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Colorectal carcinoma in pediatric patients: A comparison with adult tumors, treatment and outcomes from the National Cancer Database

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ABSTRACT

Background: Pediatric colorectal cancer (CRC) is rare. Comparison with adult CRC tumors, management, and outcomes may identify opportunities for improvement in pediatric CRC care.
Study Design: CRC patients in the National Cancer Data Base from 1998 to 2011, were grouped into Pediatric (≤21 years), early onset adult (22–50) and older adult (>50) patients. Groups were compared with χ^2 and survival analysis.
Results: A total of 918 pediatric (Ped), 157,779 early onset adult (EA), and 1,304,085 older adults (OA) were identified ($p < 0.01$ for all comparisons). Patients ≤50 presented more frequently with stage 3 and 4 disease (Ped: 62.0%, EA: 49.7%, OA: 37.3%) and rectal cancer (Ped: 23.6%, EA: 27.5%, OA: 19.2%). Pediatric histology was more likely signet ring, mucinous, and poorly differentiated. Initial treatment was usually surgery, but patients ≤50 were more likely to have radiation (Ped: 15.1%, EA: 18.6%, and OA: 9.2%) and chemotherapy (Ped: 42.0%, EA: 38.2%, and OA: 22.7%). Children and older adults showed poorer overall survival at 5 years when compared to early onset adults. Adjusting for covariates, age ≤21 was a significant predictor of mortality for colon and rectal cancers (colon HR: 1.22, rectal HR: 1.69).
Conclusions: This is the largest cohort of pediatric CRC patients, revealing more aggressive tumor histology and behavior in children, particularly in rectal cancer. Despite standard oncologic treatment, age ≤21 was a significant predictor of mortality. This is likely owing to worse tumor biology rather than treatment disparities and may signal the need for different therapeutic strategies.

Colorectal cancer (CRC) is the third most common cancer in adults and the second leading cause of cancer-related death in the United States. In contrast, colorectal adenocarcinoma is a rare pediatric tumor, representing only 1% of all pediatric malignancies, with an incidence of approximately 1 per million [1]. There is a robust body of evidence in adults, but studies of pediatric CRC have been limited by small numbers of patients, with no large institutional experience or prospective studies to guide treatment. The largest database study to date used the Surveillance, Epidemiology, and End Results Project (SEER) database, studying 159 patients, and the largest single center study reviewed 77 patients [2,3]. Despite small numbers, these studies demonstrated differences between pediatric and adults CRC patients, showing a significantly higher proportion of aggressive histology, particularly signet ring and mucinous and a higher proportion presenting with metastatic disease [2,4–7]. However, no studies specifically compare rectal cancer outcomes in children and adults.

Utilizing the National Cancer Database (NCDB) data, our study compares pediatric and adult CRC patients with regards to demographics, histology, and treatment regimens and survival outcomes. Comparison with adult patients may uncover unique features of pediatric CRC and suggest opportunities for improvements in pediatric CRC care.

1. Methods

Ethical approval for this study was granted by the Maine Medical Center Institutional Review Board. All patients with a histologic diagnosis of colorectal adenocarcinoma, using ICD-O-3 classification, diagnosed between years 1998 and 2011 were identified from the NCDB. The NCDB, a joint project of the American Cancer Society and the Commission

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on Cancer (CoC) of the American College of Surgeons, is a nationwide, facility-based, comprehensive clinical surveillance resource oncology data set that currently captures 70% of all newly diagnosed malignancies in the US annually [8].

