Clin Orthop Relat Res (2016) 474:684–686 / DOI 10.1007/s11999-015-4416-5

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

Published online: 20 June 2015

CORR Insights

CORR Insights®: Do Surgical Margins Affect Local Recurrence and Survival in Extremity, Nonmetastatic, High-grade Osteosarcoma?

Kathleen S. Beebe MD

Where Are We Now?

While there is certainly no consensus as to how wide a margin of resection should be [1], surgeons agree that oncologic outcome must take priority over functional results when performing surgery for patients with osteosarcoma. The debate begins with the understanding that the patient's survival can be affected by the hands of the surgeon, despite the enormous benefits of chemotherapy and the confusing effects of local recurrence on survival.

In a study of patients with locally recurrent osteosarcoma published almost a decade ago by Nathan et al. [5], it is noted that six of 13 patients with positive margins and 14 of 389 with negative margins developed local recurrence. The strongest correlation with poor survival was local recurrence within the first year after primary resection [5].

It would seem from this study alone that positive margins and local recurrence should be avoided at all cost. However, a study by Rougraff and colleagues [6] found that despite having no local recurrences after hip disarticulation for osteosarcoma of the femur, there was no difference in duration of survival or of disease-free survival when compared to patients undergoing limb-salvage surgery or above knee amputations in spite of higher local recurrence rates in these groups. One of the reasons for this, the authors speculate, is that the small percentage difference in local control, confounded by nearly 50% of the patients dying, represents such a small discrepancy that it did not affect the overall survival statistics.

The literature can be confusing when considering margins, local recurrence, and survival. Readers should consider how words like "only" or "small" may influence decisions about margins. A study by Kong and colleagues [3], with the title, "Local Recurrence Has Only a Small Effect on Survival in High-risk Extremity Osteosarcoma" might allow us as surgeons to let down our guard a bit, relax, or push the envelope when the margin is "close."

In the current study, Bertrand and his colleagues showed that after controlling for relevant confounding variables, the presence of a positive

This CORR Insights® *is a commentary on the article* "Do Surgical Margins Affect Local Recurrence and Survival in Extremity, Nonmetastatic, High-grade Osteosarcoma?" *by Bertrand and colleagues available at:* DOI: 10.1007/s11999-015-4359-x.

The author certifies that he, or any member of his immediate family, has no funding or commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research*® editors and board members are on file with the publication and can be viewed on request.

This *CORR* Insights® comment refers to the article available at DOI: 10.1007/s11999-015-4359-x.

K. S. Beebe MD (✉)
Musculoskeletal Oncology and Limb Salvage, Rutgers-New Jersey Medical School, 140 Bergen St., Newark, NJ 07101-1709, USA
e-mail: kathleen.beebe@rutgers.edu

CORR Insights

margin compared with a negative margin of greater than 1 mm was the only independent predictor of local recurrence and that patients with positive margins were more likely to die from disease than those with negative margins. The study further showed that negative margins less than or equal to 1 mm did not show an increase likelihood of local recurrence compared with margins greater than 1 mm. They suggest that surgeons should strive to obtain negative margins while attempting to maximize function and quality of life.

Where Do We Need To Go?

The ideal resection margin in osteosarcoma is becoming harder and harder to define as we strive to obtain negative margins while also inching closer and closer to the tumor at hand. We must determine how close we can get without negatively affecting local recurrence, which has unclear ramifications ranging from "only a small effect on survival" to the "strongest correlation with poor survival" [3, 5]. A previous study compared margins of greater than 5 mm to those of less than 5 mm. An additional study also compared margins of greater than 2 mm and less than 2 mm with neither study showing an increase in local recurrence [2, 4].

With the study by Bertrand and colleagues adding to the available literature, we can perhaps begin carefully dismissing recommendations from previous generations that request margins in the greater than 1-cm range.

How Do We Get There?

As we continue our quest to provide more patients with limb salvage surgery, we must remember that inadequate margins and local recurrence appear to influence survival [3]. Measuring the effects of local recurrence on survival has been extremely difficult primarily because we, as surgeons, have been vigilant about obtaining negative margins and thus, avoiding local recurrence in many cases. This has had the effect of allowing us to study survival in only a small subset of patients with osteosarcoma. As we place our knives closer and closer to the malignant entity that may ultimately kill our patient, we must continue to remain vigilant. The study by Bertrand and colleagues should allow us to continue our quest to preserve function by obtaining exceedingly small margins, but does not support an acceptance of a positive margin.

An osteosarcoma resection complicated by a positive margin is potentially life-threatening complication. As was the case in the Bertrand study, reresection at the time of the positive intraoperative frozen section seems prudent. It is unclear from this study, what the course should be if the margin is reported to be positive after the surgery is complete. However, with the addition of the current study to the literature, it is becoming clearer that removing vital structures is unnecessary as long as negative margins are obtained. We also do not need to compromise function in order to obtain generous margins since those seem to provide no benefit in terms of local control; negative margins suffice.

As we move forward and continue to operate with closer and closer margins, we must continue to reassess (through research, cooperative collection of data, and our specialty societies) how our approaches to close margins may affect patient survival. Collaborative, multi-institutional studies with measured margins, local recurrence rates, and survival statistics would allow us to move beyond the limited information and conclusions that can be drawn from single institutional studies, studies that look only at if the margins are macroscopically or microscopically negative or positive or

CORR Insights

studies that look only at specific disease sites.

References

1. Biermann JS (ed). *Orthopaedic Knowledge Update: Musculoskeletal Tumors 3*. Rosemont, IL: American Academy Of Orthopaedic Surgeons; 2014.
2. Bispo Junior RZ, Camargo OP. Prognostic factors in the survival of patients diagnosed with primary non-metastatic osteosarcoma with a poor response to neoadjuvant chemotherapy. *Clinics*. 2009;64:1177–1186.
3. Kong CB, Song WS, Cho WH, Oh JM, Jeon DG. Local recurrence has only a small effect on survival in high-risk extremity osteosarcoma. *Clin Orthop Relat Res*. 2012;470:1482–1490.
4. Li X, Moretti VM, Ashana AO, Lackman RD. Impact of close surgical margin on local recurrence and survival in osteosarcoma. *Int Orthop*. 2012;36:131–137.
5. Nathan SS, Gorlick R, Bukata S, Chou A, Morris CD, Boland PJ, Huvos AG, Meyers PA, Healey JH.Treatment algorithm for locally recurrent osteosarcoma based on local disease-free interval and the presence of lung metastasis. *Cancer*. 2006;107:1607–1616.
6. Rougraff BT, Simon MA, Kneisl JS, Greenberg DB, Mankin HJ. Limb salvage compared with amputation for osteosarcoma of the distal end of the femur. A long-term oncological, functional, and quality-of-life study. *J Bone Joint Surg Am*. 1994;76:649–656.