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A Retrospective Epidemiological Study and Prognostic Factors of Lower Rectal and Anal Carcinoma

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Abstract

Background: Anorectal carcinoma includes tumors of the anal margin, the anal canal, and the low rectum. The incidence of rectal cancer is 40% of all colorectal cancers, but anal tumors represent 2.5% of all gastrointestinal tumors. The incidence of anal malignancy has been increased in the last 30 years, both in the USA and elsewhere. Adenocarcinomas are the most frequent pathological subtype.

Patients and methods: Our study is retrospective and was conducted for 5 years. Patient's data were collected from the medical records through a predesigned sheet that included the following information: demographic data, medical history, past history, presenting symptoms, pathological data, treatment details and treatments outcomes in the form of PFS and OS.

Results: Of 181 cases, 11.6% were anal adenocarcinoma, 39.2% were rectal adenocarcinoma, 74% were anorectal adenocarcinoma, and 2.2% were anal squamous cell carcinoma. The median age for AA was 55 years, 52 years for RA, and 51 years for ARA. The median OS was lower for AA (41 months); compared with RA (62.3 months) and ARA (61.1 months) (P value 0.3) that needs further evaluation. Early stages had a better OS (63 months) while advanced and metastatic stages were associated with shorter OS (30.2 and 12.4months) respectively with highly statistically significant. Positive safety margin and positive lymphovascular/perineural invasion were associated with shorter OS (31.9 months) in comparison to higher survival in patients with the negativity of these two factors (61.6 months) and this was significantly high (p-value: 0.03). Univariate analysis for PFS revealed that the age only can affect PFS significantly as the younger age group has a median survival of 54 months in comparison to 33.5 months for the older age.

Conclusion: AA has poor prognosis than ARA, RA. The early-stage has a better OS that needs more effort for early diagnosis and treatment.

Keywords: Anorectal cancers; Adenocarcinoma; Chemoradiotherapy; Preserving surgery; Anal cancer; CRT; Neoadjuvant; Adjuvant; TAB

Introduction

Colorectal cancer (CRC) represents the 3rd most prevalent cancer and the 4th common cause of cancer deaths worldwide. It accounts for 9.7% of the incidence of all cancers worldwide and 6.5% in Egypt [1]. The incidence of rectal cancer is 40% of all colorectal cancers; However anal tumors forms 2.5% of all gastrointestinal tumors [2]. In Egypt, colorectal cancer cases are increasing annually, diagnosed in 13% of patients who experiencing colonoscopy [3]. This is due to generational changes such as the effect of dietary patterns, obesity, and lifestyle. In developed countries the mortality rates decrease due to selection of more best practices in cancer treatment and hence improve the survival [4].

CRC is mostly found in people aged 50 years or older in developed countries [5]. In Egypt, there are relatively higher CRC rates in patients under 40 years of age than reported in the west. This has implications relating to future epidemiological trends in Egypt [3]. The incidence of anal malignancy has been increased in the last 30 years, both in the United States (USA) and elsewhere particularly in women [6]. Females are more likely to develop anal cancer than males (ratio of 5:1) [7]. This is due to high prevalence of human papilloma virus (HPV) [8].

High red meat intake and low fibers strongly linked to CRC due to production of carcinogen (N-nitroso compounds) by bacterial flora and heme iron in red meat [9]. Smoking is an independent factor for anal cancer due to genotoxic damage to the anal epithelium and has a role in formation and rate of growth of adenomatous polyps. Which are precursors lesions for CRC [10]. Homosexuality is increasing the risk of developing anal cancer. Among heterosexual, the number of lifetime sexual partners and the young age at first intercourse are associated with high risk of developing anal cancer [10].

Adenocarcinomas are the most frequent pathological subtype than squamous cell carcinoma (SCC) due to the anorectal region is formed mainly of glandular structure [11]. Our aim is to study Clinico-epidemiological characteristics of the patients with low rectal and anal carcinoma presented to Clinical Oncology & Nuclear Medicine Department at Mansoura University Hospital from the period of 2012 up to 2016 and this is the primary end point. The Secondary end point is to assess progression free survival (PFS) and overall survival (OS) of the patients with different methods of treatment and evaluation of prognostic factors.

