Systematic review

doi:10.1111/codi.12868

Segmental *vs* extended colectomy in the management of hereditary nonpolyposis colorectal cancer: a systematic review and meta-analysis

H. M. Heneghan, S. T. Martin and D. C. Winter

Centre for Colorectal Disease, St Vincent's University Hospital, Dublin, Ireland

Received 20 July 2014; accepted 27 October 2014; Accepted Article online 15 December 2014

Abstract

Aim The optimal surgical approach to the management of colorectal cancer in the setting of hereditary nonpolyposis colorectal cancer (HNPCC) is contentious. While some advocate total colectomy, others perform segmental resection followed by regular endoscopic surveillance. This systematic review evaluates the evidence for segmental colectomy (SC) and total (extended) colectomy (TC) in the management of HNPCC.

Method Two major databases (PubMed and Cochrane) were searched using predefined terms. All original articles, published in English, comparing the oncological outcomes of SC and TC in HNPCC patients from January 1950 to July 2013 were included.

Results Eighty-four studies were identified. After applying exclusion criteria, six studies involving 948 patients were included (mean age 47.4 years, 51.8% male). SC was more commonly performed than TC ($n = 780$; 82.3%). Mean follow-up was 106.5 months. Metachronous high-risk adenomas were detected more often after SC, although the difference was not statistically significant (23.4% *vs* 9.6%; OR 2.258, $P = 0.057$). Metachronous cancers occurred more frequently after SC than after TC (23.5% *vs* 6.8%; OR 3.679, $P < 0.005$). However, there was no difference in overall survival (90.7% *vs* 89.8% for SC and TC, respectively; $P = 0.085$). Only one study reported operative mortality (0% in each group), there was no report of operative morbidity or functional outcome.

Conclusion The optimal surgical approach in the management of HNPCC remains unclear. More adenomas and cancers occur after SC than after TC but there certainly is no evidence to suggest that more radical surgery leads to improved survival.

Keywords Segmental colectomy, extended colectomy, total colectomy, HNPCC, prophylactic surgery

Introduction

Hereditary nonpolyposis colorectal cancer (HNPCC) is an autosomal dominant syndrome that accounts for up to 5% of all colorectal carcinomas [1]. Patients with HNPCC have an 80% lifetime risk of developing colorectal cancer, which usually presents at an earlier age than sporadic colon cancers in the general population. Those affected are at increased risk of other malignancies, particularly in the urogenital, gastrointestinal, central nervous and cutaneous systems [2]. HNPCC is currently divided into two clinical syndromes, namely Lynch syndromes I and II. Lynch syndrome I is characterized by an inherited susceptibility to nonpolyposis colorectal carcinoma specifically, with a predilection for the right colon and increased risk of synchronous colorectal tumours. Lynch syndrome II has similar features, but is also associated with extracolonic tumours, particularly endometrial carcinoma [3,4].

The genetic defects responsible for HNPCC are germline mutations in deoxyribonucleic acid (DNA) mismatch repair genes. Five mutations occur most frequently (*MLH1*, *MSH2*, *MSH6*, *PMS1*, *PMS2*); however it has been suggested that more than 500 gene mutations may be implicated in the development of HNPCC-associated cancers [5,6]. In 1991 an international collaborative group agreed upon criteria for diagnosing HNPCC; these became known as the Amsterdam Criteria (AC) [7]. These were broadened in 1999 to include a diagnostic role for

Correspondence to: Helen M. Heneghan, St Vincent's University Hospital, Elm Park, Dublin 4, Ireland.
E-mail: helenheneghan@hotmail.com

extracolonic tumours, and subsequently became known as the Amsterdam Criteria II (AC-II) (Table 1) [8].

One of the key facets of managing HNPCC patients is educating the patient (and his or her relatives) about their risk of developing cancer at specific sites and of means to reduce or even eliminate this risk [9]. The role of prophylactic surgery in the management of individuals with HNPCC is controversial. Lynch and others advocate prophylactic total colectomy with ileorectal anastomosis, on the basis that there is a high risk of CRC with potential for rapid progression [10–14]. However, there is no evidence to suggest that segmental resection of established colon or rectal cancers compromises survival among HNPCC patients. Furthermore, even if a patient with HNPCC undergoes a total or subtotal colectomy, their risk of future rectal cancer persists and they must remain committed to careful endoscopic surveillance of the rectal segment. Panproctocolectomy, with an ileostomy or an ileal pouch anal anastomosis if the sphincters can be preserved, is not often advocated, although the advantage is complete elimination of CRC risk in susceptible individuals.

