

Uterine body cancer mass screening at Tokai University Hospital

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A total of 1,512 women participated in mass screenings for uterine body cancer (UBC) from 1998 to 2003 at Tokai University Hospital. Their rate in the examinees of uterine cervical cancer (UCC) mass screenings was 4.7 %. Among the 1,512 examinees, endometrial cytological abnormalities (class III or higher) were found in 17 (1.1 %) cases. As a result, UBC was detected in two patients (0.13 %). One case was diagnosed as class V, adenocarcinoma, and she underwent hysterectomy. In another case, adenocarcinoma was found to be associated with atypical endometrial hyperplasia in hysterectomy specimens. For the remaining 15 cases diagnosed as class III, the cytological abnormalities disappeared after a follow-up except for 3 patients who were not followed at Tokai University Hospital. In a comparison of the examinees with or without genital bleeding, the cytological abnormalities were more frequently detected in the former group; 4.2 % (6/142) vs. 0.6 % (5/819) ($p < 0.05$). We recommend examinees aged 40 years or higher with a complaint of genital bleeding to participate in UBC mass screening for detection of endometrial adenocarcinoma at early stages.

Key words : mass screening, uterine body cancer, cytology

INTRODUCTION

Uterine body cancer (UBC) composed mainly of endometrial adenocarcinoma is steadily increasing in Japan as well as in Western countries. It accounted for more than 10 % of overall uterine cancers in the 70's, and exceeded 45 % in 2001 [1]. According to a nation-wide UBC mass screening as required by the Health and Medical Service Law for the Aged (the *Law*) since 1987 [2], the number of examinees who participated in the screening for UBC and uterine cervical cancer (UCC) was 20,115 and 3,674,936 in 1987 and 332,495 and 3,825,670 in 2001, respectively [3], with the rate of UBC examinees in those of UCC being 0.5 % in 1987 and 8.7 % in 2001. Although UBC has recently become a major gynecologic malignancy in Japan, examinees for UBC mass screening are

selected when gynecologists consider that the examination is necessary according to the *Law*. The essential criterion for UBC mass screening is that female examinees have experienced abnormal genital bleeding within 6 months of mass screening. The following three conditions need to be met; 50 years or older, postmenopausal, and nulligravid with irregular menstruation. Examinees with cytologically positive or suspicious results are referred to a diagnostic close work-up.

Our hospital established an institute for thorough medical check-ups in 1975, when UCC mass screening commenced. However, UBC mass screening has been optionally carried out since 1998. Between 1998 and 2003, 1,512 women participated in the UBC mass screening, resulting in detection rates of 1.1 % for endometrial cytological abnormalities and 0.13 % for endometrial adenocarcinoma. Two patients underwent hysterectomy

because the tumors were in early stages. The present study includes a discussion on the examinee profiles and the significance of UBC mass screening.

SUBJECTS AND METHODS

Statistics

On average, 18,000 examinees including 6,500 women (36.1 %) each year have participated in thorough medical check-ups including UCC screening at Tokai University Hospital since May, 1975. Between April, 1998 and January, 2003, 32,325 female examinees (the number of subjects 11,300, the mean age 52.2 years) participated in UCC

mass screening with 168 (0.5 %) in their 20's, 2,172 (6.7 %) in their 30's, 10,230 (31.6 %) in their 40's, 13,222 (40.9 %) in their 50's, 5,282 (16.3 %) in their 60's, and 1,251 (3.9 %) 70 years or older (Fig. 1). Among the examinees, 4.7 % (total 1,512, the number of subjects 961, the mean age 52.8 years) participated in UBC mass screening. The age distribution of the 1,512 examinees was 15 (1.0 %) in their 20's, 90 (6.0 %) in their 30's, 392 (25.9 %) in their 40's, 651 (43.1 %) in their 50's, 336 (22.2 %) in their 60's, and 28 (1.9 %) at 70 years or older (Fig. 2). The rate of examinees who participated in UBC mass screening in each generation was 8.9 % (15/168) for those

