



## Comparison of oncologic outcomes of unanticipated cervical carcinoma in women undergoing inadvertent simple hysterectomy and those undergoing surgical treatment after preoperative diagnosis

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### HIGHLIGHTS

- Cervical carcinoma patients (10.8%) were diagnosed after simple hysterectomy.
- Median survival of the inadvertent simple hysterectomy group was comparable to that of the standard treatment group.
- Additional appropriate treatment would help achieve favorable oncologic outcomes.

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### ABSTRACT

**Objectives.** To determine the proportion of women with undiagnosed cervical carcinoma before simple hysterectomy and its causes and to compare the oncologic outcomes of women diagnosed and treated with standard therapy to those undergoing inadvertent simple hysterectomy with subsequent treatment.

**Methods.** Medical records were reviewed for patients with cervical carcinoma who underwent hysterectomy between 1 January 2004 and 31 December 2014. Demographic data, chemotherapeutic agents, and response rates were analyzed using descriptive statistics. The categorical variables were compared using chi-square or Fisher's exact test. The continuous data were compared using the independent *t*-test and Mann–Whitney test, as appropriate. The Kaplan–Meier method was used to evaluate the survival outcomes.

**Results.** Of the 526 patients with cervical carcinoma who underwent hysterectomy, 57 patients (10.8%) were diagnosed with cervical carcinoma after simple hysterectomy. After excluding 121 patients with invasion of <3 mm and without lymphovascular space invasion (LVSI), 353 patients were preoperatively diagnosed with cervical carcinoma stage IA1 with LVSI to IIA and underwent proper surgical treatment. Fifty-two patients were encountered for inadvertent hysterectomy. Forty-four of 52 patients in the inadvertent hysterectomy group consented to subsequent treatment, with 43 patients receiving concurrent chemoradiotherapy and one undergoing additional surgery. The median time before subsequent treatment initiation was 1.6 months [0.5–9.2 months]. The 5-year DFS rates of the standard surgical treatment group and inadvertent hysterectomy group were 88.4% vs. 93.2%, respectively ( $P = 0.147$ ). The 5-year OS rates of the standard surgical treatment group and the inadvertent hysterectomy group were 98.9% vs. 100%, respectively ( $P = 0.767$ ).

**Conclusions.** Women with cervical carcinoma who had small tumors and underwent inadvertent simple hysterectomy with appropriate consequent management had oncologic outcomes comparable to those in the standard surgical treatment group.

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## 1. Introduction

Cervical carcinoma is one of the most important health issues, ranking fourth among cancers in terms of its incidence and mortality rate among women worldwide, with an estimated 569,847 new cases and 311,365 deaths in 2018 [1]. In Thailand, it is the second most common cancer in women after breast cancer, with 5513 new cases diagnosed in 2017 [2]. The standard primary treatment for cervical carcinoma is based on clinical staging. In stage I-IIA, it is usually curable with primary treatment either by surgery or by concurrent chemoradiation (CCRT) but with different treatment-associated complications [3]. A randomized study of patients with stage IB-IIA cervical carcinoma who were treated by either radical surgery or radiotherapy alone showed that after a median follow-up of 87 months, the two groups achieved identical 5-year disease-free survival (DFS) and overall survival (OS) rates of 74% and 83%, respectively. However, severe morbidity was higher in the surgery group than in the radiotherapy group (28% vs. 12%,  $P = 0.0004$ ) [4]. Similar outcomes were confirmed using long-term follow-up data, which revealed that the 20-year OS rates of radical surgery and radiotherapy groups were 72% and 77%, respectively ( $P = 0.280$ ) [5]. The usual surgical procedures for patients with cervical carcinoma clinical stage IA1 without lymphovascular space invasion (LVSI), patients with stage IA1 with LVSI and stage IA2, and patients with stage IB1-IIA are simple hysterectomy, modified radical hysterectomy with pelvic lymphadenectomy (mRHPL), and radical hysterectomy with pelvic lymphadenectomy (RHPL), respectively [3].

Occasionally, cervical carcinoma is discovered after simple hysterectomy. Inadvertent hysterectomy means there has been a postoperative diagnosis of cervical carcinoma, for which simple hysterectomy is inadequate treatment. For complete primary treatment, such patients need additional surgery or CCRT. To the best of our knowledge, there are no comparative data on the oncologic outcomes of patients with cervical carcinoma who received standard surgical treatment versus those who were diagnosed after inadvertent hysterectomy.

The current study had three aims: (1) to determine the proportion of patients for whom cervical carcinoma was diagnosed after simple hysterectomy, (2) to identify the possible causes of patients undergoing inadvertent simple hysterectomy, and (3) to assess and compare the oncologic outcomes of the patients with cervical carcinoma who underwent inadvertent simple hysterectomy with subsequent treatment and patients for whom cervical carcinoma was diagnosed before standard surgical treatment.

## 2. Materials and methods

After approval by the institutional review board (COA no. Si 123/2016), the medical records of all eligible patients were retrieved to collect their demographic data, indications of hysterectomy, tumor characteristics, histopathology, subsequent treatment, and oncologic outcomes. The eligibility criteria were patients for whom cervical carcinoma was diagnosed after simple hysterectomy without evidence of residual diseases. The demographic and clinical data collected included age, body mass index (BMI), menopausal status, parity, underlying diseases, presenting symptoms, and tumor characteristics (including gross appearance, histopathology types and grading, and the International Federation of Gynecology and Obstetrics [FIGO] stage). Cancer stage was assigned retrospectively according to the FIGO 2018 by pathology size instead of clinical staging [3]. Data of all the study patients were analyzed for the proportion of patients for whom cervical carcinoma was diagnosed before and after hysterectomy.

