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Influences of Estrogen-dependent Diseases, Premature Oophorectomy and Anti-cancer Chemotherapy on Skin Age in Japanese Women

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Abstract

Aim: The purpose of the present study was to investigate the influences of estrogen-dependent diseases, premature oophorectomy and anti-cancer chemotherapy on skin age in Japanese women.

Materials and methods: A total of 68 Japanese women were recruited between July 2016 and May 2018 at the Department of Obstetrics and Gynecology, Kagoshima University Hospital. This study included three subjects. Subject 1: A total of 57 premenopausal women were divided into two groups: those with estrogen-dependent diseases (n=19) and estrogen-independent diseases (n=38). Subject 2: A total of 26 premenopausal women were divided into two groups: those with premature oophorectomy (n=15) and ovarian preservation (n=11) during gynecological surgery. Subject 3: A total of 11 postmenopausal women who had received oophorectomy during their cancer operations were divided into two groups: those with postoperative anti-cancer chemotherapy (n=6) and those without chemotherapy (control, n=5). Facial skin parameters including skin age, relative skin age (i.e., skin age minus chronological age) and skin health conditions were assessed using a bioelectrical impedance analysis device.

Results: 1) Relative skin age was significantly younger in women with estrogen-dependent diseases than in those with estrogen-independent diseases (-1.0 ± 1.4 vs. 2.5 ± 0.6 years, respectively, $p<0.01$). 2) Longitudinal changes in relative skin age at 6 months postoperatively in the oophorectomy group had progressed significantly compared with the ovarian preservation group (3.5 ± 1.4 vs. -0.2 ± 0.8 years, respectively, $p<0.05$). 3) Longitudinal changes in relative skin age at 12 months after chemotherapy in postmenopausal women who received 6 courses of postoperative anti-cancer chemotherapy had progressed significantly compared with control (10.5 ± 3.3 vs. -3.8 ± 3.4 years, respectively, $p<0.05$). The ratio of young skin conditions was also significantly decreased after chemotherapy (from 5/6 to 1/6, respectively, $p<0.05$).

Conclusions: Women with estrogen-dependent diseases maintain a younger facial skin age than those with estrogen-independent diseases. However, skin aging is accelerated by premature oophorectomy and markedly accelerated by anti-cancer chemotherapy.

Key Words: words: anti-cancer chemotherapy, estrogen-dependent diseases, premature oophorectomy, skin age, skin health conditions

Introduction

Estrogens are the most important sex hormones that promote the development and maintenance of female characteristics. The menopause causes hypoestrogenism, accelerating age-related deterioration, which results in thinner skin, an increased number of wrinkles, increased skin dryness and decreased skin elasticity[1, 2]. From gynecological aspects, factors affecting the skin age include simple aging, natural or iatrogenic menopause (i.e., premature oophorectomy), radiotherapy and anti-cancer chemotherapy. As for estrogen-dependent gynecological diseases[3-5], developments of uterine leiomyoma and endometrial cancer are estrogen-dependent, differing from uterine cervical cancer. In particular, most risk factors for endometrial cancer are associated with prolonged and unopposed exposure of the endometrium to estrogen. The development of endometrial cancer reflects the cumulative effects of uncontrolled estrogen exposure[6]. Estrogen is one of the important determinants of women's skin conditions[1, 7-9]. Thus, it is likely that women with estrogen-dependent diseases have a younger skin age. Anti-cancer chemotherapy also affects patients' skin, mucous membranes, hair and nails[10]. Recent developments of anti-cancer chemotherapy have extended patients' survival. Thus, in cancer survivors as well, maintenance of the skin condition after anti-cancer chemotherapy is becoming more important. In the gynecological field, however, the relationship of estrogen-dependent diseases with skin aging and the effects of premature oophorectomy and anti-cancer chemotherapy on skin aging have been insufficiently investigated. One of the possible reasons for this may be the difficulty of objective assessment of skin aging by gynecologists. In addition, special attention has not been paid to the skin condition around the periods of premature oophorectomy and anti-cancer chemotherapy. Recent technological advances in bioelectrical impedance analysis have enabled us to objectively assess the skin age[11].

In the present study, we investigated the influences of estrogen-dependent diseases, premature oophorectomy and anti-cancer chemotherapy on the skin age in Japanese women with various gynecological diseases using bioelectrical impedance analysis.

