>
</tr>
<tr>
<td>Platelets, units</td>
<td>2.3 ± 1.5</td>
<td>2.8 ± 1.7</td>
<td>.02</td>
</tr>
<tr>
<td>AT, units</td>
<td>12 ± 8</td>
<td>12 ± 8</td>
<td>.93</td>
</tr>
<tr>
<td>PRBC:FFP</td>
<td>1.5 ± 0.8</td>
<td>1.8 ± 1.4</td>
<td>.30</td>
</tr>
<tr>
<td>TRBC:FFP</td>
<td>2.9 ± 1.9</td>
<td>2.7 ± 1.7</td>
<td>.66</td>
</tr>
<tr>
<td>AT:PRBC</td>
<td>1.4 ± 1.0</td>
<td>1.1 ± 0.7</td>
<td>.07</td>
</tr>
<tr>
<td>High ATb</td>
<td>31 (65)</td>
<td>16 (41)</td>
<td>.05</td>
</tr>
</tbody>
</table>

AT, Autotransfusion; EBL, estimated blood loss; FFP, fresh frozen plasma; PRBC, packed red blood cells; SBP, lowest preoperative systolic blood pressure; TRBC, total red blood cells (includes AT).

*Continuous data are presented as mean ± standard deviation.

bDefined as AT:PRBC ≥1.
mean TRBC:FFP ratios were similar between those who died (2.7) and those who lived (2.9; \(P = .30\)). Among 39 patients with a TRBC:FFP ratio \(\leqslant 2\) (high FFP), mortality was 49\%, whereas among 48 patients with TRBC:FFP >2 (low FFP), mortality was 40\% \((P = .39)\).

The AT:PRBC transfusion ratio trended toward significance on the univariate mortality analysis, with an increased ratio predicting survival \((P = .07, \text{Table I})\). When dichotomized at the group median, an AT:PRBC ratio of \(\geq 1\) (high AT) was a significant predictor of survival \((P = .05)\). In 47 patients with high AT after open repair of RAAA, mortality was 34\%; in the 38 with low AT, mortality was 55\% \((P = .05)\). The high-AT group received an average of 9.6 units of PRBC vs 10.9 units in the low-AT group \((P = .24)\). The high-AT group also received about twice the amount of AT \((15.2 \text{ vs } 7.2 \text{ units}; \ P < .001)\) and had greater mean blood loss \((832 \text{ vs } 6547 \text{ mL}; \ P = .09)\).

Multivariate logistic regression was performed to test whether the AT:PRBC ratio was associated with death independent of other pertinent risk factors identified on univariate analysis. Variables were selected if their \(P\) value on univariate analysis was \(\leq .1\). We did not include PRBC, FFP, and platelet transfusion and crystalloid infusion because they were covariates with estimated blood loss. Age >74 years, lowest preinduction SBP pressure <90 mm Hg, estimated blood loss >6 liters (the group median), and high AT were entered into a logistic regression model. Age >74 years \((P = .03)\) and low AT \((P = .02)\) were independent predictors of death \((\text{Table I})\).

The mortality rate did not change significantly over time during the study period. From April 1989 through December 1999 (early period, 38 patients) there were 18 deaths for a 47% mortality rate. From January 2000 through November 2009 (late period, 51 patients), there were 21 deaths for a 41% mortality rate \((P = .56)\). From the early to the late period, the mean TRBC:FFP decreased significantly, from 3.6 to 2.2 \((P = .0007)\), indicating progressively more liberal administration of FFP. Between the two intervals, the mean AT:PRBC was similar \((1.4-1.2, \ P = .18)\), indicating stability in the relative amount of AT infused (Fig 1).

The rate of major complications among the 89 massively transfused patients was 73\%. Of the 85 patients who received AT, 69 (82\%) survived >24 hours. There were no significant differences between the high-AT and low-AT groups in the incidence of overall or infectious complications, postoperative bleeding requiring reoperation, or colon ischemia (Fig 2).

**DISCUSSION**

We examined the influence of intraoperative blood product resuscitation on in-hospital death among massively transfused patients after primary operation for RAAAs at our institution. This study revealed two significant findings: the first and more unexpected was that an increased FFP:PRBC ratio was not associated with improved survival. The second was that an increased AT:PRBC ratio was associated with a decreased mortality rate.

Increased FFP:PRBC ratios have been associated with improved survival after massive transfusion in trauma patients and in patients with RAAAs. The phenomenon has been best studied in trauma patients, with numerous reports of retrospective series from military and civilian experiences. This has led to the widespread adoption of “damage control” or “hemostatic” resuscitation practices in severely injured patients who are believed to be at risk for requiring a massive transfusion. Such practices principally include the liberalizing of FFP administration to aim for a PRBC:FFP ratio of \(\leq 2:1\).
The population that has seemed to benefit the most from increased FFP transfusion has been severely injured, acidic, and coagulopathic at the time of resuscitation. The principal proposed explanation for the observed benefits involves the early replacement of coagulation factors, which theoretically prevents or treats the acquired coagulopathy associated with tissue trauma, massive hemorrhage, and transfusion. This explanation is reinforced by the finding that in both trauma and RAAA reports, the patient population benefitting from increased FFP:PRBC ratios has had documented coagulopathy on arrival to the hospital. Additional proposed benefits of increased FFP transfusion include prevention of acidosis through the buffering capacity of plasma and through the avoidance of crystalloids, with their low pH and proinflammatory properties.

