

Paper Alert

Perioperative Blood Transfusions and Bladder Cancer Outcomes

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There are many reasons to restrict administration of allogeneic perioperative blood transfusions (PBTs) including avoiding transfusion reactions, transmission of infections, sensitization against future transfusions and organ transplantations, and of course, “waste” of a precious and scarce resource. However, the one that concerns bladder cancer surgeons the most is having worse oncologic outcomes, particularly reducing cause specific (CSS) and overall survival (OS) for patients undergoing radical cystectomy. The most compelling articles which point to this possibility are two structured reviews [1, 2] which show marginal improvements in OS and CSS and reduction in all-cause mortality (ACM) in patients who have not received a PBT. However, neither review has had the opportunity to analyze patient specific data and very few of the individual studies comprising the reviews actually show a benefit on their own. Moreover, the two structured reviews share 6 studies. The biggest concern with this type of analysis is that they only included retrospective studies with many uncontrolled variables, including different thresholds for administering transfusions, and of course, complicating factors such as prior surgery and or radiation therapy, which lengthen cases and increase the likelihood of administering PBTs. While demographics and stage of disease were often controlled for in the studies, other factors including tumor size, patient frailty, and specific comorbidities

were not. Each of these greatly impacts surgeons’ and anesthesiologists’ decisions to administer blood.

It thus comes as somewhat of a surprise that a consortium of 18 academic tertiary care centers reported on a prospective series of 679 consecutive patients undergoing radical cystectomy in 2011 [3] in which individual patient data beyond demographics and tumor stage were known. These included use of neoadjuvant and adjuvant chemotherapy, soft tissue margins, ASA scores, Charlson comorbidity indices, BMIs, presence of lymphovascular invasion, number of lymph nodes involved and removed, estimated blood loss (EBL) and post-operative complications. All of these influence oncologic and overall outcomes. Moreover, these authors looked at cystectomy caseload for each institution. While before statistical weighting was done, many of these factors were associated with worse 3 year outcomes (cancer specific and other cause mortality and CSS), as was PBT status (negative or positive), these differences all disappeared with weighting. Interestingly, further questioning the impact of PBTs with disease outcome, both unadjusted and adjusted analyses failed to find a negative impact of PBTs on recurrence free survival (RFS), perhaps the oncologic outcome that best reflects the effectiveness of bladder cancer treatment and which is most accurately reported (other than OS).

Even so, this study had some limitations. It did not control for when PBTs were administered and did not report whether the number of PBTs influenced outcomes. Despite this, given the impossibility of conducting a randomized clinical trial on this subject,

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it makes one question whether PBTs adversely influence oncologic outcomes.

Certainly using vaso-pressors, restricting overall fluid volume, and administering agents that “expand” intravascular volume can help, but at times anesthesiologists ad/or surgeons have little choice in administering PBTs. Further confusing matters is a report from Germany for patients undergoing several oncologic surgical procedures (not only cystectomy) where careful attention was paid to pre- and peri-operative “blood status”. This led to better outcomes, particularly for patients who actually received one PBT [4].

That said, as mentioned above, there are several reasons to try to avoid administering PBTs beyond whatever impact they have, if any, on oncologic outcomes, and there are several ways to achieve this. One is to use minimally invasive surgical approaches. These clearly reduce intraoperative blood loss, although other than this feature and reduced immediate postoperative pain, robotic cystectomy does not appear to hold the same advantages as robotic approaches do for prostatic and renal surgery [5]. It is generally associated with longer operative times [5] and requires expensive equipment that even in the United States is not always available. It is less available in other countries.

There are approaches in open surgery which may also reduce the administration of PBTs including fluid restriction, employing a cell saver (although there are theoretical concerns for using cell savers in patients with malignancies and who have urine and bowel contamination in the operative field), and factors which stabilize clot formation. Particularly intraoperative infusion of tranexamic acid (TA), which blocks the breakdown of fibrin by preventing binding of the plasimogen-plasmin tissue activator complex, and appears not to increase venous thrombotic events (VTEs). Indeed, in a nonrandomized but consecutive radical cystectomy series, Zaid and colleagues from the Mayo Clinic [6] reported that intraoperative use of TA reduced PBT from 57.7% in matched controls to 31.1% in those receiving TA ($p < 0.0001$), without any increase in VTEs. Moreover, the cost of administering TA at \$267 for 1

patient (bolus and 5 hour infusion) compared with \$1583 for administering 1 unit of packed red blood cells. Surprisingly, reported EBL was not significantly reduced in patients receiving TA, which the authors attributed to inaccurate assessment of EBL during cystectomy. Additionally, when PBTs were given, the same number of transfusions were administered to patients receiving TA and to controls. A randomized trial would address these issues as well as definitively demonstrating an advantage for TA.

In summary, radical cystectomy is a major operation where substantial blood loss can occur. Even if not impacting oncologic outcomes negatively, there are many reasons to try to limit PBTs to what is absolutely necessary.

CONFLICTS OF INTEREST

Conflicts of interest can be found under Board Disclosures on the website: <https://www.bladdercancerjournal.com>.

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