Materials and methods

Japanese women with gynecological diseases were recruited between July 2016 and May 2018 at the Department of Obstetrics and Gynecology, Faculty of Medicine, Kagoshima University Hospital. Fully informed written consent was obtained from 68 patients before entry into the study. This study was conducted in accordance with IRB approval (No.28-84) at Kagoshima University Hospital, and was also conducted in accordance with Helsinki Declaration (as revised in Tokyo 2004).

Subjects

Subject 1: A total of 57 premenopausal women were divided into two groups: those with estrogen-dependent diseases (n=19) and estrogen-independent diseases (n=38). Estrogen-dependent diseases included endometrial cancer (n=12), atypical endometrial hyperplasia (n=1) and uterine leiomyoma (n=6). Estrogen-independent diseases included uterine cervical cancer (n=20), cervical intraepithelial neoplasia (n=5) and non-estrogen-producing ovarian tumor (n=13).

Subject 2: A total of 26 premenopausal women were divided into two groups: those with premature oophorectomy (n=15) and ovarian preservation (n=11) during gynecological surgery. The oophorectomy group included women with endometrial cancer (n=9), cervical cancer (n=4), ovarian cancer (n=1) and another gynecological disease (n=1). The ovarian preservation group included those with cervical cancer (n=7) and other gynecological diseases (n=4).

Subject 3: A total of 11 postmenopausal women who had received cancer operations were divided into two groups: those with postoperative anti-cancer chemotherapy (n=6) and those without chemotherapy (control, n=5). The principal cancer operations included hysterectomy, bilateral salpingo-oophorectomy, pelvic lymphadenectomy and/or omentectomy. Chemotherapy regimens included paclitaxel and carboplatin (TC) (n=5) and docetaxel and carboplatin (DC) (n=1).

Baseline characteristics included the chronological age (years), height (cm), body weight (kg), body mass index (BMI), parity, smoking status and amenorrhea status. Facial skin parameters including skin age, relative skin age (i.e., skin age minus chronological age) and skin health conditions were assessed using a bioelectrical impedance analysis device. BMI was calculated as the weight (kg) divided by height squared (m^2).

Some patients overlapped with Subject 1 and 2. Exclusion criteria included patients with skin disease, heart pace-maker, pregnancy, radiation exposure, excessive ultraviolet radiation exposure (e.g., female athletes), heavy makeup and a heavy drinking or smoking habit.

Measurement of skin age

Bioelectrical impedance of the skin shows an age-related increase[12]. This is due to the fact that hyaluronic acid, collagen and hydration contents in the skin show age-related declines and are negatively correlated with bioelectrical impedance[12]. In this study, the skin age was measured with a bioelectrical impedance analysis device, Well-Beauty® (AC100V, 50/60HZ) (Wellup, CO., Ltd., Yokohama, Japan). During measurements of skin age, wearing makeup did not matter. In subject 1, skin ages were measured after admission of patients and before gynecological treatments. In subject 2, skin ages were measured at three time points. The first measurements were performed after admission of patients and before gynecological treatments, the second measurements were performed at 6 months after the operation and the third measurements were performed at 12 months after the operation. In subject 3, skin ages were also measured at three time points: before cancer operations and 6 and 12 months after 6 courses of postoperative anti-cancer chemotherapy. We input their sex and age using the touch panel monitor of the device. After fixing electrodes to the patient's bilateral palms and cheek skin, impedance to the weak flow of an electric current between the layers of the epidermis and dermis was measured for 40 seconds. This impedance was plotted on an age-related decline curve of 1/impedance obtained from pooled standard data, and then the measurement result (i.e., skin age) was displayed on the touch panel. Facial skin health conditions were ranked from A to E according to the relative skin age (skin age minus chronological age) and results were displayed on the touch panel. The ranking comprised five categories: A (much younger skin), B (younger skin), C (normal range skin), D (older skin) and E (much older skin), compared with the chronological age, as shown in Table 1. In this study, skin health rank A or B was defined as a "young skin condition", whereas skin health rank D or E was defined as an "old skin condition", and C was a "normal skin condition".

Table 1. Facial skin health conditions (rank)

Rank		Relative skin age* (years)
A	Much younger skin	～ -11
B	Younger skin	-10 ～ -5
C	Normal range skin	-4 ～ +4
D	Older skin	+5
E	Much older skin	+6 ～

* Relative skin age = skin age –chronological age (years)

Statistical analysis

All data show the mean ± standard error of the mean. Inter- and intra-group comparisons were made of the relative skin age, changes in the relative skin age and skin health conditions using paired or unpaired Student's t-test or the Chi-square test, as appropriate. $p<0.05$ was considered significant.

