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Effectiveness of Radiotherapy in Preventing Heterotopic Ossification: A Meta-Analysis of Randomized Controlled Trials Beyond Total Hip Arthroplasty

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Data analysis.

Conflicts of interest - The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

INPLASY registration number: INPLASY202530092

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 March 2025 and was last updated on 22 March 2025.

INTRODUCTION

Review question / Objective The investigation applied the PICO framework as follows: Population (P): Trauma or surgery patients requiring prophylaxis against HO. Intervention (I): Prophylactic Radiotherapy (RT). Comparator (C): Non-radiated controls undergoing standard rehabilitation; Outcomes (O): Primary outcome: Radiologically confirmed HO incidence (Brooker Grade). Secondary outcome: Adverse reactions.

Condition being studied Heterotopic ossification (HO) frequently occurs after procedures such as hip replacements, acetabular fractures, and elbow

fractures. While radiotherapy (RT) has been a longstanding preventive measure against HO, its efficacy remains controversial, with some studies questioning its effectiveness and noting potential side effects. Previous research has predominantly focused on total hip arthroplasty (THA), leading to a gap in comprehensive evaluation of RT's efficacy and safety across other conditions.

METHODS

Search strategy Our comprehensive search strategy integrated controlled vocabulary (MeSH terms including "RT", "Ossification, Heterotopic", and "Randomized Controlled Trials as Topic") with free-text keywords.

Participant or population Trauma or surgery patients requiring prophylaxis against HO.

Intervention Prophylactic RT.

Comparator Non-radiated controls undergoing standard rehabilitation.

Study designs to be included RCTs.

Eligibility criteria Inclusion criteria encompassed trauma or surgery patients requiring HO prophylaxis, those undergoing radiotherapeutic intervention or standard care, and human clinical trials published in peer-reviewed randomized controlled trials up to January 2025, with mandatory 12-week radiographic surveillance. Exclusion criteria included retrospective analyses, case series, conference abstracts, and secondary systematic reviews.

Information sources Searches were executed across four major biomedical databases: PubMed, Embase, Cochrane Library, and Web of Science.

Main outcome(s) Heterotopic ossification (HO).

Additional outcome(s) Adverse reactions.

Quality assessment / Risk of bias analysis Two investigators assessed methodological quality using Cochrane's standardized risk of bias criteria. For unresolved discrepancies, an independent arbiter adjudicated final determinations.

Strategy of data synthesis The included studies underwent quantitative synthesis via RevMan 5.4 (Version 5.4.1, Cochrane Collaboration), with results visualized through forest plot diagrams. Continuous outcomes were expressed as weighted mean differences (WMD) with 95% confidence intervals (CIs), whereas dichotomous outcomes were reported as risk ratios (RR) with corresponding 95% CIs. Inter-study heterogeneity was quantified using Cochran's Q statistic (χ^2 test) supplemented by I^2 index. For analyses demonstrating low heterogeneity ($I^2 < 50\%$), a Mantel-Haenszel fixed-effect model was implemented; conversely, when substantial heterogeneity was present ($I^2 \geq 50\%$), a DerSimonian-Laird random-effects model was employed to account for between-study variance. The statistical significance threshold was set at $p=0.05$ for all inferential tests.

Subgroup analysis THA and non-THA subgroup analyses were performed using RevMan if needed.

Sensitivity analysis Sensitivity analyses were performed using StataSE software if required.

Country(ies) involved China.

Keywords Radiotherapy, Heterotopic Ossification, Meta-Analysis.

Contributions of each author

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