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Prevalence of Depression, Anxiety and Suicidal Ideation in Patients with Ovarian Cancer: Trend Analysis from 1977 to 2022

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Abstract

Objective: We planned to estimate the epidemiological data on mental disorders in patients with ovarian cancer.

Method: We searched PubMed, Embase, Elsevier ScienceDirect, China National Knowledge Infrastructure, Wanfang Data Knowledge Service Platform, and Duxiu Academic Search Platform to determine observational studies on depression, anxiety, and suicidal ideation in patients with ovarian cancer published before December 31st, 2023, and estimated the prevalence of mental disorder in patients with ovarian cancer worldwide and estimated the combined prevalence of different regions, countries, research periods, and assessment scales.

Results: This research included 31 studies involving 8,315 patients with ovarian cancer. The prevalence of depression and anxiety in patients with ovarian cancer was 35% (95% CI: 25%-45%) and 37% (95% CI: 27%-48%), respectively. The suicidal ideation of patients with ovarian cancer was 32% (95% CI: 28%-35%) in China. Patients with ovarian cancer in Asia had the highest prevalence of depression, while those in Oceania had the lowest. The prevalence of depression and anxiety in patients with ovarian cancer increased significantly after 2000 worldwide and gradually stabilized. The prevalence of psychiatric disorders was significantly higher with the use of self-report tools than with diagnostic tools.

Conclusion: These findings estimated the prevalence of comorbid mental disorders in patients with ovarian cancer, increasing the awareness of doctors and patients about the ovarian cancer-related mental problems.

Keywords: Ovarian cancer; Epidemiology; Depression; Anxiety; Suicidal ideation

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Introduction

Ovarian cancer is one of the most common malignant tumors of the female reproductive system, with the second-highest mortality rate among gynecological malignant tumors [1]. In 2020, approximately 19,880 new cases of ovarian cancer have been reported in the United States [2]. Despite standardized treatment, women with ovarian cancer have a poor prognosis due to a low rate of early diagnosis. The risk of mental illness in cancer survivors is significantly higher than in healthy people, and it is often underestimated [3]. Compared to general cancer patients, patients with ovarian cancer must also deal with loss of fertility, sexual dysfunction, concerns about female offspring inheritance, fewer treatment options, and worse prognosis, resulting in higher levels of mental distress. Previous studies have observed that 46% of patients with ovarian cancer have moderate to severe psychological distress [4], and psychological disorders, such as depression and anxiety, can increase the risk of poor prognosis of ovarian cancer [5]. Therefore, it is of great clinical and social value to improve our understanding of mental health complications in patients with ovarian cancer. A meta-analysis of 3,626 patients with ovarian cancer, published in 2015, revealed that women with ovarian cancer had significantly higher rates of depression and anxiety than healthy women [6]. There is currently no high-quality, evidence-based medical research or large-scale observational study that analyzes the prevalence of mental disorders in patients with ovarian cancer worldwide. Therefore, we aimed to analyze the epidemiology of depression, anxiety, and

suicidal ideations in patients with ovarian cancer while focusing on three types of mental health disorders.

Methods

This study was conducted according to the PRISMA [7] and epidemiological observational study (MOOSE) [8] guidelines and was registered in the PROSPERO database (ID: CRD42023490509).

Literature search strategy

As of December 31st, 2023, we comprehensively searched PubMed, Embase, Elsevier ScienceDirect, China National Knowledge Infrastructure, the Wanfang Data Knowledge Service Platform, and the Duxiu Academic Search Platform. And as far as possible from the references of the included studies and clinical research registration website to find relevant research. Two research investigators (TZ and YRW) independently reviewed the titles and abstracts of the studies identified in the search to exclude those that did not meet the criteria. They also reviewed the full and supplementary texts of the remaining studies to determine whether they contained relevant information. At this stage, conflicts in research selection were resolved by consulting the original articles and senior researchers (WHL). Supplementary materials 1 illustrates the search strategy.

The inclusion criteria were as follows: (a) patients with a pathological diagnosis of malignant ovarian cancer (including fallopian tube cancer and female peritoneal cancer, as they have similar morphology and behavior to ovarian cancer), with a focus on the prevalence of depression, anxiety, and suicidal ideation. (b) observational studies, including cohort studies, case-control studies, cross-sectional studies, computer-based joint analysis experiments, real-world studies, and retrospective studies. (c) studies using the International Classification of Diseases, Hamilton Anxiety and Depression Scale, Patient Health Questionnaire-9, and other scales as diagnostic criteria. The scales selected in the included studies were all well-established versions and the classification of the same scale is roughly similar. This study observed the number of ovarian cancer patients with depression, anxiety, and suicidal ideations, i.e., as long as the scores were outside the normal range, they were considered to have depression, anxiety, and suicidal ideations. For example, according to the Hamilton Depression Scale, patients with scores ≥ 8 considered 'may be cases' can be included in the study. (d) research reports published in Chinese and/or English.

