

## **Abstract**

**Objective:** Strict follow-up is recommended for branch-duct intraductal papillary mucinous neoplasms (BD-IPMNs) to avoid missing the development of high-risk stigmata (HRS) at a premalignant stage. This study explored the risk factors associated with the development of HRS during follow-up.

**Methods:** We performed a retrospective analysis of 283 patients with BD-IPMN, treated at Okayama University Hospital in Japan between January 2009 and December 2016. Only patients with imaging studies indicative of classical features of BD-IPMN without HRS and followed for over one year were included in the study. We performed radiological follow-up every six months and collected patients' demographic data, cyst characteristics, and clinical outcomes and used univariate logistic regression models to determine the odds of developing HRS.

**Results:** Ten patients (3.5%) developed HRS after a median surveillance period of 55.8 months. The main pancreatic duct (MPD) size (5-9 mm) and cyst growth rate (>2.5 mm/year) were both suggested to be possible risk factors for the development of HRS (odds ratio, 14.2; 95% confidence interval [CI], 3.1-65.2, P=0.0006, and odds ratio, 6.1; 95% CI 1.5-25.5, P=0.014). Regarding the number of worrisome features (WFs), the rate of HRS development was 2.0% (4/199) in cases with no WF, 1.6% (1/62) in cases with single WF and 22.7% (5/22) in cases

with multiple WFs, respectively. The rate of HRS development was significantly higher in cases with multiple WFs than in the other cases ( $P < 0.0001$ ).

**Conclusion:** MPD dilation, rapid cyst growth, and multiple WFs were significant risk factors for the development of HRS. In the presence of such features, it is necessary to closely follow the development of HRS and avoid missing the best opportunity to perform surgical intervention.