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## Management of Large Colon Polyps



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**Colorectal cancer is the third most common cancer in the United States. Pre-cancerous colon polyps are precursors to most colorectal cancers, and colonoscopy reduces the incidence of colorectal cancer by removal of these polyps. The risk of cancer is especially higher in polyps > 20 mm in size, NICE 3 or Kudos VI or VN features. Management of large colon polyps includes optimal detection and recognition especially for sessile polyps, assessment of polyp morphology and histology, endoscopist's comfort in advanced polypectomy techniques as well as managing associated adverse events.**

### INTRODUCTION

**C**olorectal cancer (CRC) is the third most common cause of cancer-related deaths in the United States.<sup>1</sup> Colon polyps with certain histology are the precursors to most CRCs.<sup>2</sup> Colonoscopy with polypectomy reduces both the incidence as well as the mortality associated with CRC.<sup>3,4</sup> Previous studies have shown that removal of adenomatous polyps during colonoscopy is associated with 50% reduction in CRC-related mortality.<sup>3,4</sup> Therefore, optimizing the management of colon polyps is essential. This is especially important in large polyps. When the size of polyps is larger than 20 mm, the risk of cancer in these polyps increases.<sup>5</sup> In this review, we will discuss techniques of management of large colon polyps.

### INSPECTION

#### *Inspection*

The first step in managing large colon polyps is being able to recognize them. Flat or sessile polyps especially in the right colon can be often missed. Hence, studies have shown that a second look in the right colon whether in forward view or in retroflexion during colonoscopy can improve the detection rates of these polyps.<sup>6</sup> Needless to add that high-quality colonoscopy is essential in recognizing polyps. This includes a good bowel preparation, adequate withdrawal time and an endoscopist with an adenoma detection rate meeting standard guidelines.<sup>7,8</sup>

Once a large polyp is identified, the next step is to carefully assess the polyp for size, location and morphology.<sup>9-11</sup> This is important to determine whether endoscopic resection is safely possible and the optimal modality of endoscopic resection. While studies have shown that there is

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only moderate agreement among experts when it comes to classifying large polyps according to various classifications,<sup>12</sup> there are several available classifications. In the US, the most commonly used are the Paris classification,<sup>13</sup> narrow band imaging international colorectal endoscopic (NICE) classification,<sup>14</sup> and Kudo's classification of polyp pit pattern among others.<sup>15</sup>

### **Classification Systems to assess polyps**

The Paris classification classifies polyps as pedunculated (1p), sessile (1s), flat (IIa, IIb, IIc) or ulcerated (III).<sup>13</sup> For non-pedunculated polyps (Paris classification 1s and II), surface morphology should also be classified as granular or non-granular laterally spreading tumors. The NICE classification classifies lesions as type 1 (serrated class: either hyperplastic or sessile serrated polyp), type 2 (conventional adenomas) or type 3 (deep submucosal invasive cancer).<sup>14</sup> Another classification system, especially popular in Eastern part of the world is the Kudo pit pattern classification system.<sup>15</sup> It requires magnification during colonoscopy using chromoendoscopy and evaluation of the pit pattern of the polyps. Pits are openings for the crypts. The Kudo classification classifies pit pattern as round / normal (Type I), asteroid (Type II), tubular or round pit smaller than normal pit (Type IIIS), tubular or round pit larger than normal pit (Type IIIL), gyrus/dendritic (IV), irregular arrangement (VI), and loss of decrease of pits with amorphous structure (VN). Polyps with type I to IV pit pattern are endoscopically resectable, while those with type VI and VN are suggestive of invasion and neoplasia.

### **What makes a polyp unresectable?**

While all the above classifications are helpful in standardizing the nomenclature of how we describe large polyps, it is important to note that reports have shown variability in agreement among experts regarding polyp classifications.<sup>12</sup> Therefore, the most practical recommendation for endoscopists is to recognize which polyps are amenable to endoscopic resection. Histological features that are unfavorable (lymphovascular invasion, tumor budding, poor differentiation) are not always predictable before resection.<sup>16</sup>

Depth of submucosal invasion can be predicted based upon lesion morphology and pit pattern as described above. Non-granular surface particularly pseudodepressed subtype, redness, expansion, firmness and fold convergence can all be associated with submucosal invasive carcinoma.<sup>17</sup> Areas in polyp which do not lift with submucosal injection are also worrisome for invasive cancer.<sup>18,19</sup> Prior reports have shown that the positive predictive value for invasive cancer if non-lifting sign is present can be 80% in treatment-naïve lesions.<sup>19,20</sup> Non-lifting sign can be seen in lesions which have been previously biopsied or endoscopic resection has been attempted, and in these cases, this does not predict submucosal invasion.

