Research Article

Quality of Life and Its Predictor Factors Among Iranian Gastrointestinal Cancer Survivors

Musab Ghaderi[1], Afzal Shamsi[2], Azad Rahmani[3]

1. Department of Nursing, Khalkhal University of Medical Sciences, Khalkhal, Iran; 2. Anesthesiology Department, School of Allied Medicine, Tehran University of Medical Sciences, Iran, Islamic Republic of; 3. Tabriz University of Medical Sciences, Iran, Islamic Republic of

Background: Quality of life (QoL(is an important factor in cancer patients through which the important consequences of disease treatment can be evaluated. This study aimed to identify QoL and its factors influencing Gastric and colorectal cancer survivors.

Materials and Methods: A descriptive-correlation study was conducted among 120 GI cancer survivors in Tabriz city per year 2019. which was done on patients with GI cancer referred to the clinic and inpatient departments of Ghazi Hospital in Tabriz. Participants were recruited using the convenience sampling method. After obtaining the consent of the patients and data were collected by private interview method in a private environment. Data were collected using cancer-related quality of life questionnaire (QLQ-C30). The predictor factors were identified using a linear regression model.

Results: The average overall QoL score was 48.98. Based on the threshold defined in the scales of physical performance, cognitive performance, emotional performance, fatigue, pain and financial problems, more than half of the patients had problems. anemia and marriage were the most predictors in all scales. HTN for global QoL scale and physical activity for symptom scale was identified as the strongest predictors. These factors predicted a significant proportion of variance for QoL, 84% for global QoL, 83.5% for functional scale, and 67.3% for symptom scale.

Conclusions: Our results indicated that the Qol of Iranian GI cancer survivors was poor. Therefore, managing some comorbidities and developing supportive care programs is essential to improve the QoL of these patients.

Corresponding authors: Musab Ghaderi, Musab.ghaderi@gmail.com; Afzal Shamsi, ashamsi@sina.tums.ac.ir; Azad Rahmani, Azad.rahmani@yahoo.com

 doi.org/10.32388/J5Y5LR

Introduction

One of the major public health problems worldwide is cancer. Among existing cancers, gastrointestinal cancers account for approximately one-third of all cancer incidence and mortality worldwide. Gastrointestinal (GI) cancers, esophageal, stomach, and colorectal malignancies are among the most common cancers in humans. Based on data from GLOBOCAN 2020, gastrointestinal cancers [colorectal cancer (CRC), gastric cancer, and esophageal cancer] accounted for 18.7% of new cancer cases and 22.6% of cancer deaths in 2020. Both have the highest rates among all types of cancer. and are a significant public health burden for most people [1][1][1]. Colorectal cancer (CCR) is the second-largest cause of death related to cancer and the third leading cause of cancer worldwide [1]. The five-year survival rate for colorectal cancer was calculated as 64-67% [2]. According to a study in Iran, the 5-year survival rate among Iranian patients with colorectal cancer was estimated at 54%, which this rate is lower than that reported in developed countries due to late diagnosis [3].

Cancer can negatively affect patients′ Qol due to their destructive effects on patients' life processes [4]. QoL is considered an important factor to assess the quality of care provided to cancer survivors, through which consequences of cancer treatment can be assessed [5]. Additionally, survival for most cancer sites was estimated to be 75% after one year and 50% after five years. The increase in the proportion of people who survive cancer may be attributed to the aging population and advances in anti-cancer treatments that have improved treatment outcomes. On the other hand, many negative factors affecting cancer survival have been highlighted and include lower socioeconomic status along with unhealthy lifestyle choices. It is now clear that as survival increases, long-term health issues related to cancer emerge as a significant public health concern, and this is reflected in health care strategies[2].

The World Health Organization (WHO) defines QoL as "individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [6]. The concept of QoL seems to be a highly appropriate one to indicate the global individuals′ QoL in health and disease situations [7]. As a result, estimating the impact of chronic diseases on patients′ QoL is necessary to better plan and distribute health care resources. There have been many international studies reviewing the QoL of cancer survivors. Although Han has reported that the QoL of cancer survivors is largely comparable to a healthy population [8], other studies have reported that cancer diagnosis can still have a devastating effect on the QoL of cancer survivors even 2 to 26 years after diagnosis [9]. In particular, studies conducted in Iran [3], Asia [10] and some European

countries [11] have shown that the various aspects of QoL in cancer survivors are lower than in the general population.

In this regard, studies in Iran have examined the QoL of patients with colorectal cancer. These studies showed QoL in Iranian patients with colorectal cancer was low or moderate [12][13]. To the best of our knowledge, few studies have studied the QoL of Iranian colorectal cancer survivors, and the results of these studies were inconsistent, and some reported QoL in these survivors as moderate [14] or low [13]. Hence, further studies are needed in this field. A better understanding of cancer survivors' QoL and examining its influencing factors are important in developing a care plan for these survivors. We conducted a cross-sectional study to determine predictors of quality of life in these survivors. Considering this issue and the fact that Tabriz Shahid Ghazi Hospital is the referral center for these patients in the northwest of Iran, researchers in 2019 decided to evaluate the quality of life of the survivors and the predictive factors that may increase their quality of life.

Materials and Methods

This study used a descriptive-correlation design conducted in the Tabriz University of Medical Sciences-affiliated outpatient cancer clinic. Data were collected from January to October 2019. The study population were GI cancer survivors (colon, rectum and gastric) whose initial treatments had been completed and had no signs or symptoms of active cancer. Inclusion criteria were as follows: 1) They were eligible if they had survived at least 1 year from diagnosis; of gastric or colorectal cancer, 2) absence of any symptoms of active cancer, 3) at least 18 years old up to 80 years old, 4) ability to communicate, Patients suffered from another cancer were excluded. The sample size was calculated based on our pilot study (sample size estimation was performed based on a pilot study data (n = 120). A total of 135 eligible patients were invited to participate in the study using the convenience sampling method. Patients (n=15) not willing to participate in the study were excluded. Finally, we included 120 GI cancer survivors in the analysis (Participation rate = 0. 89).

The questionnaire used in this research included two parts. The first one was designed to collect demographic and disease-related characteristics of patients (including: blood pressure, blood sugar, CBC, BUN, creatinine,..) In this study, the presence of anemia in patients was determined based on hemoglobin level. Hemoglobin level in women and men was marked as value <12 g/dL and <13 g/dL, respectively [15]. The physical activity of patients was recorded daily as time (minutes).

The second part was the cancer-related quality of life questionnaire (QLQ-C30) with 30-item which assessed cancer patients' QoL in 15 scales. The questionnaire incorporates five functional scales (physical functioning, role functioning, cognitive, emotional and social functioning), nine symptom scales (fatigue, pain, nausea and vomiting, dyspnea, insomnia, appetite loss, constipation, diarrhea and financial difficulties), and global health and QOL scale. The scoring of 28 items was rated on 4-point Likert scales, ranging from "not at all" [1] to "very much" [4], and the scoring of two items was rated on 7-point Likert scales, ranging from " extremely bad[1]" to "extremely good[7]". The questionnaire items were scored on a scale ranging from 0 to 100. A higher score for the functional scales and global QoL scale indicated better functioning and QOL. For symptom scales, a higher score indicated more frequent and/or more intense symptoms [16]. The threshold for clinical importance was recently developed to improve the interpretation of the QLQ-C30 scales [17]. The Iranian version of the questionnaire was validated in a previous study [18]. In this study, face validity and content validity were assessed and verified by an expert panel including 10 faculty members of Tabriz University of Medical Sciences, Iran. The final version of the questionnaire was tested for reliability in a pilot study involving 30 cancer patients. The Cronbach's alpha value for items of QLQ-30 questionnaire was 85%. To perform data collection, first, this research project was approved by the Regional Ethics Committee at the Tabriz University of Medical Sciences (Ethics code: IR.TBZMED.REC.1396.345). Then, the necessary permissions were obtained from the research environment (clinic of Shahid Ghazi Hospital in Tabriz). The first author attended the hospital clinic during the sampling period and identified eligible patients who were referred to the clinic for the follow-up visit. After providing the necessary information to the patients regarding the aims of the study, the patients were invited to participate in the study. Moreover, after providing verbal consent, a written informed consent was obtained from all participants. Since most of the participants were illiterate (55.4%), their data were collected through an interview in a private room in the hospital's clinic.

Data were analyzed using SPSS software version 14. The Kolmogorov-Smirnov test was used to assess the normal distribution of data. Mean ± standard deviation (SD), frequency, and percentages were used to describe the characteristics of the study subjects. Paired sample t-test, chi-square and ANOVA were used to assess the association between fatigue and marital status, employment status, anemia, blood pressure, diabetes, smoking, physical activity and BUN/Cr ratio. Furthermore, a linear regression model was used to identify predictor variables. The significance level was considered at P-value = 0.05.

Ethical considerations

This study was approved by the Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1396.345). Written informed consent was obtained from all patients prior to participation in the study.

Results

The general characteristics of the study participants are shown in Table 1. A total of 120 GI cancer survivors were included in this study. The mean age ± SD of the participants was 56.01 ± 11.07 years. 55% of the participants were male, and 87% were married. The mean ± SD of BUN and Creatinine was estimated at 24.10 ± 1.39 and 1.11 ± 0.41, respectively. Table 2 reports the mean ± SD scores of participants in scales of functional, symptoms and global QoL and reports the percentage of patients who had problems in the scales as mentioned above based on the determined threshold. The results of the linear regression analysis of the possible predicting factors of QoL are reported in Table 3. Variables of HTN, marital status, anemia and BUN/Cr ratio were the strongest predictors of QoL, respectively. Global, these variables predicted 84% of the variance of the QoL variable. The results also showed that marital status, anemia, BUN/Cr ratio and activity were the strongest predictors of functional scale, respectively. These variables predicted 83.5% of the variance of the global functional scale (Table 4). According to the linear regression model results, marital status and anemia were the most important predictors of symptom, respectively. These variables predicted 67.3% of the variance of the symptom scale (Table 5).

Variables	Categories	Frequency (%)
Job	Housekeeper	38(31.7)
	self-employed	34(28.3)
	Retired	27(22.5)
	Unemployment	12(10)
	Employee	9(7.5)
Education	Primary	52(43.3)
	Diploma	46(38.3)
	University degree	22(18.3)
Type of cancer	Colorectal	87(72.5)
	Gastric	33(27.5)
Anemia	Yes	77(64.1)
	No	43(35.9)
Diabetes	Yes	33(27.5)
	No	87(72.5)
Hypertension	Yes	49(40.8)
	No	71(59.2)
Smoking	Yes	42(35)
	No	78(65)
Physical activity (min/day)	Nothing	83(69.2)
	<60	15(12.5)
	60-120	18(15)
	>120	4(3.3)

Table 1. Demographic and disease related characteristics of cancer patients

Thresholds for Clinical Importance		SD	MD		Domains of QOL
NO	Yes *				
n (%)	n (%)				
28 (23.3)	92 (76.7)	2.23	62.22	Physical function	Function
79 (65.8)	41 (34.2)	2.70	67.50	Role function	
44 (36.7)	76 (63.3)	2.62	64.58	Cognitive. Function	
42 (35.0)	78 (65.0)	2.75	55.34	Emotional functional	
66 (55)	54 (45.0)	2.33	65.69	Social function	
		2.52	63.06	Function. Total	
43 (35.8)	77 (64.2)	2.59	49.62	Fatigue	Symptoms
68 (56.7)	52 (43.3)	1.99	13.61	Nausea/vomiting	
42 (35.0)	78 (65.0)	3.11	46.66	Pain	
63 (52.5)	57 (47.5)	2.77	23.88	Dyspnea	
69 (57.5)	51(42.5)	2.71	38.88	Insomnia	
90 (75.0)	30 (25.0)	3.20	32.77	Appetite. Loss	
94 (78.3)	26 (21.7)	3.37	27.50	Constipation	
65 (54.2)	55 (45.8)	2.95	23.05	Diarrhea	
26 (21.7)	94 (78.3)	2.25	35.55	Financial problems	
		2.53	32.39	Symptoms total	
		2.61	48.12	global QOL	

Table 2. the mean ± SD scores of participants QoL in functional, symptoms and global QoL

*Clinically significance problem

Variable	B	SE	β
Constant	53.317	0.465	
Marital status (single= 0)	10.383	0.181	0.153*
Anemia (anemia= 0)	16.65	0.194	0.245**
Hypertension (yes= 0)	35.28	0.208	0.463***
Diabetes (yes= 0)	0.63	0.298	0.001
Smoking (yes= 0)	0.263	0.162	0.004
Activity	1.611	0.098	0.044
BUN/Cr	0.957	0.005	0.578***

Table 3. linear regression analysis of the possible predicting factors of global of GI cancer survivors

Adjusted R2=0.845, f=48.95, * p=0.045, ** p= 0.002, ***p<0.001

Variable	B	SE	β
Constant	53.317	0.465	
Marital status (single= 0)	10.383	0.181	0.153*
Anemia (anemia= 0)	16.65	0.194	0.245**
Hypertension (yes= 0)	35.28	0.208	0.463***
Diabetes (yes= 0)	0.63	0.298	0.001
Smoking (yes= 0)	0.263	0.162	0.004
Activity	1.611	0.098	0.044
BUN/Cr	0.957	0.005	0.578***

Table 4. linear regression analysis of the possible predicting factors of function of GI cancer survivors

*Adjusted R2=0.835, f=44.99, * p<0.001, ** p= 0.005,***p= 0.015*

doi.org/10.32388/J5Y5LR

Variable	B	SE	β
Constant	54.991	11.702	
Marital status (single= 0)	-18.599	4.730	-0.453*
Anemia (anemia= 0)	-26.524	4.869	-0.464*
Hypertension (yes= 0)	-0.841	5.230	-0.019
Diabetes (yes= 0)	-2.429	7.490	-0.033
Smoking (yes= 0)	0.802	4.076	0.018
Activity	4.519	2.467	0.202
BUN/Cr	-0.047	0.115	-0.47

Table 5. Linear regression analysis of the possible predicting factors of symptoms of GI cancer survivors

*Adjusted R2=0.673, f=15.88, *p<0.001*

Discussion

This study was carried out in order to investigate the quality of life of patients who survived GI cancer. If we put the score from 0 to 100 in the base questionnaire. An average of 50 with a standard deviation of 10 can be considered as a standard and acceptable index. The results of the present study showed that the score of the general quality of life of the patients is lower than the norm and an acceptable level, which is lower than the majority of studies. [4][5][6][7] Consistent with the present study, Lee et al.'s study found that survivors 5 years after treatment still needed symptom management, food control, maintaining self-esteem, maintaining social competitiveness, and financial support.[8] By comparing the QoL levels of our participants with those of colorectal cancer populations in previous studies [19], we found that the GI cancer survivors had lower QoL in this study. Based on the threshold, the QoL of most participants was poor. It should be noted that this study was conducted among GI cancer survivors, and this low level of QoL are expected to decrease after completing the treatment process of colorectal cancer, and patients report fewer symptoms after finishing chemotherapy [19].

Some symptoms and factors such as fatigue, pain, insomnia, appetite loss, nausea and vomiting, problems with eating, financial difficulty and reduction of family support would have a cumulative effect on the QoL of patients [20]. Worsening of debilitating symptoms, pain, insomnia, loss of appetite, nausea and vomiting, and eating problems, increasing financial problems and reducing joint support, all can have a negative cumulative effect on the quality of life of patients [13].In the symptom scale, the lowest score of QoL was related to the fatigue dimension. In a previous study, fatigue was identified as one of the most frequent side-effects of cancer treatment in patients with colorectal cancer [21]. Patients suffer from various problems (physical, emotional and cognitive) related to their fatigue. Emotional problems that include problems related to decreased energy and decreased desire and interest in activities and issues. The results of the present study showed that the score of the performance domain was average. This result was similar to Charalambous et al.'s study [14]. Cancer and its treatment can have harmful effects on social functioning, including work and life, relationships with family, friends, relatives, and colleagues, and other social activities. Studies in Asian countries have demonstrated a low level of QoL among cancer survivors [10][22]. Also, previous studies in Iran reported that patients with colorectal cancer had a moderate [14] or low QoL or low [13].

The results of the study showed that men had a better quality of life, which was in line with the study of Nikbakht et al[9]. It was also inconsistent with the results of the study by Momeni et al.[3], who showed that the quality of life in women is at a lower level than men. The sensitivity of women in facing unfortunate life events and women's greater responsibility towards the family can be the reason for justifying this difference.

The results of the study showed a significant correlation between quality of life and age. This result is consistent with other studies. Larson et al.'s study showed that younger people have a lower quality of life[10]. On the other hand, the results of Sio et al.'s study showed that elderly patients have a lower overall quality of life score than middle-aged and young women [11]. Probably because more aggressive treatments are given to patients in young patients, the complications of treatment are more in these patients. These complications and symptoms affect the patients' quality of life.

results of the study showed that there is a significant correlation between the employment status and income of patients with quality of life and performance. In Nikbakht et al.'s study, there was a significant correlation between employment and the quality of life and performance of individuals [9]. Employment

and income strengthen people's motivation. On the other hand, not having a suitable job or sufficient income creates an additional burden for the patient in addition to the disease.

The results of the study showed that there is a significant correlation between education level and quality of life. This result is consistent with other studies. The results of Cagayan et al.'s study showed that the level of education of people has a significant relationship with their quality of life [12].

In our study, anemia was identified as one of the most important predictor factors of QoL. Anemia is a relatively frequent comorbidity in cancer patients that jeopardize patients' QoL, life expectancy and survival [23]. In other hand Wouters report that anemia did not have an impact on survival in individuals younger than 60 years [15]. Anemia is highly prevalent, especially among colorectal cancer patients, which nowadays, iron supplements are most often used to treat anemia [24]. In the Wouters study demonstrated the detrimental effect of anemia on cancer patients' QoL [25]. A recent study showed that an increase in hemoglobin was significantly associated with improvement in cancer survivors' QoL [26].

In this study, marital status was identified as one of the predictor factors of QoL. Married patients were more likely to have better QoL than unmarried patients. The presence of a support person can play an important role in responding to treatment and patients' QoL. Spouses can increase the patient's willingness to continue the treatment process by encouraging the patient. A study showed that unmarried patients are less likely to receive social support [27].

Moreover, this study did identify physical activity as a predictor factor for QoL, especially for global QoL and functional scale, which is in line with previous studies [28] Another study reported that having a special exercise program like yoga can improve QoL and the daily functioning of cancer patients [29]. However, these results are inconsistent with a previous study reporting no association between exercise and Qol among cancer patients [30].

Another predictor factor for QoL among cancer survivors was found to be hypertension. Studies have demonstrated that patients with hypertension were more likely to have lower QoL [31][32]. A systematic review also showed lower QoL in patients with hypertension [32].

Furthermore, the BUN/Cr ratio was another predictor factor of QoL among cancer survivors. BUN/Cr is an important biochemical parameter related to physical function. High BUN levels indicate increased protein breakdown, which strongly affects the strength of muscle contraction and leads to fatigue and decreased physical function. When the body is deficient in energy, protein is consumed, and BUN levels elevate in

response to activity [33]. Previous studies have demonstrated a positive correlation between BUN level and activity tolerance [34], fatigue level [35].

The most important limitation of this study is that some patients went to physicians' private offices for their treatment, and we did not include them in our analysis. So, this limits our ability to generalize our results to all GI cancer survivors.

Conclusion

Our findings highlighted that the QoL level of GI cancer patients was low. In our study, variables of anemia, marital status, BUN/Cr, creatinine, HTN, and physical activity were identified as the most important predictor factors of QoL and predicted a high percentage of the variance of QoL. Therefore, it seems that the formulation and implementation of supportive care programs can play a crucial role in improving the QoL of patients.

Application of Findings

Quality of life related to cancer should be considered as a serious problem along with cancer and its treatment. Guidelines suggest that patients should be screened for quality of life and related issues during initial visits. The cause of the decline in the quality of life and the treatable factors should be identified, along with the cancer treatment, the improvement of the quality of life should also begin, and continue after the cancer treatment. The results of the present study can be used as a guide for clinical trials, experimental and semi-experimental studies, as well as future systematic review studies in identifying factors related to the quality of life of cancer survivors. It can also be used as a guide for the treatment team. Anemia was one of the most important variables that played a greater role in predicting the quality of life. It is recommended to identify the cause of anemia (deficiency of vitamin B12, iron deficiency, or bone marrow depression) in these patients as soon as possible and take measures to resolve it. Nutritional status of patients and adequate fluid intake should be monitored by the treatment team and patients. The use of supplements that can provide the nutritional needs of patients can also help in this field, which should be the attention of researchers and treatment staff. Modifying the lifestyle of patients and having regular meal plans to get enough food, sports activities, adjusting activities in such a way that balance between activity and rest of patients is recommended both in hospitalized patients and surviving patients. Correction of background problems such as blood pressure and diabetes control of patients as variables that can affect quality of life should be considered by the treatment team.

Other References

- Ghaderi M, Azadi A, Rahmani A, Sanaat Z, Nazemiyeh H, Shamsi A, et al. Fatigue and Its Related Factors Among Iranian Cancer Survivors. Journal of caring sciences. 2021;10(4):210.

References

1. a, b, c, d *Xie Y, Shi L, He X, Luo Y. Gastrointestinal cancers in China, the USA, and Europe. Gastroenterology Report. 2021;9(2):91-104. DOI: 10.1093/gastro/goab010.*
2. a, b *Granados-Romero JJ, Valderrama-Treviño AI, Contreras-Flores EH, Barrera-Mera B, Herrera Enríquez M, Uriarte-Ruíz K, et al. Colorectal cancer: a review. Int J Res Med Sci. 2017;5(11):4667-76.*
3. a, b, c *Mattiuzzi C, Sanchis-Gomar F, Lippi G. Concise update on colorectal cancer epidemiology. Annals of translational medicine. 2019;7(21):609. DOI: 10.21037/atm.2019.07.91.*
4. a, b, c *Maajani K, Khodadost M, Fattahi A, Shahrestanaki E, Pirouzi A, Khalili F, et al. Survival rate of colorectal cancer in Iran: a systematic review and meta-analysis. Asian Pacific journal of cancer prevention: APJCP. 2019;20(1):13. DOI: 10.31557/APJCP.2019.20.1.13.*
5. a, b *Drury A, Payne S, Brady A-M. Cancer survivorship: advancing the concept in the context of colorectal cancer. European Journal of Oncology Nursing. 2017;29:135-47. DOI: 10.1016/j.ejon.2017.06.006.*
6. a, b *Adams SV, Ceballos R, Newcomb PA. Quality of life and mortality of long-term colorectal cancer survivors in the Seattle Colorectal Cancer Family Registry. PloS one. 2016;11(6):e0156534. DOI: 10.1371/journal.pone.0156534.*
7. a, b, c *Haraldstad K, Wahl A, Andenæs R, Andersen JR, Andersen MH, Beisland E, et al. A systematic review of quality of life research in medicine and health sciences. Quality of life Research. 2019;28(10):2641-50. DOI: 10.1007/s11136-019-02214-9.*
8. a, b *Pinto S, Fumincelli L, Mazzo A, Caldeira S, Martins JC. Comfort, well-being and quality of life: Discussion of the differences and similarities among the concepts. Porto Biomedical Journal. 2017;2(1):6-12.*
9. a, b, c *Han X, Robinson LA, Jensen RE, Smith TG, Yabroff KR. Factors associated with health-related quality of life among cancer survivors in the United States. JNCI cancer spectrum. 2021;5(1):pkaa123.*
10. a, b, c *Firkins J, Hansen L, Driessnack M, Dieckmann N. Quality of life in "chronic" cancer survivors: a meta-analysis. Journal of Cancer Survivorship. 2020:1-14.*

11. a, b *Liao L-J, Hsu W-L, Lo W-C, Cheng P-W, Shueng P-W, Hsieh C-H. Health-related quality of life and utility i n head and neck cancer survivors. BMC cancer. 2019;19(1):1-10. DOI: 10.1186/s12885-019-5614-4.*

12. a, b *Annunziata MA, Muzzatti B, Flaiban C, Gipponi K, Carnaghi C, Tralongo P, et al. Long-term quality of lif e profile in oncology: a comparison between cancer survivors and the general population. Supportive Care i n Cancer. 2018;26(2):651-6.*

13. a, b, c, d *Akhondi-Meybodi M, Akhondi-Meybodi S, Vakili M, Javaheri Z. Quality of life in patients with colore ctal cancer in Iran. Arab J Gastroenterol. 2016;17(3):127-30. DOI: 10.1016/j.ajg.2016.06.001.*

14. a, b, c *Momeni M, Ghanbari A, Jokar F, Rahimi A, Leyli EK. Predictors of quality of life in patients with colorec tal cancer in Iran. Indian journal of cancer. 2014;51(4):550. DOI: 10.4103/0019-509X.175331.*

15. a, b *Nikbakht HA, Sani NA, Jafarabadi MA, Hosseini SR. Quality of life and its determinants among colorecta l cancer survivors. Journal of Kermanshah University of Medical Sciences. 2015;19(2):84-92.*

16. ^ *Ferrari M, Manea L, Anton K, Bruzzone P, Meneghello M, Zamboni F, et al. Anemia and hemoglobin serum levels are associated with exercise capacity and quality of life in chronic obstructive pulmonary disease. B MC pulmonary medicine. 2015;15(1):1-8. DOI: 10.1186/s12890-015-0050-y.*

17. ^ *Scott NW, Fayers P, Aaronson NK, Bottomley A, de Graeff A, Groenvold M, et al. EORTC QLQ-C30 reference values manual. 2008.*

18. ^ *Giesinger JM, Loth FL, Aaronson NK, Arraras JI, Caocci G, Efficace F, et al. Thresholds for clinical importanc e were established to improve interpretation of the EORTC QLQ-C30 in clinical practice and research. Journ al of clinical epidemiology. 2020;118:1-8.*

19. a, b *Safaee A, Dehkordi Moghimi B, Tabatabaie S. Reliability and validity of the QLQ-C30 questionnaire in c ancer patients. Armaghane danesh. 2007;12(2):79-88.*

20. ^ *Russell L, Gough K, Drosdowsky A, Schofield P, Aranda S, Butow PN, et al. Psychological distress, quality of life, symptoms and unmet needs of colorectal cancer survivors near the end of treatment. Journal of cancer survivorship. 2015;9(3):462-70.*

21. ^ *Talagala IA, Arambepola C. Changes in quality of life following initial treatment of oesophageal carcinom a: a cohort study from Sri Lanka. BMC cancer. 2018;18(1):1-9. DOI: 10.1186/s12885-018-5106-y.*

22. ^ *Ma Y, He B, Jiang M, Yang Y, Wang C, Huang C, et al. Prevalence and risk factors of cancer-related fatigue: A systematic review and meta-analysis. International journal of nursing studies. 2020;111:103707. DOI: 10.101 6/j.ijnurstu.2020.103707.*

23. ^ *Ho PJ, Gernaat SA, Hartman M, Verkooijen HM. Health-related quality of life in Asian patients with breast cancer: a systematic review. BMJ open. 2018;8(4):e020512. DOI: 10.1136/bmjopen-2017-020512.*

24. ^Busti F, Marchi G, Ugolini S, Castagna A, Girelli D. Anemia and iron deficiency in cancer patients: role of iro n replacement therapy. Pharmaceuticals. 2018;11(4):94. DOI: 10.3390/ph11040094.

25. ^Wilson M, Harlaar JJ, Jeekel J, Schipperus M, Zwaginga J. Iron therapy as treatment of anemia: A potentiall y detrimental and hazardous strategy in colorectal cancer patients. Medical hypotheses. 2018;110:110-3.

26. ^Wouters HJ, van der Klauw MM, de Witte T, Stauder R, Swinkels DW, Wolffenbuttel BH, et al. Association of anemia with health-related quality of life and survival: a large population-based cohort study. haematolog ica. 2019;104(3):468. DOI: 10.3324/haematol.2018.195552.

27. ^Gascón P, Arranz R, Bargay J, Ramos F. Fatigue- and health-related quality-of-life in anemic patients with lymphoma or multiple myeloma. Supportive care in cancer: official journal of the Multinational Associatio n of Supportive Care in Cancer. 2018;26(4):1253-64. DOI: 10.1007/s00520-017-3948-5.

28. ^Bower JE. Cancer-related fatigue—mechanisms, risk factors, and treatments. Nature reviews Clinical oncol ogy. 2014;11(10):597-609.

29. ^Wong JN, McAuley E, Trinh L. Physical activity programming and counseling preferences among cancer su rvivors: a systematic review. International Journal of Behavioral Nutrition and Physical Activity. 2018;15(1):1 -21.

30. ^Yagli NV, Ulger O. The effects of yoga on the quality of life and depression in elderly breast cancer patients. Complementary therapies in clinical practice. 2015;21(1):7-10. DOI: 10.1016/j.ctcp.2015.01.002.

31. ^Dhillon H, Bell M, van der Ploeg H, Turner J, Kabourakis M, Spencer L, et al. Impact of physical activity on f atigue and quality of life in people with advanced lung cancer: a randomized controlled trial. Annals of Onc ology. 2017;28(8):1889-97. DOI: 10.1093/annonc/mdx205.

32. a, bChin YR, Lee IS, Lee HY. Effects of hypertension, diabetes, and/or cardiovascular disease on health-relate d quality of life in elderly Korean individuals: a population-based cross-sectional survey. Asian Nursing Res earch. 2014;8(4):267-73.

33. ^Trevisol DJ, Moreira LB, Kerkhoff A, Fuchs SC, Fuchs FD. Health-related quality of life and hypertension: a s ystematic review and meta-analysis of observational studies. Journal of hypertension. 2011;29(2):179-88. D OI: 10.1097/HJH.0b013e328340d76f.

34. ^Wang J, Sun C, Zheng Y, Pan H, Zhou Y, Fan Y. The effective mechanism of the polysaccharides from Panax ginseng on chronic fatigue syndrome. Archives of pharmacal research. 2014;37(4):530-8. DOI: 10.1007/s1227 2-013-0235-y.

35. ^Miao X, Xiao B, Shui S, Yang J, Huang R, Dong J. Metabolomics analysis of serum reveals the effect of Dang gui Buxue Tang on fatigued mice induced by exhausting physical exercise. Journal of pharmaceutical and b

iomedical analysis. 2018;151:301-9. DOI: 10.1016/j.jpba.2018.01.028.

Declarations

Funding: No specific funding was received for this work.

Potential competing interests: No potential competing interests to declare.