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Comparison of Selected Older and Younger Patients Regarding Optimal Surgical Treatment of Colorectal Cancer: A Prospective Cohort Study

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Abstract. *Background/Aim: Current evidence regarding the optimal management of older colorectal cancer patients, is conflicting. Functional deficits impact long-term survival prognosis, while frailty often results to optimal treatment postponement. Thus, the characteristics of this subgroup combined with treatment deviations further perplex optimal oncological management. The study aim was to compare survival and optimal surgery rates between older and younger colorectal cancer patients. Patients and Methods: This study was designed as a prospective cohort. All adult (≥18 years) colorectal cancer patients operated, during the 2016-2020 period, in the Department of Surgery, University Hospital of Larissa, were considered as eligible. The primary endpoint of the study was the difference in terms of the overall survival between older (>70 year) and younger (<70 years) colorectal cancer patients. Results: Overall, 166 patients (60 younger and 106 older) were enrolled. Although the older subgroup displayed a higher rate (p=0.007) of ASA II and ASA III patients, mean CCI scores were comparable (p=0.384). The two subgroups were similar in terms of performed operations (p=0.140). No delay in surgery was noted. Most operations were performed using an open approach (open: 57.8% vs. laparoscopic: 42.2%), under an elective status (elective: 91% vs. emergency: 1.8%). There was no difference in terms of overall complications rate (p=0.859). Overall survival was similar (p=0.227) between the older and younger subgroups (25.68 vs. 28.48 months). Conclusion: Older operated patients did not differ from their younger counterparts with regard to their overall survival. Due to several study limitations, further trials are required to confirm these findings.*

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Colorectal cancer is among the most common gastrointestinal malignancies. Current epidemiologic studies confirm the stabilization or the decrease of standardized incidence and mortality rates in high income countries, while a considerable increase in early-onset colorectal cancer is, also, noted (1, 2). Furthermore, it is estimated that, over 300,000 new cases per year are diagnosed in Europe alone, while the pooled 5-year survival rate is approximately 65% (2-5). Additionally, almost 60% of these patients are older than 70 years old, with considerable comorbidities and physical impairments (3-5).

However, older patients (>65 years of age) are a very heterogeneous group, with notable deviations in terms of fitness and frailty (6-11). More specifically, the presence of underlying functional and mobility deficits combined with suboptimal nutritional status and ageism impact the prognosis of such patients (12-14). Therefore, a formal geriatric assessment with validated tools, generally provides more accurate classification, compared to a simple age cut-off point (12-15). These patients have been, traditionally, undertreated, receiving in many cases suboptimal oncological operations.

Additionally, due to the accompanying comorbidities and reduced survival expectancy, these patients are systematically excluded from clinical trials (6-11). Moreover, besides strict inclusion criteria, the lack of family support and the surgeons' prejudice for increased risk of morbidity, led to a systematic under-representation of these patients in colorectal cancer studies (13, 14). However, these disparities

are quite problematic since older patients have the highest rates of malignancies, alongside major socioeconomic obstacles (13, 14).

Surgical resection alongside perioperative therapy is the gold standard approach in colorectal cancer (7, 9-11, 16-18). However, radical resections are associated with a considerable morbidity and mortality burden. Thus, especially in older patients, frailty, and physical reserves limitations, often lead to the postponement or deviations from the optimal treatment (7, 9-11, 16-18).

Current evidence regarding the optimal management of older colorectal cancer patients, is still a matter of controversy (19-24). More specifically, initial cohorts suggested that older patients display a higher risk of perioperative complications, whereas recent studies reported that optimal oncological resections can be safely performed in this age subgroup (19-24). The significance of these is that optimal management of colorectal cancer in older patients has a direct impact on the oncological outcomes, including survival and recurrence.

Therefore, the aim of this prospective study was to compare the differences between older and younger colorectal cancer patients in terms of survival and the delivery of optimal surgical treatment.

Patients and Methods

Study endpoints. The primary endpoint of the study was comparison of the older (>70 year) and younger (<70 years) patient subgroups in terms of overall survival (OS) (25). Secondary endpoints included optimal surgery rates and OS comparisons based on optimal treatment and the interaction of optimal and age subgroups.