The exclusion criteria were as follows: (a) studies with incomplete or unavailable data. (b) repetitively published studies. (c) non-observational and/or non-clinical studies.

Data extraction and quality assessment

For each eligible study, the following variables were independently extracted by two researchers (TZ and YRW): First author, publication year, study period, region, recruitment methods, subject age, pathological type and stage of ovarian cancer, treatment, rating scale, type of mental health disease, cut-off value of the scale, number of cases of ovarian cancer combined with mental health disease, and prevalence. Two authors independently completed this process. If any differences were present, the original literature was reviewed and discussed until the results remained unchanged. If multiple publications of the same trial were identified, the publication with the most complete data was included. For studies with longer follow-up time, the data at the first observation time point after diagnosis were selected because the data were the least missing at this time.

Two researchers (TZ and YRW) evaluated the quality of the included studies. For cross-sectional studies, the Health Care Research and Quality Agency (AHRQ) tool was used to assess the risk of bias. The Newcastle-Ottawa Scale (NOS) was used to evaluate the case-control and cohort studies [9]. Each study was assigned a separate specific score based on the following scale: 0 to 3 for low quality, 4 to 7 for medium quality, and 8 to 11 for high quality. Cohen's Kappa statistical coefficient was used to evaluate the consistency of the quality evaluation results. When the Kappa value exceeded 0.6, consistency was strong. Otherwise, it was considered that the two quality evaluations were quite different, which could be resolved by consulting senior researchers (WHL), retraining, re-evaluation, and other methods.

Statistical analysis

The inconsistency index (I^2) was used to evaluate the heterogeneity between study-specific estimates, with a cut-off value of <30%, 30% to 59%, 60% to 75% and >75% representing low, medium, high, and considerable heterogeneity, respectively. Egger's linear test was used to assess publication bias. $P<0.05$ was considered as significant bias, needing further correction using the trimmed method. Depending on the inevitable differences between observational studies, all included studies used a random-effects model. The combined prevalence and 95% Confidence Interval (CI) were calculated using the inverse and Freeman-Tukey Double arcsine Transformation (PFT) methods. All statistical analyses were performed using R software (version 4.3.2).

Results

Characteristics of the included studies

A total of 1,921 studies were identified. After deleting duplicates, the titles and abstracts of the remaining 956 studies were screened. After reviewing 219 studies in the full text, 188 were deleted due to unclear diagnostic criteria, outcome indicators, study type, and incomplete data. Finally, this meta-analysis included 31 studies involving 8,315 patients with ovarian cancer (Figure 1) [10-39].

Among the 31 studies, 29 studies observed the prevalence rate of depression [10,11,13-38], 19 studies observed the prevalence rate of anxiety [13-17,20-29,32,33,36,37,40], and 2 studies reported the prevalence of suicidal ideation in patients with ovarian cancer [12,39]. One study recruited patients through the internet [28], and 1 case-control study was based on the statewide SEER Utah Cancer Registry [23], the rest were mostly recruited patients through the inpatient department or outpatient department. Specific information can be seen in Supplementary materials 2.

Study quality

The included studies were of various quality: two low-quality studies [33,38], seven high-quality studies [10,16,23,24,26,27,37], and twenty-two moderate-quality studies. Supplementary materials 3 presents the details of the quality evaluation.

Outcomes

Prevalence: Depression: The total prevalence of depression was 35% (95% CI: 25%-45%) in patients with ovarian cancer (Figure S1). We conducted a subgroup analysis of the prevalence of ovarian cancer, examining the relationship between depression and ovarian cancer in various regions, countries, research stages and evaluation scales (Table 1). The research stages were grouped before 2000, 2000-2009, 2010-2019, and after 2019. If a study's observation time spans multiple groups, it is judged to be a partition with more than 70%

