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Deciphering the Prognostic Efficacy of MRI Radiomics in Nasopharyngeal Carcinoma: A Comprehensive Meta-Analysis

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ADMINISTRATIVE INFORMATION

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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 23 February 2024 and was last updated on 18 March 2024.

INTRODUCTION

Review question / Objective How effective is MRI radiomics in predicting the prognosis of patients with nasopharyngeal cancer in terms of local relapse-free survival, distant metastasis-free survival, disease-free survival, local recurrence, local control, and local failure, compared to traditional MRI imaging methods?
This question can be further broken down into more specific questions to address the various aspects of the main question, using the PICOS framework for clarity:

Population-Specific Question: Among patients diagnosed with nasopharyngeal cancer, how does the prognostic accuracy of MRI radiomics compare with conventional MRI imaging in predicting local relapse-free survival?

Intervention-Specific Question: In the context of MRI imaging for nasopharyngeal cancer, how do radiomics-based machine learning (ML) and deep learning (DL) methods contribute to the accuracy of prognosis predictions?
Comparison-Specific Question: How do traditional MRI imaging outcomes differ from those obtained using MRI radiomics in terms of predicting distant metastasis-free survival in nasopharyngeal cancer patients?
Outcome-Specific Question: Which radiomic features derived from MRI imaging are most predictive of disease-free survival, local recurrence, local control, and local failure in nasopharyngeal cancer?
Study Design-Specific Question: Do retrospective and prospective cohort studies offer consistent evidence on the prognostic value of MRI radiomics in nasopharyngeal cancer management?

These questions aim to dissect the overarching inquiry into manageable, focused segments that collectively provide a thorough understanding of the prognostic efficacy of MRI radiomics in nasopharyngeal carcinoma. Each question is tailored to explore different dimensions of the research topic, facilitating a comprehensive meta-analytical review.

Condition being studied Nasopharyngeal carcinoma (NPC) is a unique form of head and neck cancer distinguished by its occurrence in the nasopharynx, the upper part of the throat behind the nose. This disease is geographically and ethnically distinct, with higher prevalence rates in East Asia, North Africa, and some Arctic regions, suggesting both genetic susceptibilities and environmental factors, such as Epstein-Barr virus (EBV) infection, play roles in its development. NPC manifests in a region rich in lymphatic tissues, contributing to its aggressive nature and propensity for early lymphatic spread.

Clinical management of NPC involves a multidisciplinary approach, with radiotherapy and chemotherapy being the mainstays of treatment due to the anatomical complexity and sensitivity of the surrounding structures. Despite advancements in treatment, prognosis remains variable, heavily dependent on stage at diagnosis, with distant metastasis and locoregional recurrence being significant challenges.

The introduction of Magnetic Resonance Imaging (MRI) radiomics, which utilizes advanced image processing and analysis to extract detailed features from MRI scans, promises to enhance the precision of prognosis, treatment planning, and outcome prediction in NPC. By analyzing the tumor's shape, texture, and other radiographic features, radiomics aims to uncover patterns not visible to the naked eye, offering a potential leap forward in personalized cancer care.

METHODS

Participant or population The participants in this systematic review are individuals diagnosed with nasopharyngeal cancer, irrespective of age, gender, ethnicity, and disease stage at diagnosis. This includes patients who have undergone any standard treatment modalities for nasopharyngeal cancer, such as radiation therapy, chemotherapy, or a combination of both.

Intervention The intervention of interest in this review is MRI radiomics, which involves extracting a large number of features from MRI images using advanced computational methods, .The intervention of interest in this review is MRI radiomics, which involves extracting a large number of features from MRI images using advanced computational methods, including both Machine Learning (ML) and Deep Learning (DL) techniques. These radiomic features may relate to the shape, texture, and intensity of the tumor and surrounding tissues, potentially providing prognostic information beyond what can be seen by the naked eye or through traditional imaging analysis.The intervention of interest in this review is MRI radiomics, which involves extracting a large number of features from MRI images using advanced computational methods, including both Machine Learning (ML) and Deep Learning (DL) techniques. These radiomic features may relate to the shape, texture, and intensity of the tumor and surrounding tissues, potentially providing prognostic information beyond what can be seen by the naked eye or through traditional imaging analysis. These radiomic features may relate to the shape, texture, and intensity of the tumor and surrounding tissues, potentially providing prognostic information beyond what can be seen by the naked eye or through traditional imaging analysis.