The aim of this systematic review and meta-analysis is to evaluate and compare the oncological outcomes after segmental and total colectomy in HNPCC patients. The primary outcomes of interest are 10-year overall survival (OS), and the rates of metachronous colorectal cancers and high-risk adenomas. We also aim to ascertain the morbidity and mortality associated with segmental and total colectomy in this setting.

Methodology

This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [15].

Search strategy for identification of studies

A systematic literature search of the Cochrane and PubMed databases was performed. The Cochrane database search was performed by combining the following search terms using the Boolean AND/OR operators: 'hereditary non-polyposis colorectal cancer', 'HNPCC', 'Lynch syndrome' and 'surgery'. For the PubMed database search, these same keywords (and variants) were used as both text words and Medical Search Headings (MeSH terms), and were combined using Boolean operators. The search was limited to original papers based on human studies, and there was no restriction on the date of publication. In addition to the primary electronic search we reviewed the 'related citations' linked to each citation in PubMed, and manually reviewed the bibliographies of selected articles and relevant review papers to identify other studies for inclusion.

Study selection

Only articles published in the English language from January 1950 to July 2013 were included for review. Other inclusion criteria were as follows: studies of patients with HNPCC or Lynch syndrome who underwent surgical treatment in the form of a colec-

Table 1 Features of Lynch syndrome and a summary of the Amsterdam criteria.

Features of Lynch syndrome	Amsterdam criteria
Germline mutation in a mismatch repair gene (MLH1, MSH2, MSH6 or PMS2)	AC-I: At least three relatives with histologically confirmed CRC
Autosomal dominant inheritance pattern for cancers in the family pedigree	**1** One is a first degree relative of the other two
Early age of onset of CRC	**2** At least two successive generations affected
Proximal (right-sided) colonic cancer predilection	**3** At least one relative with CRC was diagnosed at < 50 years of age
Accelerated carcinogenesis (small adenomas can rapidly develop into carcinomas)	**4** FAP has been excluded
High risk of metachronous CRC	AC-II: As above, but at least three relatives have had a HNPCC-associated cancer [colorectal cancer, or cancer of the endometrium, stomach, ovary, ureter/renal pelvis, brain, small bowel, hepatobiliary tract, or skin (sebaceous tumours)]
Increased risk of cancers at certain extracolonic sites (endometrium, ovary, stomach, ureter, small bowel, hepatobiliary, brain)	
Pathology of CRCs is more often poorly differentiated, with an excess of mucoid and signet-cell features, a Crohn's-like reaction, and a significant excess of tumour-infiltrating lymphocytes within the tumour	
Increased survival from CRC	

CRC, colorectal cancer; FAP, familial adenomatous polyposis.

tomy (total, subtotal or segmental), which reported subsequent development of metachronous cancers, high risk adenomas and survival data. A minimum average (or median) follow-up duration of 60 months and a minimum cohort of 40 patients were required for included studies. Exclusion criteria were: case reports or small case series (fewer than 40 patients), review articles, studies reporting on surgical technique or short-term postoperative outcomes only, studies reporting the management of malignancies associated with extracolonic HNPCC and those predominantly reporting on the genetic mutations associated with HNPCC.

Multiple publications involving the same series of patients (or duplicate patient populations) were identified; only the most recent or parent study was included in this review to avoid double counting of patients. In cases in which we were uncertain about duplicate patient groups (same group or institution reporting outcomes for a similar period, without clear indications that the smaller report was a substudy or interim results) a consensus was reached among the authors regarding its inclusion or exclusion.