The authors excluded patients who had invasive lesions <3 mm in depth and without LVSI. The study patients were classified into two groups: (i) standard surgical treatment group (patients with cervical carcinoma diagnosed and who underwent clinical staging before hysterectomy), and (ii) inadvertent hysterectomy group (patients with cervical carcinoma diagnosed after simple hysterectomy). Possible causes

of inadvertent hysterectomy were extracted. For the oncologic outcome analyses including DFS and OS, the authors excluded patients who had not consented to subsequent treatments or declined follow-up.

The subsequent radiotherapy consisted of external beam radiation therapy to a total dose of 42–50 Gy in 21–25 fractions (1.8–2 Gy per fraction), followed by high-dose rate intracavitary radiation therapy (ICRT) in 2–3 fractions with doses of 5–5.5 Gy per fraction. The intracavitary radiation therapy could be either vaginal cylinder or ovoids based on the vaginal shape and length. The ICRT dose was prescribed at a 5 mm depth from the vaginal surface for approximately the upper half of the vaginal length. Cisplatin 40 mg/m<sup>2</sup> was administered weekly for a concurrent purpose. The surgical treatment after inadvertent hysterectomy was pelvic lymphadenectomy, radical parametrectomy, and upper vaginectomy. Follow-up visits were scheduled every 3 months for the first two years after the completion of the treatment, subsequently every 6 months for another 3–5 years. Follow-up data were retrieved until 31 December 2017. Recurrent disease was defined by clinical and imaging assessment with or without histology. The DFS time was counted from either the date of inadvertent hysterectomy or the date of the surgical treatment in the standard group to the date of disease recurrence. The OS time was calculated from the date of the initial surgery to the date of death or last contact.

SPSS for Windows, version 18.0 (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis. Data were presented as number with percentage, mean  $\pm$  standard deviation (SD), and median with interquartile range (IQR). The mean values of age and BMI of both study groups were compared using the independent *t*-test. The categorical variables were compared using chi-square or Fisher's exact test. Survival was estimated by the Kaplan–Meier method, and a Cox regression analysis was used to compare the effects of inadvertent simple hysterectomy.

## 3. Results

Overall, 526 patients with cervical carcinoma received hysterectomy, of which, 57 patients (10.8%) were diagnosed after simple hysterectomy. One hundred twenty-one patients were excluded by the pathology of invasion, which was <3 mm in depth, without LVSI. Fifty-two patients were included in the inadvertent hysterectomy group, while 353 patients were included in the standard surgical treatment group (Fig. 1). The possible causes for the inadvertent hysterectomy in the 52 patients in the inadvertent hysterectomy group are summarized in Table 1. The data of patient characteristics, histology, pathology as clinical stages, and subsequent treatment of 52 patients in the inadvertent hysterectomy group are detailed in Table 2. Most of them were in menopause with invasive lesions in pathology stage IB1. Forty-four of 52 patients in the inadvertent hysterectomy group consented to subsequent treatment; all but one of the 44 received a subsequent CCRT.

Patient characteristics and treatment outcomes of the two study groups are compared and represented in Table 3. Patients in the inadvertent hysterectomy group were older and had higher BMI than those in the standard surgical treatment group, significantly. The proportions of histopathology subtype, number and duration of recurrence, and death of the two groups were similar. With regard to the treatment for the 43 recurrent patients in the standard group, 12 patients received systemic chemotherapy, another 12 received radiation therapy or CCRT, 3 underwent surgery, and 16 were given symptomatic treatment. In the case of the 4 recurrent patients in the inadvertent group, one was treated by CCRT and three by chemotherapy.

The median follow-up time was 42 months [IQR, 19.2–68.4 months]. Figs. 2 and 3 showed DFS curves and OS curves of the two study groups. The mean DFS times of the standard surgical treatment and inadvertent hysterectomy groups were 105.6  $\pm$  4.9 vs. 104.9  $\pm$  4.3 months, respectively, while the 5-year DFS rates were 88.4% vs. 93.2% ( $P = 0.147$ ), respectively. The mean OS times of the standard surgical treatment and inadvertent hysterectomy groups were 125.7  $\pm$  0.9 vs. 111.9  $\pm$

