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Research Article

Does Gender Matter in Colorectal Cancer?

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Received date: November 28, 2022; **Accepted date:** December 23, 2022; **Published date:** January 11, 2023

Citation: Ashfaq Chandio, Mehak Chandio, Zainab Shaikh, Zawar Khichi, Najeeb Memon,Aijaz , Memon Katherine Brown, (2023) Does Gender Matter in Colorectal Cancer?. *Cancer Research and Cellular Therapeutics*. 7(1) ; **DOI:** 10.31579/2693-4779/132

Abstract:

Colorectal cancer is one of the most common and lethal cancer worldwide,and it exhibits differences in incidence,pathogenesis, molecular pathways, and outcome depending on the location of the tumour. Colorectal cancer is a disease strongly influenced by gender, mortality rates in males considerably higher than females

Aim: To determine the gender disparities in the incidence of Colorectal cancer

Methods: All patients managed with colorectal cancer from January 2015 through December 2019 were retrospectively identified from the referral database created by the colorectal specialist nurses in the colorectal service.Inclusion: All patients diagnosed with colorectal cancer

Exclusion: Tumour in the Appendix, Anal canal, small bowel, metastatic tumours of unknown primary

Results: 976 patients were diagnosed with bowel cancer percentages of studied participant were Male 52.60% and Female 47.40%. The mean age of 74.14 years. Sixty six (66) 6.76% patients were excluded from the study. The location of colon cancer is also changing. The incidence rate of Right side colon cancer in women was much higher than that in men 1.20:1, and on Left side colon cancer including rectum was much higher in men than that in women this was especially exhibited in cases of rectal cancer, for which the male to female ratio was increased to 1.54:1 whereas the male to female ratio of left colon cancer 1.26:1 The incidence rates were increasing in all groups over time, especially in the 50 -79 years group. Incidence of colorectal cancer was greater for cancers of the left side of colon than right colon (62.41% vs 37.58%).

Conclusion:

There are not significant sex differences in access to and effectiveness of Colorectal cancer treatment. Screening provides effective opportunity to prevent Colorectal cancer. Gender-specific guidelines for screening, treatment, and prevention protocols for colorectal cancer can be established to decrease the mortality and increase the quality of life.

Keywords: colorectal cancer; gender difference; routes to diagnosis; staging; survival

Introduction

Colorectal cancer is the third most commonly diagnosed cancer in the world and is a major health problem, incidence and mortality rates vary markedly around the world. Globally, Colorectal cancer is the second most common cause of cancer death causing almost one million deaths. The incidence of Colorectal cancer is more among men than women and 3–4 times more common in developed than in developing nations. Worldwide Age-standardised incidence rates per 100,000 of Colorectal cancer in both sexes is 19.7, in males is 23.6, and in females is 16.31 While the age-standardised incidence rate among men is 30.1/100,000, in high human development index nations (Canada, the United Kingdom (UK), Denmark, and Singapore), it is 8.4, in low human development index nations (the same statistics for women are 20.9 and 5.9, respectively).2 With increasing age, the proportion of proximal Colorectal cancer gradually increased in women, whereas that of rectal cancer gradually decreased. Most colorectal cancers (CRC) arise from adenomatous colon polyps that progress from small (<8 mm) to large (≥8 mm) polyps, then to dysplasia and carcinoma. Colo rectal cancer is a disease that has both biological sex differences and socio-cultural gender components.3-10 Detecting colorectal cancer is challenging patients may present with slight symptoms or asymptomatic. A diagnosis of colorectal cancer results either from an evaluation of a patient symptoms, or as a result of screening. When colorectal cancer or its precursor lesion is diagnosed early, its 5-year relative survival rate is very high, however advanced colorectal cancer reduces the quality of life of patients.

Sex differences recommend more targeted interventions might expedite prevention and early diagnosis in both gender. There are not significant sex differences in access to and effectiveness of Colorectal cancer treatment. Therefore, novel methods that would allow the early diagnosis

of colorectal cancer are chosen. Greater awareness of how sex and gender impact on Colorectal cancer may therefore lead to new insights into how improvements in prevention, early diagnosis, treatment and survival can be made.

