



Colorectal Carcinoma in Children and Adolescents

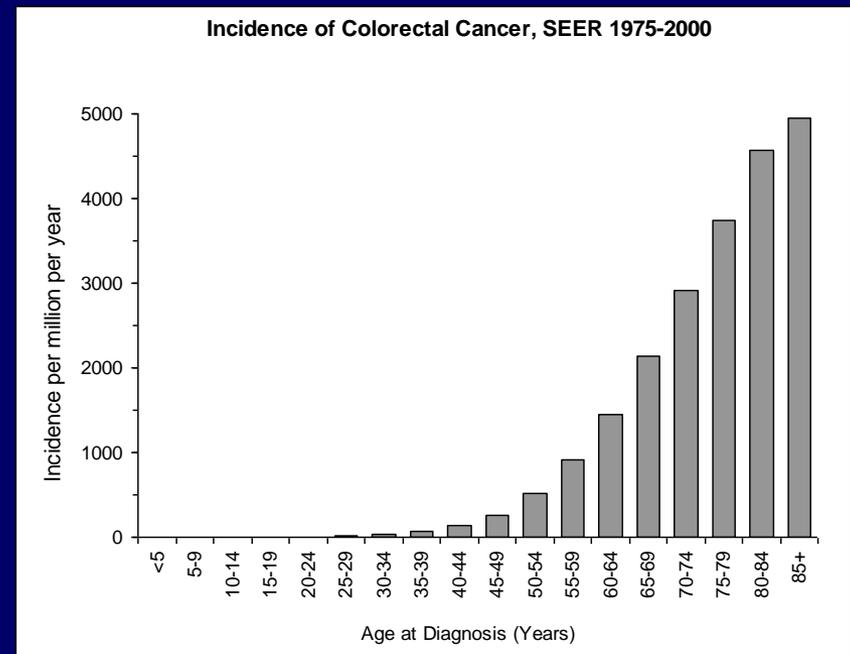
Review of 77 patients from St. Jude
Analysis in progress

D. Ashley Hill, M.D.

Colorectal carcinoma



- 3rd most common malignant tumor in adults
- In 2004
 - 147,000 cases of CRC
 - 56,730 deaths
- 90% of cases occur after age 50
- 1 case in 10⁶ in persons less than 20 years of age
- 2.1% of malignant neoplasms in 15-29 year olds



Colorectal carcinoma



- **Etiology**

- Adenomatous polyps are precursors of CRC in adults (most cases)
- Diet
 - High fat intake, red meat, alcohol increase risk
 - Fiber, COX-2 inhibitors decrease risk
- Other predisposing conditions
 - IBD, prior radiation, hereditary cancer predisposition syndromes

Colorectal carcinoma in Children



- Colorectal CA has a poor prognosis in children and adolescents
- Myth or Reality?

Small single institution or referral institution studies of CRC in children



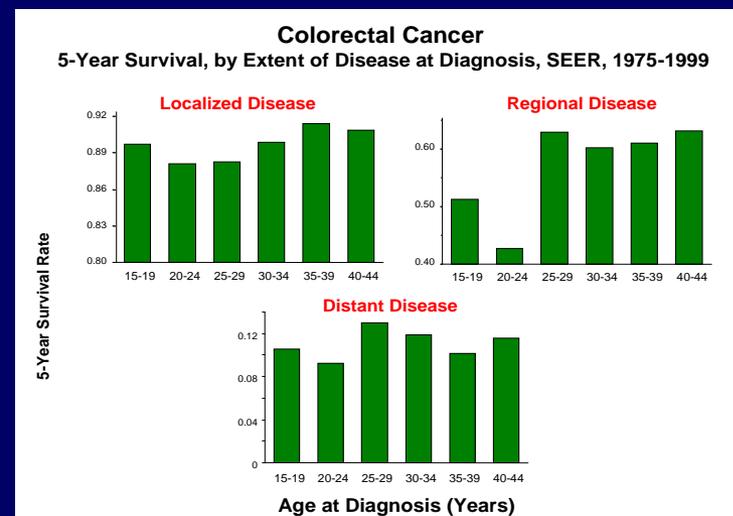
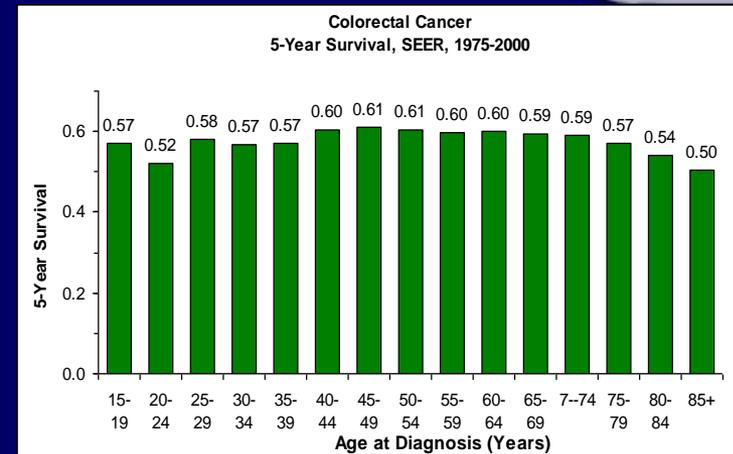
- (14) Sharma AK, Gupta CR. Colorectal cancer in children: case report and review of literature. *Trop Gastroenterol* 2001 Jan - Mar.22:36-39.
- (15) Minardi AJ, Jr., Sittig KM, Zibari GB, McDonald JC. Colorectal cancer in the young patient. *Am Surg.* 1998;64:849-853.
- (16) Sebbag G, Lantsberg L, Arish A, Levi I, Hoda J. Colon carcinoma in the adolescent. *Pediatr Surg Int.* 1997;12:446-448.
- (17) Ferguson E Jr, Obi LJ. Carcinoma of the colon and rectum in patients up to 25 years of age. *Am Surg.* 1971;37:181-189.
- (18) Andersson A, Bergdahl L. Carcinoma of the colon in children: a report of six new cases and a review of the literature. *J Pediatr Surg.* 1976;11:967-971.
- (19) Radhakrishnan CN, Bruce J. Colorectal cancers in children without any predisposing factors. A report of eight cases and review of the literature. *Eur J Pediatr Surg* 2003 Feb.13:66-68.
- (20) Karnak I, Ciftci AO, Senocak ME, Buyukpamukcu N. Colorectal carcinoma in children. *J Pediatr Surg.* 1999;34:1499-1504.
- (21) Odone V, Chang L, Caces J, George SL, Pratt CB. The natural history of colorectal carcinoma in adolescents. *Cancer.* 1982;49:1716-1720.
- (22) Lamego CM, Torloni H. Colorectal adenocarcinoma in childhood and adolescent. Report of 11 cases and review of the literature. *Pediatr Radiol.* 1989;19:504-508.
- (23) Steinberg JB, Tuggle DW, Postier RG. Adenocarcinoma of the colon in adolescents. *Am J Surg.* 1988;156:460-462.
- (24) Cain AS, Longino LA. Carcinoma of the colon in children. *J Pediatr Surg.* 1970;5:527-532.
- (35) LaQuaglia MP, Heller G, Filippa DA et al. Prognostic factors and outcome in patients 21 years and under with colorectal carcinoma. *J Pediatr Surg.* 1992;27:1085-1089.
- (32) Rao BN, Pratt CB, Fleming ID et al. Colon carcinoma in children and adolescents. A review of 30 cases. *Cancer.* 1985;55:1322-1326.

