Author's response to reviews

Title: Prophylactic Antibiotic Regimens In Tumor Surgery (PARITY) Survey

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Author's response to reviews: see over
Dear BioMed Central Journal Editorial Office,

My co-authors and I would like to thank you and the reviewers for the careful review and constructive feedback provided for our manuscript entitled ‘Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) Survey’. We have revised the manuscript based on the reviewer recommendations as outlined below.

We feel that the manuscript has been greatly improved and we request that the manuscript be considered for publication in *BMC Musculoskeletal Disorders*.

We thank-you very much for your time and attention and we look forward to your reply.

Sincerely,

Michelle Ghert, MD, FRCSC (corresponding author)

**REVIEWER 1**

Specific comments:

1. Page 5
Specific questions (section A-D) should be noted in the methods

Response:
The Methods section does include a summary of each of the section questions (see below). However, in order to provide more detail, we have attached the survey itself as an Appendix, which will provide the readers with a broader understanding of the questions that were asked in the survey.

“These surgeons also commented on the clarity and comprehensiveness of the questionnaire. The questionnaire itself consisted four sections, and presented closed-ended questions as multiple-choice or five-point Likert scale formats. Section A encompasses eight questions relating to surgeons’ backgrounds (i.e. age, gender, years in practice, type of practice [academic versus community setting], fellowship training in orthopaedic oncology, and supervision of resident trainees) and surgical volume. Section
B sought information regarding surgeons’ management of oncology cases, specifically with regards how long after chemotherapy, and at what white blood cell count, should surgical resection of the long bone sarcoma be performed. Section C consists of nine questions that address features of a particular surgeon’s antibiotic regimen (i.e. reconstruction type, specific antibiotics used, time period [pre- and/or post-operatively] and dosages administered). Section D addresses the need for future research in this area and provides participants with an opportunity to offer comments and/or suggestions.”

2. Page 9

Description about dose of Cephalosporin is ambiguous. Per day or per one administration?

Response:
This has been clarified in the manuscript and as follows:

“Thirteen percent (95% CI: 7, 23%) of surgeons responded to prescribing one gram of Ancef (Cefazolin) per dose while 33% (95% CI: 23, 44%) prescribe two grams of Ancef per dose (Table 4).”

3. Page 10

The discussion is very poor and redundant description of the results. The authors should discuss more specific strategy to propose a further study for regimens of prophylactic antibiotics in tumor prosthesis surgery, compared with the studies to define standard guidelines for prophylactic antibiotics as indicated by AAOS.

Response:
The discussion has been developed further in the manuscript and the following 2 paragraphs have been added:

“These results signify a significant lack of evidence and guidelines directing the prescription of prophylactic antibiotic regimens in musculoskeletal tumor surgery. With the emergence of resistant antimicrobial organisms and outbreaks of clostridium difficile in healthcare facilities, duration and prescription of antibiotics has proven to be an important clinical entity. At the same time, a high infection rate of 15-30% reported in many studies (2,3,4,5,6) highlights the importance of optimizing antibiotic regimens. There is no doubt that the development of clinical guidelines is of paramount and immediate importance.

Due to the fact that bone sarcomas are rare, a randomized clinical trial designed to create high level evidence would require multi-institutional and likely international participation. To date, this type of study has not been attempted in the Orthopaedic Oncology community. However, such a study is possible with support from a Surgical Trials Methods Center which exists at the institution of the primary authors for this study. A trial has been designed and is under funding and ethics review, which will involve
randomizing patients undergoing lower extremity tumor prosthesis reconstruction to either 24 hours or 5 days of cephalosporin coverage. The study will be double-blinded as randomization will be completed by the Pharmacy Department at each institution. Thus, with completion of this study, there is the possibility that eventually guidelines such as those provided by the AAOS will be created for this very challenging peri-operative issue in Orthopaedic Oncology.'

**REVIEWER 2**

**Major Compulsory Revisions**

1. The sample size formula provided in the Methods; Sample Size section appears to be incorrect. Given the formula provided along with parameters indicated, the formula yields a sample size of 9.4. I do believe the sample size formula should appear as:

   \[ N = z^2 \frac{p(1-p)}{w^2} \]

   This formula a typing error and should be 36.9 as calculated using the above formula.

**Response:**

This has been clarified by our statistical expert who has provided the following calculation:

\[ N = \left( z^2 \times \left( \frac{\sqrt{p(1-p)}}{w^2} \right) \right) \]

\[ N = (1.9) \]

\[ N = 368.8 \]

**Minor Essential Revisions**

3. In the Abstract, Results, first sentence, the authors indicate that 97 surgeons received the questionnaire, however in the Manuscript Methods, Sample Size, second paragraph: the authors indicate that a total of 96 surgeons were approached to participate. Please confirm sample size in both abstract and manuscript.

**Response:**

This was corrected in the abstract and manuscript to state that 96 surgeons received our questionnaire.
4. The references are not cited consecutively in order of appearance. For example, in the Background section, end of first paragraph last sentence:
references 2,3,4,5, and 10 are cited, in the next paragraph, first sentence:
references 2,3,5 and 6 are cited.

Response:
This was corrected in the manuscript and the references are now listed in order of appearance.

 Minor Issues Not for Publication
I find the following sentences read awkwardly and could be revised to improve readability as follows:
5. Methods, Pretesting and Validity Assessments, second paragraph, third sentence. “Section B sought information regarding surgeons’ management of oncology cases, specifically with regard to how long after chemotherapy, and at what white blood cell count surgical resection of the long bone sarcoma should be performed.”

Response: This was revised in the manuscript as follows
“Section B sought information regarding surgeons’ management of oncology cases - specifically with regards to how long after chemotherapy can surgery be safely performed, at what white blood cell count the patient is safe for surgery.”

6. Methods, Questionnaire Administration, first sentence: remove comma after “…were surveyed” and remove comma after “voluntarily”.

Response
This was corrected in the manuscript which now reads:

“All Active Members of the Musculoskeletal Tumor Society (MSTS) and all members of the Canadian Orthopaedic Oncology Society (CANOOS) (duplicates were excluded) were surveyed voluntarily via a web-based method (Survey Monkey).”

7. Authors’ contributions section: “KH carried out and assisted…”

Response
This was completed as follows:

“Authors' contributions

KH carried assisted in the conception and design of the survey as well as data acquisition. KH assisted in analyzing and interpreting the data as well as drafting and revising the final manuscript. AR assisted in developing the figures and participated in revising the manuscript. BD assisted in study design, providing background knowledge as well as
revising the manuscript. FF assisted in data analysis and interpretation. JW, PF, BP, and MB provided critical revisions to the manuscript as well as assisting in developing study design. MG conceived and designed the survey and the study. MG provided critical revisions and assisted in drafting the manuscript as well as approving the final manuscript for submission for publication.”