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Quality of Life in Colorectal Cancer Patients with Oxaliplatin Induced Peripheral Neuropathy

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Abstract

Background: Oxaliplatin has demonstrated modest activity in patients with metastatic CRC, generating a response rate between 10% and 24%. Neurotoxicity is the most frequent dose limiting toxicity of oxaliplatin. Acute sensory neurotoxicity manifests as rapid onset of cold induced distal dysesthesia and/or paresthesia, sometimes accompanied by cold dependent muscular contractions of the extremities or the jaw. The symptoms, often occurs during or shortly after infusion, are usually transient and mild. A cumulative sensory peripheral neuropathy may also develop with prolonged treatment with oxaliplatin , eventually causing superficial and deep sensory loss, sensory ataxia and functional impairment.

Aim of Study: This study aimed at estimating QoL in CRC patients treated with oxaliplatin-based regimen and having neurotoxicity.

Patients and Methods: In this cross-sectional study, 62 patients with colorectal cancer treated with oxaliplatin-containing regimen were recruited from the Clinical Oncology Department Ain Shams University Hospitals.

All consecutive patients were assessed by means of two questionnaires, the QLQ-CIPN20 for assessment of neuropathy and the QLQ-C30 core questionnaire for assessment of quality of life in cancer patients from the European Organization for Study and Treatment of Cancer after being translated to Arabic.

Results: The sensory scale revealed that around 46% of the patients suffered little tingling in the fingers or hands (mild) and 21.0% had quite a bit (moderate). Almost 42% suffered little tingling toes or feet (mild) and 16% suffered quite a bit (moderate). Furthermore, 38.7% had little numbness in fingers or hands (mild) and 14.5% suffered quite a bit (moderate). Furthermore, in our study, motor scale revealed that patients who suffered “Quite a bit” (moderate) cramps in their hands were 6.45% while those with cramps in their feet were 16.1%. Also, 19.4% had a little (mild) struggle holding a pen and 4.8% had quite a bit (moderate) struggle holding their hands. Finally, the assessment of autonomic function in our study revealed that 47% had a little (mild) dizziness when standing up from a sitting or lying position and 7% had quite a bit (moderate) dizziness. 17.4% had a little (mild) blurred vision. Regarding erection function, 30.64 had quite a bit (moderate) difficulty getting or maintaining an erection while 19.35 had a little (mild) difficulty. Generally, the EORTC-QLQ questionnaire revealed overall moderate quality of life. One fifth or less suffered problems in role functioning followed by social and emotional functioning.

Conclusion: The use of oxaliplatin as an anticancer agent mostly associated with neurological disorders, including motor, sensory, and some other autonomic disorders which significantly affects the quality of life of those patients. Chemotherapy induced peripheral neuropathy is also the most frequent reason for treatment discontinuation. Physicians should actively assess for CIPN in order to prevent chronic neuropathy.

Key Words: *Colorectal Cancer – Oxaliplatin – QoL – Peripheral Neuropathy.*

Introduction

COLORECTAL Cancer (CRC) represents 9.2% in women and 10.0% in men and is the fourth cause of cancer death worldwide. Males in Egypt are more likely to develop colorectal cancer than females, at a rate of 5.1% against 4.7%. Egypt has the highest rate of early CRC in the world as 35% of 1,600 Egyptian CRC patients were under 40. It was reported that Egyptian patients who have CRC below the age of 30 have a threefold increased risk of dying within 5 years compared to those who have CRC over the age of 50, from 75 to 25% **[1].**

Although chemotherapy prolongs survival in cancer patients, some chemotherapeutic agents can cause Chemotherapy-Induced Peripheral Neuropathy (CIPN), which affects Quality of Life (QoL) **[2].** Depending on the severity of the neuron damage, CIPN may appear weeks to months after exposure to

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chemotherapeutic medicines, can persist even after the chemotherapy has stopped, and may be irreversible. The chemotherapy drugs thalidomide, bortezomib, platinum compounds, vinca alkaloids, and taxanes most frequently result in CIPN [3]. CIPN is classified into axonopathy, neuronopathy and myelinopathy based on the etiological mechanism. Oxaliplatin causes neuronopathy, which occurs due to cell death in neural ganglia of the dorsal spinal nerve root. Neuronopathy is thought to be hard to reverse because of damage to the neuron itself, even if drug administration is stopped [4].

The main chemotherapy drug for the treatment of CRC is oxaliplatin, a third-generation platinum-based drug that is also used to treat pancreatic, gastric, and other malignancies in individuals. Oxaliplatin has increased overall survival rates, but it still has a treatment-limiting side effect known as Oxaliplatin-Induced Peripheral Neuropathy (OIPN) [5]. The symptoms of acute neurotoxicity and chronic oxaliplatin-induced neuropathy are caused by hyperexcitability of axons, changes in voltage-gated sodium and/or potassium channels causing repetitive discharges and oxidative stress, and neuronal damage caused by oxaliplatin accumulation in the dorsal root ganglia, respectively [6]. By combining with DNA in dorsal root ganglion neurons to create complexes (adducts), the platinum in oxaliplatin causes chronic CIPN. Next, the adducts prevent DNA replication and result in apoptosis [2].

OIPN has been reported as dose-dependent, with symptoms more likely to occur as the cumulative dose exceeds 780–850mg/m^2. Unlike acute OIPN which is transient, chronic OIPN can persist for months or years and includes pain, numbness, and dysesthesias that lead to reduced quality of life and function [5]. However, 40% of patients with neurotoxic adverse events show complete recovery 8 months after oxaliplatin is stopped [4].

The sensory nerves are primarily affected by neuropathy in the majority of oxaliplatin-induced CIPN patients. The prevalence of motor symptoms is rather low. Numbness, tingling, and paresthesia brought on by coldness in the limbs, paresthesia around the mouth, trouble swallowing cold liquids, shortness of breath, numbness, cramps, stiffness of the jaw, and changes in the auditory and visual receptive fields are some of the acute symptoms that may appear several hours to several days after the injection [7]. Exceeding 175 to 200mg/m^2 of oxaliplatin can result in paresthesia of the distal ends of limbs and hypoesthesia unrelated to coldness. Loss of sensory function, a decrease in deep tendon reflexes, and impaired proprioception are examples of chronic symptoms [2].

Aim of the work:

The aim of this study was to estimate QoL in CRC patients treated with oxaliplatin-based regimen and having neurotoxicity.

Patients and Methods

This cross-sectional study included 62 patients with colorectal cancer treated with oxaliplatin containing regimen, recruited from clinical oncology department, Ain Shams University Hospitals after obtaining a written informed consent and explaining to them the objectives of the study and the procedure to be done from all patients. The study was approved from Ethical Committee of Clinical Oncology Department, Ain Shams University Hospitals. From February 2023 – September 2023.

Any colorectal cancer patient receiving treatment with oxaliplatin containing regimens were included in the study. While diabetic patients with autoimmune diseases (systemic lupus erythematosus, rheumatoid arthritis, vasculitis), alcoholism, exposed to industrial chemicals and mechanical entrapment of nerves were excluded from the study.

European Organization for Study and Treatment of Cancer Quality of Life Questionnaire–Chemotherapy Induced Peripheral Neuropathy (EORTC QLQ-CIPN20) questionnaire [8] and QLQ-C30 core questionnaire from EORTC after being translated to Arabic were used to the assess the quality of life of the participants [9].

Assessment of quality of life in patients with CRC treated with oxaliplatin-based regimen was measured using EORTC QLQ – CIPN20.

While reporting scale level data, it is highly recommended that some basic psychometric analyses be carried out. Minimally, the internal consistency of the scales should be examined using the reliability program of SPSS or a similar software package that calculates a Cronbach's alpha coefficient. That coefficient should preferably be above 0.70 for any given multi-item scale (for purposes of group comparisons). You do not need to recode the items to perform the reliability analysis.

If forming a scale appears to be justified, then the same algorithm can be used as is presented in the scoring manual for the QLQ-C30 for linearly converting items and/or scales to 0-100 scales.

The module items can also be reported individually. If this is done, it may be more useful to report the percentage of patients endorsing each of the response categories, rather than mean scores. It may be even more useful to recode the response categories to yield a dichotomous outcome per item (e.g., "not at all" and "a little" vs. "quite a bit" and "very much"). This allows one, for example, to report the percentage of patients with moderate to severe symptoms or problems. If item mean scores are being presented, the items should first be linearly converted to a 0 to 100 scale.

Both multi-item scales and single-item measures are included in the QLQ-C30. These comprise a global health status/QoL scale, three symptom

scales, five functional scales, and six single items. There are various sets of items in each of the multi-item scales; no item appears in more than one scale.

The scores for all scales and single-item measurements range from 0 to 100. A high scale score indicates a higher level of responsiveness. Therefore, a high score on a functional scale denotes a high or healthy level of functioning, but a high score on a global health status or quality of life scale denotes a high QoL or level of symptomatology.

Statistical analysis: EORTC-CIPN20 questionnaire items were presented as frequencies and percentages. The QLQ-C30 questionnaire scores were presented as the mean ± standard deviation (SD) and as the median [interquartile range, IQR]. Comparisons between groups of patients were assessed using the Chi-squared test for categorical variables Mann-Whitney U tests & Kruskal-Wallisto test for differences in continuous variables. To examine which factors, influence QoL in patients with colorectal cancer while holding the other factors constant, multiple linear regression of age, gender, chemo protocol, and performance status on QoL summary score.

Results

A total of 62 colorectal cancer patients were recruited. Baseline demographics are presented in Table (1). According to Table (1), males comprise most of our sample with 67.7%. Mean age of the included patients is 50.13 (±11.15) years with the youngest had 27 years and the oldest patient had 70 years old. Fifty-five of the participants were on the lower Oxiplatin chemo protocol (FOLFOX), and 45% on the higher dose (CAPEOX). Seventy-seven percent of the patients were in the stages 0 and 1 of the Eastern European Oncology Group Performance status, almost one quarter of them in the stages 2&3.

Table (1-A): Demographic and clinical characteristics of patients included in the sample.

	N=62
Gender[1]*:*	
Female	20 (32.3)
Male	42 (67.7)
Age (years)[2]	50.13±11.15
Chemo protocol:	
CAPEOX	28 (45)
FOLFOX	34 (55)
EGOC-PS[3]*:*	
0	15 (24)
1	33 (53)
2	9 (15)
3	5 (8)

[1]Data expressed as frequency (percent).
[2]Data expressed as mean ± SD.
[3]EGOC-PS Eastern European Oncology Group Performance status.

Table (1-B): Quality of life domains for patients included in the sample.

Quality of life Domains (n=62)	n	Mean ± SD	Median (IQR)
Functional scales (higher is better functioning):			
Physical functioning	62	75.6±19.6	80.0 (30)
Role functioning	62	54.8±27.9	66.7 (16.7)
Emotional functioning	62	67.5±32.6	79.2 (45.8)
Cognitive functioning	62	86.0±25.5	100 (29.2)
Social functioning	62	55.9±28.6	50 (45.8)
Symptoms scales (higher is more symptoms, worse functioning):			
Fatigue	62	46.6±27	33.3 (44.4)
Nausea and vomiting	62	19.9±19.5	16.7 (16.7)
Pain	62	30.6±31.8	16.7 (33.3)
Single-item symptom scores (higher is more symptoms, worse functioning):			
Dyspnea	62	21±29	0 (33.3)
Insomnia	62	32.3±29.5	33 (33)
Appetite loss	62	31.7±29.8	33 (66.7)
Constipation	62	37.1±29.6	33 (58.3)
Diarrhea	62	27.4±28.6	33 (33)
Financial impact	62	73.1±16.9	66.7 (0)
Global health status/QoL	62	63.6±31	75 (39.6)
Quality of life-summary score	62	68.7±24	81.4 (37)

Patients exhibit moderate level of functioning and quality of life with role and social functioning, the most affected functional domains. Symptom scales show mild suffering. The extremely affected domain is the financial impact.

Table (1-C): Demographic and clinical characteristics of patients included in the sample.

Domain	Frequency	Percentage (%)
Symptoms scales (higher is more symptoms, worse functioning):		
Fatigue	14	22.5
Nausea and vomiting	0	0
Pain	7	11.3
Single-item symptom scores (higher is more symptoms, worse functioning):		
Dyspnea	2	3
Insomnia	5	8
Appetite loss	3	4.8
Constipation	5	8
Diarrhea	3	4.8
Financial impact	15	25

Table (1-C) showed that the main concern is that 25% were suffering from financial difficulties, followed by 22.5% had fatigue problems, and pain problems were in 11.3% of patients. 8% have sleeping problems and constipation 4.8% appetite loss and diarrhea, 3% suffered from dyspnea and no one showed nausea or vomiting problems (exceeding 66.7% cutoff value for problematic symptoms).

Table (1-D): Quality of life Domains showing problems (<33.3% on functional scale).

Domain	Frequency	Percentage (%)
Functional scales (higher is better functioning):		
Physical functioning	3	4.8
Role functioning	12	19
Emotional functioning	11	17.7
Cognitive functioning	2	3
Social functioning	10	16
Global health status/ QoL	11	17.7
Quality of life-summary score	7	11.3

Based on the functional scales where those values that lie below the cut off value of 33.3 to be considered as showing problems, there were role functioning problems in 12 patients (19%) followed by emotional 11 (17.7), and 10 patients (16%) had social functioning problems.

Overall, seventy-one percent of the patients are functioning well as they score greater than or equal to 66.7 total QoL summary score, fifty-nine percent of them were on FOLFOX and forty-one percent were on CAPEOX, but this effect was not statistically significant (*p*-value=0.44). The quality-of-life summary score median value is higher among the chemo protocol with the lower Oxiplatin dose; FOLFOX 82.8 versus 77.5 among those on CAPEOX, however the difference was not statistically significant (*p*-value=0.10).

A somewhat similar relationship found in the comparison between males and females. Overall males seem to have higher QoL; median 82.1 compared to females 76. Based on Wilcoxon test w= 293, *p*-value is borderline = 0.05669. On conducting multiple linear regression analysis to assess the impact of age, sex, performance status, and chemo protocol on QoL summary score, it seems that both sex and performance status explained almost half of the variability in QoL (adjusted R^2 = 49%) (Fig. 1).

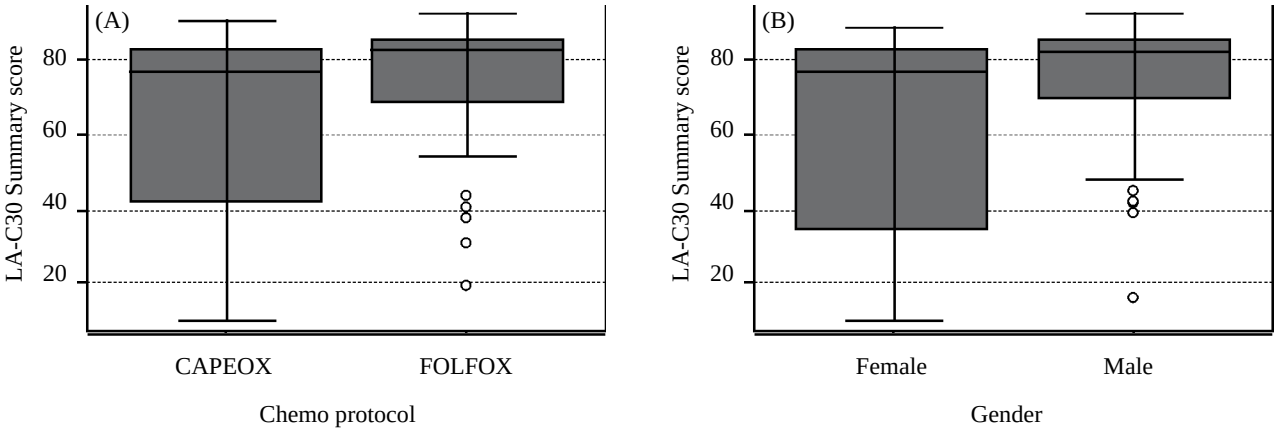

Fig. (1): (A) Quality of life summary scores distribution among those on FOLFOX versus CAPEOX. (B) Quality of life summary scores distribution among males versus females.

The plot shows high correlation between stages of EGOC and QoL summary score. Median QoL summary score values among the ECOG-PS stages were as follow: 81.9 in zero stage, 83.1 for first stage, 43.9 in the second, 16.4 in the third stage. Kruskal-Wallis chi square test value of 21.166 and *p*-value <0.001* is statistically significant.

Health status, physical functioning and the overall summary score median and mean values are higher and better among those on FOLFOX, emotional functioning median is higher with almost the same mean value for those on CAPEOX, both protocols show similarity in role and cognitive functioning as shown in Table (2).

Symptoms scales demonstrated more symptoms for those on CAPEOX, where fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation and diarrhea all showed elevated mean and third quartile values compared to FOLFOX. Financial difficulties expressed from both groups with slightly greater mean effect among CAPOEX.

Table (2): Quality of life domains in patients according to different chemo protocols.

Domain	Chemo Protocol	Median	First Quartile	Third Quartile	IQR	Mean	SD
QL	CAPEOX	58.33	31.25	83.33	52.08	55.66	34.25
	FOLFOX	83.33	54.17	83.33	29.17	70.10	27.69
PF	CAPEOX	76.67	60	80	20	69.76	21.28
	FOLFOX	86.67	75	93.33	18.33	80.392	16.89
RF	CAPEOX	66.67	16.67	66.67	50	48.81	30.41
	FOLFOX	66.67	50	66.67	16.67	59.80	24.99
EF	CAPEOX	83.33	41.67	100	58.33	67.26	35.42
	FOLFOX	75	60.42	91.67	31.25	67.65	30.55
CF	CAPEOX	100	66.67	100	33.33	83.93	26.64
	FOLFOX	100	100	100	0	87.75	24.72
SF	CAPEOX	50	29.17	70.83	41.67	49.41	31.26
	FOLFOX	66.67	50	83.33	33.33	61.28	25.53
FA	CAPEOX	44.44	22.22	80.56	58.33	50.40	29.70
	FOLFOX	33.33	22.22	52.78	30.56	43.46	24.83
NV	CAPEOX	16.67	0	37.5	37.5	20.83	24.69
	FOLFOX	16.67	16.67	16.67	0	19.12	14.29
PA	CAPEOX	16.67	16.67	66.67	50	36.31	36.02
	FOLFOX	16.67	4.17	33.33	29.17	25.98	27.58
DY	CAPEOX	0	0	66.67	66.67	26.19	31.89
	FOLFOX	0	0	33.33	33.33	16.67	26.27
SL	CAPEOX	33.33	33.33	66.67	33.33	39.29	30.16
	FOLFOX	33.33	0	33.33	33.33	26.47	28.16
AP	CAPEOX	33.33	25	66.67	41.67	38.10	29.696
	FOLFOX	33.33	0	33.33	33.33	26.47	29.34
CO	CAPEOX	33.33	33.33	66.67	33.33	46.43	31.87
	FOLFOX	33.33	0	33.33	33.33	29.41	25.64
DI	CAPEOX	33.33	0	41.67	41.67	30.95	33.86
	FOLFOX	33.33	0	33.33	33.33	24.51	23.65
FI	CAPEOX	66.67	66.67	75	8.33	75	14.70
	FOLFOX	66.67	66.67	66.67	0	71.57	18.59
QLQTOTAL	CAPEOX	77.52	41.73	82.54	40.81	63.90	27.10
	FOLFOX	82.82	69.88	85.60	15.72	72.68	20.78

QL : Global health status/ QoL.
PF : Physical functioning.
RF : Role functioning.
EF : Emotional functioning.
CF : Cognitive functioning.
SF : Social functioning.
FA : Fatigue.
NV : Nausea and vomiting.
PA : Pain.
DY : Dyspnea.
SL : Insomnia.
AP : Appetite loss.
CO : Constipation.
DI : Diarrhea.
FI : Financial impact.
QLQTOTAL: Quality of life-summary score.
IQR: Interquartile range.
SD : Standard deviation.

According to Table (3), females seem to have lower global health status and overall quality of life summary scores. For the other domains, same median score pattern for both sexes, however, twenty five percent of the females showed lower functioning scores (first quartile) and higher symptom scores (third quartile) compared to males.

Table (3): Quality of life domains in patients according to patients' gender.

Domain	Gender	Median	First Quartile	Third Quartile	IQR	Mean	SD
QL	Female	66.67	20.83	83.33	62.50	55.00	36.91
	Male	75.00	52.08	83.33	31.25	67.66	27.99
PF	Female	80.00	46.67	86.67	40.00	70.33	23.04
	Male	80.00	73.33	93.33	20.00	78.10	17.44
RF	Female	66.67	25.00	66.67	41.67	48.33	31.02
	Male	66.67	50.00	66.67	16.67	57.94	26.09
EF	Female	66.67	20.83	77.08	56.25	50.83	34.08
	Male	83.33	66.67	100.00	33.33	75.40	28.98
CF	Female	100.00	50.00	100.00	50.00	75.83	35.24
	Male	100.00	100.00	100.00	0.00	90.87	17.73
SF	Female	50.00	29.17	83.33	54.17	49.17	31.75
	Male	50.00	50.00	83.33	33.33	59.13	26.85
FA	Female	44.44	33.33	88.89	55.56	54.44	28.82
	Male	33.33	22.22	55.56	33.33	42.86	25.81
NV	Female	16.67	16.67	37.50	20.83	24.17	19.10
	Male	16.67	0.00	16.67	16.67	17.86	19.61
PA	Female	16.67	16.67	66.67	50.00	41.67	35.66
	Male	16.67	0.00	33.33	33.33	25.40	28.81
DY	Female	0.00	0.00	66.67	66.67	26.67	36.83
	Male	0.00	0.00	33.33	33.33	18.25	24.64
SL	Female	33.33	33.33	66.67	33.33	45.00	34.67
	Male	33.33	0.00	33.33	33.33	26.19	25.01
AP	Female	33.33	0.00	66.67	66.67	36.67	34.03
	Male	33.33	0.00	33.33	33.33	29.37	27.75
CO	Female	33.33	0.00	41.67	41.67	36.67	34.03
	Male	33.33	33.33	66.67	33.33	37.30	27.75
DI	Female	33.33	25.00	66.67	41.67	38.33	31.11
	Male	16.67	0.00	33.33	33.33	22.22	26.20
FI	Female	66.67	66.67	100.00	33.33	76.67	19.04
	Male	66.67	66.67	66.67	0.00	71.43	15.74
QLQTOTAL	Female	75.96	35.16	82.27	47.11	60.84	28.42
	Male	82.14	69.88	85.60	15.72	72.46	21.00

QL : Global health status/ QoL.
PF : Physical functioning.
RF : Role functioning.
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QLQTOTAL: Quality of life-summary score.
IQR: Interquartile range.
SD : Standard deviation.

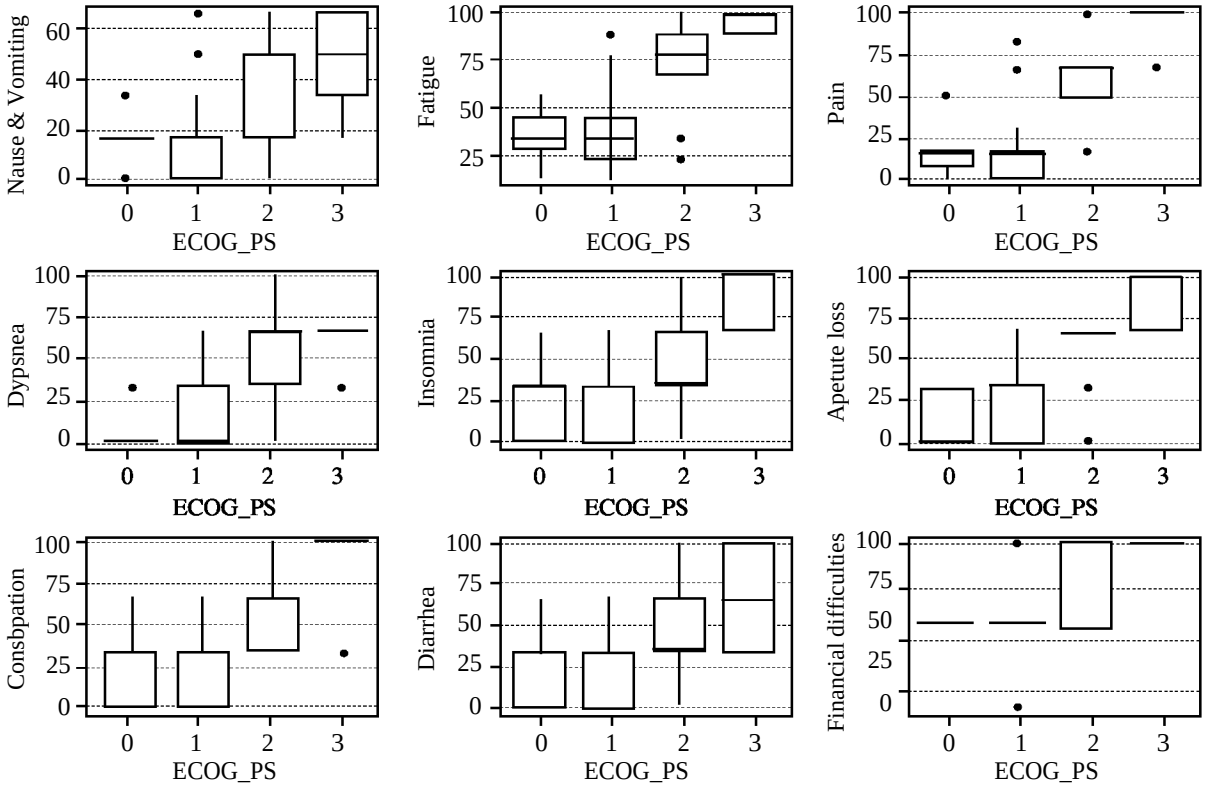

Fig. (2): Symptoms scales of quality-of-life questionnaire "QLQ-c30" and Eastern Cooperative Oncology Group-Performance Status.

ECOG-PS was significantly correlated with deteriorating QoL functional and symptom scales, QLQ symptoms scales show strong correlation with ECOG-PS stages (Fig. 2) where symptom scales higher scores were associated with class 3, and to some extent class 2. In stage 3, the main domains that exhibits the worst scores (>66.7%) include: fatigue, pain, insomnia, appetite loss. Financial difficulties seem affecting all study participants. Similarly, QLQ functional scales were deteriorating more in stages 3 and 2 (Fig. 3), the worst functioning scores were related to role, emotional, social, and global health status.

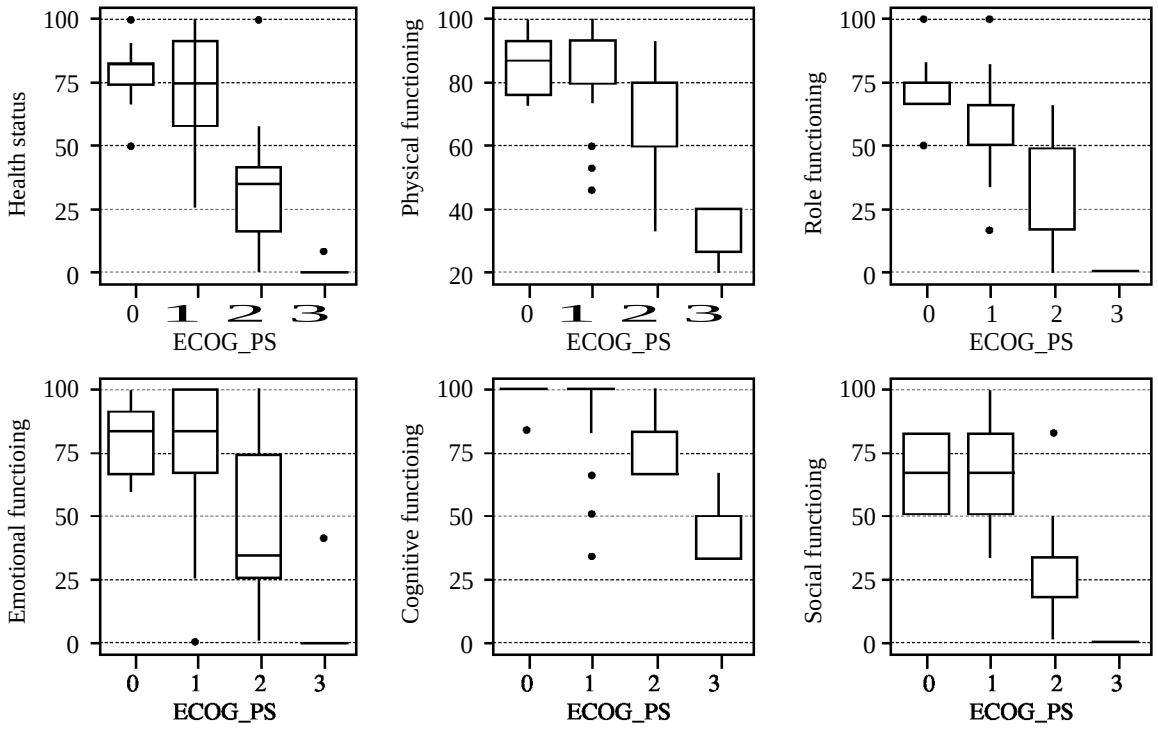

Fig. (3): Functional scales of quality-of-life questionnaire "QLQ-c30" and Eastern Cooperative Oncology Group-Performance Status.

According to Table (4-A), around 46% of the patients suffered little tingling in the fingers or hands and 21.0% had quite a bit. Almost 42% suffered little tingling toes or feet and 16% suffered quite a bit. Furthermore, 38.7% had little numbness in fingers or hands and 14.5% suffered quite a bit. In 60% of patients had no numbness in toes or feet while 33% had a little numbness. 21.0% had a little shooting or burning pain while almost 13% had quite a bit. Moreover, 19.4% had little problems standing or walking because of difficulty feeling the ground under their feet and 3.2% suffered quite a bit. 17.7% had little difficulty distinguishing between hot and cold water and 12.9% had quite a bit. Regarding hearing problems, almost 98% had no hearing problems.

Table (4-A): Sensory scale of CIPN20 questionnaire.

CINP20 Questions	Not at all		A little (Mil)		Quite a bit (Moderate)		Very much (Sever)	
	N	%	N	%	N	%	N	%
Did you have tingling fingers or hands?	19	30.6	28	45.2	13	21.0	2	3.2
Did you have tingling toes or feet?	20	32.3	26	41.9	10	16.1	6	9.7
Did you have numbness in your fingers or hands?	25	40.3	24	38.7	9	14.5	4	6.5
Did you have numbness in your toes or feet?	37	59.7	20	32.3	5	8.1	0	0.0
Did you have shooting or burning pain in your fingers or hands?	28	45.2	18	29.0	15	24.2	1	1.6
Did you have shooting or burning pain in your toes or feet?	41	66.1	13	21.0	8	12.9	0	0.0
Did you have problems standing or walking because of difficulty feeling the ground under your feet?	48	77.4	12	19.4	2	3.2	0	0.0
Did you have difficulty distinguishing between hot and cold water?	42	67.7	11	17.7	8	12.9	1	1.6
Did you have difficulty hearing?	61	98.4	1	1.6	0	0.0	0	0.0

Table (4-B): Motor scale of CIPN20 questionnaire.

CIPN Questions	Not at all		A little (Mil)		Quite a bit (Moderate)		Very much (Sever)	
	N	%	N	%	N	%	N	%
Did you have cramps in your hands?	45	72.58	13	20.96	4	6.45	0	0
Did you have cramps in your feet?	24	38.7	28	45.2	10	16.1	0	0.0
Did you have a problem holding a pen, which made writing difficult?	45	72.6	12	19.4	3	4.8	2	3.2
Did you have difficulty manipulating small objects with your fingers (for example, fastening small buttons)?	31	50.0	21	33.9	7	11.3	3	4.8
Did you have difficulty opening a jar or bottle because of weakness in your hands?	28	45.2	23	37.1	6	9.7	5	8.1
Did you have difficulty walking because your feet dropped downwards?	57	91.9	4	6.5	0	0.0	1	1.6
Did you have difficulty climbing stairs or getting up out of a chair because of weakness in your legs?	29	46.8	16	25.8	13	21.0	4	6.5
Did you have difficulty using the pedals?	9	14.51	1	1.61	5	8.06	1	1.61

Table (4-C): Autonomic scale of CIPN20 questionnaire.

CINP20 Questions	N	%
Were you dizzy when standing up from a sitting or lying position?		
Not at all	29	46.77
A little	29	46.77
Quite a bit	4	6.45
Very much	0	0
Did you have blurred vision?		
Not at all	51	82.25
A little	11	17.74
Quite a bit	0	0
Very much	0	0
Did you have difficulty getting or maintaining an erection?		
Missed	10*	16.12
Not at all	6	9.67
A little	12	19.35
Quite a bit	19	30.64
Very much	6	9.67
No	9	14.51

* Female patients.

Discussion

This study aimed at estimating QoL in CRC patients treated with oxaliplatin-based regimen and having peripheral neuritis.

In this cross-sectional study, 62 patients with colorectal cancer treated with oxaliplatin-containing regimen were recruited from the Clinical Oncology Department Ain shams University Hospitals.

Our study revealed that males comprises the majority of our sample with 67.7% with a mean age of 50.13 (±11.15) years. This comes in the line with another study reports where CRC represents 3% in women and 3.47 in men, in Egypt. Additionally, It was reported that Egyptian patients who have CRC below the age of 30 have a threefold increased risk of dying within 5 years compared to those who have CRC over the age of 50, from 75 to 25% *[1]*.

The sensory scale revealed that around 46% of the patients suffered little tingling in the fingers or hands and 21.0% had quite a bit. Almost 42% suffered little tingling toes or feet and 16% suffered quite a bit. Furthermore, 38.7% had little numbness in fingers or hands and 14.5% suffered quite a bit. In 60% of patients had no numbness in toes or feet while 33% had a little numbness. 21.0% had a little shooting or burning pain while almost 13% had quite a bit. Moreover, 19.4% had little problems standing or walking because of difficulty feeling the ground under their feet and 3.2% suffered quite a bit. 17.7% had little difficulty distinguishing between hot and cold water and 12.9% had quite a bit. Regarding hearing problems, almost 98% had no hearing problems.

Similarly, one study detected rapid-onset acute sensory neuropathy associated with multiple doses of oxaliplatin along with a late-onset cumulative sensory neuropathy. In about 75% of patients, neurotoxicity was recoverable with a median time for recovery of 13 weeks following treatment cessation *[10]*. In Attal et al. study, 48 patients had oxaliplatin for different cancer treatment. The study revealed that almost 96% displayed abnormal sensations in the hands following each cycle. These sensations were continuously activated by cold and corresponded to paresthesia, dysesthesia or pain (71% of the patients at Cycle 3. Their intensity and duration augmented after cumulative cycles. Other neurological symptoms in the hands, include electric shocks, burning, or brush- or pressure-evoked pain (<5% of cases after cycle 3 and 6). A small number of the patients had transient sensory symptoms at the face after each cycle, including cold-induced throat dysesthesia (32%), difficulty with swallowing (14%), jaw cramping (10%), or ear/nose dysesthesia (7%) *[11]*. In the same line, another study assessing neurotoxicity revealed that among 20 patients with a median time of 12.6±2.8 months following treatment cessation (mean cumulative oxaliplatin dose, 789mg/m^2), 40% displayed neurotoxicity that required early termination of treatment. Only 10% of patients were chosen by physicians with severe neurotoxicity, whereas, in the contrary, patient self-reporting questionnaires displayed remarkable physical limitations due to neuropathic symptoms in 60% of patients. Around 85% of patients had obvious sensory neuropathy symptoms with nerve conduction *[12]*. Furthermore, comparing oxaliplatin QoL in comparison to fluoropyrimidine, revealed worse QoL scores through all domains, with statistically and clinically significant differences for role and social function, nausea/loss of appetite and financial problems. The mean cumulative oxaliplatin dose used was 567mg/m^2 (55% of intentional dose). Oxaliplatin demonstrated statistically and clinically significant worse sensory and motor scale scores, predominated by symptoms from the feet. Additionally, 37% had severe tingling and 38% had numbness in toes/feet against 8% only who were on fluoropyrimidine alone (p<0.001) *[13]*. Barbosa et al. revealed that patients on oxaliplatin suffered significantly cooler skin temperature in the fingertips before chemotherapy than the healthy controls. The patient pre-treatment warm detection threshold was significantly higher than that detected in healthy volunteers. Nevertheless, warm detection threshold significantly increased from the patient baseline in the 6-month follow-up group *[14]*. Also, around one-fourth of the patients had to stop treatment due to neuropathies. In almost 70% of the patients, neuropathies were chronic even after 22 months of treatment cessation *[15]*. Among 207 patients diagnosed with CRC between 2000 and 2009 assessed using EORTC QLQ-CIPN20 2–11 years after diagnosis, patients who received a cumulative dose of ≥842mg/m^2 had a significantly lesser EORTC

QLQ-CIPN20 sensory score in comparison with those who had lower cumulative doses of <421mg/m^2 (mean 19 vs. 8; p=0.02). They displayed tingling toes/feet (13% vs. 2%, respectively; p=0.01) [16].

Furthermore, in our study, motor scale revealed that patients who suffered "Quite a bit" cramps in their hands were 6.45% while those with cramps in their feet were 16.1%. Also, 19.4% had a little struggle holding a pen and 4.8% had quite a bit struggle holding their hands. In the same line, McHugh et al. revealed that upon assessment of neuropathy in 17 patients on oxaliplatin compared with 105 control, oxaliplatin caused a length-dependent sensory neuropathy. The utmost sensitive early marker of neuropathy was irregular vibration perception threshold in the foot and followed by reduced sensory nerve action potential amplitudes. Vibration perception threshold is feasible and validated marker for neuropathy at low cumulative doses of oxaliplatin [17]. Similar significant association between the increase in channelopathy of axonal sodium and advanced irregularities developed in sensory axons followed by detected neuropathy was revealed by Park et al. study [18]. Correspondingly, Banach et al., revealed that among 32 CRC patients on oxaliplatin treatment, 66.6% displayed neurological symptoms and/or electrophysiologically measured signs of peripheral neuropathy; of those, 33.4% exhibited only electrophysiological changes and the remaining 66.6% showed fully symptomatic peripheral neuropathy [19]. Similar conclusion was revealed by other studies in patients with cumulative doses of oxaliplatin [5,20]. In the contrary, according to Kun Lee et al., study, using oxaliplatin intravenous doe of (85mg/m^2) every two-weeks in the form of FOLFOX revealed no significant changes detected in the overall QoL assessment (EuroQoL-VAS) score through the treatment. Furthermore, sensory and motor neuropathy symptoms evaluated by the EORTC-QoL-CIPN20 did not reveal significant change over time [21].

Finally, the assessment of autonomic function in our study revealed that 47% had a little dizziness when standing up from a sitting or lying position and 7% had quite a bit dizziness. 17.4% had a little blurred vision. Regarding erection function, 30.64 had quite a bit difficulty getting or maintaining an erection while 19.35 had a little difficulty.

Although oxaliplatin-caused erectile dysfunction has not been reported in clinical studies, two in vivo studies has revealed the association between erectile dyfunction and oxaliplatin as a result of decreased neuronal nitric oxide and endothelial NO synthase protein levels in rats [22]. To our knowledge only one clinical study has revelaed negative changes following the administration of oxaliplatin on autonomic function, including erectile dysfunction Dal et al., [23] which contradicts our study findings.

Generally, the EORTC-QLQ questionnaire revealed overall moderate quality of life. One fifth or less suffered problems in role functioning followed by social and emotional functioning. Similarly, about one fifth suffered fatigue then pain suffering was in 10% of study participants.

Of the important finidings upon assessment of quality of life is the somewhat higher summary scores, and functioning scores among those on the lower Oxiplatin dose, the average scores of all fatigue, pain, dyspnea, and other symptoms were higher when prescribed high dose compared to those on low dose of Oxiplatin.

Based on the 15 outcomes generated by the EORTC-QLQ questionnaire, Performance status and female sex predicted poorer overall QoL summary score in colorectal cancer patients, findings that were similar to Daly study EORTC, [9] in the close association between ECOG-PS assessment and QoL impact on colorectal cancer patients.

Conclusion:

The findings of this study highlight the significant impact of oxaliplatin-based chemotherapy on the quality of life (QoL) of colorectal cancer (CRC) patients, particularly due to the onset of oxaliplatin-induced peripheral neuropathy (OIPN). Sensory neuropathy, including tingling, numbness, and burning pain in the extremities, was prevalent among the patients, with many of them reported that these symptoms interfered with their day-to-day activities. The study also showed that some subgroups saw a higher decline in QoL, including women and those with lower performance status. The cumulative dose of oxaliplatin was linked to more severe symptoms, highlighting the necessity of cautious dose management to strike a balance between patient safety and treatment effectiveness. Given these findings, healthcare providers should prioritize monitoring and mitigating these side effects to improve patient outcomes and maintain a better QoL during and after treatment.

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جودة الحياة فى مرضى سرطان القولون والمستقيم الذين يعانون من اعتلال الأعصاب المحيطية الناتج عن عقار أوكساليبلاتين

المقدمـــة: أظهـر أوكسـاليباتين نشـاطاً متواضعـاً فـى المرضـى المصابـين بسـرطان القولـون والمسـتقيم النقيلـى، حيـث حقـق معـدل اسـتجابة يتـراوح بـين ١٠٪ و٢٤٪. يُعـرف OIPN مـع التأثـر الحسـى بتنميـل حـاد عابـر و/أو تنميـل وبسـمة عصبيـة مسـتمرة تراكميـة للمرضـى الذيـن يعانـون مـن أربـع سـنوات إمـا مـن تنميـل محـدود مسـتمر بشـدة متوسـطة (٢,٧٪) أو تنميـل قـد يتداخـل مـع الأنشـطة الوظيفيـة (٠,٧٪).

الهـدف مـن الدراسـة: هدفـت هـذه الدراسـة إلـى تقديـر جـودة الحيـاة لـدى مرضـى سـرطان القولـون والمسـتقيم المعالجـين بنظـام قائـم علـى أوكسـاليباتين والذيـن يعانـون مـن التهـاب الأعصـاب الطرفيـة.

المرضـى وطـرق العـلاج: فـى هـذه الدراسـة المقطعيـة، تم تجنيـد ٦٢ مريضـاً مصابـاً بسـرطان القولـون والمسـتقيم المعالجـين بنظـام يحتـوى علـى أوكسـاليباتين مـن قسـم الأورام السـريرية بمستشـفيات جامعـة عـين شـمس.

النتائـج: أظهـر المقيـاس الحسـى أن حوالـى ٤٦٪ مـن المرضـى عانـوا مـن وخـز بسـيط فـى الأصابـع أو اليديـن و ٢١,٠٪ عانـوا مـن وخـز بسـيط. عانـى مـا يقـرب مـن ٤٢٪ مـن وخـز بسـيط فـى أصابـع القدمـين أو القدمـين و١٦٪ عانـوا مـن وخـز بسـيط. وعـلاوة علـى ذلـك، عانـى ٣٨,٧٪ مـن خـدر بسـيط فـى الأصابـع أو اليديـن و١٤,٥٪ عانـوا مـن خـدر بسـيط. وفـى ٦٠٪ مـن المرضـى لـم يكـن لديهـم خـدر فـى أصابـع القدمـين أو القدمـين بينمـا عانـى ٣٣٪ مـن خـدر بسـيط. وعانـى ٢١,٠٪ مـن ألـم خفيـف أو حـارق بينمـا عانـى مـا يقـرب مـن ١٣٪ مـن خـدر بسـيط. وعـلاوة علـى ذلـك، عانـى ١٩,٤٪ مـن مشـاكل بسـيطة فـى الوقـوب أو المشـى بسـبب صعوبـة الشـعور بـالأرض تحـت أقدامهـم و٣,٢٪ عانـوا مـن خـدر بسـيط. وعانـى ١٧,٧٪ مـن صعوبـة بسـيطة فـى التمييـز بـين المـاء السـاخن والبـارد و١٢,٩٪ عانـوا مـن خـدر بسـيط. وفيمـا يتعلـق بمشـاكل السـمع، لـم يعانـى مـا يقـرب مـن ٩٨٪ مـن مشـاكل السـمع. وأخيـراً، كشـف تقييـم الوظيفـة اللاراديـة فـى درسـتنا أن ٤٧٪ عانـوا مـن دوار بسـيط عنـد الوقـوب مـن وضـع الجلـوس أو الاسـتلقاء و٧٪ عانـوا مـن دوار بسـيط. وعانـى ١٧,٤٪ مـن عـدم وضـوح الرؤيـة. فيمـا يتعلـق بوظيفـة الانتصـاب، واجـه ٣٠,٦٤ صعوبـة كبيـرة فـى الحصـول علـى الانتصـاب أو الحفـاظ عليـه بينمـا واجـه ١٩,٣٥ صعوبـة بسـيطة.

الخلاصـة: مـن النتائـج المهمـة عنـد تقييـم جـودة الحيـاة هـى الدرجـات الإجماليـة الأعلـى إلـى حـد مـا، ودرجـات الأداء بـين أولئـك الذيـن تناولـوا جرعـة أقـل مـن أوكسـيبلاتين، وكانـت الدرجـات المتوسـطة لجميـع التعـب والألـم وضيـق التنفـس والأعـراض الأخـرى أعلـى عنـد وصـف جرعـة عاليـة مقارنـة بأولئـك الذيـن تناولـوا جرعـة منخفضـة مـن أوكسـيبلاتين.