

# Analysis of gynecologic cancer patients visiting emergency department: a population-based cohort study in Taiwan

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## Summary

**Purpose:** To investigate the characteristics of gynecologic cancer patients visiting the emergency department (ED). **Materials and Methods:** A retrospective cohort of gynecologic cancer patients in ED visits from 2000 to 2012 was analyzed using the Longitudinal Health Insurance Database 2000 (LHID2000) which randomly selected 1,000,000 beneficiaries from the year 2000 Registry of Beneficiaries (n = 23.72 million). **Results:** There were 5,893 ED visits by 1,400 gynecologic cancer patients. The mean age was 55.22 ± 14.60 years. The mean number of ED visits was 4.21 ± 5.18. 657 (46.93%) patients that were admitted to hospital; 70.57% ED visits occurred in medical center. Abdominal pain (19.04%), complications of surgical and medical care (13.28%) and intestinal obstruction without mention of hernia (10.69%) are the most three common presenting symptoms except other symptoms, signs, and ill-defined conditions (24.79%); 62.56% of the medications prescribed in ED visits are of gastrointestinal category. The overall survival rate of ED visits was significantly lower than that of no ED visits ( $p < 0.0001$ ). **Conclusions:** Relatively low rate of hospital admission may indicate unnecessary ED visits resulting in healthcare costs. Abdominal pain is the most common specific symptoms at presentation. Most medications belong to the gastrointestinal category reminding us of the importance of nutrition support. ED visits were a significant poor prognostic factor for overall survival.

**Key words:** Gynecologic cancer; Emergency department; Admittance; Taiwan National Health Insurance Research Database (NHIRD).

## Introduction

Cancer is a major cause of morbidity and mortality in the world. Results from GLOBOCAN reveal that in 2012, there were approximately 14 million new cases and eight million cancer-related deaths.[1] These estimates correspond to age-standardized incidence and mortality rates of 182 and 102 per 100,000. Among women, cervix uteri (7.9%), corpus uteri (4.8%), and ovary (3.6%) were the fourth, sixth, and eighth common incident site of cancer. These gynecologic cancers underwent single or combined therapy such as surgery, chemotherapy, and radiotherapy to the pelvic region. Improvement in cancer treatment and supportive care measures over the past two decades have resulted in the improvement of relative survival rates. However, much cancer patients suffered from treatment and disease-related symptoms coming to emergency department (ED) for medical recommendation. Earle *et al.* reported poor quality indicators for end-of-life care [2, 3]. A high number of emergency room visits, inpatient hospital admissions, or intensive care unit days near the end of life are major indications of poor quality of end-of-life cancer care.

In 2011 in Taiwan, there were over 4,600 new cases of

gynecologic cancer and approximately 1,300 deaths. It is the fifth leading cause of cancer-related deaths in women, after lung, liver, colorectal, and breast cancer [4]. Therefore, life care in gynecologic oncology is an important health issue among women. The present authors used the Taiwan National Health Insurance Research Database (NHIRD) to deal with the gynecologic cancer patients visiting the ED.

## Materials and Methods

### Database

The authors used data sourced from the Longitudinal Health Insurance Database 2000 (LHID2000), which is derived from National Health Insurance Bureau (NHIB) records and released by the Taiwan National Health Research Institute (NHRI). Taiwan initiated its NHI program in 1995, and coverage has been about 98% of the entire population since its inception. The LHID2000 comprises registration files and medical claims data for reimbursements of 1,000,000 beneficiaries under the Taiwanese NHI program. The Taiwan NHRI randomly selected these 1,000,000 beneficiaries from the year 2000 Registry of Beneficiaries (n = 23.72 million) of the NHI program. Prior studies demonstrated the validity of the claims data of the NHI database (NHIRD) [5, 6]. To date, hundreds of studies have been published in internationally peer-reviewed journals using

