Colorectal cancer outcomes in patients aged over 85 years

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ABSTRACT

INTRODUCTION The prevalence of colorectal cancer is increasing in the elderly. We examined the treatment and outcomes in our institution of patients aged over 85 years with proven colorectal adenocarcinoma.

METHODS One hundred and five patients were identified and stratified by treatment received: curative surgery (CS), other treatments (OT) or best supportive care (BSC). Data on demographics, staging, treatment and survival was collected and analysed.

RESULTS Forty two patients received CS, 36 OT and 27 BSC. While the treated groups (CS and OT) were similar in terms of age ($p=0.35$) and staging ($p=0.16$), BSC patients were significantly older and had higher stage disease ($p<0.01$). Survival was significantly poorer among BSC patients, at a mean of 9.7 months (95% confidence interval [CI] 4.7–14.7) versus 41.6 months (95% CI 32.5–50.7) and OT 27.3 months (95% CI 20.4–34.1) for the CS and OT groups ($p<0.001$). There was no significant survival difference between CS and OT groups within 2 years of treatment ($p=0.12$). Thereafter, OT patients had a very similar 5-year survival to that of the BSC group, at 13% versus 43% in CS patients ($p<0.001$).

CONCLUSIONS These data suggest that, up to 2 years following treatment, the risks of resectional surgery for colorectal cancer may neutralise any benefit. However, those that survive beyond this period show improvements. The challenge of improving patient selection is most acute in the growing ageing population, and highlights the current focus on presenting all treatment options to 'a reasonable patient'.

KEYWORDS

Colorectal neoplasms – Aged 80 and over – Mortality

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Sporadic colorectal cancer is a disease of the elderly, with over 43% of cases in the UK arising in people aged over 75 years.^{1,2} The proportion of the UK population aged over 85 – 'the oldest old' – is set to nearly double, from 7.9% of the population in 2012 to 13% in 2037. An ageing population combined with bowel cancer rates increasing 1.4–2.5-fold with each successive decade of life will significantly increase the prevalence of colorectal cancer in this cohort in the coming years.³ Furthermore, improved awareness, better access to investigations and the recognition that chronological age is no longer a barrier to individualised treatment renders colorectal cancer increasingly important in this age group.

Generally, segmental resection is the first-line treatment for stage I–III colorectal cancer. Although the morbidity and mortality associated with surgery increase progressively with advancing age, they are confounded by older patients presenting with later-stage disease and thus having more emergency and less curative surgery.^{4,5} Those aged over 80 years have a 15% increase in postoperative

all-cause 30-day mortality.⁶ Charlson comorbidity scores >5 also increase mortality by 24%, while emergency surgery increases mortality rates by 14.9%.⁶

Life expectancy in the absence of cancer at 85 years of age is 5.8 years for men and 6.8 years for women, and is expected to rise.⁷ Nevertheless, the older a patient becomes, the less likely they are to undergo curative treatment, even after adjusting for confounding factors such as comorbidity and performance status.^{4,8}

Frequently, robust assessment of fitness for surgery to objectively determine an individual's ability to undergo treatment is not performed. Decision-making instead relies on clinician experience, influenced by chronological patient age, the historically observed shorter life expectancies, a paucity of good evidence for treatment in the elderly and wider preconceptions about the ability of elderly patients to cope with the treatment.⁹

Our study examines the outcomes of patients aged over 85 years diagnosed with colorectal adenocarcinoma to determine survival patterns in treatment groups.

Methods

All patients aged over 85 years diagnosed with colorectal cancer and considered in our colorectal multidisciplinary team (MDT) meetings between 1 January 2008 and 31 December 2010 were considered for inclusion. Mortality and treatment data were collected from electronic clinical notes, general practice records and public records. Charlson comorbidity scores were derived from clinic letters, investigations, prescriptions and discharge letters.