Patients were grouped based on age — pediatric (≤21 years), young adults (22–50) and older adults (>50). The dataset was queried using tumor histology codes from the International Classification of Disease for Oncology 3rd Edition (ICD-O-3) for all colorectal adenocarcinoma codes, including in situ disease, and classified as 1) adenocarcinoma (codes 8050–8052, 8140–8148, 8210–8231, 8255–8263, 8510, and 8560–8576), 2) signet ring cell carcinoma (code 8490), and 3) mucinous adenocarcinoma (codes 8480–8481). Non-adenocarcinoma histologies were excluded including carcinoid, sarcomas, GISTs, and lymphomas. Familial adenomatous polyposis (FAP) was identified by pathology (codes 8220–8221). Tumor location from cecum to rectosigmoid was classified as "colon"; tumors located distal to this were classified "rectal". Only cases for which this cancer was either the first or the only cancer diagnosis in their lifetime, and those diagnosed or treated at the reporting facility, were included. Demographic variables, pathology, as well as surgical, chemotherapy and radiation treatments were compared between groups. Charlson Deyo score was used as a measure of patient comorbidities [9]. TNM staging based on pathology was used preferentially owing to less change between years with new editions of the TNM staging system. If TNM stage was unavailable, owing to missing histologic stage, clinical stage was used. Groups were compared with chi-squared analysis for demographic data, histology, stage, surgical and adjuvant therapy, and outcomes. Patients with missing data were excluded from the univariate analysis. Factors found to be significant in a univariate analysis were then entered into a multivariate analysis using the Cox proportional hazards model, which was limited to patients ≤50 years of age owing to difficulty interpreting all-cause mortality in the oldest age group (age >50). Appropriateness of a proportional hazards model was investigated to determine graphically whether the hazards for subjects with and without a given covariate were approximately proportional over time. Hazard ratios for colon and rectal cancers were examined separately. Potential effect modification was explored by including interaction terms for each combination of covariates. In addition to the variables included in the reported models, preliminary models considered other racial categories and comorbidities, none of which were independently significant ($p > .05$). After considering interactions between age group and sex, race, stage, pathologic characteristics, and colon/rectal location, only the last of these appeared significant, which was most easily expressed by reporting separate models for colon and rectal locations.

Concordance probability estimates using the method of Gönen and Heller were performed for each model [10].

Five and ten year overall survival was estimated using the Kaplan–Meier method. Survival was calculated from the time of the initial diagnosis to the date of death, with survival curves for each stage for colon and rectal location of presenting tumor separately. Those excluded from the survival analysis were patients who were lost to follow up, those who had more than one cancer diagnosis, and those diagnosed in 2007 or later as they would not have had the 5 years of follow up required by NCDB. Data analysis was conducted using the statistical program Stata (Version 13.0, StataCorp, College Station, Texas).

2. Results

2.1. Demographics (Table 1)

A total of 918 pediatric (Ped), 157, 577 early onset adult (EA), and 1,303,655 older adult (OA) patients were identified (Fig. 1). There were no significant differences in gender or race among the 3 age groups. Comorbidities, as measured by the Charlson Deyo score, increased with increasing age. Significant differences exist in presenting location of tumor, with older adults presenting with a higher proportion of right colon cancer (Ped: 23.7%, EA: 22.9%, OA: 35.8%, $p < 0.001$) whereas the early onset adults had a slightly higher proportion of left colon cancer (including splenic flexure, descending, sigmoid and rectosigmoid) as

Table 1
Patient demographics.

