Author’s response to reviews

Title: Oncological, surgical and functional results of the treatment of patients after hemipelvectomy due to metastases

Authors:
Grzegorz Guzik (grzegorz.guzik@vp.pl)

Version: 1 Date: 26 Nov 2017

Author's response to reviews:

COVER LETTER

Dear Editors

I would like to thanks Editors and Reviewers for valuable comments which improved the quality of my article. All comments were considered and highlighted in the manuscript.

BMSD-D-17-00624

Oncological, surgical and functional results of the treatment of patients after hemipelvectomy due to metastases

Grzegorz Guzik

BMC Musculoskeletal Disorders

Dear Dr Guzik,

Your manuscript "Oncological, surgical and functional results of the treatment of patients after hemipelvectomy due to metastases" (BMSD-D-17-00624) has been assessed by our reviewers.
They have raised a number of points which we believe would improve the manuscript and may allow a revised version to be published in BMC Musculoskeletal Disorders.

A decision will be made once we have received your revised manuscript, which we expect by 13 Dec 2017.

I look forward to receiving your revised manuscript and please do not hesitate to contact us if you have any questions.

Best wishes,

James Mockridge

BMC Musculoskeletal Disorders

https://bmcmusculoskeletdisord.biomedcentral.com/

Technical Comments:

- Tables should not be embedded in the main text but placed after the reference list

All tables was placed after references.

- Authorship: it is unusual for papers to have a sole author. Please can you confirm that no other researchers had a contribution to the study that would warrant authorship or highlighting in the acknowledgements.

I confirm that I am sole author of this manuscript.
Reviewer reports:

Reviewer 1:

- The article is acceptable for publication with minor revision

It adds to current literature on hemipelvectomy due to metastases.

The current literature was added:


- The author can add a table about review of literature showing the comparison of the results of current study with published data on hemipelveectomy for primary and metastatic bone tumors

The table with literature review showing treatment results was added.

Tab.6 Oncological and surgical results of treatment of pelvic metastases in current literature.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Number of patients</th>
<th>Type of surgery</th>
<th>Complications</th>
<th>Mean follow-up (months)</th>
<th>Local recurrence</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruggieri et al.</td>
<td>21</td>
<td>9 - curetage</td>
<td>1 - urinary fistula</td>
<td>28</td>
<td>30%</td>
<td>15% - 66 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 en-bloc wide resection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 - THR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yasko et al.</td>
<td>14</td>
<td>14 - en bloc resection and THR</td>
<td>1 - prosthesis dislocation</td>
<td>53</td>
<td>0</td>
<td>56% - 60 months</td>
</tr>
<tr>
<td>Nillson et al.</td>
<td>32</td>
<td>Intralesional and Harrington reconstruction</td>
<td>2 - bleeding, 2 - dislocations, 1 - infection</td>
<td>range 0.5-106</td>
<td>0</td>
<td>40% - 11 months</td>
</tr>
<tr>
<td>Marco et al.</td>
<td>55</td>
<td>54 - protrusio cup with Harrington procedure</td>
<td>14 - early complications, 5 - fixation failure</td>
<td>16</td>
<td>25%</td>
<td>median - 9 months</td>
</tr>
<tr>
<td>Giurea et al.</td>
<td>43</td>
<td>37 intralesional resections, 6 wide resections</td>
<td>24%</td>
<td>19%</td>
<td>0</td>
<td>median -13</td>
</tr>
<tr>
<td>Guzik</td>
<td>34</td>
<td>9 - Lumic prosthesis, 16 - Harrington procedure, 9 - no reconstruction</td>
<td>4 - infections, 2 - Lumic dislocations, 1 - implant loosening, 1 - nerve damage</td>
<td>25</td>
<td>18%</td>
<td>48.2% - 60 months</td>
</tr>
</tbody>
</table>

Reviewer 2: Thank you for inviting me to review this case series of patients with metastases of the pelvis. The topic is interesting, however, not appropriately presented by the authors. These are my comments:
Metastatic lesions localized in the pelvis cause pain, pathological fractures and decrease quality of patients life. Limited data are available to compare the oncological, surgical and functional outcomes after different surgeries in patients with metastatic pelvic tumors. Most of the works presents the results of hemipelvectomy performed in patients with primary malignant bone tumors. The objectives of this study were to assess the outcome of patients after internal hemipelvectomy due to cancer metastases.

Material and methods: Over the period 2010-2015 at the Department of Orthopaedic Oncology in Brzozów, 34 patients with metastases to the pelvis were treated. This study group comprised of 21 men and 13 women. The mean age was 67 (range: 51-79) for men and 56 (range: 41-77) for women. The majority of the treated patients suffered from myeloma (12 patients) and breast cancer (8 patients). Following the Enneking system classification guidelines, tumours were found in zone I (5 cases), zone II (18 cases), zone III (4 cases). Tumour involvement of both zones (II and III) considered 7 patients. The following resections were accomplished: wide in 11 cases, marginal in 17 cases, and intralesional in 6 cases. 18 patients were postoperatively treated with 8 Gy single-dose radiotherapy. 25 patients underwent bone reconstruction using either Lumic prostheses (9 cases) or the Harrington technique (16 cases). The mean follow-up period was 2.1 years (range: 1.2-6 years). The analysis covered patients' survival, number of local recurrences, functional results and effectiveness of surgical treatment, considering the type, number and reason of complications.