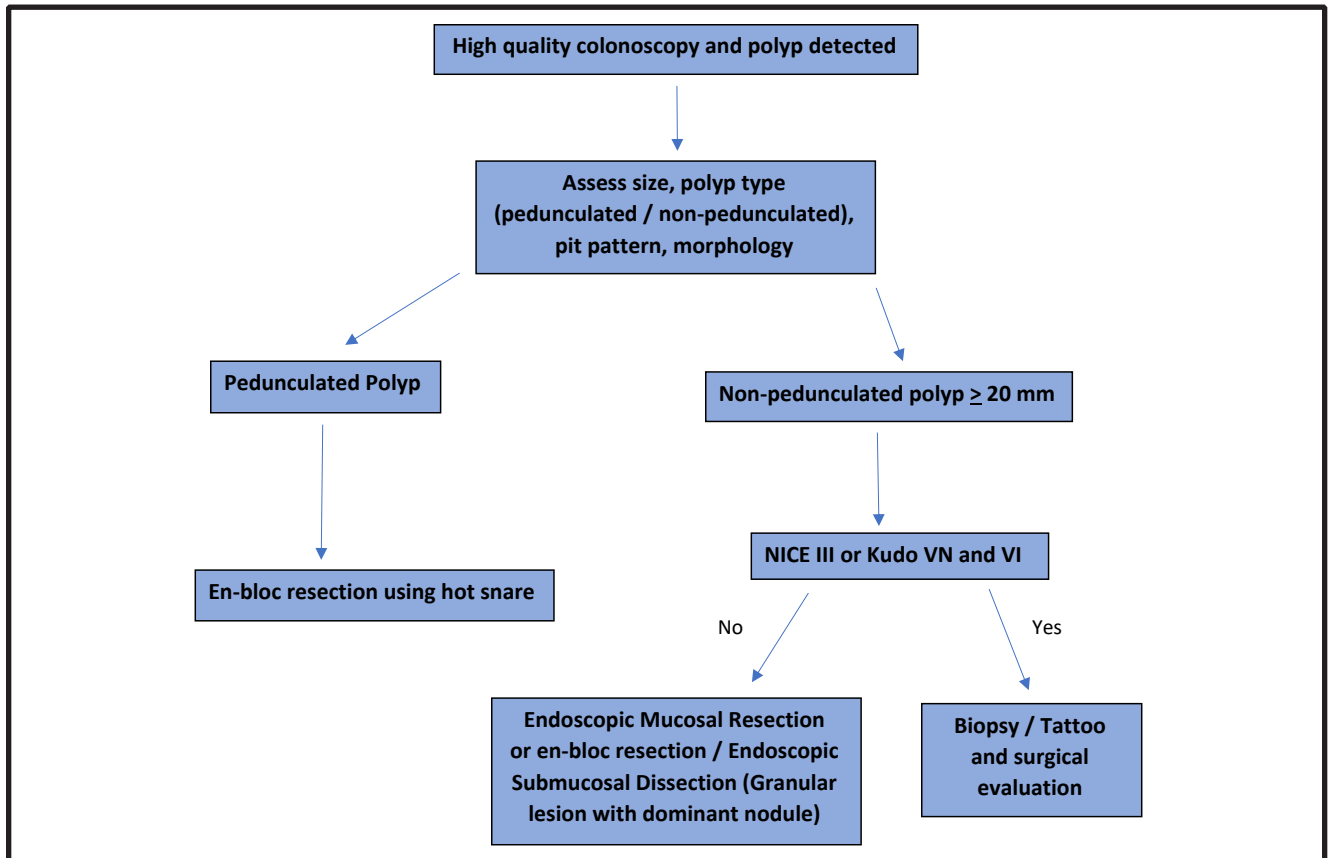
### **Knowing your expertise**

As mentioned above, optimal and complete resection of large colon polyps is essential in preventing CRC. The United States Multi-Society Task Force (USMSTF) recommends an advanced endoscopist experienced in advanced polypectomy to manage polyps larger than  $\geq 20$  mm in size.<sup>9</sup> It is important to know your expertise and resources. This is because studies have shown that polyps which are endoscopically resectable are often sent for surgery.<sup>21</sup> According to one report, after endoscopic resection by expert endoscopists, only about 5-10% of patient subsequently require surgery.<sup>22</sup> Therefore, resection should not be attempted unless the endoscopist is comfortable that resection will be complete. Incomplete polyp resections and biopsies cause submucosal fibrosis. Partial resections make subsequent endoscopic resection challenging, hence, the first attempt should always be aimed to complete resection.<sup>23</sup> If an endoscopist feels a polyp will be challenging to resect or does not have available time for that, it is better to refer the patient to an endoscopist who is comfortable with advanced polypectomy techniques.

### **Tattoo placement**

If an endoscopist deems that a polyp is unresectable, it is often advisable to place a tattoo so that polyp can be recognized easily by the endoscopist who the patient will be referred to. However, if cecal landmarks are in view, then tattoo placement is not necessary.<sup>9</sup> It is important to remember that tattoo

Figure 1. Algorithm for Management of Large Colon Polyps



placement can be problematic at times as well. Tattoo should never be placed in or under polyp itself. Carbon black spreads in the submucosa even if it is a few centimeters from the site of injection and extends beneath polyps causing submucosal fibrosis and rendering future endoscopic attempts complicated.<sup>23,24</sup> Tattoos should be placed on an opposite wall from the polyp, or 5 cm distal to the polyp, with images depicting the lesion and its relationship to the tattoo.<sup>23,24</sup>

## Endoscopic Management

### *Pedunculated Polyps*

As mentioned above large polyps can be pedunculated or non-pedunculated. For pedunculated polyps that are greater than 10 mm in size, hot snare polypectomy is suggested.<sup>9</sup> Attempts should be made to perform polypectomy towards the lower end of the stalk so assessment of stalk invasion can be made on histological analysis.<sup>9</sup> For larger pedunculated polyps, consideration of epinephrine into the head or stalk of polyp can also be considered to reduce the size and make

