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The Risk of Cancer in Patients With Obsessive-Compulsive Disorder

A Nationwide Population-Based Retrospective Cohort Study

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Abstract: Previous studies suggest a link between anxiety disorders and cancer. The aim of the study was to evaluate the risk of cancer among patients with obsessive-compulsive disorder (OCD) using a nationwide population-based dataset.

We recruited newly diagnosed OCD patients without antecedent cancer from the Taiwan National Health Insurance Research Database between 2002 and 2011. The standardized incidence ratios (SIRs) were estimated for 22 specific cancer types among OCD patients and we determined the SIRs for subgroups according to age and sex group. In addition, because of a potential detection bias, a subgroup analysis stratified with the duration of the OCD diagnosis was carried out.

Among the 52,656 OCD patients, who were followed up for 259,945 person-years (median follow-up = 4.9 years), there were 718 cases of cancer. Patients with OCD did not exhibit an increased overall cancer risk relative to the general population (SIR 1.05, 95% confidence interval [CI] 0.98–1.13). An increased SIR was observed among OCD patients only within the first year of OCD diagnosis (SIR 1.21, 95% CI 1.01–1.43).

This study indicated that the overall cancer risk was not elevated among OCD patients. An increased SIR observed among OCD patients within the first year of OCD diagnosis may be caused by a surveillance bias, and because paraneoplastic manifestations presented with obsessive-compulsive behaviors. Prospective study is necessary to confirm these findings.

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Abbreviations: CI = confidence interval, GAD = generalized anxiety disorder, ICD-9-CM = the International Classification of Diseases, ninth revision, Clinical Modification, IQR = interquartile range, NHI = National Health Insurance, NHIRD = National Health Insurance Research Database, NHRI = the National Health Research Institutes, OCD = obsessive-compulsive disorder, SIRs = standardized incidence ratios, UK = the United Kingdom.

INTRODUCTION

O bsessive-compulsive disorder (OCD) is a type of anxiety disorder with a lifetime prevalence of 1.6% to 2.5% among the general adult population.[1–3] It is characterized by the presence of either obsessions or compulsions that cause marked distress or interfere with normal functioning at work, home, or during social activities.[4] Despite the availability of treatment options, OCD remains a major public health concern. It is associated with considerable impairment and disability, and patients with OCD often experience severe social and interpersonal difficulties, familial dysfunction, occupational problems, and impaired quality of life.[5–8] The World Health Organization classified OCD as one of the top 10 most debilitating illnesses.[9]

Emotional distress, such as chronic depression and anxiety, has been associated with poorer survival among cancer patients.[10] However, whether psychological factors increase the cancer incidence remains unclear.[11] Although substantial studies have been performed on the associations between psychosocial factors and cancer incidence, there is no research evidence to support a direct causal relationship between the 2 events.[11–22] In addition, only a few of these studies focused on anxiety or anxiety disorders.[17–19,22] A study in Taiwan has suggested that patients with anxiety disorders may increase the risk of prostate cancer and marginally decrease the risk of cervical cancer,[17] and a study in the United Kingdom (UK) has indicated that patients with anxiety disorders may have a higher risk for lung and brain cancers.[18] In both the studies, the results showed no significant effect of anxiety disorders on overall cancer risk.

The present study was designed to determine the links between OCD and cancers. To our knowledge, this is the first large population-based retrospective cohort study to evaluate the risk of cancer among OCD patients.

METHODS

Data Sources

The National Health Insurance (NHI) program was implemented in Taiwan in 1995, and offers affordable and comprehensive health-care coverage to nearly 99% of all Taiwan residents.[23] The NHI Research Database (NHIRD) contains comprehensive information about every billing order, including details on both inpatients and outpatients services. The NHIRD is managed by the National Health Research Institutes (NHRI) and confidentiality is maintained according to the directives of the Bureau of the NHI. For researchers' convenience, the NHRI issues the Longitudinal Health Insurance Database (LHID) as a representative NHIRD subset. The LHID contains original claims data for 1,000,000 randomly selected beneficiaries in the registry of beneficiaries. Its representativeness is supported by similar distributions in age, sex, and health-care cost from the original NHIRD.