Patients were included if they had a histologically proven diagnosis of colorectal adenocarcinoma and an age at diagnosis of 85 years or older. Patients with recurrent disease, suspicious pathology proven to be benign after surgery and those with disseminated malignancy and an uncertain primary diagnosis were excluded.

Patients were stratified by treatment arm into three groups: curative surgery (CS), other treatments (OT) and best supportive care (BSC). CS was defined as those patients who received a surgical resection with curative intent as part of their treatment. OT included all procedures aimed at loco-regional disease control. BSC included patients who declined curative or other treatment or had treatment and procedures for palliation of symptoms.

Statistical analyses were performed using SPSS version 22.0 (IBM, Armonk, NY, USA). Patient age was normally distributed, and the mean and standard deviation was calculated. Statistical significance between groups was calculated using the Kruskal-Wallis test or one way analysis of variance (ANOVA), where appropriate.

Survival was calculated from the date of diagnosis (as recorded in the MDT discussion) to the date of death or last confirmed survival. The study ended on the 30 September 2014 and survival time was censored if the participant was still alive. Kaplan Meier survival curves were constructed and significance tested using the log-rank test. The level of significance was set at a $p < 0.05$.

Results

One hundred and five patients were included in the study (Table 1). The mean age was 88 years (range 85–98 years). Those patients who received BSC were significantly older than the treated groups, at a mean age of 91 years versus 88 years ($p < 0.001$). There was no significant age difference between CS and OT groups ($p = 0.351$). The median Charlson comorbidity score for both treated groups (CS and OT) was 5 (interquartile range [IQR] 2), but was significantly higher in the BSC group 6.5 (IQR 4; $p < 0.001$).

Forty two patients received CS, with 35 having open and seven laparoscopic resections (one procedure was converted to an open resection). Almost one-third (31%) of these procedures were performed as an emergency.

Thirty one patients had OT, including 11 who received long-course chemoradiotherapy and nine treated with radiotherapy alone. There were also six transanal endoscopic local excisions (TEO/TEMS), two transanal resections of tumour (TART), and three endoscopic procedures.

Thirty two patients were treated with BSC, including five who declined surgery or other treatments. One patient received a colonic stent, alongside three bypass procedures and one defunctioning stoma.

BSC patients had higher stage disease ($p < 0.001$) compared to those who had CS or OT. There was no statistically significant difference in staging between CS and OT patients ($p = 0.165$). Staging was incomplete in the OT and BSC arms (three patients missing in each group) and could not be determined retrospectively.

Survival

Figure 1 shows 5-year survival from colorectal cancer by treatment arm. Those given BSC had significantly poorer survival than those who were treated surgically, at a mean of 9.7 months (95% confidence interval [CI] 4.7–14.7) versus 41.6 months (95% CI 32.5–50.7) for CS and 27.3 months

Table 1 Summary of patient characteristics

	Curative surgery	Other treatment	Best Supportive care	All patients
Number of patients	42 (40)	31 (29.5)	32 (30.5)	105 (100)
Age (mean [SD])	87.4 (2.3)	88.5 (2.6)	89.7 (3.5)	88.4 (2.9)
Gender F:M (%F)	20:22 (47)	24:12 (67)	19:8 (70)	64:42 (60)
Charlson comorbidity score (median [IQR])	5 (2)	5 (2)	6.5 (4)	
Stage I-III	41 (97.6)	29 (80.5)	15 (55)	85 (80.9)
Stage IV	1 (2.4)	4 (11.1)	9 (33.3)	14 (13.3)
Emergency treatment	13 (31)	2 (6.5)	1 (3.1)	
Laparoscopic surgery	7 (17)	0	0	
Right sided tumour – caecum to distal transverse colon	28 (66.7)	3 (9.7)	16 (50.0)	47 (44.8)
Left sided tumour – splenic flexure to sigmoid colon	11 (26.2)	3 (9.7)	7 (21.9)	21 (20)
Rectal tumour	3 (7.1)	25 (80.6)	9 (28.1)	37 (35.2)
All values mean (%), unless otherwise stated. Abbreviations: IQR, interquartile range; F, female; M, male; SD, standard deviation