Optimal treatment was defined as the operation that allowed complete oncological clearance based on tumor location and stage. More specifically, for right and left colon cancer that was translated to colectomy adhering to the CME/CVL principles, with adequate resection margins. Similarly optimal treatment for rectal cancer was considered resection based on the TME principles followed by anastomosis when applicable. Any deviation from these principles, or any salvage operation (*e.g.*, bypass procedures or defunctioning stomas) was considered as suboptimal treatment.

Study design. This prospective observational study was conducted at the Department of Surgery, University Hospital of Larissa, Larissa, Greece. All patients submitted to colorectal cancer surgery during the January of 2016 -April of 2020 period, were included in this study. Prior to patient inclusion, the appropriate local ethics committee approval and informed consent were received. The present study results are reported based on the STROBE guidelines (26).

Eligibility criteria. Eligible patients were considered all consecutive adult patients (^{3}18 years), diagnosed with colorectal cancer and operated in our Department during the aforementioned period. The following exclusion criteria were considered: 1) non-adult patients, 2) refusal to participate and provide a signed informed consent, 3) operations performed outside the investigation period, 4) recurrent tumors and 5) patients not submitted or unfit for surgical treatment.

Treatment. All operations were performed by a group of 4 consultant surgeons. All surgeons had previous experience in open and laparoscopic colorectal surgery and had completed the respective learning curves. A standardized surgical technique was used in all cases. Dissection was performed with an energy source.

Data collection. Data regarding demographics [age, sex, American Society of Anesthesiologists -ASA score, Eastern Cooperative Oncology Group (ECOG) status, comorbidities, and Charlson Comorbidities Index (CCI)], tumor characteristics (TNM classification and tumor location) and operative and perioperative treatment outcomes (resection type, surgery delay, operation status, surgical approach, additional resections, and perioperative therapy) were recorded. Moreover, all perioperative adverse events, readmission and reoperation rates were recorded. Patient characteristics were retrieved from institutional databases, whereas morbidity and survival data were recorded during follow-up. The latter included scheduled outpatient visits and telephonic call evaluations.

Statistical analysis. Prior to statistical analyses, a Kolmogorov-Smirnoff normality test was performed. Chi-square test was applied in categorical variables, whereas a *t*-test and a Mann-Whitney *U*-test was used for normal and non-normal continuous outcomes, respectively. Pearson's correlation coefficient was also introduced for association analyses. Survival analysis was based on the Kaplan-Meier curves and the Log-Rank test. Continuous data were provided in the form of Mean (Standard Deviation) or Median (Interquartile Range) on the basis of normality results, while categorical variables were reported as N (Percentage). Significance was considered at the level of $P<0.05$. Statistical analyses were completed by SPSS v.21 software.

Ethics approval. This study was performed in line with the principles of the Declaration of Helsinki.

Informed consent. Informed consent was obtained from all individual participants included in the study. Patients signed informed consent regarding publishing their data and photographs.

Results

Patient characteristics. Overall, 166 patients were enrolled in the study (Table I). More specifically, 60 (36.1%) younger and 106 (63.9%) older patients were submitted to colorectal cancer surgery. Mean age in the former and the latter group was 62.27 and 77.8 years, respectively. There was no difference in terms of mean weight and sex allocation. Even though the older subgroup displayed a higher rate (p=0.007) of ASA II (56.7% *vs*. 61.3%) and ASA III (0% *vs*. 11.3%) patients, mean CCI scores were comparable (p=0.384) between the two groups. Older patients were not associated with increased rates of high ECOG (p=0.384) status. Similarly, besides coronary heart disease (1.7% *vs*. 12.3%), overall and specific comorbidities rates did not differ among the older and younger patients.

Treatment characteristics. In Table II, a summary of the TNM classification characteristics is displayed. In total, 35

Table I. *Patient characteristics and comorbidities*.