COLON CANCER IN YOUNG PATIENTS IS ASSOCIATED WITH INCREASE IN MUCINOUS HISTOLOGY, HIGH STAGE DISEASE AND POOR OUTCOME

SEER data for CRC in children



- SEER data from 1975-1999 does not appear to substantiate these reports
- 5 year survival rates of 57% in 15-19 year olds
- Nor is there evidence that CRC in kids present with advanced stage disease
- Clearly there is some reporting and/or referral bias in institutional studies
- Numbers of CRC picked up on screening (after 15 years of age) in the SEER data unknown



Colorectal carcinoma in Children



- Why might CRC in children have a poor outcome?

Colorectal carcinoma in Children



- **Delay in diagnosis?**
 - Vague or unusual symptoms
 - Rarity of disease
 - No general population screening

Colorectal carcinoma in Children



- **Different natural history and biology?**
 - Lack of a dysplasia, adenoma, cancer progression
 - Cancer type differences? More frequent mucinous histology?
 - Different genetics?

Colorectal carcinoma in Children



- **Inadequate treatment?**
 - Surgery issues
 - Cancer surgery
 - Appropriate lymph node recovery and evaluation

Colorectal Carcinoma in Children



- Review of 77 cases referred to SJCRH between February 1964 and September 2003
- SJCRH is a major referral center for pediatric cancer
- Ran 5 consecutive colorectal carcinoma treatment protocols from 1972 to present

Colorectal Carcinoma in Children



- **Cases were identified from files based on diagnosis of GI tract carcinoma**
 - Excluded from review
 - 9 patients > age 21 with CRC as second malignancy
 - 3 patients with gastric or small intestinal primaries
 - 7 patients with carcinoid tumors
 - 4 patients with limited follow up
 - 77 cases had pathologic review, chart review and outcome analysis

Colorectal Carcinoma in Children



- **Chart review included**
 - Presenting symptoms, duration of symptoms
 - Initial diagnostic impression or differential diagnosis
 - Procedure used to establish diagnosis
 - Length of time from presentation to medical care to diagnosis
 - Physical exam findings
 - Hemoccult results

Colorectal Carcinoma in Children



- **Chart review included**
 - Laboratory abnormalities
 - Relevant past medical history
 - Family history of cancer
 - Presence or absence of polyps or polyposis syndrome
 - Data regarding treatment administered
 - Site and timing of relapse
 - Disease status or cause of death

Colorectal Carcinoma in Children



- Pathology review
 - Site
 - Tumor classification
 - Adenocarcinoma
 - Mucinous adenocarcinoma
 - Signet ring adenocarcinoma
 - Degree of differentiation
 - Polyps
 - In-situ dysplasia adjacent to tumor
 - Staging

Colorectal Carcinoma in Children



Characteristic	N	%
Gender		
Male	46	60%
Female	31	40%
Race		
White	48	62%
Black	29	38%
Age at diagnosis (years)	15.5	-
Median	7.5 - 19.9	-
Range		

Colorectal carcinoma in Children



- **Ten patients had known predisposing conditions**
 - Familial JP (n=4)
 - FAP (n=1)
 - Polyposis, not specified (n=1)
 - Previous XRT for bladder RMS (n=2)
 - UC (n=1)
 - NF-1 (n=1)

Colorectal carcinoma in Children



- **Symptoms**

- 76/77 patients were symptomatic from cancer
- Abdominal pain, weight loss and bowel alterations were the most common symptoms

Colorectal Carcinoma in Children



Pain	
No. of patients with data recorded	75
No. of patients with Pain	64 (85%)
Abdomen	58
Abdomen, NOS	46
Abdomen localized	12
Rectum	2
Back	2
Side	1
Unspecified site	1
No. of patients without Pain	11 (15%)