Data collection and statistical analysis

The data extracted from selected studies included: year of publication, authors' institution and country, number of patients and their demographics, location of the primary colonic tumour, type of colectomy performed, rate of metachronous adenomas and cancers, duration of follow-up, early postoperative morbidity and mortality, survival statistics (5-year and/or 10-year OS). Statistical analyses were performed only on extracted summarized data from the selected studies. Basic descriptive statistics (percentages and weighted means) were used to summarize the patient, study and outcome data. Weighted means were calculated for oncological outcomes across all studies. The software package Comprehensive Meta-Analysis Version 2.0 (Biostat™, Englewood, New Jersey, USA) was used to perform the meta-analysis and to generate forest plots. Where possible, pooled analyses were performed to compute the odds ratio (OR) and the corresponding 95% confidence interval (CI). The degree of heterogeneity between studies was calculated for each analysis; a fixed effects model was used if heterogeneity was low, and the DerSimonian–Laird random-effects model was used if there was a high degree of heterogeneity between studies. The *P*-value for overall effect was calculated with the *Z*-test and significance was set at $P < 0.05$. The pooled OR and 95% CI are presented graphically as forest plots. The degree of heterogeneity is presented using the Q and I^2 statistics. The I^2 index of heterogeneity represents the percentage of the total variation which is due to variation between studies. For interpreting I^2, Higgins *et al.* [16] proposed that a value of 0% indicated no heterogeneity, 25% represented low heterogeneity, 50% was moderate heterogeneity and 75% indicated high heterogeneity between the studies.

Results

Search yields and data retrieval

The initial literature search yielded 84 citations. After an initial screening of titles and abstracts, 75 studies were excluded and nine papers were reviewed in full to determine whether they met the inclusion criteria. Of these, four were rejected because they did not fulfil the inclusion criteria. Upon thorough review of the remaining five publications, one further study was identified from bibliographies and related citations which was deemed suitable for inclusion. These six studies met the above criteria to merit inclusion in the extractable and analysable dataset (Fig. 1).

Study characteristics

The dataset consisted of six original studies involving 948 patients who had undergone either segmental (762) or total colectomy (186) for HNPCC. Of these six studies, half were from the USA ($n = 3$), with one study each from Europe, New Zealand and South Africa. Data from two studies by the colorectal surgery group in Cleveland, Ohio, USA were included, as the populations did not appear to overlap [17,18]. These papers are summarized in Table 2.

Patient characteristics

In total, 948 patients were investigated in the six studies. Preoperatively, the mean age of the patients was 47.4 years, and 51.8% of the population was male. Only three studies reported tumour location; 60.2% of colon cancers were right-sided. The specific genetic mutation(s) responsible for HNPCC were reported in four of the six included studies, and not every patient in these studies was tested for germline mutations in their mismatch repair genes. Among those tested, mutations in the *MLH1* and *MSH2* genes were most commonly identified (*MLH1* in 49.5%, *MSH2* in 42.5%) of HNPCC patients who underwent genetic testing.

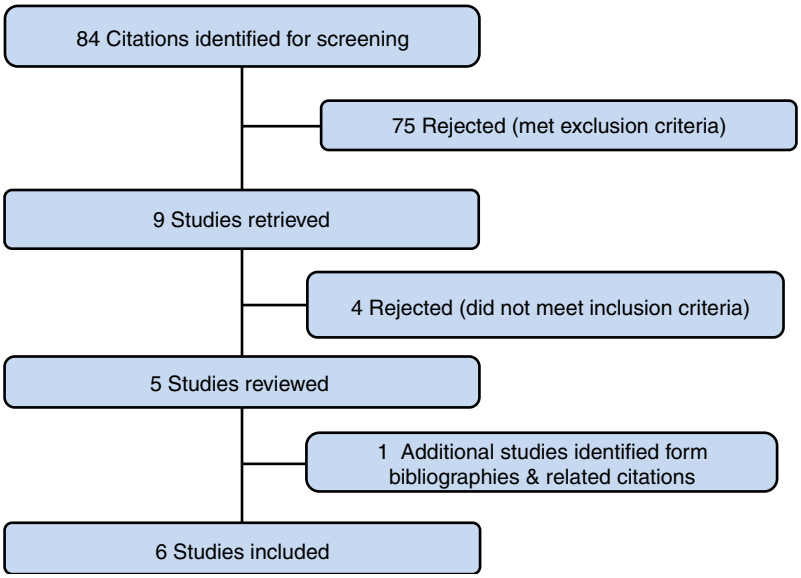

Figure 1 PRISMA flow chart illustrating the study screening and selection process.