Patients and Methods

This study is a retrospective study and was conducted for five years includes a review of the total number of available registered cases of

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patients with lower rectal and anal carcinoma. They were 181 patients presented to Mansoura Clinical Oncology and Nuclear Medicine Department, Mansoura University Hospital during the period from January 2012 to December 2016 inclusive.

Patient's data were collected from the medical records through a predesigned sheet that included the following information: demographic data as age, sex, marital status and occupation. Medical history was collected as well as family history, risk factors as smoking, nutritional status, viral infection and sexual behavior then past history to previous operations and/or pelvic irradiation.

The presenting symptoms and signs were collected as bleeding per rectum, perianal pain, change in the bowel habit or loss of weight, anal swelling, abscess or fistula and intestinal obstruction (IO). Pathological data were obtained as histopathology, primary tumor size and extent, number of metastatic lymph nodes, safety margin and presence of vascular invasion. The laboratory, endoscopic and radiological investigations and metastatic work up done to the patients were collected. Treatment details including surgery with different surgical modalities, external beam radiotherapy (EBRT) and chemotherapy (CTH) were reported. Treatments outcomes in the form of PFS and OS were calculated for all our patients.

Statistical Analysis

Data were revised, coded and analyzed using the computer program, SPSS version "23". Numerical data were expressed as mean and standard deviation or median and range as appropriate. Qualitative data were expressed as frequency and percentage. Chi-square test (fisher exact test) was used to examine the relation between qualitative variables. P-value considered significant when <0.05. Survival was evaluated using Kaplan-Meier method.

Results

Anal adenocarcinomas (AA), lower rectal adenocarcinomas (RA), anorectal adenocarcinomas (ARA) and anal squamous cell carcinoma (SCCA) were identified. Only, pathologically confirmed cases were included. Cases with more than one primary were excluded.

Patient's characteristics were shown in Table 1. Median age was 53 years, 67 patients (37%) were less than 50 years old, and 114 patients (63%) were ≥ 50 years old. One hundred patients were male (55.2%) while females were 81 patients (44.8%). Positive family history of colon, or anorectal cancers in first degree relatives was found in 7 (3.9%) patients only. ECOG (0-1) was the most common performance status among 129 (71.2%) patients while ECOG (2-3) was found in 52 patients (28.8%).

Regarding symptoms and signs, bleeding per rectum, change in bowel habit, perianal pain and less common complaint like abscess, fistula or mass and intestinal obstruction were found as first presentation in 125 (69.1%), 52 (28.7%), 50 (27.6%), 13 (7.2%) and 4 (2.2%) patients respectively.

As regard tumor extension, 47% of patients had anorectal disease, 39.2% had lower rectal cancer, while anal cancer was encountered in 13.8% of cases only. Adenocarcinoma predominance was found in 97.8%. The majority of them (47%) have anorectal adenocarcinomas (ARA) while the lower rectal adenocarcinomas (RA) showed 39.2% and 11.6% had anal adenocarcinomas (AA). Squamous cell carcinoma (SCC) was found in 4 patients (2.2%) of the total 181 patients.

Only 15 patients (8.3%) were diagnosed as stage I, whereas 86 patients (47.5%) had stage II disease, stage III disease was found in 61 patients (33.7%) while, 19 patients (10.5%) had stage IV disease at the time of diagnosis of the reported 181 cases. Moderate differentiated tumors are the most common among 65.7% of tumors; poorly differentiated tumors constitute 22.1% while well differentiated tumors found in 12.2%.

Table 2 shows the clinical staging of the study population. Locally advanced tumors (stage II and III) are most prevalent in anal and rectal carcinoma 88%, 80.7% respectively. The metastatic disease found in 12% of anal cancer and 9.6% for lower rectal and anorectal carcinoma. The localized disease only found in 9.6% of rectal cancer cases.