	Younger	Older	Total	*p*-Value
N	60	106	166	
	36.1%	63.9%	100.0%	
Age	62.27 (5.3)	77.8 (4.8)	72.19 (9)	**<0.001**
Weight	70.6 (8.2)	72.5 (9.4)	71.81 (9)	0.192
Sex				
Male	32	59	91	0.772
	53.3%	55.7%	54.8%	
Female	28	47	75	
	46.7%	44.3%	45.2%	
ASA				
I	26	29	55	**0.007**
	43.3%	27.4%	33.1%	
II	34	65	99	
	56.7%	61.3%	59.6%	
III	0	12	12	
	0.0%	11.3%	7.2%	
ECOG				
0	23	27	50	0.074
	38.3%	25.5%	30.1%	
1	19	34	53	
	31.7%	32.1%	31.9%	
2	15	26	41	
	25.0%	24.5%	24.7%	
3	3	19	22	
	5.0%	17.9%	13.3%	
CCI	2.67 (1.46)	2.88 (1.5)	2.8 (1.49)	0.384
Comorbidities				
Total	58	99	157	0.371
	96.7%	93.4%	94.6%	
Arterial hypertension	27	51	78	0.699
	45.0%	48.1%	47.0%	
Coronary heart disease	1	13	14	**0.018**
	1.7%	12.3%	8.4%	
Atrial fibrillation	4	12	16	0.329
	6.7%	11.3%	9.6%	
Diabetes mellitus	10	21	31	0.617
	16.7%	19.8%	18.7%	
COPD	8	17	25	0.640
	13.3%	16.0%	15.1%	
Thyroid disease	2	9	11	0.199
	3.3%	8.5%	6.6%	
Benign prostatic hyperplasia	1	6	7	0.219
	1.7%	5.7%	4.2%	
Renal failure	2	8	10	0.273
	3.3%	7.5%	6.0%	
Hepatitis	1	2	3	0.919
	1.7%	1.9%	1.8%	
Stroke	1	8	9	0.108
	1.7%	7.5%	5.4%	
Psychiatric disease	8	6	14	0.087
	13.3%	5.7%	8.4%	
Malignancy history	7	5	12	0.097
	11.7%	4.7%	7.2%	
Other	17	27	44	0.688
	28.3%	25.5%	26.5%	

Data are presented as means (standard deviation) and N, percentage. ASA: American Society of Anesthesiologists; ECOG: Eastern Cooperative Oncology Group; CCI: Charlson Comorbidity Index; COPD: chronic obstructive pulmonary disease. Statistically significant *p*-values are shown in bold.

Table II. *Tumor characteristics of included patients.*

	Younger	Older	Total	*p*-Value
N	60	106	166	
	36.1%	63.9%	100.0%	
T				
0	0	1	1	0.818
	0%	0.9%	0.6%	
1	5	11	16	
	8.3%	10.4%	9.6%	
2	11	16	27	
	18.3%	15.1%	16.3%	
3	20	41	61	
	33.3%	38.7%	36.7%	
4	24	37	61	
	40.0%	34.9%	36.7%	
N				
0	0	4	4	0.309
	0%	3.8%	2.4%	
1	50	84	134	
	83.3%	79.2%	80.7%	
2	10	18	28	
	16.7%	17.0%	16.9%	
M				
0	39	71	110	0.795
	65.0%	67.0%	66.3%	
1	21	35	56	
	35.0%	33.0%	33.7%	
Tumor location				
Cecum/Ascending colon	9	26	35	
	15.0%	24.5%	21.1%	0.469
Transverse colon	5	9	14	
	8.3%	8.5%	8.4%	
Descending colon	22	38	60	
	36.7%	35.8%	36.1%	
Rectum	24	33	57	
	40.0%	31.1%	34.3%	

Data are presented as means (standard deviation) and N, percentage.

cecum/ascending colon, 14 transverse colon, 60 descending colon and 57 rectal were introduced in this study. Moreover, 55 right colectomies, 2 extended right colectomies, 18 left colectomies, 24 sigmoidectomies, 40 low anterior resections, 3 abdominoperineal resections, 6 transverse colostomies, 8 loop ileostomies, 6 Hartmann's procedures, 3 subtotal colectomies and 1 bypass were performed (Table III). There was no significant difference between the two subgroups in terms of the performed operations (p=0.140). Furthermore, there was no delay in surgery. Most of the operations were performed in an open approach (57.8%), under an elective status (91%). Additional resections were implemented in 2.4% of total cases. Additionally, a homogeneous allocation, in terms of neoadjuvant and adjuvant schemes (p=0.138), was recorded. A R0 resection was achieved in 95.5% of cases. Median follow-up for the pooled patient sample was 24 months.

Postoperative outcomes. There was no difference between older and younger patients (18.9% *vs*. 20%) in terms of overall complications rate (p=0.859). The pooled anastomotic leakage rate was 4.8%. Comparable readmission (p=0.67), reoperation (p=0.260) and ICU (p=0.855) admission rates were also noted. There was no difference in any other perioperative adverse event.

