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A Clinically Feasible Prognostic Scoring System By Integrating KRAS Codon 12 Mutant Dosage From Targeted Sequencing With Preoperative Clinical Variables

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Background : Most studies on cancer mutation profiling are still on the bench, not the bedside. For clinical application, it is necessary to focus on key genes and integrate with clinical variables. Among the key variants, KRAS codon 12 (G12) mutation is receiving the most attention, but the prognostic value of the mutant dosage is still unknown. Therefore, we aimed to evaluate the prognostic values of KRAS G12 mutant dosage in pancreatic ductal adenocarcinoma (PDAC) and establish a prognostic scoring system.

Methods : One hundred ninety-three patients with PDAC who underwent pancreatectomy between 2009 and 2016 were included. RNA, whole exome, and KRAS targeted sequencing data were generated and processed for estimating KRAS G12 mutant dosage. A prognostic scoring system was established by combining the mutant dosage from targeted sequencing (> 0.195, 1 point) with two clinical variables such as maximal tumor diameter at preoperative image (>20 mm, 1 point) and carbohydrate antigen 19-9 (>150 U/ml, 1 point).

Results : Of these 193 patients, 24 (12.4%), 65 (33.7%), 81 (42.0%), and 23 (11.9%) patients had 0-point, 1 point, 2 points, and 3 points, respectively. Patients with 0-point had superior median, 1-year, 3-year, and 5-year overall survival of 97.0 months, 95.8%, 70.8%, and 66.4%, respectively. In contrast, patients with 3 points had significantly worse median, 1-year, 3-year, and 5-year overall survival of only 16.0 months, 65.2%, 8.7%, and 8.7%, respectively.

Conclusions : Addition of KRAS G12 mutant dosage variable can improve clinical variable-based survival prediction, thereby the integrated scoring system is fully feasible with clinical significance.

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