International Journal of Colorectal Disease (2019) 34:1879–1885
https://doi.org/10.1007/s00384-019-03402-2

ORIGINAL ARTICLE

# Colon cancer in the young: contributing factors and short-term surgical outcomes

Kamil Hanna[1] · Muhammad Zeeshan[1] · Mohammad Hamidi[1] · Viraj Pandit[1] · Pamela Omesiete[1] · Alejandro Cruz[1] · Agnes Ewongwo[1] · Bellal Joseph[1] · Valentine Nfonsam[1]

Accepted: 23 August 2019 / Published online: 17 October 2019


## Abstract

**Background** The incidence in young patients has increased significantly over the last few decades. The aim of this study is to evaluate demographic and tumor characteristics of young patients and analyze the short-term surgical outcomes of patients undergoing surgery.

**Methods** We performed a 2-year review (2015–2016) of the ACS-NSQIP and included all patients with CC who underwent surgical management. Patients were stratified into two groups: early-onset CC (< 50 years old) and late-onset CC (≥ 50 years old). Outcome measures were hospital length of stay, 30-day complications, mortality, and readmission.

**Results** We included a total of 15,957 patients in the analysis. Mean age was 65 ± 13 years, and 52% were male. Overall 10% of the patients had early-onset CC. Patients with early-onset CC were more likely to be black (11% vs 7%, $p = 0.04$) and Hispanic (8% vs 4%, $p = 0.02$). Additionally, they presented with a more aggressive tumor and higher TNM staging. Patients with early onset CC had lower 30-day complications (18% vs 22%, $p = 0.02$), shorter hospital length of stay (6[3–8] vs 8[5–11], $p = 0.03$) and lower 30-day mortality (0.4% vs 1.8%, $p = 0.04$) compared to their counterparts. However, there was no difference between the two groups regarding 30-day readmission. On regression analysis, there was no difference between the two groups regarding study outcomes.

**Conclusions** Racial disparity does exist in the incidence of colon cancer in the young with higher incidence in blacks. Younger patients with CC tend to have better surgical outcomes on univariate analysis. On regression analysis, the surgical outcomes between the two groups are comparable.

**Keywords** Colon cancer · Young patients · Nationwide Surgical Quality Improvement Program · Racial disparities · Ethnic disparities

Level of Evidence: Level III, Retrospective Observational Study

✉ Valentine Nfonsam
vnfonsam@surgery.arizona.edu

Kamil Hanna
kamilhanna@surgery.arizona.edu

Muhammad Zeeshan
Muhammad.Zeeshan@wmchealth.org

Mohammad Hamidi
hamidi@surgery.arizona.edu

Viraj Pandit
virajpandit@email.arizona.edu

Pamela Omesiete
npo@email.arizona.edu

Alejandro Cruz
acruz700@surgery.arizona.edu

Agnes Ewongwo
ewongwo@email.arizona.edu

Bellal Joseph
bjoseph@surgery.arizona.edu

[1] Department of Surgery, University of Arizona Medical Center, Tucson, AZ, USA

## Introduction

Colon cancer (CC) is the third most common incident cancer and cause of cancer-related deaths in the USA [1]. According to estimates by the International Agency for Research on Cancer (IARC), CC accounted for around 10% of all cancers incident globally, with approximately 814,000 cases in men and 664,000 cases in women [2]. Annually, around 50,630 Americans die of CC. This accounts for approximately one in 12 of all cancer-related deaths [3]. Thus, CC remains a major cause of morbidity and mortality in the USA and is a significant burden on the population and the healthcare system. More than a million US residents were estimated to have been living with CC cancer in 2013 [1].

