INPLASY

Adjuvant Radiotherapy in Resected Primary Adrenocortical Carcinoma: A Systematic Review and Meta-analysis of Oncological Outcomes

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Murthy, V; Subramani, V; Chauhan, H; Maitre, P.

Corresponding author:
Vedang Murthy

vedangmurthy@gmail.com

Author Affiliation:
Tata Memorial Centre.

ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202540090

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 April 2025 and was last updated on 25 April 2025.

INTRODUCTION

Review question / Objective What is the impact of adjuvant radiotherapy on disease control outcomes and toxicity in adult patients with surgically resected, primary adrenocortical carcinoma?

Rationale Adrenocortical carcinoma (ACC) is a rare, aggressive malignancy with high recurrence rates even after complete surgical resection. The role of adjuvant radiotherapy (RT) in reducing local recurrence and improving survival remains controversial due to the rarity of the disease and absence of large randomized trials. This review aims to synthesize the available evidence on the effectiveness and safety of adjuvant RT in adult patients with resected primary ACC.

Condition being studied Adrenocortical carcinoma (ACC) is a rare and aggressive cancer of the adrenal cortex. The focus of the protocol is to evaluate the impact of adjuvant radiotherapy on disease control outcomes (local recurrence free survival, overall survival) and treatment-related toxicity in patients who had undergone surgical resection for primary ACC.

METHODS

Search strategy

Databases to be searched:
– PubMed/MEDLINE
– Embase
– Scopus
– Cochrane Library
Additionally, one institutional dataset from Tata Memorial Centre will be included as a source of primary data.
Grey literature (if feasible): clinical trial registries, Google Scholar, and institutional repositories. A comprehensive search strategy using MeSH and free-text terms will be developed for each database. Only articles published since 2000 will be included.

Participant or population Adult patients (≥18 years) with histologically confirmed primary ACC

– Treated with curative-intent surgery and
– Received adjuvant radiotherapy post surgery.

Intervention Patients who received adjuvant radiotherapy after primary resection of Adrenocortical carcinoma.

Comparator Patients who had only primary surgical resection for Adrenocortical carcinoma.

Study designs to be included Comparative or non-comparative studies (RCTs, cohorts, case series >10 patients) and Peer-reviewed full-text articles.

Eligibility criteria
Inclusion Criteria:
Institutional or unpublished datasets may be included if they meet all predefined eligibility criteria and provide sufficient methodological detail.
– Adult patients (≥18 years) with histologically confirmed primary ACC
– Treated with curative-intent surgery
– Received adjuvant radiotherapy
– Reports at least one of: DFS, LRFS, OS, recurrence/local control, toxicity – Comparative or non-comparative studies (RCTs, cohorts, case series >10 patients)
– Peer-reviewed full-text articles
Exclusion Criteria:
– Pediatric patients
– Palliative RT or radiotherapy for recurrent/metastatic ACC
– No primary surgery
– Studies using SEER/NCDB without detailed RT/disease control data – Case reports (≤10 patients), reviews, editorials, letters, meta analysis
– Non-English studies.

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Main outcome(s) To evaluate the effect of adjuvant radiotherapy on:
1. Local recurrence free survival (LRFS)
2. Disease-free survival (DFS)
3. Local or distant recurrence
4. Overall survival (OS)
5. Treatment-related toxicity.

Quality assessment / Risk of bias analysis Newcastle-Ottawa Scale (NOS) and Risk of bias tools.

Strategy of data synthesis
– A qualitative synthesis will be performed
– Where feasible, meta-analysis using RevMan will be conducted
– Effect sizes: Hazard ratios (HR) for time-to-event outcomes, odds ratios (OR) for dichotomous outcomes
– Heterogeneity will be assessed using I^2 and χ^2 tests.

Subgroup analysis The following subgroups will be considered:
– Radiotherapy technique (e.g., 3D-CRT, IMRT,)
– Use of concurrent or sequential mitotane or chemotherapy
– Margin status after surgery (R0/R1/R2)
– Stage at diagnosis
– Radiation dose/fractionation schemes .
These analyses aim to assess whether specific factors modify the effect of adjuvant radiotherapy on outcomes.

Sensitivity analysis Given the limited number of studies and anticipated heterogeneity, sensitivity analyses will focus on:
– Performing leave-one-out analysis to assess the influence of individual studies on pooled estimates
– Stratification by radiotherapy technique (e.g., 3DCRT, IMRT,) will be considered only if sufficient and consistent data are available
– Exclusion of non-comparative studies will not be performed, as they constitute a significant portion of the evidence base in this rare disease context
These approaches aim to ensure the robustness of findings while preserving the clinical relevance of available data.

Language restriction English Only.

Country(ies) involved INDIA.

Keywords Adrenocortical Carcinoma; Adjuvant Radiotherapy; Primary surgical resection.

Dissemination plans The findings of this systematic review and meta-analysis will be disseminated through publication in a peer-reviewed oncology journal and presentation at relevant national and international conferences.

The results will also be shared with clinical collaborators and disseminated through institutional platforms of Tata Memorial Centre. Where applicable, findings will inform clinical practice guidelines and multidisciplinary tumor board discussions regarding adjuvant radiotherapy in adrenocortical carcinoma.

Contributions of each author

Author 1 - Vedang Murthy.
Email: vedangmurthy@gmail.com
Author 2 - Vasanthapriya Subramani.
Email: dr.vasanthapriyas@gmail.com
Author 3 - Harshdeep Chauhan.
Email: chauhanharshdeep020@gmail.com
Author 4 - Priyamvada Maitre.
Email: priyamvadamaitre@gmail.com