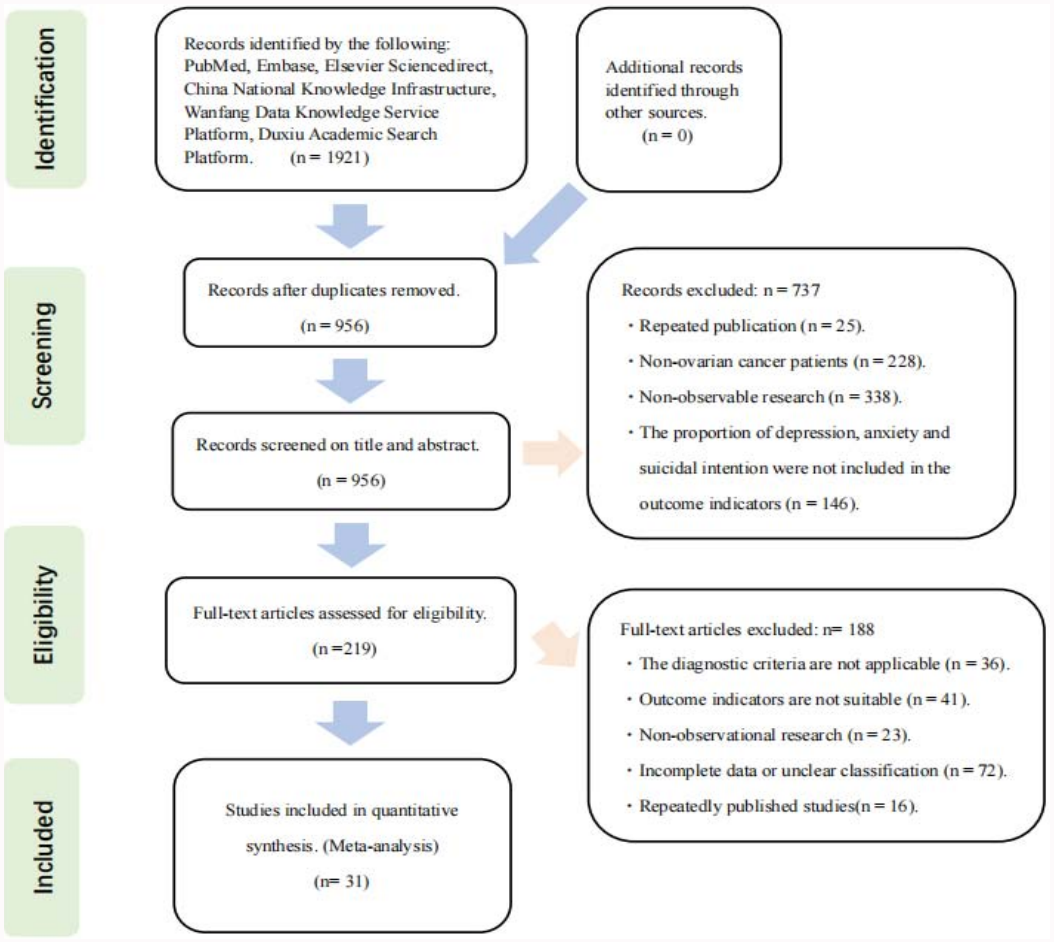

Figure 1: Flowchart of search strategy.

observation time, otherwise it is considered unclear.

The prevalence of depression in patients with ovarian cancer has been studied across different continents (Figure S2): 13 studies in Asia revealed a combined prevalence of 45% (95% CI: 28%-62%); 3 studies in Oceania had a combined prevalence of 10% (95% CI: 4%-16%); 8 studies in North America had the combined prevalence of 33% (95% CI: 20%-47%); 6 studies in Europe had combined prevalence of 31% (95% CI: 13%-52%).

The prevalence of depression among patients with ovarian cancer was calculated for each country (Figure S3): 10 studies in China had a combined prevalence of 51% (95% CI: 33%-69%); 3 studies in Australia had a combined prevalence of 10% (95% CI: 4%-16%); 7 studies in the United States had combined prevalence of 33% (95% CI: 20%-47%); in UK, the combined prevalence was 31% (95% CI: 25%-48%). Some countries had only 1 study that met the inclusion criteria and could not be combined for analysis. According to their respective research results, the prevalence of depression in patients with ovarian cancer was 4% (95% CI: 0%-12%) in Thailand, 18% (95% CI: 14%-22%) in France, 10% (95% CI: 6%-15%) in Norway, 21% (95% CI: 13%-30%) in Poland, 83% (95% CI: 65%-94%) in the Czech Republic, 22% (95% CI: 20%-23%) in South Korea, and 56% (95% CI: 44%-68%) in Japan (Figure 2).

The prevalence of depression in patients with ovarian cancer was observed during different time periods (Figure S4): 2 studies earlier than 2,000 reported the prevalence of 12% (95% CI: 6%-18%); 8 studies from 2000 to 2009 showed the prevalence of 48% (95% CI: 27%-69%); 8 studies from 2010 to 2019 indicated the prevalence of 30% (95% CI: 11%-54%); only 1 study after 2019 suggested the prevalence of 52% (95% CI: 38%-65%).

The prevalence of depression in patients with ovarian cancer was analyzed using different evaluation scales (Figure S5). Two studies were evaluated using the Self-rating Depression Scale (SDS), which was 71% (95% CI: 64%-77%). Seventeen studies were evaluated using the Hamilton Depression Scale (HAMD), and the combined result was 27% (95% CI: 16%-40%). Four studies were evaluated using the Center for Epidemiologic Studies Depression scale (CES-D), and the pooled result was 36% (95% CI: 18%-55%). Two studies were evaluated using the Patient Health Questionnaire-9 (PHQ-9), and the pooled result was 48% (95% CI: 42%-54%). Four studies were evaluated using the International Classification of Diseases, 9th Revision (ICD-9), International Classification of Diseases, 10th Revision (ICD-10), Beck Depression Inventory (BDI), and Zung self-rating depression scale for ovarian cancer with depression and reported prevalence rates of 16% (95% CI: 13%-16%), 22% (95% CI: 20%-23%), 55% (95% CI: 47%-64%), and 83% (95% CI: 65%-93%), respectively.