There is widespread variation in the overall incidence, mortality rates, and epidemiological trends across different countries, and the incidence has been changing over the past two decades especially in high-income countries [4]. More specifically, CC occurrence and mortality have been decreasing significantly since 1990, and multiple reasons behind these shifting epidemiological trends have been identified [5–7]. The widespread implementation of effective screening practices and the resection of adenomatous polyps along with other precursor regions in individuals considered to be at average risk has decreased the annual incidence by 4% per year [8, 9]. There has also been advances in the disease's management which has led to improvement in cancer-free survival [10–13]. Despite all these significant progress made, during the same time period, there is an alarming increase in the incidence of CC in individuals below the age of 50 especially in high-income counties [14–16]. Rates are projected to increase by 124% for patients aged 20–34 years, and by 46% for patients aged 35–49 years by 2030 [17].

Unlike middle-aged individuals, there is a paucity of data describing the unique characteristics of CC in young patients [18]. Understanding the unique risk profile of patients below the screening age threshold, along with their surgical outcomes following resection provides insight into the pathogenesis of the disease in light of our understanding of its genetic and environmental underpinnings. Furthermore, it will also guide efforts for prevention and early detection [18]. The aim of this study is to evaluate demographic and tumor characteristics of young patients and analyze the short-term surgical outcomes of patients undergoing surgery.

## Methods

### Data source

We queried the American College of Surgeons – National Surgical Improvement Program (ACS-NSQIP) database. ACS-NSQIP is a nationwide compiled surgical database that can guide national quality improvement programs by providing risk-adjusted information on surgical outcomes. Data from > 550 institutions across the USA and Canada is collected based on current procedural terminology (CPT) codes. This study was an exempt from the Institutional Review Board as the ACS-NSQIP database contains deidentified patient data.

### Patient selection (inclusion and exclusion criteria)

We performed a 2-year (2015–2016) retrospective cohort analysis and selected all adult patients (age ≥ 18) diagnosed with CC and underwent surgical management. Patients who non-surgically managed were excluded from the analysis.

### Patient stratification

Patients were stratified into two groups on the basis of age at presentation: Early-onset CC (< 50 years old) and late-onset CC (≥ 50 years old). The age of 50 years was used as a cutoff for stratification because it is the age beyond which screening is recommended for individuals considered to be at average risk of CC and it is the age below which the incidence of CC is noted to be rising unlike middle-aged and older adults.

### Data points and study outcomes

The following data points were collected for each patient from the dataset: age, gender, race, ethnicity, body mass index, functional status, comorbidities, type of anesthesia, procedure type, and wound classification. Outcome measures were hospital length of stay, 30-day complications, mortality, and readmission. The post-operative complications analyzed were stratified as follows: respiratory (pneumonia, re-intubation, and ventilator support), cardiac (cardiac arrest and myocardial infarction), hematologic (deep venous thrombosis and pulmonary embolism), septic, renal (acute and progressive renal failure), neurological (coma and cerebrovascular incident), wound complications (infection or dehiscence), and urinary tract infection. A complication was defined as suffering from at least one of the aforementioned complications.

### Outcome measures

Surgical outcome measures were hospital length of stay, 30-day complications, 30-day mortality, and 30-day readmission.

### Statistical analysis

We reported descriptive statistics. Data are reported as mean ± standard deviation (SD) for continuous variables with normal distribution, as median [interquartile range (IQR)] for continuous variables without normal distribution, and as proportions (% percentage) for the categorical variables. To analyze the

differences between the two patient groups on the univariate level, we used a chi-square test for categorical variables, the Mann-Whitney *U* test for continuous nonparametric data, and the independent Student's *t* test for continuous parametric data.

A multivariate logistic regression was used to control for the following covariates: patient's demographics, comorbidities, TNM stage, ASA class, type of surgery, anesthesia, and recipient of chemotherapy. First, we evaluated the association between each covariate and the binary outcomes, on a univariate level. Variables with a $p$ value of less than 0.2 in the univariate model were included in multivariable logistic regression model. On the multivariable logistic regression analysis, variables were considered significant at $p$ value of $< 0.05$. To assess the model fit, Hosmer-Lemeshow test was performed. In the logistic regression model, the Hosmer-Lemeshow test exceeded 0.05 and the tolerance was greater than 0.1 for all independent variables with a variance inflation factor of less than 10.0. In our study, alpha was set at 5% and a value of $p < 0.05$ was considered statistically significant. All statistical analyses were conducted using the Statistical Package for Social Sciences software (SPSS, version 24; SPSS, Inc.).

