

INPLASY PROTOCOL

To cite: Liang et al. Optimal treatment and clinical outcomes of intramedullary spinal cord metastasis from breast cancer: a systematic review. Inplasy protocol 202040064. doi: 10.37766/inplasy2020.4.0064

Received: 12 April 2020

Published: 12 April 2020

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Support: Not applicable.

Review Stage at time of this submission: The review has not yet started.

Conflicts of interest: No.

Optimal treatment and clinical outcomes of intramedullary spinal cord metastasis from breast cancer: a systematic review

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Review question / Objective: To identify risk factors for progression-free survival and overall survival in intramedullary spinal cord metastasis from breast cancer and to purpose the optimal treatment protocol.

Condition being studied: Intramedullary spinal cord metastases (ISCM) are rare but devastating issues of systematic malignancy. They reportedly affect 0.1-0.4% of all cancer patients and constitute 8.5% of neuraxis masses as well as 1-3% of intramedullary neoplasms. Among them, ISCM from breast cancer were estimated to be the second most common type. However, due to a lack of awareness and limited researches, ISCM are easily ignored by medical staff. As the diagnosis and management of breast cancer improve profoundly over the past decades, the incidence of ISCM from breast cancer increases gradually. Patients diagnosed with it usually present with severe neurological deficits, such as paraplegia, dysesthesia and sphincter dysfunction. Thus, prompt identification become necessary to guide further intervention. However, the treatment modalities, including surgery, chemotherapy, radiotherapy, and immunotherapy are rather inconsistent owing to limited researches and low volume of patients. Besides, the outcomes of ISCM patients and risky factors were poorly studied, leading to the lack of guidance. Therefore, we badly need more systematic reviews of ISCM, especially from breast cancer, and evidence-based conclusions drawn from them for future clinical decision making.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 April 2020 and was last updated on 12 April 2020 (registration number INPLASY202040064).

INTRODUCTION

Review question / Objective: To identify risk factors for progression-free survival and

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METHODS

Search strategy: Search Terms: “breast cancer,” or “breast carcinoma” and “intramedullary spinal cord metastasis.”; Sources: Ovid MEDLINE, Embase, PubMed, and Cochrane database; Search Dates: From May 1, 2020 to June 1, 2020; Language: English; Publication period: January 1, 1954 to May 1, 2020.

Participant or population: Inclusion criteria: 1. pathological diagnosis of any type of breast cancer; 2. metastasis to intramedullary spinal cord location; 3. detailed information of treatment, neurological outcome, status of recurrence, metastasis, or death; Exclusion criteria: 1.unavailable or incomplete clinical

data; 2. basic research rather than clinical report without data which was necessary for statistical analysis; 3. pathological diagnosis was undefined; and/or 4. duplicated report.

Intervention: Surgical treatment (gross total resection, subtotal resection, partial resection, or biopsy); 2. Radiation (radiotherapy type and dose); 3. Chemotherapy (drug and regimen); 4. Immunotherapy (drug and regimen).

Comparator: Not applicable.

Study designs to be included: No restrictions on the types of study design due to the rarity of the disease.

Eligibility criteria: Clinical information including demographic features (age, sex), location of tumor, duration of symptoms, extent of resection, treatment modalities, Ki-67 index, PFS, recurrence status, follow-up time, patient clinical status on the last follow-up, and OS were extracted from the included cases. Similar studies done in the same place were not included in our analysis to exclude the duplicate patients. Reports from the same institution in different time frames were included after careful examination. Two review authors independently assessed the bias in the included studies by considering the completeness of outcome data and selective outcome reporting. Disagreement between the review authors over the bias in particular studies was resolved by discussion, with involvement of a third review author when necessary.

Information sources: Search Terms: “breast cancer,” or “breast carcinoma” and “intramedullary spinal cord metastasis.”; Sources: Ovid MEDLINE, Embase, PubMed, and Cochrane database; Search Dates: From May 1, 2020 to June 1, 2020; Language: English; Publication period: January 1, 1954 to May 1, 2020. The reference lists of all selected studies will be checked as well as the grey literature. In addition, references to relevant assessments, guidelines and comments

identified in MEDLINE, Embase, PubMed, and Cochrane Library will be found.

Main outcome(s): Adverse factors for recurrence, progression-free survival and overall survival.

Additional outcome(s): Optimal treatment for intramedullary spinal cord metastasis from breast cancer.

Data management: The following data were extracted independently by two authors from each study whenever possible, and discrepancies rendered to Dr Liang Wu. Data to be extracted: author and year of diagnosis, main preoperative complaint, tumor location, tumor size, tumor volume, surgical approach, symptom duration, magnetic resonance imaging features, histological types, extent of resection, adjuvant therapy of type, status of survival and duration of follow-up.

Quality assessment / Risk of bias analysis: Two review authors will independently assess the risk of bias in included studies by considering the following discrepancies, with involvement of a third review author where necessary. Quality of individual studies: (1) patients with a pathological diagnosis of intramedullary spinal cord metastasis from breast cancer who underwent neurosurgery and histological types were not restricted; (2) intramedullary spinal cord metastasis location; (3) detailed information on treatment, status of survival. This will define the risk factors and appropriate treatment for patients with intramedullary spinal cord metastasis from breast cancer.

Strategy of data synthesis: Individual participant data will be used, and we will provide a narrative synthesis of the findings from the included studies (univariate analysis and multivariate analysis), structured around the type of intervention, target population characteristics, type of outcome and intervention content.

Subgroup analysis: If the necessary data are available, subgroup analysis will be

done for people with different treatment protocol.

Sensibility analysis: If it is necessary, sensitivity analysis will be performed by Stata 15.1 using the leave-one-out approach.

Language: English.

Country(ies) involved: China.

Keywords: Breast cancer; Intramedullary spinal cord metastasis; Surgery; Radiotherapy; Chemotherapy; Immunotherapy; Systematic review.

Contributions of each author:

Author 1 - The author drafted the manuscript and read, provided feedback and approved the final manuscript.

Author 2 - The author provided statistical expertise.

Author 3 - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.

Author 4 - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.