However, rather than using the LHID, in the current study we analyzed a specific database from the NHRI, which was composed of all beneficiaries with OCD in the registry of beneficiaries. Thus, nearly all OCD patients in Taiwan were included in this dataset. The registry of catastrophic illness patients in the NHIRD provides comprehensive enrollment information for all patients with severe diseases, such as cancer, who have received a copayment exemption in the NHI program.

Standard Protocol Approvals, Registrations, and Patient Consent

The Institutional Review Board of the Taipei Veterans General Hospital approved this study (2012-12-013BC). Written consent from study patients was not obtained because the NHI dataset consists of deidentified secondary data used for research purposes, and the Institutional Review Board of Taipei Veterans General Hospital issued a formal written waiver regarding the need for consent.

Study Population

We conducted a retrospective cohort study from January 1, 2001 to December 31, 2011. Patients newly diagnosed with OCD between January 1, 2002 and December 31, 2010, who had no prior malignancies, were enrolled. OCD was defined according to the International Classification of Diseases, ninth revision, Clinical Modification (ICD-9-CM) code 300.3. In addition, we included only patients who were diagnosed with OCD by a clinical psychiatrist to ensure the diagnostic validity and patient homogeneity.

Statistical Analysis

The main dependent variable was the occurrence of cancer, as reported in the registry of catastrophic illness patients. The cancer diagnoses of patients in the registry were histologically confirmed. OCD patients were followed until the development of cancer, death, withdrawal from the NHI program, or the end of the year 2011.

The risk of cancer among the OCD cohort was determined based on standardized incidence ratios (SIRs), an analysis often used to determine if the occurrence of cancer in a relatively small population, such as the patients with OCD, is high or low. The SIR is obtained by dividing the observed number of cases of cancer and the expected number of cases. In our study, the observed number of cases was the absolute number of cancer diagnoses among the patients with OCD and the expected number of cancer occurrences in OCD patients was derived by multiplying the national cancer incidence rate, stratified according to calendar period, age groups in 5-year intervals and sex, with the corresponding stratum-specific person-time accrued in the patients with OCD. The national cancer incidence rates were obtained from the Taiwan Cancer Registry. The 95% confidence intervals (CIs) of the SIRs were estimated based on the assumption that the observed numbers of cancers have a Poisson probability distribution. To avoid biased conclusions, especially those caused by the potential surveillance bias, subgroups were stratified according to the follow-up duration since OCD diagnosis. For the same reason, only patients with cancers diagnosed beyond the first year following OCD diagnoses were included to calculate the SIRs for the overall cancer risk and the risk of each cancer type. In addition, the Bonferroni correction was used for the concern of the multiple comparisons in statistics. Categorical variables were compared using χ^2 tests, and continuous variables were compared using independent t tests.

The Perl programming language (version 5.12.2) was used to extract, match, and compute data. The Microsoft SQL Server 2005 (Microsoft Corporation, Redmond, WA) was used for further data processing. Statistical analysis was performed using IBM SPSS 17.0 software (SPSS Inc, Chicago, IL). The comparisons resulting in a P value of less than 0.05 were considered to present a statistically significant relationship.

RESULTS

Patient Demographics

Overall, the cohort was observed for 259,945 person-years from 2002 to 2011. A total of 52,656 patients with OCD (50.9% female) were identified. The median age at diagnosis was 32 years (interquartile range [IQR] = 23–45 years), and the median follow-up period was 4.9 years (IQR = 2.5–7.4 years). The patient demographics are shown in Table 1.