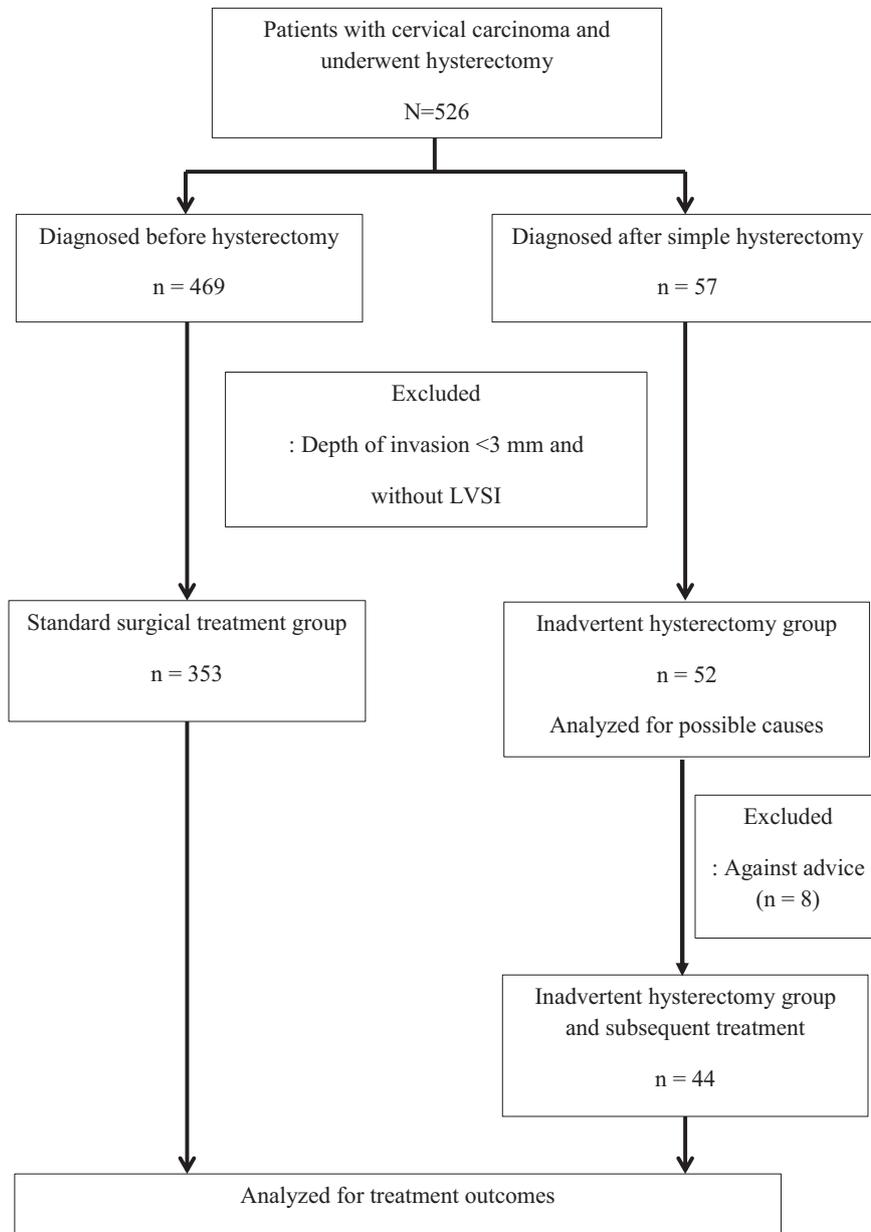


Fig. 1. Flowchart of enrolment and analysis process.

2.4 months, respectively. The 5-year OS rates were 98.9% vs. 100% ( $P = 0.767$ ), respectively.

#### 4. Discussion

The majority of the patients with early-stage cervical carcinoma were primarily treated by surgery. On the basis of the FIGO recommendations for surgical treatment, stage IA1 without LVSI can be treated by

**Table 1**  
Possible causes of 52 patients with cervical carcinoma who underwent inadvertent hysterectomy.

Causes	Number (%)
Cone margins positive/not evaluated	14 (26.9)
False-negative Pap test	12 (23.1)
Inappropriate diagnostic workup	9 (17.3)
Endometrial origin or error of pathology	9 (17.3)
Emergency hysterectomy	3 (5.8)
No available data	5 (9.6)

simple hysterectomy or conization to retain the fertility function. Patients in stage IA1 with LVSI and stage IA2 should be managed by mRHPL. RHPL is suitable for patients in stage IB1-IIA2 [3]. Thus, simple hysterectomy is insufficient for patients with cervical carcinoma stage IA1 with LVSI or higher stages, called inadvertent hysterectomy.

Concordant with previous studies, the current study showed that the most common causes of inadvertent hysterectomy were understaging or the presence of invasive lesions/inadequate evaluation of the cone margins [6–9]. From the cumulative data of 4 previous studies, the potential causes in 197 patients who underwent inadvertent simple hysterectomy were the understaged disease (52%–79.6%), lack of preoperative cervical cancer screening in cases of benign diseases such as myoma uteri (9.4%–12.2%), uterine prolapse (3.3%–16%), and emergency hysterectomy (6.3%–44%) [6–9]. Hence, the pitfall of inadvertent hysterectomy had 4 main causes. First, cervical cancer screening is neglected to be performed before hysterectomy in benign conditions or emergency hysterectomy or there is false-negative cervical cancer screening test results. Second, an inappropriate management of abnormal cervical cancer screening test results, such as making the diagnosis

**Table 2**

Characteristic and subsequent treatment of 52 patients with cervical carcinoma who underwent inadvertent hysterectomy.

