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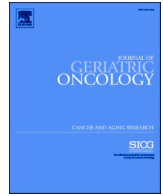
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Research Paper

Emergency presentation of colorectal cancer in older adults: A retrospective cohort analysis

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ABSTRACT

Introduction: Adults aged 70 years and over account for almost 60% of colorectal cancer (CRC) diagnoses in the United Kingdom. Whilst emergency presentation of CRC is known to be associated with poorer outcomes across all ages, older adults are less likely to be treated with curative intent and have poorer overall survival (OS). We aimed to investigate whether presentation, management, or outcome differed in older (≥ 70 years) versus younger (< 70 years) adults in our population.

Materials and Methods: The electronic records of patients diagnosed with CRC within the period 2016 to 2019 in National Health Service (NHS) Tayside, Scotland were retrospectively analysed. Patients were grouped by age (< 70 years and ≥ 70 years). Demographics were compared by Chi-squared or *t*-test, and Kaplan-Meier and Cox proportional hazard regression were used for survival analyses.

Results: In total, 1245 patients were diagnosed with CRC (median age 71 years, range 20–98). Of these, 215 patients (17.3%) presented emergently and were included in the analysis. Older adults accounted for 65.1% ($n = 140$) of emergency presentations. Older adults were less likely to present with classical symptoms of CRC (80.0% vs 90.7%, $p = 0.04$) and more likely to present via the medical assessment unit (46.4% vs 30.7%, $p = 0.03$). Additionally, older adults were less likely to receive a histological diagnosis of CRC (71.4% vs 97.3%, $p < 0.001$) or have complete staging investigations performed (78.6% vs 96.0%, $p < 0.001$). Fewer older adults underwent surgical management (55.0% vs 86.7%, $p < 0.001$) and fewer were treated with chemotherapy (14.3% vs 69.3%, $p < 0.001$). Whilst older adults had poorer median OS than those aged < 70 years (12.0 vs 34.4 months, $p < 0.001$), multivariate Cox proportional hazards regression demonstrated that higher stage (stage III hazard ratio [HR] 2.7, 95% confidence interval [CI] 1.6–4.7, stage IV HR 16.7, 95% CI 9.7–28.8, incomplete HR 8.2, 95% CI 4.6–14.7) and not receiving chemotherapy (HR 2.6, 95% CI 1.7–4.0) were associated with poorer survival, whereas age and sex were not.

Discussion: Emergency presentation of colorectal cancer was more common in older adults. Older adults were more likely to present atypically, less likely to have completed staging, and had lower rates of intervention, which were associated with poorer survival outcome.

1. Introduction

Older adults (those aged 70 years and over) account for almost 60% of colorectal cancer (CRC) diagnoses in the United Kingdom (UK) [1]. Around 15–30% of all CRC cases are diagnosed as a result of an emergency attendance to hospital [2]. A multitude of factors influence emergency presentation of malignancy, often in combination. These can

be considered as patient factors (including older age, female sex, deprivation, minority ethnicity, co-morbidities, and health-seeking behaviours), tumour characteristics (biology, stage, and site) and health service factors (such as missed diagnosis or system delays) [3–6].

Ageing is a variable process and chronological age is not always representative of physiological fitness and reserve. However, survival is known to be poorer for older adults presenting emergently and they are

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less likely to be treated with curative intent. This was described in a large systematic review incorporating 34,194 patients in 2000 [7]. Similar findings have been reported over the subsequent two decades, including the observation that older patients are less likely to receive chemotherapy [3,8].

We aimed to explore the issue of emergency presentation of CRC in our local population, with a particular focus on older adults. Specifically, we aimed to investigate whether presentation, management, or outcome differed in older versus younger adults.

2. Methods

All patients diagnosed with CRC between January 2016 and December 2019 were identified from the local Cancer Registry for NHS Tayside (Scotland, UK), which serves a population of approximately 400,000 people. Patients with CRC whose diagnosis was a direct result of an emergency presentation to secondary care (defined, using the National Quality Performance Indicator [QPI] methodology [9], as presentation via the Emergency Department or referral from primary care for same-day assessment by medicine or surgery) were identified and included in the main analysis. Electronic patient records were retrospectively interrogated for information related to the emergency presentation (precipitant, symptoms, mode of presentation, blood test results), diagnosis, and staging of CRC, treatment, and survival.