resection easier. Other strategies include using a detachable loop or placing clips at the polyp stalk before resection via hot snare. The USMSTF recommends that after resection, attempts should be made to retrieve large pedunculated polyps en-bloc so that accurate histological assessment can be made.<sup>9</sup>

### *Non-pedunculated polyps*

The vast majority of non-pedunculated polyps can be removed using endoscopic mucosal resection (EMR). The various modalities implied in resection of large non-pedunculated polyps are described below. Algorithm for approaching management of large colon polyps is outlined in Figure 1.

### **Endoscopic mucosal resection**

Endoscopic mucosal resection (EMR) involves submucosal injection of fluid to lift the lesion away from muscle and allow resection in single or multiple pieces. This technique has now evolved, and several sub-categories of this

technique exists including hot EMR, cold EMR and underwater EMR. In expert hands, EMR is safe and effective. According to a systematic review of 50 studies, the reported rate of severe adverse events was 10% and the review also reported low rates of local recurrence (14%).<sup>25</sup>

#### *Hot EMR*

Hot snare EMR involves the use of electrocautery in polyp resection. The first step is submucosal injection. Submucosal injection can be achieved with using dye such as methylene blue with saline or there are commercially available submucosal injections available as well. Polyps which are  $\leq 20$  mm in size can be removed en-bloc while polyps which are  $> 20$  mm in size can be removed in piecemeal fashion. After submucosal injection is achieved and the lesion is adequately lifted, a snare is used to capture the tissue. After the lesion is captured in the snare, the snare is lifted up away from the mucosa and lesion is removed using electrocautery. When a polyp is removed piecemeal, ablation of the normal margins of the EMR defect using argon plasma coagulation or snare tip soft coagulation can burn microscopic residual tissue and reduce the risk of recurrence.<sup>9</sup>

#### *Cold snare EMR*

Over the past few years, another technique of EMR which has gained popularity is cold snare EMR.<sup>26,27</sup> This technique allows for resection of large polyps without the use for electrocautery. The advantage of this technique is that it significantly reduces the adverse events associated with electrocautery such as bleeding and perforation. Initial data has been encouraging and has shown low rates of adverse events and comparable recurrence rates to hot snare EMR.<sup>28</sup> While there is variation in technique, the basic principles involve using submucosal injection and using small diameter snare and removal of the polyp in multiple pieces.

