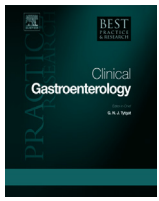
Best Practice & Research Clinical Gastroenterology 29 (2015) 675–686

Contents lists available at ScienceDirect

Best Practice & Research Clinical Gastroenterology



13

Serrated lesions of the colon and rectum: The role of advanced endoscopic imaging

J.L.A. Vleugels, MD, Research fellow [1],
J.E.G. IJspeert, MD, Research fellow [2],
E. Dekker, MD, PhD, Professor [*]

Department of Gastroenterology and Hepatology, Academic Medical Centre, Meibergdreef 9, 1105 AZ, Amsterdam, The Netherlands

Keywords:
Cancer prevention
Colonic polyps
Colonoscopy
Colorectal cancer
Endoscopic polypectomy
Review

A B S T R A C T

Conventional adenomas were traditionally thought to be the only precursors to colorectal cancer (CRC). Nowadays, also serrated polyps are acknowledged as precursor lesions for CRC, responsible for up to 30% of all CRCs and probably a larger percentage of interval CRCs after colonoscopy. In recent years, much research is being done to unravel the serrated neoplasia pathway. Endoscopic detection of serrated polyps is still a challenge for gastroenterologists, which is illustrated by large variations in detection rates of serrated polyps in the proximal colon. Clinical practice is further inhibited by poor optical differentiation of SSA/Ps from conventional adenomas and HPs and difficult delineation of those lesions, resulting in incomplete resection. The main focus of this review is to highlight recent advancements in endoscopic imaging techniques with regards to detection, differentiation and resection of serrated polyps.

* Corresponding author. Tel.: +31 20 566 4702; fax: +31 20 691 7033.
E-mail addresses: j.l.vleugels@amc.uva.nl (J.L.A. Vleugels), j.e.ijspeert@amc.uva.nl (J.E.G. IJspeert), e.dekker@amc.uva.nl (E. Dekker).
[1] Tel.: +31 20 566 2249; fax: +31 20 691 7033.
[2] Tel.: +31 20 566 2199; fax: +31 20 691 7033.

http://dx.doi.org/10.1016/j.bpg.2015.05.009
1521-6918/

Introduction

In current medicine, colorectal cancer (CRC) is a major challenge for gastroenterologists, oncologists and surgeons worldwide [1]. According to the World Health Organization, in 2012 approximately 1.4 million individuals were diagnosed with CRC [1]. In the same year, an estimated 700,000 persons died from this disease [1]. Since CRC slowly progresses from precursor lesions in a matter of many years, it is a disease that is largely preventable. A landmark study highlighted that colonoscopy with detection and resection of adenomas can reduce the mortality rate of CRC by more than 50% [2].

However, colonoscopy is not perfect in preventing CRC. Several large population-based studies showed that colonoscopy is markedly less protective for the development of right-sided than for left-sided CRC [3–5]. Correspondingly, interval CRCs after colonoscopy, i.e. CRCs that occur after a complete, negative colonoscopy and within the time-period to the recommended next surveillance procedure, are more often located in the proximal colon [6,7]. Studies focusing on interval CRCs after colonoscopy have tried to identify potential causes and a clear correlation with quality parameters of colonoscopy is seen. A high adenoma detection rate of the endoscopist, i.e. the proportion of colonoscopies in which an endoscopist detects at least one adenoma, is inversely correlated with the risk of interval CRC [8,9]. Other important quality parameters are cecal intubation rate, bowel preparation, withdrawal times and complete polyp resection [10–14]. Besides these procedural quality parameters, also specific biological behavior is increasingly acknowledged as a cause for interval CRC after colonoscopy [5]. Those CRCs are associated with microsatellite instable (MSI-high) and often show tumor-suppressor silencing due to promoter hypermethylation, suggesting that these tumors might have developed from serrated polyps [5,15].

For several decades, conventional adenomas were thought to be the only precursors to CRC via the traditional adenoma-carcinoma pathway [16]. Hyperplastic polyps were historically considered as innocent lesions. Recent literature reports that the route to CRC is more heterogeneous and that this cancer might also arise from serrated polyps via the serrated neoplasia pathway. In 2010, the World Health Organization has re-classified the hyperplastic polyps into the group of serrated polyps [17]. Serrated polyps (Fig. 1) are sub-classified into three main categories: hyperplastic polyps (HPs), sessile serrated adenomas/polyps (SSA/Ps) and traditional serrated adenomas (TSAs) [17]. SSA/Ps can develop dysplasia, while TSAs per definition harbor a dysplastic component and HPs do not [17].

The serrated neoplasia pathway

In the serrated neoplasia pathway, two major oncogenic mechanisms are appreciated. A mutation in the *BRAF* proto-oncogene, which is a molecular switch in cellular growth control, seems to play a major role. *BRAF* mutations are frequently seen in both HPs as well as SSA/Ps [18–20]. The second important mechanism is CpG island hypermethylation of gene promoter regions and subsequent silencing of associated tumor suppressor genes [21]. Silencing of *MLH1* is probably the most well described example of this mechanism, resulting in sporadic MSI and subsequent accelerating carcinogenesis [20,21]. Molecular analysis of interval CRCs after colonoscopy highlighted an independent association with both the CpG island methylator phenotype (CIMP) (OR 2.4; CI 1.2–4.9) as well as with MSI (OR 3.7; CI 1.5–9.1) [5,15]. Furthermore, both the presence of a *BRAF*-mutation and CIMP status are also closely related to MSI [20]. Evaluation of the correlation between MSI, CIMP and *BRAF* with both serrated polyps and adenomas, has led to the appraisal of the serrated neoplasia pathway originating from serrated polyps as an alternative to the adenoma-carcinoma pathway [21–25]. The correlation between SSA/Ps and CRC has been well described, while for HPs no such correlation seems present [26,27]. However, it has been suggested that proximally located HPs could be the precursor lesions of the SSA/Ps, since *BRAF* mutations are also frequently seen in a large subset of these HPs [21,23]. The clinical importance of TSAs is less well understood, mainly due to their low prevalence, but the neoplastic progression of TSAs seems distinct from that of SSA/Ps [28]. In conclusion, although scientific research in the past decade has improved the knowledge of serrated polyps, the debate on their natural history is ongoing and yet largely unknown [29,30].