International Urogynecology Journal (2018) 29:1669–1674
https://doi.org/10.1007/s00192-018-3689-0

ORIGINAL ARTICLE

Pelvic organ prolapse surgery following hysterectomy with benign indication: a national cohort study in Taiwan

Huei-Kai Huang[1] · Dah-Ching Ding[2,3]

Received: 9 February 2018 / Accepted: 6 June 2018 / Published online: 19 June 2018

Abstract

Introduction and hypothesis Hysterectomy and pelvic organ prolapse (POP) surgeries are two of the most common gynecologic surgeries conducted for benign conditions. This nationwide retrospective cohort study explored the risk of subsequent POP surgery following hysterectomy without simultaneous POP surgery.

Methods This study identified 7298 patients who underwent hysterectomy between January 1, 2000, and December 31, 2012, from the Taiwan National Health Insurance (NHI) Research Database. A comparison cohort was constructed comprising 29,192 age-matched patients who had not undergone hysterectomy. All hysterectomy and control patients were followed until they required POP surgery, withdrew from the NHI system, died, or December 31, 2012. Patients were excluded if they underwent POP surgery before or at the time of hysterectomy.

Results The adjusted hazard ratio (aHR) of subsequent POP surgery in subjects with hysterectomy was higher [2.60, 95% confidence interval (CI) 1.79–3.78] than that of controls during the follow-up period. Compared with patients who had not undergone hysterectomy, the highest risks of subsequent POP surgery was noted in those who had undergone vaginal hysterectomy (VH; HR 6.29, 95% CI 1.54–25.79) followed by those who underwent laparoscopy-assisted VH (LAVH; HR 3.77, 95% CI 2.43–5.85).

Conclusions Hysterectomy may increase the risk of subsequent POP surgery, and various hysterectomy techniques, particularly VH and LAVH, may increase the risk of subsequent POP surgery.

Keywords Hysterectomy · Pelvic organ prolapse · Cohort · Risk

Introduction

Hysterectomy and pelvic organ prolapse (POP) surgeries are two of the most common gynecologic surgeries performed for benign conditions [1], and the incidence of hysterectomy among Taiwanese women is 2.68–3.03 per 1000 women and 3.0 per 10,000 women, respectively [2, 3].

POP affects approximately 8% of women, and the need for POP surgery is expected to increase by nearly 50% over the next 40 years [4]. The risk factors of POP included parity, advanced age, chronic constipation, connective tissue disorder, obesity, race, and ethnicity [5]. However, the role of hysterectomy in the development of subsequent POP is controversial [6–9], making its epidemiology a subject of considerable discussion. The risk may depend on age, whether prolapse is present at the time of hysterectomy, and the surgical approach [10, 11].

We hypothesized hysterectomy might be associated with the risk of subsequent POP surgery. We use Taiwan's National Health Insurance Research Database (NHIRD) to explore the risk of POP surgery following hysterectomy for those who had not previously experienced POP between 2000 and 2013.

Materials and methods

Data sources

The sampling cohort data set was obtained from the Taiwan's National Health Insurance Research Database (NHIRD). The

✉ Dah-Ching Ding
dah1003@yahoo.com.tw

[1] Department of Family Medicine, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan

[2] Department of Obstetrics and Gynecology, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Tzu Chi University, Hualien, Taiwan

[3] Institute of Medical Sciences, Tzu Chi University, Hualien, Taiwan

National Health Insurance (NHI) program of Taiwan is a single-payer health insurance system administered by the government and implemented in 1995. It covers more than 99% of the Taiwanese population and is in a contractual relationship with 97% of Taiwanese hospitals and clinics. For research purposes, the National Health Research Institute (NHRI) of Taiwan randomly and systemically sampled a representative database using the registry of all NHI beneficiaries from the year 2000; this database, called the Longitudinal Health Insurance Database (LHID), includes data of 1 million people. As reported by NHRI, there are no statistically significant differences between the ages and healthcare expenditures of the sample cohort in LHID and all NHI beneficiaries in Taiwan. For data security and patient privacy, the NHI Bureau encrypted personal identification prior to releasing the database [12].

