INPLASY PROTOCOL

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Corresponding author:
Gang Qian

qiangang65@163.com

Author Affiliation:
The Affiliated Hospital of Jiaxing University.

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None declared.

Association between aromatase inhibitors and myocardial infarction morbidity in women with estrogen receptor-positive breast cancer: A meta-analysis of observational studies

Sun, JC[1]; Sun, ZF[2]; He, CJ[3]; Zhai, CL[4]; Qian, G[5].

Review question / Objective: **We conducted the meta-analysis focused on the association between AI treatment and the risk of MI in the real world.**
Condition being studied: **Breast cancer has become the most commonly diagnosed malignancy in females in various nations, and it is matched by the highest mortality. As mainstay medicines, aromatase inhibitors (AIs, i.e., anastrozole, letrozole, and exemestane) and tamoxifen are generally prescribed for women with estrogen receptor-positive breast cancer. AIs have been proven superior to tamoxifen, with third-generation AIs displacing tamoxifen as the cornerstone endocrine treatment for estrogen receptor-positive breast carcinoma. Data from several trials showed that AIs significantly reduced the recurrence and improved the overall survival rates of breast cancer. However, cardiovascular adverse events (CVAEs) have turned into a major cause of noncancer-related chronic morbidity and mortality, and as breast cancer mortality showed a decline, the cardiovascular toxicity of therapies has been observed in recent years.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 July 2022 and was last updated on 18 July 2022 (registration number INPLASY202270086).

INTRODUCTION

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generally prescribed for women with estrogen receptor-positive breast cancer. AIs have been proven superior to tamoxifen, with third-generation AIs displacing tamoxifen as the cornerstone endocrine treatment for estrogen receptor-positive breast carcinoma. Data from several trials showed that AIs significantly reduced the recurrence and improved the overall survival rates of breast cancer. However, cardiovascular adverse events (CVAEs) have turned into a major cause of noncancer-related chronic morbidity and mortality, and as breast cancer mortality showed a decline, the cardiovascular toxicity of therapies has been observed in recent years.

METHODS

Participant or population: Participants were female with estrogen receptor-positive breast cancer and with age more than 18 years old.

Intervention: AIs as adjuvant endocrine therapy or extended adjuvant endocrine therapy.

Comparator: Comparison involving AI treatment versus tamoxifen or no hormonal treatment.

Study designs to be included: Cohort or case-control study

Eligibility criteria: We excluded articles without odds ratio, hazard ratio, and risk ratio (RR) or publications without available data to calculate these values.

Information sources: PubMed, Embase, and Cochrane Library.

Main outcome(s): Pooled results of the studies showed no statistical significance difference when comparing the association between AIs and the control group (RR: 0.98, 95% CI: 0.83–1.17). The I2 = 57.52% demonstrated heterogeneity between studies. In terms of the absolute risks, 1.20% of the participants in the AI groups experienced MI, and 0.96% in the control group experienced MI (difference in absolute risk = 0.3%, NNH = 416).

Additional outcome(s): AI-treated subjects were associated with a slightly reduced risk of IS (NNH: 609) compared with the control group, but the difference was not statistically significant (RR: 0.93, 95% CI: 0.82–1.07; I2 = 37%). No significant difference in the occurrence of HF was found (RR: 1.24, 95% CI: 0.92–1.66; I2 = 77%).

Data management: Stata and Endnote softwares were used to manage records and data.

Quality assessment / Risk of bias analysis: Newcastle–Ottawa Scale (NOS) was used to evaluate the risk of bias in observational studies. The NOS was used to assess the quality of included studies through three parameters: selection, comparability, and outcome. Maximum scores of 4, 2, and 3 were assigned to the selection, comparability, and outcome, respectively. The score of 9 was the highest, and the studies were categorized into low- (fewer than 5 points), moderate- (5–7 points), and high-quality (more than 7 points) research.

Strategy of data synthesis: This meta-analysis was conducted using Stata (Stata Version 16.0; Stata Corporation, College Station, TX, USA). A pooled RR and 95% confidence intervals (CIs) were calculated for binary outcomes, and a P value of less than 0.05 was defined as a statistically significant difference. The heterogeneity between included trials was evaluated using the I-square (I2) statistic. The random effect model was applied to the present meta-analysis, considering the probably high heterogeneity due to clinical and methodological factors.

Subgroup analysis: Subgroup analysis was performed based on the history of CVD, propensity score, control groups, and the age of included patients. In addition, we performed another subgroup analysis on the enrolled population-based studies to explore the association between AI usage and MI morbidity in real-world settings.

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Sensitivity analysis: To assess the stability of the primary outcome, we performed a sensitivity analysis by sequentially deleting trials.

Language: The search was restricted to articles published in English.

Country(ies) involved: China.

Keywords: myocardial infarction, aromatase inhibitors, tamoxifen, breast cancer, meta-analysis.

Contributions of each author:

Author 1 - Jing-Chao Sun - Author 1 contributed to the study design, the data acquisition, analysis, interpretation, the drafting, and revision of the manuscript and agreed to be accountable for all aspects of the work.
Email: 15990657855@163.com
Author 2 - Ze-Fan Sun - Author 2 contributed to the study design, the data acquisition, analysis, interpretation, the drafting, and revision of the manuscript.
Email: sunzhewei0211@163.com
Author 3 - Chao-Jie He - Author 3 contributed to the study design, the data acquisition, analysis, interpretation, the drafting, and revision of the manuscript.
Email: hechaojie824@163.com
Author 4 - Chang-Lin Zhai - Author 4 contributed to the study conceive, the supervision, data interpretation, and performed revision of the manuscript.
Email: yesterdaygun@126.com
Author 5 - Gang Qian - Author 5 contributed to the study conceive, design, data analysis, interpretation, and revised the manuscript.
Email: qiangang65@163.com

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