Comparator The comparator in this systematic review is traditional MRI imaging techniques without the application of radiomics analysis. This encompasses standard MRI interpretations used in the diagnosis, monitoring, and evaluation of treatment response in nasopharyngeal cancer patients. The comparison aims to assess whether MRI radiomics provides additional prognostic value over conventional MRI imaging practices.

Study designs to be included Randomized Controlled Trials (RCTs), Cohorts, Case-Control Studies.

Eligibility criteria Inclusion criteria were specified for participants definitively diagnosed with naso-pharyngeal carcinoma (NPC), focusing exclusively on adult populations of both sexes. Required imaging criteria stipulated that subjects must have undergone magnetic res-onance imaging (MRI) for initial radiomic assessment. This criterion was applicable to both individuals receiving a new diagnosis and those previously subjected to medical interventions such as surgery, radiation, or chemotherapy. Only studies that included the concordance index (c-index) were considered. The c-index, a measure of the prognostic accuracy of models in time-to-event analysis where data may be censored, was selected based on its utilization in prior research [13], owing to its advantage in

providing consistent results across studies with variable endpoints, in contrast to the time-independent area under the curve (AUC) which may lead to heterogeneous out-comes.Exclusion criteria were established as follows: studies concerning cancers other than NPC; research employing deep learning-based radiomics, attributed to its lower inter-pretability; documents in the form of letters, conference proceedings, retracted papers, or those devoid of images. Further, studies using imaging modalities other than MRI, covering topics or outcomes irrelevant to the study aims, presenting data unsuitable for quantitative analysis, or not reporting the c-index were excluded.

Information sources Pubmed, Embase, Web of science.

Main outcome(s) LRFS, DMFS, OS, PFS.

Quality assessment / Risk of bias analysis QUIPS, RQS.

Strategy of data synthesis Data Synthesis Approach:
The synthesis of data will involve both quantitative and qualitative analyses. Quantitative data, particularly from studies providing comparable outcomes, will be pooled in a meta-analysis. Qualitative synthesis will summarize findings from studies that are not amenable to meta-analysis due to heterogeneity in methodologies or reported outcomes.

Meta-analysis Procedure:
Models to be Used: Both fixed-effect and random-effects models will be employed. The choice between these models will be guided by the degree of heterogeneity among study results. The fixed-effect model will be used when studies are sufficiently homogenous, while the random-effects model will be applied in the presence of significant heterogeneity.
Assessment of Heterogeneity: Heterogeneity among study results will be quantitatively assessed using the I^2 statistic, which measures the percentage of total variation across studies due to heterogeneity rather than chance. An I^2 value greater than 50% will be considered indicative of substantial heterogeneity.
Subgroup Analyses and Meta-regression: If substantial heterogeneity is detected, subgroup analyses will be conducted based on predefined characteristics (e.g., study design, patient population, MRI radiomics methodology). Meta-regression may also be employed to explore the impact of continuous variables on effect sizes.
Sensitivity Analysis: To assess the robustness of the meta-analysis findings, sensitivity analyses will be performed by systematically excluding studies one at a time and evaluating the impact on the overall results.
Publication Bias: The presence of publication bias will be investigated using funnel plots and Egger's regression test.
Software Package:
Data synthesis, including the meta-analysis, will be conducted using the Comprehensive Meta-Analysis (CMA) software and STATA software, and additional analyses may be performed using R, specifically the 'meta' and 'metafor' packages, which are well-suited for advanced meta-analytic techniques.

This strategy is designed to provide a rigorous and comprehensive assessment of the available evidence regarding the prognostic value of MRI radiomics in patients with nasopharyngeal carcinoma, ensuring that conclusions drawn are both reliable and informative for clinical practice and future research.

Subgroup analysis Subgroup analyses were conducted based on geographical location, validation method-ology, MRI sequence, and radiomics software, alongside meta-regressions on publication year, training sample size, and the number of features used.

Sensitivity analysis Leave one out.

Country(ies) involved Taiwan.

Keywords Radiomics; Prognostic Models; Meta-analysis; Survival.

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