Treatment details are described in Table 3. Total abdominal resection (TAB) was the mainstay for treatment of stage I disease. It is associated with or without adjuvant chemoradiotherapy (CRT) with a percent from total number of stage I (15 patients) as 53.3%, 46.7% respectively. Neoadjuvant treatment followed by TAB resection was the treatment found in locally advanced tumors stage II (57.8%)

Characteristics of 181 patients	No (%)
Age in years	
Median (Minimum - Maximum)	53 (21 - 80)
Age < 50 years	67 (37%)
Age ≥ 50 years	114 (63%)
Sex	
Male	100 (55.2%)
Female	81 (44.8%)
Family history	
Positive family history	7 (3.9%)
Presentation*	
Bleeding per rectum	125 (69.1%)
Change in the bowel habit	52 (28.7)
Perianal pain	50 (27.6%)
Perianal abscess	8(4.4%)
Anal mass	5 (2.8%)
Intestinal obstruction	4 (2.2%)
ECOG performance status	
ECOG 0	10 (5.5%)
ECOG 1	119 (65.7%)
ECOG 2	47 (26%)
ECOG 3	5 (2.8%)
Site of primary tumor	
Anorectal	85 (47%)
Lower rectum	71 (39.2%)
Anal	25 (13.8%)
Histopathological types	
Anorectal adenocarcinomas	85 (46.9%)
Lower rectal adenocarcinomas	71 (39.2%)
Anal adenocarcinomas	21 (11.6%)
Anal squamous cell carcinoma	4 (2.2%)
Clinical stage	
Stage I	15 (8.3%)
Stage II	87 (48.1%)
Stage III	61 (33.7%)
Stage IV	18 (9.9%)
Grade	
Grade I	22 (12.2%)
Grade II	119 (65.7%)
Grade III	40 (22.1%)
* Some patients presented with more than one symptom.	

Table 1: Patient's and tumor characteristics.

Clinical Staging		Lower Rectum/Anorectal (156 patients)		Anal Carcinoma (25 patients)	
		No	%	No	%
Localized	Stage I	15	9.6	-	-
Locally advanced	Stage II	69	44.2	18	72
	Stage III	57	36.5	4	16
Metastatic	Stage IV	15	9.6	3	12
Total		156	100 %	25	100%
		181 cases			

Table 2: Clinical staging of 181 patients of the lower rectum, anorectal and anal carcinoma.

Treatment analysis	No	(%)
Stage I 15		
TAB resection without adjuvant treatment	7	46.7%
TAB resection with adjuvant treatment	8	53.3%
Stage II 64		
Neoadjuvant treatment followed by TAB resection	37	57.8%
TAB resection followed by adjuvant CRT	27	42.2%
Stage III 58		
Neoadjuvant treatment followed by TAB resection TAB resection followed by adjuvant CRT	30	51.7%
	28	48.3%
Stage IV 17		
Palliative chemotherapy	12	70.6%
Palliative radiotherapy	3	17.6%
Palliative surgery	2	11.8%

Table 3: Treatment algorithm of 154 lower (lower rectal, anorectal, anal adenocarcinoma who received treatment).

and stage III (51.7%) despite, primary TAB followed by adjuvant chemoradiotherapy 42.2%, 48.3% respectively. Palliative chemotherapy was the prevalent among metastatic disease 70.6% than palliative radiotherapy 17.6% and palliative surgery 11.8%. Only 3 patients with ASCC, stage II underwent primary TAB and only one received definitive chemoradiotherapy.

The mean overall survival (OS) for 154 patients with adenocarcinoma who received treatment in the study was 56.6 months with 95% confidence interval (CI: 49.8 to 63.4 months), while, the mean progression free survival (PFS) was 46.7 months (95% CI: 38.9 to 54.6 months) as in Figures 1 and 2.