All Cancers

A total of 718 cancers occurrences were recorded within the observation period. Compared with the general population, patients with OCD did not exhibit an increased overall cancer risk, as indicated by the SIR of 1.05 (95% CI 0.98–1.13). An

TABLE 1. Characteristics of Patients With Obsessive Compulsive Disorder

	Total	**Male**	**Female**
No. of patients	52,656	25,880	26,776
Person-years at risk	259,945	127,776	132,168
Median follow-up, yr (interquartile range)	4.9 (2.5–7.4)	5.0 (2.4–7.4)	4.9 (2.5–7.5)
Median age, yr (interquartile range)	32 (23–45)	30 (21–43)	35 (25–47)
Distribution of patients according to age			
0–19	9649	5993	3656
20–39	24,920	12,069	12,851
40–59	14,018	6031	7987
60–79	3706	1616	2090
≥80	363	171	192

TABLE 2. Standardized Incidence Ratios (SIRs) According to Age, Sex, and Duration of Obsessive Compulsive Disorder

Characteristics	Total			Male			Female		
	Observed	Expected	SIR (95% CI)	Observed	Expected	SIR (95% CI)	Observed	Expected	SIR (95% CI)
All cancers	718	682.82	1.05 (0.98–1.13)	355	326.75	1.09 (0.98–1.21)	363	356.07	1.02 (0.92–1.13)
Age, yr									
0–19	11	4.10	2.68 (1.34–4.80)	7	2.65	2.64 (1.06–5.44)	4	1.45	2.76 (0.75–7.07)
20–39	89	88.73	1.00 (0.81–1.23)	41	35.77	1.15 (0.82–1.55)	48	52.96	0.91 (0.67–1.20)
40–59	304	315.97	0.96 (0.86–1.08)	127	137.17	0.93 (0.77–1.10)	177	178.80	0.99 (0.85–1.15)
60–79	260	232.68	1.12 (0.99–1.26)	144	127.58	1.13 (0.95–1.33)	116	105.10	1.10 (0.91–1.32)
≥80	54	41.34	1.31 (0.98–1.70)	36	23.58	1.53 (1.07–2.11)	18	17.76	1.01 (0.60–1.60)
Duration									
0–1	134	110.63	1.21 (1.01–1.43)	64	52.36	1.22 (0.94–1.56)	70	58.27	1.20 (0.94–1.52)
≥1	584	572.19	1.02 (0.94–1.11)	291	274.40	1.06 (0.94–1.19)	293	297.79	0.98 (0.87–1.10)
1–5	373	371.24	1.00 (0.91–1.11)	192	176.32	1.09 (0.94–1.25)	181	194.91	0.93 (0.80–1.07)
≥5	211	200.95	1.05 (0.91–1.20)	99	98.07	1.01 (0.82–1.23)	112	102.88	1.09 (0.90–1.31)

CI = confidence interval, SIR = standardized incidence ratio.

analysis of subgroups stratified according to sex showed that neither male nor female patients exhibited increased SIRs (1.09, 95% CI 0.98–1.21 and 1.02, 95% CI 0.92–1.13, respectively). An analysis of subgroups stratified according to age showed that patients younger than 20 years exhibited an increased SIR (2.68, 95% CI 1.34–4.80, $P = 0.01$), but those aged 20 years and older did not. Male patients under 20 years of age also exhibited an increased SIR (2.64, 95% CI 1.06–5.44, $P = 0.04$). Within the first year of OCD diagnosis, 134 cancers were reported, with an SIR of 1.21 (95% CI 1.01–1.43, $P = 0.03$). Excluding the first year following, did not significantly increase the SIR (1.02, 95% CI 0.94–1.11). The results of the subgroup analyses are summarized in Table 2.

Specific Cancer Types (Excluding Patients Whose Cancer Was Diagnosed Within the First Year of OCD Diagnosis)

Among the OCD patients, breast cancer (n = 96) was most common, followed by liver and biliary tract cancers (n = 79), and colon and rectum cancers (n = 75). An increased SIR was observed for prostate cancer (1.64, 95% CI 1.11–2.35, $P = 0.01$) and bladder cancer (1.74, 95% CI 1.13–2.57, $P = 0.01$). However, a decreased SIR was observed for uterine cancer (0.45, 95% CI 0.16–0.98, $P = 0.04$). An increased SIR was observed among male OCD patients for prostate (1.64, 95% CI 1.11–2.35, $P = 0.01$), bladder (1.98, 95% CI 1.19–3.09, $P = 0.01$), and hematologic cancers (1.84, 95% CI 1.21–2.67, $P = 0.01$). Among female OCD patients, a decreased SIR was observed for uterine cancer (0.45, 95%

CI 0.16–0.98, $P = 0.04$). The SIRs for specific types of cancer are presented in Table 3.