Variable	Age ≤ 21 % (No)	Age 22–50 % (No.)	Age >50 % (No.)	P-value
Sex				
Male	54.6 (502)	52.8 (83,248)	50.6 (659,718)	p < 0.001
Female	45.3 (416)	47.1 (74,329)	49.3 (643,937)	
Race				
White	78.2 (718)	78.7 (124,043)	85.7 (1,118,166)	p < 0.001
Black	14.4 (133)	15.0 (23,711)	10.3 (134,402)	
Asian	3.2 (30)	3.4 (5491)	2.1 (28,207)	
Other	4.0 (37)	2.7 (4332)	1.7 (22,880)	
Charlson Deyo Score				
0	94.4 (578)	88.7 (93,519)	69.9 (565,629)	p < 0.001
1	4.7 (29)	9.3 (9876)	21.9 (177,406)	
2	0.8 (5)	1.8 (1952)	8.1 (65,501)	
Site				
Right Colon	23.7 (218)	22.9 (36,212)	35.8 (466,723)	p < 0.001
Transverse Colon	8.3 (77)	5.0 (7892)	6.7 (88,337)	
Left Colon	34.8 (320)	40.6 (64,016)	34.6 (451,234)	
Rectum	23.6 (217)	27.5 (43,373)	19.2 (250,508)	
Large intestine, NOS	9.3 (86)	3.8 (6084)	3.6 (46,853)	
Histology				
Adenocarcinoma	66.9 (615)	88.2 (139,094)	90.2 (1,176,551)	p < 0.001
Mucinous Adeno	17.5 (161)	9.7 (15,304)	8.7 (114,256)	
Signet Ring	15.4 (142)	2.0 (3179)	0.9 (12,848)	
FAP (pathologic diagnosis)	2.6 (24)	0.2 (318)	0.03 (427)	P < 0.001
Microsatellite instability (MSI)				
No MSI (stable)	58.7 (27)	76.1 (4184)	73.3 (16,369)	P < 0.001
MSI (unstable)	41.3 (19)	23.9 (1313)	26.7 (5967)	
Grade				
Well differentiated	7.8 (72)	8.6 (13,546)	9.7 (126,753)	p < 0.001
Mod. differentiated	39.5 (363)	57.7 (90,961)	58.5 (762,809)	
Poorly differentiated	29.5 (271)	16.9 (26,726)	15.3 (200,673)	
Undifferentiated	3.3 (31)	1.2 (1977)	1.1 (14,651)	
Unknown	19.7 (181)	15.4 (24,367)	15.2 (198,769)	
TNM Stage (combined)				
0	5.2 (48)	6.1 (9611)	7.2 (93,895)	p < 0.001
1	8.3 (77)	17.2 (27,137)	22.4 (292,285)	
2	14.2 (131)	19.7 (31,120)	24.3 (318,015)	
3	32.7 (301)	28.0 (44,166)	22.4 (292,508)	
4	29.3 (269)	21.7 (34,213)	14.9 (195,088)	
Unknown	10.0 (92)	7.1 (11,330)	8.5 (111,864)	
Treatment Started after diagnosis				
Within 1 month	88.1 (743)	84.5 (122,973)	83.2 (968,069)	p < 0.001
1–3 months	10.2 (86)	14.1 (20,546)	15.2 (177,269)	
3–6 months	0.3 (3)	0.6 (978)	0.8 (9523)	
6 months–1 year	1.1 (10)	0.5 (855)	0.6 (7734)	
>1 year	0.1 (1)	0.08 (115)	0.06 (663)	
Surgery				
No excision/ unknown	17.4 (160)	11.4 (17,991)	12.2 (159,920)	p < 0.001
Local excision	3.5 (33)	7.5 (11,962)	8.2 (107,830)	
Segmental resection	54.1 (497)	68.1 (107,321)	71.5 (933,231)	
Total colectomy, proctectomy, or proctocolectomy	22.3 (205)	11.1 (88,432)	6.7 (88,432)	
Surgery, NOS	2.5 (23)	1.7 (2804)	1.0 (14,242)	
Lymph Nodes Removed				
<12	17.39 (160)	27.29 (43,063)	35.29 (460,282)	p < 0.001
≥12 nodes	53.59 (493)	47.85 (75,503)	39.35 (513,153)	
Unknown or none	29.01 (267)	24.85 (39,213)	25.36 (330,750)	
Chemotherapy				
Yes	70.1 (644)	59.7 (94,167)	32.6 (426,084)	p < 0.001
No or unknown	29.6 (274)	40.2 (63,410)	67.2 (877,571)	
Radiation				
Yes	19.5 (179)	22.9 (36,180)	12.2 (160,014)	p < 0.001
No	79.0 (726)	75.8 (119,536)	86.7 (1,130,225)	
Unknown	1.4 (13)	1.1 (1861)	1.0 (13,416)	