Results: 8 patients died. The mean cumulative percentage of 5-year survival calculated with Kaplan-Meier curve was 48.2% for 34 patients. Medial survival was 3.85 years. In this group, local tumour recurrences concerned 6 patients. The extent of tumour resection and the use of
postoperative radiotherapy were statistically significantly related to local recurrences. Functional results were better in a group of patients without reconstruction. Postoperative VAS score was 2.7, Karnofsky status 71 and MSTS 23(86%). After Lumic prosthesis implantation VAS score was 3.4, Karnofsky status 65 and MSTS 19(63%). The worst results were observed after Harrington procedure. We noticed 9 perioperative complications in 6 (18%) of patients. Most frequently, the problems included impaired wound healing due to infection (4 patients) and dislocation of Lumic prosthesis (2 patients).

Conclusions: The frequency of local recurrences after hemipelvectomies is related to the radicality of tumour resection and the postoperative application of radiotherapy. Survival time depends on the type and stage of cancer. The best functional results were obtained in patients after type I resection followed by no reconstruction of the bone. Lumic prosthesis implantation gave better results than Harrington procedure.

- Introduction: the authors should clarify what is missing from the literature regarding these patients.

The informations what is missing in literature was added.

Although numerous publications have presented oncological and functional outcomes of patients with primary bone sarcomas in the pelvis, there is only a few data about the results of managing metastases in this location. There is no clear data if radical metastasis resection can significantly improve the quality of life and increase overall survival of patients. Many authors presents different numbers of postoperative complications and implants damage. Most publications come from large oncological centers where the treatment seems to be optimal but a large number of patients with bone metastases force to perform the surgery also in smaller, not such experienced oncological centers. Analysis of treatment outcomes coming from different centers provides the opportunity to develop optimal treatment options [13-19].
The literature should be updated. By a simple search, the authors did not include a citation from a major tumor center with important results on the topic (Ruggieri P, Mavrogenis AF, Angelini A, Mercuri M. Metastases of the pelvis: does resection improve survival? Orthopedics. 2011 Jul 7;34(7):e236-44.; this is an important paper which findings should be discussed and compared to the present paper)

The current literature was added:


- Materials: the authors should clarify the margins of resections and compare to those with wide/marginal vs intralesional.

The informations about margins of resections were added.

The indications for wide margins surgery were: solitary bone metastases, prolonged disease-free survival and good life expectancy. In patients with poor life expectancy and with multiple metastases curettage were performed. Qualification for surgical treatment was supported by the Capana et al system, which distinguishes 4 Classes of patients [14]. Two experienced pathologists assessed resection margins in each patient to determine the radicality of surgery. The following resections were achieved: wide resections (11 cases), marginal (17 cases) and intralesional (6 cases).
- Results: a tumor paper should provide the outcome (survival, metastases, local recurrences) of the patients, and the outcome (survival and complications) of the reconstructions. Instead of merely reporting observational data, the authors should perform a formal analysis of the patients who benefit and those who did not from wide resection.

Outcome informations was added.

The follow up of patients was every 3 months. 8 patients died before the last visit. The mean cumulative percentage of 5-year survival calculated with Kaplan-Meier curve was 48.2% for 34 patients. Medial survival was 3.85 years - fig.1.

Fig. 1 Overal survival to death of patients with pelvic bone metastases.

Symptoms of local recurrences were observed in 6 of 34 patients. Only 2 factors (extent of neoplasm resection and postoperative radiotherapy) were significantly statistically related to local recurrences of the disease - tab. 2.

- Discussion: the authors should discuss regarding the need and benefit for resection (wide margins) for metastatic bone disease (please see comment above). To my opinion and other surgeons as well, wide resection does not offer much to patients with metastatic bone disease. The authors should comment on that and discuss the related literature. They should also discuss palliative options for these patients (please consider: Rossi G, Mavrogenis AF, Casadei R, Bianchi G, Romagnoli C, Rimondi E, Ruggieri P. Embolisation of bone metastases from renal cancer. Radiol Med. 2013 Mar;118(2):291-302., and Rossi G, Mavrogenis AF, Rimondi E, Braccaiol L, Calabrò T, Ruggieri P. Selective embolization with N-butyl cyanoacrylate for metastatic bone disease. J Vasc Interv Radiol. 2011 Apr;22(4):462-70.)

Informations about wide margin benefit and palliative treatment methods was added.
Surgical treatment was rarely used because of patients' short-term life prognosis. In supportive treatment, bisphosphonates, hormone therapy, chemotherapy or percutaneous cementoplasty can be used. Recent studies have also included the use of tumor embolization as a pre-operative treatment or as an independent treatment method. Rossi and Mavrogenis et al. have presented good treatment results with use of selective tumor embolization. In 107 patients with renal metastatic cancer, tumor necrosis were observed in all cases and ossification in 41 cases. For 2-4 days after embolisation patients had ischaemic pain. In group of 309 patients after embolization with N-butyl cyanoacrylate they have obtained tumor devascularisation in 80% of cases. In 97% of patients, greater than 50% pain decrease was achieved. Ossification were observed in 65 cases [20,21].

Doubt exists regarding radical resection compared to marginal or intralesional pelvic metastases resections. Ruggieri et al. have presented oncological results after wide en-bloc resections in 12 cases compared to curettage in 9 cases in patients with pelvic metastases. Authors have noted no significant statistical differences in survival to death and survival to local recurrence between patients groups. They reported one postoperative complication in patient treated with wide resection [17,19].

- Illustrations: please add a couple of cases in sets of figures (intraoperative images are not necessary).

Illustrations was added.

Fig.2 Preoperative and postoperative radiograph series of patients with metastatic pelvis tumours. Figure (a) showed preoperative radiograph of metastatic renal cancer (type III involvement), and (b) after resection without bone reconstruction. Figure (c) showed breast metastatic cancer in periacetabular area, and (d) after type II resection and Lumic prosthesis implantation. Figure (e) showed periacetabular myeloma metastasis, and (f) Harrington bone reconstruction.
Please positive review my article.

Yours faithfully Grzegorz Guzik

I,m waiting Your answer.