Oncological outcomes: rates of metachronous adenomas, cancers and long-term survival

After an average (weighted) follow-up period of 106.5 months (range 69.6–144), the rate of metachronous high-risk adenomas was 23.4% among patients who had undergone segmental colectomy and 9.6% among those who had undergone total colectomy. Only three studies adequately reported this data; meta-analysis of these three studies shows that metachronous adenomas are detected more often after SC, although this difference did not meet statistical significance (OR 2.258, 95% CI 0.975–5.231, $P = 0.057$). The rates of development of metachronous cancer after segmental and total colectomy (reported in five of the six studies included in this review) were 23.5% and 6.8%, respectively (OR 3.679, 95% CI 1.899–7.125, $P < 0.005$). The OS was only reported in three of the six studies [19–21]. On average, long-term survival was 90.7% after segmental colectomy and 89.8% after total colectomy ($P = 0.085$). A summary of outcomes is presented in Table 3 and forest plots illustrating the data from the meta-analysis are presented in Figs. 2–4.

Operative morbidity and mortality

Operative mortality, defined as death within 30 days of surgery, was only reported by Stupart *et al.* [21]. In this South African study of 60 HNPCC patients who underwent segmental or total colectomy, there were no early postoperative deaths. None of the six studies reported morbidity, quality of life or functional outcomes Table 4.

Discussion

The surgical management of colonic cancer in HNPCC is contentious. The decision to undertake a segmental colectomy or extended resection (total

Table 2 Baseline study characteristics.

Author	Year	Country	*n*	Segmental colectomy (*n*)	Total colectomy (*n*)	Mean age (years)	% Male	Follow-up (months)
Mecklin [7]	1993	Finland	54	37	17	36.7	n.r.	69.6
Kalady [18]	2010	USA	296	253	43	52	47.9	104
Natarajan [19]	2010	USA	106	69	37	45.3	52.5	144
Parry [20]	2011	New Zealand	382	332	50	45.9	51.4	108
Stupart [21]	2011	South Africa	60	39	21	42.1	59.2	80.4
Kalady [17]	2012	USA	50	50	0	53	68.0	101.7
Summary data*			948	780	168	47.4	51.8	106.5

n, number of patients; n.r., not reported.
*Weighted means presented.

Table 3 Oncological outcomes after segmental colectomy (SC) or total colectomy (TC) in HNPCC patients.

Author	Year	*n* (SC/TC)	Metachronous adenomas after SC (%)	Metachronous adenomas after TC (%)	Metachronous cancers after SC (%)	Metachronous cancers after TC (%)	10-year OS for SC (%)	10-year OS for TC (%)
Mecklin [7]	1993	54 (37/17)	27.0	11.8	21.6	11.8	n.r.	n.r.
Kalady [18]	2010	296 (253/43)	22.0	11.0	25.0	8.0	n.r.	n.r.
Natarajan [19]	2010	106 (69/37)	n.r.	n.r.	33.3	10.8	76.8	86.5
Parry [20]	2011	382 (332/50)	n.r.	n.r.	22.0	0.0	97.0	98.0
Stupart [21]	2011	60 (39/21)	17.9	4.8	21.0	9.5	62.0	76.0
Kalady [17]	2012	50 (50/0)	39.4	n.r.	15.2	n.r.	n.r.	n.r.
Summary data*		948 (780/168)	23.4	9.6	23.5	6.8	90.7	89.8

n.r., not reported.
*Weighted means presented.

Table 4 Early postoperative outcomes.

Author	Year	*n* (SC/TC)	30-day mortality for SC	30-day mortality for TC	Morbidity for SC	Morbidity for TC
Mecklin [7]	1993	54 (37/17)	n.r.	n.r.	n.r.	n.r.
Kalady [18]	2010	296 (253/43)	n.r.	n.r.	n.r.	n.r.
Natarajan [19]	2010	106 (69/37)	n.r.	n.r.	n.r.	n.r.
Parry [20]	2011	382 (332/50)	n.r.	n.r.	n.r.	n.r.
Stupart [21]	2011	60 (21/39)	0	0	n.r.	n.r.
Kalady [17]	2012	50 (50/0)	n.r.	n.r.	n.r.	n.r.
Summary data		948 (780/168)	0.0%	0.0%	n.r.	n.r.

SC, segmental colectomy; TC, total colectomy; n.r., not reported.