Of 14 patients with localized abdominal pain or rectal pain, 12 had a tumor in the colonic region corresponding to site of pain and all had pT3 or pT4 disease

Colorectal Carcinoma in Children



Bowel Habit Alterations	
No. of patients with data recorded	76
Vomiting	35
Constipation	20
Diarrhea	17
Hematochezia/rectal bleeding	16
Nausea	12
Distension/bloating	8
Bloody diarrhea	1
Tarry stools	1
Pain with eating	1
Flatus	1
Tenesmus	1
No bowel symptoms	14

Colorectal Carcinoma in Children



Weight Loss	
No. of patients with data recorded	72
No. of patients experiencing weight loss	47 (65%)
Median weight loss (n=33)	20 lbs
Range (n=33)	5 – 81 lbs
No. of patients without weight loss	25 (35%)

Colorectal Carcinoma in Children



Other Symptoms/Signs	
Anemia (recorded as iron deficiency anemia, anemia, and/or pallor)	16
Anorexia	14
Fever	6
Fatigue	4
Malaise	4
Urinary symptoms (dysuria, nocturia)	3
Weakness	2
Aphthous ulcers	1
Dehydration	1
Irregular periods	1
Jaundice	1
Ascites	1
Cervical adenopathy	1

Colorectal carcinoma in Children



- **Physical examination**

- 21/33 patients with initial physical examination in chart had palpable abdominal masses or fullness
- 10/12 patients with hemoccult recorded had positive tests (3/10 had gross hematochezia)

Colorectal carcinoma in Children



- Laboratory evaluation
- 44 patients had HGB levels at initial presentation

Hemoglobin level	Number of patients (of 44)
> 12 g/dl	16
10-12 g/dl	10
6.5-10 g/dl	14
<6.5 g/dl	4

- Additional 6 patients had Hct data:
 - 16%, 20%, 24%, 29%, 31%, 38%

Initial clinical diagnosis or differential diagnosis	
Abdominal inflammatory process	22
Acute appendicitis	8
Chronic appendicitis	2
Abscess or infection	7
Pancreatitis	1
Hepatitis	1
Prostatitis	1
Urinary tract infection	1
Bowel perforation	1
Inflammatory bowel disease	7
Constipation/"gas" / functional bowel syndrome	5
Intussusception	6
Malignancy	4
Peptic ulcer disease, gastritis, GERD	4
Anemia	4
Bowel obstruction	4
Ovarian mass/cyst	3
Polyp/polyposis	2
Rectal ulcer syndrome/rectal stricture	2
Food poisoning	1
Rheumatic fever	1

Colorectal Carcinoma in Children



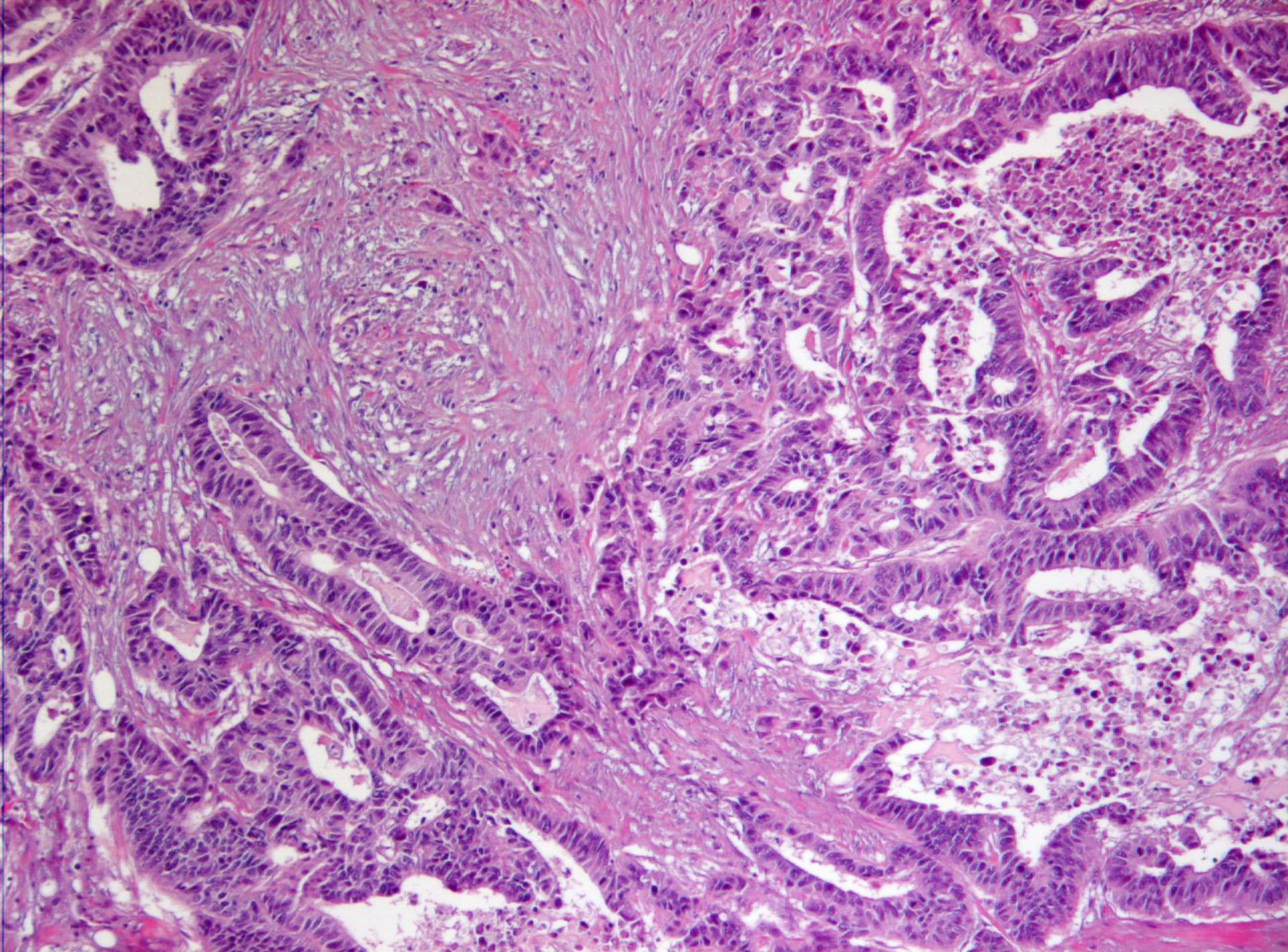
- Time from presentation to diagnosis (32 patients had documentation)
- 14/32 were diagnosed within 1 week
 - 11 within 48 hours (symptoms of appendicitis)
- 12/32 patients had more than 2 months of observation before diagnosis
 - 4 patients went 6 months