DISCUSSION

According to our thorough review of relevant research, this is the first large population-based study to evaluate the risk of cancer among patients with OCD. This study analyzed 52,656 patients followed up for 259,945 person-years. The data showed no increase in overall cancer risk among OCD patients relative to the general population. However, an increased SIR was observed among OCD patients aged less than 19 years (SIR = 2.68) and within the first year of OCD diagnosis (SIR = 1.21).

This study used unbiased patient selection and performed SIR estimation; the patients were matched according to calendar period, age, and sex. Because participation in the NHI is mandatory and offered to all residents of Taiwan, and copayments are low, referral bias was not present and the follow-up was complete. Patients with a certificate of catastrophic illness are exempted from related medical expenses, in particular, hospital costs. To apply for a catastrophic illness certificate for cancer, pathologic proof of malignancy is required, and laboratory and imaging studies must be provided. Therefore, the cancer diagnoses analyzed in this study were reliable and thorough.

Numerous studies have investigated the association between anxiety and subsequent cancer risk.[17–19] A study in Taiwan reported that patients with anxiety exhibited a higher risk for prostate cancer and a marginally lower risk for cervical

TABLE 3. Standardized Incidence Ratios (SIRs) for Specific Cancer Types Among Patients With Obsessive Compulsive Disorder (Excluding Patients Whose Cancer Was Diagnosed Within First Year of OCD Diagnosis)

Site of Cancers	Total			Male			Female		
	Observed	Expected	SIR (95% CI)	Observed	Expected	SIR (95% CI)	Observed	Expected	SIR (95% CI)
All cancers	584	572.19	1.02 (0.94−1.11)	291	274.40	1.06 (0.94−1.19)	293	297.79	0.98 (0.87−1.10)
Head and neck	55	63.41	0.87 (0.65−1.13)	48	53.71	0.89 (0.66−1.18)	7	9.70	0.72 (0.29−1.49)
Digestive	180	188.21	0.96 (0.82−1.11)	109	114.53	0.95 (0.78−1.15)	71	73.67	0.96 (0.75−1.22)
Esophagus	8	12.19	0.66 (0.28−1.29)	5	11.30	0.44 (0.14−1.03)	3	0.89	3.38 (0.70−9.88)
Stomach	14	21.69	0.65 (0.35−1.08)	6	12.22	0.49 (0.18−1.07)	8	9.48	0.84 (0.36−1.66)
Colon and rectum	75	74.84	1.00 (0.79−1.26)	43	38.61	1.11 (0.81−1.50)	32	36.23	0.88 (0.60−1.25)
Liver and biliary tract	79	71.00	1.11 (0.88−1.39)	53	47.96	1.11 (0.83−1.45)	26	23.04	1.13 (0.74−1.65)
Pancreas	4	8.48	0.47 (0.13−1.21)	2	4.45	0.45 (0.05−1.62)	2	4.03	0.50 (0.06−1.79)
Lung and mediastinum	49	56.88	0.86 (0.64−1.14)	25	32.15	0.78 (0.50−1.15)	24	24.73	0.97 (0.62−1.44)
Bone and soft tissue	7	6.21	1.13 (0.45−2.32)	6	3.42	1.76 (0.64−3.82)	1	2.79	0.36 (0.01−1.99)
Skin	12	9.47	1.27 (0.65−2.21)	2	4.61	0.43 (0.05−1.57)	10	4.86	2.06 (0.99−3.79)
Breast	96	88.42	1.09 (0.88−1.33)	0	0.26	0.00 (0.00−14.39)	96	88.17	1.09 (0.88−1.33)
Genitourinary	102	87.54	1.17 (0.95−1.41)	57	34.52	1.65 (1.25−2.14)	45	53.02	0.85 (0.62−1.14)
Cervix	9	16.89	0.53 (0.24−1.01)	–	–		9	16.89	0.53 (0.24−1.01)
Uterus	6	13.35	0.45 (0.16−0.98)	–	–		6	13.35	0.45 (0.16−0.98)
Ovary	12	11.51	1.04 (0.54−1.82)	–	–		12	11.51	1.04 (0.54−1.82)
Prostate	30	18.25	1.64 (1.11−2.35)	30	18.25	1.64 (1.11−2.35)	–	–	
Bladder	25	14.35	1.74 (1.13−2.57)	19	9.61	1.98 (1.19−3.09)	6	4.75	1.26 (0.46−2.75)
Kidney	20	13.19	1.52 (0.93−2.34)	8	6.66	1.20 (0.52−2.37)	12	6.53	1.84 (0.95−3.21)
Thyroid	22	22.09	1.00 (0.62−1.51)	3	4.05	0.74 (0.15−2.16)	19	18.04	1.05 (0.63−1.64)
Hematologic malignancies	37	27.64	1.34 (0.94−1.84)	27	14.69	1.84 (1.21−2.67)	10	12.95	0.77 (0.37−1.42)
All Others	24	22.30	1.08 (0.69−1.60)	14	12.45	1.12 (0.61−1.89)	10	9.85	1.01 (0.49−1.87)