Results

The relationship of estrogen-dependent diseases with relative skin age in premenopausal women (Subject 1)

Table 2 shows comparisons of backgrounds of 57 premenopausal women with estrogen-dependent and estrogen-independent diseases. The chronological age was significantly older in women with estrogen-dependent diseases. The difference in skin age was not significant between the two groups. However, the relative skin age was significantly younger in women with estrogen-dependent diseases, compared with those with estrogen-independent diseases (-1.0 ± 1.4 vs. 2.5 ± 0.6 years, respectively, $p<0.01$) (Figure 1). Table 3 shows the differences in the facial skin health conditions of the 57 premenopausal women between the two groups. The ratio of young skin conditions (the number of A + B/the total number) was significantly higher in women with estrogen-dependent diseases than in those with estrogen-independent diseases (5/19 vs. 2/38, respectively, $p<0.05$). However, the ratio of old skin conditions (the number of D + E/the total number) was not different between the two groups.

The influence of premature oophorectomy on skin aging in premenopausal women (Subject 2)

We measured the skin age of oophorectomy and ovarian

Table 2. Background of 57 premenopausal women with estrogen-dependent and estrogen-independent diseases

	Estrogen-dependent disease (n=19)	Estrogen-independent disease (n=38)	p-value
Age (years)	44.1±1.6	38.1±1.1	$p<0.05$
Skin age (years)	43.1±1.7	40.6±1.2	0.12
Height (cm)	157.6±1.3	156.9±0.9	0.67
Weight (kg)	60.7±2.47	55.8±1.32	0.06
BMI* (kg/m^2)	24.5±1.01	22.7±0.53	0.08
Parity	0.79±0.22	1.13±0.17	0.25
Amenorrhea (%)	0%	0%	NS†
Smokers (%)	15.8% (n=3)	36.8% (n=14)	0.10

Data are mean ±SEM
*BMI =body mass index
†NS = not significant

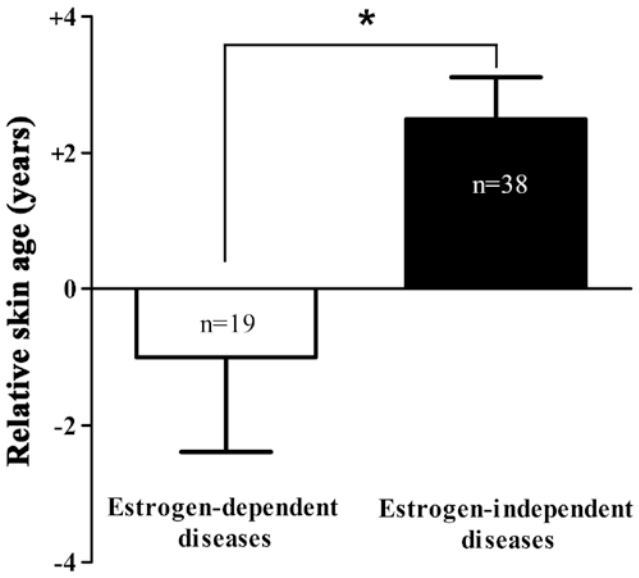

Figure 1. Relative skin age of 57 premenopausal women with estrogen-dependent and estrogen-independent diseases. *p<0.05

Table 3. Facial skin health conditions of 57 premenopausal women with estrogen-dependent and estrogen-independent diseases

Facial skin health conditions (rank)		Estrogen-dependent diseases (n=19)	Estrogen-independent diseases (n=38)	
Young skin	A+B	5	2	$p<0.05$
	A	3	1	(5/19 vs. 2/38)
	B	2	1	
Normal skin	C	12	28	NS*
Old skin	D+E	2	8	p=0.32
	D	2	4	(2/19 vs. 8/38)
	E	0	4	

*NS = not significant

preservation groups before and 6 and 12 months after the operation. Tables 4 and 5 show the backgrounds of the two groups of premenopausal women (skin age measurements 6 and 12 months after the operation, respectively). At 6 months postoperatively, the chronological age and skin age in the oophorectomy group were both significantly older than in the ovarian preservation group. At 12 months postoperatively, the chronological age and skin age in the oophorectomy group were also older than in the ovarian preservation group, although the difference in the skin age was not significant. Longitudinal changes in relative skin age at 6 months postoperatively in the oophorectomy group had progressed significantly compared with that in the ovarian preservation group (3.5 ± 1.4 vs. -0.2 ± 0.8 years, respectively, $p<0.05$) (Figure 2). Longitudinal changes in relative skin age at 12 months postoperatively in the oophorectomy group tended to progress compared with that in ovarian preservation group (3.5 ± 1.8 vs. 0.1 ± 0.3 years, respectively, $p=0.08$) (Figure 3). On inter-group comparison in the oophorectomy group, longitudinal changes in relative skin age had progressed significantly at 12 months postoperatively (Figure 4, $p<0.05$). In the ovarian preservation group, the relative skin age showed no longitudinal change at 12 months postoperatively.