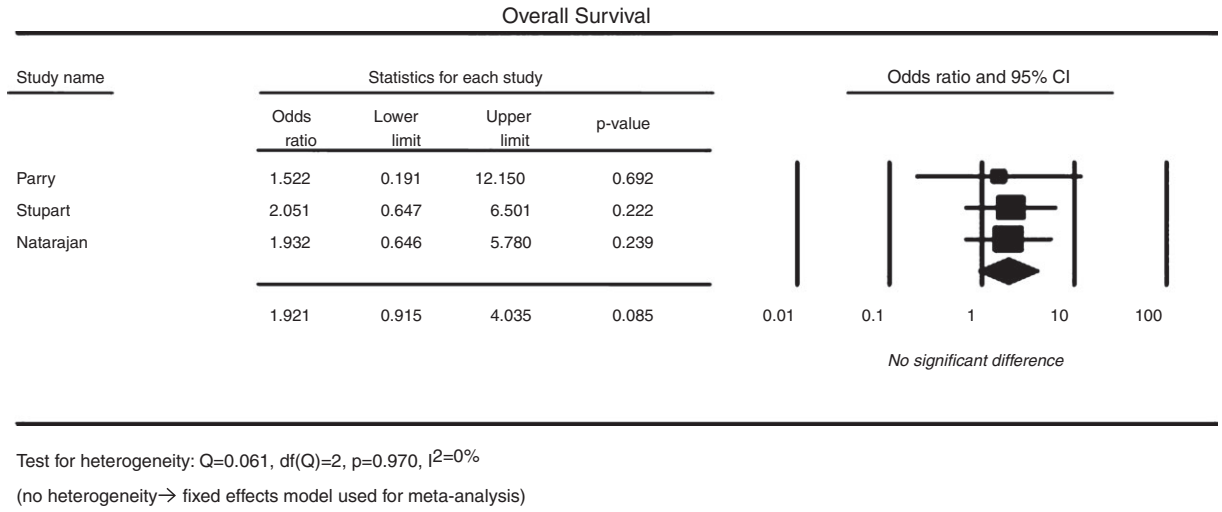

Figure 2 Forest plot showing pooled data comparing 10-year overall survival after segmental and total colectomy for HNPCC.

colectomy or proctocolectomy) remains largely at the surgeon's discretion. Thus far, no good evidence exists to guide this decision-making process. It is strongly influenced by expert opinion or institutional practices. The advocates for total colectomy in the setting of an HNPCC-associated colon cancer claim that this approach eliminates patients' future risk of metachronous high-risk colonic adenomas or cancers.

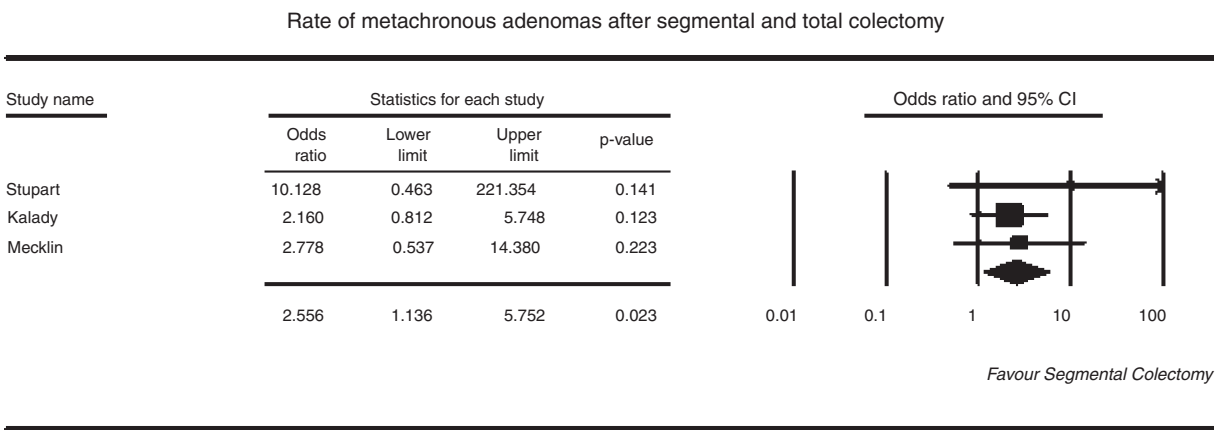

Figure 3 Forest plot showing pooled data comparing rates of metachronous high-risk adenomas after segmental and total colectomy for HNPCC.