CI = confidence interval, OCD = obsessive-compulsive disorder, SIR = standardized incidence ratio.

cancer.[17] In addition, a UK study revealed that the anxiety patients appeared to be at a increased risk for lung and brain cancer.[18] Moreover, a prospective large-scale study in Finland, with a 6 to 9-year follow-up, suggested that anxiety was not a risk factor for breast cancer.[19] To sum up, there is no general consensus on the association between anxiety and the subsequent cancer occurrence. The inconsistency in the results from the above-mentioned studies may be attributed to the varying definitions of anxiety and the different inclusion criteria used. For example, the Taiwan study included patients with all types of anxiety disorders defined in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision and only anxiety patients who had been admitted for at least 3 times were included. The inclusion criteria may have caused a

tendency for including only patients with severe anxiety disorders. Similarly, the UK study might have tended to include severely anxious patients, because it also included only those having been admitted for anxiety disorders according to the ICD systems, including ICD-7, ICD-8, ICD-9, and ICD-10 codes for anxiety disorders. Therefore, different ICD systems and numerous ICD codes were used to define anxiety disorders in this study. Moreover, in the Finland study, the Spielberger State-Trait Anxiety Inventory, rather than psychiatrist diagnosis, was used to evaluate anxiety.[19] Thus, the diversity of results among these studies might be attributed to the different definitions of anxiety and inclusion criteria used and the fact that anxiety disorders comprise a relatively heterogeneous group of clinical conditions.

It has been hypothesized that psychological factors, including stress-related anxiety, may impair immune and endocrine

TABLE 4. Standardized Incidence Ratios (SIRs) for Specific Cancer Types Among Patients With Obsessive Compulsive Disorder