(95% CI 20.4–34.1) for OT ($p < 0.001$). Surgery showed a higher 90-day mortality, at 12% ($n=6$) versus 3% for OT ($n=1$), which was related to early deaths in the postoperative period. However, CS and OT had very similar early postoperative survival, at 53% in both groups at 2 years ($p=0.115$). This remained unchanged following removal of emergency surgery from the analysis. After 2 years, survival in the OT group declined towards that for BSC, at 5-year survival in both groups of 13% versus 43% for CS ($p < 0.001$).

Median survival following emergency surgery was 30.7 months (95% CI 17.5–45.9) compared to 45 months (95% CI 35.9–56) with elective surgery, although the difference did not reach statistical significance ($p=0.298$).

A large proportion of CS patients had right-sided tumours (Table 1). A sub-analysis by tumour site revealed that these tumours did not have significantly better survival following CS than others ($p=0.227$) (Figure 2). Thirty (66.7%) of all right-sided tumours underwent CS versus only three (7.1%) rectal tumours.

Among patients receiving OT, rectal tumours, which formed the majority of cases, had significantly better survival than other tumours ($p < 0.05$) (Figure 3). They were treated with radiotherapy with or without chemotherapy, as well as local procedures such as TEO/TEMS and TART.

Discussion

Management of colorectal cancer in the oldest old, with its unique challenges, will become increasingly important

over the coming decades. Patients aged over 85 years are most likely to ask: What happens if I don't have a big operation? Indeed, all patients should now expect a full explanation of all the possible treatment options available to them, and clinicians are now legally bound to present these dispassionately.¹⁰ Such discussions require clear information and time, both during and outside clinic consultations. Better perioperative assessment of the elderly and information regarding life expectancy and quality of life, both with and without treatment, are also paramount. Perhaps the most challenging aspects of such discussions is the avoidance of 'framing' when discussing risk or survival, and excluding the transference of clinician or MDT preferences (perhaps even prejudices). Few healthcare pathways are designed to accommodate such an approach, especially in systems dominated by targets.

This study is a retrospective analysis and has clear limitations. Notably, the numbers are small and we are unable to present quality of life data for the patients included. We therefore do not know if those who had surgery had functional disturbances or other problems thereafter, or if the group who had other treatment had uncontrolled symptoms of cancer detrimental to their quality of life. In terms of overall survival, it nevertheless appears that CS for colorectal cancer in this patient group does not yield a benefit over the first 2 years compared to other treatments. Beyond 2 years, a clear survival benefit is apparent. There are, of course, many potential confounding factors and it is noteworthy that five patients in this study considered fit for surgery declined the offer of CS in favour of BSC.

These results suggest that the site of the cancer may matter, in determining both survival and the treatment offered. Right-sided cancers were more likely to be treated in the elderly with surgical resection in our service. By contrast, rectal tumours were more likely to receive other treatment such as local excision and/or radiotherapy. This may highlight early rectal cancer as an important subgroup in the over 85-year-old for treatment with local techniques such as TEMS and TART. Complete responses to neoadjuvant chemoradiation have been reported in some studies, allowing a non-operative strategy to be employed with some success.^{11–15} The predominance of right-sided cancers in the CS group and rectal cancers in the OT group may be confounding the survival analysis into a comparison of survival between these two sites, rather than between differing treatment strategies. Furthermore, recognition that resection surgery for rectal cancer carries higher morbidity and mortality may underlie a bias against offering resection to elderly patients, as local excision and radiotherapy can be used instead. The role of 'rectal preservation' is attracting great interest in terms of the management of early rectal cancer and late rectal cancer that responds completely to long-course radiotherapy. However, there remain as many questions as answers in both areas. Interestingly, more left-sided cancer patients, where no such alternative is available, were treated with CS. They had the poorest survival of all three sites, and outcomes were worse than for those undergoing other treatments.