Table 4. Background of oophorectomy and ovarian preservation groups in 26 premenopausal women (skin age measurements at 6 months postoperatively)

	Oophorectomy (n=15)	Ovarian preservation (n=11)	p-value
Age (years)	47.2±1.3	37.1±1.4	$p<0.05$
Skin age (years)	46.6±1.7	39.7±1.5	$p<0.05$
Height (cm)	158.2±1.1	156.8±1.6	0.45
Weight (kg)	59.1±2.45	53.0±1.77	0.07
BMI* (kg/m^2)	23.7±1.02	21.6±0.70	0.14
Parity	1.00±0.31	0.91±0.25	0.83
Amenorrhea (%)	0%	0%	NS†
Smokers (%)	20.0% (n=3)	36.4% (n=4)	0.37

Data are mean ±SEM
*BMI =body mass index
†NS = not significant

Table 5. Background of oophorectomy and ovarian preservation groups in 17 premenopausal women (skin age measurements at 12 months postoperatively)

	Oophorectomy (n=10)	Ovarian preservation (n=7)	p-value
Age (years)	45.7±1.8	38.6±1.8	$p<0.05$
Skin age (years)	45.2±1.9	41.7±1.7	0.11
Height (cm)	157.4±1.4	158.3±2.2	0.72
Weight (kg)	62.6±4.06	53.1±2.56	0.09
BMI* (kg/m^2)	25.2±1.53	21.2±1.01	0.07
Parity	1.30±0.40	1.14±0.34	0.78
Amenorrhea (%)	0%	0%	NS†
Smokers (%)	20.0% (n=2)	42.9% (n=3)	0.34

Data are mean ±SEM
*BMI =body mass index
†NS = not significant

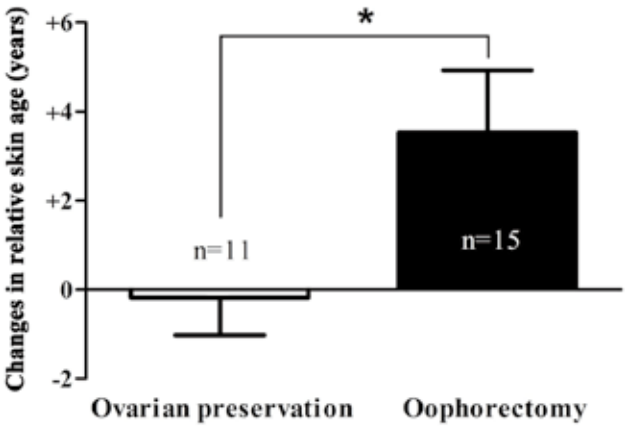

Figure 2. Changes in relative skin age of ovarian preservation and premature oophorectomy groups in 26 premenopausal women (6 months after operation). *p<0.05

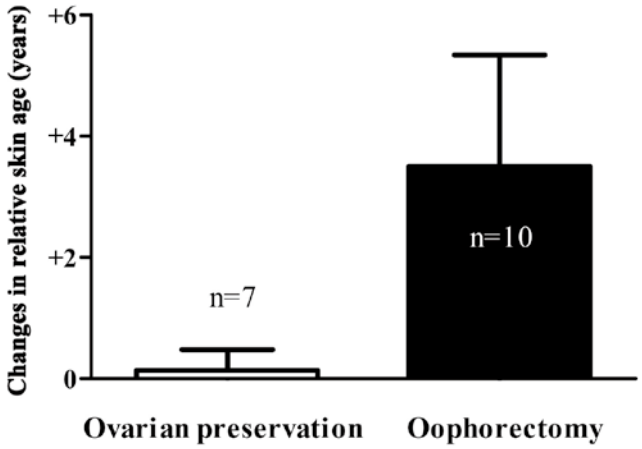

Figure 3. Changes in relative skin age of ovarian preservation and premature oophorectomy groups in 17 premenopausal women (12 months after operation). p=0.08

