Introduction

Colorectal cancer (CRC) is the third most common malignancy worldwide, with a 6% lifetime risk of developing this cancer. Most CRCs develop from adenomatous polyp with a mean observed sojourn time of 3 - 6 years. Screening colonoscopy with polypectomy can reduce the incidence and mortality associated with colon cancer. However CRC develops even though previous colonoscopy was normal or polyp was completely removed, colon cancer developed during unexpected short time period. Like this case, colon cancer is called as interval cancer.

Clinical features of interval colorectal cancer

Interval CRC is CRC that is found before the next recommended screening or surveillance interval within 5 years after a negative colonoscopy or within 3 years after a polypectomy for advanced adenoma.

The overall prevalence of interval CRC ranged from 1.8 to 9.0% from Singh’s meta-analysis study of interval CRC. On pooled analysis, the prevalence of interval CRCs was 3.7% within 6 - 36 months of previous colonoscopy. But when they defined interval CRCs as those diagnosed within 6 - 60 months, the pooled prevalence of interval CRCs was 6%.

Regarding location, the prevalence of proximal interval CRCs was 6.5%. This corresponds to 1 in 15 proximal CRCs being interval CRCs. the prevalence of distal interval CRCs was 2.9%. This corresponds to 1 in 34 distal CRCs being interval CRCs. As compared with detected CRCs, interval CRCs were 2.4 times more likely to be proximal CRC than distal CRCs.

Although meta-analysis study reported females were no more likely than males to develop interval CRCs, several studies individually reported a higher prevalence of interval CRCs in females as compared with males.

Generally, interval CRCs are classified as missed lesions, incomplete colonoscopy, incomplete resection of polyps and newly developed cancers or rapid tumor progression (de novo I-CRCs). Among them, the most colon etiology is missed lesion.
Biological features of interval colorectal cancer

Many studies have primarily focused on the proportion of I-CRCs due to false-negative colonoscopies. Rapid growing features of I-CRC could be another cause of I-CRCs that is specific aberrant biology that drives their de novo and rapid growth.

The characteristics of SSA/Ps are pale, flat lesion or covered with mucus, which cause missing the lesion or incomplete resection and they was located predominantly within the proximal colon. Serrated pathway of colorectal cancer carcinogenesis has BRAF, CIMP and MSI mutations and MLH1 methylation. Sessile serrated adenomas/polyps (SSA/Ps) share many genomic and colonic site characteristics with I-CRCs, and consequently have been suggested to be a precursor lesion for I-CRCs.

The reason why SSAPs have been suggested to be a precursor lesion for I-CRCs as follow First, I-CRCs were almost 4 times as likely as non-interval colon cancers to be associated with mismatch repair gene dysfunction, and hence demonstrate microsatellite instability (MSI). Second, the risk of I-CRCs is high in patients with a proximal mucinous cancer. And synchronous colorectal cancers had more frequent mutations in BRAF, were more frequently (CpG island methylation phenotype (CIMP)-high and MSI-high. These suggest that biologic characteristics of I-CRCs are associated with serrated neoplastic pathway.

Conclusion

The prevalence of interval CRCs ranges from 2.8 to 9.0% of all sporadic CRCs. As compared with sporadic CRCs, interval CRCs was 2.4 times more likely to be proximal CRC than distal CRCs. And higher prevalence of interval CRCs in females as compared with males. While I-CRCs may arise due to false negative colonoscopies, a portion is also likely attributed to aberrant molecular biology. Due to the physical and molecular similarities shared between sessile serrated adenoma (SSA/Ps) and I-CRCs. Since SSA/Ps possess the CIMP, this could explain the increased prevalence of CIMP and MSI-High observed in I-CRCs. And hypermethylation and/or mutation of other genes (i.e., p16INK4a, IGFBP7, Wnt pathway) may occur concurrently and effectively synergize to produce a tumorigenic phenotype conferring rapid development.

References