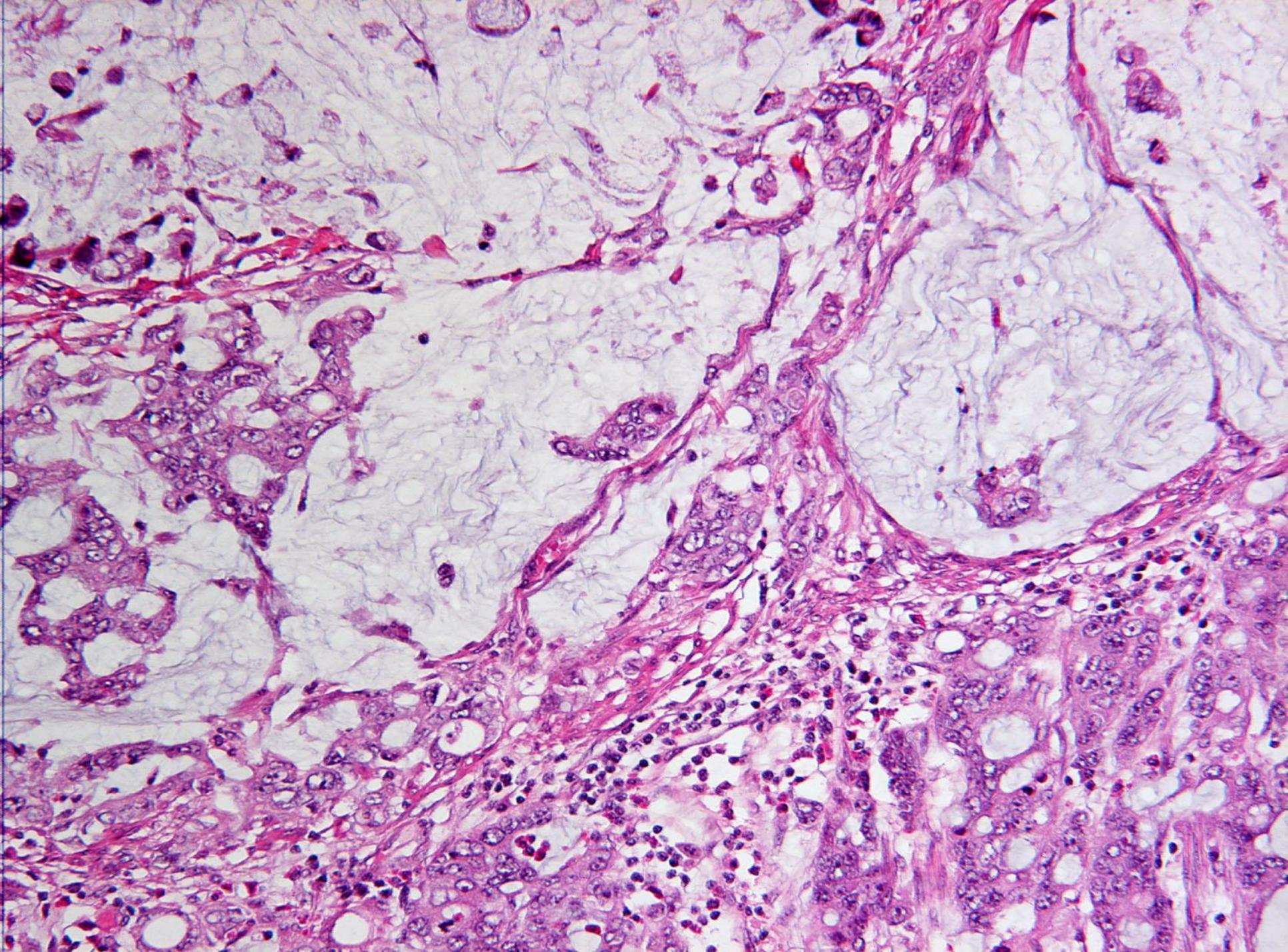
Colorectal Carcinoma in Children

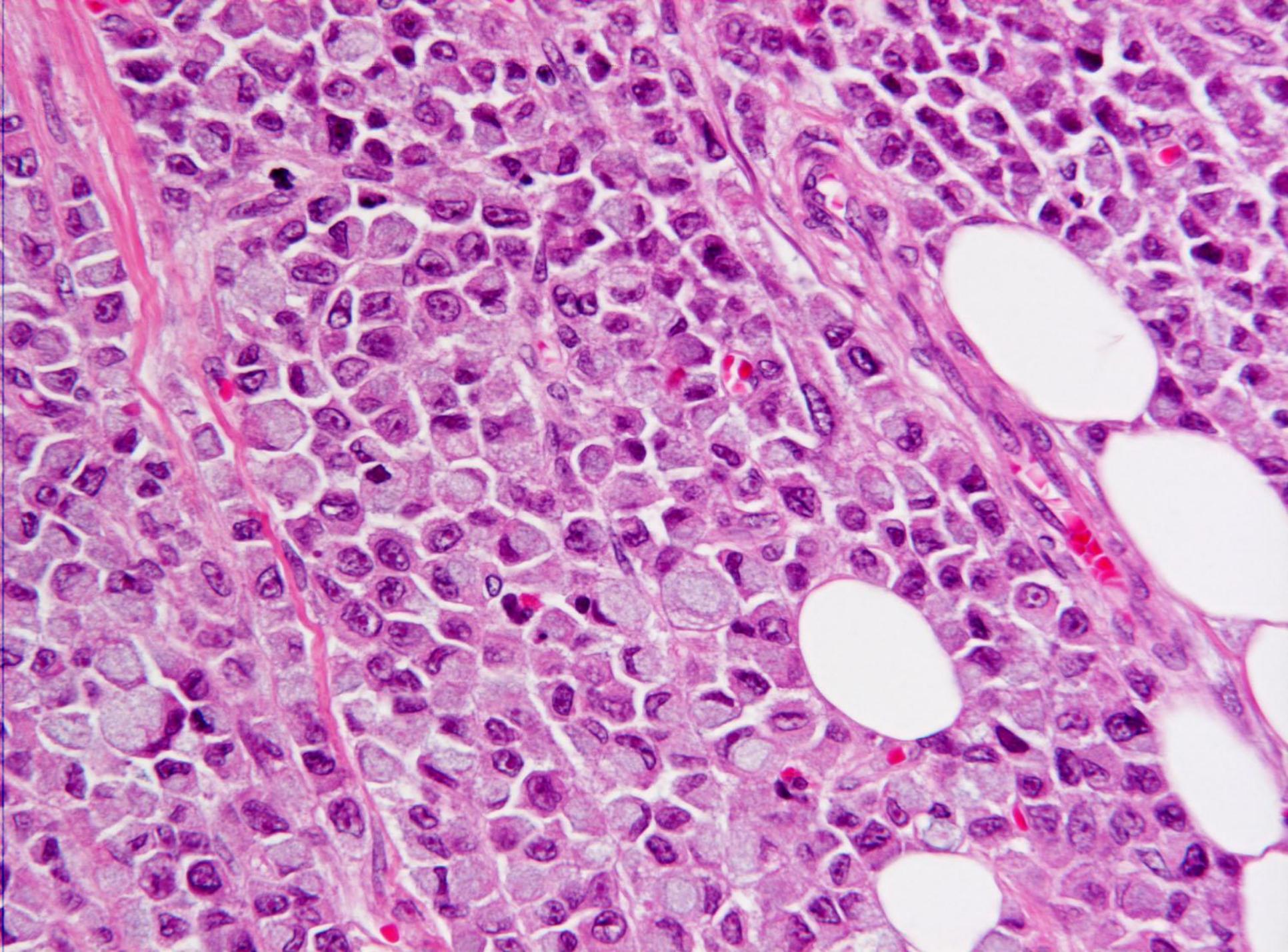


Characteristic	N	%
Site Group		
Right	33	43%
Cecum	15	
Ascending colon	5	
Hepatic flexure	7	
Right colon, NOS	6	
Transverse	9	12%
Left	34	44%
Splenic flexure	6	
Descending colon	6	
Sigmoid colon	10	
Rectum*	12	
Multiple primary sites (ascending, transverse, descending)	1	1%

Tumors relatively evenly divided between right and left colon







Colorectal Carcinoma in Children



Characteristic	N	%
Mucinous adenocarcinoma (>50% tumor composed of mucin)	48	62%
Non-mucinous adenocarcinoma	29	38%