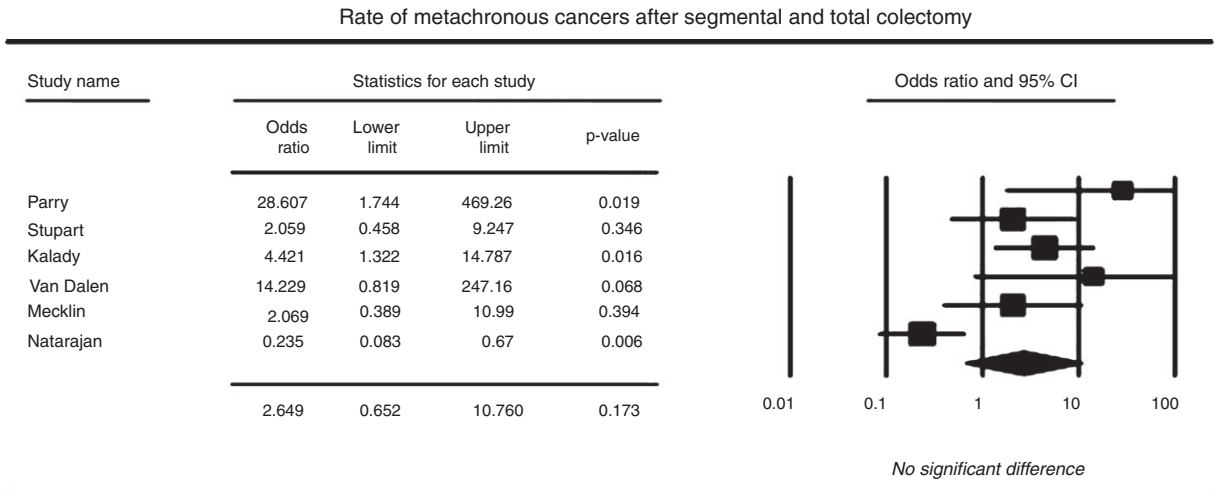

Figure 4 Forest plot showing pooled data comparing rates of metachronous cancers after segmental and total colectomy for HNPCC.

Proponents of a limited or segmental colectomy maintain that this is the standard of care for sporadic colorectal cancers; that the morbidity is less than that of total colectomy or proctocolectomy; and that with regular endoscopic surveillance metachronous colonic lesions can be treated if they arise. Furthermore, the latter group point out that total colectomy doesn't remove the need for endoscopic surveillance of the rectal segment. Also, it isn't clear if a more radical surgical approach confers a survival benefit.

This systematic review aimed to evaluate and compare oncological outcomes following therapeutic (segmental) and prophylactic (total) colectomy for the management of HNPCC-associated colon cancers. Data from this review confirm the logical expectation that metachronous high-risk adenomas and cancers are more commonly detected after segmental than total colectomy. However, OS data were almost identical for HNPCC patients irrespective of the surgical approach taken. What is notably absent in all of the included studies is a comparison of surgical morbidity and mortality after both procedures. It is premature to recommend either surgical approach to HNPCC (total or segmental colectomy) without weighing the surgical risks against the benefits of each procedure. Total colectomy with ileorectal anastomosis is

associated with greater morbidity than right or left colonic anastomoses [22,23]. This morbidity rate is as high as 53% for open total colectomy and ileorectal anastomosis [24,25].

When considering the relatively high rate of metachronous adenomas after segmental colectomy compared with total colectomy in the HNPCC population (23.4% *vs* 9.6%, respectively, in this study) it may be put into context by comparing it with the detection rates for metachronous adenoma and cancer after sporadic colorectal cancer resections. After segmental resection of a sporadic colorectal cancer, the adenoma detection rate is as high as 25% and metachronous cancers are found in approximately 4% of patients within 2 years [26]. Admittedly, the detection of metachronous cancers after segmental resection is almost four times higher than after total colectomy in HNPCC patients (23.5% *vs* 6.8%, respectively). However, these cancers are usually detected at an early stage and do not compromise patients' OS in the long-term. We believe this is not convincing enough data to recommend more extensive resection for HNPCC.

Aside from oncological outcomes after segmental and extended surgical approaches to HNPCC, other important considerations are patient-related outcomes such as quality of life and postoperative bowel function. In addition to higher overall morbidity rates, subtotal or total colectomy with ileorectal anastomosis are associated with an increase in the frequency of bowel movements, poorer functional outcome and lower quality of life compared with segmental colectomy [27–29]. Given that segmental colectomy appears equivalent to total colectomy in terms of survival, and those patients who have total colectomy report poorer functional outcomes while retaining a 12% risk of developing rectal cancer after 12 years [30] that requires endoscopic surveillance of the rectum, the recommendations for prophylactic 'extended' surgery for HNPCC must be questioned. These data also prompt the question whether true prophylactic surgery in young patients with HNPCC should involve a restorative proctocolectomy rather than a total colectomy and ileorectal anastomosis? In advocating 'prophylactic surgery' for HNPCC one must also consider management of the gynaecological and genitourinary tracts, which are also at risk of tumour development; should we be offering prophylactic hysterectomy and oophorectomy to all women with HNPCC, or at least to those women beyond child-bearing age?

