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CORR Insights

CORR Insights®: Are Allogeneic Blood Transfusions Associated With Decreased Survival After Surgery for Long-bone Metastatic Fractures?

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Where Are We Now?

Substantial progress has been made in the medical management of patients with metastatic cancer of the bone, and patients are living longer with their cancers more than ever before. Still, metastatic bone disease remains a major source of morbidity and mortality for patients afflicted with advanced cancers of the breast, prostate, lung, kidney, thyroid, myeloma, and more. As the population in the United States ages, the prevalence of cancer is expected to rise. Presently, the prevalence of cancer is about 5 million cases per year. In 2015, more than 1.2 million people will receive a cancer diagnosis, most of whom will be older than 40 years of age. Approximately half of these newly diagnosed cases will involve the skeleton. As of 2007, the cost of treating metastatic bone cancer in the United States reached USD 12.6 billion, making up almost 20% of all societal cancer costs, as estimated by the NIH [6]. These numbers will continue to rise as the population ages, and are not restricted to the United States. Metastatic bone disease is a major global health care challenge [5].

Janssen and colleagues attempt to answer whether allogeneic blood transfusions are associated with worse survival after surgery in patients with pathologic long bone fractures. The current study poses a clear clinical question, which it tries to answer with a relatively large and homogeneous patient population while reviewing a robust number of clinical variables. This work is commendable for the volume of patients and clinical factors it evaluates. Additionally, it demonstrates statistically significant information apart from the primary objective that would be consistent with expectations. By their own admission, the work by Janssen and colleagues is underpowered to definitively demonstrate a lack of correlation between perioperative transfusions and patient survival. Still, it is hard to imagine a much larger or more thorough

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conducted survey in this patient population for this clinical question.

Where Do We Need To Go?

Given then that these patients live longer with these diagnoses, the question arises as to whether any of our treatments are adversely affecting patient outcomes. One area of keen interest is the role of allogeneic blood transfusions in patients with cancer. The relationship between perioperative allogeneic blood transfusions and adverse oncologic outcomes is controversial. It has been postulated that the immunomodulation that results from allogeneic blood transfusions puts patients at increased risk of recurrence and death. As such, many oncologic disciplines are starting to look at this effect. Chaflin et al. [1] have shown that allogenic blood transfusions is not independently associated with worse overall survival, cancer-specific survival, or recurrence in prostatectomy. In fact, autologous blood transfusions, as compared to allogeneic, was associated with a worse overall survival and cancer-specific survival in the colorectal population [3]. The question then becomes how do we best manage this patient population's acute chronic anemia in the perioperative setting?

How Do We Get There?

The controversy remains as to the potential nefarious effects of allogeneic blood transfusions for patients with advanced cancer involving the musculoskeletal system or elsewhere. Given the myriad of heath challenges facing this unfortunate population, including bone marrow depletion, to not transfuse in the acute setting is as risky as the potential immunomodulation imposed by transfusing allogeneic blood. As the prevalence of anemia in these patients is common, routine autodonation is also unreasonable. The role of erythropoietin or other erythropoietin stimulating agents in cancer associated anemia may confer some benefit, but it has no real role in the acute setting. Additionally, erythropoietin treatment may play an insidious role as some tumor cells express the erythropoietin receptor and exogenous erythropoietin may stimulate tumor progression [2, 4].

Therefore, if the question is to transfuse or not to transfuse, the treating surgeon must use his or her best judgment and clinical acumen. It would be inappropriate, and perhaps even unethical, to consider a prospective randomized controlled trial on this issue. As the emphasis for surgical intervention in these patients is to restore a semblance of quality of life as quickly as possible, investigators could potentially consider applying patient reported outcome metrics to these patients postopertatively, controlling for hematocrit and blood transfusions. Such information could ultimately enable some standardization of surgical treatment algorithms to optimize short-term functional gains.

In the interim, diligent and proactive communication with the managing medical oncologist pre and post operatively is of the utmost importance. Checking for iron and B12 deficiencies, the most common reasons for chronic anemia in this circumstance, is easy and readily reversible. In fact, the prevalence of these conditions could easily be studied in this patient population. Specifically asking the medical oncologist about a patient's marrow reserve is critical to knowing how to optimally manage the acute anemia. If the patient is relatively young and otherwise healthy without much marrow burden, a mild acute anemia, as long as asymptomatic, could be watched. Conversely, with advanced tumor burden and expected weeks to months to live, allogeneic transfusion should be considered with alacrity. As always, when making a clinical decision, do unto others as one would want done unto oneself.

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References

1. Chalfin HJ, Frank SM, Feng Z, Trock BJ, Drake CG, Partin AW, Humphreys E, Ness PM, Jeong BC, Lee SB, Han M. Allogeneic versus autologous blood transfusion and survival after radical prostatectomy. *Transfusion*. 2014;54:2168–2174.
2. Glaspy J. Current status of use of erythropoietic agents in cancer patients. *Semin Thromb Hemost*. 2014;40:306–312.
3. Harlaar JJ, Gosselink MP, Hop WC, Lange JF, Busch OR, Jeekel H. Blood transfusions and prognosis in colorectal cancer: Long-term results of a randomized controlled trial. *Ann Surg*. 2012;256:681–686; discussion 686–687.
4. Nayak-Rao S, McCormick B. Erythropoietin use in CKD patients with cancer: To tread with caution? *J Nephrol*. 2013;26:829–835.
5. Randall RL. A promise to our patients with metastatic bone disease. *Ann Surg Oncol*. 2014;21:4049–4050.
6. Schulman KL, Kohles J. Economic burden of metastatic bone disease in the U.S. *Cancer*. 2007;109:2334–2342.