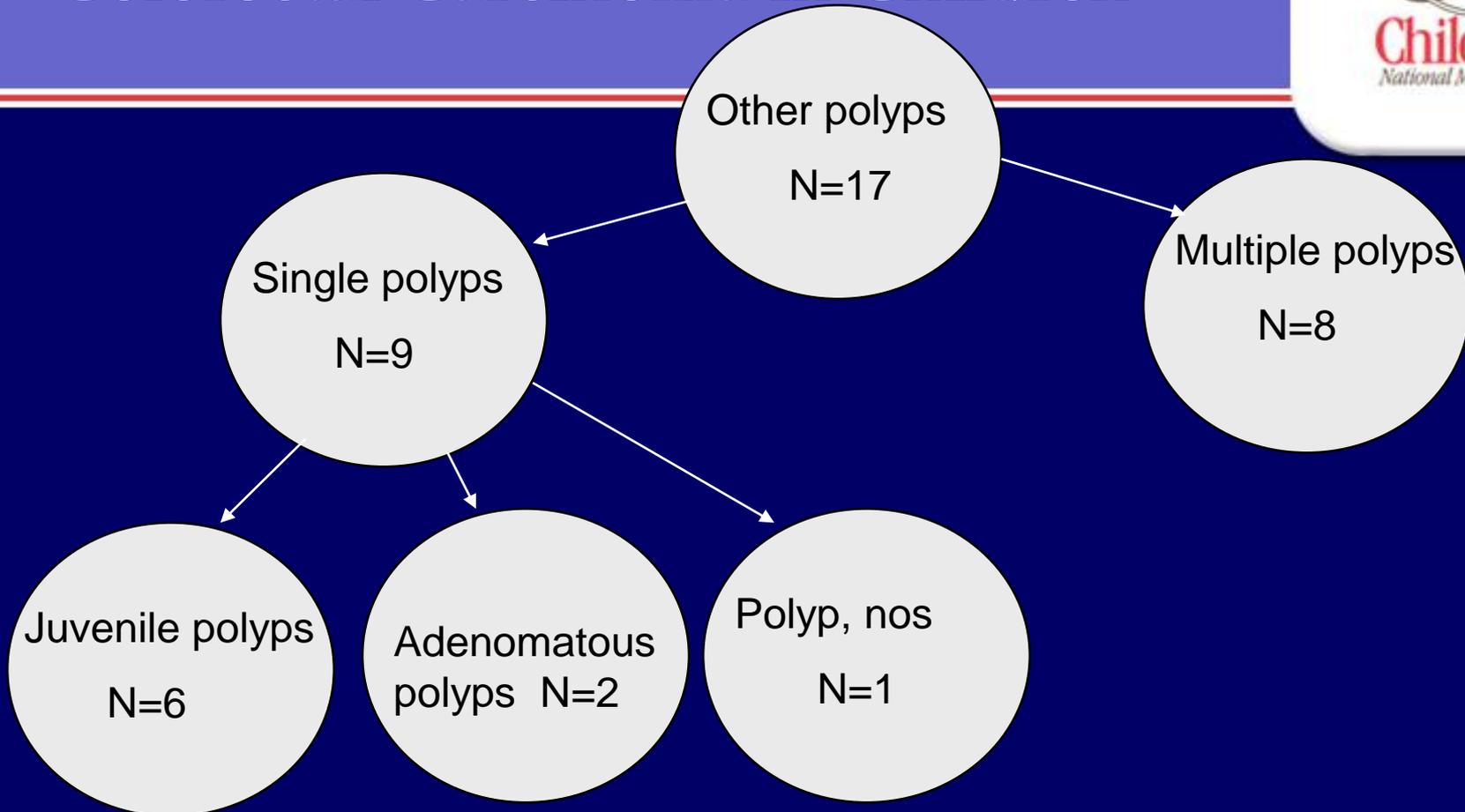
Majority of tumors were mucinous

Colorectal Carcinoma in Children

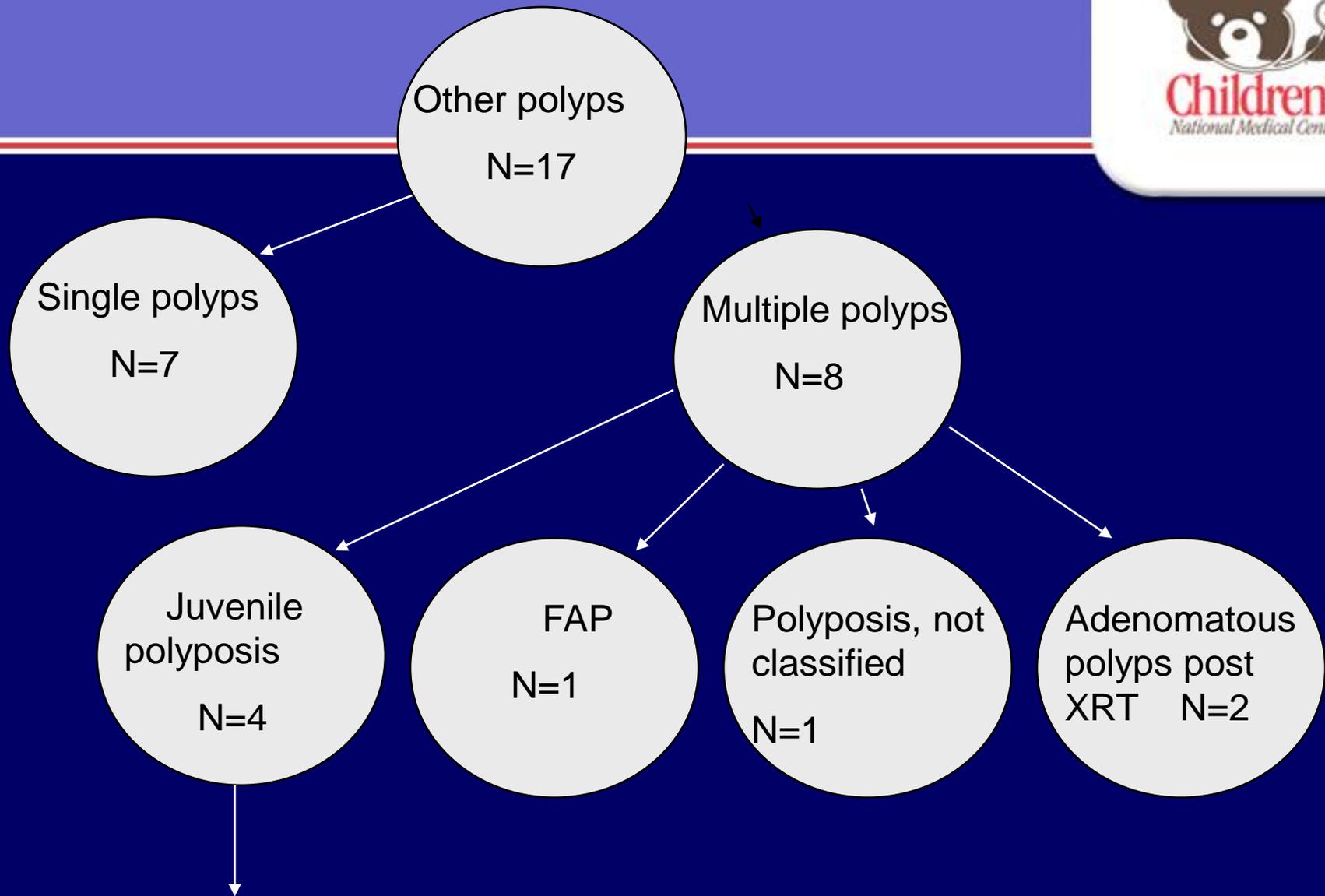


Characteristic	N	%
In-situ component		
Yes	13	17%
No	47	61%
Not evaluable	17	22%
Other polyps identified at time of operation		
Yes	17	22%
Multiple polyps	8	
Single polyp	9	
No	51	66%
Not evaluable or not recorded	9	12%