Site of Cancers	Total			Male			Female		
	Observed	Expected	SIR (95% CI)	Observed	Expected	SIR (95% CI)	Observed	Expected	SIR (95% CI)
All cancers	718	682.82	1.05 (0.98−1.13)	355	326.75	1.09 (0.98−1.21)	363	356.07	1.02 (0.92−1.13)
Head and neck	66	75.68	0.87 (0.65−1.11)	57	64.00	0.89 (0.67−1.15)	9	11.68	0.77 (0.35−1.46)
Digestive	218	224.36	0.97 (0.85−1.11)	131	136.46	0.96 (0.80−1.14)	87	87.89	0.99 (0.79−1.22)
Esophagus	12	14.43	0.83 (0.43−1.45)	8	13.37	0.60 (0.26−1.18)	4	1.05	3.80 (1.03−9.72)
Stomach	21	26.13	0.80 (0.50−1.23)	13	14.70	0.88 (0.47−1.51)	8	11.43	0.70 (0.30−1.38)
Colon and rectum	90	88.71	1.01 (0.82−1.25)	48	45.63	1.05 (0.78−1.39)	42	43.08	0.97 (0.70−1.32)
Liver and biliary tract	91	85.03	1.14 (0.93−1.39)	60	57.48	1.04 (0.80−1.33)	31	27.54	1.13 (0.78−1.58)
Pancreas	4	10.06	0.40 (0.11−1.02)	2	5.27	0.38 (0.05−1.37)	2	4.79	0.42 (0.05−1.51)
Lung and mediastinum	61	67.44	0.90 (0.69−1.16)	32	38.18	0.84 (0.57−1.18)	29	29.25	0.99 (0.66−1.42)
Bone and Soft tissue	7	7.52	0.93 (0.37−1.92)	6	4.12	1.46 (0.53−3.17)	1	3.40	0.29 (0.01−1.64)
Skin	15	11.23	1.34 (0.75−2.20)	2	5.46	0.37 (0.04−1.32)	13	5.77	2.25 (1.20−3.85)
Breast	114	105.33	1.08 (0.89−1.30)	0	0.31	0.00 (0.00−12.04)	114	105.02	1.09 (0.90−1.30)
Genitourinary	128	104.60	1.22 (1.02−1.46)	69	40.66	1.70 (1.32−2.15)	59	63.93	0.92 (0.70−1.19)
Cervix	15	20.87	0.72 (0.40−1.19)	–	–		15	20.87	0.72 (0.40−1.19)
Uterus	9	15.78	0.57 (0.26−1.08)	–	–		9	15.78	0.57 (0.26−1.08)
Ovary	13	13.86	0.94 (0.50−1.60)	–	–		13	13.86	0.94 (0.50−1.60)
Prostate	35	21.35	1.64 (1.14−2.28)	35	21.35	1.64 (1.14−2.28)	–	–	
Bladder	31	17.08	1.81 (1.23−2.58)	24	11.43	2.10 (1.35−3.13)	7	5.66	1.24 (0.50−2.55)
Kidney	25	15.65	1.60 (1.03−2.36)	10	7.89	1.27 (0.61−2.33)	15	7.76	1.93 (1.08−3.19)
Thyroid	25	26.32	0.95 (0.61−1.40)	3	4.78	0.63 (0.13−1.83)	22	21.54	1.02 (0.64−1.55)
Hematologic malignancies	50	33.24	1.50 (1.12−1.98)	33	17.67	1.87 (1.29−2.62)	17	15.58	1.09 (0.64−1.75)
All Others	34	27.11	1.25 (0.87−1.75)	22	15.10	1.46 (0.91−2.21)	12	12.00	1.00 (0.52−1.75)

CI = confidence interval, OCD = obsessive-compulsive disorder, SIR = standardized incidence ratio.

functions,[4,24,25] and that the impaired immune and endocrine function might play an essential role in specific stages of cancer development and in the pathogenesis of certain cancer types.[26–29] However, the present study suggested that the overall cancer risk among OCD patients was not higher than that among general population (SIR = 1.05, 95% CI 0.98–1.13). There are 2 explanations for the possibility of false-negative finding. First, carcinogenesis is a multistage process, and second, a latency period may separate a potential carcinogenic agent and the appearance of a cancer. The phenomenon of increasing cancer incidence rates with age might further enforce these arguments.[30] Although the onset of OCD typically occurs during childhood or early adulthood[31]which implicated that the population of OCD would have more opportunity to live long enough to see the cancer fully develop, the median follow-up period in the current study was 4.9 years, which may have been insufficient for detecting an increased risk of certain malignancies, especially cancers with long latency periods.