This systematic review is limited by the heterogeneity and paucity of data available for inclusion in the analysis. In particular, survival data have been infrequently and poorly reported after segmental and total colectomy for HNPCC. Furthermore, many of the included studies were retrospective reviews of prospectively collected databases/registries and so carry the inherent limitations of retrospectively gathered data. To date there are no prospective randomized studies comparing segmental and total colectomy for HNPCC patients; such studies would provide stronger evidence upon which treatment decisions could be based. Additionally, it would be interesting to assess for associations between the rates of metachronous cancers in HNPCC patients according to an individual's genetic mutation. While it is known that *MLH1* and *MSH2* account for almost 90% of all identified mutations in HNPCC cohorts, it is not known if any one mutation confers greater risk of metachronous cancers than another. There is also concern for outcome reporting bias given that not every study reported all outcomes of interest (metachronous adenomas, cancers and OS). Finally, this review is limited by the notable absence of morbidity and mortality data. These data are critical in order to perform a more balanced risk–benefit analysis of segmental *vs* extended colectomy in the setting of HNPCC.

Given these limitations, this review indicates that prophylactic colectomy does not lead to improved survival and does not eliminate the risk of metachronous cancers. Therefore it fails as a truly prophylactic operation. Although morbidity for both procedures in the HNPCC setting is not well described, it is likely that total colectomy with ileorectal anastomosis has higher morbidity and worse function. True prophylactic surgery would require complete proctocolectomy as a non-restorative (ileostomy) or restorative (pouch) procedure. There would be significant morbidity and functional consequences with this approach, and there is little evidence to support it as yet. Until we have better data on outcomes, the best conclusion is that segmental resection of HNPCC is the standard of care unless the patient's preference is prophylactic extended resection. Under those circumstances, the true prophylactic procedure to eliminate CRC risk would be a proctocolectomy.

Author contributions

All authors were involved in study concept, design, data collection & analysis, writing and editing of the manuscript.

Disclaimers and source of funding

The authors have no relevant financial disclosures or conflicts of interest. No funding was sought or received for this study.

References

1 Hegde MR, Roa BB. Genetic testing for hereditary nonpolyposis colorectal cancer (HNPCC). *Curr Protoc Hum Genet* 2009; **Chapter 10:** Unit 10 2.

2 Watson P, Lynch HT. The tumor spectrum in HNPCC. *Anticancer Res* 1994; **14:** 1635–9.

3 Silva FC, Valentin MD, FerreiraFde O, Carraro DM, Rossi BM. Mismatch repair genes in Lynch syndrome: a review. *Sao Paulo Med J* 2009; **127:** 46–51.

4 Lynch HT, Watson P, Kriegler M *et al.* Differential diagnosis of hereditary nonpolyposis colorectal cancer (Lynch syndrome I and Lynch syndrome II). *Dis Colon Rectum* 1988; **31:** 372–7.

5 Papp J, Kovacs ME, Olah E. Germline MLH1 and MSH2 mutational spectrum including frequent large genomic aberrations in Hungarian hereditary non-polyposis colorectal cancer families: implications for genetic testing. *World J Gastroenterol* 2007; **13:** 2727–32.

6 Lynch HT, Lynch J. Lynch syndrome: genetics, natural history, genetic counseling, and prevention. *J Clin Oncol* 2000; **18:** 19S–31S.

7 Vasen HF, Mecklin JP, Watson P *et al.* Surveillance in hereditary nonpolyposis colorectal cancer: an international cooperative study of 165 families. The International Collaborative Group on HNPCC. *Dis Colon Rectum* 1993; **36:** 1–4.

8 Vasen HF, Watson P, Mecklin JP, Lynch HT. New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative group on HNPCC. *Gastroenterology* 1999; **116:** 1453–6.

9 Lynch HT, de la Chapelle A. Hereditary colorectal cancer. *N Engl J Med* 2003; **348:** 919–32.

10 Lynch HT, Lynch JF, Fitzgibbons R Jr. Role of prophylactic colectomy in Lynch syndrome. *Clin Colorectal Cancer* 2003; **3:** 99–101.

