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Review article

A comparative study between limb-salvage and amputation for treating osteosarcoma



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ABSTRACT

Purpose: Osteosarcoma is an aggressive malignant neoplasm, and conflicting findings have been reported on the survival and function recovery in osteosarcoma patients experiencing limb salvage or amputation. In the present study, we compared clinical outcomes regarding limb salvage surgery vs. amputation for osteosarcoma patients by a meta-analysis.

Method: Literature search was conducted in CNKI, Medline, Embase, the Cochrane Database, and Web of Sciences, and the quality of included studies was evaluated based on Newcastle-Ottawa scale quality assessment. Odds ratio and 95% confidence interval of the local recurrence, 5-year overall survival, and metastasis occurrence were calculated.

Results: 17 articles were included according to selection criteria. There were 1343 patients in total derived from these studies. Our result showed that there was no significant difference between limb salvage surgery and amputation with respect to local recurrence, and patients with limb salvage surgery had a higher 5-year overall survival, and a lower metastasis occurrence.

Conclusions: The present study provided more comprehensive evidences to support limb salvage surgery as an optimal treatment of osteosarcoma patients.

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Abbreviations: LSS, limb salvage surgery

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1. Introduction

Osteosarcoma is an aggressive bone neoplasm arising from primitive transformed cells of mesenchymal origin. It was such a fatal disease that “months to metastasis” rather than actual survival time, was used to measure the outcomes of treatment in studies of early stage. In the 1950s, there was no optional therapy that could significantly increase the survival rate, with a 5-year survival rate of 22% [1]. However, with the aid of effective chemotherapeutic drugs the survival rate of osteosarcoma has been significantly improved since the late 1970s [2,3]. Recently, the gold standard of osteosarcoma chemotherapy have been based on around 5 drugs; high-dose methotrexate (HDMTX) with leucovorin rescue, doxorubicin (adriamycin), cisplatin, ifosfamide, and etoposide [4]. Combinations of these drugs, mostly in the form of neoadjuvant as well as adjuvant MAP, are the current management for osteosarcoma [5], and various chemotherapy protocols are still under investigation. The experience with radiotherapy is limited, as osteosarcoma is long considered resistant to applicable doses of radiation. However, recent data suggest that the combined approach of irradiation with chemotherapy may be useful in patients who have microscopic residual tumor foci following intralesional resection [6].

With the advent of effective neoadjuvant chemotherapy in the 1970s, limb salvage surgery (LSS) has been taken as a potential treatment for osteosarcoma [7,8]. Usually, LSS has functional and physiological advantages over traditional amputative procedures when combined with neoadjuvant or adjuvant chemotherapy [9]. It is now generally accepted that LSS is indicative for localized osteosarcoma, while surgical amputation is adopted for high malignancy osteosarcoma. However, there are still some surgeons holding the view that immediate and aggressive removal of the tumor will prevent the progression of fracture-induced disease, and consequently amputation is considered to be a better option for osteosarcoma patients with pathological fracture [10–13].

Conflicting findings have been reported on the survival and function recovery between treatments of LSS and amputation in patients with osteosarcoma. Toward this end, a meta-analysis of published clinical trials was performed to compare the clinical efficacy of LSS and amputation treatments in terms of local recurrence, 5-year overall survival rate, and metastatic occurrence. Several studies have attempted similar meta-analysis [14]; however, the included studies were much smaller, and their scopes were restricted to specific therapies compared with this meta-analysis. Through more extensive osteosarcoma literature, this meta-analysis tries to give a comprehensive conclusion on the outcomes in osteosarcoma patients receiving LSS and amputation. Such information will help us determine the most appropriate osteosarcoma-treating method.

2. Material and methods

2.1. Literature search

A comprehensive and complete search of Medline, Embase, Cochrane Database, Web of Sciences, and CNKI was performed from June 2014 to July 2014, using the search terms: “osteosarcoma”, “limb salvage” and “amputation”. There was no language or other restrictions. All articles with raw descriptive data were included, including original research, clinical trials, case reports, databases, letters, and reviews.

2.2. Included studies

Articles were included if they were (1) comparative study between LSS and amputation groups, (2) patients with osteosarcoma in their lower limb, (3) sufficient data was provide in terms of local recurrence, 5-year overall survival rate, or occurrence of metastasis. Exclusion criteria were as follows: (1) studies only reported data related to LSS or amputation groups without a comparison, (2) general case series with less than 20 total patients, (3) letters, case reports, editorials or reviews.

2.3. Data extraction

Outcome data were collected from the articles by two authors of our study. The authors used a structured sheet, and then gathered all the data into a database. Study characteristics included year of publication, number of patient with LSS and amputation, study period, gender, Enneking stage, response to chemotherapy, follow-up, etc. Any disagreement was resolved by continuing discussions until a consensus was reached.

2.4. Study quality

With the Newcastle–Ottawa scale (NOS) quality assessment as recommended by the Cochrane Observational Studies Method Working Group, the quality of included articles was evaluated by two independent reviewers. This scale has a maximum nine points concerning quality of selection, comparability, exposure, and outcome of study participants. Because of the variable quality of the observational studies, we took the criteria of 5 or more NOS scores as studies with good quality.

2.5. Statistical analysis

The outcome of measurement used in our study was local recurrence, 5-year overall survival rate, and occurrence of metastasis, which were all dichotomous data. We used the software of the Cochrane Collaboration (Review Manager 5.2) to calculate OR and 95% CI for all outcomes. Statistical heterogeneity among the included studies was assessed by the Chi squared and I^2 tests. Statistically significant heterogeneity was defined as an I^2 value > 0.5. A random effects model was selected for heterogeneous data; otherwise, a fixed effect model was selected.

Funnel plots were used to test the possibility of publication bias, which exhibited the intervention effect from the individual study against the respective standard error. A symmetrical plot represents no bias, and any asymmetry of the plot suggests the existence of publication bias.

3. Results

3.1. Literature information

In the preliminary literature search, 137 potentially relevant articles were identified. However, according to the inclusion criteria, only 17 articles [15–31] were selected (Fig. 1; Table S1). All of the 17 research articles were retrospective studies. The publication dates ranged from 1996 to 2012. 1343 patients with osteosarcoma were comprised totally, of whom 617 patients received LSS and 726 received amputation. The results of quality assessment by NOS are shown in Table 1, and the detail information of patients in each articles were listed in Table 2. Among 5 of the studies

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