## Results

A total of 15,957 adult patients diagnosed with CC and managed operatively were identified throughout the study period. The sample was stratified based on the age at presentation into the early CC group which includes those who presented < 50 years of age ($n = 1567$) and the late CC group which includes those who presented ≥ 50 years of age ($n = 14{,}390$). Mean age was 64 ± 9 years and 49% were male. In terms of race and ethnicity, 7.3% were black and 4.3% were Hispanic. The overwhelming majority of patients were functionally independent at the time of presentation (96%). The patient cohort was not free from comorbidities. The most commonly noticed comorbidity was hypertension 55% followed by smoking 14%. Regarding their operative intervention, the overwhelming majority of patients were operated on under general anesthesia (99.6%), under non-emergent conditions, with a clean/contaminated wound classification (87.3%).

Patients with early-onset CC were more likely to be male (53.2% vs. 38.9%; $p < 0.01$), black (11% vs 7%, $p < 0.01$), and Hispanic (8% vs 4%, $p < 0.01$). Additionally, patients in the early-onset group were more likely to be functionally independent (98.5% vs. 95.8%, $p < 0.01$) and were more likely to have a lower ASA Class ≥ 3 (40.2% vs. 66.9%, $p < 0.01$) compared to patients in the late-onset group. In terms of comorbidities, patients in the late-onset group are more likely to present with higher rates of comorbidities including diabetes mellitus ($p < 0.01$), hypertension ($p < 0.01$), CHF ($p < 0.01$), and dyspnea ($p < 0.01$). On the other hand, patients in the early-onset group had higher rates of smoking ($p < 0.01$), and weight loss ($p < 0.01$) (Table 1).

On analysis of surgical outcomes, patients with early-onset CC had a shorter hospital length of stay (6[3–8] vs. 8[5–11]; $p = 0.03$), along with lower rates of 30-day complications (18% vs 22%, $p = 0.02$), and 30-day mortality (0.4% vs 1.8%, $p = 0.04$) compared to their counterparts. However, there was no difference between the two groups regarding the rate of 30-day readmission (11.9% vs. 12.2%, $p = 0.29$) (Table 2). Regarding tumor characteristics, patients in the early-onset were more likely to present with aggressive tumor and higher TNM staging. Patients in the early onset CC were more likely to have a larger tumor size $T > 2$ (64% vs. 58%; $p = 0.02$), an increased likelihood of lymph node involvement (49% vs. 38%; $p = 0.02$), and distant metastasis (12% vs. 7%; $p = 0.01$) (Table 3). Additionally, these patients were also more likely to undergo emergent surgery (20% vs 16%, $p = 0.01$) compared to patients with late-onset CC.

On multivariate regression analysis after controlling for demographics, comorbidities, type and approach of surgery, TNM stage, and ASA class, there was no difference between the two groups regarding 30-day complications (OR 0.97 [0.79–2.45], $p = 0.26$), 30-day mortality (OR 0.92 [0.82–3.15], $p = 0.28$), and 30-day readmission (OR 1.11 [0.92–3.58], $p = 0.59$) (Table 4).

## Discussion

The results of our study indicate that in a nationally representative sample of CC patients, around 10% has early onset CC. Therefore, the increasing incidence of early onset CC is significant and is an alarming epidemiological trend and warrants further investigation. In an effort to outline the unique set of patient-related factors that define the risk profile of early onset CC, our results can help identify and risk stratify patients, and this may help guide disease surveillance and promote early diagnosis. In addition, the results show no apparent difference in surgical outcomes when comparing early versus late onset CC after adjusting for measurable confounding variables.