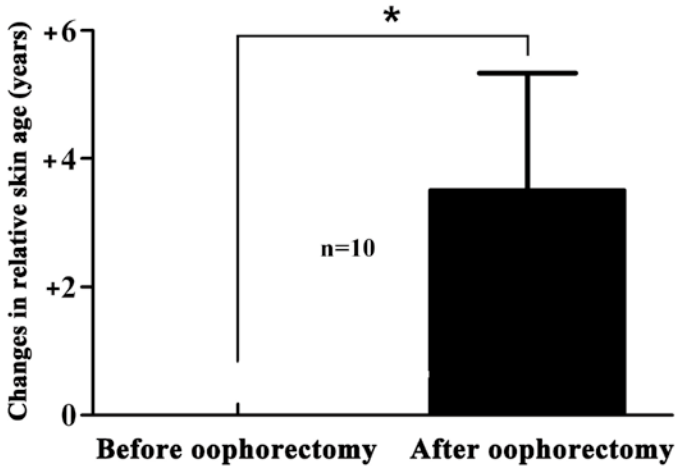

Figure 4. Longitudinal changes in relative skin age of premature oophorectomy group before and 12 months after oophorectomy (n=10). *p<0.05

The influence of anti-cancer chemotherapy on skin aging in postmenopausal women (Subject 3)

Table 6 shows the background of operation followed by chemotherapy and operation alone (control) groups (total of 11 postmenopausal women). Differences in the chronological age and skin age between the two groups were not significant. Longitudinal changes in relative skin age of the two groups were observed 6 and 12 months after chemotherapy. Six months after chemotherapy, longitudinal changes in relative skin age had progressed significantly in chemotherapy group compared with control group (8.7 ± 3.6 vs. -3.4 ± 3.0 years, respectively, $p<0.05$) (Figure 5). Twelve months after chemotherapy, similar results were obtained (10.5 ± 3.3 vs. -3.8 ± 3.4 years, respectively, $p<0.05$) (Figure 6). Table 7 presents the changes in the skin health condition before and 12 months after anti-cancer chemotherapy. The ratio of young skin conditions was also significantly decreased after chemotherapy (from 5/6 to 1/6, respectively, $p<0.05$). Longitudinal changes in relative skin age were observed before and after chemotherapy at 6-month intervals (Figure 7). Relative skin ages significantly progressed 6 and 12 months after chemotherapy, respectively.

Table 6. Background of chemotherapy and control groups in 11 postmenopausal women

	Chemotherapy (n=6)	Control (n=5)	p-value
Age (years)	63.3±1.3	58.6±2.6	0.12
Skin age (years)	53.5±2.8	57.8±3.0	0.16
Height (cm)	158.5±2.4	156.4±1.8	0.52
Weight (kg)	52.8±4.09	60.4±2.78	0.18
BMI* (kg/m^2)	21.0±1.46	24.8±1.40	0.10
Parity	1.67±0.56	1.40±0.40	0.72
Smokers (%)	0% (n=0)	20.0% (n=1)	0.34

Data are mean ±SEM
*BMI =body mass index

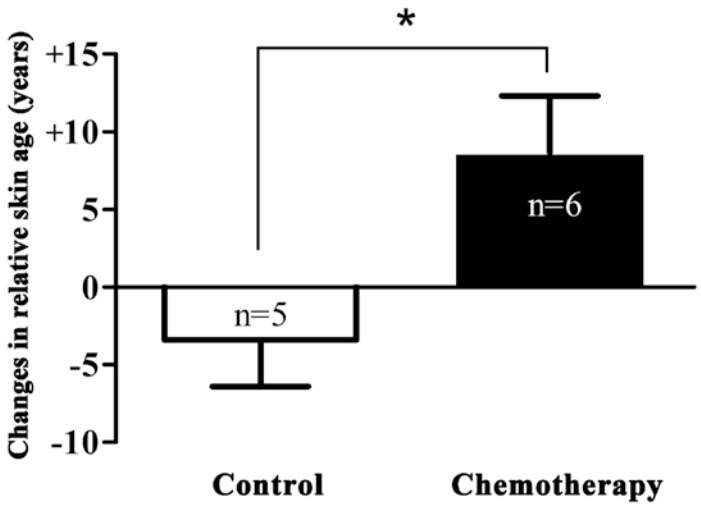

Figure 5. Changes in relative skin age of chemotherapy and control groups in 11 postmenopausal women (6 months after chemotherapy). *$p<0.05$

