INPLASY PROTOCOL

To cite: Zhang et al. Factors influencing survival benefit in patients with de novo stage IV breast cancer: a systematic review and meta-analysis. Inplasy protocol 202270053. doi: 10.37766/inplasy2022.7.0053

Received: 10 July 2022

Published: 10 July 2022

Corresponding author:
Ang Zheng

812144104@qq.com

Author Affiliation:
Department of Burn Plastic Surgery, Chaoyang Central Hospital, Chaoyang, Liaoning Province, China.

Support: **NSFC.**

Review Stage at time of this submission: **Completed but not published.**

Conflicts of interest:
None declared.

Factors influencing survival benefit in patients with de novo stage IV breast cancer: a systematic review and meta-analysis

Zhang, ML[1]; Zheng, A[2].

Review question / Objective: **There are significant differences in the prognosis of patients with de novo stage IV breast cancer. This study aimed to conduct a comprehensive meta-analysis of the factors influencing de novo stage IV breast cancer, which will enable clinicians to facilitate individualized and precise treatment for patients.**
Eligibility criteria: **Inclusion criteria: (i) source of case was patient with de novo stage IV breast cancer confirmed at a medical institution, (ii) study design was a case-control study or cohort study, (iii) relevant studies included factors influencing de novo stage IV breast cancer, and (iv) odds ratio (OR)/hazard ratio (HR) and corresponding 95% confidence interval (CI) were provided or adequate data were available for calculation. Exclusion criteria: (i) duplicate publications, (ii) reviews, meta-analyses, commentaries, case reports, or animal studies, (iii) full text unavailable, incomplete data, or improper statistical methods, and (iv) Newcastle-Ottawa Scale (NOS) score < six.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 July 2022 and was last updated on 10 July 2022 (registration number INPLASY202270053).

INTRODUCTION

Review question / Objective: **There are significant differences in the prognosis of patients with de novo stage IV breast cancer. This study aimed to conduct a comprehensive meta-analysis of the factors influencing de novo stage IV breast cancer, which will enable clinicians to facilitate individualized and precise treatment for patients.**

Condition being studied: **Breast cancer is the most common malignancy among females worldwide. [1] Stage IV breast cancer is defined as breast cancer with any T stage, any N stage, and an M stage of M1. [2] De novo stage IV breast cancer**

refers to breast cancer that is stage IV at initial diagnosis, which accounts for about 6-10% of all cases of breast cancer. [3] The Chinese Society of Breast Surgery (CSBrS) found that de novo stage IV breast cancer accounted for 1.07% of breast surgery-related admissions in China and that the median age of onset was 51.5 years. [4]

The median survival period for advanced breast cancer has increased annually worldwide, and in 2017, a US research group reported that over 60% of advanced breast cancer patients survived for more than 2 years and 17% survived for more than 10 years. [5] Furthermore, the survival of patients with de novo stage IV breast cancer was also improved. [6] In fact, patients with de novo stage IV breast cancer are a large group of patients with very different individual characteristics, which results in significant prognostic differences between these patients. Clinical researchers need to know which patients with de novo stage IV breast cancer are likely to exhibit long-term survival and which are at risk of poor prognosis so as to establish individualized and precise treatment for patients with de novo stage IV breast cancer. Accordingly, this article is the first comprehensive review of the factors influencing the prognosis of de novo stage IV breast cancer, and a meta-analysis was conducted to identify the factors affecting progression-free survival (PFS), breast cancer-specific survival (BCSS), and overall survival (OS) in de novo stage IV breast cancer patients and further distinguish protective factors and high-risk factors for prognosis.

With improvements in diagnosis and treatment, the survival period and quality of life of patients with de novo stage IV breast cancer have improved tremendously, and the principles associated with local surgical management have become a major clinical concern. The CSBrS-002 study [4] showed that 54.2% of Chinese patients with de novo stage IV breast cancer underwent mastectomy. The clinical benefit of surgery for localized lesions in de novo stage IV breast cancer has become a key consideration for clinical decision-makers.[7, 8] Most current prospective studies are limited to a single study center, with very different baseline characteristics of the patients, as well as selection bias. Therefore, this study intends to add evidence-based medical practices to perform a meta-analysis to determine whether primary site surgery provides survival benefit for patients with de novo stage IV breast cancer.

