A Systematic Literature Review of Prognostic Factors in Advanced Merkel Cell Carcinoma

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INTRODUCTION

- Advanced merkel cell carcinoma (aMCC) is a rare, highly aggressive neuroendocrine skin tumor, characterized by a significant frequency of locoregional recurrence, metastasis, and poor prognosis[1,2]
- Despite its rarity, the rising prevalence of aMCC underscores the need for a thorough understanding of prognostic factors to inform clinical decision-making and enhance patient outcomes
- The current systematic literature review (SLR) aims to provide a comprehensive overview of prognostic factors associated with aMCC outcomes

METHODS

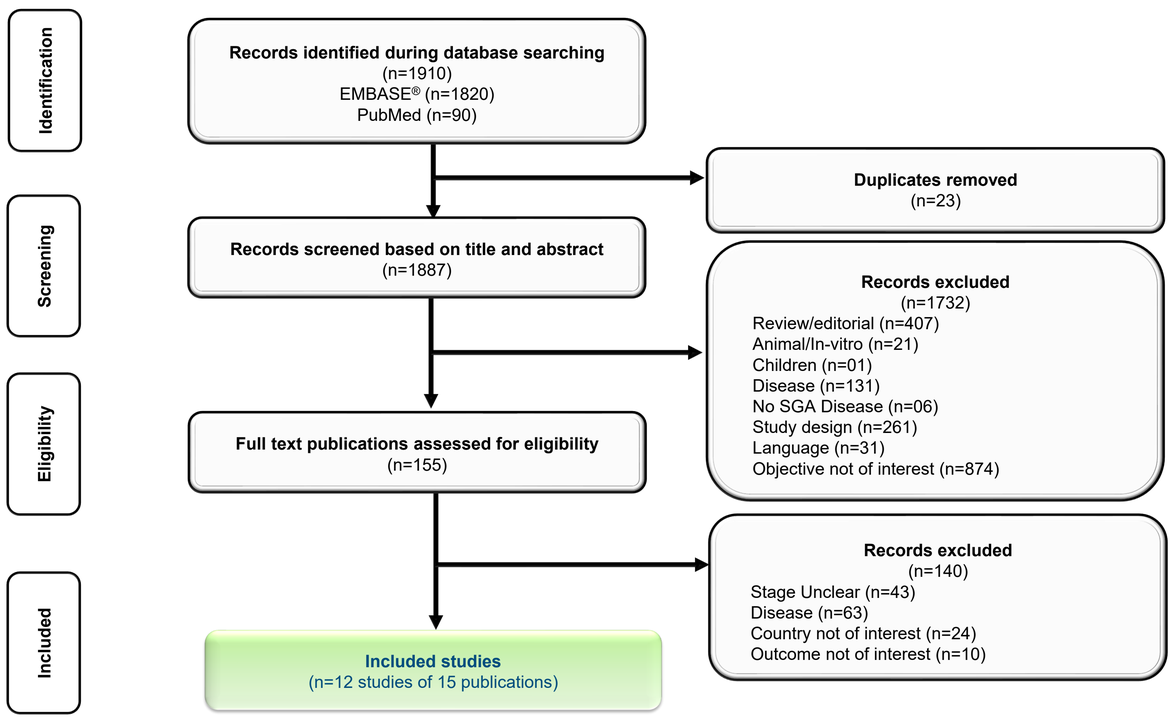
- Electronic databases such as Embase® and Medline® were searched using a combination of relevant keywords related to prognosis and aMCC
- Articles published in the English language from the last five years (2020-2025), specific to the United States (US) and Europe, that investigated prognostic factors in aMCC were included
- The prespecified eligibility criteria are presented in **Figure 1**
- Two independent reviewers collected data, and a third independent reviewer performed a quality check
- The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological rigor[3]