Assessment of fitness of the elderly for surgery must be more holistic than in the general population. It requires consideration of cardiorespiratory fitness and other comorbidities but also assessment of function, frailty and quality of life. Several tools and tests are available to assess cardiorespiratory reserve. Cardiopulmonary exercise testing (CPET) provides an objective measurement of physiological fitness that predicts postoperative cardiorespiratory mortality and is superior to simple self-reported questionnaires or shuttle walk tests.^{14,15} However, CPET and other similar tools are expensive resources and not available universally. In our institution, we now strive to ensure that these patients are routinely assessed preoperatively by a consultant anaesthetist but, again, this requires additional resources at a time when financial pressures on the NHS are ever-increasing.

Frailty, as a phenotype of physiological reserve and resistance to stressors, is increasingly seen as an independent predictor of outcome after surgery.¹⁶ Frailty scores independently predict postoperative complications and length of stay and mortality.^{17,18} Few colorectal surgeons, if any, have expertise in assessing frailty and there is increasing interest in specialist teams, often with healthcare of the elderly input, contributing to such assessments. Comprehensive Geriatric Assessment (CGA) is a multidimensional, multiprofessional iterative process providing detailed analysis of an individual across a broad range of health domains, and provides the basis of ongoing care and management. As an intervention applied to older people in a wide variety of settings, CGA has significant positive effects

on mortality, morbidity, functional performance and independence.¹⁹ There is mounting evidence that the use of CGA in elective non-malignant surgery is effective in reducing poor outcomes for frail elders.²⁰ We have recently incorporated CGA into the care of our patients aged over 80 years. It is envisaged that this should help to improve patient selection and empower patients to make more informed decisions about their treatment, but must of course be subject to considered cost-benefit analysis in the future.

In this study, only seven patients underwent laparoscopic colorectal resections. However, laparoscopic surgery is increasingly being offered to patients, with proven benefits for postoperative pain, hospital stay and recovery versus conventional open surgery.^{21–25} These benefits may be especially important in the poorly mobile and comorbid elderly but are sometimes offset by concerns regarding the effects of a pneumoperitoneum and longer operating times. Enhanced recovery after surgery programmes may require modification in a sub-population who often have lower levels of baseline function.²⁴

Conclusions

Patients aged over 85 years with colorectal cancer are increasing in number. Under our duty of informed consent, outcomes and alternatives to surgery must be discussed. This study has shown similar survival over the first 2 years for those who had CS and those who received OT. Patients treated curatively for right-sided cancers survived longer, while those with rectal tumours who received radiotherapy or local surgical treatments might expect similar survival over the first two years. Notwithstanding the difficulties inherent to this type of analysis, these data have helped to inform discussions with our patients and helped to identify areas where further data is required. More comprehensive assessment of fitness, including not only cardiorespiratory reserve but also function, frailty and quality of life might allow patients to make more informed choices. Crucially, the aspiration must be to improve the selection of patients who might benefit from CS and identify those better served by alternative strategies.

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References

1. Cancer Statistics Registrations, England (Series MB1), No. 41, 2010. Office for National Statistics. <http://www.ons.gov.uk/ons/rel/vsob1/cancer-statistics-registrations-england-series-mb1/no-41-2010/index.html> (cited October 2015).