Primary endpoint. Regarding the primary outcome, mean survival was 26.69 months. There was no difference (28.48 *vs*. 25.68 months) between the two study arms (p=0.227). Similar were the results from the survival analysis function (Figure 1, Log-Rank test p=0.224).

Secondary endpoints. The optimal surgery rate was similar (p=0.074) between the younger and older subgroups (80% *vs*. 67%). There was no difference in terms of diagnosis to

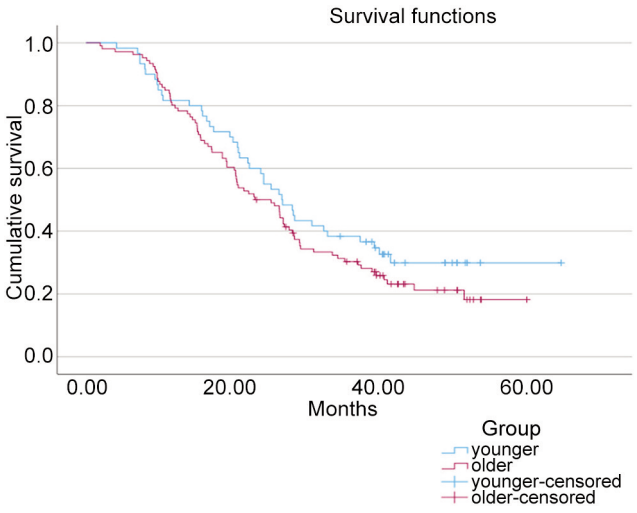

Figure 1. *Overall survival of older and younger patients. Median follow-up was 24 months (range=1-65 months).*

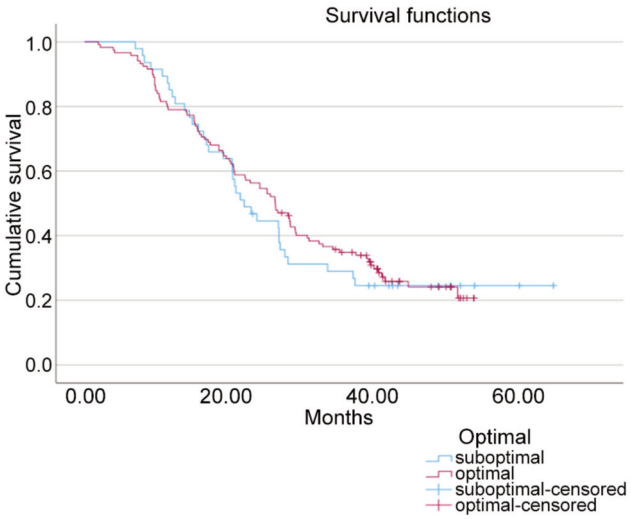

Figure 2. *Overall survival of optimal and suboptimal treatment groups. Median survival was 26.1 vs. 21.9 months, respectively (Log-Rank test p=0.674).*

admission (p=0.973), admission to operation (p=0.893) and diagnosis to operation (p=0.992) time.

Finally, there was no survival discrepancy between the optimal and the suboptimal surgery groups (Figure 2, Log-Rank test p=0.674). Subgroup analyses (older & suboptimal, older & optimal, younger & suboptimal, younger & optimal) did not highlight any statistically significant survival difference (Figure 3, Log-Rank test p=0.467).

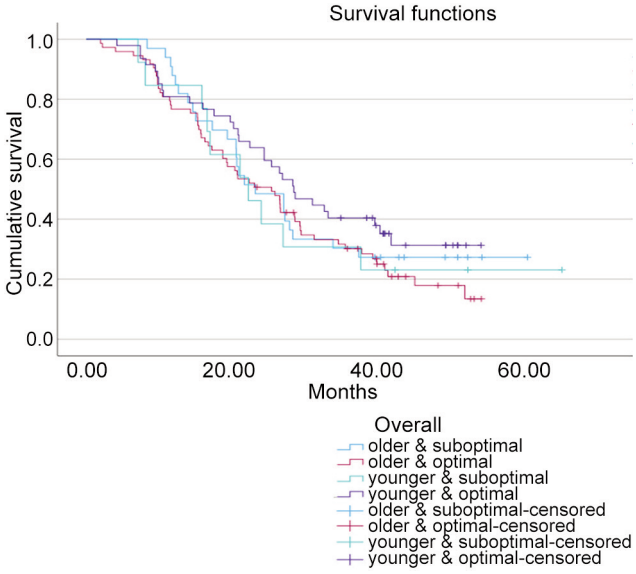

Figure 3. *Comparison of overall survival in the combined subgroups (age & optimal treatment). Median survival of subgroups: older & suboptimal treatment 22.8 months; older & optimal treatment: 25 months; younger & suboptimal treatment: 21.9 months; younger & optimal treatment: 28 months (Log-Rank test p=0.467).*

Discussion

Colorectal cancer is among the most frequently encountered malignancies. Almost 760,000 males and 614,000 females are diagnosed with colorectal cancer every year, worldwide (19). This corresponds to almost 5% of the total population developing a colorectal tumor at least once in their life span (19).

Recent innovations in medicine have allowed an increase in the life expectancy of the Western countries' population. It is estimated that the average life span of the developed nations ranges from 78.6 to 84.2 years, with an increasing trend (27). However, the definition of the term 'older' is still unclear (28). Conventionally, patients aged over 65 years old were regarded as older (28). However, in current literature, definitions up to 75 years old were reported (28-31). Furthermore, recent definition proposals incorporated the loss of functional independence and frailty as an additional differentiation characteristic of elderly (28-31). Based on previous cohorts, we defined the two subgroups of our study by the 70 years age key-point.

Overall, cancer is considered as a disease of the older patients; in terms of colorectal cancer, a parallel tendency of the prevalence rate, with the increasing age is noted (22). For instance, patients aged 60-64 years have, almost, the half incidence of colorectal malignancies, compared to the respective 80-84 years old cases. Based on these and alongside the escalation of the pooled incidence, it becomes apparent that the total number of older patients with colorectal cancer is expected to increase (22).

Table III. *Operative and perioperative treatment characteristics of patients.*

	Younger	Older	Total	*p*-Value
N	60	106	166	
	36.1%	63.9%	100.0%	
Resection				
Right colectomy	16	39	55	0.140
	26.7%	36.8%	33.1%	
Extended right colectomy	0	2	2	
	0.0%	1.9%	1.2%	
Left colectomy	8	10	18	
	13.3%	9.4%	10.8%	
Sigmoidectomy	8	16	24	
	13.3%	15.1%	14.5%	
LAR	17	23	40	
	28.3%	21.7%	24.1%	
APR	3	0	3	
	5.0%	0.0%	1.8%	
Transverse colostomy	2	4	6	
	3.3%	3.8%	3.6%	
Loop ileostomy	4	4	8	
	6.7%	3.8%	4.8%	
Hartmann's	0	6	6	
	0.0%	5.7%	3.6%	
Subtotal colectomy	2	1	3	
	3.3%	0.9%	1.8%	
Bypass	0	1	1	
	0.0%	0.9%	0.6%	
Complications				
Overall	12	20	32	0.859
	20.0%	18.9%	19.3%	
SSI	4	6	10	0.793
	6.7%	5.7%	6%	
Bleeding	1	1	2	0.682
	1.7%	0.9%	1.2%	
Leakage	4	4	8	0.403
	6.7%	3.8%	4.8%	
Pulmonary	0	3	3	0.188
	0.0%	2.8%	1.8%	
Ileus	0	3	3	0.188
	0.0%	2.8%	1.8%	
ICU	2	3	5	0.855
	3.3%	2.8%	3%	
Readmission	2	5	7	0.67
	3.3%	4.7%	4.2%	
Stoma related	1	1	2	0.682
	1.7%	0.9%	1.2%	
Incisional hernia	2	2	4	0.559
	3.3%	1.9%	2.4%	
Reoperation	3	3	5	0.260
	5%	1.9%	3%	
Delay	0	0	0	-
	0%	0%	0%	
Status				
Elective	57	94	151	0.341
	95.0%	88.7%	91.0%	
Semi-elective	2	10	12	
	3.3%	9.4%	7.2%	
Emergency	1	2	3	
	1.7%	1.9%	1.8%	

Table III. *Continued*

Table III. *Continued*

	Younger	Older	Total	*p*-Value
Approach				
Open	32	64	96	0.377
	53.3%	60.4%	57.8%	
Laparoscopic	28	42	70	
	46.7%	39.6%	42.2%	
Additional resection	2	2	4	0.559
	3.3%	1.9%	2.4%	
Resection status				
R0	53	97	150	0.685
	94.6%	96.0%	95.5%	
R1	3	4	7	
	5.4%	4.0%	4.5%	
Perioperative therapy				
None	11	33	44	0.138
	18.3%	31.1%	26.5%	
Adjuvant	32	54	86	
chemotherapy	53.3%	50.9%	51.8%	
Neoadjuvant	13	17	30	
chemo-radiotherapy	21.7%	16.0%	18.1%	
Adjuvant	4	2	6	
chemo-radiotherapy	6.7%	1.9%	3.6%	
Follow pp (months)*	23.5 (23.75)	24 (26)	24 (25)	0.792
Optimal surgery	48	71	119	0.074
	80.0%	67.0%	71.7%	
Diagnosis to admission (days)*	60.5 (38)	62.5 (38)	62 (37.25)	0.973
Admission to operation (days)*	4 (3)	3.5 (3)	4 (3)	0.893
Diagnosis to operation (days)*	65.5 (41.75)	66.5 (38.75)	66 (38.5)	0.992
Survival (months)	28.48 (14.81)	25.68 (13.9)	26.69 (14.28)	0.227

Data are presented as means (standard deviation) and N, percentage. *Non-parametric analysis; presented as Median (interquartile range). LAR: Low anterior resection; APR: abdominal perineal resection; SSI: surgical site infection; ICU: intensive care unit.

A multimodal approach is the current gold standard treatment for colorectal cancer (32). Radical resection combined with neo-adjuvant and adjuvant modalities allowed prolongation of the overall and disease-free survival, while in parallel minimizing the local and distant recurrence rates (32, 33). However, the former, still, remains a controversial issue for older patients, since many cohorts confirmed that age is an independent prognostic factor of postoperative morbidity and mortality (21). More specifically, the increasing burden of systematic comorbidities reduces the physiological reserves, thus jeopardizing the final, postoperative outcome.

Several clinical studies have compared the two age groups in terms of perioperative endpoints. Fiscon *et al*. (34) reported a 24% complications rate in older patients, compared to the respective 8% of their younger counterparts. In the study of Bottino *et al*. (23), although no difference in overall complication rate was noted, older patients were associated with an increased risk for cardiopulmonary adverse events. In our study pooled complications rate was comparable between older and younger patients. Specific postoperative adverse event analyses showed similar results. These findings are in contrast with the results of a recent meta-analysis, where a significant difference in terms of pooled morbidity was found (20). However, Hoshino *et al*. (20) noted that despite statistical significance, the magnitude of difference was quite small. Possible confounders that may affect these results could be the lack of randomization, the absence of reporting standardization and the inherent heterogeneity of patient, tumor, and operation characteristics (20).

During the previous decades an age over 80 years was considered as an exclusion criterium for radical oncological resection (22). Therefore, in these patients, a palliative approach, such as diverting stoma or bypass, was often introduced. However, the advances in preoperative rehabilitation, optimization of comorbidities, intraoperative monitoring and surgical innovations allowed the safe implementation of more extensive resections (22). In our trial, oncological resections were the primarily surgical approach in both groups. Moreover, palliative procedures were performed in a comparable rate, while in parallel we confirmed that the delivery of optimal treatment was not affected by the age subgroup.

The benefits of minimal invasive colorectal resections are well established. The minimization of surgical trauma further reduces the perioperative inflammatory cascade (35). Improved cosmesis, reduced postoperative pain, enhanced mobilization and bowel function recovery are amongst the several advantages of laparoscopic colectomies (36). Nonetheless, the safety of laparoscopic colorectal resections in octogenarians is, still, a matter of controversy. The hemodynamic changes induced by the pneumoperitoneum combined with the prolonged operative times and the extreme intraoperative positions challenge the already reduced reserves of patients with cardiopulmonary comorbidities (20, 21, 37). However, in a clinical study by Akiyoshi *et al*. (37), an improved morbidity profile was suggested when a minimal invasive approach was applied in older patients. In our study 42.2% of the pooled resections were performed laparoscopically. There was no notable difference between the two groups in terms of morbidity.