Anxiety: The overall prevalence of anxiety in patients with ovarian cancer was 37% (95% CI: 27%-48%) (Figure S6). Like depression, we performed a subgroup analysis of the prevalence of anxiety in patients with ovarian cancer based on the region, country, study stage, and evaluation scale (Table 2).

Table 1: Prevalence of depression in ovarian cancer patients.

Study or Subgroup	Number of studies (Sample size)	Prevalence (95% CI)	I^2	P value
Depression				
Overall prevalence		35% (25%-45%)	97%	<0.01
1. Region				
Asia	13 (3609)	45% (28%-62%)	98%	<0.01
Oceania	3 (908)	10% (4%-16%)	73%	0.02
North America	7 (2324)	33% (20%-47%)	97%	<0.01
Europe	6 (824)	31% (13%-52%)	84%	<0.01
2. Country				
China	10 (1151)	51% (33%-69%)	98%	<0.01
Australia	3 (908)	10% (4%-16%)	73%	0.02
Thailand	1 (56)	4% (0%-12%)		
USA	7 (2324)	33% (20%-47%)	97%	<0.01
UK	2 (181)	31% (25%-48%)	0%	0.69
France	1 (318)	18% (14%-22%)		
Norway	1 (189)	10% (6%-15%)		
Poland	1 (106)	21% (13%-30%)		
Czech	1 (30)	83% (65%-94%)		
Korea	1 (2329)	22% (20%-23%)		
Japan	1 (73)	56% (44%-68%)		
3. Research period				
Before 2000	2 (238)	12% (6%-18%)	35%	0.22
2000-2009	8 (1272)	48% (27%-69%)	98%	<0.01
2010-2019	8 (3310)	35% (18%-55%)	98%	<0.01
After 2019	1 (56)	52% (38%-65%)		
4. Scale				
SDS	2 (218)	71% (64%-77%)	0%	0.7
HAMD	17 (2563)	27% (16%-40%)	97%	<0.01
CES-D	4 (409)	36% (18%-55%)	91%	<0.01
PHQ-9	2 (284)	48% (42%-54%)	0%	0.56
ICD-9	1 (1689)	16% (13%-16%)		
BDI	1 (143)	55% (47%-64%)		
ICD-10	1 (2329)	22% (20%-23%)		
Zung self-rating depression scale	1 (30)	83% (65%-93%)		

The prevalence of anxiety in patients with ovarian cancer varied on a continent-by-continent basis (Figure S7): 9 studies in Asia combined reported a prevalence of 38% (95% CI: 21%-57%); 3 studies in Oceania indicated a prevalence of 28% (95% CI: 23%-34%); 2 studies in North America revealed a prevalence of 24% (95% CI: 6%-50%), and 5 studies in Europe reported a prevalence of 48% (95% CI: 33%-64%).

For different countries, the prevalence of ovarian cancer in patients with anxiety was 44% (95% CI: 23%-66%) in 7 studies from China. The pooled prevalence of the 3 Australian studies was 28% (95% CI: 23%-34%). The pooled prevalence of the 2 American studies was 24% (95% CI: 6%-50%). The pooled prevalence of the 2 UK studies was 47% (95% CI: 31%-64%). Only 1 study from Thailand, France, Norway, Poland and South Korea reported the prevalence of anxiety in ovarian cancer patients was 7% (95% CI: 2%-17%), 43% (95% CI: 38%-49%), 30% (95% CI: 23%-37%), 75% (95% CI: 65%-82%) and 35% (95% CI: 33%-37%), respectively (Figure 3 and Figure S8).

The prevalence of anxiety in patients with ovarian cancer was reported during the different observation periods (Figure S9): 2 studies were conducted before 2000, with a prevalence of 29% (95% CI: 24%-35%); 4 studies were conducted from 2000 to 2009, and the combined prevalence was 39% (95% CI: 20%-59%); 8 studies were conducted from 2010 to 2019, and the prevalence of post-merger anxiety was 35% (95% CI: 15%-58%); 1 post-2019 study reported a prevalence of 38% (95% CI: 25%-51%).

According to the evaluation scale (Figure S10), 16 studies were evaluated using Hamilton Anxiety Scale (HAMA), and the prevalence of anxiety in patients with ovarian cancer was 41% (95% CI: 29%-53%). Three studies were evaluated using ICD-9, ICD-10, and Generalized Anxiety Disorder-7 (GAD-7) scales, which reported

Table 2: Prevalence of anxiety in ovarian cancer patients.