In this study, the LHID was used to retrieve patient characteristics and medical records, including inpatient care claims, outpatient records, and the registry of beneficiaries. The study protocol was approved by the Institutional Review Board of Tzu Chi Medical Center (REC No.: IRB104-118-C).

Study population

The study population comprised hysterectomy and nonhysterectomy (comparison) cohorts. The hysterectomy cohort comprised adult women, aged 20–50 years, who had received hysterectomy for benign indications between January 2000 and December 2012. Patients recruited in 2012 were followed up for at least 1 year. The date of admission for hysterectomy was defined as the index date. Hysterectomies were first identified using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure codes, combined with the operation code in the NHIRD, and further classified into four different categories according to the operation method used: subtotal abdominal hysterectomy (STAH), total abdominal hysterectomy (TAH), vaginal hysterectomy (VH), and laparoscopy-assisted VH (LAVH). To ensure that patients underwent hysterectomy for a benign indication, patients who had previously received a diagnosis of cervical, ovarian, or endometrial cancer were excluded (ICD-9-CM codes: 179–180, 182, and 183), together with those who underwent radical hysterectomy. Patients aged < 20 years were excluded; in addition, those aged > 50 years were excluded because menopause is a risk factor for POP. Patients who had been diagnosed with POP (ICD-9-CM code: 618) or had undergone any surgery for POP before the index date were also excluded. Besides, patients who already had symptoms of urinary system (ICD-9-CM code: 788) previously were also excluded (Fig. 1).

The comparison cohort was selected from LHID. Four patients who had not undergone hysterectomy were matched with one patient who had received hysterectomy (1:4) by age and index year. In both cohorts, patients were excluded if they had a history of cervical, ovarian, or endometrial cancer, POP, POP surgery, or symptoms of urinary system before the index date. The index dates of patients in the comparison cohort were defined according to the same index dates of their matched cases, and the nonhysterectomy patients began their follow-ups from this date.

Primary outcome and covariates

The primary outcome was defined as having undergone POP surgery during the follow-up period. Surgical procedures for POP included anterior colporrhaphy, posterior colporrhaphy, the Manchester procedure, abdominal sacrocolpopexy, vaginal sacrospinous fixation, abdominal and vaginal enterocele obliteration and colpocleisis, and pelvic reconstruction surgery. All surgical procedures for POP were considered as single outcomes in our analyses. The patients were followed from the index date until they underwent POP surgery, withdrew from LHID, died, or December 31, 2013 (the last date in the database). The risks of POP surgery following hysterectomy were compared between the hysterectomy and nonhysterectomy cohorts. To evaluate the effect of different hysterectomy operation methods, the hysterectomy cohort was further divided into four subgroups, namely STAH, TAH, VH, and LAVH, which were respectively compared with the comparison cohort.

The baseline comorbidities listed in Table 1 were identified according to ICD-9-CM codes: diabetes mellitus (250), hypertension (401–405), COPD (490–496), connective tissue diseases (710), and urinary tract infection (590, 595, 597, and 599.0). These comorbidities had to be diagnosed by at least by one inpatient service or two outpatient services within a 1-year period before the index date. Socioeconomic status was assessed on the basis of each individual's income level and urbanization level of their place of residence, according to NHIRD data. Income levels were determined according to NHI premiums (through income-related insurance premiums as a proxy of income) and classified into four intervals [financially dependent, New Taiwan Dollar (NT$) 1–NT$19,999, NT$20,000–NT$39,999, and ≥ NT$40,000]. Urbanization levels were divided into five levels for analysis [13]. The detailed descriptions used to identify income and urbanization levels have been described in previous studies [14].