Among the patients with OCD, the cancer incidence significantly increased only within the first year after the diagnosis of OCD, with an SIR of 1.21. The most reasonable explanations for this result are surveillance bias[32] and that patients with paraneoplastic syndrome might be misdiagnosed with OCD initially. Patients with OCD are likely to have more outpatient visits than the general population, leading to an earlier detection of undiagnosed cancers. In addition, the close temporal relationship demonstrated in this study between OCD diagnosis and newly diagnosed cancer may support the argument that obsessive-compulsive behaviors are a paraneoplastic manifestation among patients with an undiagnosed malignancy.[33–36] While excluding data from OCD patients with cancer development within the first-year follow-up, the result found no statistically significant difference in cancer risk between the patient with OCD and the general population (SIR = 1.02, 95% CI 0.94–1.11).

In our study, an increased SIR was observed among OCD patients aged less than 19 years (SIR = 2.68). Previous studies have shown that testicular teratoma and anti-Ma2 antibodies were associated with OCD, and have suggested that these were causative, based on data indicating the involvement of the limbic region in OCD.[36,37] Because testicular teratoma is the most common malignancy in male adolescents and young adults,[38] it is reasonable to conclude that the increased SIR among OCD patients aged less than 19 years may be attributed to paraneoplastic manifestation.

After excluding patients whose cancer was diagnosed within the first year of OCD diagnosis, a higher risk of prostate (1.64, 95% CI 1.11–2.35, $P = 0.01$), bladder (1.98, 95% CI 1.19–3.09, $P = 0.01$), and hematologic cancers (1.84, 95% CI 1.21–2.67, $P = 0.01$) was noted among male OCD patients. By contrast, a lower risk of uterine cancer (0.45, 95% CI 0.16–0.98, $P = 0.04$) was noted among female OCD patients. An increased risk of prostate cancer among patients with anxiety disorder was previously reported; however, this may be attributed mainly to surveillance bias, and it was observed that a higher proportion of patients with anxiety disorder underwent a prostate-specific antigen test.[17,22] However, that OCD increased the risk of bladder and hematologic cancers, and reduced the risk of uterine cancer, has not been previously reported. Our findings require confirmation by further studies, because when taking into account multiple comparisons, the P values of the results presented in this study did not indicate statistical significance (a P value equal to or less than 0.05 divided by 22, approximately 0.002, was considered significant when adjusting using

the Bonferroni correction). Thus, the values determined in this study may be chance findings.

In our study, patients with a newly diagnosed cancer within the first year of OCD diagnosis were excluded from our original analysis for the concerns of detection bias and bias caused by paraneoplastic syndrome. However, based on the fact that the final numbers of cases in each cancer category are relatively small and an increased SIR was indeed observed within the first year of OCD diagnosis (Table 2), it is appropriate to perform the same analysis using all cancer cases without follow-up year stratification. As shown in Table 4, the results of the further analysis are consistent with original one in our study, showing no increase in overall cancer risk among OCD patients relative to the general population and the increased SIRs of specific types of cancer were considered to lack statistical significance after using Bonferroni correction.

There are limitations to our findings. First, information regarding the family history of cancer, environmental exposures, diet, cigarette smoking, and alcohol use is not included in the NHIRD. Second, the NHIRD does not specify how diagnostic classifications were performed. Therefore, the diagnostic accuracy of OCD in our study could not be ascertained. Additional studies of OCD patients who were diagnosed through structured interviews should be conducted. Third, OCD severity was not considered in this study, and whether severity influences the risk of developing cancer warrants further study. Finally, the duration of the follow-up period in this study may have been insufficient for detecting the carcinogenesis of certain types of cancer. Thus, future studies with longer follow-up periods are required to determine the long-term risk of cancer among OCD patients.

CONCLUSIONS

In conclusion, this population-based retrospective cohort study observed no increase of overall cancer risk among patients with OCD compared with the general population. An increased cancer risk in the first year after the diagnosis of OCD among OCD patients may be attributed to surveillance bias and the paraneoplastic manifestation of certain cancers. Risks of prostate, bladder, and hematologic cancers were specifically determined to have increased among male OCD patients, whereas the risk of uterine cancer among female OCD patients was observed to be reduced. Additional large, unbiased population-based prospective studies with longer follow-up periods are required to investigate the association between OCD and cancer risk.

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