Univariate analysis for OS of patients with adenocarcinoma according to prognostic factors as shown in Table 4 revealed that age, ECOG, stage and lymphovascular invasion were significant independent prognostic factors for OS. The younger age was associated with shorter OS (34.5) months in comparison to the older age group (60.1 months) and this was statistically significant (p: 0.007). Bad performance status ECOG 2-3 was associated with shorter OS (35 months) than ECOG 0-1 (61.5 months) and this was statistically significant (p: 0.01). Based on tumor stage, early stages had better OS (63 months) while, advanced and metastatic stages were associated with shorter OS (30.2 and 12.4 months) respectively and this was highly statistically significant (p: 0.000*). On the concern of positive safety margin and positive lymphovascular/perineural invasion, they were associated with shorter OS (31.9 months) in comparison to higher survival in patients with negativity of these two factors (61.6 months) and this was significantly high (p: 0.03). Univariate analysis for PFS of patients with adenocarcinoma according to prognostic factors as shown in Table 4 revealed that the age only can affect PFS significantly as the younger age group has median survival of 54 months in comparison to 33.5 months for the older age group (p: 0.03).

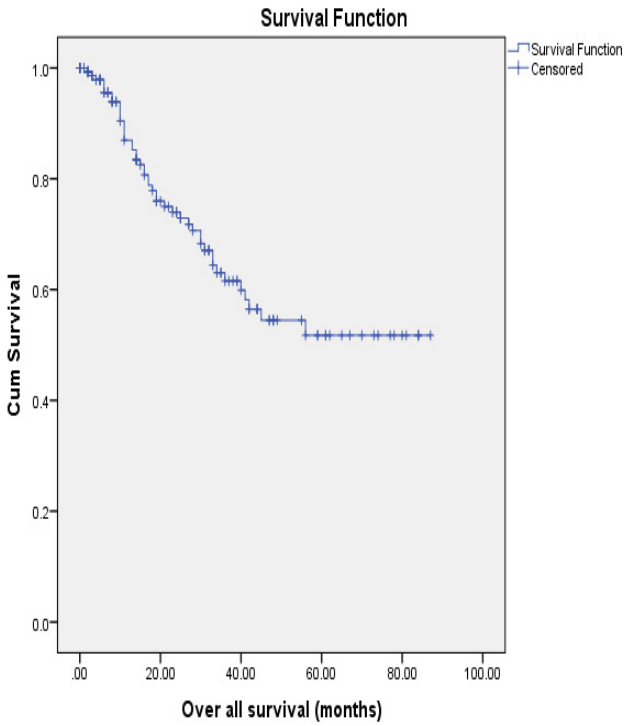

Figure 1: Overall Survival (OS).

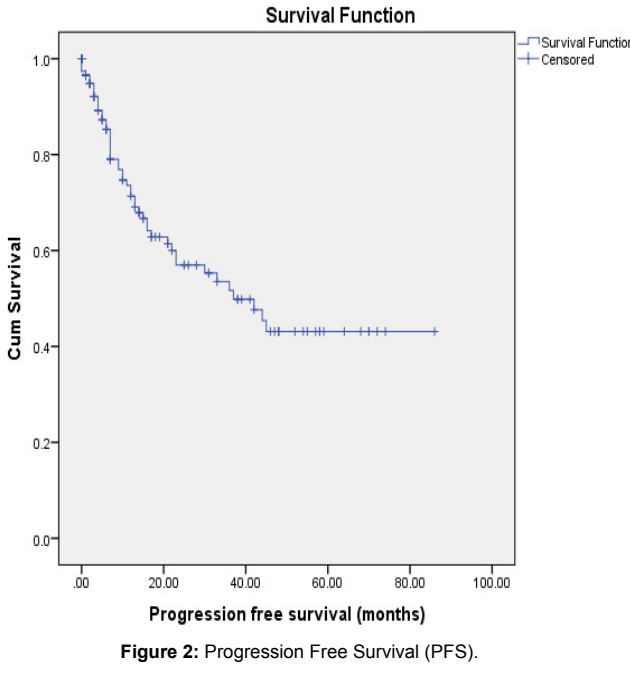

Figure 2: Progression Free Survival (PFS).

