The Natural History of Colorectal Polyps

Overview of Predictive Static and Dynamic Features

Perry J. Pickhardt, MD[a,b,*], Bryan Dustin Pooler, MD[b], David H. Kim, MD[b], Cesare Hassan, MD[b], Kristina A. Matkowskyj, MD, PhD[b], Richard B. Halberg, PhD[b]

KEYWORDS

• Colorectal cancer • Colorectal polyps • CT colonography • Virtual colonoscopy • Optical colonoscopy

KEY POINTS

- Subcentimeter colorectal polyps are highly prevalent in adults.
- Subcentimeter colorectal polyps are invariably benign, and the vast majority will never develop into cancer.
- Polyp size is an important determinant of clinical relevance and management.
- Polyp growth rates provide further insight into natural history and clinical significance.
- CT colonography is unique among screening tools by allowing for accurate assessment of volumetric growth rates, which are likely tied to underlying genetic and epigenetic alterations.

INTRODUCTION

It is widely accepted that colorectal cancers (CRC) generally derive from once benign dysplastic colorectal polyps. However, it is also true that colorectal polyps are a highly prevalent human condition, affecting most of the adults according to recent

Disclosures: Dr P.J. Pickhardt is the co-founder of VirtuoCTC; advisor to Check-Cap and Bracco; and shareholder in SHINE, Elucent, and Cellectar Biosciences; Dr D.H. Kim is the co-founder of VirtuoCTC and shareholder in Elucent and Cellectar Biosciences. This work was supported in part by NIH NCI grant 1R01 CA220004-01.

[a] University of Wisconsin School of Medicine & Public Health, 600 Highland Avenue, Madison, WI, 53793 USA; [b] Digestive Endoscopy Unit, Nuovo Regina Margherita Hospital, Via Emilio Morosini 30, 00153, Rome, Italy

* Corresponding author. University of Wisconsin School of Medicine & Public Health, 600 Highland Avenue, Madison, WI, 53793 USA.

E-mail address: ppickhardt2@uwhealth.org

Gastroenterol Clin N Am ■ (2018) ■–■

https://doi.org/10.1016/j.gtc.2018.04.004

gastro.theclinics.com

endoscopic screening data. As such, the most of the colorectal polyps behave in a benign fashion and will of course never develop into cancer. Furthermore, although the precise timing and sequence of events for progression to cancer have not yet been fully elucidated, the typical dwell time for this infrequent transformation is likely a decade or more, whether via the classic adenocarcinoma sequence or the serrated polyp pathway. When taking all these factors into consideration, CRC can clearly be effectively prevented through the detection and removal of benign dysplastic colorectal polyps, but also a strategy of universal polypectomy is an inefficient approach, leading to excessive resource utilization, costs, and complications. At the other end of the spectrum, tests that primarily target cancer detection ignore the larger benefit of cancer prevention. Between these 2 extremes, a more rational CRC screening approach that targets large and/or growing polyps and early cancers likely represents a more clinically efficacious and cost-effective strategy.

A large and ever-growing volume of data exist surrounding static cross-sectional features of colorectal polyps, such as lesion size, morphology, and location, and their relationship to underlying histologic features. Much of these data come from large colonoscopic databases, where detected polyps are removed without any knowledge of their preceding growth rates. With the emergence of computed tomography colonography (CTC) as an attractive CRC screening tool, the authors have the ability to follow polyps longitudinally before resection. This dynamic in vivo investigation also provides unique opportunities for studying the natural history of polyps, such as correlating growth rates with underlying polyp histology and genetic alterations. These insights could ultimately inform future strategies for screening and surveillance, as well as fuel novel theories on tumor evolution.

CROSS-SECTIONAL (STATIC) POLYP DATA: SIZE, MORPHOLOGY, AND LOCATION

Static polyp features, including lesion size, morphology, and anatomic location, have long served as the major determinants of clinical significance. Of these, polyp size is likely the single most important consideration, because it directly correlates with important histologic features such as high-grade dysplasia (HGD) and invasive cancer.[1,2] However, polyp morphology and segmental location can both further enhance classification and risk stratification, as discussed later after polyp size considerations. Implicit in this discussion on static polyp features is ensuring sensitive detection by both CTC and optical colonoscopy (OC), because this represents the only means for preventing polyp progression.

Given the extremely high prevalence of subcentimeter (sub-cm) colorectal polyps and their potential influence on screening algorithms, it is critical to first focus attention on this subset. Sub-cm polyps are further subdivided into diminutive ($\leq$5 mm) and small (6–9 mm) size categories. Although abundant prior cumulative evidence has demonstrated very low rates of HGD and exceedingly low (or even nonexistent) rates of cancer among sub-cm polyps,[1–3] a recent study by Ponugoti and colleagues[4] has further crystallized these findings. This report on greater than 40,000 sub-cm colorectal polyps resected at OC has substantially increased our cumulative experience. From prior observational series, rates of HGD and invasive cancer typically ranged from 0.5% to 0.8% and 0% to 0.5%, respectively for small polyps, and would be even lower for diminutive lesions.[2] The large study by Ponugoti and colleagues[4] essentially doubles the cumulative data on sub-cm polyps. In this study, rates of HGD and invasive cancer among diminutive conventional adenomas and small conventional adenomas were 0.3% and 0% and 0.8% and 0%, respectively. Reported rates of advanced histology (villous component, HGD, or invasive cancer) are