European Journal of Obstetrics & Gynecology and Reproductive Biology 190 (2015) 26–30

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

The effect of coexisting squamous cell lesions on prognosis in patients with cervical adenocarcinoma in situ

Taejong Song [a], Yoo-Young Lee [b], Chel Hun Choi [b], Tae-Joong Kim [b], Jeong-Won Lee [b], Duk-Soo Bae [b], Byoung-Gie Kim [b,*]

[a] Department of Obstetrics & Gynecology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
[b] Department of Obstetrics & Gynecology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

ARTICLE INFO

Article history:
Received 23 September 2014
Received in revised form 31 March 2015
Accepted 8 April 2015

Keywords:
Adenocarcinoma in situ
Carcinoma in situ
Squamous cell lesions
Cervix
Conization
Recurrence

ABSTRACT

Objective: The aim of this study was to assess the relative incidences of cervical adenocarcinoma in situ (AIS) and squamous cell carcinoma in situ (sCIS) and to determine the effect of coexisting squamous cell lesions on prognosis in patients with cervical AIS.
Study design: We performed a retrospective review of patients diagnosed with AIS or sCIS who underwent cervical conization at a University hospital between 2000 and 2011.
Results: A total of 1184 patients with cervical carcinoma in situ were included. The ratio of sCIS to AIS was 16:1. Among 71 patients with AIS, AIS with coexisting squamous cell lesions and AIS alone were detected in 41 patients (58%) and 30 patients (42%), respectively. During the median follow-up of 57.1 months, 5 episodes of AIS recurrences and one episode of invasive recurrence occurred. The recurrence rate was significantly higher in patients with AIS alone than in patients with AIS and coexisting squamous cell lesions (17% versus 2%; $P = 0.043$).
Conclusion: These results suggest that patients with cervical AIS and coexisting squamous cell lesions have a more favorable prognosis than patients with AIS alone.

Introduction

Adenocarcinoma in situ (AIS) of the uterine cervix, which was first described in 1952 by Hepler et al. [1], is considered a precursor lesion of invasive adenocarcinoma [2,3]. Adenocarcinoma comprises about 20% of all cervical cancers [4] and its incidence is increasing worldwide [4,5]. The frequency of cervical AIS has also increased along with the increase in frequency of adenocarcinoma of the cervix [6,7]. AIS is more difficult to detect and treat because the lesions are often located high in the cervical canal, are not readily visible on colposcopic examination, and may be multifocal [1,3]. Although definitive treatment traditionally involves hysterectomy, a growing body of evidence supports the use of conservative management, such as loop electrosurgical conization or cold-knife conization [8–10].

Squamous cell lesions can be detected concurrently in cone biopsy specimens of AIS [8,11–13]. However, no data are currently available on the clinico-pathologic characteristics and prognosis of patients with AIS and coexisting squamous cell lesions. Also, the relative incidences of different existing squamous cell lesions in AIS patients are not well-known. Considering the increasing incidence of AIS of the cervix and the common use of conservative treatment in young patients with AIS, a study focusing on patients with AIS and coexisting squamous cell lesions is needed. The aims of this study were to determine the relative incidences of cervical AIS and cervical squamous carcinoma in situ (sCIS), and to compare the clinico-pathologic characteristics and recurrence rate of patients with AIS and coexisting squamous cell lesions versus patients with AIS alone.

Materials and methods

After approval by the Institutional Review Board, a retrospective review of the tumor registry and institutional pathology database was performed between January 2000 and December 2011 at Samsung Medical Center (SMC, Seoul, Korea) to identify all patients with carcinoma in situ (either AIS or sCIS) of the cervix on cone biopsy. Patients with synchronous AIS and sCIS were also included in this study. However, patients were excluded if carcinoma in situ was found to coexist with microinvasive or

* Corresponding author at: Department of Obstetrics and Gynecology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-Dong, Gangnam-gu, Seoul 135-710, Republic of Korea. Tel.: +82 2 3410 3513; fax: +82 2 3410 0630.
E-mail address: bgkim@skku.edu (B.-G. Kim).

http://dx.doi.org/10.1016/j.ejogrb.2015.04.005
0301-2115/

invasive carcinoma in the initial cervical biopsy or subsequent hysterectomy specimen. In all cases, the method of conization used was electrosurgical conization using a triangular loop, which has been previously reported in detail [14].

Demographic data, Papanicolaou (Pap) smear history, colposcopy results, human papilloma virus (HPV) results, pathology results, treatment, and follow-up data were abstracted from medical records. Pathology reports were analyzed for descriptions of histology, margin status of the specimen, location of positive margins, and final pathologic diagnosis. Residual disease was defined as the presence of carcinoma in situ in a repeat cone biopsy or in a hysterectomy specimen received immediately after initial conization. Follow-up of patients included a Pap smears, every 6 months for 3 years, and then yearly thereafter. In addition, endocervical curettage was performed in cases with an insufficient endocervical sample or a stenotic cervical os. Punch biopsy and/or endocervical curettage were performed in all patients with abnormal Pap smears. The follow-up period was defined as the time interval between the date of initial diagnosis of cervical carcinoma in situ and the date of last contact. Recurrence of disease was defined as the histologic documentation of original cervical carcinoma in situ, microinvasive cancer, or invasive cancer after the initial treatment, with all intervening cytologic and histologic assessments being negative. Recurrence-free interval was defined as the time interval from the date of initial diagnosis of cervical carcinoma in situ to the date of recurrence or last contact.