Statistical analysis

All statistical analyses were conducted using Stata (version 13; Stata Corp., College Station, TX, USA), and a two-sided p value of <0.05 was considered statistically significant. Categorical variables, presented as number and percentage, were analyzed using the chi-square test. The Kaplan-Meier

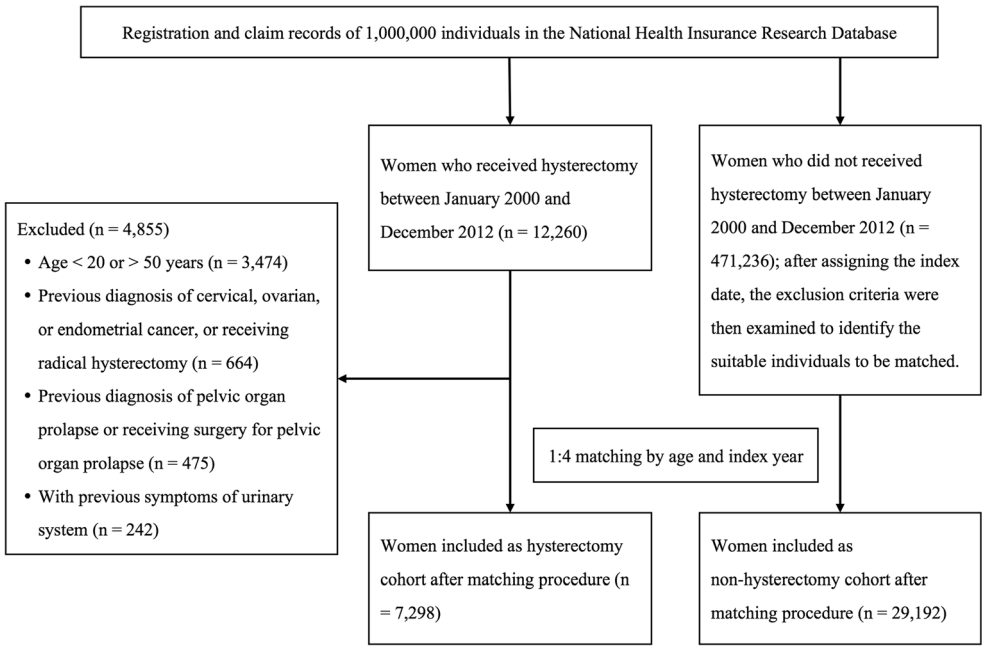

Fig. 1 Flow chart for identifying the study cohorts from the National Health Insurance Research Database

Table 1 Baseline characteristics of patients with and without hysterectomy

	Hysterectomy		
	Yes ($n = 7298$)	No ($n = 29,192$)	P value
Age (years)			1.000
< 40	1145 (15.7%)	4580 (15.7%)	
40–44	2857 (39.1%)	11,428 (39.1%)	
45–50	3296 (45.2%)	13,184 (45.2%)	
Income level (NTD)			< 0.001
Financially dependent	1280 (17.5%)	5412 (18.5%)	
1–19,999	4137 (56.7%)	15,722 (53.9%)	
20,000–39,999	1326 (18.2%)	5659 (19.4%)	
≥ 40,000	555 (7.6%)	2399 (8.2%)	
Urbanization level			< 0.001
1 (Most urbanized)	2444 (33.5%)	10,666 (36.5%)	
2	2220 (30.4%)	8479 (29.0%)	
3	1305 (17.9%)	5043 (17.3%)	
4	857 (11.7%)	3305 (11.3%)	
5 (Least urbanized)	472 (6.5%)	1699 (5.8%)	
Comorbidities			
Hypertension	646 (8.9%)	1514 (5.2%)	< 0.001
Diabetes mellitus	250 (3.4%)	661 (2.3%)	< 0.001
COPD	141 (1.9%)	411 (1.4%)	0.001
Connective tissue diseases	38 (0.5%)	151 (0.5%)	0.971
Urinary tract infection	685 (9.4%)	1488 (5.1%)	< 0.001

Categorical data were expressed as number (%)

COPD, chronic obstructive pulmonary disease; NTD, new Taiwan dollars

method was used to estimate the cumulative incidence curves, and the log-rank test was employed to determine differences between group curves. Univariate and multivariate Cox proportional hazard regression models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for undergoing POP surgery. All baseline characteristics (Table 1) were used for adjustment when employing the multivariate Cox proportional hazard regression model.