As 70 years of age is the most commonly used threshold to define ‘older adults’ in oncological research, patients were grouped by age (<70 years and ≥70 years) at presentation [10]. Demographics were compared by Chi-squared or *t*-test, as appropriate. Kaplan-Meier and Cox proportional hazard regression were used for survival analysis. Statistical analysis was performed using R (version 4.3.1, 2023).

Caldicott Guardian approval was granted by NHS Tayside for use of patient-identifiable data for research purposes.

3. Results

During the study period, 1,245 patients were diagnosed with CRC, with a median age of 71 years (range 20–98). Of these, 215 patients (17.3%) presented emergently and were included in the analysis. Patients presenting emergently were significantly older (median age 74 vs 70 years, *p* < 0.001). Older adults accounted for 65.1% (*n* = 140) of emergency presentations. Sex and tumour-sidedness were similar between age groups (male sex: 50.7% of older adults vs 56.0%, *p* = 0.55, right-sided tumour: 55.0% for older adults vs 50.7%, *p* = 0.64) (Table 1).

3.1. Presentation

Emergency presentation was generally precipitated by symptoms, although one in eight patients were referred for same-day assessment due to abnormal blood results (significant anaemia), imaging (impending bowel obstruction), or examination findings (palpable masses).

Older adults were less likely than younger counterparts to present with classical symptoms of CRC such as abdominal pain, rectal bleeding, change in bowel habit, symptomatic anaemia, or bowel obstruction (80.0% vs 90.7%, *p* = 0.04). Instead, older adults presented acutely with other symptoms including those related to geriatric domains such as increasing frailty and delirium. Of note, older adults were more likely to present via the medical assessment unit, likely due to their differing symptomology (46.4% vs 30.7%, *p* = 0.03). At presentation, older adults were also more likely to demonstrate anaemia (though not microcytosis), hypoalbuminaemia (albumin <35 g/L), and renal dysfunction than those under 70 years of age (Table 1).

3.2. Diagnosis and Staging

Older adults were less likely to receive a histological diagnosis of

Table 1

Demographics, presentation, diagnosis and staging by age group. *Classical symptoms of CRC: abdominal pain, rectal bleeding, change in bowel habit, symptomatic anaemia or bowel obstruction. +Other: Chest pain, infective symptoms, leg swelling. MCV = mean corpuscular volume, CRC = colorectal cancer, Hb = hemoglobin, TNM = tumour, node, metastasis.

	Patients aged ≥ 70 (<i>n</i> = 140)	Patients aged < 70 (<i>n</i> = 75)	<i>p</i> -value
Age (years)			
Mean (SD)	80.4 (6.46)	58.8 (9.23)	
Median [Min, Max]	81 [70, 96]	62 [29, 69]	
Sex, <i>n</i> (%)			
Female	69 (49.3%)	33 (44.0%)	0.55
Male	71 (50.7%)	42 (56.0%)	
Tumour side, <i>n</i> (%)			
Left	63 (45.0%)	37 (49.3%)	0.64
Right	77 (55.0%)	38 (50.7%)	
Precipitant of emergency presentation, <i>n</i> (%)			
Symptoms	121 (86.4%)	67 (89.3%)	0.60
Blood test result	10 (7.1%)	6 (8.0%)	
Imaging result	7 (5.0%)	1 (1.3%)	
Examination findings	2 (1.4%)	1 (1.3%)	
Primary symptom, <i>n</i> (%)			
Classical symptoms of CRC*	112 (80.0%)	68 (90.7%)	0.11
Frailty or confusion	12 (8.6%)	2 (2.7%)	
Other ⁺	16 (11.4%)	5 (6.7%)	
Route of presentation, <i>n</i> (%)			
Emergency department	24 (17.1%)	11 (14.7%)	0.03
Surgical assessment unit	51 (36.4%)	41 (54.7%)	
Medical assessment unit	65 (46.4%)	23 (30.7%)	
Blood results at presentation, median [min, max]			
Hb (g/L)	119 [42, 169]	127 [51, 182]	0.007
MCV (fL)	88.2 [58.8, 115]	86.6 [57.5, 108]	0.28
Albumin (g/L)	32 [12, 44]	35 [11, 42]	<0.001
Urea (mmol/L)	7.65 [2.9, 26.9]	5.50 [1.9, 15.0]	<0.001
Creatinine (µmol/L)	80 [9, 366]	69 [35, 124]	<0.001
Histological diagnosis, <i>n</i> (%)			
Yes	100 (71.4%)	73 (97.3%)	<0.001
No	40 (28.6%)	2 (2.7%)	
TNM stage, <i>n</i> (%)			
1	4 (2.9%)	2 (2.7%)	0.04
2 A	22 (15.7%)	13 (17.3%)	
2B	12 (8.6%)	7 (9.3%)	
3 A	14 (10.0%)	12 (16.0%)	
3B	11 (7.9%)	11 (14.7%)	
4	48 (34.3%)	27 (36.0%)	
Incomplete	29 (20.7%)	3 (4.0%)	

