

## ABSTRACT

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Pretreatment ADC Histogram Analysis as a Prognostic Imaging Biomarker for Patients with Recurrent Glioblastoma Treated with Bevacizumab: A Systematic Review and Meta-analysis.

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**BACKGROUND:** The mean ADC value of the lower Gaussian curve (ADCL) derived from the bi-Gaussian curve-fitting histogram analysis has been reported as a predictive/prognostic imaging biomarker in patients with recurrent glioblastoma treated with bevacizumab; however, its systematic summary has been lacking.

**PURPOSE:** We applied a systematic review and meta-analysis to investigate the predictive/prognostic performance of ADCL in patients with recurrent glioblastoma treated with bevacizumab.

**DATA SOURCES:** We performed a literature search using PubMed, Scopus, and EMBASE.

**STUDY SELECTION:** A total of 1344 abstracts were screened, of which 83 articles were considered potentially relevant. Data were finally extracted from 6 studies including 578 patients.

**DATA ANALYSIS:** Forest plots were generated to illustrate the hazard ratios of overall survival and progression-free survival. The heterogeneity across the studies was assessed using the Cochrane Q test and I<sup>2</sup> values.

**DATA SYNTHESIS:** The pooled hazard ratios for overall survival and progression-free survival in patients with an ADCL lower than the cutoff values were 1.89 (95% CI, 1.53-2.31) and 1.98 (95% CI, 1.54-2.55) with low heterogeneity among the studies. Subgroup analysis of the bevacizumab-free cohort showed a pooled hazard ratio for overall survival of 1.20 (95% CI, 1.08-1.34) with low heterogeneity.

**LIMITATIONS:** The conclusions are limited by the difference in the definition of recurrence among the included studies.

**CONCLUSIONS:** This systematic review with meta-analysis supports the prognostic value of ADCL in patients with recurrent glioblastoma treated with bevacizumab, with a low ADCL demonstrating decreased overall survival and progression-free survival. On the other hand, the predictive role of ADCL for bevacizumab treatment was not confirmed.

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