The consistently observed mortality benefit of an increased FFP:PRBC ratio was not seen in our study. Our ratio of TRBC (inclusive of AT) to FFP was similar in survivors and nonsurvivors, and the ratios of both groups were near 3:1, which is that reported among the nonsurvivors in a study of transfusion and RAAAs by Mell et al. Over time, our massively transfused RAAA patients received proportionally more FFP but did not experience a coincident decrement in mortality.

Almost 90% of our RAAA patients were transferred from other institutions. This likely presents a survival bias in our RAAA population, with transferred patients likely being more physiologically stable on arrival and thus at the time of operation. This phenomenon has been postulated in other reports, which have noted no difference in survival between transfer and nontransfer patients despite the treatment delay incurred upon transfer. Preoperative physiologic stability may be the result of less severe preoperative hemorrhage, which is supported by the relatively high preoperative mean SBP of 99 ± 30 mm Hg observed in our population.

Although our data do not include direct evidence of this, additional characteristics of a more physiologically stable RAAA population on presentation may have included decreased incidence of acquired coagulopathy and acidosis, which are believed to develop with severe injury and after larger blood losses. The absence of significant coagulopathy and acidosis in our population would mitigate some of the aforementioned beneficial effects of increased FFP transfusion on survival and might explain the observed lack of a survival benefit with increased FFP transfusion.

The use of AT in surgery for RAAAs has undergone limited study, and reported results have been heterogeneous. Posacioglu et al reported no difference in mortality rates between RAAA patients who received AT (40%) vs no AT (50%; P = .50). The equivalence of mortality was seen even though the AT group received greater transfusions of PRBC and FFP, indicating that the AT group likely had more significant hemorrhage. This interpretation is supported by the fact that patients who received >3 liters of AT had increased incidences of inpatient complications. In another report, Marty-Ane et al documented decreased intraoperative, 1-month, and 3-month mortality and decreased intraoperative PRBC transfusion following the institution of a policy of more liberal use of AT in RAAA surgery. Their report found the use of AT was an independent predictor of survival from RAAA at 1 month.

In our study, an increased ratio of AT:PRBC was predictive of survival on univariate analysis. The volume of AT delivered to survivors and nonsurvivors was similar at 12 units, but nonsurvivors received an average of 4 more units of PRBC. This coincided with greater operative blood loss among nonsurvivors and suggests that the pace of operative bleeding was higher in nonsurvivors, potentially outpacing the availability of AT for transfusion. This situation may have resulted in survivors being more fully resuscitated through their operation and may account for the survival difference noted.

On multivariate analysis controlling for other predictors of death, survival was associated with a high AT ratio (AT:PRBC ratio ≥1) independent of age, estimated blood loss, and the presence of preoperative hypotension. The high-AT group received a similar amount of PRBC, on average, compared with the low-AT group while receiving about twice the amount of AT and having greater mean blood loss. In this context, high AT resulted in a survival advantage of 21% despite increased blood loss. This may represent that the high-AT group was more fully resuscitated through the operation than the low-AT group, resulting in improved postoperative physiology and decreased in-hospital mortality. An additional contributing explanation may be that the low AT ratios were driven (at least partially) by these patients requiring more PRBC due to their greater pace of hemorrhage and that this pace of hemorrhage contributed to mortality.

Allogenic blood transfusion has been associated with the development of infection, multiple organ failure, and acute respiratory distress syndrome in trauma patients, as well as being identified as an independent risk factor for death after injury. The relationship between transfusion of PRBC and adverse outcomes strengthens with increasing transfusion volume. In addition, PRBC transfusion amounts were correlated with the incidence of postoperative infection in patients undergoing cardiac surgery. These relationships have not been directly studied in RAAA patients, and we did not observe a difference in the rate of inpatient complications between the high-AT and low-AT groups, a finding which may be related to the similarity in the PRBC transfusion amounts between the groups. Our findings, as well as those in the reports cited above, nonetheless support the use of AT in RAAA operations to decrease the burden of allogenic transfusion in this patient population.

The benefits of using AT in the setting of massive transfusion for RAAA extend beyond the potential for a more effective resuscitation. Using AT to replace even some PRBC requirement avoids the additional risk of transfusion reaction and infectious disease transmission incurred with additional PRBC units. The replacement of PRBC
with AT also results in a cost savings: The average cost of a unit of PRBC is $\sim 300$, whereas the cost of the disposables used at our institution to set up and process AT for an RAAA is $190$. If each of the 9 units of AT transfused, on average, to our RAAA patients were replaced with an equivalent RBC mass at the conversion of 1.5 units of AT per unit of PRBC, there would have been 6 additional PRBC units transfused per patient at a cost of $\sim 1800$. This is substantially greater than the $216 ($190 setup cost, plus nine autologous blood transfer bags at $2.90 each) that the 9 units of AT cost.

This study has several limitations that bear mentioning. It may have been underpowered to detect a significant effect of increased FFP transfusion on survival. The principal limitation is the potential for reporting bias in this retrospective study. We cannot be certain that all inpatient events were captured in our population, and this may have biased the results.

In addition, we lack data on the initial coagulation and acid–base status of our patients, which hampers our ability to explain the lack of benefit of increased FFP transfusion in contrast to other published studies.

CONCLUSIONS

This study did not demonstrate the improved survival with increased FFP administration in massively transfused RAAA patients seen in other reports. Proportionally greater use of AT was associated with a decreased mortality rate, however. On the basis of these findings, we recommend regular use of AT and judicious transfusion of FFP in hemodynamically stable patients undergoing operation for RAAs. Further study to prospectively identify the population of RAAA patients who will require massive operative transfusion should be undertaken so a potentially greater risk of mortality after massive transfusion. J Trauma 2008;65:986-93.


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