Results

Patient characteristics

The hysterectomy cohort included 7298 women who had undergone hysterectomy, whereas as the nonhysterectomy cohort comprised 1:4 age- and index date-matched patients who had not undergone hysterectomy ($n = 29,192$). The mean age of the study population was 43.6 years. The results showed differences in the baseline characteristics of income levels, urbanization levels, and comorbidities between the two cohorts; nevertheless, differences in income and urbanization levels were proportionally minor between the groups (Table 1). However, the hysterectomy cohort had a higher proportion of comorbidities, including hypertension, diabetes mellitus, COPD, and urinary tract infection (Table 1).

Risk of subsequent POP surgery

The median follow-up time is 7.9 years, with interquartile range of 4.5 to 11.2 years. During the follow-up period, 47

hysterectomy and 69 nonhysterectomy patients underwent POP surgery (8.3/10,000 and 3.0/10,000 person-years, respectively). For women undergoing POP surgery, the median interval between the index date and POP surgery was 3.8 years, with POP surgery being performed at a mean age of 48.0 years. The Kaplan-Meier analysis revealed that the hysterectomy cohort had a significantly higher cumulative incidence of undergoing POP surgery than did the nonhysterectomy cohort (log-rank test, $p < 0.0001$; Fig. 2). Compared with the nonhysterectomy cohort, Cox proportional hazard regression models showed an increased risk of POP surgery in the hysterectomy cohort in both univariate (crude HR 2.74, 95% CI 1.89–3.96, $p < 0.001$) and multivariate [adjusted HR (aHR) 2.60, 95% CI 1.79–3.78, $p < 0.001$] models (Table 2).

Association of subsequent POP surgery risk with hysterectomy techniques

Compared with the nonhysterectomy patients, the risk of receiving POP surgery was significantly higher in patients who had undergone TAH, LAVH, and VH. Patients who underwent VH had the highest risk of subsequent POP surgery (aHR 6.29, 95% CI 1.54–25.79, $p = 0.011$) followed by those who underwent LAVH (aHR 3.77, 95% CI 2.43–5.85, $p < 0.001$) and then by those who underwent TAH (aHR 1.92, 95% CI 1.11–3.32, $p = 0.020$). However, because of an insufficient number of cases, HRs could not be calculated for STAH (Table 3).

Discussion

Our patients underwent hysterectomy at a median age of 43.6 years (range 40–50 years); with an income of < NT$20000, they were more urbanized and had high comorbidity rates. Compared with the comparison cohort, the risk of POP surgery following hysterectomy was higher (aHR 2.63; Table 2); relatively higher HRs for subsequent POP surgery risk were also noted for VH, LAVH, and TAH individually.

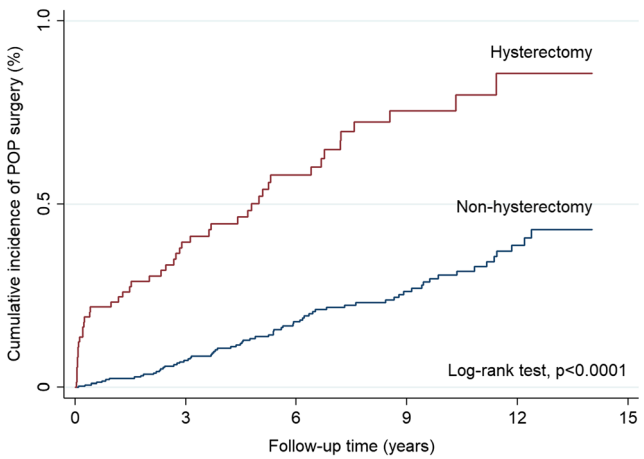

Fig. 2 Cumulative incidences of undergoing subsequent pelvic organ prolapse (POP) surgery for hysterectomy and nonhysterectomy patients

Table 2 Risks of receiving pelvic organ prolapse surgery among patients with and without hysterectomy

	Hysterectomy	
	Yes	No
Patient numbers	7298	29,192
POP surgery cases	47	69
Person-years	56,790.2	228,123.4
Incidence rate*	8.3	3.0
Univariate model		
Crude HR (95% CI)	2.74 (1.89–3.96)	1 (ref.)
p value	< 0.001	
Multivariate model†		
Adjusted HR (95% CI)	2.60 (1.79–3.78)	1 (ref.)
p value	< 0.001	

*Per 10,000 person-years

†Multivariate Cox proportional hazard regression model, adjusting for all baseline characteristics listed in Table 1

POP, pelvic organ prolapse; HR, hazard ratio; CI, confidence interval

A case-control study in Sweden showed an increased risk of POP surgery for hysterectomized women compared with nonhysterectomized controls [15], where the risk of POP was found to be highest in the first 5 years following hysterectomy. The Rochester Epidemiology Project database case-control study selected 144 pairs from 8220 women who had undergone hysterectomy; the results showed a median time of 13 years between hysterectomy and pelvic floor repair (POP surgery) [16]. The only risk factor currently identified for developing POP after hysterectomy is chronic obstructive pulmonary disease (COPD) [16]. Another Swedish study showed that women who underwent POP surgery were younger when they received hysterectomy than were women who had not undergone POP surgery [17]. Furthermore, a Danish population-based study showed that 12% of POPs occurred as a long-term complication after hysterectomy. In addition, undergoing hysterectomy at younger age was a risk factor for POP [18]. Our results support the findings of the above studies.

Regarding the surgical methods, the results of previous studies are inconsistent. For instance, the results of a stratified analysis in the US [8]—different from those of our study—revealed that women without POP who underwent VH had the same risk of subsequent POP surgery as did those who underwent TAH. In another Swedish study [19], no difference was found between the STAH and TAH groups for the

Table 3 Risks of receiving pelvic organ prolapse surgery among patients with different hysterectomy procedures

Procedures	n	POP surgery cases	Person-years	Incidence rate*	Univariate model		Multivariate model†	
					Crude HR‡ (95% CI)	*p* value	Adjusted HR‡ (95% CI)	*p* value
Subtotal abdominal hysterectomy	509	0	3254.5	0	None&		None&	
Total abdominal hysterectomy	3509	16	28,018.9	5.7	1.89 (1.10–3.26)	0.022	1.92 (1.11–3.32)	0.020
Laparoscopy-assisted vaginal hysterectomy	3181	29	24,495.9	11.8	3.91 (2.54–6.04)	<0.001	3.77 (2.43–5.85)	<0.001
Vaginal hysterectomy	99	2	1020.9	19.6	6.65 (1.63–27.1)	0.008	6.29 (1.54–25.79)	0.011

*Per 10,000 person-years

†Multivariate Cox proportional hazard regression model, adjusting for all baseline characteristics listed in Table 1

‡The HR of each procedure of hysterectomy was calculated using non-hysterectomy patients as reference

& The HR could not be calculated because of insufficient cases of POP surgery

POP, pelvic organ prolapse; HR, hazard ratio; CI, confidence interval

presence of POP during follow-up. A Danish cohort study [9] found a small difference (HR 1.25) between those undergoing VH and TAH. Nevertheless, a Swedish study [15] found the risk of POP surgery to be 33% higher for women who had undergone STAH than those who had undergone TAH. In our study, no subsequent POP surgeries were noted in the STAH group, but the incidence of POP surgery was 5.9/10,000 person-years in the TAH group (Table 3). Patients who underwent VH had significantly higher risk of subsequent POP surgery (aHR 6.29, 95% CI 1.54–25.79) followed by LAVH (aHR 3.77, 95% CI 2.43–5.85).

Recent trends in hysterectomy have used minimally invasive surgical techniques [2, 3]; therefore, the use of LAVH is currently popular. LAVH has not previously been reported to be associated with the risk of subsequent POP surgery, and this study demonstrated that LAVH carries an aHR of 3.77 (95% CI 2.43–5.85; Table 3). Although we concede the slight possibility that low-grade POP may have been misclassified during registration, we consider that our sources are dependable with respect to the registration of patients with POP grades 2 or higher. The possible reason for the greater risk of POP in patients who underwent VH and LAVH could be the smaller uterine size in these patients compared with those who underwent TAH or that they had greater extendability of the vagina.

The vaginas of parous women may be more extendable than those of nonparous women. In addition, stretching the vaginal, cardinal, and other pelvic region ligaments during vaginal surgery may also predispose patients to subsequent POP [8]. Surgeons generally favor VH for women with a higher parity and a relatively descended uterus, both of which are risk factors for later prolapse. Therefore, the higher rate of prolapse repair after VH may simply reflect that women who are more likely to have prolapses are those who are better candidates for VH, but not that the method of hysterectomy is related to the incidence of prolapse. Thus, an approach using a natural orifice is ideal for surgery, as reflected by the ACOG recommendation that VH be considered as the first choice for route of hysterectomy, when appropriate [20].

A lack of POP surgery following supracervical hysterectomy was noted in our study. In the previous study, the outcomes of patients diagnosed with POP of stage 2 or higher did not significantly differ between patients who underwent TAH and STAH [19]. We speculated the lack of POP surgery following supracervical hysterectomy might have occurred because this type of surgery preserves most ligaments attached to the uterus, which can maintain pelvic cavity stability. However, the previous literature has shown no difference in POP between the two surgeries [10, 11].

The strengths of this study include the use of a national database that includes the majority of the Taiwan population, thereby limiting selection bias, and the long follow-up period of almost 8 years. The registration of all surgeries in NHIRD is mandatory by law to prevent any sampling bias. Furthermore, based on its quality, this registry is suitable for epidemiologic studies [21].

However, our study has several limitations. First, we focused only on women who had undergone POP surgery, but not women with POP who had not undergone POP surgery. Women with lower stages of prolapse are recommended to first try conservative measures, such as pessaries and pelvic floor physical therapy; these are not reflected in our results. Second, this study could not consider potential confounders or modifiers, such as parity, mode of delivery, obesity, race, ethnicity, weight of uterus, body mass index, and smoking, because of no records in our database. Nevertheless, these factors may have affected the results. However, we considered POP surgery status at the time of hysterectomy to be the most important confounder and thus excluded women who had undergone POP surgery before or at the time of hysterectomy. In addition, some of the increased number of comorbidities in the hysterectomy cohort, such as COPD, could have

accounted for the increase in the number of subsequent POP surgeries in the hysterectomy cohort compared with the nonhysterectomy group. Nevertheless, the prevalence of POP in both groups was adjusted for these factors. The status of prophylactic anti-prolapse techniques at the time of hysterectomy was not recorded in the database. Thus, this may cause different surgical techniques to have different POP prevalences.

In conclusion, our nationwide population-based retrospective cohort study provides further evidence of the significant risk of requiring POP surgery following hysterectomy. Furthermore, different hysterectomy techniques may carry significantly higher risks of subsequent POP surgery, particularly VH and LAVH. However, interventions for reducing the risk of POP surgery after hysterectomy should be addressed for all surgery types.

Acknowledgements The authors thank Dr. Jon-Son Kuo for the English editing. This manuscript was edited by Wallace Academic Editing.

Compliance with ethical standards

Conflict of interest None.