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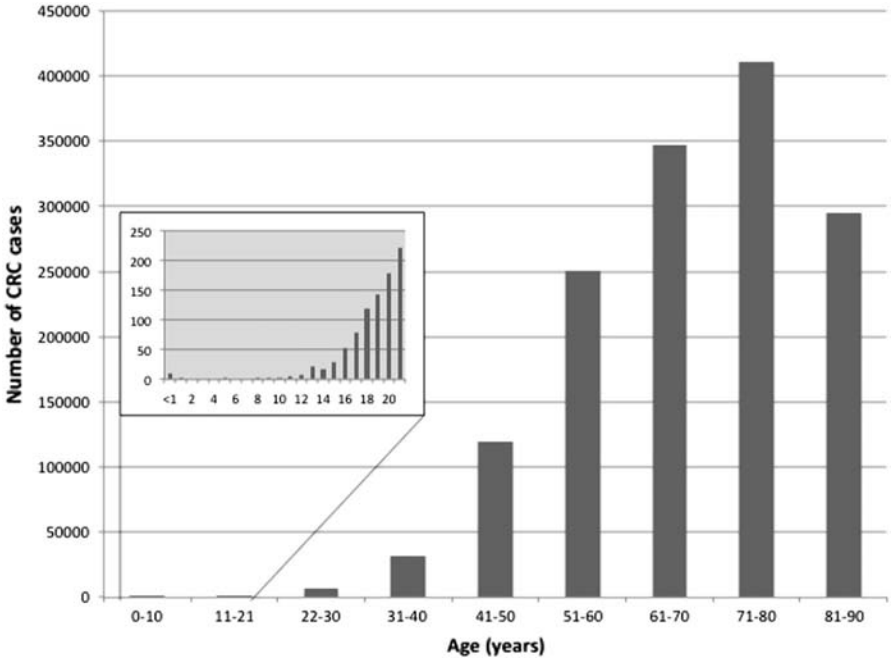

Fig. 1. Frequency of colorectal cancer by age. Pediatric (age 0–21 years) histogram inset.

compared to the other 2 groups (Ped: 34.8%, EA: 40.6%, OA: 34.6%, $p < 0.001$). Both early onset adults and, to a lesser degree, children had a higher proportion of rectal cancer compared to the older adults (Ped: 23.6%, EA: 27.5%, OA: 19.2%, $p < 0.001$).

2.2. Histology (Table 1)

With respect to histology, the proportion of mucinous adenocarcinoma in pediatric patients was almost twice that seen in the other two age groups (Ped: 17.5%, EA: 9.7%, OA: 8.7%, $p < 0.001$). Furthermore, signet ring was 8–17 times higher in pediatric patients than the other 2 groups (Ped: 15.4%, EA: 2.0%, OA: 0.9%, $p < 0.001$). The proportion of patients with a diagnosis of FAP was small for all groups but significantly higher in the pediatric group (Ped: 2.6%, EA: 0.2%, OA: 0.03%, $p < 0.001$). Of the 0.2% of patients who had microsatellite instability (MSI) tested, the proportion of unstable MSI was highest in the young patients (Ped: 41.3%, EA: 23.9%, OA: 26.7%). Pediatric patients also had significantly worse histologic grade with a higher proportion of poorly differentiated tumors (Ped: 29.5%, EA: 16.9%, OA: 15.3%, $p < 0.001$). Pediatric patients presented more frequently with stage 3 and 4 disease when compared to the other two age groups (Ped: 62.0%, EA: 49.7%, OA: 37.3%, $p < 0.001$).

2.3. Treatment

Time from diagnosis to treatment was similar for all groups, with most starting treatment within one month (Ped: 88.1%, EA: 84.5%, OA: 83.2%). Initial treatment was usually surgery and most patients had a segmental resection, regardless of age group (Ped: 54.1%, EA: 68.1%, OA: 71.5%) with >12 lymph nodes resected in the majority of pediatric patients, but less than 50% of adults (Ped: 53.6%, EA: 47.9%, OA: 39.4%, $p < 0.001$). Pediatric patients more often had a total colectomy, proctocolectomy or proctectomy (Ped: 22.3%, EA: 11.1%, OA: 6.7%, $p < 0.001$). Both pediatric and early onset adult patients were more likely to have radiation (Ped: 19.5%, EA: 22.9%, OA: 12.2%, $p < 0.001$) and chemotherapy (Ped: 70.1%, EA: 59.7%, OA: 32.6%, $p < 0.001$), even when adjusted for stage as well as rectal location of tumor.