Methods:

All patients managed with colorectal cancer at the Luton and Dunstable University Hospital UK from January 2015 through December 2019 were retrospectively identified from the referral database created by the colorectal specialist nurses in the colorectal service. Data were retrieved by detailed review of the hospital case notes, ICE / Evolve (Computer database for investigations and correspondence) including endoscopy; radiographic imaging; operative course and cancer follow up. The following parameters were recorded: age, gender, and source of referral, presentation, stage of the disease, MDT discussion, intervention, and outcome. Tumour locations were classified as the right colon (i.e. caecum, ascending colon, hepatic flexure, transverse colon, and the left colon (i.e. spleenic flexure, descending colon, sigmoid, Recto sigmoid, and rectum.

Inclusion: All patients diagnosed with colorectal cancer

Exclusion: Tumour in the Appendix, Anal canal, small bowel, metastatic tumours of unknown primary

Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 26). Mean values were compared using the Student t test (Table 1).

One-Sample Statistics					
	N	Mean	Std. Deviatio	Std. Error Mean	
Age	910	6.6978	1.33494	0.04425	
Gender	910	1.5297	0.49939	0.01655	
cancer	910	1.6242	0.4846	0.01606	
Colon	910	6.6681	3.08083	0.10213	

Table 1:

Univariate analysis of categorical variables was performed by the chi-square test (Table 2).

Test Statistics								
	Age	Gender	cancer	Colon				
Chi-Square	869.844a	3.204b	56.127b	620.376a				
df	8	1	1	8				
Asymp. Sig.	0	0.073	0	0				
a 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 101.1.								
b 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 455.0.								

Table 2:

Pearson's chi squared test was used for comparing two proportions (Table 3).

Risk Estimate			
	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for Gender (Female / Male)	1.733	1.322	2.272
For cohort cancer = Right colon	1.408	1.189	1.667
For cohort cancer = Left colon	0.812	0.732	0.901
N of Valid Cases	910		

Table 3

An OR with corresponding 95% confidence interval >1 implied a positive association where as an OR with corresponding 95% confidence interval <1 implied a negative association. Two-sided p values <0.05 were considered significant. (Table 4)

	Cancer / Gender		
Year	**Male**	**Female**	**Total**
2015	87	69	156
2016	96	106	202
2017	104	77	181
2018	110	83	193
2019	83	95	178
Total	**480**	**430**	**910**

Table 4

The results are mainly illustrated by descriptive statistics. (Table 5)

One-Sample Test

One-Sample Test						
	Test Value = 0					
	t	df	Sig. (2-tailed	Mean Differenc	95% Confidence Interval of the Differen	
					Lower	Upper
Age	149.626	975	0	6.62398	6.5371	6.7109
Gender	95.4	975	0	1.52561	1.4942	1.557
cancer	94.321	975	0	1.59324	1.5601	1.6264
Colon	65.014	975	0	6.79508	6.59	7.0002
Year	66.938	975	0	2.95287	2.8663	3.0394
Referral	58.964	974	0	1.61538	1.5616	1.6691
Intervention	88.361	975	0	1.34734	1.3174	1.3773
Mortality	10.41	971	0	0.31687	0.2571	0.3766
Missing	184.457	964	0	1.03109	1.0201	1.0421

Table 5

Chi-Square tests for intervention

Chi-Square Tests						
	Value	df	Asymptotic Significance (2-sided)			
Pearson Chi-	54.610a	9	0			
Likelihood Ra	54.331	9	0			
Linear-by-Lin	19.77	1	0			
N of Valid Ca	976					
a 6 cells (30.0%) have expected count less than 5. The minimum expected count is .69.						

Table 6

Results:

In the study period 976 patients were diagnosed with bowel cancer percentages of studied participant were Male 52.60% and Female 47.40%. (figure 1)

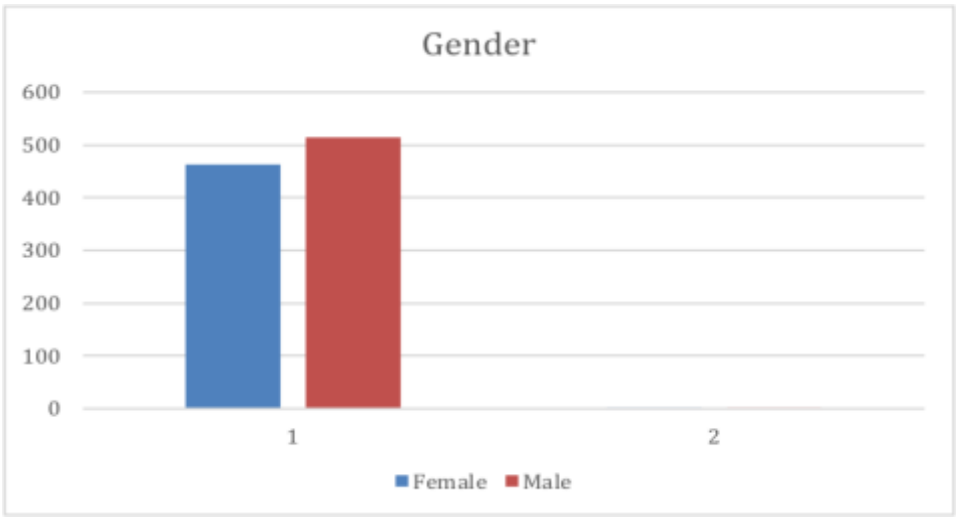

Figure 1: *Characteristics and incidence*

The mean age of 74.14 years (range, 25 to 101). 6.76% patients were excluded from the study on the account of Tumours in the Appendix, Anal canal, Small bowel and metastatic tumor of unknown primary. (Figure 2).

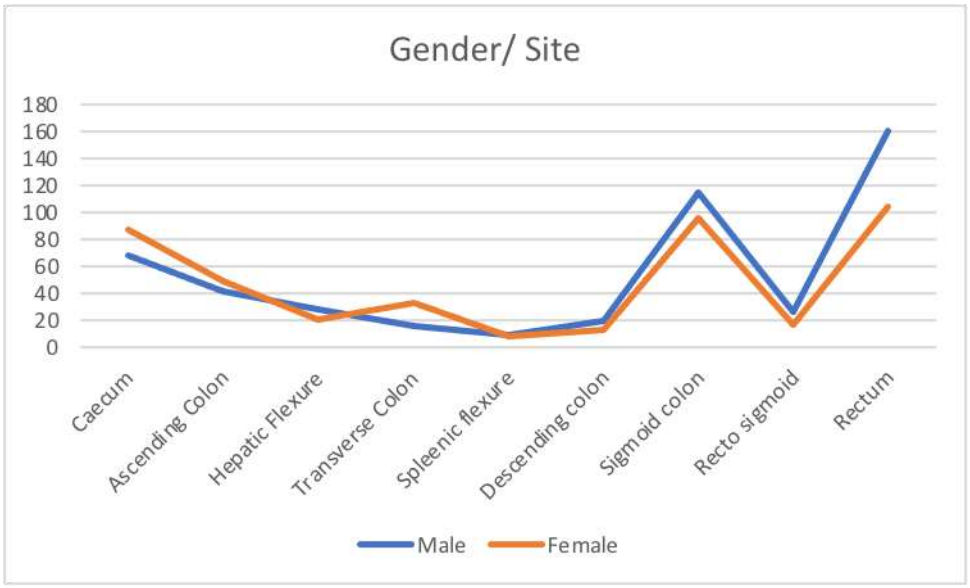

Figure 3

The location of colon cancer is also changing, (Figure 3). The incidence rate of Right side colon cancer in women was much higher than that in men 1.20:1, and on Left side colon cancer including rectum was much higher in men than that in women this was especially exhibited in cases of rectal cancer, for which the male to female ratio was increased to 1.54:1 whereas the male to female ratio of left colon cancer 1.26:1 (Table 1,2). In the univariate analysis, tumour location was associated with age in both men and women. The shift of tumour location to the proximal colon with increasing age was more prominent 5.38% aged < 50 years had right-sided colorectal cancer, compared with 65.05% of those aged 50 –79 years. while Age group 80-99 years incidence 28.90% and over age group 100 years 0.65%. In a multivariate analysis, right-sided colorectal cancer was the only independent variable that correlated with age. The rectal cancer incidence increased from 20.75% in 2015 to 21.88% in 2018. The most significant increase was noted 22.64% in 2017. High male to female rate ratios were found in 2017,1.35:1 and 2018, 1.32:1. The proportion of distal colon cancer was increasing annually, rising to 22.88% in 2018. The proportion of Colorectal cancer in women increase from 7.58% in 2015 to 10.43% in 20190. (Table 3) All studied cases were classified into four groups according to the age at diagnosis. The incidence rates were increasing in all groups over time, especially in the 50 -79 years group. 69.89% patients underwent surgical intervention. 24.50% patients deemed unsuitable for resection surgery were treated with best supportive care palliatively.(Table 4,5,6) In the Right colon subset of patients there was a total of 37.58% patients 189 Female and 153 Male, In 33.29% patients with Left Colon cancer there were 169 Male and 134 Female. Of 29.12% Rectal cancer patients there were 161 Male and 104 Female. 32.08 % patients died during the study period. Incidence of colorectal cancer was greater for cancers of the left side of colon than right colon (62.41% vs 37.58%).

Discussion:

Colorectal cancer is one of the most common and lethal cancer worldwide, and it exhibits differences in incidence, pathogenesis, molecular pathways, and outcome depending on the location of the tumour. Colorectal cancer is a disease strongly influenced by gender, mortality rates in males considerably higher than females. There is scarcity to appreciative whether sex differences exist along the pathway from presentation to survival. Most colorectal cancers arise from adenomatous colon polyps that progress from small (<8 mm) to large (≥8 mm) polyps, then to dysplasia and carcinoma. Bowel cancer can affect anyone of any age, in the United Kingdom, age-standardised incidence have remained constant, but incidence rates in aged 20–39 have increased in the last 25 years.11 Age-standardised incidence rates of bowel cancer for females in the UK remained stable between 1993-1995 and 2015-2017, and for males, bowel cancer age-standardised incidence rates in the UK decreased by 3% between 1993-1995 and 2015-2017. In the UK between 2005-2007 and 2015-2017, bowel cancer age-standardised incidence rates for males and females combined decreased by 4%. In males age-standardised incidence rates decreased by 6%., and in females rates decreased by 2%. Generally prevalence of colon cancer is higher in males than in females. This increased liability of men to develop colorectal may be due to a number of genetic and gender related (developmental) factors.12-15 Men are more likely to have a diet rich in processed and red meat,16 be more alcohol consumers,17 and more prone to smoke.18 Men also have a more tendency to deposit visceral fat19 which is related with increased risk of developing colorectal cancer.20-22 Conversely, female gender is more associated with BRAF V600E mutation, CpG island methylator phenotype (CIMP)-high, hypermethylation, microsatellite instability,23 which are more liable to result in the sessile serrated polyps. Females are furthermore found to have higher frequency of KRAS mutations in codon 12 than males, that again are linked with more advanced adenomas.24 Published Studies have shown that Women, are more constant with relationships and appeared more familiar about colorectal cancer screening, and better able to expressive views on screening.25,26,27-30 Men reported less clear interactions, less knowledgeable and often kept decision making processes vague and emotionally distanced. In the UK bowel cancer is the 3rd most common cancer In both sexes. In males (13% of all new male cancer cases) and in females, (10% of all new female cancer cases). A comparable or greater proportion of patients with Right colon cancer are female, and the median age of patients with Right colon cancer at diagnosis is higher compared to patients with Left colon cancer.31-33 56 % of bowel cancer cases in the UK are in males, and 56% are in females. This is in contrast to our study, in our study there were 52.74% Male and 47.25% Female. In current study Bowel cancer incidence is strongly related to age, with the highest incidence rates being in older people. Age-specific incidence rates rise steeply from around age 50-79. The highest rates are in the 70 to 79 age group for females and males, while Age group 80-99 years incidence 28.90% and over age group 100 years 0.65%. In our study the proportion of cancer in the distal colon and rectum is considerably lower among women than among men this is similar to other published studies (Stewart et al, 1983; Bonithon-Kopp and Benhamiche, 1999; McCashland et al, 2001). Many studies have reported that oncologic outcomes of colon cancer are different according to the tumour location. Most studies have reported poorer oncologic outcomes in patients with Right colon cancer compared with patients with Left colon cancer.34-38 However, our study have reported that the prognosis of Right colon cancer is better than that of Left colon cancer this is similar to other published studies.39,40 Five-year survival for bowel cancer shows an unusual pattern with age: survival overall decreases with increasing age.41 In 1990 report on prognostic effect of primary tumour localisation on clinical outcome was first reported.42 In a FIRE-1 trial, Right colon cancer patients had a considerably shorter progression-free survival and overall survival compared with Left colon cancer.43 This is similar to our study, Overall 5-year survival in our study for right-sided tumours was 24.94%. In comparison, survival rates were 42.96% for patients with left-sided tumours. In our study 15.10% had complications after surgery (Fig. 6) and age is not a predictor of post-operative complications. Increased circulating levels of oestrogens and progestin subsequent to exogenous exposure through contraceptives or hormone replacement therapy (HRT) in post-menopausal, have shown to lower risk of colorectal cancer in women, possibly by preventing the loss of oestrogen receptor beta signalling in the colonic mucosa (Rennert, 2017; Barzi et al., 2013). Similarly, reduced testosterone levels as a result of androgen deprivation therapy, androgen receptor polymorphisms or obesity associates with increased cancer risk in men (Rennert, 2017; Lin et al., 2013). Gender differences have been also observed in body fat storage/distribution and lifestyle (Vari et al., 2016; Bredella, 2017). One of the strengths of our study is that the sample size is not small, Patients admitted as an emergency and scheduled for elective surgery for confirmed colorectal cancer were included and long follow-up period. The limitations of this study is single center, retrospective. The choice of treatment is based on several factors, including conditions of the patient stage at presentation, and the location of tumour. Surgery remains the core in curative treatment for colorectal cancer. Age on its own would not be taken as for less aggressive therapy; Careful assessment of the patient taking into consideration comorbidities, functional status and patient wishes are essential in decision making and choosing appropriate management plan. Management of comorbidities preceding surgery may impact postoperative outcome. Colon cancer is a common and highly treatable cancer. Advances in screening and treatment have led to better outcomes for patients. Greater awareness of how gender impact on colorectal cancer may have led to innovative comprehensions in what way to prevent, early diagnosis, treatment and survival can be made.

Conclusion:

Screening provides effective opportunity to prevent Colorectal cancer. Conversely, there are no gender-specific guidelines or screening tools. Gender-specific guidelines for screening, treatment, and prevention protocols for colorectal cancer can be established to decrease the mortality and increase the quality of life. There are not significant sex differences in access to and effectiveness of Colorectal cancer treatment.

Reference:

1. Ferlay J, Ervik M, Lam F, et al. (2018). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from:
2. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68: 394-424.
3. Kim SE, Paik HY, Yoon H, Lee JE, Kim N, Sung MK. (2015) Sex- and gender-specific disparities in colorectal cancer risk. World J Gastroenterol. 21:5167–5175.
4. Brenner H, Hoffmeister M, Arndt V, Haug U. (2007) Gender differences in colorectal cancer: implications for age at initiation of screening. Br J Cancer. 96: 828–831.
5. Payne S. (2007) Not an equal opportunity disease – a sex and gender-based review of colorectal cancer in men and women: part I. J Men's Heal Gend. 4:131–139.
6. Chacko L, Macaron C, Burke CA. (2015) Colorectal cancer screening and prevention in women. Dig Dis Sci. 60:698–710.
7. Christy SM, Mosher CE, Rawl SM. (2014) Integrating men's health and masculinity theories to explain colorectal cancer screening behavior. Am J Mens Health. 8:54–65.
8. Nguyen SP, Bent S, Chen Y-H, Terdiman JP. (2009) Gender as a risk factor for advanced neoplasia and colorectal cancer: a

systematic review and meta- analysis. Clin Gastroenterol Hepatol. 7:676–681.
9. Clarke N, Gallagher P, Kearney PM, Mcnamara D, Sharp L. (2016) Impact of gender on decisions to participate in faecal immunochemical test-based colorectal cancer screening: a qualitative study. Psycho-Oncology. 25:1456–1462.
10. Wang Y, Freemantle N, Nazareth I, Hunt K. (2014) Gender differences in survival and the use of primary care prior to diagnosis of three cancers: an analysis of routinely collected UK general practice data. PLoS One. 9:e101562..
11. Vuik FE, Nieuwenburg SA, Bardou M, Lansdorp-Vogelaar I, Dinis-Ribeiro M, Bento MJ, et al. (2019) Increasing incidence of colorectal cancer in young adults in Europe over the last 25 years. Gut.
12. Cook MB, Dawsey SM, Freedman ND, Inskip PD, Wichner SM, Quraishi SM, et al. (2009) Sex disparities in cancer incidence by period and age. Cancer Epidemiol Biomark Prev. 18:1174–1182.
13. CRUK/NCIN. Excess cancer burden in men. London: Cancer Research UK, NCIN, Leeds Met University, Men's Health Forum; 2013.
14. Edgren G, Liang L, Adami H-O, Chang E. (2012) Enigmatic sex disparities in cancer incidence. Eur J Epidemiol. 27:187–196.
15. Cook MB, McGlynn KA, Devesa SS, Freedman ND, Anderson WF. (2011) Sex disparities in cancer mortality and survival. Cancer Epidemiol Biomark Prev. 20:1629–1637.
16. Bates B, Cox L, Nicholson S, Page P, Prentice A, Steer T, et al. (2016) National Diet and Nutrition Survey: Results from Years 5 and 6 (combined) of the Rolling Programme (2012/2013–2013/2014). London: Public Health England;
17. Schütze M, Boeing H, Pischon T, Rehm J, Kehoe T, Gmel G, et al. (2011) Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study. BMJ. 342:d1584.
18. Chang LC, Wu MS, Tu CH, Lee YC, Shun CT, Chiu HM. (2014) Metabolic syndrome and smoking may justify earlier colorectal cancer screening in men. Gastrointest Endosc. 79:961–969.
19. Tchernof A, Després J-P. (2013) Pathophysiology of human visceral obesity: an update. Physiol Rev. 93:359–404.
20. Bassett JK, Severi G, (2010) English DR, Baglietto L, Krishnan K, Hopper JL, et al. Body size, weight change, and risk of colon cancer. Cancer Epidemiol Biomark Prev. 19:2978–2986.
21. Marino M, Masella R, Bulzomi P, Campesi I, Malorni W, Franconi F. (2011) Nutrition and human health from a sex-gender perspective. Mol Asp Med. 32:1–70.
22. Moghaddam AA, Woodward M, Huxley R. (2007) Obesity and risk of colorectal cancer: a meta-analysis of 31 studies with 70,000 events. Cancer Epidemiol Biomark Prev. 16:2533–2547.
23. Chacko L, Macaron C, Burke CA. (2015) Colorectal cancer screening and prevention in women. Dig Dis Sci. 60:698–710.
24. Lorentzen JA, Grzyb K, De Angelis PM, Hoff G, Eide TJ, Andresen PA. (2016) Oncogene mutations in colorectal polyps identified in the Norwegian colorectal cancer prevention (NORCCAP) screening study. Clin Med Insights Pathol. 9:19–28.
25. Mahalik JR, Good GE, Englar-Carlson M: (2003) Masculinity scripts, presenting concerns, and help seeking: implications for practice and training. Prof Psychol Res Pr 34:123–131.
26. Addis ME, Mahalik JR: (2003) Men, masculinity, and the contexts of help seeking. Am Psychol 58(1):5–14.
27. Macdonald J, (2002) Crawford DH: Recent developments concerning men's health in Australia. Aust J Primary Health 8:77–82.
28. Denner BJ: (2000) MAN model: health promotion. Aust J Primary Health 6:230–240.
29. Dalziel A, Leishman J (2003) Stop men losing out in the healthcare stakes: men are reluctant users of health services, particularly primary care. Practice Nurse 26:24.
30. Lumb PB: (2003) Why is men's health and well-being policy not implemented in Australia? Int J Men's Health 2:73–88
31. Hemminki K, Santi I, Weires M, Thomsen H, Sundquist J, Bermejo JL. (2010) Tumor location and patient characteristics of colon and rectal adenocarcinomas in relation to survival and TNM classes. BMC Cancer 10:688.
32. Loupakis F, Yang D, Yau L, Feng S, Cremolini C, Zhang W, et al. (2015) Primary tumor location as a prognostic factor in metastatic colorectal cancer. J Natl Cancer Inst 107(3).
33. Sinicrope FA, Mahoney MR, Yoon HH, Smyrk TC, Thibodeau SN, Goldberg RM, et al. (2015) Analysis of molecular markers by anatomic tumor site in stage III colon carcinomas from adjuvant chemotherapy trial NCCTG N0147 (alliance). Clin Cancer Res 21(23):5294–5304.
34. Benedix F, Kube R, Meyer F, et al. (2010) Colon/Rectum Carcinomas (Primary Tumor) Study GroupComparison of 17,641 patients with right and left sided colon cancer: differences in epidermilogy, perioperative course, histology, and survival. Dis Colon Rectum 53:57–64
35. Suttie SA, Shaikh I, Mullen R, et al. (2011) Outcome of right- and left-sided colonic and rectal cancer following surgical resection. Colorectal Dis 13:884–889.
36. Huang CW, Tsai HL, Huang MY, et al. (2015) Different clinicopathologic features and favorable outcomes of patients with stage III left-sided colon cancer. World J Surg Oncol 13:257.
37. Meguid RA, Slidell MB, Wolfgang CL, et al. (2008) Is there a difference in survival between right- versus left-sided colon cancers? Ann Surg Oncol 15:2388–2394.
38. Jess P, Hansen IO, Gamborg M, et al. (2013) Danish Colorectal Cancer GroupA nationwide Danish cohort study challenging the categorization into right-sided and left-sided colon cancer. BMJ Open 3: 002608.
39. Warschkow R, Sulz MC, Marti L, et al. (2016) Better survival in right-sided versus left-sided stage I-III colon cancer patients. BMC Cancer 16:554.
40. Moritani K, Hasegawa H, Okabayashi K, et al. (2014) Difference in the recurrence rate between right- and left-sided colon cancer: a 17-year experience at a single institution. Surg Today 44:1685–1691.
41. Office for National Statistics. (2014) Cancer survival in England: adults diagnosed in 2009 to 2013, followed up to Newport: ONS; 2015
42. Bufill JA. (1990) Colorectal cancer: evidence for distinct genetic categories based on proximal or distal tumor location. Ann Intern Med 113(10):779–788.
43. Modest DP, Schulz C, von Weikersthal LF, Quietzsch D, von Einem JC, Schalhorn A, et al. (2014) Outcome of patients with metastatic colorectal cancer depends on the primary tumor site (midgut vs. hindgut): analysis of the FIRE1-trial (FuFIRI or mIROX as first-line treatment). Anticancer Drugs 25(2): 212–218.

DOI: 10.31579/2693-4779/132