Characteristics	Number (%)
Age, years	56 [IQR 46.75–62.75]
Parity	2 [IQR 1–3]
Menopausal status	
Premenopause	10 (19.2)
Postmenopause	42 (80.8)
Histopathology	
Squamous cell carcinoma	29 (55.8)
Adenocarcinoma	21 (40.4)
Endometrioid carcinoma	1 (1.9)
Neuroendocrine	1 (1.9)
Pathology was similar to FIGO stage	
IA2	11 (21.2)
IB1	39 (75.0)
IB2	2 (3.8)
Depth of invasion	
Inner-third	22 (42.3)
Middle-third	7 (13.5)
Outer-third	23 (44.2)
Lymphovascular space invasion	
No	34 (65.4)
Yes	18 (34.6)
Margin status	
Negative	44 (84.6)
Positive for HSIL	1 (1.9)
Positive for carcinoma	7 (13.5)
Uterine involvement	
Negative	47 (90.4)
Positive for carcinoma	5 (9.6)
Adnexal involvement (n = 44)	
Negative	42 (95.5)
Positive for carcinoma	2 (4.5)
Further treatment	
Refuse	8 (15.4)
Radiation	43 (82.7)
Re-operation	1 (1.9)

Abbreviations: IQR, interquartile range; FIGO, International Federation of Gynecology and Obstetrics; HSIL, high-grade squamous intraepithelial neoplasia.

by colposcopy without a biopsy or diagnostic conization. Third, the squamocolumnar junction and transformation zone are difficult to evaluate in some situations such as menopausal women or nulliparous or women with endocervical lesions and also a missed interpretation of pathology. To overcome these causes, clinicians should be careful in the pelvic examination and choose the preoperatively appropriate cervical cancer screening methods for patients who have benign diseases with simple hysterectomy schedules. In the case of abnormal cervical cancer screening tests, the mandatory step of diagnostic investigations has to be followed. In the operative theater, meticulous organ exploration and frozen section pathology should be considered in selected cases. Obtaining a second opinion on a pathology report or requesting an additional immunohistochemistry test might be helpful in difficult situations. Essentially, clinicians should avoid inadvertent hysterectomy to the greatest extent possible.

After inadvertent hysterectomy, subsequent treatment is necessary for cure, such as (i) additional parametrectomy with upper vaginectomy with bilateral pelvic lymphadenectomy or (ii) CCRT; however, there is no “best choice.” In a study in France on 29 patients with inadvertent hysterectomy, 13 patients underwent the second operation and 8/13 patients (61.6%) had no adjuvant treatment. The remaining 16 patients received secondary treatment with radiation, with or without cisplatin. The surgery group had significantly better survival outcomes than the radiation group; the 5-year DFS rates were 86% vs. 37% ( $P = 0.02$ ), while the 5-year OS rates were 100% vs. 77% ( $P = 0.04$ ), respectively [10]. However, the researchers did not define the criteria for patient-group selection. Moreover, 11/18 of patients (61.1%) who were in pathological stages IA2&IB1 underwent the second operation and 7/9 patients (77.8%) who were in pathological stage IB2&IIB

**Table 3**

Patient characteristics and treatment outcomes of 353 patients in the standard surgical treatment group compared with 44 patients in the inadvertent hysterectomy group who received subsequent treatment.

Variables	Standard, n (%)	Inadvertent, n (%)	P
	N = 353	N = 44	
Age, years	48.7 ± 10.1	54.4 ± 9.5	<0.001
Body mass index, kg/m <sup>2</sup>	24.3 ± 4.2	26.0 ± 4.9	0.014
Stage as			
IA2	13 (3.7)	8 (18.2)	<0.001
IB1	199 (56.4)	34 (77.3)	
IB2	104 (29.5)	2 (4.5)	
IB3	37 (10.4)	0	
Histopathology			
SCCA	191 (54.1)	22 (50.0)	0.606
Non-SCCA	162 (45.9)	22 (50.0)	
Depth of invasion			0.004
Inner-third	136 (38.5)	14 (31.8)	
Middle-third	92 (26.1)	7 (15.9)	
Outer-third	114 (32.3)	23 (52.3)	
Aborted hysterectomy	11 (3.1)	0	
LVSI			0.297
No	228 (64.6)	26 (59.1)	
Yes	114 (32.3)	18 (40.9)	
Aborted hysterectomy	11 (3.1)	0	
Margin status			0.001
Negative	326 (92.4)	36 (81.8)	
Positive for HSIL/AIS	6 (1.7)	1 (2.3)	
Positive for carcinoma	10 (2.8)	7 (15.9)	
Aborted hysterectomy	11 (3.1)	0	
Uterine involvement			0.044
Negative	316 (89.5)	39 (88.6)	
Positive for HSIL/AIS	12 (3.4)	0	
Positive for carcinoma	13 (3.7)	5 (11.4)	
Aborted hysterectomy	11 (3.1)	0	
Adnexal involvement			0.001
Negative	265 (75.1)	36 (81.8)	
Positive for carcinoma	3 (0.8)	2 (4.5)	
Did not perform SO	85 (24.1)	6 (13.7)	
Recurrence	43 (12.2)	4 (9.2)	0.147
Locoregional	22	2	
Distant	14	2	
Both	7	0	
Recurrence within			
12 months	12 (3.8)	0	
24 months	30 (10.3)	2 (5.2)	
36 months	38 (13.8)	3 (8.0)	
Death	4 (1.1)	1 (2.3)	0.767
Death within			
12 months	0	0	
24 months	1 (0.4)	0	
36 months	2 (0.8)	0	

Abbreviations: AIS, adenocarcinoma in situ; HSIL, high-grade squamous intraepithelial neoplasia; LVSI, Lymphovascular space invasion; SCCA, squamous cell carcinoma.