CRC (71.4% vs 97.3%, *p* < 0.001), with diagnosis based on imaging in over a quarter of cases. In all, 29.3% of older adults and 30.7% of those <70 were discharged from their emergency presentation with planned outpatient investigation for suspected CRC. The length of time between emergency presentation and diagnosis varied considerably (range 0–305 days), but overall was similar between groups (median 4 days for older adults vs 3 days for those <70 years of age).

Older adults were much less likely to have complete staging investigations performed (79.3% vs 96.0%, *p* = 0.002), primarily due to lack of surgical specimens for histology leaving nodal status unknown.

For those who were staged, the distribution was similar between groups (Supplementary Table S1). Around one-third of all patients presented with stage IV disease (34.3% of older adults and 36.0% of those <70 years of age).

3.3. Management

Overall, fewer older adults underwent surgical intervention (55.0% vs 86.7%, $p < 0.001$) and fewer were treated with chemotherapy (14.3% vs 69.3%, $p < 0.001$) (Table 2). Older adults were less likely to be treated with curative intent (43.6% vs 61.3%, $p = 0.02$), and less likely to receive adjuvant chemotherapy (16.4% vs 65.2% of those treated curatively, $p < 0.001$). Where treated with palliative intent, chemotherapy was used in 12.7% of older adults and 75.9% of younger adults ($p < 0.001$). A further 12 older adults (15.2%) and six younger adults (20.7%) underwent palliative surgical procedures without palliative chemotherapy. Among older adults, 40.7% received best supportive care only, compared with just one patient (1.3%) <70 years of age ($p < 0.001$). Post-operative length of stay was longer in older adults but did not meet significance (15 vs 11 days, $p = 0.14$). Where chemotherapy was used, older adults were more likely to be prescribed monotherapy (65.0% v 25.0%, $p < 0.001$). Demographics, diagnosis, staging, and chemotherapy use by treatment intent group can be found in Supplementary Table 2.

3.4. Prognosis

Older adults had poorer median overall survival (OS) than those aged <70 years (12.0 vs 34.4 months, $p < 0.001$) (Fig. 1A). Univariate and multivariate Cox proportional hazards regression was performed to assess the association of age, sex, stage, and chemotherapy on survival (Fig. 1B and Supplementary Table 3). Although associated with poorer survival on univariate analysis, age did not meet significance on multivariate analysis (age ≥ 70 years hazard ratio [HR] 1.4, 95% confidence interval [CI] 0.93–2.1, $p = 0.10$). However, higher stage (stage III HR 2.7, 95% CI 1.6–4.7, stage IV HR 16.7, 95% CI 9.7–28.8, incomplete HR 8.2, 95% CI 4.6–14.7) and not receiving chemotherapy (HR 2.6, 95% CI 1.7–4.0) were strongly associated with poorer survival. Univariate and multivariate analysis was also performed within groups; for older adults both higher stage and not receiving chemotherapy were

Table 2
Treatment intent and management by age group.