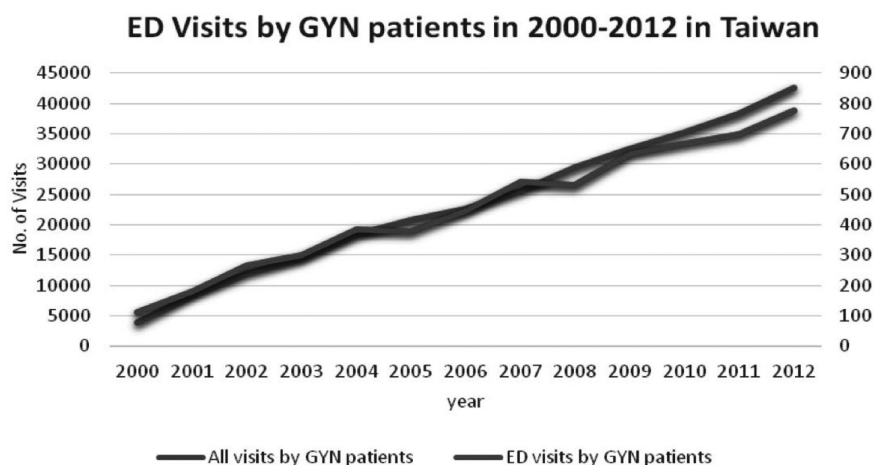


Figure 1. — Number of all visits (blue line) and emergency department (ED) visits (red line) made by gynecologic cancer (GYN) patients per year from 2000 to 2012.

data from the NHIRD. Particularly, the NHIRD has been used in a prior study to examine ED utilization of patients in Taiwan [7]. The LHID2000 consists of encrypted de-identified secondary data released to the public for research purposes and was therefore exempted from full review following consultation with the Veterans General Hospital Kaohsiung (VGHS's) Institutional Review Board.

Patients with gynecologic cancer were identified from an analysis of ED encounters from 2000 to 2012, using the LHID2000, compiled by the Taiwan NHI program. Data elements within the LHID2000 include international classification of diseases, ninth revision, clinical modification (ICD-9-CM) codes, patient demographic characteristics, hospital characteristics, and inpatient data for ED admissions.

#### Identification of sample

The gynecologic cancer patient subpopulation was identified using the LHID2000 (HV) codes, which encompass all types of malignancies. The HV is a diagnosis and procedure categorization scheme that collapses ICD-9-CM codes into a smaller number of clinically meaningful categories. To select the study cohort, the authors identified 1,400 subjects who had been diagnosed with gynecologic cancer (ICD-9-CM codes 180, 182, 183) after ED visit between January 1, 2000 and December 31, 2012. According to the centers for disease control and prevention, the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) is the official system of assigning codes to diagnoses and procedures associated with hospital use (including the ED) in Taiwan. Hospital employees typically assign more than one ICD-9-CM code per visit. The ICD-9-CM code listed in diagnosis position one (i.e., listed first) for a visit is considered the primary diagnosis, the ICD-9-CM code in diagnosis position two (i.e., listed second) is considered the secondary diagnosis, and so forth.

#### Outcome/end-point assessment

Patient and visit demographic variables for gynecologic cancer-related visits from LHID2000 included visit month, patient sex, age at first visit, teaching level of hospital, region of hospital, diagnostic position of gynecologic cancer, frequency of ED visits, frequency of admittance, survival and interval of ED visit and death. Descriptive statistics, both counts and percentages, were calculated for each of these variables.

Frequencies of categorized primary ICD-9-CM discharge diagnosis were assessed. The reason prompting an ED visit was defined as the primary ICD-9-CM discharge diagnosis associ-

ated with the visit, unless the primary diagnosis was a cancer diagnosis (ICD-9-CM Codes 180, 182, 183). In cases where a cancer diagnosis was the primary diagnosis (22.16% of visits), the second listed ICD-9-CM diagnosis was considered to be the reason prompting the ED visit. Cancer diagnoses were excluded from the present analysis in order to focus on symptom or complication diagnoses among gynecologic cancer patients with cancer who present to the ED. Frequencies of categorized medicines were also assessed and the ten most common categories were listed.

#### Data analysis

Descriptive statistics are represented as numbers of cases, percentages, and means with standard deviation (SD) of ED and admittance frequency. The proportion of visits made by patients with gynecologic cancer and the disposition status was determined for the top ten primary non-cancer diagnoses. The cumulative survival curves were estimated using the Kaplan-Meier method. The comparison of the survival curves was performed by the log-rank test and value of  $p < 0.05$  (two-sided) was considered significant. All statistical calculations were performed using the Statistical Package for SAS statistical package (version 9.4).

## Results

### ED visits by gynecologic cancer patients in Taiwan from 2000-2012

From 2000-2012, there were a total of 304,656 gynecologic cancer-related visits, including inpatient, outpatient, and ED services. The number of visits increased steadily from 3,777 in 2000 to 42,657 in 2012. Among these visits, 1,400 gynecologic cancer patients made 5893 ED visits, ranging from the lowest number of visits (111) in 2000 to the highest number of visits (775) in 2012 (Figure 1). ED visits were further categorized by month of the year (Figure 2). August (9.16%) was the month with the highest number of visits, and February (7.36%) was the month with the lowest number of visits.

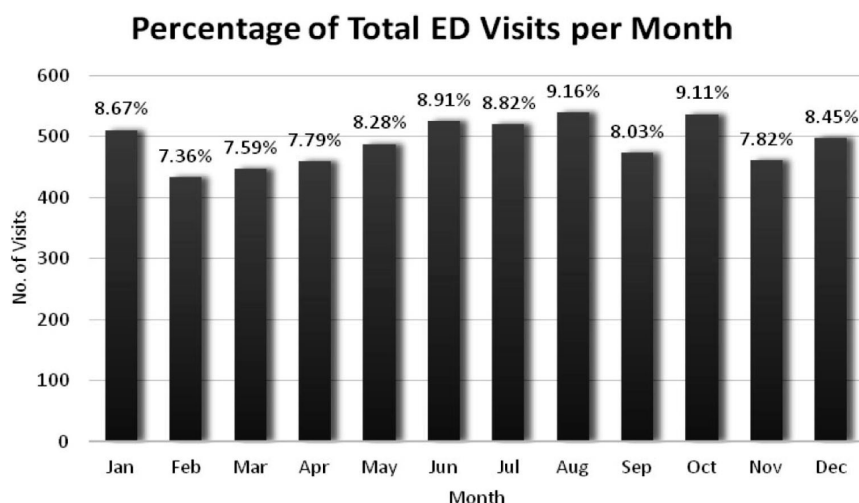


Figure 2. — Percentage of emergency department (ED) visits made by gynecologic cancer patients per month from 2000 to 2012.

Table 1. — Demographic characteristics of gynecologic cancer patients presenting to the ED ( $n = 1,400$ ).

Characteristic	No.	%
Age at diagnosis, years	Mean/SD (55.22/14.60)	Min/max (5.70/98.69)
< 20	10	0.71
20–29	42	3
30–39	137	9.79
40–49	353	25.21
50–59	349	24.93
60–69	273	19.5
> 70	236	16.86
Teaching level of the hospital		
Medical center	988	70.57
Regional, district hospital	412	29.43
Geographic region		
Northern	703	50.21
Central	258	18.43
Southern	415	29.64
Eastern	24	1.71
Site		
Cervix	753	53.79
Body of uterus	307	21.93
Ovary and other uterine adnexa	340	24.29
Chemotherapy		
No	788	56.29
Yes	612	43.71
ED visits (n)	Mean/SD (4.21/5.18)	Min/max (1/72)
1	435	31.07
2	272	19.43
3	172	12.29
4	132	9.43
5	93	6.64
> 5	296	21.14
Admittances (n)	Mean/SD (0.99/1.72)	Min/max (0/21)
0	743	53.07
1	352	25.14
2	145	10.36
≥ 3	160	11.43

#### Characteristics of the study population

The patient characteristics are detailed in Table 1. Over a period of 12 years (2000–2012), 1,400 patients with gynecologic cancer visited the ED. The mean age of these patients was  $55.22 \pm 14.60$  years. Most of them were between 40 and 60 years (age 40–49 years, 25.21%; age 50–59 years, 24.93%). The majority of the ED visits occurred at medical center ( $n=988$ , 70.57%) rather than regional or district hospital ( $n=412$ , 29.43%). In addition, the majority of the patients visited the ED in densely populated cities in Taiwan (northern, central, and southern) rather than in sparsely populated area (eastern:  $n=24$ , 1.71%). The most common site of gynecologic cancer was cervix (ICD-9-CM Codes 180) (53.79%), followed by ovary, and other uterine adnexa (ICD-9-CM Codes 183) (24.29%), and the floor of body of uterus (ICD-9-CM Codes 182) (21.93%).

#### Frequency of ED visits and hospitalizations

In Table 1, regarding the proportion of ED visits, 435 (31.07%) patients visited the ED one time, 272 (19.43%) patients two times, 172 (12.29%) patients three times, 132 (9.43%) patients four times, 93 (6.64%) patients five times, and 296 (21.14%) patients more than five times. The mean number of ED visits was  $4.21 \pm 5.18$  (min/max=1/72). Although 743 (53.07%) patients did not require admission to the hospital, 352 (25.14%) patients were admitted one time, 145 (10.36%) patients two times, and 160 (11.43%) patients more than three times. The mean number of admittances was  $0.99 \pm 1.72$  (min/max=0/21).

#### Prognosis and survival

The overall survival rate of gynecologic cancer patients significantly decreased over time in the ED visitor group compared with the non-ED visitor group ( $p < 0.0001$ ) (Figure 3). There was no significant difference in the ovary and other uterine adnexa cancer group ( $p = 0.0649$ ) (Figure 4).

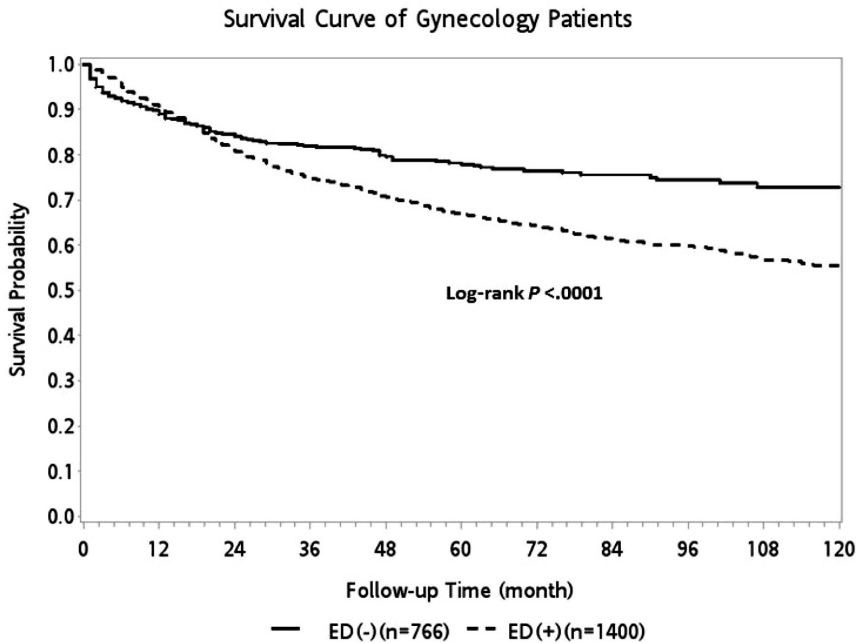


Figure 3. — Kaplan-Meier survival curves for gynecologic cancer patients who visited the emergency department (ED) (dashed line) and who did not visit the emergency department (ED) (solid line).

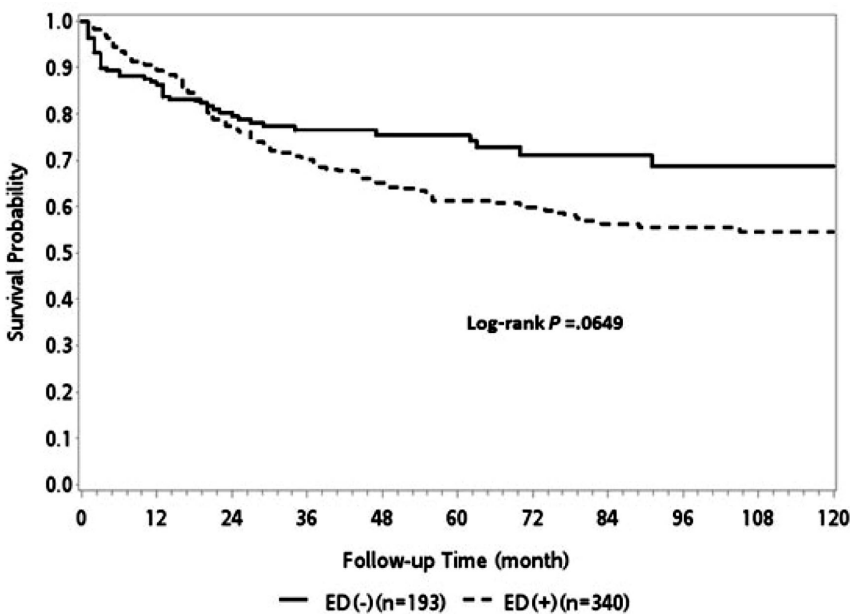


Figure 4. — Kaplan-Meier survival curves for ovary and other uterine adnexa cancer patients who visited the emergency department (ED) (dashed line) and who did not visit the emergency department (ED) (solid line).

*Diagnoses and medicines prescribed at ED visits*

As shown in Table 2, a rank-order list of diagnoses was generated, and ED visits were categorized based on the top ten diagnoses (accounting for 98.63% of all diagnoses) and were ranked as follows: other symptoms, signs, and ill-defined conditions (ICD-9-CM: 7800-7805, 7807-784, 7854-7859, 7861-787, 7881, 7883-7889, 7891-796, 7981-7989, 7990, 7992-7999; percentage: 24.79%), abdominal pain

(ICD-9-CM: 7890; percentage: 19.04%), complications of surgical and medical care (ICD-9-CM: 996-999, E870-E879, E930-E949; percentage: 13.28%), intestinal obstruction without mention of hernia (ICD-9-CM: 540-562; percentage: 10.69%), pyrexia (fever) of unknown origin (ICD-9-CM: 7806; percentage: 10.36%), open wounds and injury to blood vessels (ICD-9-CM: 870-904; percentage: 6.66%), fractures (ICD-9-CM: 800-829, E800-E848; per-



Table 2. — Presenting diagnosis and drug categories of gynecologic cancer patients who visited the ED (n = 1,400).

Ranking	Diagnosis	No.	%	Drug category	No.	%
1	Other symptoms, signs, and ill-defined conditions	603	24.79	Alimentary tract and metabolism	5468	20.81
2	Abdominal pain	463	19.04	Drugs for acid-related disorders	4705	17.91
3	Complications of surgical and medical care	323	13.28	Antiemetics and antinauseants	3582	13.63
4	Intestinal obstruction without mention of hernia	260	10.69	Drugs for functional gastrointestinal disorders	2684	10.21
5	Pyrexia (fever) of unknown origin	252	10.36	Antihemorrhagics	2649	10.08
6	Open wounds and injury to blood vessels	162	6.66	Stomatological preparations	1883	7.17
7	Fractures	82	3.37	Nervous system	1733	6.6
8	Intracranial and internal injuries, including nerves	54	2.22	Antithrombotic agents	1559	5.93
9	Renal colic	41	1.69	Anesthetics	431	1.64
10	Constipation	35	1.44	Anti-infectives for systemic	253	0.96

centage: 3.37%), intracranial and internal injuries, including nerves (ICD-9-CM: 850-869, 950-957; percentage: 2.22%), renal colic (ICD-9-CM: 7880; percentage: 1.69%), constipation (ICD-9-CM: 5640; percentage: 1.44%). According to the drug use characteristics of the patients with gynecologic cancer who presented to the ED, ten categories (accounted for 94.94% of all medicines) are also listed and ranked in Table 2. Within these ten drugs categories, four of them were gastrointestinal related medicines (62.56%), including alimentary tract and metabolism (20.81%), acid related disorders (17.91%), antiemetics, and antinauseants (13.63%), and functional gastrointestinal disorders (10.21%). The remaining categories were antihemorrhagics (10.08%), stomatological preparations (7.17%), nervous system (6.6%), antithrombotic agents (5.93%), anesthetics (1.64%), and anti-infectives for systemic use (0.96%).

## Discussion

The age distribution of the gynecological cancer patients with ED visits in the present study was mainly above the age of 40 years and accounted for 86.5% of all visits. In the 1990s, the incidence rate of cervical cancer in Taiwan was about 26% and declined to less than 20% after 2005. This decline largely is the result of many women getting regular Pap smear test, which can detect cervical dysplasia before it turns into cancer. Though the incidence of cervical cancer decreased gradually in the last ten years in Taiwan, malignant neoplasm of cervix uteri still account for 53.79% of the gynecologic cancer ED visits.