Study or Subgroup	Number of studies (Sample size)	Prevalence (95%CI)	I^2	P value
Anxiety				
Overall prevalence		37% (27%-48%)	97%	<0.01
1. Region				
Asia	9 (3154)	38% (21%-57%)	97%	<0.01
Oceania	3 (908)	28% (23%-34%)	34%	0.22
North America	2 (1772)	24% (6%-50%)	93%	<0.01
Europe	5 (799)	48% (33%-64%)	94%	<0.01
2. Country				
China	7 (769)	44% (23%-66%)	97%	<0.01
Australia	3 (908)	28% (23%-34%)	34%	0.22
Thailand	1 (56)	7% (2%-17%)		
USA	2 (1772)	24% (6%-50%)	96%	<0.01
UK	2 (181)	47% (31%-64%)	79%	0.03
France	1 (318)	43% (38%-49%)		
Norway	1 (189)	30% (23%-37%)		
Poland	1 (106)	75% (65%-82%)		
Korea	1 (2329)	35% (33%-37%)		
3. Research period				
Before 2000	2 (251)	29% (24%-35%)	0%	0.77
2000-2009	4 (951)	39% (20%-59%)	89%	<0.01
2010-2019	7 (981)	35% (15%-58%)	93%	<0.01
After 2019	1 (56)	38% (25%-51%)		
4. Scale				
HAMA	16 (2490)	39% (28%-51%)	96%	<0.01
ICD-9	1 (1689)	14% (12%-15%)		
ICD-10	1 (2329)	35% (33%-37%)		
GAD-7	1 (56)	38% (25%-51%)		

Table 3: The results of the publication bias assessment.

	Depression	Anxiety
Egger's test p value	0.007	0.15
Proportion before trim-and-fill method	35% (25%-45%)	37% (27%-48%)
Increased number of studies	8	5
Proportion after trim-and-fill method	21% (12%-32%)	27% (16%-39%)

prevalence rates of 14% (95% CI: 12%-15%), 38% (95% CI: 25%-51%), and 35% (95% CI: 33%-37%), respectively.

Suicidal ideation: 2 studies from China observed the proportion of patients with ovarian cancer with Suicidal ideation, and the results of the combined analysis were 32% (95% CI: 28%-35%), with minimal heterogeneity between the studies (Figure S11).

Publication bias: We assessed the publication bias for depression and anxiety in patients with ovarian cancer using Egger's linear test. The results showed publication bias (Table 3). Then, we assessed the prevalence of depression and anxiety in patients with ovarian cancer using the trim-and-fill method. Eight and five additional studies were added, respectively. Meta-analysis showed that the prevalence of depression in patients with ovarian cancer was reduced to 21% (95% CI: 12%-32%), and the prevalence of anxiety was reduced to 27% (95% CI: 16%-39%) (Figures S12-S17).

Consistency of quality evaluation: Cohen's kappa statistical coefficient was used to evaluate the literature quality evaluation table of the two researchers. The Kappa statistical coefficient for each item by the two researchers was >0.6, indicating good consistency (Supplementary materials 4).

Discussion

Depression and anxiety are common, disabling mental disorders. Suicidal ideation is a cognitive structure related to suicide risk and is a sign of extreme mental distress [41]. The medical community and public have recognized that mental health greatly affects the quality of life and prognosis of patients with ovarian cancer, and it is of great significance to improve the psychological status related to cancer diagnosis and treatment. It is crucial to screen for mental illness during multidisciplinary assessment of patients with ovarian cancer and provide appropriate mental health care [42]. This study investigated the global epidemiology of depression, anxiety, and suicidal ideation in patients with ovarian cancer, aiming to provide basic data on mental disorders in patients with ovarian cancer to improve their mental health and quality of life.

The economic level, medical insurance policy, mental nursing level, education level, and cultural background of the different regions

