The management of inherited gastric cancer syndromes is a challenging field, with prophylactic total gastrectomy (PTG) the only effective preventive measure for at risk individuals. Germline mutations in CDH1, encoding E-cadherin, account for around 30% of cases of hereditary diffuse gastric cancer (HDGC). Individuals carrying a pathogenic mutation in CDH1 have a high lifetime risk of developing diffuse gastric cancer, estimated to be 70% in men and 56% in women (1). Current international consensus guidelines recommend that PTG should be offered to carriers of pathogenic mutations (1). Individuals electing to defer surgery should undergo annual endoscopy with multiple biopsies following the Cambridge protocol (1). Our current limited understanding of what triggers the progression from non-invasive to invasive signet ring adenocarcinoma in this setting means that early surgery remains the chosen course of action for many.

The decision to proceed to PTG is life-changing and often a source of significant anxiety for a patient and their family. The recent study by Muir et al. is an examination of the issues surrounding quality of life, surgery and decision making in a population at risk of HDGC (2). Eighteen patients who were offered PTG were recruited to a longitudinal questionnaire study extending up to 24 months post-PTG. Thirteen patients proceeded to surgery, and the five who declined or deferred surgery completed baseline questionnaires. Patients completed standard quality of life questionnaires (EORTC QLQ-C30 and STO22) and this was combined with assessments of body image, regret, decisional conflict and psychological symptoms.

The inclusion of an assessment of decisional conflict is welcome given the magnitude of the decision and it is interesting that most patients expressed little regret. In a qualitative interview study about the factors influencing decision to undergo PTG there appear to be many factors influencing the decision making process including the perception of risk and perceptions of life post-surgery (3).

Interestingly, there were no long-term psychological or body image consequences of PTG in this cohort. However, chronic low-severity health related quality of life (HRQL) limiting symptoms were common. Unsurprisingly, at 2–4 weeks post-gastrectomy, significant reductions in global HRQL, role and social functioning, and symptom scores, were commonly observed. Intriguingly, global HRQL and role/social functioning subscales returned to baseline 12 months following PTG, prior to dropping once again at 24 months, although this analysis is based on only three patients and may not be generalizable. It would be interesting to know the correlation between body image and global QOL scores.

Post-gastrectomy symptoms, as reported by the EORTC STO22, were common, with more than half of patients experiencing reflux, eating restriction and dry mouth. Health-based anxiety was not reduced by surgery, reflecting the complex balance of cancer risk versus post-gastrectomy difficulties for this patient group. Despite the early prevalence of symptoms and reduced quality of life, only...
half of participants expressed regret about their decision to proceed to PTG in the immediate post-operative period, which reduced over subsequent assessments.

The findings of Muir et al. reflect those published by Worster et al. from Cambridge, UK (4), who demonstrated good recovery of physical functioning and HRQL at 12 months post PTG despite ongoing symptoms. Interestingly, in the cohort studied by Worster, 44% complained of body image concerns at 12 months and it may be relevant that this cohort had a greater proportion of men than this study by Muir et al. which comprised mainly women (11 women and 2 men) who proceeded to surgery. In a qualitative interview study age was also shown to impact on recovery time, with younger patients reporting faster recovery (5).

Gastrectomy is a significant undertaking, with infrequent but major short-term risks and uncertain long-term consequences. There is very limited data on the long-term outcomes of gastrectomy in young people. Comparisons can be drawn with the long-term outcomes of surgical treatment of peptic ulcer disease; however this has not been commonplace for 40 years. Patient cohorts undergoing gastrectomy for invasive cancer tend to be older and, until recent improvements in oncological therapy, had a poor long-term prognosis (6).

A major and persisting consequence of upper gastrointestinal surgery is the poorly named “dumping syndrome”. Initially described in 1913, it encompasses a loosely connected constellation of symptoms experienced after meals, with early symptoms being predominantly vasomotor and late symptoms related to reactive hypoglycaemia (7,8). Over 50% of 269 post-total gastrectomy patients complained of some dumping symptoms in a large Japanese study (9). Whilst dumping explains many of the specific symptoms in Muir’s study, pathophysiological understanding of this syndrome is poor. Assuming that similar physiological mechanisms underpin the beneficial metabolic effects of bariatric surgery and the detrimental effects of gastric resection in lean patients, there are potential roles for altered bile acid, gut hormone and microbiome profiles (10-12). An improved understanding of the metabolic sequelae of gastrectomy may allow better physiological characterisation of dumping symptoms and more specific treatments than dietary advice, acarbose or somatostatin analogues. An exciting prospect is the development of glucagon like peptide 1 (GLP-1) antagonists (13).

Weight loss is a consistent outcome of gastrectomy and the extent of nutritional compromise appears to directly impact on quality of life (14). Nutritional support and loss of weight were key factors mentioned in open questioning by Muir et al. (2). A recent study from Dublin demonstrated a high incidence of pancreatic exocrine insufficiency, small intestinal bacterial overgrowth and fat soluble vitamin deficiency in 15 patients’ post-gastrectomy (15). In association with post-prandial dumping symptoms, these represent common but potentially treatable causes of significant weight loss after PTG.

One approach that has potential to reduce gastrointestinal symptoms is preservation of the vagus at the time of gastrectomy. A recently published randomised controlled trial of vagus preserving versus conventional distal gastrectomy, including 163 patients, demonstrated reduced diarrhoea and appetite loss at 12 months post-surgery (16). In our experience, it is possible to preserve the posterior vagus while performing a PTG with adequate oncological clearance for a T1 signet ring adenocarcinoma.

It is unclear whether PTG in early adult life results in long-term nutritional consequences beyond weight loss. Patients undergoing Roux-en-Y gastric bypass (RYGB) for obesity, a similar operation to PTG in terms of enteric reconstruction, are recognised to be at risk of a range of micronutrient deficiencies (17). In a study by Adachi et al., 59 patients of mean age 64 underwent bone mineral density assessment greater than 5 years after gastrectomy for cancer: 71% of women, and 18% of men, were found to have bone mineral density measurements consistent with a diagnosis of osteoporosis (18). At present, there is insufficient evidence to say whether micronutrient deficiency will become a problem after PTG but it is reasonable to expect some degree of vitamin and mineral malabsorption in this patient group.

In conclusion, the study by Muir et al. is an important recognition of the wide-ranging psychological and quality of life issues affecting the small, but important subgroup of patients undergoing gastrectomy when otherwise fit and healthy (2). Global HRQL appears to return to baseline within 1 year of surgery, which is encouraging; however the chronic nature of gastrointestinal symptoms, persistent weight loss and uncertainty over long-term nutritional deficiencies represents a burden in the post-PTG patient group, perhaps reflected in their persisting health-related anxiety. Patients with CDH1 mutation advised to have risk-reducing gastrectomy require cautious genetic and surgical counselling, including discussion of the long-term post-PTG uncertainties to aid them in their decision making. Contact with other patients who have been through this process can be very useful in our experience. Life-
long surgical and nutritional follow-up should monitor for treatable complications of gastrectomy as well as late presenting micronutrient deficiencies. In view of the rarity of HDGC it is important that the data is collected across multiple centres with long-term follow-up so that we can optimise the management for these individuals.

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**Footnote**

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

**References**


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