2.4. Survival analysis and predictors of survival (Table 2)

Kaplan–Meier analysis demonstrates better overall survival in the early onset adult group but similar survival in children and older adults at 5 years for colon cancer, $p < 0.001$ for all comparisons. This was also true in a stage by stage comparison (Fig. 2). For rectal cancer, survival was worse in the pediatric age group at stages 2, 3 and 4 when compared to both adult groups (Fig. 3).

Patients 0–50 years of age were examined using a Cox proportional hazards model to examine predictors of mortality in colon and rectal cancers (Table 2). Concordance probability estimates were .759 for the colon model and .725 for the rectal model. For colon cancer subjects, the hazard for pediatric subjects was similar to the hazard for young adults for the first few weeks, after which an approximately proportional relationship was seen. For rectal cancer subjects, the hazards were approximately proportional.

The most important predictor of mortality was stage, which increased in a nonlinear fashion with Stage 4 disease resulting in a 31 times greater mortality for colon cancer (stage 4 HR = 31.21; 95% CI 29.08–33.50, stage 3 HR = 5.82; 95% CI 5.41–6.26, stage 2 HR = 2.55; 95% CI 2.36–2.76) when compared to stage 1. Rectal cancer showed similar relationship between stage and survival, with nearly 20 times greater mortality in patients with stage 4 disease when compared to stage 1 (stage 4 HR = 19.97; 95% CI 18.25–21.85, stage 3 HR = 3.80; 95% CI 3.47–4.17, stage 2 HR = 2.78; 95% CI: 2.53–3.07). Age ≤21 was an independent predictor of mortality for both colon cancer (HR = 1.22; 95% CI 1.05–1.42), and rectal cancer (HR = 1.69; 95% CI 1.31–2.18) even when adjusting for the other covariates.

Other significant predictors of mortality include a Charlson Score of 2 (colon HR = 1.65; 95% CI 1.45–1.89, rectal HR = 1.59; 95% CI 1.22–2.07), poorly differentiated grade (colon HR = 1.42; 95% CI 1.38–1.47, rectal HR = 1.49; 95% CI 1.41–1.58), black race (colon HR = 1.35; 95% CI 1.30–1.39, rectal HR = 1.43; 95% CI 1.33–1.53), and male gender (colon HR = 1.22; 95% CI 1.18–1.25, rectal HR = 1.20; 95% CI 1.14–1.25). Signet ring histology was a significant predictor of mortality for colon, but had a greater effect in rectal cancer (colon HR = 1.50, 95% CI 1.41–1.61, rectal HR = 2.11; 95% CI 1.85–2.41). Mucinous histology was a significant predictor of mortality for rectal but not colon cancer (colon HR = 0.91; 95% CI 0.88–0.95, rectal HR = 1.31; 95% CI

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Table 2
Predictors of mortality, Cox proportional hazards model.

Variable	Colon excluding rectal		Rectal	
	HR	95% CI	HR	95% CI
Age 0–21 (ref 22–50)	1.22	1.05, 1.42	1.69	1.31, 2.18
Male (ref Female)	1.22	1.18, 1.25	1.20	1.14, 1.25
Black (ref other race)	1.35	1.30, 1.39	1.43	1.33, 1.53
Charlson Score > =2 (ref Charlson <2)	1.65	1.45, 1.89	1.59	1.22, 2.07
Stage 2 (ref Stage 0–1)	2.55	2.36, 2.76	2.78	2.53, 3.07
Stage 3 (ref Stage 0–1)	5.82	5.41, 6.26	3.80	3.47, 4.17
Stage 4 (ref Stage 0–1)	31.21	29.08, 33.50	19.97	18.25, 21.85
Poorly differentiated (ref other)	1.42	1.38, 1.47	1.49	1.41, 1.58
Signet ring histology (ref other)	1.50	1.41, 1.61	2.11	1.85, 2.41
Mucinous histology (ref other)	0.91	0.88, 0.95	1.31	1.21, 1.42
FAP (ref other)	0.88	0.64, 1.22	0.91	0.47, 1.74
Any chemotherapy (ref none)	0.74	0.71, 0.76	0.82	0.76, 0.89
Any radiation (ref none)	1.26	1.21, 1.32	0.95	0.89, 1.01