	Patients aged ≥ 70 (n = 140)	Patients aged < 70 (n = 75)	p-value
Treatment intent, n (%)			
Curative	61 (43.6%)	46 (61.3%)	0.02
Palliative	79 (56.4%)	29 (38.7%)	
Palliative chemotherapy	10 (7.1%)	22 (29.3%)	<0.001
Palliative surgery only	12 (8.6%)	6 (8.0%)	
Best supportive care	57 (40.7%)	1 (1.3%)	
Surgical management, n (%)			
Yes	77 (55.0%)	65 (86.7%)	<0.001
No	63 (45.0%)	10 (13.3%)	
Chemotherapy, n (%)			
Adjuvant	10 (7.1%)	30 (40.0%)	<0.001
Palliative	10 (7.1%)	22 (29.3%)	
None	120 (85.7%)	23 (30.7%)	
Chemotherapy regime, n (%)			
Combination	5 (3.6%)	38 (50.7%)	<0.001
Single therapy	13 (9.3%)	13 (17.3%)	
Unknown	2 (1.4%)	1 (1.3%)	

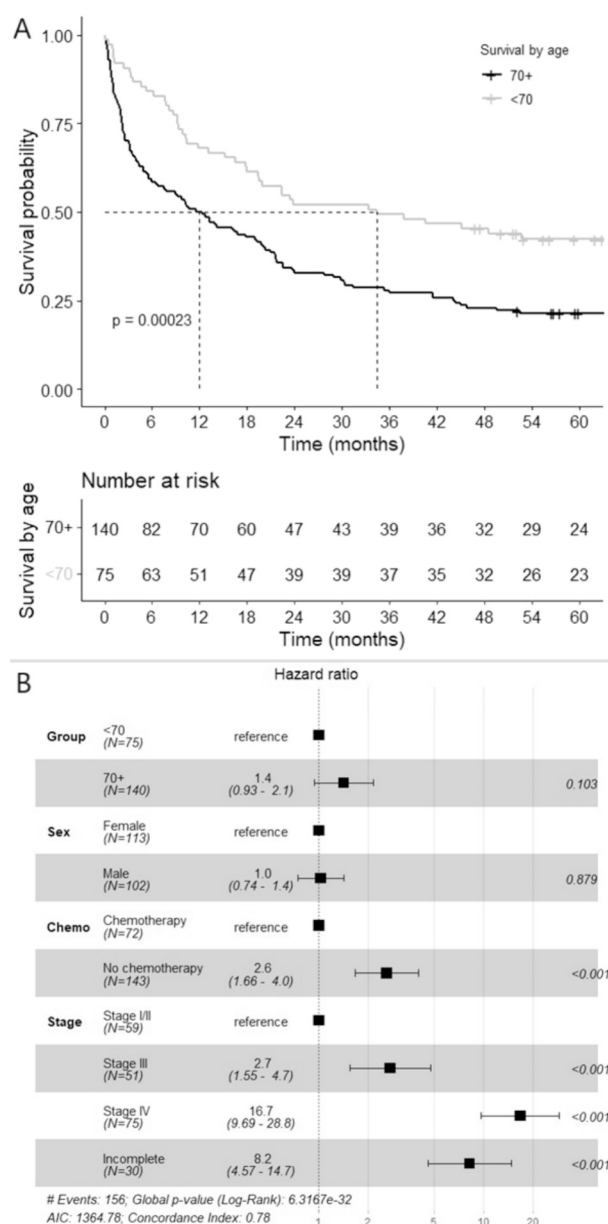


Fig. 1. A) Kaplan-Meier plot demonstrating overall survival by age group. B) Cox proportional hazard regression demonstrating hazard ratios for age group, sex, chemotherapy use, and stage.

associated with poorer survival, whereas for younger adults only stage was significant (Supplementary Tables 4 and 5 and Fig. S1). The poorer OS observed in older adults may therefore be driven by stage of disease at diagnosis and subsequent management, rather than purely by age.

For patients treated with curative intent, OS tended to be poorer for older adults – particularly at five years – but did not meet significance; one-year survival was 80.3% for older adults vs 89.1% for <70 years ($p = 0.22$), and five-year survival was 49.2% for older adults vs 65.2% for <70 years ($p = 0.10$). Fig. 2 shows OS by age group and treatment intent. Across the whole cohort, OS was calculated for patients undergoing palliative treatment; median OS was 10.3 months with palliative chemotherapy, 3.2 months with palliative surgery, and 2.5 months with best supportive care (Fig. 3). A considerable number of patients died during their emergency admission – thirteen older adults (9.3%) and three adults under 70 years of age (4.0%).