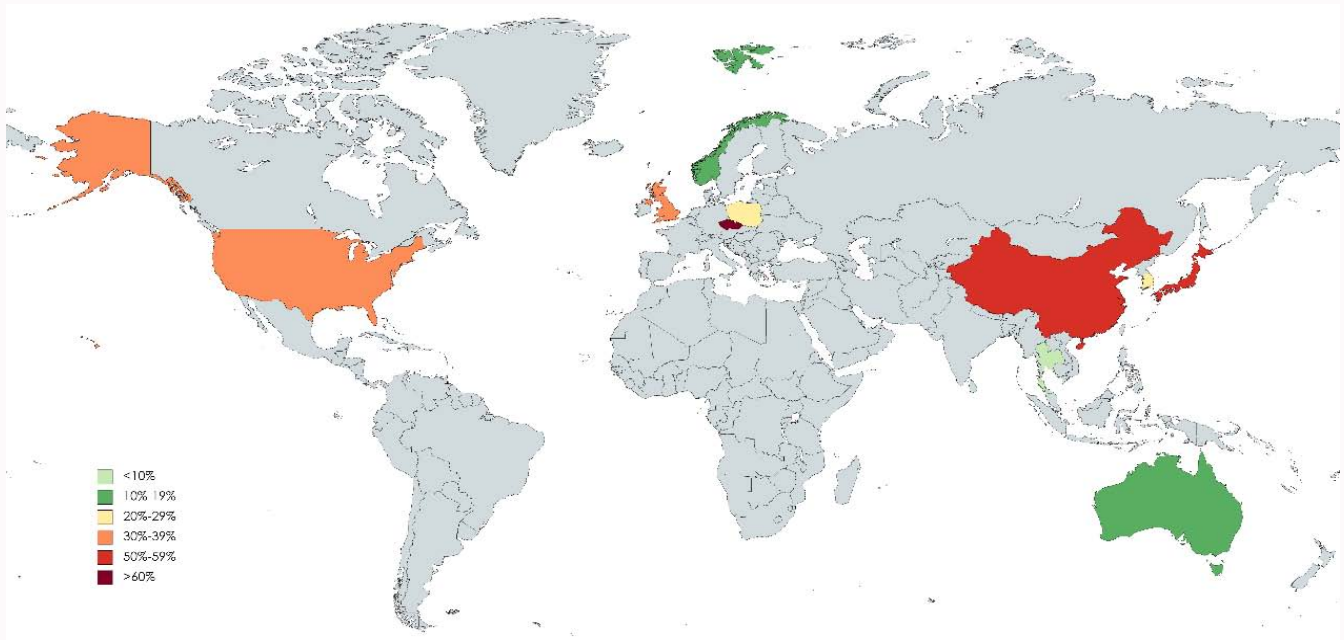

Figure 2: Global prevalence of depression among patients with ovarian cancer.

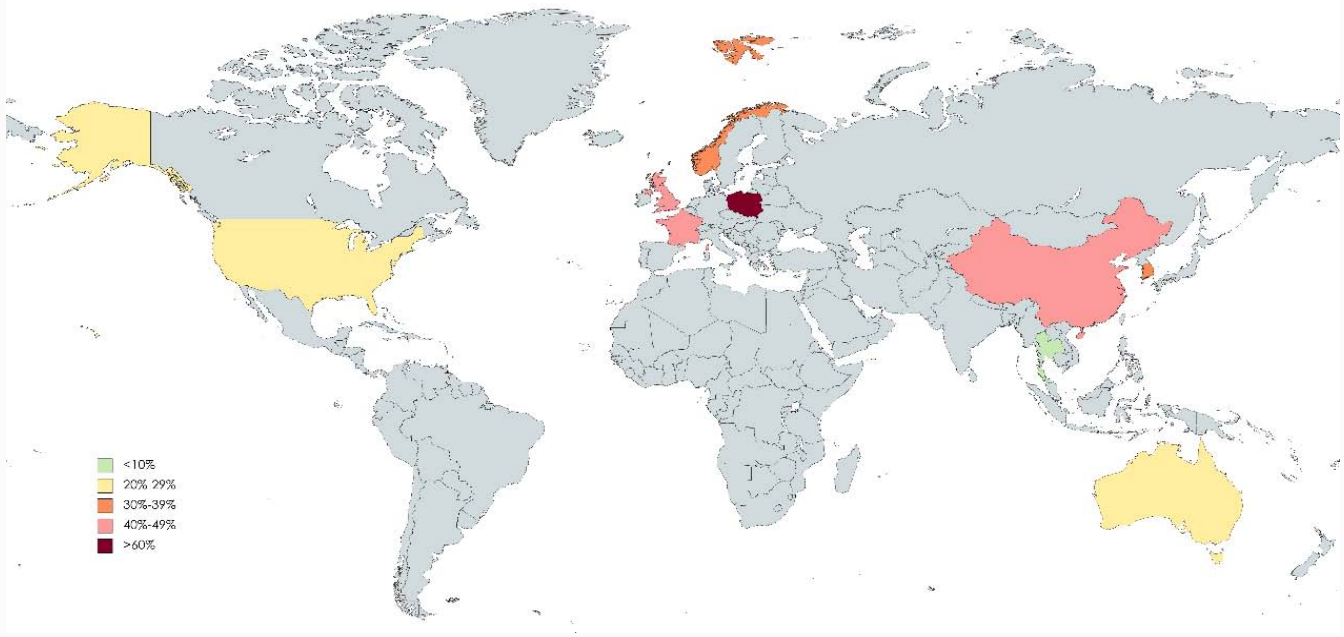

Figure 3: Global prevalence of anxiety among patients with ovarian cancer.