Patients with early onset CC are more likely to be functionally independent according to the results, and these patients have the potential to lose a large number of productive years [19]. It is therefore imperative to explore the unique risk factors in this vulnerable age group. Kolligs et al. conducted a recent epidemiological review of CC and reported that the incidence in individuals below the age of 50 was around 10% [20]. The incidence is in line with the results of this study. Nationally compiled databases like the NSQIP can capture a large number of patients from multiple centers, and this can allow clinicians to explore pertinent characteristics and recognize trends that can allow the early identification of high-risk individuals for the purpose of screening and early diagnosis.

**Table 1** Patient characteristics

| Variable | Early ($n = 1567$) | Late ($n = 14,390$) | $p$ value |
|---|---|---|---|
| Age, mean ± SD | 42 ± 5 | 66 ± 14 | < 0.01* |
| Male, *n* (%) | 53.2% | 48.9% | < 0.01* |
| Black, *n* (%) | 11% | 7% | 0.04* |
| Hispanic, *n* (%) | 8% | 4% | 0.02* |
| BMI, mean ± SD | 28.7 ± 7.7 | 28 ± 7.0 | < 0.01* |
| Functional status, *n* (%) | | | |
| Independent | 98.5% | 95.8% | < 0.01* |
| Partially dependent | 0.7% | 3.3% | < 0.01* |
| Totally dependent | 0.3% | 0.4% | < 0.01* |
| Unknown | 0.6% | 0.5% | < 0.01* |
| ASA Class ≥ 3, *n* (%) | 40.2% | 66.9% | < 0.01* |
| Comorbidities, *n* (%) | | | |
| Diabetes mellitus (non-insulin) | 5.5% | 14.1% | < 0.01* |
| Hypertension | 21.0% | 59.5% | < 0.01* |
| Current smoker | 18.9% | 12.9% | < 0.01* |
| CHF (30-day before surgery) | 0.2% | 2.1% | < 0.01* |
| History of severe COPD | 0.7% | 7.2% | < 0.01* |
| Bleeding disorder | 1.7% | 4.8% | < 0.01* |
| Dyspnea (at rest) | 0.3% | 0.8% | < 0.01* |
| Steroids use for chronic condition | 2.8% | 3.3% | 0.35 |
| Systemic sepsis, *n* (%) | 6.4% | 4.6% | < 0.01* |
| Sepsis | 2.0% | 1.7% | < 0.01* |
| Septic shock | 0.1% | 0.2% | < 0.01* |
| SIRS | 4.3% | 2.7% | < 0.01* |
| Currently on pre-op dialysis | 0.1% | 0.7% | 0.01* |
| Ascites | 1.4% | 1.0% | < 0.1* |
| > 10% weight loss | 7.9% | 5.9% | < 0.01* |
| Type of anesthesia | | | |
| General, % | 99.5% | 99.7% | 0.49 |
| Wound classification, *n* (%) | | | |
| Clean | 2.0% | 1.6% | < 0.01* |
| Clean/contaminated | 84.7% | 87.6% | < 0.01* |
| Contaminated | 7.7% | 7.0% | < 0.01* |
| Dirty | 5.6% | 3.8% | < 0.01* |
| Type of surgery | | | |
| Emergent procedure | 20% | 16% | 0.01* |

*SD* standard deviation, *ASA* American Society for Anesthesiology, *CHF* congestive heart failure, *COPD* chronic obstructive pulmonary disease

*Statistically significant, $p < 0.05$

For example, the results shed light on noticeable racial and ethnic disparities in the incidence of early onset CC. The patients with early onset CC are more likely to be black and Hispanic. These findings are consistent with previously published studies. Compared to other races, the incidence and mortality of CC differ significantly among African-Americans. According to the American Cancer Society estimates, incidence rates were 25% higher and mortality rates were 50% higher in African-Americans compared to Caucasians in the period between 2006 and 2010 [21]. Stefanis et al. analyzed a single-center tumor registry, and they looked into the incidence of CC in Hispanics and reported results that are in line with the findings of this study [22]. Hispanic patients are more likely to be younger at the time of diagnosis and are more likely to have more metastatic disease leading to a poor prognosis relative to non-Hispanics.