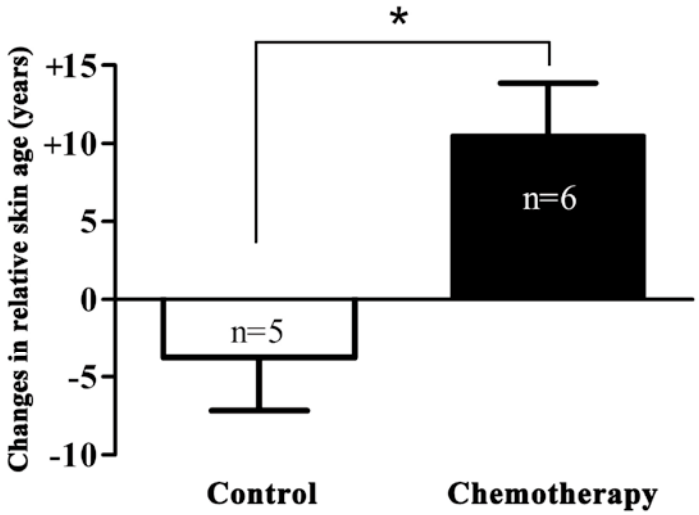

Figure 6. Changes in relative skin age of chemotherapy and control groups in 11 postmenopausal women (12 months after chemotherapy). *p<0.05

Table 7. Changes in skin health conditions before and 12 months after anti-cancer chemotherapy in 6 postmenopausal women

Facial skin health conditions (rank)		Before chemotherapy	After chemotherapy	
Young skin	A+B	5	1	p＜0.05 (5/6 vs. 1/6)
	A	5	1	
	B	0	0	
Normal skin	C	1	5	p＜0.05 (1/6 vs. 5/6)
Old skin	D+E	0	0	NS*
	D	0	0	
	E	0	0	

*NS = not significant

Figure 8 presents longitudinal changes in relative skin age in a 38-year-old patient with cervical cancer, who received 6 courses of anti-cancer TC chemotherapy after radical trachelectomy with ovarian preservation. Skin ages were measured before and 6 and 12 months after chemotherapy. The relative skin age markedly progressed from -10 years at the baseline to +3 years at 6 months after chemotherapy. During the 6-month period, the skin age became 13 years older. However, skin aging reached a plateau between 6 and 12 months after chemotherapy. Skin health conditions showed rank B at the baseline, and rank C at both 6- and 12-month intervals, being consistent with longitudinal changes in the relative skin age (Figures 5, 6 and 7). During chemotherapy and the follow-up period, she maintained her regular menstrual cycle.

Discussion

The skin is one of the important non-reproductive target organs of estrogen, which is known to play an essential role in regulating skin maintenance and turnover[13, 14]. Postmenopausal skin shows increased dryness[15, 16], decreased elasticity[17] and increased wrinkling[18]. Postmenopausal hormone replacement therapy (HRT) improves skin conditions[7, 19, 20] through

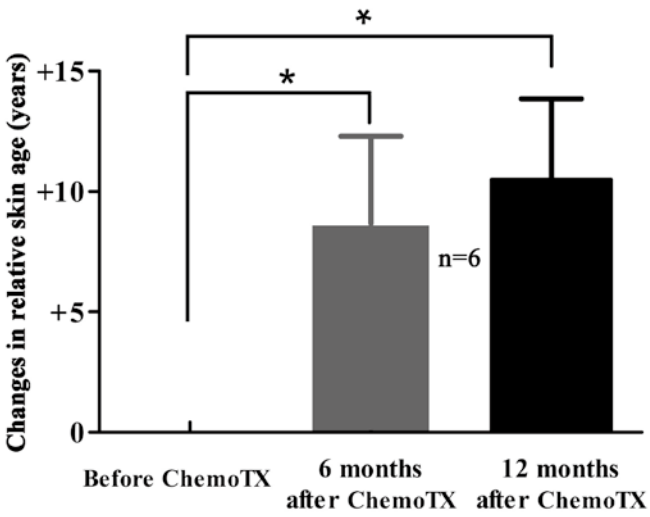

Figure 7. Longitudinal changes in relative skin age before and after chemotherapy in 6 postmenopausal women (at 6-month intervals). ChemoTX: chemotherapy. *p<0.05