1.21–1.42). Chemotherapy was a protective factor for both colon (HR = 0.74; 95% CI 0.71–0.76), and rectal (HR = 0.82; 95% CI 0.76–0.89) cancers. Radiation was not an independent predictor of survival in rectal cancer and was associated with worse survival in colon cancer (colon HR = 1.26; 95% CI 1.21–1.32, rectal HR = 0.95; 95% CI 0.89–1.01). FAP was not found to be a significant predictor of mortality.

3. Discussion

To our knowledge, the current study represents the largest cohort (N = 918) of pediatric colorectal cancer patients studied. These results reveal poorer survival in children, even when adjusted for known prognostic factors such as stage, pathology, and behavior. Notably, the mortality risk associated with the pediatric age group was affected by the tumor location, with a greater effect on mortality for rectal tumors. This study also confirms findings from prior studies demonstrating more aggressive tumor biology in children with higher proportions of signet ring and mucinous histology, less differentiation, and presentation at later stage [2–4,7].

It is not clear why children more commonly present at a later stage than adults, but postulated causes include delays in diagnosis owing to its low incidence and mimicry of more common pathologies including infectious and inflammatory bowel disease [11]. Differences in tumor biology not fully captured by differentiation and histology may also account for presentation at a higher stage and the worse outcomes observed in children [3,6,7].

There are several pathogenic mechanisms proposed in adults that first result in adenomatous polyps that then undergo dysplastic and finally malignant transformation; changes which occur over approximately 10 years [12–14]. However, in the cohort assessed here there are cases of colorectal adenocarcinoma in patients less than 10 years of age and even less than 1 year, suggesting an accelerated or alternate mechanism for pediatric CRC development than that which occurs in adults [14–16]. Pediatric CRC may arise in the setting of predisposing genetic or polyposis syndromes such as FAP, Lynch syndrome or familial juvenile polyposis, as well as in the setting of inflammatory bowel disease, but CRC more frequently develops in children without known predisposing syndromes [17]. The numbers of patients with predisposing syndromes may be underestimated within this database owing to the limited genetic testing of patients diagnosed in earlier years, but still likely represent a minority of patients based on previous studies [2,3,18]. The SEER study, representing data from 1973 to 2005, found an FAP prevalence of 10% in children and 0.1% in adult CRC populations, but the prevalence was 2–4 fold lower in our cohort: 2.6% of children and 0.05% of adults [2]. This may be a relative underrepresentation of pediatric FAP within this database or the effect of a change in timing of surgery in our more contemporary cohort [19]. Microsatellite instability (MSI) is much more common in pediatric CRC but, unlike adult CRC, it correlates poorly with Lynch Syndrome [18]. Genetic testing for microsatellite instability (MSI) confirmed relatively high proportions (46%) of unstable MSI in pediatric patients tested, but these data were only available for 5% of the pediatric group, with insufficient numbers to make meaningful comparisons between groups. As more data are collected, it may be valuable to compare pediatric and adult rates of MSI, as well as loss of heterozygosity at chromosome 18q and KRAS mutations, which are not reported here as both had 98%–100% of data missing, and assess how much they may account for differences in behavior.