11 Burke W, Petersen G, Lynch P *et al.* Recommendations for follow-up care of individuals with an inherited predisposition to cancer. I. Hereditary nonpolyposis colon cancer. Cancer Genetics Studies Consortium. *JAMA* 1997; **277:** 915–9.

12 Guillem JG, Smith AJ, Calle JP, Ruo L. Gastrointestinal polyposis syndromes. *Curr Probl Surg* 1999; **36:** 217–323.

13 Vasen HF. Clinical diagnosis and management of hereditary colorectal cancer syndromes. *J Clin Oncol* 2000; **18:** 81S–92S.

14 Fitzgibbons RJ Jr, Lynch HT, Stanislav GV *et al.* Recognition and treatment of patients with hereditary nonpolyposis colon cancer (Lynch syndromes I and II). *Ann Surg* 1987; **206:** 289–95.

15 Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009; **339:** b2535.

16 Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; **327:** 557–60.

17 Kalady MF, Lipman J, McGannon E, Church JM. Risk of colonic neoplasia after proctectomy for rectal cancer in hereditary nonpolyposis colorectal cancer. *Ann Surg* 2012; **255:** 1121–5.

18 Kalady MF, McGannon E, Vogel JD, Manilich E, Fazio VW, Church JM. Risk of colorectal adenoma and carcinoma after colectomy for colorectal cancer in patients meeting Amsterdam criteria. *Ann Surg* 2010; **252:** 507–11; discussion 11–3.

19 Natarajan N, Watson P, Silva-Lopez E, Lynch HT. Comparison of extended colectomy and limited resection in patients with Lynch syndrome. *Dis Colon Rectum* 2010; **53:** 77–82.

20 Parry S, Win AK, Parry B *et al.* Metachronous colorectal cancer risk for mismatch repair gene mutation carriers: the advantage of more extensive colon surgery. *Gut* 2011; **60:** 950–7.

21 Stupart DA, Goldberg PA, Baigrie RJ, Algar U, Ramesar R. Surgery for colonic cancer in HNPCC: total vs segmental colectomy. *Colorectal Dis* 2011; **13:** 1395–9.

22 Hyman N, Manchester TL, Osler T, Burns B, Cataldo PA. Anastomotic leaks after intestinal anastomosis: it's later than you think. *Ann Surg* 2007; **245:** 254–8.

23 Veyrie N, Ata T, Muscari F *et al.* Anastomotic leakage after elective right versus left colectomy for cancer: prevalence and independent risk factors. *J Am Coll Surg* 2007; **205:** 785–93.

24 Ahmed Ali U, Keus F, Heikens JT *et al.* Open versus laparoscopic (assisted) ileo pouch anal anastomosis for ulcerative colitis and familial adenomatous polyposis. *Cochrane Database Syst Rev* 2009: CD006267.

25 McNicol FJ, Kennedy RH, Phillips RK, Clark SK. Laparoscopic total colectomy and ileorectal anastomosis (IRA), supported by an enhanced recovery programme in cases of familial adenomatous polyposis. *Colorectal Dis* 2012; **14:** 458–62.

26 Balleste B, Bessa X, Pinol V *et al.* Detection of metachronous neoplasms in colorectal cancer patients: identification of risk factors. *Dis Colon Rectum* 2007; **50:** 971–80.

27 You YN, Chua HK, Nelson H, Hassan I, Barnes SA, Harrington J. Segmental vs. extended colectomy: measurable differences in morbidity, function, and quality of life. *Dis Colon Rectum* 2008; **51:** 1036–43.

28 Lim JF, Ho YH. Total colectomy with ileorectal anastomosis leads to appreciable loss in quality of life irrespective of primary diagnosis. *Tech Coloproctol* 2001; **5:** 79–83.

29 Haanstra JF, de Vos Tot Nederveen Cappel WH, Gopie JP *et al.* Quality of life after surgery for colon cancer in patients with Lynch syndrome: partial versus subtotal colectomy. *Dis Colon Rectum* 2012; **55:** 653–9.

30 Rodriguez-Bigas MA, Vasen HF, Pekka-Mecklin J *et al.* Rectal cancer risk in hereditary nonpolyposis colorectal cancer after abdominal colectomy. International Collaborative Group on HNPCC. *Ann Surg* 1997; **225:** 202–7.