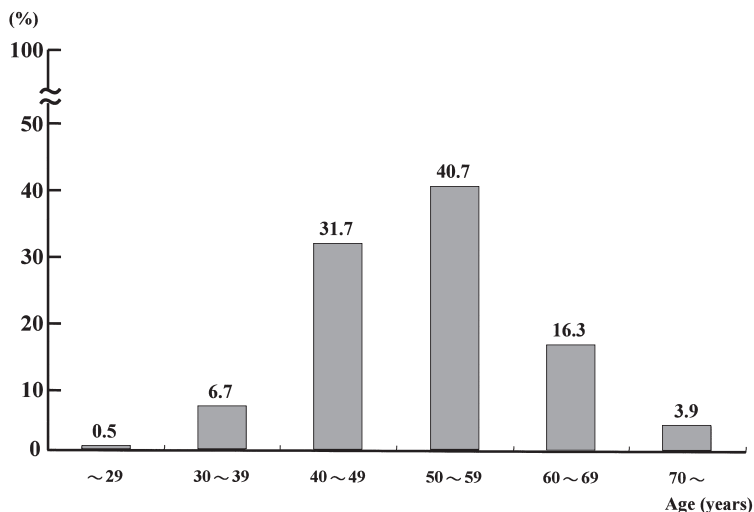


Fig. 1 Age distribution of overall female examinees

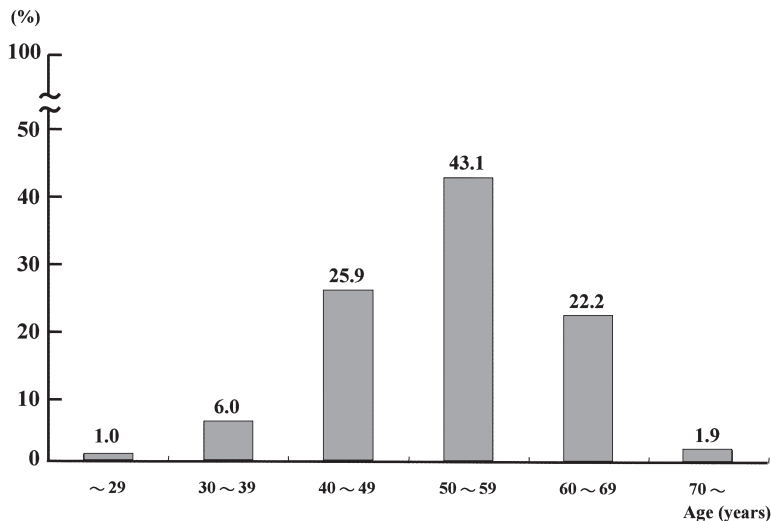


Fig. 2 Age distribution of endometrial cytological examinees

in their 20's, 4.1 % (90/2,172) in their 30's, 3.8 % (392/10,230) in their 40's, 4.9 % (651/13,222) in their 50's, 6.4 % (336/5,282) in their 60's, and 2.2 % (28/1,251) for those 70 years or older (Fig. 3). Among the 32,325 examinees, 5.2 % (1,667) noticed genital bleeding within 1 year of the screening. The rate of the examinees who complained of genital bleeding in each generation was 14.9 % (25/168) for those in their 20's, 11.2 % (244/2,172) in their 30's, 8.7 % (888/10,230) in their 40's, 3.4 % (450/13,222) in their 50's, 1.1 % (58/5,282) in their 60's, and 0.2 % (2/1,251) for those 70 years or older (Fig. 4). Among the 1,512 UBC examinees, 40.0

% (605) were postmenopausal, and 9.4 % (142) complained of genital bleeding within 1 year of the screening. Statistical analysis was performed using the z-test; $p < 0.05$ was regarded as significant.

Cytology

UBC mass screening was performed involving cytological endometrial examinations by gynecologists using endocytoscopy. Smear preparations were routinely processed and evaluated by cytotechnologists and pathologists and classified into the following five categories; class I, no abnormal findings; class II, hyperplastic or inflammatory changes;

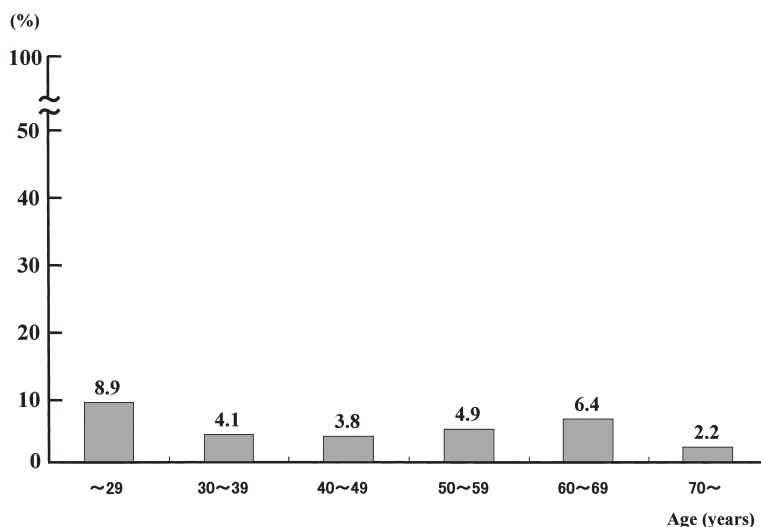


Fig. 3 Age distribution of participation rates of endometrial cytological examinees