Importantly, this study also found that age less than or equal to 21 was an independent predictor of mortality, even when controlling for known prognostic factors. Furthermore, this effect was modified by

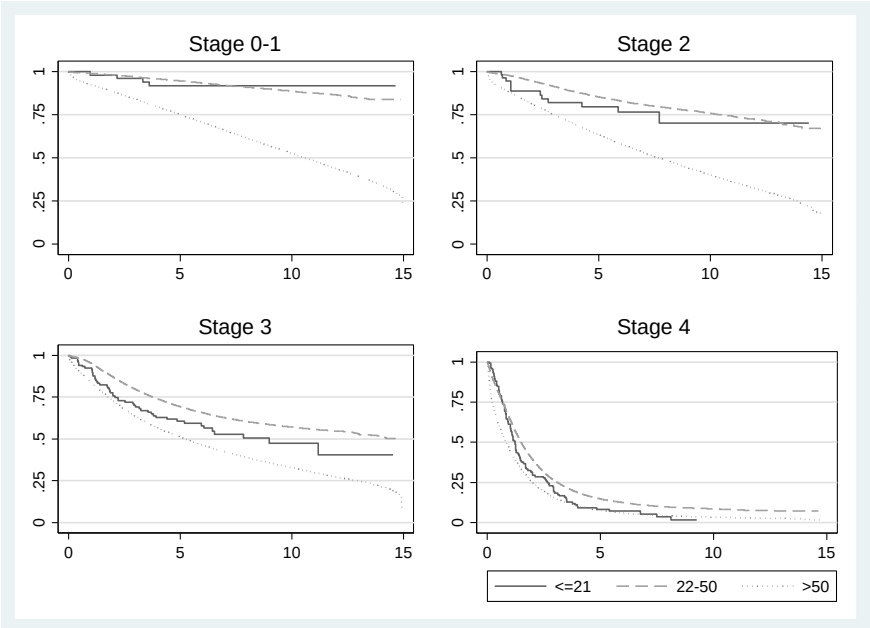

Fig. 2. Kaplan–Meier survival curves by stage for colon cancer patients. No significant difference between children (0–21) and early onset adults (22–50) for stages 1 and 2, but children have poorer survival for stage 3 and 4. Older adults have the lowest survival at each stage, except for stage 4 patients when it is equivalent to children.

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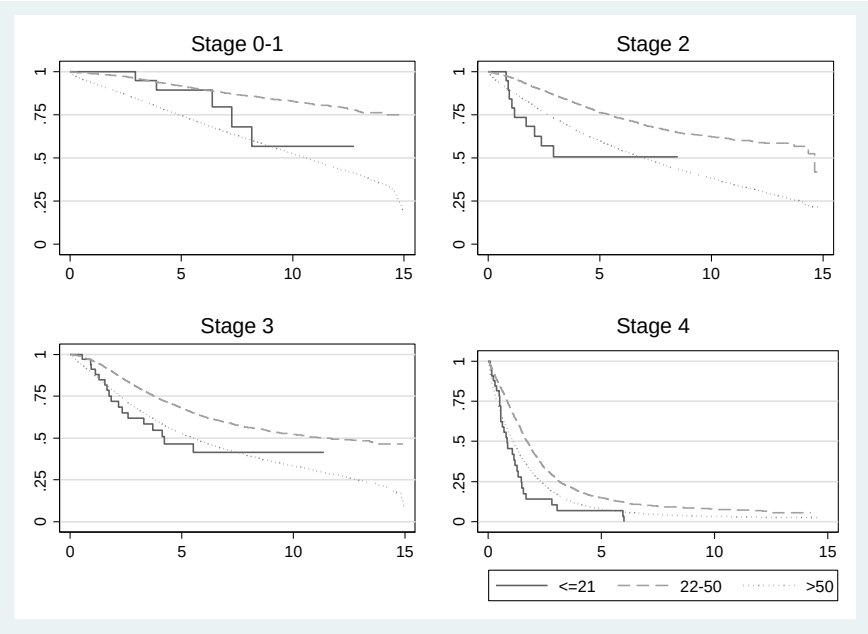