For comparative analysis, patients with AIS were classified into two groups based on histology: patients with AIS and coexisting squamous cell lesions (the group 1) and patients with AIS alone (the group 2). Categorical variables were compared using chi-square or Fisher exact test, and continuous variables were compared using the Student's *t*-test or Mann–Whitney *U* test. The recurrence rates were calculated using the Kaplan–Meier method and compared using the log-rank test. A P value <0.05 was considered statistically significant. Statistical analyses were performed with SPSS software (version 12.0; SPSS, Inc., Chicago, IL).

Results

Incidence

During the 12-year study period, 5035 cone biopsies were performed. Among them, the following 3851 cases were excluded: 3413 cases diagnosed with cervical intraepithelial neoplasia (CIN) without accompanying the in situ lesion; 375 cases diagnosed with chronic cervicitis, koilocytotic atypia, or condyloma; 41 cases in which repeat cone biopsies were performed; 22 cases with microinvasive or invasive cancer (Fig. 1). Finally, a total of 1184 patients with carcinoma in situ of the cervix were included. One thousand one hundred thirteen patients (94%) had sCIS alone and 71 patients (6%) had AIS with or without squamous cell abnormalities (Fig. 2). Therefore, the ratio of sCIS to AIS was 16:1. Of the 71 patients with AIS, 30 patients (42%) had AIS alone, 26 patients (37%) had synchronous AIS and sCIS, and 15 patients (21%) had AIS with coexisting squamous CIN without accompanying the in situ lesion. Synchronous AIS and sCIS comprised 2.2% of all carcinomas in situ of the cervix. AIS with coexisting squamous cell lesions comprised 58% of all AIS cases.

Characteristics

The clinico-pathologic characteristics of patients with AIS according to the presence of coexisting squamous cell lesions are detailed in Table 1. Patients' median age and body mass index at the time of initial conization were 42 years (range, 25–67 years)

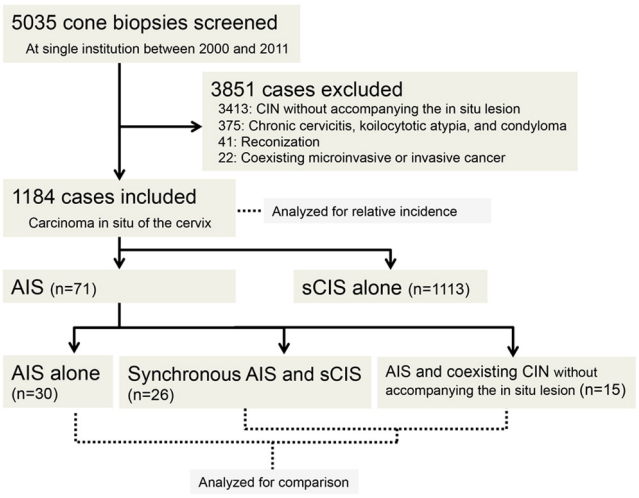

Fig. 1. Consort diagram for case selection. *Abbreviations*: CIN, cervical intraepithelial neoplasia; AIS, adenocarcinoma in situ; sCIS, squamous cell carcinoma in situ.

and 22.8 kg/m^2 (range, 16.1–34.7 kg/m^2), respectively, with no statistically significant differences between the two groups. Results of the referral Pap smear before conization between the two groups were different ($P < 0.001$): in the group 1 (patients with AIS and coexisting squamous cell lesions), squamous cell abnormalities were observed in 93% of patients, glandular cell abnormalities were observed in 2% of patients, and combined squamous and glandular cell abnormalities were observed in 2% of patients, while in the group 2 (patients with AIS alone), squamous cell abnormalities were observed in 37% of patients, glandular cell abnormalities were observed in 43% of patients, and combined squamous and glandular cell abnormalities were observed in 10% of patients. High-risk HPV was detected in 66% of all patients with AIS, with no significant differences between the two groups. Results of punch biopsy before conization were also different between the two groups ($P < 0.001$): in the group 1, squamous cell lesions were observed in 73% of patients, glandular cell lesions were observed in 7% of patients, and combined squamous and glandular cell lesions were observed in 12% of patients, whereas in the group 2, glandular cell lesions were observed in 67% of patients and negative findings such as cervicitis or koilocytosis were observed in 30% of patients. Ninety-six percent of the group

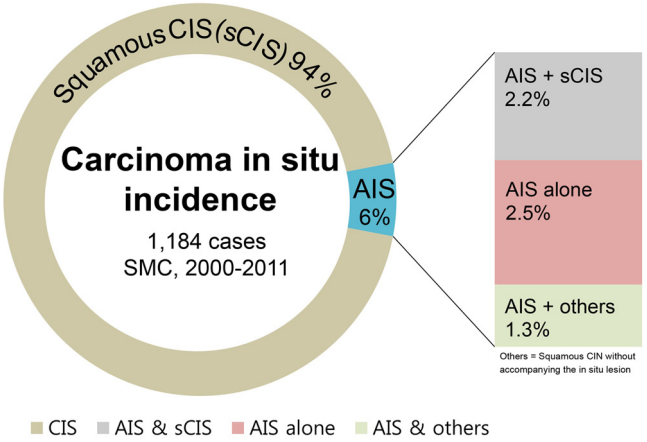

Fig. 2. The histological distribution in 1184 cases of carcinoma in situ of the cervix diagnosed at Samsung Medical Center (SMC) during the 12-year study period. *Abbreviations*: CIS, carcinoma in situ; AIS, adenocarcinoma in situ; sCIS, squamous cell carcinoma in situ.