References

1. Oliphant SS, Jones KA, Wang L, et al. Trends over time with commonly performed obstetric and gynecologic inpatient procedures. Obstet Gynecol. 2010;116:926–31.
2. Ding DC, Chu TY, Chang YH. Trend changes in the proportion of minimal invasive hysterectomies over a five-year period: a single-center experience. Tzu Chi Med J. 2012;24:136–8.
3. Wu MP, Huang KH, Long CY, et al. Trends in various types of surgery for hysterectomy and distribution by patient age, surgeon age, and hospital accreditation: 10-year population-based study in Taiwan. J Minim Invasive Gynecol. 2010;17:612–9.
4. Geynisman-Tan J, Kenton K. Surgical updates in the treatment of pelvic organ prolapse. Rambam Maimonides Med J. https://doi.org/10.5041/RMMJ.10294.
5. Jelovsek JE, Maher C, Barber MD. Pelvic organ prolapse. Lancet. 2007;369:1027–38.
6. Dällenbach P, Kaelin-Gambirasio I, Dubuisson JB, Boulvain M. Risk factors for pelvic organ prolapse repair after hysterectomy. Obstet Gynecol. 2007;110:625–32.
7. Lukanovic A, Drazic K. Risk factors for vaginal prolapse after hysterectomy. Int J Gynaecol Obstet. 2010;110:27–30.
8. Blandon RE, Bharucha AE, Melton LJ 3rd, et al. Incidence of pelvic floor repair after hysterectomy: a population-based cohort study. Am J Obstet Gynecol. 2007;197:664. **e1–7**
9. Lykke R, Løwenstein E, Blaakær J, Gimbel H. Hysterectomy technique and risk of pelvic organ prolapse repair: a Danish nationwide cohort study. Arch Gynecol Obstet. https://doi.org/10.1007/s00404-017-4470-1.
10. Lethaby A, Mukhopadhyay A, Naik R. Total versus subtotal hysterectomy for benign gynaecological conditions. Cochrane Database Syst Rev. 2012;4:CD004993.
11. Andersen LL, Alling Møller LM, Gimbel HM. Objective comparison of subtotal vs. total abdominal hysterectomy regarding pelvic organ prolapse and urinary incontinence: a randomized controlled trial with 14-year follow-up. Eur J Obstet Gynecol Reprod Biol. 2015;193:40–5.
12. Tsan YT, Lee CH, Wang JD, Chen PC. Statins and the risk of hepatocellular carcinoma in patients with hepatitis B virus infection. J Clin Oncol. 2012;30:623–30.
13. Liu CY, Hung YT, Chuang YL, et al. Incorporating development stratification of Taiwan townships into sampling design of large scale health interview survey.
14. Lin SM, Yang SH, Cheng HY, et al. Thiazide diuretics and the risk of hip fracture after stroke: a population-based propensity-matched cohort study using Taiwan's National Health Insurance Research Database. BMJ Open. 2017;7:e016992.
15. Altman D, Falconer C, Cnattingius S, Granath F. Pelvic organ prolapse surgery following hysterectomy on benign indications. Am J Obstet Gynecol. 2008;198:572. **e1–6**
16. Blandon RE, Bharucha AE, Melton LJ 3rd, et al. Risk factors for pelvic floor repair after hysterectomy. Obstet Gynecol. 2009;113:601–8.
17. Forsgren C, Zetterström J, López A, Altman D. Risk factors for vaginal vault prolapse surgery in postmenopausal hysterectomized women. Menopause. 2008;15:1115–9.
18. Lykke R, Blaakær J, Ottesen B, Gimbel H. Pelvic organ prolapse (POP) surgery among Danish women hysterectomized for benign conditions: age at hysterectomy, age at subsequent POP operation, and risk of POP after hysterectomy. Int Urogynecol J. 2015;26:527–32.
19. Persson P, Brynhildsen J, Kjølhede P. Hysterectomy multicentre study Group in South-East Sweden. Pelvic organ prolapse after subtotal and total hysterectomy: a long-term follow-up of an open randomised controlled multicentre study. BJOG. 2013;120:1556–65.
20. Committee on Gynecologic Practice. Committee opinion, number 701, June 2017, choosing the route of hysterectomy for benign disease.
21. Chien HC, Kao Yang YH, Bai JPF. Trastuzumab-related cardiotoxic effects in Taiwanese women: a nationwide cohort study. JAMA Oncol. 2016;2:1317–25.