may be due to differences in the incidence of depression in patients with ovarian cancer. Few studies have been conducted in low- and middle-income countries on the mental health status of patients with ovarian cancer. Although fewer resources are available once diagnosed with ovarian cancer in these environments, the economic and mental assistance needs of patients with ovarian cancer are greater [43]. Patients with ovarian cancer in China, Japan, South Korea, and other Asian countries are prone to psychological disorders for the following reasons: (1) the social and emotional support of ovarian cancer patients is insufficient, especially the lack of support for subjective feelings and the imperfect ways for patients to seek social support actively [10]. (2) Patients with ovarian cancer in some Asian countries have a low level of education, lack a correct understanding of major stress events, or cannot reduce the harm properly caused by stress events [15]. (3) Patients with cancer in Asian countries also have a sense of tumor stigma that is rare in patients in other regions [44]. Numerous studies have confirmed that patients with ovarian cancer have the highest risk of suicide (>50%) among all gynecological malignancies [45]. The two studies on suicidal ideation included in this study were from China. The study results discovered that the women with ovarian cancer in China had suicidal ideations of 32%, which was much higher than that of healthy women (4.9%) [46] and other cancer survivors [47].

Because of the popularization of tumor diagnosis, more patients with ovarian cancer were found. The 21st century's information explosion undoubtedly increased the awareness of ovarian cancer, but the diversification of disease information also increased patients' anxiety and fear, triggering a series of mental problems. However, there are no matching psychological support channels and methods. The prevalence of depression in patients with ovarian cancer increased significantly after the epidemic of COVID-19. Although this conclusion comes from only one study, the effects of treatment delay, viral infection, and other factors on the incidence of mental health during the epidemic cannot be ignored [48].

The diagnostic tools and evaluation scales for mental disorders also affected this study's results. Most studies included in this review were evaluated using patient-self-reported scales, and individual studies used clinical standard diagnostic tools, such as ICD-9. Self-reporting tools have a significantly higher prevalence of mental disorders than diagnostic tools. The diagnostic interview is a standardized tool that adheres to strict clinical standards. The self-reporting tool can analyze the risk or severity of mental disorders but cannot diagnose them. Consequently, the use of self-report tools may overestimate the existence of mental disorders. In addition, we found that a small number of studies selected ≥ 11 points as the inclusion criteria for depression or anxiety when using the Hamilton scale for evaluation. Through subgroup analysis of studies with different cut-off values of the scale (Figure S18~19), we found that the prevalence of depression and anxiety was 32% (17%~50%) and 46% (33%~60%), respectively, when the equivalent scale score was ≥ 8 (possible cases). The prevalence of depression and anxiety was 18% (5%-36%) and 20% (12%-29%), respectively, when the equivalent scale score was ≥ 11 (defined cases). The improvement of this standard means that the number of patients with depression and anxiety included in the study is less, which will inevitably reduce the estimation of the prevalence of depression and anxiety in this study.

We focused on several areas where the prevalence of mental disorders in this study was striking. Another study by Slovacek showed that the prevalence of depression in female cancer patients in the Czech Republic was 71.8% [49], which was slightly lower than that in patients with ovarian cancer [34]. A study conducted by Chittrakul et al. in Thailand exhibited a low prevalence of depression and anxiety [17], and the age-standardized incidence of depression in South Asia was also found to decreased significantly between 1990 and 2017 [50]. However, a study in southern Thailand showed that 23% of patients with cancer receiving radiotherapy had mild depression [51], another study conducted in Thailand found that the prevalence of depression and anxiety in patients with epithelial ovarian cancer exceeded 20% [52]. According to Ostovar et al., the prevalence of anxiety disorders in different types of patients with cancer in Southeast Asian countries ranges from 7% to 88%, while the prevalence of depression ranges from 3% to 65.5% [53]. A study in Poland found that the prevalence of anxiety in female patients with cancer was 33% [54], far lower than Mielcarek's study [29]. A study involving patients with ovarian cancer showed that the combined prevalence of depression and suicidal ideation in Chinese patients with cancer was 44.63% and 24.95%, respectively [55]. Another Chinese study including ovarian cancer patients also found that the prevalence of anxiety and depression in patients with cancer was higher than 38% [56], while another study excluding patients with ovarian cancer found that the prevalence of anxiety and depression in 2,930 Chinese patients with advanced cancer was 29% and 11% [57]. It shows that the prevalence of mental disorders in patients with ovarian cancer in China was higher than other cancers. Additionally, studies in many countries were missing because they did not meet the inclusion criteria of this study. There are some differences between these findings and our study conclusions. For example, Irene et al. found that the proportion of patients with advanced cancer in Singapore with both depression and anxiety was 19%, while the proportion of anxiety and depression alone was 4% and 3%, respectively [58]. A Canadian study showed that 46% of cancer patients reported positive depressive symptoms at a median of 66 days after diagnosis [59]. An Indian study found that 33.5% of patients with cancer were diagnosed with anxiety or depression [60]. The small sample size and insufficient inclusion studies are undoubtedly the root causes of these differences. Therefore, more studies are needed to understand the prevalence and potential causes of depression and anxiety in patients with ovarian cancer in these countries.

