INTRODUCTION

Review question / Objective: To provide evidence for early detection of adverse cardiac events and improve management by evaluating the incidence of cardiotoxicity associated with ICI therapy for lung cancer.

Condition being studied: Although people are more and more aware of the cardiotoxicity caused by Immune checkpoint inhibitors (ICIs) in the treatment of lung cancer, its incidence rate has not been systematically analyzed.

Information sources: Search for relevant publications in PubMed and Scopus from inception to 19 April 2022. Review articles, case series, conference abstracts, and articles not published in English were excluded.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 May 2022 and was last updated on 07 May 2022 (registration number INPLASY202250042).

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METHODS

Participant or population: Lung cancer patients undergoing immunotherapy.

Intervention: Immunotherapy.

Comparator: Combination immunotherapy or immunotherapy combined with radiotherapy or chemotherapy.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: We considered all randomized studies on ICIs for lung cancer. Studies were eligible if they reported outcome data with regards to immune related adverse events.

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Main outcome(s): The primary outcome of the present meta-analysis is incidence of ICI-associated cardiotoxicity.

Additional outcome(s): The secondary outcomes are incidence of ICI-associated myocarditis, pericardial effusion, heart failure, cardiopulmonary events, cardiac arrest, atrial fibrillation, arrhythmia, and myocardial infarction.

Quality assessment / Risk of bias analysis: Risks of bias were assessed independently using the Risk of Bias Tool developed by the Cochrane.

Strategy of data synthesis: The incidence of cardiotoxicity may be very rare, even no event occurring in either or both arms of a study. Meta-analysis of incidence using inverse variance methods has the problem that the variance becomes very small when the incidence is small or large, with the consequence that such studies get a large weight in the meta-analysis. Transformation methods can be used to avoid an undue large weight for studies with small or large incidence. The double arcsine transformation has properties that make it the clearly preferred option over the often used logit transformation. Pooled incidence and risk ratios (RRs) with 95% confidence intervals (95% CIs) for cardiotoxicity events were calculated. This meta-analysis was conducted in MetaXL 5.3 (EpiGear International) using the inverse variance heterogeneity (IVhet) model.

Subgroup analysis: The incidence of any cardiac AEs in SCLC and NSCLC subgroups will be analyzed.

Sensitivity analysis: Sensitivity analyses will be performed by a leave-one-out analysis.

Country(ies) involved: China.

Keywords: Immune checkpoint inhibitor, immunotherapy, cardiotoxicity, myocarditis.

Contributions of each author:
Author 1 - Xiaotong Zhang.
Email: zhangxtpumch@126.com
Author 2 - Nan Ge.
Email: genan32@163.com
Author 3 - Zijian Xiang.
Email: xiangzj@xy-data.net
Author 4 - Tao Liu.
Email: 15601089300@163.com