#### *Underwater EMR*

Underwater EMR is another technique for resection of large colon polyps which allows full water immersion for polypectomy.<sup>29</sup> It obviates the need for submucosal injection prior to polypectomy. Some experts report using argon plasma coagulation to mark the borders of the polyp.<sup>29,30</sup>

This is followed by immersing the segment of the colon polyp under water. All gas is aspirated from the colon and the mucosa and submucosa involute as folds into the colon.

#### **Post resection considerations**

##### *Endoscopic clip placement*

Bleeding is the most common adverse event after endoscopic mucosal resection. Risk factors for post-polypectomy bleeding include polyp size  $\geq 1$  cm, presence of a thick stalk, use of anti-coagulation, right sided polyps and co-morbid conditions such as cardiovascular disease or renal dysfunction.<sup>31</sup> In these cases, endoscopic clip placement after polypectomy can be considered. Endoscopic clip placement is usually not necessary after cold snare EMR since the risk of delayed bleeding is extremely low.<sup>30</sup>

##### *Tattoo placement and surveillance*

Tattoo placement should be considered when a polyp is resected in piecemeal fashion and is in a location which will be challenging to localize in the future.<sup>9</sup> Tattoo placement is usually recommended 3-5 cm anatomically distal to the lesion.<sup>9</sup>

For large colon polyps that have been removed using piecemeal EMR, the USMSTF recommends the first surveillance colonoscopy at 6 months, and if there is no recurrence of polyp, then following examination should be performed at 1 and 3 year intervals respectively.<sup>9</sup> Endoscopists should perform a careful exam of the resection site using high-definition white light endoscopy and narrow band imaging. Post-resection sites that demonstrate normal macroscopic and histological examination have high predictive values for long-term eradication.<sup>32</sup> If recurrence of polyp is seen on surveillance examination, attempts should be made at endoscopic resection with either repeat EMR, snare or avulsion method.<sup>9</sup>

#### **Endoscopic Submucosal Dissection**

Endoscopic submucosal dissection (ESD) allows for higher en-bloc resection rates as compared to EMR for lesions  $\geq 20$  mm in size. Other instances when ESD should be considered include lesions where there is suspicion for submucosal

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invasion, local early carcinoma, and pseudo-depressed laterally spreading tumor.<sup>33</sup> ESD involves submucosal injection followed by use of an ESD knife to perform a mucosal incision. This is followed by trimming of the submucosal edges to facilitate access to the submucosal plane. Submucosal dissection is then performed resulting in en-bloc resection. While ESD has excellent rates of en-bloc resection, it has higher rates of adverse events compared to EMR, including perforation, hospitalization related to procedure and costs.<sup>34</sup>

### Endoscopic Full-Thickness Resection

Endoscopic full-thickness resection (EFTR) is a relatively new approach which allows for removal of all layers of the colon wall.<sup>35,36</sup> EFTR is indicated in lesions < 30 mm in size which do not lift or those which involve a diverticulum or lesions in the appendiceal orifice which are challenging to resect with traditional polypectomy methods.<sup>37</sup> Commercially available full-thickness resection device is available (Ovesco Endoscopy AG, Tübingen, Germany) which is an over-the-scope system with a cap and a ready to use mounted clip and fitted snare.

### CONCLUSION

Over the last decade, there has been a paradigm shift for management of large colon polyps from surgery to endoscopic resection. Optimal resection of large colon polyps is essential for preventing the incidence and mortality associated with colorectal cancer. Endoscopists should be comfortable at recognizing large colon polyps. Resection of large colon polyps should only be attempted by endoscopists who feel comfortable with advanced polypectomy techniques and if resources are not available, patients should be referred to an endoscopist who is familiar with large polyp resection. ■

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Answers to this month's crossword puzzle:

