رَبِّ اشْرَحْ لِي صَدْرِي وَيَسِّرْ لِي أَمْرِي
وَاحْلُلْ عُقْدَةً مِّن لِّسَانِي يَفْقَهُواقولى

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Women with adenomyosis are at higher risks of endometrial and thyroid cancers: A population-based historical cohort study

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Introduction

Endometriosis is a disorder in which tissue that normally lines the inside of uterus (the endometrium) grows outside of uterus. Endometriosis most commonly involves ovaries, fallopian tubes and the tissue lining your pelvis. Rarely, endometrial tissue may spread beyond pelvic organs.

Common signs and symptoms of endometriosis may include:

- **Painful periods** (dysmenorrhea). Pelvic pain and cramping

- **Pain with intercourse**.

- **Pain with bowel movements or urination**.

- **Excessive bleeding**. You may experience occasional heavy periods (menorrhagia) or bleeding between periods (menometrorrhagia).

- **Infertility**

- **Other symptoms**. fatigue, diarrhea, constipation, bloating or nausea

Introduction

Adenomyosis is a common condition. It is most often diagnosed in middle-aged women and women who have had children. Some studies also suggest that women who have had prior uterine surgery may be at risk for adenomyosis .

Introduction

The cause of Adenomyosis isn't known, studies have suggested that various hormones including estrogen, progesterone, prolactin, and follicle stimulating hormone -- may trigger the condition.

Introduction

Adenomyosis is a condition in which the inner lining of the uterus (the endometrium) breaks through the muscle wall of the uterus (the myometrium)

Introduction

Adenomyosis can cause menstrual cramps, lower abdominal pressure, and bloatingbefore menstrual periods and can result in heavy periods. The condition can be located throughout the entire uterus or localized in one spot.

Introduction

Adenomyosis and endometriosis are two common gynecologic diseases, and both are characterized by the presence of ectopic endometrial glands and stroma .These diseases are commonly diagnosed in reproductive-age women, and they can result in pelvic pain, dysmenorrhea, and infertility

Introduction

Although adenomyosis and endometriosis are generally considered benign conditions, they have been suggested to share some characteristics with malignant tumors, such as angiogenesis, abnormal tissue growth, and invasion

Introduction

in recent years, an increasing number of studies have investigated the association of endometriosis with several cancer types particularly ovarian cancer. However, few studies have examined the association of adenomyosis with cancer risk

Materials and methods

A total of ۴۸۶,۰۷۷ women were contained in the LHID۲۰۰۰ which is a subset of the National Health Insurance Research Database (NHIRD) in Taiwan. we stratified these women by their birth year, and calculated the proportions of women having at least one diagnostic record of adenomyosis or endometriosis in individual strata

Materials and methods

we selected women born between ۱۹۵۱ and ۱۹۸۴ as the study population because more than ۵% of women had a diagnosis of adenomyosis or endometriosis in each of these strata.

The study population was divided into four cohorts:

(١) adenomyosis cohort,

(٢) endometriosis cohort

(٣) both adenomyosis and endometriosis cohort,

(٤) adenomyosis-and-endometriosis-free cohort.

Methods

This study included a cohort of ١٢,٤٤٧ women with adenomyosis but not endometriosis, born in ١٩٥١–١٩٨٤, and a cohort of ١٢٤,٤٧٠ adenomyosis-free women matched by birth year

Methods

For each patient in the adenomyosis only cohort, ١٠ women matched by birth year were randomly sampled from the adenomyosis-and-endometriosis-free cohort.

The cancer risks for a cohort of ١٠,٩٦٢ women with endometriosis but not adenomyosis and a birth-year matched cohort of ١٠٩,٦٢٠ endometriosis-free women.

Methods

We first compared the distribution of cancer-free survival (CFS) between cohorts with and without adenomyosis

Methods

Subsequently, within the adenomyosis cohort, we examined whether time-to-onset of the identified cancer type was correlated with time-to-onset of adenomyosis.