The results of our study updated and supplemented other studies. A meta-analysis of 211 studies revealed that the average prevalence of depression in patients with cancer was between 8% and 24% [61]. Linden et al. found that 41.6% of patients with cancer had anxiety symptoms above subclinical, and 29.4% of patients with cancer reported depressive symptoms above subclinical [62]. A study of 182,521 patients showed that the prevalence of depression in women with cancer was 31% and increased by 0.6% per year [63]. A few study results are inconsistent with our results. Mitchell et al. showed that the prevalence of depression and anxiety in patients with cancer was 11.6% and 17.9%, respectively [64]. Watts conducted a meta-analysis on the prevalence of mental disorders in patients with ovarian cancer and found that the prevalence of depression before, during, and after treatment was 25.34%, 22.99%, and 12.71%, respectively. The prevalence of anxiety in patients with ovarian cancer before, during, and after treatment were 19.12%, 26.23%, and 27.09%, respectively [6]. Compared with this study, we found a higher prevalence of depression and anxiety in patients with ovarian cancer. The reasons may be the following: (1) Social pressure increases with the increase of economic level. Women are expected to undertake certain social duties while completing family affairs, which inevitably brings greater mental pressure. (2) With the popularization of tumor screening awareness and methods, the number of new ovarian cancer patients has increased compared with 2015, and the age of onset is younger. At the same time, the screening of mental disorders in cancer patients is also timelier and more appropriate than before. The studies' conclusions differ due to differences in research period, subjects, and methods, but our study is the only one to comprehensively analyze the epidemiology of three mental health disorders (depression, anxiety, and suicidal ideation) in patients with ovarian cancer.

Psychological disorders can affect cancer by reducing treatment compliance and immune system function, increasing health risk behaviors, and reducing the effectiveness of cancer treatment [65], and are associated with higher cancer mortality and progression [66]. Activation of the hypothalamic-pituitary-adrenal axis and sympathetic nervous system is a direct target of mental stress exposure [67]. Subsequent release of stress hormones such as catecholamines may reduce the number and activity of immune cells and inhibit T lymphocyte-mediated immune responses, thereby reducing anti-tumor immune responses [68]. Stress hormones also promote oncogene expression in cancer cells, thereby promoting their proliferation, invasion, and migration [69]. Studies have demonstrated that physical function and fatigue are associated with

higher Interleukin-6 (IL-6) in peripheral blood. Women diagnosed with advanced ovarian cancer have elevated IL-6 in peripheral blood and tumor-surrounding areas [19]. The proportion of CD3+, CD4+, and NK cells in patients with major depression decreased, and anti-tumor immunity decreased [70]. Depression increases the levels of CA-125, human epididymis protein-4, and insulin I in the serum and ascites of patients with ovarian cancer and increases the risk of tumor progression and recurrence [71]. In summary, there is a potential mechanism of interaction between ovarian cancer and mental disorders, which may focus on abnormalities in immune function, tumor genes, and inflammatory cytokines.

This study had some limitations. (1) The included studies were published in Chinese and English, and there was inevitable language and citation bias. (2) Some countries have not reported the prevalence of ovarian cancer combined with mental disorders; thus, we could not include these countries in our study. (3) When researching the regions, the data distribution was uneven. For example, research in Asia is mostly concentrated in East Asia. (4) The lost follow-up population included in the study might have a higher level of mental disorders, but this part of the data was unavailable. (5) Subgroup analyses were performed only for the region, country, study period, and evaluation scales. However, other elements related to mental disorders, such as tumor type, treatment stage and/or method, and physical performance status, could not be analyzed due to insufficient data. (6) For studies with multiple observation points, we selected the first time point after diagnosis for combined analysis. This ensures as complete data as possible, but ignores the impact of treatment on the mental health of patients with ovarian cancer.

This study highlights the importance of mental illness screening in the multidisciplinary assessment of ovarian cancer patients to improve their quality of life. However, due to the limited number of included studies, more in-depth studies are needed to clarify the prevalence of mental disorders in patients with ovarian cancer and to explore the potential biological mechanisms of mental disorders in cancer patients.

Conclusion

We combined the evidence from numerous observational studies to illustrate the epidemiology of mental illness in patients with ovarian cancer. The prevalence of ovarian cancer with mental disorders in different continents, different countries, different periods and different assessment methods was estimated.

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