This meta-analysis focuses on the prognostic factors of de novo stage IV breast cancer. This study aimed to screen for patients with de novo stage IV breast cancer who can achieve survival benefits, thus providing new evidence and insights to improve the precision diagnostics and individualized therapeutics of de novo stage IV breast cancer.

METHODS

Participant or population: Patients with de novo stage IV breast cancer.

Intervention: Not applicable.

Comparator: Not applicable.

Study designs to be included: Study design was a case-control study or cohort study.

Eligibility criteria: Inclusion criteria: (i) source of case was patient with de novo stage IV breast cancer confirmed at a medical institution, (ii) study design was a case-control study or cohort study, (iii) relevant studies included factors influencing de novo stage IV breast cancer, and (iv) odds ratio (OR)/hazard ratio (HR) and corresponding 95% confidence interval (CI) were provided or adequate data were available for calculation. Exclusion criteria: (i) duplicate publications, (ii) reviews, meta-analyses, commentaries, case reports, or animal studies, (iii) full text unavailable, incomplete data, or improper statistical methods, and (iv) Newcastle-Ottawa Scale (NOS) score < six.

Information sources: PubMed, the Cochrane Library, Embase, and Web of Science.

Main outcome(s): A total of 37 studies were included and a pooled analysis of 21

influencing factors was performed. The results indicated that surgery of primary tumor was a protective factor for progression-free survival (PFS), breast cancer-specific survival (BCSS), and overall survival (OS) in patients with de novo stage IV breast cancer ($p < 0.05$). For BCSS and OS, hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) positive was the molecular subtype with the best prognosis, while HR-HER2- had the worst prognosis. Patients with brain metastases had a significantly higher risk of death compared to those with bone metastases (HR = 1.81, 95% CI: 1.45-2.27, $p < 0.00001$). Additionally, we found that the absence of visceral metastases was a protective factor for patient OS (HR = 0.75, 95% CI: 0.72-0.79, $p < 0.00001$).

Quality assessment / Risk of bias analysis: The meta-analysis used the Newcastle-Ottawa scale (NOS) recommended by the Cochrane Collaboration for literature quality assessment (add NOS reference). Scores ranged from zero to nine, with higher scores indicating better quality of the included literature. The NOS was performed independently by two researchers (Meilin Zhang and Ang Zheng), and a third researcher (Feng Jin) made the final decision in case of disagreement.

Strategy of data synthesis: Statistical analyses were performed using ReviewManager 5. 3 software (Cochrane Collaboration, Copenhagen, Denmark). The Cochrane Q test was used to analyze the heterogeneity and the I^2 value was used to evaluate the heterogeneity among the included studies. $p > 0.1$ and $I^2 < 50\%$ indicated no statistical heterogeneity between the studies and we used a fixed effect model. If there was statistical heterogeneity, we used sensitivity analysis to find the source of heterogeneity, otherwise we used a random effect model, and the final results were displayed in forest plots. Publication bias was performed for influencing factors included in five or more studies. $p > 0.05$ indicates no obvious publication bias in the Egger's test and Begg's test, which was performed in Stata 14 software. In the meta-analysis, $p < 0.05$ was considered statistically significant.

Subgroup analysis: We judged the heterogeneity according to Cochran Q and I^2 value. Cochran Q $P < 0.1$ or $I^2 \geq 50\%$ indicated that there was heterogeneity among the included studies. We further performed subgroup analysis or sensitivity analysis, otherwise random effect model was used.

Sensitivity analysis: We judged the heterogeneity according to Cochran Q and I^2 value. Cochran Q $P < 0.1$ or $I^2 \geq 50\%$ indicated that there was heterogeneity among the included studies. We further performed subgroup analysis or sensitivity analysis, otherwise random effect model was used.

Country(ies) involved: China.

Keywords: de novo stage IV breast cancer, risk Factor; protective Factor, meta-analysis.

Contributions of each author:
Author 1 - Meilin Zhang.
Author 2 - Ang Zheng.