Methods

The Cox proportional hazards model was used to compare the distribution of CFS between the adenomyosis and adenomyosis-free cohorts and between the early- and late-diagnosed adenomyosis groups

The distribution of cancer types in the adenomyosis cohort was summarized in Table ١. In this study, we only analyzed cancer types for which the patient numbers were more than or equal to ١٠.

Site of cancer (ICD-9-CM)	Number of cancer	Adenomyosis diagnosed before cancer				Cancer diagnosed before adenomyosis			
		More than 6 months		Within 6 months		Within 6 months		More than 6 months	
	patients	n	%	n	%	n	%	n	%
Head and neck (140–149)	24	13	54	0	0	0	0	11	46
Esophagus (150)	0	0	0	0	0	0	0	0	0
Stomach (151)	9	5	56	0	0	0	0	4	44
Colon and rectum (153, 154)	44	27	61	8	18	1	2	8	18
Liver (155)	13	10	77	1	8	0	0	2	15
Gallbladder and extra hepatic bile duct (156)	2	2	100	0	0	0	0	0	0
Pancreas (157)	1	1	100	0	0	0	0	0	0
Lung (162)	27	21	78	2	7	2	7	2	7
Melanoma (172)	3	1	33	0	0	0	0	2	67
Skin (173)	3	1	33	0	0	0	0	2	67
Breast (174)	202	94	47	13	6	11	5	84	42
Endometrium (182)	76	22	29	40	53	9	12	5	7
Cervix (179, 180)	76	8	11	31	41	33	43	4	5
Ovary (183)	34	12	35	11	32	7	21	4	12
Bladder (188)	1	0	0	0	0	1	100	0	0
Kidney (189)	8	6	75	1	13	0	0	1	13
Brain (191)	6	5	83	0	0	0	0	1	17
Thyroid (193)	66	24	36	4	6	3	5	35	53
Lymphatic and hematopoietic tissue (200–208)	20	11	55	2	10	0	0	7	35

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S2 Table. Distribution of cancer types in the endometriosis cohort.

Site of cancer (ICD-9-CM)	Number of cancer patients	Endometriosis diagnosed before cancer				Cancer diagnosed before endometriosis			
		More than 6 months		Within 6 months		Within 6 months		More than 6 months	
		n	%	n	%	n	%	n	%
Head and neck (140-149)	**11**	**4**	**36**	**0**	**0**	**0**	**0**	**7**	**64**
Esophagus (150)	0	0	0	0	0	0	0	0	0
Stomach (151)	**10**	**6**	**60**	**1**	**10**	**1**	**10**	**2**	**20**
Colon and rectum (153-154)	**24**	**13**	**54**	**1**	**4**	**2**	**8**	**8**	**33**
Liver (155)	6	5	83	0	0	0	0	1	17
Gallbladder and extra hepatic bile duct (156)	1	1	100	0	0	0	0	0	0
Pancreas (157)	0	0	0	0	0	0	0	0	0
Lung (162)	9	8	89	0	0	1	11	0	0
Melanoma (172)	1	1	100	0	0	0	0	0	0
Skin (173)	4	2	50	0	0	0	0	2	50
Breast (174)	**97**	**57**	**59**	**2**	**2**	**2**	**2**	**36**	**37**
Endometrium (182)	**21**	**8**	**38**	**6**	**29**	**5**	**24**	**2**	**10**
Cervix (179, 180)	**19**	**3**	**16**	**7**	**37**	**5**	**26**	**4**	**21**
Ovary (183)	**45**	**17**	**38**	**22**	**49**	**3**	**7**	**3**	**7**
Bladder (188)	1	1	100	0	0	0	0	0	0
Kidney (189)	8	6	75	0	0	0	0	2	25
Brain (191)	1	0	0	0	0	0	0	1	100
Thyroid (193)	**30**	**18**	**60**	**1**	**3**	**1**	**3**	**10**	**33**

For each cancer type, the patients were further classified into four subsets, according to the order of diagnoses of cancer and adenomyosis (adenomyosis diagnosed before cancer or cancer diagnosed before adenomyosis) and the interval between these two events (within or more than ۶ months)

Statistical analysis

The Pearson chi-squared test was used to compare demographic characteristics and comorbidities between adenomyosis and adenomyosis-free cohorts. The demographic characteristics examined were geographic region, occupation, urbanization level, and monthly income

Table ۲. Comparisons of demographic characteristics and comorbidities between adenomyosis and adenomyosis-free cohorts.