received radiation therapy. In addition, 5/13 patients (38.5%) in the surgery group received adjuvant radiation. These treatment approaches might have worsened the prognosis of the radiation group, confounded by the more advanced stage of the disease and the benefit of adjuvant radiation in the surgery group. In contrast, in another study of IA2-IIA lesions arising from inadvertent hysterectomy, there was a similar therapeutic efficacy of additional radical surgery (29 patients) and radiotherapy with or without chemotherapy (44 patients): the 10-year DFS rates were 100% vs. 93% ( $P = 0.315$ ) and the 10-year OS rates were 100% vs. 94% ( $P = 0.935$ ), respectively [11]. To prevent the compounding of treatment-related complications, an additional surgery is preferred in patients who are less likely to require postoperative adjuvant radiotherapy with or without chemotherapy according to the Gynecologic Oncology Group criteria (GOG) [12,13]. Briefly, patients who have one of the high pathologic risk factors such as pelvic lymph node metastasis, parametrium metastasis, or surgical margin involving high-grade squamous intraepithelial neoplasia (HSIL) or carcinoma were considered to have a high risk of disease recurrence and need

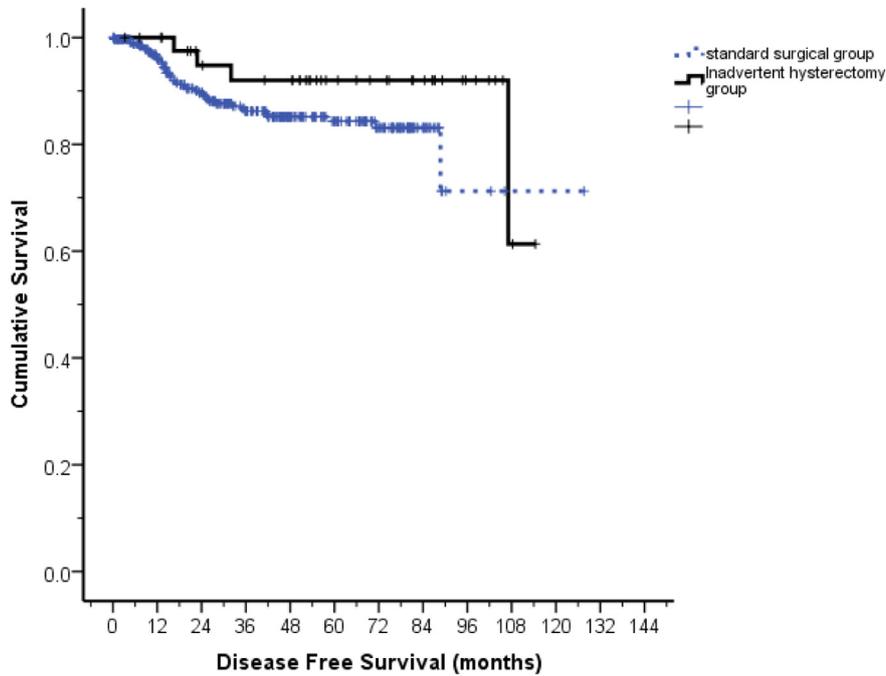


Fig. 2. Disease-free survival curves of 353 patients in the standard surgical treatment group and 44 patients in the inadvertent hysterectomy group ( $P = 0.147$ ).

CCRT after radical surgery to obtain DFS and OS benefits [12]. Patients who have the intermediate pathologic risk factors specified in the GOG 92 criteria (i.e., more than one-third cervical stromal invasion, a tumor diameter  $\geq 4$  cm, and the presence of LVSI) should receive further adjuvant external-beam radiotherapy [13,14]. Other substantial considerations are the complications associated with subsequent treatment. For example, young women who want to preserve their ovarian and vaginal functions prefer additional surgery. On the basis of the cumulative data of previous studies, a total of 173 patients who underwent inadvertent hysterectomy and received additional surgery had negative malignancies as high as 76.3% in their surgical specimens [8,10,11,15–19]. To avoid multimodality treatment, investigations

such as magnetic resonance imaging (MRI), computed tomography (CT), or positron emission computed tomography (PET-CT) would be helpful to triage the risk of adjacent organ metastasis before choosing the subsequent treatment [3,20].

Data from literature reporting subsequent treatment outcomes of inadvertent hysterectomy showed average 5-year OS of radiotherapy was 30%–100% (mostly without chemotherapy) and additional surgery was 38.3%–100% (Table 4) [7,8,10,11,15–19,21–36]. For primary treatment of FIGO stage IB1, IB2, or IIA cervical cancer, both radical surgery and radiotherapy have been shown to be equally effective with 5-year OS rates of 83%–95% and 5-year DFS rate of 70%–74% [4,37]. These rates were consistent with those in the current study. Interestingly, the survival