Figure 1: Eligibility criteria for selection of evidence

RESULTS

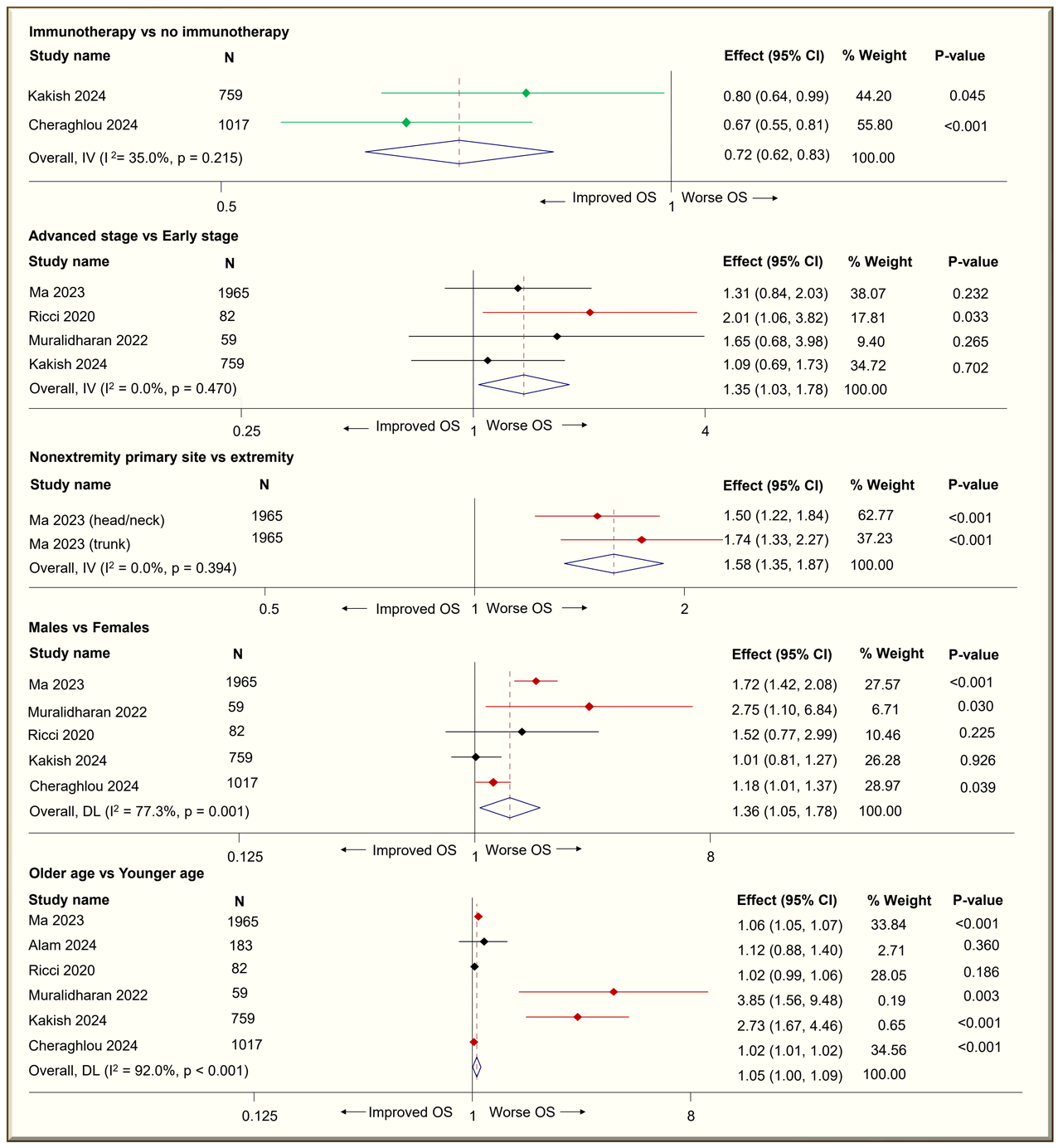
- A PRISMA diagram for the screening process is presented in **Figure 2**
- Among the 1910 publications screened, 12 studies were identified across the US (n=8), EU-4 (n=3), and one globally, reporting the prognostic factors for aMCC
- Findings revealed that in the multivariable analysis, first-line immunotherapy (n=2), treatment at high-volume centers (n=1), and Eastern Cooperative Oncology Group score >1 (n=1) were associated with prolonged overall survival (OS) **(Figure 3)**
- Further, older age (n=4), male gender (n=3), advanced disease stage (n=1), high baseline neutrophil-lymphocyte ratio, positive merkel cell polyomavirus status (MCPyV) and delayed time to radiation (≥79 days), nonextremity (head/neck/trunk) vs extremity sites (n=1) had a significant, independent, adverse impact on OS (p<0.05)
- The findings of the univariable analyses were aligned with multivariable analyses. In addition, bone metastases and larger tumor size were also significant factors for worse OS
- The independent predictors for shorter progression-free survival included gender (Hazard ratio/HR: 2.08; p=0.018) and advanced disease stage (HR: 20.57; p<0.0001)
- Regional lymph node irradiation and adjuvant radiotherapy were associated with improved recurrence-free survival, disease-specific survival (DSS), and disease-free survival, while brain metastasis and advanced disease stage were associated with a threefold (HR: 3.85; p=0.003 and a twofold (HR: 2.16; p=0.161) worse DSS, respectively

Figure 2: PRISMA diagram for the screening process



SGA: Subgroup analyses

Figure 3: Prognostic factors for overall survival (Multivariate analyses)



CI: Confidence interval; DL: DerSimonian & Laird; HR: Hazard ratio; IV: Inverse variance; n: Sample size; OS: Overall Survival
Statistically significant factors for improved overall survival ; Statistically significant factors for worse overall survival
For DL method, weights were from random-effects model

LIMITATIONS

- Exclusion of non-English-language studies may have led to the omission of some studies with valid findings
- The SLR only included studies from the past five years, potentially overlooking older research that could provide valuable insights into the evolution of prognostic factors in aMCC

CONCLUSIONS

- ❖ This systematic review highlights that patient characteristics (age and gender), disease-related factors (stage, tumor size, metastasis), and treatment-related factors (type and timing of therapy, and treatment setting) collectively influence clinical outcomes in aMCC
- ❖ Understanding these prognostic indicators is essential to inform clinical decision-making and improve patient management strategies in this rare but aggressive cancer

References

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