In the present study, 31.07% of gynecologic cancer patients had one ED visit and 27.78% of patients had more than four times ED visits. The mean number of ED visits was  $4.21 \pm 5.18$ . Surprisingly, the maximal ED visits was 72 times. According to the statistics of Health Promotion Administration in Taiwan, the crude incidence rates (per 100,000) from 2000 to 2011 of cervical cancer, corpus uteri cancer, and ovarian cancer were from 26.78% to 14.45%, 5.7% to 14.87%, and 7.26% to 10.73% respectively [4]. Though the individual incidence rate of the gynecologic

cancers had growth and declined from 2000 to 2011, the total incidence rate of gynecologic cancers remains almost consistently at about 40%. Nevertheless, the number of ED visits increased steadily from 111 in 2000 to 775 in 2012 - nearly seven times of the ED visits numbers in 2000 and 46.93% of ED visits resulted in admission to the hospital. Mayer *et al.* found that the cancer survivors living in North Carolina in 2008 had 1.4 ED visits per person and 63.2% of visits resulted in hospitalization [8]. In the systemic review of Vandyk *et al.* also found over half of ED visits (median 58%) for adult cancer patients resulted in admission [9]. The admission rate in the present gynecologic cancer patients seemed to be lower than the average rate in literature reports. In Taiwan NHI, cancer is one of the major illnesses. Patients with a valid major illness certificate who had received medical treatment for cancer-related conditions are exempted from co-payment of either outpatient or inpatient care. The policy really lightens the financial burden of those who had major illness, but it may also result in these patients group seeking medical advice more frequently. The relatively low hospital admission rate in the present cohort demonstrates the existence of unnecessary ED visits indirectly. In Taiwan, Yang *et al.* 2013 showed that the total medical expenditure on ED visits in the major illness patients group was significantly greater than that for non-major illness group [7]. Obvious increasing the number of ED visits of the gynecologic cancer patients will result in the financial burden of the present healthcare insurance system.

Kedia *et al.* found higher ED utilization for pediatric headache in January and September - the same months associated with school return from vacation. The main reasons were changes in daily lifestyle rather than school itself [10]. Hawken *et al.* revealed there was seasonal variation in rates of ED visits following infant vaccinations [11]. In Brazil, Valenca *et al.* also found that asthma consultations in ED were significantly higher in March and lower in August and September. The seasonal variations in ED visits for asthma attacks resulted from proliferation of house dust, mites, and molds [12]. From these literature reports, we can

see that if the increment of ED visits are in correlation with a specific month or season, it is always due to a specific cause. In the present study, the highest number of ED visits occurred in August and there appears to be no specific relation between disease and season or climate. The month with the lowest number of visits in the present cohort was February. Chinese New Year, the most important holiday in the Chinese culture, is always in February. The long break of Chinese New Year and the custom of avoiding hospitals during this period may be the main reason of low ED visits.

The most common presenting symptoms of ED visits were febrile neutropenia (FN), infection, pain, fever, and dyspnea [9]. Mueller *et al.* found fever and neutropenia was the most common reason for ED visit among pediatric cancers, accounting for almost 20% of visits [13]. Fever, the fifth-ranking cause in the present cohort, accounted for 10.36% of presenting symptoms. FN caused by chemotherapy should always be considered first in cancer patients. Primary granulocyte colony-stimulating factor (G-CSF) and antibiotic prophylaxis are effective in reducing FN and infections in patients with chemotherapy [14]. In the present study, the most common problem for ED visits was the group of the other symptoms, signs, and ill-defined conditions (24.79%). They reflect the individuals with cancer at ED with a large number of variable symptoms. Except in the non-specific category, the three most common symptoms were abdominal pain (19.04%), complication of surgical and medical care (13.28%), and intestinal obstruction (10.69%). With regards to gynecologic cancer, these three common symptoms were always related to disease or treatment and may occur at the same time. Like the literature reports, [8] abdominal pain was the most specific complain in the present patients. Intestinal obstruction was another critical symptom, although surgery-induced adhesion or tumor itself should be considered as a cause of the obstruction first [15]. Jackson *et al.* demonstrated that intestinal obstruction accounted for approximately 15% of all ED visits for acute abdominal pain. About 60% of cases result from prior abdominal surgery [16]. It is a medical emergency that requires prompt treatment. Treatment of stable patients with intestinal obstruction and a history of gynecologic procedures present a challenge. Having an appropriate algorithm for evaluation and treatment of patients with suspected intestinal obstruction cannot be overemphasized.