Colorectal Carcinoma in Children



5/6 adenocarcinomas were mucinous type



4 mucinous adenocarcinomas

Colorectal Carcinoma in Children



- Two patients had coexistent carcinoid tumors

Colorectal Carcinoma in Children



AJCC/UICC Staging System for Colorectal Cancer

Primary Tumor (T)		Regional Lymph Nodes (N)	
TX	Primary tumor cannot be assessed	NX	Nodes cannot be assessed (e.g., local excision only)
T0	No evidence of tumor in resected specimen (prior polypectomy or fulguration)	N0	No regional node metastases
		N1	1-3 positive nodes
Tis	Carcinoma in situ	N2	4 or more positive nodes
T1	Invades submucosa	N3	Central nodes positive
T2	Invade muscularis propria		
T3-T4	<p>Depends on whether serosa is present</p> <p><i>Serosa present:</i></p> <p>T3 Invades through muscularis propria into Subserosa Serosa (but not through) Pericolonic fat within the leaves of the mesentery</p> <p>T4 Invades through serosa into free peritoneal cavity or through serosa into a contiguous organ</p> <p><i>No serosa (distal two thirds rectum, posterior left or right colon):</i></p> <p>T3 Invades through muscularis propria</p> <p>T4 Invades other organs (vagina, prostate, ureter, kidney)</p>	Distant Metastases (M)	
		MX = Presence of distant metastases cannot be assessed	
		M0 = No distant metastases	
		M1 = Distant metastases present	

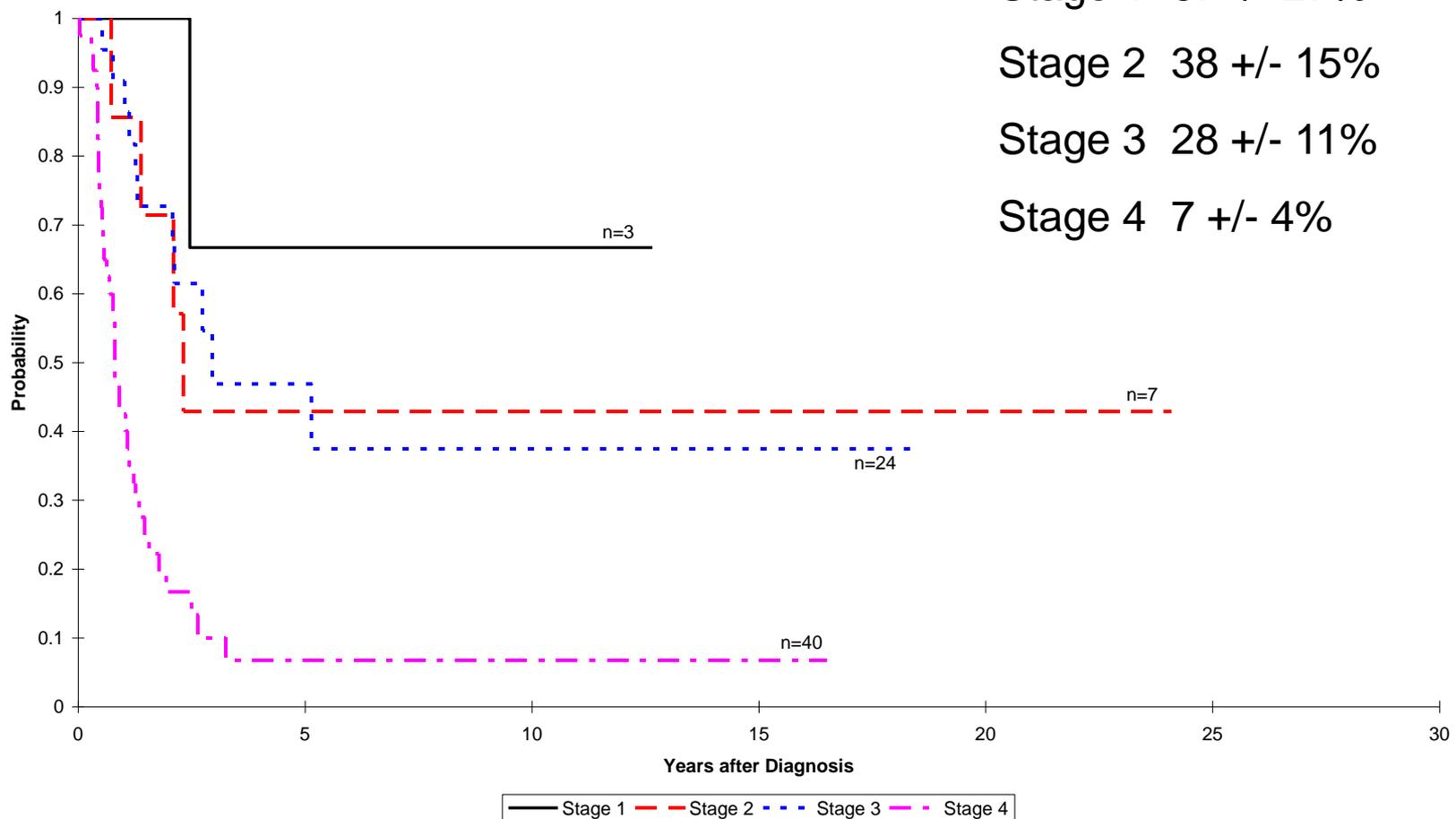
Characteristic	N	% ^
Overall Stage		
1	3	4%
2	8	10%
3	27	35%
4	39	51%
T stage		
1	1	1%
2	2	3%
3	30	39%
4	42	54%
X	2	3%
Nodal status		
0	14	18%
1	18	23%
2	37	48%
X	8	10%
M status		
0	38	49%
1	39	51%

