Surgical Decision-Making in the Management of Hereditary Tumor Syndrome-Associated Gastric Cancer

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Introduction

Background The majority of gastric cancers arise sporadically. Several hereditary tumor syndromes increase the lifetime risk of gastric cancer as well as colorectal, small bowel, endometrial, breast, pancreatobiliary and urothelial cancer. These syndromes include, but are not limited to, hereditary diffuse gastric cancer (HDGC), juvenile polyposis (JPS) and Lynch syndromes. The lifetime risk of gastric cancer varies with the syndromic entity. In general, prognosis is poor relative to sporadic cancers, with 5-year survival of approximately 20%. Therefore, presence of a hereditary tumor syndrome may impact surgical decision-making.

Objectives The scientific objectives include the discussion of:

1. The surveillance protocols of the three most common gastric cancer associated hereditary tumor syndromes
2. The surgical timing of gastrectomy
3. The operative techniques to minimize post-gastrectomy sequelae

Syndromes

1. HDGC: CDH1 mutations result in dysfunctional or absent E-cadherin expression with subsequent reduction in epithelial cell-cell adhesion and suppression of tumor invasion. The lifetime risk of HDGC-associated gastric cancer is estimated at 65-85%.[1]
2. JPS: SMAD4 mutations result in abnormal transforming growth factor beta (TGF-β) signal transduction and subsequent massive gastric polyposis. The lifetime risk of JPS-associated gastric cancer is estimated at 10 – 15%.[2]
3. Lynch: DNA mismatch repair gene mutations result in failure of their protective mechanisms and accumulation of errors during transcription. The lifetime risk of Lynch-associated gastric cancer is estimated at 5 – 13%.[3,4]

Surveillance & Surgical Timing

1. HDGC: The sensitivity of endoscopy for detecting precursor lesions may not be adequate; obtain multiple random biopsies q6 – 12 months beginning at 18 years of age. Prophylactic total gastrectomy should be considered at 18 years of age.
2. JPS: Mutation-negative cases or BMPR1A+ should be screened starting between age 15 – 25, every 5 years or contemporaneously with colonoscopy; SMAD4 mutations should be screened starting at 15 and every 1 – 2 years or contemporaneously with colonoscopy.
3. Lynch: No high-level evidence exists that demonstrate a linked precursor lesion or benefit of screening. Helicobacter pylori synergism elevates gastric cancer risk.

Benefits of an MIS Approach

A minimally invasive surgical (MIS) approach to gastrectomy should be pursued in order to:

1. Minimize postoperative adhesion burden thus facilitating future operations, especially important in patients at risk for multiple visceral malignancies.
2. Offer the other potential advantages of MIS surgery including decreased blood loss, reduced postoperative pain, accelerated recovery and reduced length of stay.

Technical Pearls

1. If gastrectomy is performed prior to colectomy, arrange the Roux limb in a retrocolic fashion to facilitate future colectomy.

Optimize enteric limb lengths to minimize malnutrition and functional disorders.

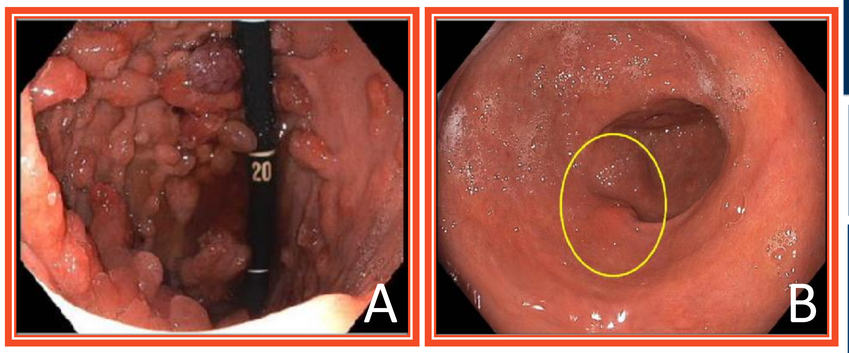
2. The biliopancreatic limb should be as short as the patient anatomy will allow. This is facilitated by a retrocolic Roux limb.
3. The Roux limb should be between 40 and 60 cm in length.
4. Roux limbs lengths less than 40 cm are at increased risk of bile reflux esophagitis.
5. Roux limb lengths greater than 60 cm are at increased risk of protein malabsorption and excessive weight loss.
6. Creation and interposition of a double jejunal pouch (J-pouch) to improve small bowel capacitance and reliable emptying.

Conclusions

The presence of hereditary tumor syndromes impacts tumor screening and surveillance strategies, surgical timing and gastrectomy technique. Patients afflicted with these syndromes should have therapy tailored to their circumstances and biology.

References

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A. Multiple gastric body polyps in a patient with juvenile polyposis syndrome.
B. Singular sessile antral sessile polyp in a patient with Lynch syndrome.