Discussion

Regarding that in Egypt, CRC incidence is increasing annually, diagnosed in 13% of patients who experiencing colonoscopy. Rectal cancer is 40% of all colorectal cancer; anal tumors represent 2.5% of all gastrointestinal tumors [3]. The chance of being diagnosed has risen in recent years, this may be attributed to increased awareness of

Items	Overall survival		Progression free survival	
	Median (CI) in months	P value	Median (CI) in months	P value
Age groups				
< 50 years old ≥ 50 years old	34.5 (25.1-43.9) 60.1 (49.8-70.3)	0.007*	33.5 (23.2-42.7) 54 (43.6-64.4)	0.03*
Sex				
Male Female	47.4 (36.1-58.7) 45.3 (36.6-54.1)	0.5	44.6 (33.5-55.6) 41.4 (32.8-50)	0.5
ECOG				
ECOG 0-1 ECOG 2-3	61.5 (53.8-69.1) 35 (27.2-42.9)	0.01*	28 (6.9-49.1) 21 (12.4-29.7)	0.6
Site				
Lower rectum Anorectal Anal canal	58.5 (47.2-69.8) 54.6 (45.9-63.3) 41 (23.1-58.9)	0.6	44 (12.9-75) 37 (23.2-50.8) 23 (11.8-33.4)	0.6
Clinical stage				
Localized Regional Distant	63 (56-70) 54.6 (45.9-63.3) 41 (23.1-58.9)	0.000*	44 (22.7-47.7) 37 (19.8-54) 9 (4.8-13.2)	0.5
Grade				
Well differentiated Moderate differentiated Poorly differentiated	66 (51.1-80.9) 56 (44.3-61) 54 (39.5-68.5)	0.2	56.3 (41.6-70.9) 33 (19.1-46.9) 21 (18-37)	0.1
Safety margin				
+ve safety margin -ve safety margin	61.6 (43.8-79.5) 65.4 (57.9-72.9)	0.5	32.2 (14.4-49) 49.5 (40.5-58.5)	0.1
Lymphovascular invasion				
+ve LV/PNI -ve LV/PNI	31.9 (20.7-43.1) 66.1 (58.9-73.4)	0.03*	26.6 (14.1-36.2) 47.9 (39.1-56.6)	0.1
Type of surgery				
Sphincter preserving Non sphincter preserving	62.9 (47.9-77.8) 65.7 (57.7-73.6)	0.5	42.1 (27.9-56.3) 48.2 (38.7-57.7)	0.1
*P-value considered significant if ≤ 0.05				

Table 4: Survival characteristics of patients with adenocarcinoma according to prognostic factors.

CRC symptoms and early detection of small lesion secondary to more widespread use of endorectal US, MRI, and fine needle aspiration of any suspicious lesion in treatment centers.

The majority of patients were above the age of 50 years old at presentation (63%). The median age were 53 years, however it is still younger than the median age of 64 years in the USA as published by SEER cancer statistics [12]. This variation may be attributed to different geographic risk factors as diet variations, smoking, obesity, genetic factors and availability of colonoscopy in treatment centers.

Gender is associated with varying incidence of anorectal cancer where it is 10.4% higher in men than women, and it is lower than the difference with Jemal and his colleagues where it is 25% [13]. Male to female ratio was found to be 1.2:1 and it is similar to research studying the difference according to gender among CRC patients, which was 1.9:1 [14].

Bleeding per rectum (69.1%) and change in bowel habit (28.7%) were the most presenting symptoms at time of diagnosis and this similar to a population based national study in USA about the epidemiology of CRC in average risk adult [15].

Most of the patients had adenocarcinoma (97.8%); that was 46.9% ARA, 39.2% lower RA and 11.6% AA. However SCC constitutes 2.2%. This differs than Franklin et al. report at 2016. They reported that ASCC predominate than AA and lower RA with 11.4%, 0.8% and 87.8% respectively [16]. This may be related to increased incidence of HPV infection in 88% of anogenital tumors in USA [17].

Regional and locally advanced stage II and III carcinoma were the predominant among our patients (81.1%); followed by metastatic carcinoma (9.9%) and the localized stage I carcinoma was (8.3%). This is different than SEER data base at USA that reported that the localized group (47%), regional (36.5%), metastatic (16.5%). This may be due to different sample size, and early diagnosis and treatment due to screening programs and health education and awareness [16].