62.56% of drug categories prescribed to the present patients were gastrointestinal related medicines. Such high percentage of using gastrointestinal drug category may result from the side effects of treatment modality such as surgery, radiotherapy, and chemotherapy or cancer cachexia itself. 43.71% of our patients were prescribed chemotherapy. Chemotherapy, either used alone or with radiation, plays an important role in the treatment of patients with gynecologic cancer [17]. Nausea used to be one of the most

unbearable side effects of chemotherapy. They may cause cancer patients to eat less and lose weight, thereby increasing morbidity. The priority of these cancer patients is enteral or parenteral nutrition support. An optimized nutritional support can prevent a further deterioration of the general status of the patients [18].

Karaca *et al.* found the mean duration for ED visits at urban hospitals were essentially higher when compared to rural hospitals in spite of patients' discharge disposition. In a similar way, mean duration of visits at teaching hospitals relative to non-teaching hospitals were abundantly longer for patients who transferred to other facilities [19]. Although Papanikolaou *et al.* do not suggest that a healthcare facility's teaching status on its own markedly improves or worsens patient outcomes [20], teaching hospital or medical centers do possess comprehensive resources and are able to care for patients with more complicated conditions. Therefore, it is not surprising that 70.57% of ED visits in the present study were in medical centers. In Taiwan, all the 14 medical centers and most metropolitan hospitals are located in Western Taiwan, where it is densely populated. Only one would be medical center is in Eastern Taiwan, located in a sparsely populated area; hence, the majority of the ED visits (98.29%) in this cohort occurred in a densely populated area.

Sadik *et al.* conducted a retrospective review of 408 cancer patients with ED visits and found the one-year median survival for all cancer patients was 7.3 months [21]. The mortality rate of cancer patients admitted to the ED was 46.8% and 61.2% died within the first month. Many studies also found that admission to the ED was a poor prognosis factor [22, 23]. Consistent with this, the present study also found the overall survival rate to be significantly better in no ED visits group than ED visits group ( $p < 0.0001$ ). From the perspective of individual cancer groups, there was no significant survival difference in the ovary and other uterine adnexa cancer patients. It may be due to more cases of advanced-stage disease in this cancer group because of the difficulty in early detection [24]. This result informs us to make a greater effort to reduce cancer patients ED visits and to identify patients with ovarian and other adnexal cancer earlier.

#### *Limitations of the study*

There were some limitations in the present study using the NHIRD database. First, the diagnoses of gynecologic cancers were dependent on ICD codes used in the NHIRD database; the registration of ICD-9-CM codes was perhaps different in various hospitals. The NHIRD database lacks information regarding cancer staging, regimen of chemotherapy, type of surgical intervention, which may be risk of some presenting symptoms. Second, the present study is limited by its retrospective nature. The relatively large number of patients ensures that the result generated from this study is minimally affected by selection and recall

bias. The major strength of this study lies in its large sample size because 99.9% of Taiwan's populations were enrolled.

## Conclusion

More than half of gynecologic cancer patients with ED visits are cervical cancer patients. Medical centers became a popular place for patients to receive medical treatment because they possess comprehensive ability to care for complicated conditions of cancer. The relatively low rate of hospital admission indicated possibility of unnecessary ED visits. Among cancer patients in the ED with diverse cancer or treatment-related symptoms, gastrointestinal-related symptoms are the major categories. An appropriate algorithm for evaluation and treatment of patients with suspected intestinal obstruction is important. Gastrointestinal medicines are the most commonly prescribed drugs and the trend of prescriptions will remind us to pay attention to the nutritional support of cancer patients. The overall survival rate of ED visits was significantly lower than that of no ED visits.

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