2. Bowel cancer statistics. Cancer Research UK. <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bowel-cancer> (cited October 2015).
3. National Population Projections, 2012-based Statistical Bulletin. Office for National Statistics. <http://www.ons.gov.uk/ons/rel/npp/national-population-projections/2012-based-projections/stb-2012-based-npp-principal-and-key-variants.html> (cited October 2015).
4. Simmonds. Surgery for colorectal cancer in elderly patients: a systematic review. Colorectal Cancer Collaborative Group. *Lancet* 2000; **356**: 968–974.
5. Barrier A, Ferro L, Houry S *et al*. Rectal cancer surgery in patients more than 80 years of age. *Am J Surg* 2003; **185**: 54–57.
6. Morris EJ, Taylor EF, Thomas JD *et al*. Thirty-day postoperative mortality after colorectal cancer surgery in England. *Gut* 2011; **60**: 806–813.
7. Office for National Statistics. Life expectancy at the age of 85 years in 2010/12, in the UK. 2014.
8. Hodgson DC, Fuchs CS, Ayanian JZ. Impact of patient and provider characteristics on the treatment and outcomes of colorectal cancer. *J Natl Cancer Inst* 2001; **93**: 501–515.
9. Turner NJ, Haward RA, Mulley GP *et al*. Cancer in old age—is it inadequately investigated and treated? *BMJ* 1999; **319**: 309–312.
10. Montgomery (Appellant) v Lanarkshire Health Board (Respondent), (2015).
11. Habr-Gama A, Perez R, Proscurshim I *et al*. Complete clinical response after neoadjuvant chemoradiation for distal rectal cancer. *Surg Oncol Clin N Am* 2010; **19**: 829–845.
12. Winde G, Nottberg H, Keller R *et al*. Surgical cure for early rectal carcinomas (T1). Transanal endoscopic microsurgery vs. anterior resection. *Dis Colon Rectum* 1996; **39**: 969–976.
13. Sgourakis G, Lanitis S, Gockel I *et al*. Transanal endoscopic microsurgery for T1 and T2 rectal cancers: a meta-analysis and meta-regression analysis of outcomes. *Am Surg* 2011; **77**: 761–772.
14. Struthers R, Erasmus P, Holmes K *et al*. Assessing fitness for surgery: a comparison of questionnaire, incremental shuttle walk, and cardiopulmonary exercise testing in general surgical patients. *Br J Anaesth* 2008; **101**: 774–780.
15. Older P, Hall A, Hader R. Cardiopulmonary exercise testing as a screening test for perioperative management of major surgery in the elderly. *Chest* 1999; **116**: 355–362.
16. Fried LP, Tangen CM, Walston J *et al*. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; **56**: M146–156.
17. Farhat JS, Velanovich V, Falvo AJ *et al*. Are the frail destined to fail? Frailty index as predictor of surgical morbidity and mortality in the elderly. *J Trauma Acute Care Surg* 2012; **72**: 1526–1530; discussion 1530–1521.
18. Makary MA, Segev DL, Pronovost PJ *et al*. Frailty as a predictor of surgical outcomes in older patients. *J Am Coll Surg* 2010; **210**: 901–908.
19. Stuck AE, Siu AL, Wieland GD *et al*. Comprehensive geriatric assessment: a meta-analysis of controlled trials. *Lancet* 1993; **342**: 1032–1036.
20. Harari D, Hopper A, Dhisi J *et al*. Proactive care of older people undergoing surgery ('POPS'): designing, embedding, evaluating and funding a comprehensive geriatric assessment service for older elective surgical patients. *Age Ageing* 2007; **36**: 190–196.
21. Clinical Outcomes of Surgical Therapy Study Group. A comparison of laparoscopically assisted and open colectomy for colon cancer. *N Engl J Med* 2004; **350**: 2050–2059.
22. Anderson C, Uman G, Pigazzi A. Oncologic outcomes of laparoscopic surgery for rectal cancer: a systematic review and meta-analysis of the literature. *Eur J Surg Oncol* 2008; **34**: 1135–1142.
23. Colon Cancer Laparoscopic or Open Resection Study Group, Buunen M, Veldkamp R *et al*. Survival after laparoscopic surgery versus open surgery for colon cancer: long-term outcome of a randomised clinical trial. *Lancet Oncol* 2009; **10**: 44–52.
24. Spanjersberg WR, Reurings J, Keus F *et al*. Fast track surgery versus conventional recovery strategies for colorectal surgery. *Cochrane Database Syst Rev* 2011: CD007635.