ABSTRACT

Background: Emerging evidence indicates that immunogenicity plays an important role in intrahepatic cholangiocarcinoma (ICC). Herein, we systematically evaluated the clinical relevance of immunogenicity in ICC.

Methods: Highly immunogenic ICCs identified in the public dataset and the Cancer Immunome Atlas (TCIA) were assessed to determine the prognostic impact of immunogenicity in ICC and key components after curative resection. We also investigated the clinical relevance of immune milieu in ICC.

Results: Using the Gene Expression Omnibus dataset 89749 and TCIA, we identified $CD8^+$/forkhead box P3 $(FoxP3)^+$ tumor-infiltrating lymphocytes (TILs), T-cell immunoglobulin and mucin domain 3 (TIM-3), and human leukocyte antigen-A (HLA-A) in highly immunogenic ICCs. Immunohistochemical analysis of the in-house cohort showed that intratumoral $FoxP3^+$ TILs correlated with $CD8^+$ TILs ($P = 0.045$, Fisher's exact test) and that high $FoxP3^+/CD8^+$ ratio (FCR) was an important marker for poor survival ($P < 0.001$, log-rank test). Furthermore, the FCR was higher in tumor-free lymph nodes in ICCs with lymph node metastases than in those without lymph node metastases ($P = 0.003$, Mann–Whitney *U* test).

Conclusions: FCR should be considered as an important biomarker that represents the immune environment of ICC based on its potentially important role in tumor progression, especially lymph node metastasis.

Key words: intrahepatic cholangiocarcinoma; forkhead box P3; $FoxP3^+/CD8^+$ ratio; lymph node metastasis