86% of patients presented with advanced stage disease (Stage 3 or 4)

Colorectal Carcinoma in Children



Survival of Colon Cancer Patients
By Overall Stage



Colorectal Carcinoma in Children



- **Of Stage 1 and 2 patients (N0 tumors)**
 - 8/11 had inadequate lymph node recovery by APDSP standards
- **pT staging was influential on outcome (related to mucinous histology)**
- **Estimated survival**
 - pT3 = 37 +/- 10%
 - pT4 = 6 +/- 4%

Factors predictive of poorer 10 year overall survival

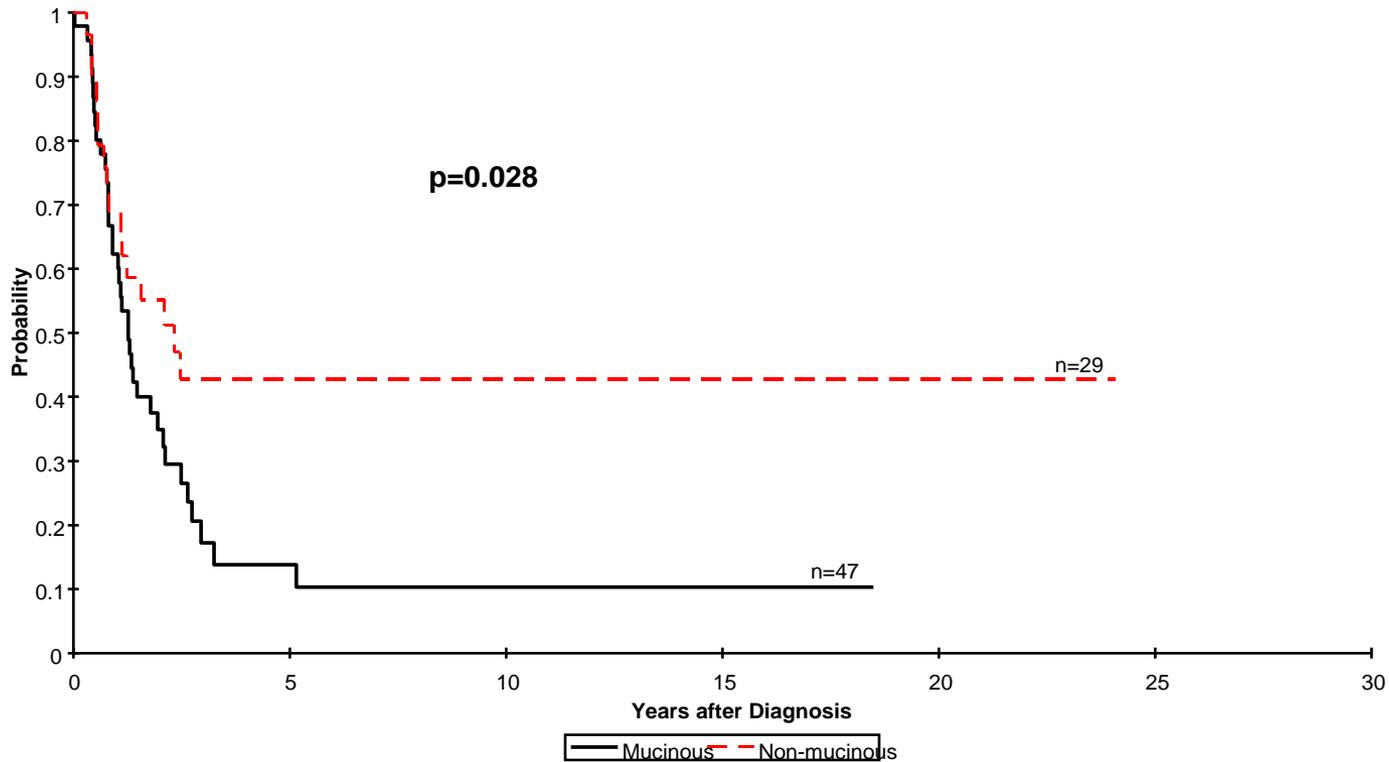


- Mucinous histology ($p=0.020$)
- Signet ring component $> 10\%$ ($p=0.040$)
- Overall stage ($p<0.001$)
- Individual T, N and M stages

Colorectal Carcinoma in Children



Survival of Colon Cancer Patients
Mucinous vs Non-mucinous



Colorectal Carcinoma in Children



- **Outcome analysis summary**
 - 16/77 patients were alive with median follow-up of 12.2 years
 - Estimated survival at 10 years was 20.1 +/- 5.4%
 - Tumor progression in 54 patients
 - Toxicity of therapy in 5 patients
 - Second malignancy in 2 patients (GBM, OS)