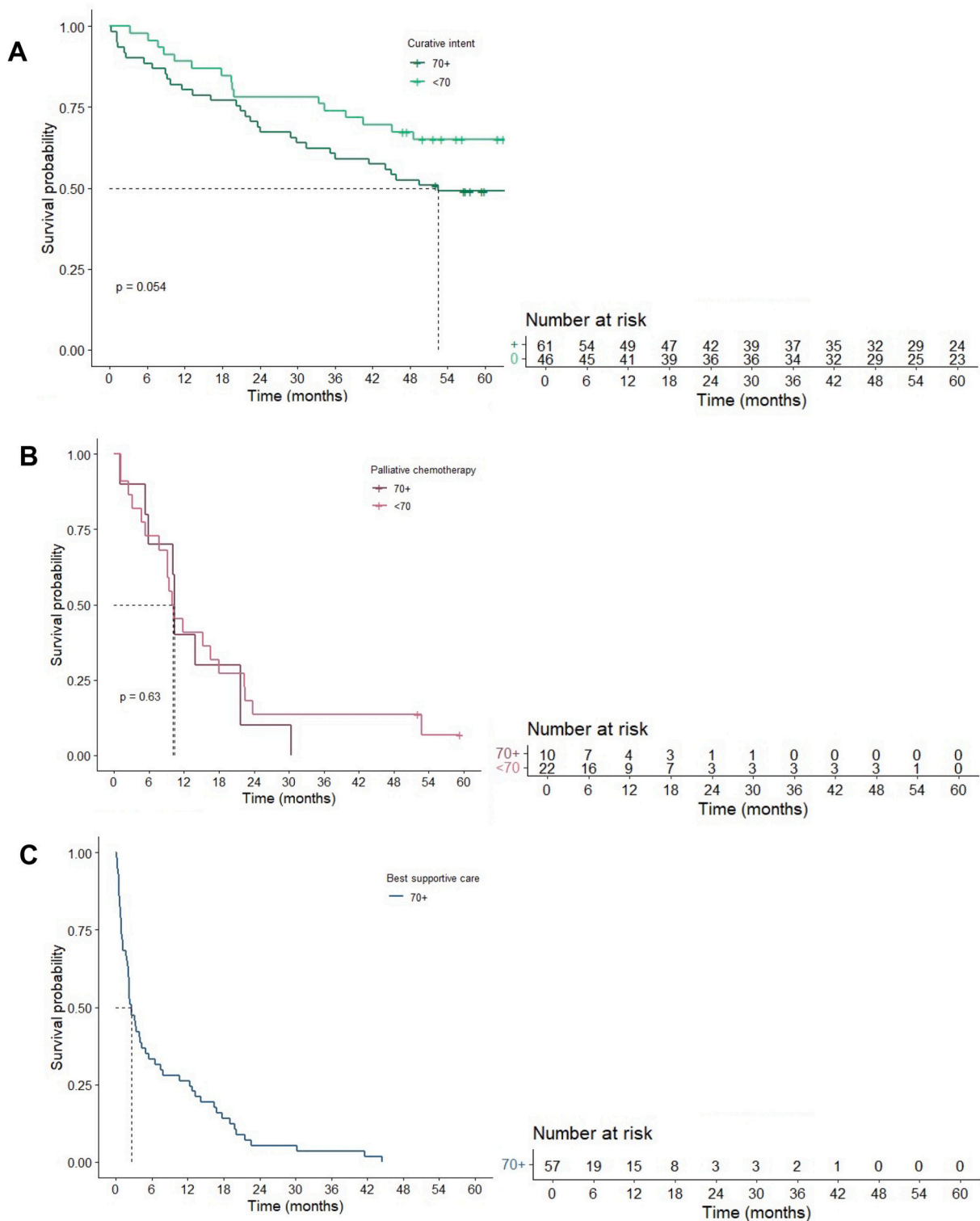


Fig. 2. Kaplan-Meier plots demonstrating overall survival by age group and treatment intent: A) Curative, B) Palliative chemotherapy, C) Best supportive care (≥70 years only, only one patient <70 years received best supportive care and was excluded).