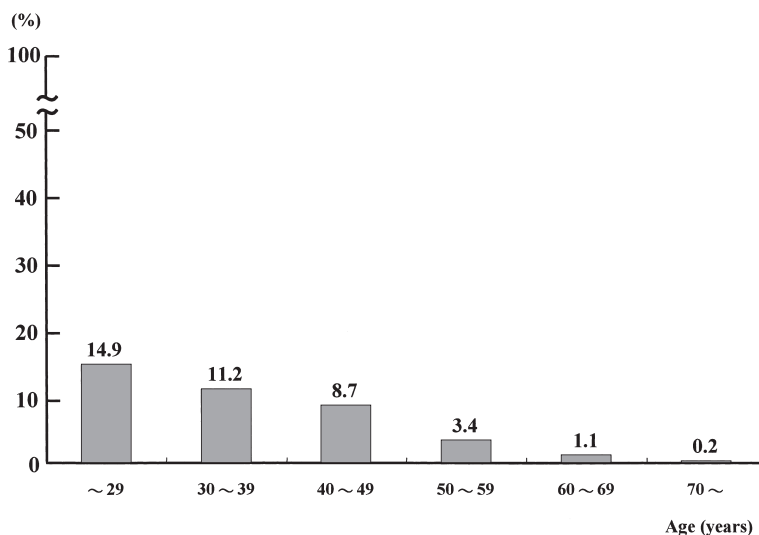


Fig. 4 Age distribution of rates of examinees with a complaint of genital bleeding

Table 1 Profiles of patients positive for endometrial cytology

Case	Age	Class	Menopause	G/P	GB	Outcome
1	40	III	Pre	2/3	+	NR
2	43	III	Pre	2/2	+	Unknown
3	45	III	Pre	0/0	+	AEH, complex: Hys.
4	47	III	Post	2/2	+	NR
5	49	III	Pre	2/2	+	Unknown
6	49	III	Pre	4/5	-	NR
7	50	III	Pre	2/4	-	NR
8	52	III	Pre	2/3	+	NR
9	53	III	Post	2/3	-	NR
10	53	III	Post	2/2	NI	NR
11	54	III	Post	3/3	-	NR
12	55	III	Post	4/5	-	Unknown
13	56	III	Post	2/4	NI	NR
14	57	III	Post	1/2	NI	NR
15	66	III	Post	2/2	NI	NR
16	67	III	Post	2/2	NI	NR
17	69	V	Post	3/3	NI	EAC: Hys.

G/P: Gravidity/Parity, GB: Genital Bleeding, NI: Not Informed, NR: Naturally Recovered
 AEH: Atypical Endometrial Hyperplasia, Hys: Hysterectomy, EAC: Endometrial Adenocarcinoma

class III, simple or complex hyperplasia, or simple atypical hyperplasia, suspected; class IV, complex atypical hyperplasia or worse (G1 endometrioid adenocarcinoma), suspected; class V, endometrial cancer, diagnosed. When examinees were evaluated as class III or higher, they were requested to consult at the Gynecologic Outpatient Clinic to receive a close work-up.

RESULTS

Seventeen examinees (the number of subjects 16) were cytologically diagnosed as having an abnormal endometrium with a detection rate of 1.1% (17/1,512). The details of the patient profiles are shown in Table. The patients were, on average, 52.9-year-old. Ten examinees (58.8 %) were postmenopausal, and 7 (41.2 %) were found to be cytologically abnormal during the first screening, 5 (29.4 %) during the second, and 5 (29.4 %) during the other screenings. The detection rate for each generation was 1.5 % (6/392) for those in their 40's, 1.2 % (8/651) in their 50's, and 0.9 % (3/336) in their 60's. Four women experienced genital bleeding within 1 year of the screening. In a comparison of the examinees with or without genital bleeding, the detection rate was higher in the former than in the latter; 4.2 % (6/142) vs.

0.6 % (5/819) ($p < 0.05$).

Fourteen of the 17 examinees were followed at the Gynecologic Outpatient Clinic of Tokai University Hospital. One patient (case 17, 69-year-old), who was cytologically diagnosed as having adenocarcinoma (class V), underwent hysterectomy at other hospital, with a final diagnosis of G1 endometrioid adenocarcinoma (stage Ia). The other patient (case 3, 45 years-old), who was cytologically evaluated as being class III, was histologically confirmed by endometrial curettage as having complex atypical endometrial hyperplasia. She also underwent hysterectomy, resulting in a diagnosis of G1 endometrioid adenocarcinoma associated with hyperplasia (stage Ia). These patients led uneventful lives after surgery. In twelve patients who were followed at 3 to 6 month intervals, no hyperplastic or neoplastic diseases were observed by cytological and histological examinations. For the remaining 3 patients, no detailed information was obtained because they did not consult at the Outpatient Clinic of Tokai University Hospital.