Demographic characteristics and comorbidities	Adenomyosis-free (n = 124,470)		Adenomyosis (n = 12,447)		*p* value
	n	%	n	%	
Birth cohort					.99
1951–1960	46200	37.1	4620	37.1	
1961–1970	52140	41.9	5214	41.9	
1971–1980	22050	17.7	2205	17.7	
1981–1984	4080	3.3	408	3.3	
Geographic region					< 0.0001
Northern	62489	50.2	5517	44.3	
Central	24011	19.3	2414	19.4	
Southern	32899	26.4	3958	31.8	
Eastern and Islands	5069	4.1	558	4.5	
Occupation					0.0031
White collar	73005	58.6	7117	57.2	
Blue collar	37816	30.4	3956	31.8	
Retired and others	13649	11.0	1374	11.0	
Urbanization level					< 0.0001
Urban	79068	63.5	7575	60.9	
Suburban	37143	29.8	3963	31.8	
Rural	8257	6.6	909	7.3	
Monthly income, NT$					< 0.0001
≤15,840	39763	32.0	3613	29.0	
15,841–25,000	61518	49.4	6481	52.1	
≥25,001	23189	18.6	2353	18.9	
Comorbidity					
Chronic obstructive pulmonary disease	22255	17.9	2999	24.1	< 0.0001
Hypertension	18176	14.6	2474	19.9	< 0.0001
Hyperlipidemia	15532	12.5	2281	18.3	< 0.0001
Diabetes	8190	6.6	1134	9.1	< 0.0001
Coronary artery disease	6240	5.0	970	7.8	< 0.0001
Chronic renal disease	4073	3.3	570	4.6	< 0.0001
Pelvic inflammatory disease	24995	20.1	4756	38.2	< 0.0001

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All statistical analyses were performed using SAS statistical software (version ٩,٤ for Windows; SAS Institute, Inc., Cary, NC, USA), and the significance level was set at ٠,٠٥

Results

As shown in S١ Table, the LHID٢٠٠٠ contained data of ٢٨٠,٤١٩ women born between ١٩٥١ and ١٩٨٤. Of them, ٢٤٩,٥٤١ (٨٩%) had been unaffected by adenomyosis or endometriosis

Results

Among the ٣٠,٨٧٨ (١١%) women affected by adenomyosis or endometriosis, ١٢,٤٤٧ (٤,٤%) women were affected by adenomyosis only, ١٠,٩٦٢ (٣,٩%) women were affected by endometriosis only, and the remaining ٧,٤٦٩ (٢,٧%) women were simultaneously affected by adenomyosis and endometriosis.

Results

When stratifying the study population by birth year, the highest proportion of women affected by adenomyosis or endometriosis (١٥,٥%) was found in the stratum of women born in ١٩٦٢

Results

All demographic characteristics and comorbidities examined were significantly different not only between the adenomyosis and adenomyosis-free cohorts but also between the endometriosis and endometriosis-free cohorts. Therefore, these variables were adjusted for in the first-stage association analysis.

Results

Compared with adenomyosis-free women, patients with adenomyosis had higher risks of endometrial and thyroid cancers, with estimated hazard ratios (HRs) (٩٥% confidence interval) of ٢,١٩ (١,٥١–٣,١٦) and ١,٧٠ (١,٢٩–٢,٢٤), respectively

Table ۳. Comparison of distribution of cancer-free survival (CFS) between adenomyosis and adenomyosis-free cohorts.