4. Discussion

Colorectal cancer is a disease associated with older age, with emergency presentation as a known risk factor for poorer outcomes. In this study, we sought to investigate the association between older age and CRC presentation, management, and outcomes.

Within our local population 17.3% of CRCs presented as an

emergency, in keeping with expected values [2]. The clinical phenotype of the patients – including age, sex distribution, stage at presentation, and tumour sidedness – was also in keeping with national data [11]. The majority of emergency presentations were older adults – 65.1% were aged 70 and older. Importantly, one in five older adults did not present with classical symptoms of colorectal cancer, likely contributing to the higher proportion of patients (46.4%) presenting via the medical

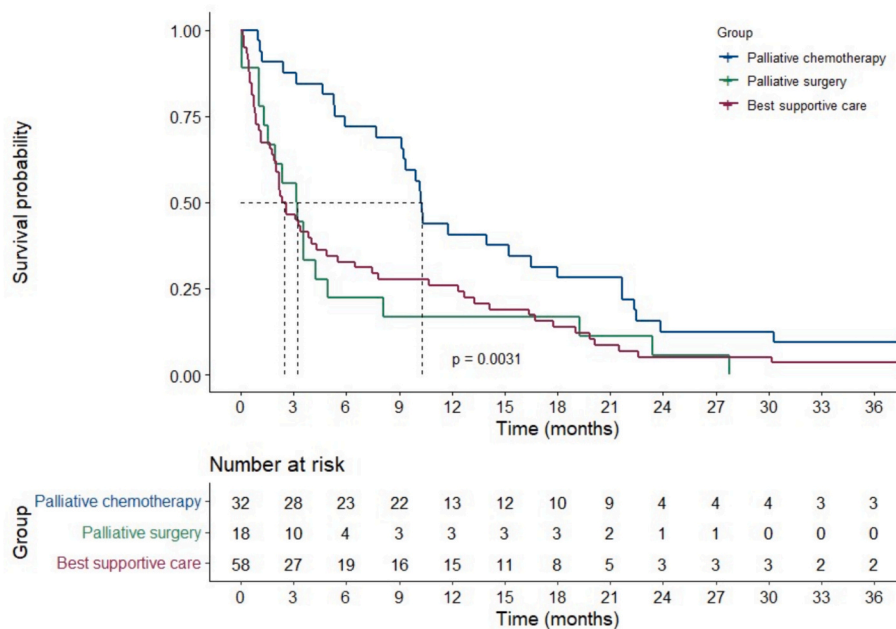


Fig. 3. Kaplan-Meier plot demonstrating overall survival of individuals who received palliative chemotherapy versus those who had palliative surgery only or best supportive care.

assessment pathway. Esteva et al. also demonstrated differing symptomology with age in a Spanish cohort; older adults in their study were less likely to present with abdominal pain or rectal bleeding and more likely to present with ‘general symptoms’ such as weight loss or fatigue [3]. Whilst other studies have not differentiated between medical and surgical admission pathway attendance [3,12], our work indicates that physicians should consider malignancy, including CRC, in the differential for older adults presenting with non-specific symptoms.

Following presentation, we found that older adults were less likely to have a histologically confirmed diagnosis and were less likely to receive full staging investigations. Despite “most valid basis of diagnosis” being included in the Scottish CRC QPI dataset, it is challenging to find recently published data on the proportion of CRC diagnoses confirmed by histology. However, age was noted to be associated with a lower rate of histological confirmation in Scottish data collated between 1992 and 1996 (85.6% for patients aged ≥ 75 vs 93.5% for those < 75) [13]. The proportion of patients with histological confirmation in our study was lower again (80.5% overall), likely reflecting the higher stage at diagnosis in our cohort of emergently presenting CRC. Clearly this issue persists and warrants further investigation – particularly given that this data is already being collected nationally.