BMI is another important risk factor captured in the results of this study. The association between BMI and CC has been

**Table 2** Univariate analysis of the study outcomes

| Outcomes | Early ($n = 1567$) | Late ($n = 14,390$) | $p$ value |
|---|---|---|---|
| Hospital length of stay, median (IQR) | 6 (3–8) | 8 (5–11) | 0.03* |
| 30-day complications, $n$ (%) | 18% | 22% | 0.02* |
| 30-day mortality, $n$ (%) | 0.4% | 1.8% | 0.04* |
| 30-day readmission, $n$ (%) | 11.9% | 12.2% | 0.29 |

*Statistically significant, $p < 0.05$

described multiple times in previous studies [23]. Even though the difference in the mean BMI between the two groups reached statistical significance in the results, the difference is not clinically significant. The contribution of BMI in increasing the risk in both early onset and late onset CC patients is expected. In light of our understanding of the pathophysiology of carcinogenesis, there is clearly an interplay of both environmental and genetic factors.

In this study, the distribution of the patients' comorbidities differed between the two groups and this could contribute to our understanding of the effect of the comorbidity profile of the patient in dictating the eventual risk of early onset CC. For example, patients in the early onset CC group had higher rates of smoking. Smoking has been shown to be associated with malignant diseases involving many organ systems and CC is no exception. In a meta-analysis of prospective cohort studies, Kelvin et al. examined the association between smoking and CC [22]. Not surprisingly, smokers exhibited a significantly higher risk of CC, findings that is consistent with other studies. Smoking is a potentially modifiable environmental and lifestyle associated risk factor that is highly relevant to the young age group [24].

When examining the disease's characteristics related to the tumor biology and aggressiveness, there is a noticeable trend towards a more aggressive disease in patients with early onset CC. This is evident when comparing tumor size, lymph node involvement, and extent of distant metastasis. Patients in the early onset CC group were more likely to have a larger tumor size, lymph node involvement, and disseminated disease. The reason behind the evident aggressive course in this group of patients is yet to be fully explained but is most likely due to the complex interplay of these patients' unique environmental risk factors along with their genetic predisposing factors. The genetics of early onset CC is growing field of research and the development of gene panels that can be used to test individuals with certain risk factors has become a subject of interest [25].

On a multivariable level analysis after controlling for measurable imbalances between the two groups including the tumor characteristics, there were no further differences in post-operative outcomes between the two groups as was shown in the univariate analysis. This demonstrates a confounding effect when examining the results of the univariate analysis. Age at presentation has been confounded by the differences in tumor characteristics observed between the two groups and that it contributes primarily to a more aggressive disease at the time of the diagnosis. However, after we adjusted for the disease characteristics between the two groups, older patients were no different than their younger counterparts.

A retrospective review of 162 CC patients performed by Habib et al. at a tertiary center to compare the presentation and survival outcomes in younger patients compared to older patients with CC showed no significant differences in surgical outcomes and post-operative complications even with the two groups having similar postoperative TNM staging. The results from this study is aligned with the findings of ours. In addition, there were no differences in survival between older and younger CC patients [26].

There are some inherent limitations of our study. There are limitations attributed to the retrospective nature of the analysis, unmeasurable confounding factors, and erroneous data entry. The NSQIP database samples more procedures from a greater number of institutions with every iteration, and it is not possible to determine the completeness of sampling year to year for any given procedure or any given hospital.

