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Therapeutic Outcomes and Toxicity of Stereotactic Body Radiotherapy (SBRT) and Stereotactic Radiosurgery (SRS) in Metastatic Anaplastic Thyroid Cancer: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 December 2024 and was last updated on 26 December 2024.

INTRODUCTION

Review question / Objective Anaplastic thyroid carcinoma (ATC) is a highly aggressive type of thyroid cancer characterized by a dismal prognosis. Stereotactic body radiotherapy (SBRT) has been employed in various centers worldwide as a local ablative therapy for metastatic ATC, whereas stereotactic radiosurgery (SRS) is utilized for the treatment of limited brain metastases. However, available data comparing the efficacy and safety of SBRT and SRS in ATC remain sparse, emphasizing the need for further investigation.

Rationale Anaplastic thyroid carcinoma (ATC) represents a therapeutic challenge. Nevertheless, the effectiveness of advanced local therapies, particularly stereotactic body radiotherapy (SBRT) or stereotactic radiosurgery (SRS), remains inconclusive. Therefore, we intend to conduct a systematic review and meta-analysis to evaluate the impact of SBRT/SRS in patients with metastatic ATC.

Condition being studied The PICO (population, intervention, comparison, outcome) setting of the current meta-analysis included: (1) P: Patients with anaplastic thyroid carcinoma (ATC); (2) I: Stereotactic radiosurgery (SRS) or stereotactic body radiotherapy (SBRT); (3) C: Standard therapy or other therapeutic modalities; and (4) O: Overall survival, progression-free survival, local control, treatment-related toxicity.

METHODS

Search strategy Two authors (R.R. and L.K.) made independent electronic searches in the PubMed/Medline, Scopus, Cochrane Library and Ovid using the Medical Subject Headings (MeSH) keywords “anaplastic thyroid cancer”, “ATC”, “stereotactic body radiotherapy”, “SBRT”, ”stereotactic radiosurgery” and “SRS”. The search was conducted between 1st June and 30th November 2024.

Participant or population Inclusion criteria were as follows: i) histological confirmed anaplastic thyroid cancer; ii) treatment with SBRT/SRS; iii)

study on humans; iv) with sufficient data on treatment-related toxicity and outcome
Exclusion criteria were as follows: i) Case reports; ii) letters; iii) reviews; iv) guideline/ editorials; v) duplicate studies. vi) reports with histology other than ATC.

Intervention Stereotactic Body Radiotherapy (SBRT) and Stereotactic Radiosurgery (SRS).

Comparator If applicabe standard therapy or other therapeutic modalities.

Study designs to be included Randomized controlled trials (RCTs), non-randomized clinical trials, observational studies, cohortstudies and retrospective studies fromoriginal research.

Eligibility criteria Inclusion criteria were as follows: i) histological confirmed anaplastic thyroid cancer; ii) treatment with SBRT/SRS; iii) study on humans; iv) with sufficient data on treatment-related toxicity and outcome
Exclusion criteria were as follows: i) Case reports; ii) letters; iii) reviews; iv) guideline/ editorials; v) duplicate studies. vi) reports with histology other than ATC.

Information sources PubMed/Medline, Scopus, Cochrane Library and Ovid.

Main outcome(s) Overall survival (OS), progression-free survival (PFS), local control.

Additional outcome(s) Treatment-related toxicity.

Data management Two independent authors (R.R. and L.K.) extracted data from the selected studies, including demographic data, study design, therapeutic details and interventions, and the values of the primary and secondary outcomes. The evaluators carefully considered the direction of effect of the scales used in each trial to prevent misinterpretation. When data were unavailable in the published articles, we contacted the corresponding authors to acquire the original data.

Quality assessment / Risk of bias analysis We assessed the methodological quality of the included studies using the Cochrane risk-of-bias tool for randomized trials, version 2 (RoB 2), which consists of six key domains: the randomization process, adherence to interventions, missing outcome data, measurement of outcomes, selective reporting, and overall risk of bias. In the intervention adherence section of RoB 2, there are two options for evaluating studies: intention-to-treat (based on intervention assignment) or per-protocol (based on intervention adherence). For this meta-analysis, we opted for per-protocol evaluation, as it aligned with the design of the studies included.

Strategy of data synthesis Due to the heterogeneity of the target populations across the included studies, we plan to conduct the current meta-analysis using a random-effects model with Comprehensive Meta-Analysis software, version 3 (Biostat, Englewood, NJ). A two-tailed p-value of less than 0.05 will be considered statistically significant. To quantify continuous outcomes, we plan to use the standard mean difference (SMD) with 95% confidence intervals (CIs). An SMD of 0.2, 0.5, and 0.8 will be interpreted as small, moderate, and large effect sizes, respectively. For discrete outcomes, we will employ odds ratios with 95% CIs. The degree of heterogeneity among studies will be assessed using the I^2 statistic and Cochran's Q test. I^2 values of 25%, 50%, and 75% will be interpreted as indicating low, moderate, and high heterogeneity, respectively.

Subgroup analysis Subgroup analyses will be conducted based on the location of metastases (brain vs. extracranial). Meta-regressions will be performed to examine whether the treatment effects of SBRT/SRS were correlated with these parameters.

Sensitivity analysis To confirm the robustness of the meta-analysis, a sensitivity analyses will be performed using one-study removal method to see if there is a significant change in the summary effect size after removing a particular trial from the analysis.

Language restriction Articles written in English.

Country(ies) involved Germany.

Keywords ATC, anaplastic thyroid cancer, metastases, SBRT, SRS.

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