DISCUSSION

Endometrial adenocarcinoma usually occurs during the postmenopausal period and the mean age is over 60 years [4]. However,

this age seems to be decreasing. In our hospital, patients 40-year-old or younger with endometrial adenocarcinoma accounted for 2.1 % of the cases 10 years ago, and the proportion recently increased to 9.7 %, indicating that the occurrence age is steadily decreasing [5]. The age criterion for UBC mass screening is still set at 50 years of age or older according to the *Law*.

According to a nation-wide survey that complied with the *Law*, the average participation rate of UBC examinees in those of UCC mass screenings is 6.8 % and the average detection rate of UBC is 0.13 % for overall population, 0.01 % for those in their 30's, 0.04 % in their 40's, 0.11 % in their 50's, 0.22 % in their 60's, and 0.55 % for those 70 years or older [6]. In our hospital, the former averaged 4.7 % (1,512/32,325) and the latter 0.13 % (2/1,512), with 0.25 % (1/392) for those in their 40's and 0.30 % (1/336) for those in their 60's. The participation and detection rates for UBC screening at Tokai University Hospital were similar to those of the nation-wide analysis.

In a large-scaled analysis in 2000 [7], endometrial cytological abnormalities were observed in 1.6 % (4,729/287,759) of the UBC examinees, and the detection rate (2.6 %) was highest for those in their 70's. As a result, 275 examinees (0.09 %) were found to have endometrial adenocarcinoma, with its detection rate of 0.02 % for those in their 30's, 0.05 % in their 40's, 0.11 % in their 50's, 0.14 % in their 60's, and 0.28 % for those 70-year-old or older. The detection rate of the examinees aged 50 years or younger was relatively lower, but they accounted for approximately 30 % of those with UBC who underwent treatment [8]. There was no significant difference in the rate between those in their 40's and those in their 50's.

Endometrial hyperplasia is usually interpreted as a precancerous state of endometrial adenocarcinoma and, in our hospital, the peak occurrence of endometrial hyperplasia has been found in the 40's. The detection rate of endometrial hyperplasia was relatively higher than that for endometrial carcinoma; in total, 0.14 %, 0.05 % for those in their 30's, 0.14 % in their 40's, 0.17 % in their 50's, 0.10 % in their 60's, and 0.12 % for those 70-years or older [6]. In a comparison of those in their 40's (0.14 %) and 50's (0.17 %), as with the tendency for

endometrial carcinoma (0.05 % in their 40's vs. 0.11 % in their 50's), there was no notable difference between the two age groups. In our study, one of the 17 examinees (case 3, 45-year-old) with cytologic abnormalities had focally developed G1 endometrial adenocarcinoma, which was associated with complex atypical endometrial hyperplasia in the background. Since endometrial hyperplasia with cytological atypia and structural complexity predicts complications with or progression to adenocarcinoma [9], patients with the disease need to be closely followed.

In general, genital bleeding is an important indicator of endometrial abnormalities. According to Berek *et al.* [10], 90 % of patients with UBC experienced genital bleeding. The rate of the examinees who complained of genital bleeding in our study was highest for those in their 20's (14.9 %) and, as the age increased, the rate steadily decreased (Fig. 4). However, cytological abnormalities were found in the examinees aged 40 years or older and the detection rate simultaneously increased (Fig. 3).

Okumura *et al.* [11] reported that the prognosis of patients whose UBC is found by mass screening is more favorable than that of patients whose UBC is found at outpatient clinics (94.0 % vs. 84.3 %, $p < 0.05$). They concluded that screenings with endometrial smears could reduce mortality from endometrial cancer. The overall death rate of uterine cancers decreased from 20.0 per 100,000 in 1950 to 7.0 in 1993 [12]. This is attributed to UCC mass screening in Japan. Nevertheless, the rate somewhat increased to 8.0 in 1999 [12]. At present, according to reports of International Union Against Cancer [13] and the Japan Public Health Association [14], the usefulness or significance of UBC mass screening is not clearly established from the point view of its contribution to a decrease in the patient mortality. However, to detect UBC at early stages, there is no practical or effective means other than mass screening for UBC.

In conclusion, to detect endometrial hyperplasia as well as adenocarcinoma at early stages, we believe that lowering the age criterion for UBC mass screening from 50 years or older to 40 years or older would be useful. At Tokai University Hospital, we recommend examinees aged 40 years or older to participate in UBC mass screening, especially for

those with a complaint of genital bleeding.

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