**Table 3** Tumor staging characteristics

| Variable | Early ($n = 1567$) | Late ($n = 14,390$) | $p$ value |
|---|---|---|---|
| Size, $T > 2$, $n$ (%) | 64% | 58% | 0.02* |
| Lymph node involvement, $n$ (%) | 49% | 38% | 0.02* |
| Distant metastasis, $n$ (%) | 12% | 7% | 0.01* |

*Statistically significant, $p < 0.05$

**Table 4** Multivariate logistic regression

| Variable | Adjusted odds ratio | 90% CI | $p$ value |
|---|---|---|---|
| 30-day complications | 0.97 | 0.79–2.45 | 0.26 |
| 30-day mortality | 0.92 | 0.82–3.15 | 0.28 |
| 30-day readmission | 1.11 | 0.92–3.58 | 0.59 |

Ref. late colon cancer. Adjusting for demographics (age, gender, race, ethnicity), Body Mass Index, functional status, comorbidities, ASA Class, TNM stage, type, and approach of surgery

Furthermore, we were not able to follow up patients for a longer period of time to determine CC recurrence, or CC free survival which are important oncological outcome measures. Patients with a more advanced disease such as the younger CC group could eventually end up having a different long-term course and mortality relative to their older counterparts. In addition, we could not capture data points regarding surgical margins which also have a bearing on oncological outcomes. However, the study analyzes a nationally representative cohort of CC patients and describes the salient characteristics of early onset CC patients, this which helps guide screening and surveillance to promote early identification of CC. The study also presents encouraging results stating that surgical outcomes in young patients are no different than their older counterparts when matched for disease stage and this signifies that the early identification of young patients with CC can allow us to achieve the same favorable epidemiological trends observed in older patients.

The study paves the way for future research studies that aim to further refine the characteristics of early onset CC patients and allows the development of screening guidelines and surveillance programs. In addition, future research studies using prospective data can also better examine surgical and longer-term oncological outcomes.

## Conclusion

Racial disparity does exist in the incidence of CC in the young with higher incidence seen in blacks. Higher rate of smoking was associated with CC in younger patients. Young patients also tend to have more aggressive disease and are more likely to undergo emergency surgery. However, younger patients with CC tend to have similar surgical outcomes at least in the immediate post-operative period.

**Author contributions** Study design and conception: VN, MH, MZ, KH, AE.
Data acquisition: AC, VN, KH, MH, PO, BJ, VP.
Statistical analysis: PO, VN, KH, MH, VP.
Manuscript writing: MZ, AE, MH, KH, VN, BJ, VP.
Critical revision: AC, VN, KH, MH, MZ, PO, BJ.

**Funding information** The study did not receive any funding.

### Compliance with ethical standards

The authors have no financial or proprietary interest in the subject matter or materials discussed in the manuscript. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Conflict of interest** The authors declare that they have no conflicts of interest.