Localized resection for early stage rectal cancer wasn't reported for clinically stage I patients (8.3%) and this is differ than USA were localized resection has been increased to be 20% of T1-T2 rectal cancer to preserve anal function as published at Huntsman Cancer Hospital at the University of Utah Salt Lake City [18]. This may be due to lack of good preoperative assessment of the patients and overestimation of the surgeons. Total abdominal resection (TAB) was the primary treatment for locally advanced stage II (42.2%) and stage III (48.3%) followed by adjuvant CRT. This is differ than Park et al. that shows all locally advanced rectal cancer patients undergo for neoadjuvant chemoradiotherapy for tumor regression and better sphincter preservation [19]. Neoadjuvant treatment is limited at our locality due to low resources for radiotherapy and prolonged waiting list.

We tried to analyze the prognostic factors affecting survival, we found that young patients less than 50 years had worse OS (34.5 m) and PFS (33.5 m); this is equal to the results of Gado and his colleagues at 2014. They found that the progression of patients less than 40 years was worse and carry a bad prognosis [3]. This needs more evaluation for the tumor biology and early detection of cancer among this age group.

There is no significant difference of OS according to sex and this is different than the results of Tsai et al. that showing there were

significant differences between male and female patients [14]. This may be due to large sample size and significant difference between gene mutations among male and female. So, this is in need for more evaluation at our nationality.

Regarding the pathological type, AA has the worst prognosis in comparison to the counterpart histological RA and ARA (OS 41 m, 58.5 m, and 54.6 m). This is in line with the results of 57.369 cases with median OS was significantly lower for AA (33 months), compared with RA (33 months) [16]. The median OS of RA among patients with positive LV/PNI was less than those with negative LV/PNI (OS 31.9m and 66.1 m respectively). This is coinciding with Hyams and his colleagues at 1997 [20].

As regard clinical stage of the tumor, localized disease has better OS (63 m) compared with regional disease (30.2 m) and metastatic disease (12.4 m). This is close to the results reported by SEER CRC statistics 2014 [6]. But lower than FLORIDA study that show survival for stage I, II, III at 87%, 72% and 59% respectively [21]. This may be due to early diagnosis and availability of facilities and multidisciplinary team approaches for best management and high prevalence of target therapy.

There is no significant difference in survival among patients underwent sphincter and non-sphincter preserving surgery 62.9 m, 65.7 m respectively and this in the same track with the result of Puthawala [22]. The independent treatment-related predictors of decreased mortality were clinical staging, LV/PNI after surgery and this more or less near to the results of McKenna and his colleagues [23].

Conclusion

Anorectal carcinoma includes tumors of lower rectum, anal canal and anal margin. This study shows adenocarcinoma predominance. Anal adenocarcinoma is often conflicted with either its common anatomic correlate in anal squamous cell carcinoma or its histological correlate in rectal adenocarcinoma. Neoadjuvant treatment followed by TAB resection was of increasing era of treatment among locally advanced tumors. All metastatic cancer patients underwent palliative treatment as chemotherapy, radiotherapy and/or surgery. The most significant prognostic factor affecting OS and PFS was age, clinical stage, performance status and presence or absence of lymphovascular/perineural invasion. Anal adenocarcinoma has the worse prognosis than histological counterpart RA, ARA in 3 cancer stage. We need more study size to compare survival statistics with 3 cancer types and compare between treatment types. We suggest future studies are needed to elucidate anal adenocarcinoma as distinct entity from anal squamous cell carcinoma and rectal adenocarcinoma and consider more aggressive treatment as appropriate.