Assessment of survival endpoints is a pivotal part of colorectal cancer trials. Overall and cancer-specific survival rates directly reflect the oncological efficacy of the investigated interventions. Interestingly, we could not verify any survival difference between older and younger colorectal cancer patients. Moreover, these results did not differentiate when the optimal surgery covariate was introduced. According to a systematic review by Colorectal Cancer Collaborative Group, older patients displayed a reduced overall survival, with minimal differences in cancer specific survival compared to their younger counterparts (38). Similarly, Golfinopoulos *et al*. reported comparable survival benefits of adjuvant and palliative chemotherapy between older and younger colorectal cancer cases (39). Moreover, colorectal cancer surgery outcomes are multifactorial and can be affected by multiple factors besides age, including stage, comorbidities, and chemotherapy scheme (38). For example, in stage IV patients, surgery has a limited effect in the overall prognosis. In our study, a relatively small cohort was assessed with a significant heterogeneity in terms of cancer staging, thus limiting the ability to safely extrapolate these results.

Our study showed that applying a suboptimal treatment in older colorectal cancer patients did not significantly affect survival outcomes. More specifically, median survival for older patients with suboptimal surgical treatment was 22.8 months compared to 25 months in the optimal arm. The best survival rate was identified in the younger and optimal subgroup (28 months). Despite these differences statistical significance was not confirmed. A possible explanation could be the previously mentioned study limitations. Current literature suggests that perioperative optimization and technological advancements allow the performance of optimal oncological resections in octogenerians with acceptable results (40). Multiple trials confirmed a survival benefit of optimal surgical treatment in older patients without documenting any safety hazard (41, 42).

Despite the therapeutic potential in colorectal cancer, surgical resection represents a major physiological trauma that derails the homeostasis of a frail patient (43, 44). More specifically, the extent of perioperative risk is directly correlated with the preoperative functional reserves of the patient (43, 44). In octogenerians, cardiac, pulmonary, and metabolic comorbidities combined with malnutrition and other psychological disorders inhibit an early and uneventful postoperative recovery (43, 44). Therefore, the introduction of multimodal pre-habilitation programs was considered as a means of improving cardiorespiratory fitness in older patients (43, 44). Although these preemptive interventions typically consist of nutritional support combined with aerobic exercise and strength training, the exact protocol and duration is, still debated (43, 44). Similarly, current evidence regarding the efficacy of such interventions is not, yet, conclusive (43-45). In our cohort no pre-habilitation protocol was applied.

Preoperative screening of biological vulnerability aims in the early identification of reduced reserve and stressor resistance in geriatric patients (46-48). During the previous years, multiple frailty assessment instruments were described (46-48). These were categorized in frailty phenotype instruments and frailty index tools; the former predominantly evaluated motor and activity scores, while the latter assessed comorbidities, social factors, cognition, and psychological disorders (46-48). Subsequently, a great discrepancy is noted among the results of these tools, and a gold standard frailty index is, yet, not established. Besides the plethora in assessment tools, the absence of hard evidence and implementation guidance, further prevents the systematic frailty evaluation of older patients (46-48). It is estimated that a frailty assessment algorithm is rarely introduced in daily clinical practice and that only in selected cases (49). In our study, a formal geriatric assessment was not performed. Patients were categorized based on a pre-defined age cut-off, while a validated comorbidity tool was also used.

Several limitations must be considered with regard to the present study. First, the study was designed as a prospective trial, thus increasing the risk of bias due to absence of masking and randomization algorithms. Furthermore, the relatively small sample size may have negatively affected the validity of our findings. Additionally, the differences in terms of tumor and operative characteristics were another noteworthy source of bias. Finally, divergences in the perioperative schemes, further, contribute to the overall heterogeneity.

Conclusion

Our cohort study highlighted that operated older colorectal cancer patients had similar survival rates with their younger counterparts. Furthermore, the two arms were comparable regarding overall morbidity and optimal surgery rates. Finally, subgroup analysis in terms of patient age and

optimal surgical approach did not reveal any survival difference. However, due to several study limitations, further trials, of a higher methodological quality and of a larger sample are required to confirm these findings.

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Conflicts of Interest

The Authors declare that they have no conflicts of interest.

Authors' Contributions

Conception and design of the study: Tepetes, Aggelakopoulou; Acquisition of data: Aggelakopoulou, Mouzakis; Drafting the article: Perivoliotis, Aggelakopoulou; Critical revision: Stergiannis, Intas. Final approval: Tepetes.

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