Fig. 3. Kaplan–Meier survival curves by stage for rectal cancer patients. Children (0–21) have the poorest 5-year survival for stages 2–4. Early onset rectal cancer in adults (22–50) has the best overall survival at every stage of presentation.

location of presenting tumor, with pediatric rectal cancer conferring a higher risk of mortality than colon cancer, which is a novel finding. Previous pediatric CRC studies have grouped pediatric colon and rectal cancers together in the analysis owing to limited numbers, so there is poor understanding of pediatric rectal tumors. This study suggests that pediatric rectal cancer may be even more aggressive than pediatric colon cancer as well as more common in pediatric and early onset adult age groups, with higher proportions of rectal cancer those age groups (23.6% and 27.5% respectively) when compared to older adults (19.2%, $p < 0.001$).

Based on the hospitals participating in the NCDB, it appears that the poorer outcomes in children are not owing to treatment disparities, as pediatric patients more frequently underwent radical excisions, were more likely to have 12 or more lymph nodes sampled, and received more adjuvant treatment. Prior studies have hypothesized that outcome differences may be in part owing to the limited knowledge of pediatric oncologists and surgeons in dealing with these diseases [2,20–22]. While this study cannot investigate individual treatment decisions, this seems less likely given that adult treatment protocols are generally used when there are no pediatric specific protocols to guide therapy and this study's findings of equal or more extensive surgical and non-surgical treatment of these tumors in a timely fashion [23].

Currently there are no specifically pediatric CRC treatment algorithms, so adult protocols are utilized, but in the absence of prospective trials it is unclear if this is the best option or how age affects individual treatment decisions. Given that the tumor biology is likely different, it may also respond differently to treatment [23]. It is clear that even within adult populations early onset colorectal cancer is associated with differences in tumor behavior that may affect outcomes of colorectal cancer [24–26]. Studies specifically on early onset CRC, as defined by age less than fifty, have demonstrated that left colon cancers were predominant, that histopathologically tumors were more often mucinous and poorly differentiated, and that they presented at a more advanced stage when compared with older patients. Survival outcomes in this group have been mixed with some studies showing a poorer prognosis and others showing equivalent and even improved outcomes when compared to older patients [27–35]. This study shows the best overall survival in the early onset adult cohort, but is limited by the inability to assess disease-specific outcomes.

3.1. Limitations

While the largest single review of CRC in the pediatric age range to date, this study suffers the limitations inherent to hospital-based registries, which may under represent chemotherapy and radiation treatment in the outpatient setting [8,36]. Furthermore, limited information was available on presenting symptoms, family history, and co-morbidities that may predispose children to CRC. Although we have identified a higher stage at presentation and worse survival in children, we are unable to determine the cause.

Disease specific mortality and disease-free survival would be helpful in comparing groups and treatment effects when age presents such a large confounding factor, but the NCDB only reports all-cause mortality. Limiting the multivariate analysis to only pediatric and early onset patients with no other cancer diagnosis partially addressed this concern. Finally, as with any database study, there are a limited number of questions can be asked and causality cannot be determined.

4. Conclusions

To our knowledge, this study represents the largest cohort of pediatric CRC patients and confirms more aggressive tumor histology and behavior in children, even with standard oncologic treatment in younger patients. This presentation is associated with a higher 5 year mortality in pediatric patients when compared to the adult cohorts. Poorer outcomes in pediatric CRC patients appear to be owing to worse tumor biology and stage rather than treatment disparities. Furthermore colon and rectal cancers do not appear to be equivalent in the pediatric age group, with a higher mortality conferred by rectal cancer. This may indicate a difference in biology or quality of treatment. Currently there are no pediatric CRC treatment protocols, with surgeons and oncologists adapting adult protocols to guide management. This approach should be reconsidered in light of the differences in behavior of adult and pediatric CRC identified here. Additional research into pediatric colorectal adenocarcinoma tumor biology may identify factors making many of these tumors more aggressive, in turn allowing for identification of more aggressive tumors in adults and helping guide development of novel targeted treatments, which could improve outcomes of CRC patients at all ages.

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