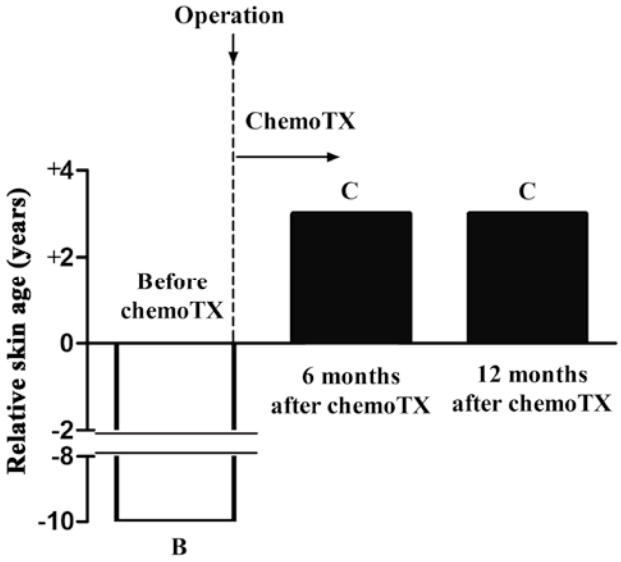

Figure 8. Relative skin age at 6-month intervals in a patient with cervical cancer who received 6 courses of postoperative anti-cancer chemotherapy after radical trachelectomy with ovarian preservation. ChemoTX: chemotherapy. B, C: Skin health condition ranks B and C.

increasing the skin collagen content, thickness, moisture and elasticity[21, 22]. A previous study showed that the decreases in the skin thickness and collagen content seen in elderly women may be more closely associated with estrogen deficiency than the chronological age[1]. In this study, we found that women with estrogen-dependent diseases had a younger skin age compared with their chronological age, and had a younger relative skin age compared with women with estrogen-independent diseases. To our best knowledge, there has been no other similar study. It is well-known that bone is also a target organ of estrogen, and that bone mineral density (BMD) is increased by HRT[23, 24]. Women with endometrial cancer have a higher BMD[25-29]. However, women with uterine cervical cancer as an estrogen-independent disease do not show a higher BMD[30]. Previous studies showed that a decrease in the skin collagen content parallels the reduction in BMD seen in postmenopausal women[1, 31]. In ovariectomized rats, marked structural alterations in skin and bone collagen

parallel hypoestrogenism[32]. Considering these findings, it is likely that cumulative estrogen exposure contributes to a younger skin age, higher BMD and the development of endometrial cancer and uterine leiomyoma.

In Japan, prophylactic salpingo-oophorectomy has been frequently performed for perimenopausal women undergoing hysterectomy even for benign conditions to prevent the later occurrence of ovarian cancer. However, women receiving premature oophorectomy have more severe and prolonged menopausal symptoms, and their risks of mood disturbance, heart disease, excessive bone resorption, sexual dysfunction and cognitive disorder are increased[33-38]. Although there have been many studies on the adverse effects of prophylactic oophorectomy on various organs to date[33-36], studies on the impact of prophylactic oophorectomy on skin conditions are limited. In the present study, longitudinal changes in the relative skin age of women who received premature oophorectomy progressed compared with the baseline level and controls with ovarian preservation at 6 months postoperatively. However, the relative skin age remained unchanged in women with ovarian preservation. Our study supports a report that prophylactic oophorectomy during hysterectomy is a significant and independent risk factor for accelerated skin aging in premenopausal women[39], reducing the quality of life (QOL). In addition, skin aging developed in an early period after oophorectomy, consistent with a previous report[39]. Many women feel a relatively early onset of skin aging several months after the beginning of menopausal symptoms[22, 40]. Thus, skin aging during menopausal transition may be an early symptom[40]. If skin aging is caused by premature oophorectomy alone, HRT soon after oophorectomy may delay the aging[7, 18], improving the QOL. However, long-term HRT may be necessary for the reversal of skin aging caused by oophorectomy, as well as the effect of postmenopausal HRT on the skin condition[7].

Standard operative procedures for ovarian cancer are hysterectomy and bilateral salpingo-oophorectomy with surgical staging (peritoneal washing cytology, omentectomy, retroperitoneal lymphadenectomy)[41]. It is well-known that the side effects of anti-cancer agents are nausea, vomiting, appetite loss, leucopenia and alopecia. Long-term side effects include the acceleration of neurocognitive decline, musculoskeletal complications such as early-onset osteoporosis, premature skin aging and ocular changes[42, 43]. Chemotherapy also affects the skin, mucous membranes, hair and nails, causing undesirable reactions including alopecia, stomatitis, hyperpigmentation, hypersensitivity reactions, and photosensitivity[10]. There is a report that skin aging is the most frequently reported unpleasant side effect[44]. In the present study, longitudinal changes in relative skin age markedly progressed in postmenopausal women with postoperative anti-cancer chemotherapy. In addition, facial skin aging in a cervical cancer patient who received radical trachelectomy with ovarian preservation markedly progressed after adjuvant anti-cancer chemotherapy. In this patient, chemotherapy-induced ovarian insufficiency (i.e., estrogen deficiency) was not observed. Based on the effects of premature oophorectomy and anti-cancer chemotherapy on the skin age, it is likely that the adverse effect of anti-cancer chemotherapy on the skin condition is greater than that of oophorectomy, leading to a greater reduction in the QOL.

