

A small-cohort study on tumor recurrence and surgery-related complications associated with proximal fibular tumors and the potential utility of biopsy

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Risk analysis of tumor recurrence and surgery-related complications associated with proximal fibular tumor biopsies

Journal of Clinical and Translational Research

Dear Dr. Sun,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Dec 28, 2020.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author.

You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Rowan van Golen
Associate Editor
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: The authors present their study on proximal fibular tumors treatment and perforative complications.

The study states that their focus is on the impact of biopsy, however only 10 out of 94 patients underwent biopsy. These results are therefore extremely inaccurate and should be taken with caution.

Regarding the iatrogenic peripheral nerve injuries, these were not noted in biopsies group, but occurred in roughly 10% of all patients. This might have also been an incidental result, as one patient with the iatrogenic injury might have changed all the results.

I consider that the results in terms of comparison between the biopsy and surgery should therefore be excluded, as a main aim, and should be included as a surgical method with less complications but also lesser surgical significance.

Please try to reorganise the study, and revise the manuscript accordingly as a study on outcomes and complications of patients with proximal fibula tumors.

Authors' response

Reviewer #1: The authors present their study on proximal fibular tumors treatment and perforative complications.

The study states that their focus is on the impact of biopsy, however only 10 out of 94 patients underwent biopsy. These results are therefore extremely inaccurate and should be taken with caution.

Indeed, we fully concur with the reviewer and have adjusted the text to reflect this important point and implications thereof. First, we have changed the title to read:

“A small-cohort study on tumor recurrence and surgery-related complications associated with proximal fibular tumors and the potential utility of biopsy”

Secondly, we have modified the abstract and used more cautionary language:

“To assess the incidence of tumor recurrence, iatrogenic peroneal never injury, and wound healing problems in a small cohort of patients with proximal fibular tumors who had undergone surgery and to determine the relative risk of pre-operative biopsies on these outcome variables.”

and

“Readers should note that, due to the relatively low incidence of this cancer type and the scarcity of pre-operative biopsies, larger cohort studies are warranted to validate the results.”

Finally, we have added more limitations to the final paragraph of section 4:

“Of the 66 included patients, only 10 patients had received pre-operative biopsy. The conclusions drawn in this study should therefore be contextualized to the very small sample size, especially with respect to the part on biopsies. Larger-cohort follow-up studies should be conducted to validate the results, although we acknowledge that this may require long inclusion times.”

The reasons why even small-cohort studies are needed is explain mainly in the relevance for patients section of the abstract:

“Patients who present with proximal fibular tumors are often young. Depending on the diagnosis of the bone cancer subtype, the surgical intervention may entail highly invasive and risky procedures. Taken together, it is imperative to ensure accurate diagnosis of the bone cancer subtype to prevent unnecessary procedures. Diagnostic accuracy can be increased by acquiring a histological specimen of the malignant bone tissue. However, it is currently not completely established whether bone biopsies in the proximal fibula can be safely performed and whether such biopsies lead to seeding metastases. Because of the rarity of these tumors and procedures, studies are needed even when these entail a small sample size.”

Regarding the iatrogenic peripheral nerve injuries, these were not noted in biopsies group, but occurred in roughly 10% of all patients. This might have also been an incidental result, as one patient with the iatrogenic injury might have changed all the results.

There were 3 cases in the biopsy group with iatrogenic peripheral nerve injury, which occurred perioperatively and were not directly caused by biopsy procedure. Our results suggest that biopsy was not statistically associated with iatrogenic peroneal nerve injury. Therefore, we did not perform binary logistic regression analysis to determine whether biopsy was an independent risk factor.

I consider that the results in terms of comparison between the biopsy and surgery should therefore be excluded, as a main aim, and should be included as a surgical method with less complications but also lesser surgical significance.

We have specified the aims of the study: (1) to assess the incidence of tumor recurrence, iatrogenic peroneal never injury, and wound healing problems in surgical patients with a proximal fibular malignancy, and (2) to determine the relative risk of pre-operative biopsies on these outcome variables. The purpose of juxtaposing biopsy to surgery was to reveal the relationship between them. Patients who had undergone biopsy were 12.4 times more likely to receive type I or type II en bloc resection ($P = 0.006$). We acknowledged that the definitiveness of these conclusions should be validated in a larger cohort and that the data should be appraised in the context of the low sample size. Nevertheless, the data in Table 4 were properly analyzed and give direction and some meaning to the relationship between biopsy and surgery. The most important finding was that biopsy may hamper wound healing,

which is critical for surgeons and peripheral caretakers to keep in mind. For that reason, we would respectfully like to keep the table and message intact.

Please try to reorganise the study, and revise the manuscript accordingly as a study on outcomes and complications of patients with proximal fibula tumors.

We have modified the text to meet your request to the best of our ability, as indicated above.

Furthermore, as you have commented, outcomes and complications of patients with proximal fibula tumors are important. We have published another paper focus on the risk factor associated with complications of patients with proximal fibula tumors as below.

Guo C, Zhang X, Gao F, Wang L, Sun T. Surgical management of proximal fibular tumors: risk factors for recurrence and complications. The Journal of international medical research. 2018;46(5):1884-1892.

In that light, we underscore the necessity of including the findings of the current study and all other studies referenced in the text in the treatment plan of this category of bone cancer patients.

2nd Editorial decision
10-Dec-2020

Ref.: Ms. No. JCTRes-D-19-00005R1

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Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Rowan van Golen
Associate Editor
Journal of Clinical and Translational Research

Comments from the editors and reviewers: