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Correlation Between Chemotherapy-Induced Nausea and Vomiting with Quality of Life in Patients with Ovarian Cancer at Dr. Cipto Mangunkusumo Hospital

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Correlation Between Chemotherapy-Induced Nausea and Vomiting with Quality of Life in Patients with Ovarian Cancer at Dr. Cipto Mangunkusumo Hospital

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Abstract

Introduction: Nausea and vomiting (NV) remain as side effects of chemotherapy, which has a detrimental effect on patients' quality of life (QOL) and treatment adherence. This study aimed to determine the effect of chemotherapy-induced NV (CINV) on the QOL of patients with ovarian cancer treated with chemotherapy at Dr. Cipto Mangunkusumo Hospital (CMH).

Methods: We conducted a cross-sectional study in patients with ovarian cancer receiving first-line chemotherapy regimens of carboplatin and paclitaxel. The European Organisation for Research and Treatment helped translate the Quality-of-Life Questionnaire-OV28 (QLQ-OV28) into Indonesian and tested it in a preliminary study. The approved Indonesian version of the QLQ-OV28, with the Quality-of-Life Questionnaire-C30 (QLQ-C30), was then used to evaluate QOL before and 1 week after chemotherapy.

Results: Several symptom scales increased, whereas function scales decreased. Moreover, 72.5% had an increase in the NV symptom scale, whereas 67.5% had a decrease in patients' scale after chemotherapy. CINV had a significant partial effect on reducing QOL (p = 0.047 and y = 12.208–0.432).

Conclusions: CINV has a significant influence on lowering the QOL of patients with ovarian cancer undergoing first-line chemotherapy regimens with carboplatin and paclitaxel in CMH.

Keywords: chemotherapy, Indonesia, ovarian neoplasms, quality of life

INTRODUCTION

In the 21st century, cancer is expected to be the primary factor responsible for mortality and presents as an essential obstacle to improving life expectancy.[1] In 2018, ovarian cancer was the seventh most common cancer in women, accounting for 295,414 cases (3.4% of all cancer diagnoses in women) and 184,799 deaths (4.4% of all women's cancer-related deaths). Among Southeast Asian countries, Indonesia accounts for approximately 50% of the incidence and mortality.[1] Despite these, various studies have shown a reduction in mortality and morbidity rates and improved quality of life (QOL) due to factors such as the approach of cytoreductive surgery followed by chemotherapy, an increase in the proportion of patients who received definitive treatment, use of less toxic analogs of platinum-based therapy (carboplatin), and adoption of targeted therapy in advanced-stage ovarian cancer.[2] In Dr. Cipto Mangunkusumo Hospital (CMH), 1,062 chemotherapy sessions were performed for patients with ovarian cancer who received adjuvant chemotherapy between November 2018 and November 2019.[3] Chemotherapy uses chemicals or cytotoxic drugs to stop the proliferation of rapidly dividing cells (e.g., cancer cells) to halt its growth and prevent its spread.[4] However, cytotoxic drugs in patients with ovarian cancer, such as carboplatin and paclitaxel, have severe side effects because of their effects on healthy cells, such as blood components, gastrointestinal (GI) mucosa, and hair roots.[3,5] Carboplatin is a cytotoxic drug with hematological side effects in thrombocytopenia (16%) and leukopenia (10%). In addition, it has non-hematological side effects such as nausea and vomiting (NV, 9%) and alopecia (4%). Meanwhile, paclitaxel exerts hematological side effects, such as granulocytopenia (96%), and non-hematological side effects, such as NV (10%).[6]

GI side effects have been a significant problem because chemotherapy is first used to treat cancer.[7] The symptoms of GI toxicity include NV, constipation, diarrhea, abdominal pain, bloating, and weight loss.[8] Approximately 60%–100% of patients on high-dose chemotherapy will experience GI side effects.[8] Abola *et al*.[9]

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emphasized the importance of the GI toxicity effect of chemotherapy by treating 10% of the GI toxicity effect, resulting in an increase in progression-free survival by 3.4% (p = 0.007) but not in overall survival. GI toxicity also affects QOL. Börjeson *et al*.[10] found that the intensity and duration of NV disrupt patients' QOL. The study also revealed that a simple drug such as ondansetron has been proven to reduce the incidence and intensity of acute nausea. Still, it cannot reduce the duration of NV.[10] The side effects of chemotherapy-related NV are known as chemotherapy-induced NV (CINV).[7] CINV can reduce QOL, disrupt treatment schedules, reduce adherence rates, and cause medical complications. Bezjak *et al*.[11] described impaired QOL by CINV using the Quality of Life Questionnaire-C30 (QLQ-C30) issued by the European Organization for Research and Treatment of Cancer (EORTC). The study revealed that the QOL decreased by 9.3 points in the cyclophosphamide plus cisplatin (CP) group and 9.8 points in the paclitaxel plus cisplatin (TP) group since the first cycle along with the highest increase in the incidence of NV from the baseline compared with subsequent cycles (24.8 points for the CP group and 22.4 points for the TP group). Haiderali *et al*.[12] used the Functional Living Index-emesis and found that 37.2% of patients reported a reduction in daily functioning and 90% of those with inadequate CINV management reported a significant reduction in daily functioning.

The EORTC QLQ-C30, a widely utilized questionnaire for assessing the QOL of patients with cancer, examines functional domains (such as physical, emotional, and role functioning) and cancer-related symptoms (including NV, pain, and fatigue).[13] The EORTC QLQ-OV28 is designed to complement the QLQ-C30 as an additional module to increase the sensitivity of the health-related QOL assessment for patients with ovarian cancer.[14] The QLQ-C30 has been validated in Indonesian.[15] However, the QLQ-OV28 has not been validated in Indonesian.

Although newer antiemetic drugs are available, CMH continues to administer basic antiemetics such as ondansetron, ranitidine, dexamethasone, and diphenhydramine since the inception of its chemotherapy services for ovarian cancer. This protocol persists owing to the limited drug options covered by the Indonesian Social Security Agency. Currently, data on the QOL of patients with ovarian cancer receiving adjuvant chemotherapy and those experiencing CINV in CMH and across Indonesia are insufficient. Consequently, evaluating and comparing these protocols with others is challenging. Thus, this study aimed to assess the effect of CINV on the QOL of patients with ovarian cancer undergoing chemotherapy at CMH and validate the Indonesian version of the EORTC QLQ-OV28.

METHODS

Ethical approval

The ethical approval to conduct this study was obtained from the Faculty of Medicine, Universitas Indonesia Health Research Ethics Committee (4428.UN2.F1/ETIK/PPM.00.02/2021).

Development of the Indonesian version of QLQ-OV28

The translation of the QLQ-OV28 took place from February to April 2021, which consisted of its translation from English to Indonesian and pilot testing.

The translation process for the new language version of the EORTC QLQ-OV28 began with an application to the EORTC Translation Unit (TU) in Belgium. The TU confirmed that no questionnaires existed or is being developed and prepared a translation package. Two native speakers of the target language translated the English version, and a reconciled translation was created. The EORTC reviewed and combined the translations for accuracy.[16]

Two native speakers translated the English questionnaire into Indonesian, and a reconciled translation was created from these versions. The EORTC reviewed and combined the translations for the best version based on accuracy and wording. Then, two translators with excellent English skills retranslated the reconciled version into English. All processes (forward translation, reconciliation, and backward translation) were reported to the TU, including comments on the reconciliation.[16]

The report was reviewed, issues resolved, and the initial translation was proofread by an external proofreader. All suggestions were discussed until a consensus was reached. Then, the translated version was subjected to linguistic validation through pilot testing, in which the translated EORTC OV-28 questionnaire was tested on 10 patients, who provided feedback on their understanding. All comments were summarized in a pilot testing report submitted to the TU. The TU then finalized the translation and closed the process.[16] The characteristics of the phase 1 sample are provided in Supplementary Table 1. The preliminary study indicated that items related to "sex activity," "passing gas," and "weakness in arms and legs" needed adjustments. These issues were resolved in the post-study discussion. In accordance with the EORTC translation protocol, a retest was not conducted because the post-study discussion resulted in unanimous understanding among all 10 patients.

Implementation of questionnaire

Data collection, data analysis, and statistical analysis were conducted from May to November 2021. Data were collected on the Indonesian EORTC OV-28 questionnaire from 40 patients with ovarian cancer before chemotherapy, excluding the 10 patients in the pilot test. Patients with ovarian cancer undergoing first-line

SUPPLEMENTARY TABLE 1. Phase 1 sample characteristics (N = 10)

Characteristics	N (%)
Age, mean (SD) years	49.9 (9.02)
Stage	
Early (1-II), n (%)	3 (30)
Advanced (III-IV), n (%)	7 (70)
History of surgery	
No history of surgery	1 (10)
Undergone surgery once	6 (60)
Undergone surgery twice	3 (30)
Undergone surgery more than two times	0 (0)
Performance Status (ECOG)	
0	10 (100)
1	0 (0)
2	0 (0)
3	0 (0)
Occupation	
Homemaker	7 (70)
Private employee	2 (20)
Researcher	1 (10)
Metastasis	
to upper gastrointestinal tract	0 (0)
to lungs	0 (0)
to brain	0 (0)
History of nausea and vomiting	
Yes	0 (0)
No	10 (100)

carboplatin and paclitaxel chemotherapy at CMH were included. Patients with chronic diseases, mental illness, psychotropic medication, and previously treated GI disease were included. A thorough history, physical examination, and laboratory tests ensured criteria fulfillment. The Indonesian version of the QLQ-C30[15] and QLQ-OV28 were completed before and 1 week after chemotherapy during control visits at the Gynaecologic Oncology Clinic.

The questionnaires were collected, and raw scores (RS) and scale scores (S) were calculated using EORTC QLQ-C30 and QLQ-OV28 formulas, values before and after chemotherapy were compared. The RS, an average of each item contributing to the scale, was calculated first. This RS was then used in the linear transformation of the functional scale, item scale/symptoms, and global health status/QOL. These calculations were performed to descriptively analyze function, symptom, and QOL scales.

RS was calculated with the following formula:

$$\text{Raw score} = RS = (I1 + I2 + I3 + .In)/n \quad (1)$$

I = value for each question item; n = number of question items.

The second stage involved linear transformation of the functional scale, item/symptom scale, and global health status/QOL. It was standardized for hospitals; thus, the scale score range ranged from 0 to 100. The three equations used for each scale are as follows.

Scoring system for the EORTC QLQ-C30:

Raw score

$$RS = \left\{\frac{(I_1 + I_2 + \ldots + I_n)}{n}\right\} \quad (2)$$

Linear transformation

Functional scales:

$$S = \left\{1 - \frac{(RS - 1)}{range}\right\} \times 100 \quad (3)$$

Symptom scale/items:

$$S = \left\{\frac{(RS - 1)}{range}\right\} \times 100 \quad (4)$$

Global health status/QOL:

$$S = \left\{\frac{(RS - 1)}{range}\right\} \times 100 \quad (5)$$

Scoring system at the EORTC QLQ-OV28:

Raw score

$$RS = \left\{\frac{(I_1 + I_2 + \ldots + I_n)}{n}\right\} \quad (6)$$

Linear transformation

Symptom scale/items:

$$S = \left\{\frac{(RS - 1)}{range}\right\} \times 100 \quad (7)$$

Statistical analysis

Statistical validity and reliability tests of the Indonesian version of the EORTC QLQ-OV28 filled before chemotherapy were performed using Pearson's and Cronbach's alpha. The questionnaire results were also analyzed using a simple linear regression test on all symptom and functional scales. A simple linear regression test for bivariate analysis was performed, followed by multivariate analysis using a multiple regression test. Statistical analysis was performed using IBM SPSS Statistics for Windows version 24.0. If the regression significance value is <0.05 and the t-count value >t-table (0.026), a significant relationship exists between the variables and QOL. The sample set for validity and reliability tests will be the same for the bivariate and multivariate analyses.

RESULTS

Sample characteristics

Between May and November 2021, 40 patient responses were received. The questionnaires were self-administered with a 100% response rate. Patients were free to ask questions if they did not understand. Moreover, 97.5% of the patients had an educational background, with the majority having graduated from senior high school (47.5%, N = 19), and one patient (2.5%) had no educational background but was literate. Most patients (85%, N = 34) have undergone at least one surgery for the primary treatment of ovarian cancer, whereas no patients underwent more than two surgeries, and 87.5% (N = 35) had an Eastern Cooperative Oncology Group (ECOG) status of 0, which indicated that most patients were fully active and could perform all activities before disease without restriction. An ECOG status of 1 (7.5%, N = 3) indicates the inability to perform strenuous activities but is still ambulatory, whereas an ECOG status of 2 (5%, N = 2) indicates that the patient is capable of self-care and ambulation but is incapable of performing any work activities.[17] No patients had an ECOG status >2. GI metastases were found in 10% (N = 4) of the cases, and a history of NV was found in 52.5% (N = 21). The characteristics of the phase 2 sample are shown in Table 1.

TABLE 1. Phase 2 sample characteristics (N = 40)

Characteristics	N (%)
Age, mean ± SD years	50 ±11
Stage	
Early (1–II)	5 (12.5)
Advanced (III–IV)	35 (87.5)
History of surgery	
No history of surgery	6 (15.0)
Undergone surgery once	27 (67.5)
Undergone surgery twice	7 (17.5)
Undergone surgery more than two times	0 (0)
Performance status (ECOG)	
0	35 (87.5)
1	3 (7.5)
2	2 (5)
3	0 (0)
Occupation	
Homemaker	25 (62.8)
Private employee	7 (17.5)
Pharmacist	1 (2.5)
Nurse	1 (2.5)
Retiree	4 (10.0)
Teacher	2 (5.0)
Metastasis	
to the upper gastrointestinal tract	4 (10.0)
to the lungs	5 (12.5)
to the brain	0 (0)
History of nausea and vomiting	
Yes	21 (52.5)
No	19 (48.5)

Validity and reliability test

For the 28 questions and answers of the EORTC QLQ-OV28 before chemotherapy, statistical validity and reliability tests were performed using Pearson's and Cronbach's alpha tests. Of the 28 questions, 25 were valid ($p < 0.05$ and R count > R table), whereas three questions (question nos. 38, 57, and 58 about symptoms of hair loss and sexual activity) were not valid ($p > 0$, 05 and R count < R table). This may be due to the small number of participants in this validity test, and 65.5% of the patients with ovarian cancer were not sexually active. Based on brief interviews, this occurred because of feelings of fear in 28% (N = 7), 24% were not interested in sex because of age factor (N = 6), and 48% were not married/divorced (N = 12). The results of the validity test are shown in Table 2. Good consistency was obtained with Cronbach's alpha of 0.881.

Results of EORTC QLQ C-30 and OV28

Tables 3 and 4 compare the symptom scale, function scale, and QOL before and after chemotherapy using the EORTC QLQ-C30 and EORTC QLQ-OV28. The GI symptom scale has the largest proportion (80%), followed by the NV symptom scale (72.5%). The largest proportion of changes in patients' QOL after chemotherapy is a decrease in QOL by 68%.

Bivariate and multivariate analysis

The results of a simple linear regression test between function and symptom scales on QOL are presented in Table 5. Based on Table 5, all symptom and function scales on the EORTC QLQ-C30 and EORTC QLQ-OV28 demonstrated a significant effect on QOL, except for symptoms of dyspnea, social function, symptoms of peripheral neuropathy, and sexual symptoms.

The relationship between CINV and QOL is significant based on a simple linear regression test ($p < 0.0001$, R square = 0.382 and y = 11.492–0.703x) and multiple linear regression test ($p < 0.047$ and y = 12.208–0.432). Because all symptom and function scales were significantly related with QOL, we determined which relationship partially affected QOL ($p < 0.05$). The partial relationship between the symptom and function scales on QOL is provided in Table 6. As shown in Table 6, NV, other chemotherapy side effects, and hormonal/menopausal symptoms have a significant partial effect on the QOL of the patients.

DISCUSSION

The cytotoxic effect of chemotherapy agents is caused by the stimulation of enteroendocrine cells in the GI mucosa that releases prostaglandins, 5-hydroxytryptamine (5-HT), cholecystokinin, and substance P, stimulating the vagal afferents to trigger emesis.[18] Antiemetics are used prophylactically to reduce the duration of NV.[10] In this study, patients were given 20 mg dexamethasone, 8 mg

ondansetron, and 150 mg ranitidine intravenously during chemotherapy, followed by 3 x 8 mg ondansetron and 2 x 150 mg ranitidine orally after chemotherapy session and returning home. Based on the results, 17.5% (N = 7) of the patients did not experience NV after chemotherapy. However, most patients (72.5%, N = 29) still experienced NV despite having been given prophylaxis.

Newer antiemetics, such as second-generation 5-HT3 receptor antagonists, D2/3 receptor antagonists, and NK-1 receptor antagonists, have shown advantages over existing antiemetic options and should be considered CINV prophylaxis.[19] Ondansetron, as a 5-HT3 receptor antagonist, was an effective antiemetic in patients receiving a cisplatin-based regimen and further

TABLE 2. Validity of EORTC QLQ-OV28

Item number	R Value	R table 5%	*p*	Criteria
31 - Abdominal pain	0.666	0.312	0.000	Valid
32 - Feeling bloated	0.615	0.312	0.000	Valid
33 - Clothes feeling tight	0.326	0.312	0.040	Valid
34 - Change in bowel habits	0.400	0.312	0.011	Valid
35 - Trouble with flatulence	0.579	0.312	0.000	Valid
36 - Feeling full too quickly	0.449	0.312	0.004	Valid
37 - Indigestion/heartburn	0.597	0.312	0.000	Valid
38 - Hair loss	0.292	0.312	0.067	Not yet valid
39 - Upset with hair loss	0.600	0.312	0.000	Valid
40 - Taste change	0.606	0.312	0.000	Valid
41 - Tingling hands or feet	0.459	0.312	0.003	Valid
42 - Finger or toe numbness	0.352	0.312	0.026	Valid
43 - Arms or legs weakness	0.524	0.312	0.001	Valid
44 - Muscle or joint aches/pains	0.536	0.312	0.000	Valid
45 - Hearing problem	0.429	0.312	0.006	Valid
46 - Frequent urination	0.431	0.312	0.005	Valid
47 - Skin problem	0.506	0.312	0.001	Valid
48 - Hot flushes	0.470	0.312	0.002	Valid
49 - Night sweats	0.398	0.312	0.011	Valid
50 - Physically feel less attractive	0.643	0.312	0.000	Valid
51 - Dissatisfied with body	0.415	0.312	0.008	Valid
52 - Disease burden	0.469	0.312	0.002	Valid
53 - Treatment burden	0.594	0.312	0.000	Valid
54 - Worry about future health	0.667	0.312	0.000	Valid
55 - Interest in sex	0.387	0.312	0.014	Valid
56 - Sexual activity	0.344	0.312	0.030	Valid
57 - Enjoyment of sex	0.264	0.312	0.100	Not yet valid
58 - Vagina	0.237	0.312	0.142	Not yet valid

TABLE 3. Comparison of the symptom scale, functional scale, and quality of life before and after chemotherapy using EORTC QLQ C-30

Item	No changes, N (%)	Scale degression, N (%)	Scale up, N (%)
Quality of life	10 (25.0)	27 (67.5)	3 (7.5)
Physical functioning	9 (22.5)	22 (55.0)	9 (22.5)
Role functioning	12 (30.0)	20 (50.0)	7 (17.5)
Emotional functioning	11 (27.5)	17 (42.5)	12 (30.0)
Cognitive functioning	17 (42.5)	15 (37.5)	8 (20.0)
Social functioning	15 (37.5)	20 (50.0)	5 (12.5)
Fatigue	4 (10.0)	9 (22.5)	27 (67.5)
Nausea and vomiting	7 (17.5)	4 (10.0)	29 (72.5)
Pain	10 (25.0)	7 (17.5)	23 (57.5)
Dyspnea	25 (62.5)	6 (15.0)	9 (22.5)
Insomnia	19 (47.5)	7 (17.5)	14 (35.0)
Appetite loss	11 (27.5)	6 (15.0)	23 (57.5)
Constipation	21 (52.5)	7 (17.5)	12 (30.0)
Diarrhea	25 (62.5)	6 (15.0)	9 (22.5)
Financial difficulties	20 (50.0)	7 (17.5)	13 (32.5)

TABLE 4. Results of EORTC QLQ-OV28

Item	No changes, N (%)	Scale degression, N (%)	Scale up, N (%)
Gastrointestinal	2 (5.0)	6 (15.0)	32 (80.0)
Peripheral neuropathy	9 (22.5)	7 (17.5)	24 (60.0)
Chemotherapy side effects	4 (10.0)	11 (27.5)	25 (62.5)
Hormonal	13 (32.5)	13 (32.5)	14 (35.0)
Body image	13 (32.5)	11 (27.5)	16 (40.0)
Attitude to disease/treatment	8 (20.0)	14 (35.0)	18 (45.0)
Sexuality	20 (50.0)	17 (42.5)	3 (7.5)

TABLE 5. Correlation between symptom scales and functional scales with the quality of life

Functional/symptom scales with QOL	T	*p*	R square
Fatigue	5.185	<0.001**	0.414
Nausea and vomiting	4.845	<0.001**	0.382
Pain	4.015	<0.001**	0.298
Dyspnea	1.337	0.189	0.045
Insomnia	3.878	<0.001**	0.284
Appetite loss	4.327	<0.001**	0.330
Constipation	2.494	0.017*	0.141
Diarrhea	2.047	0.048	0.099
Financial difficulties	3.273	0.002*	0.220
Physical functioning	2.762	0.009*	0.167
Role functioning	4.779	<0.001**	0.375
Emotional functioning	2.931	0.006*	0.184
Cognitive functioning	0.971	0.005*	0.188
Social functioning	1.633	0.111	0.066
Abdominal/GI symptoms	6.310	<0.001**	0.512
Peripheral neuropathy	1.602	0.117	0.063
Other chemotherapy side effects	2.441	0.019*	0.136
Hormonal/menopausal symptoms	3.104	0.004*	0.202
Body image	4.033	<0.001**	0.300
Attitude to disease/treatment	3.887	<0.001**	0.284
Sexuality	0.440	0.662	0.050

*$p < 0.05$; **$p < 0.001$

TABLE 6. Multivariate analysis of the symptom and function scales of EORTC QLQ-C30 and OV28

Functional/symptom scales with QOL	T	*p*
Physical functioning	1.805	0.085
Role functioning	0.057	0.955
Emotional functioning	1.560	0.133
Cognitive functioning	−1.348	0.191
Fatigue	−0.091	0.928
Nausea and vomiting	−2.100	0.047*
Pain	−0.227	0.823
Insomnia	−0.456	0.653
Appetite loss	−0.787	0.440
Constipation	−0.315	0.756
Diarrhea	−0.906	0.375
Financial difficulties	−0.951	0.352
Abdominal/GI symptoms	−1.878	0.074
Other chemotherapy side effects	2.734	0.012*
Hormonal/ menopausal symptoms	−2.358	0.028*
Body image	−1.034	0.312
Attitude to disease/treatment	−0.505	0.618

*$p < 0.05$, **$p < 0.001$

demonstrated that ondansetron was superior to metoclopramide in patients receiving both cisplatin and non-cisplatin regimens. These agents are believed to prevent CINV as a 5-HT3 receptor antagonist through the peripheral of the vagal nerve terminals and the center of the chemoreceptor trigger zone. Since its introduction, the 5-HT receptor antagonist has become part of the foundation for preventing CINV because of its effectiveness and well-tolerated side effects.[20]

Corticosteroids are beneficial when used alone to prevent NV in patients receiving low emetogenic chemotherapy and increase efficacy when combined with 5-HT3 receptor antagonists in those receiving moderate or high-emetogenicity chemotherapy. The latest guidelines recommend dexamethasone, although no studies have compared available corticosteroids. Tolerability to corticosteroids is of concern because when used to prevent delayed-type NV, common side effects include insomnia, epigastric discomfort, agitation, weight gain, and hyperglycemia.[20]

QOL is a multidimensional construct that includes physical functioning, which comprises physical well-being, mobility, ability to care for oneself, physical activity, self-activity, appetite, fatigue/sleep, and side effect symptoms; cognitive and psychological functioning, which covers emotional well-being, anxiety, depression, coping, perceptions, experiences, enjoyment, and optimism; social functioning, which comprises family interactions, time with friends, and leisure activities; symptoms of illness and treatment; spiritual or existential problems; sexual function; patient satisfaction with healthcare; and disease control.

Many instruments have been developed and validated to measure QOL issues in patients with cancer, the most commonly used instruments are the EORTC QLQ-C30 and the Functional Assessment of Cancer Therapy – General.[10] Ovarian cancer and its management significantly affect the overall QOL. Issues such as disease burden and long-term treatment effects also influence the quality of care for these patients. Modern ovarian cancer treatments increasingly aim to enhance QOL alongside survival rates and acceptable toxicity levels. To address these concerns, the EORTC QLQ-OV28 was created to complement the EORTC QLQ-C30, ensuring comprehensive assessment and documentation of ovarian cancer-specific disease and management issues. To our knowledge, this is the first study to utilize the EORTC QLQ-OV28 in Indonesian.[10]

EORTC QLQ-C30 and OV28 were used to assess patients' QOL, NV, and GI symptoms, followed by a linear regression analysis. The resulting scales were interpreted with a score range of 0–100. For the QLQ-C30, a high score on the functional scale indicates a high level of functioning, and a high score on the global health status indicates a high QOL. However, the higher the symptom scale, the more severe the symptoms.[21] For the QLQ-OV28, each symptom scale is scored separately, with each scale consisting of several or a single item. A higher score on the symptom scale indicates a severe symptom. A higher score for the functional scale, such as body image and sexual function, means a higher QOL.[10,22] Based on the results of this study, after the first-line chemotherapy regimen of carboplatin and paclitaxel, patients experienced an increase in CINV symptoms by 72.5%, an increase in GI symptoms by 80%, and a decrease in QOL by 62.5%.

The regression test on NV symptoms and QOL showed a significant effect between NV symptoms and QOL, where the regression equation for the effect of NV on QOL was 11.492–0.703x, which means that if the symptoms of NV increased by one unit, the patient's QOL after chemotherapy decreased by 0.703 units. The contribution of the NV scale in reducing the patient's QOL was 38.2% (R square = 0.382). The regression test results on symptoms and functions found in the EORTC QOL-C30 and EORTC QOL-OV28 showed that NV still affected patients' QOL after chemotherapy.

The impaired QOL by CINV, described by Bezjak *et al*.[11] using the EORTC QLQ-C30 questionnaire, decreased in patients receiving chemotherapy since the first cycle started. These results are consistent with the present study, which showed that CINV developed in 72.5% of the patients who received the first chemotherapy. Based on the multivariate test results, only the variables of NV, other chemotherapy side effects, and hormonal/menopausal symptoms demonstrated a significant partial effect on patients' QOL. These results are consistent with a study conducted by Börjeson *et al*.,[10] who studied 162 patients with ovarian cancer receiving combination chemotherapy, including cisplatin 50 mg/m^2. This study showed that NV significantly decreased the physical condition and QOL of patients, even with the administration of prophylactic antiemetics (ondansetron, dexamethasone, and metoclopramide).

Based on these results, the scale scores of GI symptoms increased (80%), which is greater than the CINV symptom scale (72.5%) and the QOL symptom reduction score (67.5%). Meanwhile, multivariate test results showed that the CINV symptom scale significantly reduced QOL, whereas GI symptoms did not. This can occur, considering other variables such as physical function, role function, emotional function, cognitive function, fatigue symptoms, pain, insomnia, decreased appetite, constipation, diarrhea, financial difficulties, other side effects of chemotherapy, hormonal/menopausal symptoms, body image, attitude toward disease/treatment, which affect the QOL as well, causing GI symptoms to have less effect in the multivariate analysis. Despite this, the QLQ-OV28 module is still necessary when evaluating the QOL of patients with ovarian cancer because it assesses a unique

set of QOL domains that are not covered by the QLQ-C30. A validation study of the QLQ-OV28 by Paradowski *et al*.[23] showed that the scales of the QLQ-OV28 demonstrated weak correlation with the scales of the QLQ-C30 (r < 0.3). The discrepancy between the CINV and GI scales can be explained by both scales assessing different symptom domains, with the GI scale evaluating abdominal pain, bloating, tightness of clothing, change in bowel habits, flatulence, and heartburn.

In this study, financial difficulty significantly affected QOL. A study of 3,670 patients with cancer by Perrone *et al*. using the EORTC QLQ-C30 revealed that patients who reported financial difficulties had worse QOL at baseline. During treatment, 74.5% of the patients who developed financial toxicity had significantly higher risk of death (HR 1.20, 95% CI 1.05–1.37, p = 0.007).[24] Although not objectively evaluated in the present study, financial difficulties in patients with cancer may have been caused by changes in their capability to work and unemployment caused by disease or treatment.[25]

In this study, sexuality was found not to have significantly affected QOL. Kim *et al*.[25] and Chie *et al*.[26] reported similar results. Sexual function may be impaired because of decreased estrogen and androgen production, increased fatigue, psychological factors such as depression and anxiety, and abdominal scarring due to surgery. This discrepancy may have been caused by not separating patients by early-stage and advanced-stage disease. Second, the culture in Indonesia, whether a serious disease affects the tendency to conduct sexual activity, was not thoroughly explored. Chie *et al*.[26] mentioned the possibility that unaffected sexual activity might have been caused by the discouragement of sexual activity during or after a serious disease.

Ovarian cancer management aims to increase survival and enhance overall QOL. Evaluating patients' QOL at various treatment stages has been crucial in refining treatment strategies. To address the needs of the Indonesian population, the EORTC QLQ-OV28 tool was translated into Indonesian. Our version is reliable and valid for assessing the QOL of patients with ovarian cancer and can be used in clinical or epidemiological studies involving Indonesian-speaking patients.

Although this study provides valuable insights into the effect of CIMV on QOL, several limitations should be acknowledged. First, the self-reporting nature of questionnaires introduced the potential for response and recall bias. Second, the questionnaire format may be prohibitive to obtain deeper information than a qualitative study. A qualitative study may provide data based on participants' perspectives and interpretations, which might otherwise have been missed in a quantitative study.

CONCLUSIONS

This study provides an Indonesian version of the EORTC QLQ-OV-28. The QLQ-C30 and QLQ-OV28 as a complementary module can be used as measuring tools to evaluate the QOL of patients with ovarian cancer. In conclusion, the presence of CINV can reduce the QOL of patients with ovarian cancer undergoing first-line chemotherapy containing carboplatin and paclitaxel (p < 0.047 and y = 12.208–0.432).

CONFLICT OF INTEREST

The authors hereby declare that there is no conflict of interest.

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