Time between presentation and diagnosis varied widely in our study, primarily due to whether the individual was diagnosed during their emergency admission or were discharged with planned outpatient investigation. Weller et al.’s study investigating CRC diagnostic time intervals across six countries reported supplementary data regarding time to diagnosis for younger (< 50 years) and older (≥ 75 years) individuals compared to a reference group of 50–74 year olds [14]. Older adults had significantly longer diagnostic intervals for non-emergency presentation but tended to have a shorter diagnostic interval than younger patients when presenting emergently (though this was only statistically significant for individuals with stage I disease). Following emergency presentation, diagnostic intervals shortened with increasing stage across both younger and older patients [14]. Whilst this was not discussed by the authors, one presumes it is again due to higher rates of inpatient rather than outpatient investigations in older adults and those with advanced disease.

Regarding staging, review of the Danish Cancer Registry reveals similar results to this study, with the proportion of incomplete staging

rising with age. As observed in our cohort, nodal staging was least likely to be complete [15]. The association between older age and incomplete staging was also observed in an English cohort of 21,522 patients with CRC, and was found to be independent of comorbid state [16]. There are a number of potential reasons for this, such as ageism, perception of frailty, and health system bias against older adults [17]. This may indicate inequality in oncological assessment of older adults and demonstrates a need for comprehensive geriatric assessment to identify patients suitable for investigation and intervention [16,18]. This has been highlighted in the recent Royal College of Radiologists guideline on assessment and management of frailty in older adults with cancer [19].

In our study, 55.0% of older patients underwent surgical intervention, compared with 86.7% of those < 70 years. Our results are comparable to other studies, showing lower rates of surgical intervention and administration of chemotherapy and resultant poorer survival in older patients [3,8,12]. Older adults had a longer median post-operative length of stay than those under the age of 70 years (15 vs 11 days) in our study although this did not meet significance, likely due to the small sub-group sizes. However, both emergency surgery and older age have previously been shown to increase the likelihood of prolonged admission in larger studies [20,21]. Where suitable for curative resection, Webster et al. observed no difference in one- or three-year survival between older (defined as ≥ 75 years) and younger patients, even with lower rates of adjuvant chemotherapy in the older group [12]. Considering the differing age thresholds and longer follow-up in our study, our findings are similar. Investigation of the use of chemotherapy in frail and older adults with CRC is the aim of several trials, such as FOCUS2 (completed) in the advanced setting, FOXTROT2 (ongoing) in the neo-adjuvant setting, and PRODIGE 34 - ADAGE (ongoing) for adjuvant chemotherapy [22–24]. The ADAGE preliminary tolerance data shows that older and/or frailer adults are less likely to commence adjuvant chemotherapy, less able to tolerate treatment toxicity, and more like to cease treatment early [22].

In the palliative setting, median OS (10.3 months with palliative chemotherapy) was similar to previously published data from trials including older adults, such as FOCUS2 [24]. Both our study and that performed by Webster et al. showed that a substantial proportion of patients received best supportive care only (27.0% and 26.4%, respectively) [12]. This is higher than national data would suggest; national

audit data for 2020–2021 reports that only 11.6% of patients presenting emergently received no cancer treatment [11]. The explanation for this is unclear but may relate to differences in clinical practice or reporting.

We acknowledge that our study has some limitations. Firstly, data collection was retrospective and therefore data was not complete for all patients. We were unable to determine if death was cancer-related or from another cause. Additionally, there is no standardised definition of ‘emergency presentation’ of CRC or absolute consensus on age threshold to define ‘older adults’ in the literature. However, we have used definitions approved by reputable organisations, namely, the European Society of Medical Oncology and Public Health Scotland. Finally, the number of included patients from a geographically broad area of Scotland adds strength to the study.

In conclusion, within our population, emergency presentation of colorectal cancer was more common in older adults. Older adults were more likely to present atypically, less likely to have completed staging, and had lower rates of intervention, which contributed to poorer survival outcome.

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CRediT authorship contribution statement

Jennifer H. Nobes: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Mark A. Baxter:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Craig Mowat:** Writing – review & editing, Supervision, Conceptualization.

Declaration of Competing Interest

Dr. Baxter reports personal fees and other from Ipsen, personal fees from Astra Zeneca, personal fees and other from Servier, personal fees from Bristol Myers Squibb, outside the submitted work.

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Appendix A. Supplementary Data

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