## References

1. Marley AR, Nan H (2016) Epidemiology of colorectal cancer. Int J Mol Epidemiol Genet 7(3):105–114
2. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F (2015) Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 136(5):E359–EE86
3. Siegel RL, Miller KD, Jemal A (2019) Cancer statistics, 2019. CA Cancer J Clin 69(1):7–34
4. Haggar FA, Boushey RP (2009) Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. Clin Colon Rectal Surg 22(04):191–197
5. Segal RL, Miller KD, Jemal A (2018) Cancer statistics, 2018. CA Cancer J Clin 68:7–30
6. Brenner H, Stock C, Hoffmeister M (2014) Effect of screening sigmoidoscopy and screening colonoscopy on colorectal cancer incidence and mortality: systematic review and meta-analysis of randomised controlled trials and observational studies. Bmj. 348: g2467
7. Murphy CC, Sandler RS, Sanoff HK, Yang YC, Lund JL, Baron JA (2017) Decrease in incidence of colorectal cancer among individuals 50 years or older after recommendations for population-based screening. Clin Gastroenterol Hepatol 15(6):903–909
8. Welch HG, Robertson DJ (2016) Colorectal cancer on the decline—why screening can't explain it all. N Engl J Med 374(17):1605–1607
9. Edwards BK, Noone AM, Mariotto AB, Simard EP, Boscoe FP, Henley SJ, Jemal A, Cho H, Anderson RN, Kohler BA, Eheman CR, Ward EM (2014) Annual report to the nation on the status of cancer, 1975-2010, featuring prevalence of comorbidity and impact on survival among persons with lung, colorectal, breast, or prostate cancer. Cancer. 120(9):1290–1314
10. Sargent D, Sobrero A, Grothey A, O'Connell MJ, Buyse M, Andre T et al (2009) Evidence for cure by adjuvant therapy in colon cancer: observations based on individual patient data from 20,898 patients on 18 randomized trials. J Clin Oncol 27(6):872
11. Saltz LB, Cox JV, Blanke C, Rosen LS, Fehrenbacher L, Moore MJ et al (2000) Irinotecan plus fluorouracil and leucovorin for metastatic colorectal cancer. N Engl J Med 343(13):905–914
12. de Gramont A, Figer A, Seymour M, Homerin M, Hmissi A, Cassidy J et al (2000) Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer. J Clin Oncol 18(16):2938–2947
13. Hall WH (1990) Adjuvant therapy for patients with colon and rectal-cancer. JAMA 264(11):1444–1450
14. Ahnen DJ, Wade SW, Jones WF, Sifri R, Silveiras JM, Greenamyer J, Guiffre S, Axilbund J, Spiegel A, You YN (2014) The increasing incidence of youngonset colorectal cancer: a call to action. In Mayo Clinic Proceedings 2014 Feb 1 (Vol. 89, No. 2). Elsevier, Amsterdam, pp 216–224
15. You YN, Xing Y, Feig BW, Chang GJ, Cormier JN (2012) Young-onset colorectal cancer: is it time to pay attention? Arch Intern Med 172(3):287–289
16. Siegel RL, Jemal A, Ward EM (2009) Increase in incidence of colorectal cancer among young men and women in the United States. Cancer Epidemiology and Prevention Biomarkers 18(6): 1695–1698
17. Bailey CE, Hu C-Y, You YN, Bednarski BK, Rodriguez-Bigas MA, Skibber JM, Cantor SB, Chang GJ (2015) Increasing disparities in the age-related incidences of colon and rectal cancers in the United States, 1975-2010. JAMA Surg 150(1):17–22
18. Deen KI, Silva H, Deen R, Chandrasinghe PC (2016) Colorectal cancer in the young, many questions, few answers. World J Gastrointest Oncol 8(6):481

19. O'Connell JB, Maggard MA, Liu JH, Etzioni DA, Livingston EH, Ko CY (2003) Rates of colon and rectal cancers are increasing in young adults. Am Surg 69(10):866–872
20. Kolligs FT (2016) Diagnostics and epidemiology of colorectal cancer. Visc Med 32(3):158–164
21. Torre LA, Siegel RL, Ward EM, Jemal A (2016) Global cancer incidence and mortality rates and trends—an update. Cancer Epidemiology and Prevention Biomarkers. 25(1):16–27
22. Tsoi KK, Pau CY, Wu WK, Chan FK, Griffiths S, Sung JJ (2009) Cigarette smoking and the risk of colorectal cancer: a meta-analysis of prospective cohort studies. Clin Gastroenterol Hepatol 7(6):682–8 e1-5
23. Shaukat A, Dostal A, Menk J, Church TR (2017) BMI is a risk factor for colorectal cancer mortality. Dig Dis Sci 62(9):2511–2517
24. Kwan LY, Stratton K, Bonnie RJ (2015) Public health implications of raising the minimum age of legal access to tobacco products. National Academies Press, Washington
25. Chung DC (2018) Genetic testing and early onset colon cancer. Gastroenterology. 154(4):788–789
26. Habib R, Gebski V, Toh J, Pathma-Nathan N, Khoury TE, Ctercteko G, Jayamohan J, Wong KYM, Wilcken N, Nagrial A (2019) Outcomes of younger patients diagnosed with locally advanced rectal cancer. Proc Am Soc Clin Oncol 37:500