Site of cancer (ICD-9-CM)	Adenomyosis-free			Adenomyosis			HR (95% CI) [b]
	n	Number of cancer	Rate [a]	n	Number of cancer	Rate [a]	
Head and neck (140–149)	124470	184	0.32	12447	24	0.41	1.27 (0.83–1.96)
Colon and rectum (153, 154)	124390	311	0.54	12439	36	0.61	1.11 (0.78–1.56)
Liver (155)	124460	104	0.18	12446	12	0.20	1.08 (0.59–1.98)
Lung (162)	124450	194	0.34	12445	25	0.43	1.20 (0.79–1.83)
Breast (174)	124340	1641	2.87	12434	189	3.22	1.12 (0.96–1.30)
Endometrium (182)	124070	151	0.26	12407	36	0.61	**2.19 (1.51–3.16)** [c]
Cervix (179, 180)	124160	454	0.79	12416	45	0.77	0.93 (0.69–1.27)
Ovary (183)	124360	181	0.32	12436	23	0.39	1.20 (0.78–1.87)
Thyroid (193)	124430	320	0.56	12443	62	1.06	**1.70 (1.29–2.24)** [c]
Lymphatic and hematopoietic tissue (200–208)	124450	173	0.30	12445	18	0.31	1.00 (0.61–1.63)

[a] per 10000 person-year.

[b] Adjusted for birth year and significant variables in Table 2.

[c] p value < 0.001.

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Results

Furthermore, compared with endometriosis-free women, patients with endometriosis had higher risks of endometrial and ovarian cancers, with HRs of ١,٨٩ (١,٠٧–٣,٣٥) and ٢,٠١ (١,٢٧–٣,١٦), respectively

Results

For both cancers, distributions of CFS were not significantly different between the early- and late-diagnosed adenomyosis groups

Table ۴. Comparison of distribution of CFS between early- and late-diagnosed adenomyosis groups.

Site of cancer (ICD-9-CM)	Early-diagnosed adenomyosis			Late-diagnosed adenomyosis			HR (95% CI) [b]
	n	Number of cancer	Rate [a]	n	Number of cancer	Rate [a]	
Endometrium (182)	6192	15	0.51	6192	12	0.41	0.79 (0.37–1.69) [c]
Thyroid (193)	6213	28	0.96	6213	31	1.06	1.10 (0.66–1.83) [c]

[a] per 10000 person-year.

[b] Adjusted for birth year.

[c] *p* value > 0.05.

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Results

Among these cancers, adenomyosis and cancer were detected within an interval of ۶ months in high proportions of the patients with cancers of the endometrium (۶۴,۴۷%), cervix (۸۴,۲۱%), and ovary (۵۲,۹۴%)

Results

Among endometriosis and cancer were detected within an interval of ۶ months in high proportions of the patients with cancers of the endometrium (۵۲,۳۸%), cervix (۶۳,۱۶%), and ovary (۵۵,۵۶%).

Discussion

This study mainly investigated cancer risk in patients with adenomyosis by using a large nationwide health insurance database collected in Taiwan.

Discussion

We found that women with adenomyosis are at elevated risks of endometrial cancer and thyroid cancer. Although the association between adenomyosis and endometrial cancer has been reported by some studies .the association between adenomyosis and thyroid cancer has rarely been reported

Discussion

Furthermore, we found that women with endometriosis have higher risks of endometrial cancer and ovarian cancer, and these observations are consistent with those of previous studies

Discussion

the etiology and pathogenesis of these two diseases remain poorly understood to date. A comprehensive understanding of the relationship between adenomyosis/endometriosis and comorbidities, such as cancer, may provide new insight into the causes of adenomyosis/endometriosis

Conclusions

According to the observations in our study, the spectrum of cancer types associated with adenomyosis did not seem to be identical to that of cancer types associated with endometriosis.

Conclusions

This study revealed a significant association of adenomyosis with endometrial cancer and thyroid cancer. However, we could not provide conclusive evidence regarding whether the time-to-onset of adenomyosis is correlated with that of endometrial cancer and thyroid cancer.

Conclusions

Women with adenomyosis are at higher risks of endometrial and thyroid cancers,

while women with endometriosis are at higher risks of endometrial and ovarian cancers.


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