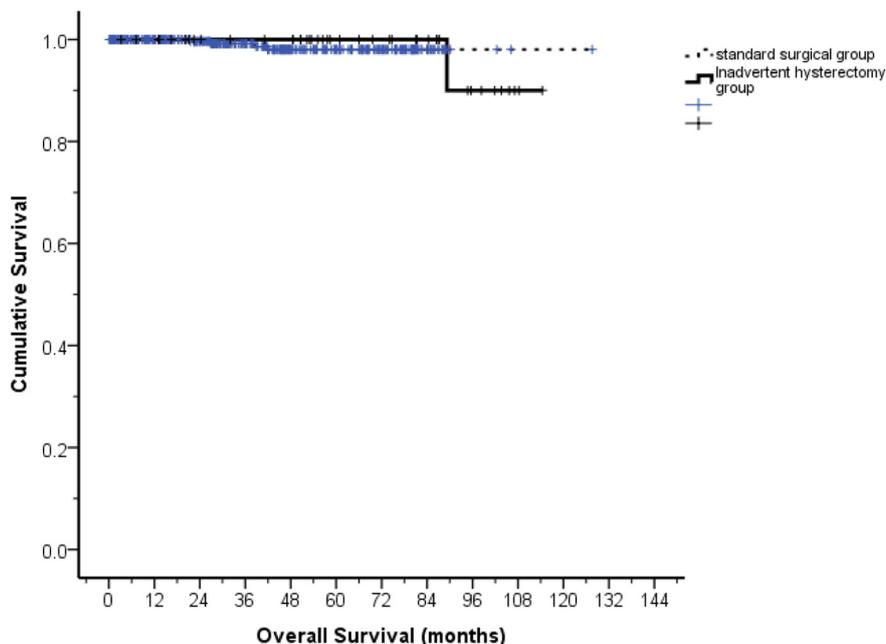


Fig. 3. Overall survival curves of 353 patients in the standard surgical treatment group and 44 patients in the inadvertent hysterectomy group ( $P = 0.767$ ).

**Table 4**

Survival outcomes of patients who underwent inadvertent simple hysterectomy and received subsequent treatment by radiotherapy or radical surgery.

Authors	N	Treatment modality	5-year DFS rate (%)	5-year OS rate (%)
Cosbie WG, et al. 1963 <sup>a</sup>	86	RT	Not reported	54
Hopkins MP, et al. 1990	78	RT	Not reported <sup>b</sup>	68 <sup>b</sup>
	4	Surgery		
Barber H, et al. 1968	81	Surgery	Not reported	38.3
Green TH, et al. 1969	30	RT	Not reported	30
	21	Surgery	Not reported	67
Andras EJ, et al. 1973	148	RT	80	89
Davy M, et al. 1977	72	RT	Not reported	60.8
Papavasiliou C, et al. 1980 <sup>a</sup>	36	RT	Not reported	89
Heller PB, et al. 1986	35	RT	Not reported	67
Orr JW, et al. 1986 <sup>a</sup>	23	Surgery	Not reported	Not reported
Kinney WK, et al. 1992 <sup>a</sup>	27	Surgery	Not reported	82
Chapman JA, et al. 1992 <sup>a</sup>	18	Surgery	Not reported	89
Roman LD, et al. 1993 <sup>a</sup>	122	RT	Not reported	65
Fang FM, et al. 1993 <sup>a</sup>	73	RT	Not reported	67
Choi DH, et al. 1997	64	RT	77.5	75.8
Crane CH, et al. 1999	18	RT	88	93
Huerta BJ, et al. 2003 <sup>a</sup>	59	RT	Not reported	59
Chen SW, et al. 2003	29	RT	90	88
Munstedt K, et al. 2004	80	RT	Not reported	83
Hsu WL, et al. 2004	91	RT	85.5	85.5
Leath CA, et al. 2004	23	Surgery	Not reported	96
Gori JR, et al. 2004	11	Surgery	Not reported	75
Ayhan A, et al. 2006	27	Surgery	88.67	88.89
Park JY, et al. 2009	44	RT/CCRT	93	94
	29	Surgery	100	100
Smith KB, et al. 2010	25	RT	96	100
Koh HK, et al. 2013	117	RT	87	87
Narducci F, et al. 2014	16	RT/CCRT	37	77
	13	Surgery	86	100
Bai H, et al. 2016	13	RT/CCRT	93.9 <sup>b</sup>	94.7 <sup>b</sup>
	76	Surgery		
Present study	43	RT/CCRT	93.2 <sup>b</sup>	100 <sup>b</sup>
	1	Surgery		

Abbreviations: CCRT, concurrent chemoradiotherapy; DFS, disease-free survival; OS, overall survival; RT, radiotherapy.

<sup>a</sup> Only the abstract available.

<sup>b</sup> Reported the survival of the entire population.

rates were similar between the standard surgical treatment group and inadvertent hysterectomy group (88.4% vs. 93.2% and 98.9% vs. 100%, respectively). This might be due to the short time interval between the date of inadvertent simple hysterectomy and the date of the definite curative treatment. The impact of the time interval after inadvertent hysterectomy to the subsequent definite treatment initiation was so important. Green et al. studied 84 patients with inadvertent hysterectomy and revealed the shorter the time interval, the higher is the cure rate. They compared the 5-year cure rates for groups with  $\leq 6$  weeks and  $> 6$  weeks' time interval between inadvertent hysterectomy and the subsequent treatment. These groups showed cure rates of 42% and 18%, respectively [28].

To the best of our knowledge, the current study is the first to compare the oncologic outcomes of inadvertent hysterectomy and standard treatment groups. However, it has the common limitations of retrospective studies, and we did not have accurate data on treatment-related complications.

In conclusion, physicians should be aware that the presence of cervical carcinoma must be excluded before performing simple hysterectomy. Patients with cervical carcinoma who had small tumors and underwent inadvertent hysterectomy with appropriate consequent management had oncologic outcomes comparable to patients receiving standard surgical treatment. Women who have inadvertent surgery for cervical cancer are at high risk for poor outcomes. The timely initiation of chemoradiation can salvage the majority of these women. More information is needed about the morbidity related to postoperative CCRT.