References

1. Foda AA, Ahmed MA, Elkalla HM, El-Zahaf E, Abdallah H, et al. (2018) Role of MEK1 and DIAPH3 expression in colorectal carcinoma. J Oncol 14: 75-82.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, et al. (2018) Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68: 394-424.
3. Gado A, Ebeid B, Abdelmohsen A, Axon A (2014) Colorectal cancer in Egypt is commoner in young people: Is this cause for alarm? Alexandria J Med 50: 197-201.
4. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, et al. (2017) Global patterns and trends in colorectal cancer incidence and mortality. Gut 66: 683-691.
5. Chung RY, Tsoi KK, Kyaw MH, Lui AR, Lai FT, et al. (2019) A population-based age-period-cohort study of colorectal cancer incidence comparing Asia against the West. Cancer Epidemiol 59: 29-36.
6. Siegel R, DeSantis C, Jemal A (2014) Colorectal cancer statistics, 2014. CA Cancer J Clin 64: 104-117.
7. Cruz A, Chen D, Hsu P, Pandit V, Omesiete P, et al. (2019) Racial and gender disparities in the incidence of anal cancer: Analysis of the Nationwide Inpatient Sample (NIS). J Gastrointest Oncol 10: 37-41.
8. Osazuwa-Peters N, Boakye EA, Rohde RL, Ganesh RN, Moiyadi AS, et al. (2019) Understanding of risk factors for the human papillomavirus (HPV) infection based on gender and race. Sci Rep 9: 297.
9. Thanikachalam K, Khan G (2019) Colorectal cancer and nutrition. Nutrients 11: 164.
10. Valvo F, Ciurlia E, Avuzzi B, Doci R, Ducreux M, et al. (2019) Cancer of the anal region. Crit Revi Oncol.
11. Matalon SA, Mamon HJ, Fuchs CS, Doyle LA, Tirumani SH, et al. (2015) Anorectal cancer: Critical anatomic and staging distinctions that affect use of radiation therapy. Radiographics 35: 2090-2107.
12. Paquette IM, Atkinson SJ (2019) The epidemiology of rectal cancer. Comprehensive rectal cancer care: Springer 3-20.
13. Jemal A, Siegel R, Xu J, Ward E (2010) Cancer statistics, 2010. CA Cancer J Clin 60: 277-300.
14. Tsai YJ, Huang SC, Lin HH, Lin CC, Lan YT, et al. (2018) Differences in gene mutations according to gender among patients with colorectal cancer. World J Surg Oncol 16: 128.
15. Glover M, Mansoor E, Panhwar M, Parasa S, Cooper GS (2019) Epidemiology of colorectal cancer in average risk adults 20–39 years of age: A population-based national study. Dig Dis Sci 1-8.
16. Franklin RA, Giri S, Valasareddy P, Lands LT, Martin MG (2016) Comparative survival of patients with anal adenocarcinoma, squamous cell carcinoma of the anus, and rectal adenocarcinoma. Clin Colorectal Cancer 15: 47-53.
17. Daling JR, Madeleine MM, Johnson LG, Schwartz SM, Shera KA, et al. (2004) Human papillomavirus, smoking, and sexual practices in the etiology of anal cancer. Cancer 101: 270-280.
18. Hazard LJ, Shrieve D, Sklow B, Pappas L, Boucher K (2009) Local excision vs. radical resection in T1-2 rectal carcinoma: results of a study from the surveillance, epidemiology, and end results (SEER) registry data. Gastrointest Cancer Res 3: 105-114.
19. Park IJ, You YN, Agarwal A, Skibber JM, Rodriguez-Bigas MA, et al. (2012) Neoadjuvant treatment response as an early response indicator for patients with rectal cancer. J Clin Oncol 30: 1770-1776.
20. Hyams DM, Mamounas EP, Petrelli N, Rockette H, Jones J, et al. (1997) A clinical trial to evaluate the worth of preoperative multimodality therapy in patients with operable carcinoma of the rectum. Dis Colon Rectum 40: 131-139.
21. Goffredo P, Robinson TJ, Frakes JM, Utria AF, Scott AT, et al. (2019) Comparison of anal versus rectal staging in the prognostication of rectal squamous cell carcinoma: A population-based analysis. Dis Colon Rectum 62: 302-308.
22. Puthawala AA, Syed AN, Gates TC, McNamara C (1982) Definitive treatment of extensive anorectal carcinoma by external and interstitial irradiation. Cancer 50: 1746-1750.
23. McKenna NP, Bergquist JR, Habermann EB, Chua HK, Kelley SR, et al. (2019) Surgery and chemotherapy are associated with improved overall survival in anal adenocarcinoma: Results of a national cohort study. Int J Colorectal Dis 34: 607-612.