## Conflicts of interest declaration

All authors declare that there are no personal or professional conflicts of interest related to the preparation and publication of this manuscript, and there was no financial support from the companies that produce and/or distribute the drugs described in this report.

## Author contribution

IR: Contributed to the design, data collection, statistical analysis of the data, interpretation of the results, and writing of the manuscript. NP: Contributed to the design, statistical analysis of the data, interpretation of the results, and review and editing of the manuscript. BV, SS, and SH: Contributed to the design and review and editing of the manuscript. JP: Contributed to data collection, review, and editing of the manuscript.

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## References

- [1] F. Bray, J. Ferlay, I. Soerjomataram, R.L. Siegel, L.A. Torre, A. Jemal, Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, *CA Cancer J. Clin.* 68 (2018) 394–424.
- [2] D. Pongnikorn, K. Suwanrungruang, R. Buasom, Cancer incidence in Thailand, in: W. Imsamran, A. Pattatag, I. Chiawiriyabunya, K. Namthaisong, M. Wongsena, P. Puttawibul, I. Chitapanarux, K. suwanrungrung, S. Sangrajan, R. Buasom (Eds.), *Cancer in Thailand*, vol. IX, International Agency for research on Cancer, Bangkok: Lyon 2017, pp. 3–9.
- [3] N. Bhatla, D. Aoki, D.N. Sharma, R. Sankaranarayanan, Cancer of the cervix uteri, *Int. J. Gynaecol. Obstet.* 143 (2018) 22–36.
- [4] F. Landoni, A. Maneo, A. Colombo, F. Placa, R. Milani, P. Perego, et al., Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer, *Lancet.* 350 (1997) 535–540.
- [5] F. Landoni, A. Colombo, R. Milani, F. Placa, V. Zanagnolo, C. Mangioni, Randomized study between radical surgery and radiotherapy for the treatment of stage IB-IIA cervical cancer: 20-year update, *J. Gynecol. Oncol.* 28 (2017) e34.
- [6] D.H. Choi, S.J. Huh, K.H. Nam, Radiation therapy results for patients undergoing inappropriate surgery in the presence of invasive cervical carcinoma, *Gynecol. Oncol.* 65 (1997) 506–511.
- [7] C.H. Crane, B.F. Schneider, Occult carcinoma discovered after simple hysterectomy treated with postoperative radiotherapy, *Int. J. Radiat. Oncol. Biol. Phys.* 43 (1999) 1049–1053.
- [8] C.A. Leath 3rd, J.M. Straughn, S.M. Bhoola, E.E. Partridge, L.C. Kilgore, R.D. Alvarez, The role of radical parametrectomy in the treatment of occult cervical carcinoma after extrafascial hysterectomy, *Gynecol. Oncol.* 92 (2004) 215–219.
- [9] W.L. Hsu, P.W. Shueng, Y.M. Jen, C.J. Wu, J.M. Hwang, L.P. Chang, et al., Long-term treatment results of invasive cervical cancer patients undergoing inadvertent hysterectomy followed by salvage radiotherapy, *Int. J. Radiat. Oncol. Biol. Phys.* 59 (2004) 521–527.
- [10] F. Narducci, B. Merlot, L. Bresson, N. Katdare, T.F. Le, A. Cordoba, et al., Occult invasive cervical cancer found after inadvertent simple hysterectomy: is the ideal management: systematic parametrectomy with or without radiotherapy or radiotherapy only? *Ann. Surg. Oncol.* 22 (2015) 1349–1352.
- [11] J.Y. Park, D.Y. Kim, J.H. Kim, Y.M. Kim, Y.T. Kim, J.H. Nam, Management of occult invasive cervical cancer found after simple hysterectomy, *Ann. Oncol.* 21 (2010) 994–1000.
- [12] W.A. 3rd Peters, P.Y. Liu, R.J. 2nd Barrett, R.J. Stock, B.J. Monk, J.S. Berek, et al., Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix, *J. Clin. Oncol.* 18 (2000) 1606–1613.
- [13] M. Rotman, A. Sedlis, M.R. Piedmonte, B. Bundy, S.S. Lentz, L.I. Muderspach, et al., A phase III randomized trial of postoperative pelvic irradiation in stage IB cervical carcinoma with poor prognostic features: follow-up of a gynecologic oncology group study, *Int. J. Radiat. Oncol. Biol. Phys.* 65 (2006) 169–176.
- [14] A. Sedlis, B.N. Bundy, M.Z. Rotman, S.S. Lentz, L.I. Muderspach, R.J. Zaino, A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: a gynecologic oncology group study, *Gynecol. Oncol.* 73 (1999) 177–183.
- [15] J.A. Chapman, R.S. Mannel, P.J. DiSaia, J.L. Walker, M.L. Berman, Surgical treatment of unexpected invasive cervical cancer found at total hysterectomy, *Obstet. Gynecol.* 80 (1992) 931–934.
- [16] W.K. Kinney, E.V. Egorshin, D.J. Ballard, K.C. Podratz, Long-term survival and sequelae after surgical management of invasive cervical carcinoma diagnosed at the time of simple hysterectomy, *Gynecol. Oncol.* 44 (1992) 24–27.

- [17] J.W. Orr Jr., G.C. Ball, S.J. Soong, K.D. Hatch, E.E. Partridge, J.M. Austin, Surgical treatment of women found to have invasive cervix cancer at the time of total hysterectomy, *Obstet. Gynecol.* 68 (1986) 353–356.
- [18] J.R. Gori, H.G. Fritsches, R. Castanno, M. Toziano, D. Habich, Radical parametrectomy for occult cervical carcinoma detected posthysterectomy, *J. Low. Genit. Tract. Dis.* 8 (2004) 102–105.
- [19] A. Ayhan, U. Otegen, S. Guven, T. Kucukali, Radical reoperation for invasive cervical cancer found in simple hysterectomy, *J. Surg. Oncol.* 94 (2006) 28–34.
- [20] H. Hricak, C. Gatsonis, F.V. Coakley, B. Snyder, C. Reinhold, L.H. Schwartz, et al., Early invasive cervical cancer: CT and MR imaging in preoperative evaluation - ACRIN/GOG comparative study of diagnostic performance and interobserver variability, *Radiology.* 245 (2007) 491–498.
- [21] K. Munstedt, P. Johnson, R. von Georgi, H. Vahrson, H.R. Tinneberg, Consequences of inadvertent, suboptimal primary surgery in carcinoma of the uterine cervix, *Gynecol. Oncol.* 94 (2004) 515–520.
- [22] E.J. Andras, G.H. Fletcher, F. Rutledge, Radiotherapy of carcinoma of the cervix following simple hysterectomy, *Am. J. Obstet. Gynecol.* 115 (1973) 647–655.
- [23] H. Bai, D. Cao, F. Yuan, H. Wang, J. Chen, Y. Wang, et al., Occult invasive cervical cancer after simple hysterectomy: a multi-center retrospective study of 89 cases, *BMC Cancer* 16 (2016) 507.
- [24] S.W. Chen, J.A. Liang, S.N. Yang, F.J. Lin, Postoperative radiotherapy for patients with invasive cervical cancer following treatment with simple hysterectomy, *Jpn. J. Clin. Oncol.* 33 (2003) 477–481.
- [25] W.G. Cosbie, Radiotherapy following hysterectomy performed for or in the presence of cancer of the cervix, *Am. J. Obstet. Gynecol.* 85 (1963) 332–337.
- [26] M. Davy, H. Bentzen, R. Jahren, Simple hysterectomy in the presence of invasive cervical cancer, *Acta Obstet. Gynecol. Scand.* 56 (1977) 105–108.
- [27] F.M. Fang, C.Y. Yeh, Y.L. Lai, J.F. Chiou, K.H. Chang, Radiotherapy following simple hysterectomy in patients with invasive carcinoma of the uterine cervix, *J. Formos. Med. Assoc.* 92 (1993) 420–425.
- [28] T.H.Jr. Green, W.J.Jr. Morse, Management of invasive cervical cancer following inadvertent simple hysterectomy, *Obstet. Gynecol.* 33 (1969) 763–769.
- [29] P.B. Heller, D.R. Barnhill, A.R. Mayer, T.P. Fontaine, W.J. Hoskins, R.C. Park, Cervical carcinoma found incidentally in a uterus removed for benign indications, *Obstet. Gynecol.* 67 (1986) 187–190.
- [30] B.J. Huerta, A.S. Labastida, A.H. Cortez, A. Calva, Postoperative radiotherapy in patients with invasive uterine cervix cancer treated previously with simple hysterectomy. Results from the hospital de Oncologia, Centro medico Nacional SXXI, *Ginecol. Obstet. Mex.* 71 (2003) 304–311.
- [31] C. Papavasiliou, D. Yiogarakis, J. Pappas, A. Keramopoulos, Treatment of cervical carcinoma by total hysterectomy and postoperative external irradiation, *Int. J. Radiat. Oncol. Biol. Phys.* 6 (1980) 871–874.
- [32] L.D. Roman, J.C. Felix, L.I. Munderspach, A. Agahjanian, D. Qian, C.P. Morrow, Risk of residual invasive disease in women with microinvasive squamous cancer in a conization specimen, *Obstet. Gynecol.* 90 (1997) 759–764.
- [33] H.R. Barber, G.V. Pece, A. Brunshwig, Operative management of patients previously operated upon for a benign lesion with cervical cancer as a surprise finding, *Am. J. Obstet. Gynecol.* 101 (1968) 959–965.
- [34] M.P. Hopkins, W.A.3rd Peters, W. Andersen, G.W. Morley, Invasive cervical cancer treated initially by standard hysterectomy, *Gynecol. Oncol.* 36 (1990) 7–12.
- [35] H.K. Koh, W. Jeon, H.J. Kim, H.G. Wu, K. Kim, E.K. Chie, et al., Outcome analysis of salvage radiotherapy for occult cervical cancer found after simple hysterectomy, *Jpn. J. Clin. Oncol.* 43 (2013) 1226–1232.
- [36] K.B. Smith, R.J. Amdur, A.R. Yeung, C.G. Morris, J. Kirwan, L.S. Morgan, Postoperative radiotherapy for cervix cancer incidentally discovered after a simple hysterectomy for either benign conditions or noninvasive pathology, *Am. J. Clin. Oncol.* 33 (2010) 229–232.
- [37] K.M. Doll, E. Donnelly, I. Helenowski, L. Rosenbloom, W. Jr. Small, J.C. Schink, et al., Radical hysterectomy compared with primary radiation for treatment of stage IB1 cervix cancer, *Am. J. Clin. Oncol.* 37 (2014) 30–34.