We could not elucidate the underlying mechanism of skin aging induced by anti-cancer chemotherapy. In addition, it remained unresolved as to which of three anti-cancer agents has the greatest impact on skin aging. Our finding of a greater impact of chemotherapy compared with oophorectomy on skin aging suggests that mechanisms of skin aging are different between chemotherapy and premature oophorectomy. We should consider that every anti-cancer chemotherapeutic agent has potential mechanisms, including the accumulation of free-radical damage, accumulation of DNA damage, telomere shortening accompanying a decline in telomerase activity and damage to the neuroendocrine/immune function[43]. The mechanisms of cyclophosphamide-induced nail pigmentation have been reported to include a genetic predisposition, toxic effect of the drug on the nail bed and matrix, photosensitization, and focal stimulation of melanocytes in the matrix[45].

It remains unclear whether skin aging due to anti-cancer chemotherapy is reversible with medical intervention. In this respect, a long period was required for recovery from chemotherapy-induced alopecia. The pigmentation of nails, as a part of the skin, usually reverses several months after withdrawal of the drugs[46]. In ovarian cancer patients, oophorectomy and anti-cancer chemotherapy are usually performed, both of which affect skin conditions. Thus, the prevention and/or treatment against facial skin worsening may require a long period even though HRT is administered. Further extensive studies are needed.

In summary, women with estrogen-dependent diseases maintain a younger facial skin age than those with estrogen-independent diseases. However, skin aging is markedly accelerated by anti-cancer chemotherapy or premature oophorectomy, and the QOL is reduced. Considering the

possible occurrence of accelerated skin aging, we must pay special attention to prophylactic oophorectomy accompanying hysterectomy for benign conditions and anti-cancer chemotherapy.

Disclosure

The authors have no conflicts of interest to disclose.

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Influences of Estrogen-dependent Diseases, Premature Oophorectomy and Anti-cancer Chemotherapy on Skin Age in Japanese Women

エストロゲン依存性疾患、外科的去勢および抗がん剤の肌年齢に及ぼす影響（日本人女性での検討）

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目的：皮膚にはエストロゲン（E）レセプターが存在し、E が複数の細胞に作用しヒアルロン酸などの生成を促進し、潤いや張りを与える。肌の老化（菲薄化、乾燥、皺の増加、弾力性の低下）には加齢、放射線療法、抗癌剤投与などが関与するが、閉経や外科的去勢でも起こる。しかし、低 E 状態による肌の老化はあまり研究されていない。我々は Bioelectrical Impedance Analysis（BIA）で肌年齢、肌の健康状態の客観的評価が可能であることに着目し、E 依存性疾患、外科的去勢および抗がん剤の肌年齢に及ぼす影響について検討した。

方法：2016 年 7 月から 2018 年 5 月までに当科を受診した患者 68 例を対象にした。Informed consent の後、肌年齢、肌加齢度（肌年齢 - 暦年齢）を Wellup 社製の肌年齢測定器（Well-Beauty、BIA 法）で測定した。①有経女性で E 依存性疾患患者（主に子宮筋腫や子宮体癌、n=19）と E 非依存性疾患患者（主に子宮頸癌、n=38）の肌年齢や肌加齢度を比較した。②有経女性で外科的去勢（n=15）による肌年齢、肌加齢度の推移を卵巣温存群（n=11）と比較した。③閉経女性で婦人科悪性腫瘍の標準手術（含:卵巣摘出術）と化学療法を受けた患者（n=6）と標準手術のみを受けた患者（対照、n=5）で肌年齢、肌加齢度の推移を比較した。有意差検定は Student t-test、χ^2 検定で適宜行った。

結果：1 ）E 依存性疾患患者では E 非依存性疾患患者に比較して肌が有意に若かった (肌加齢度：-1.0±1.4 歳 vs.+2.5±0.6 歳、$p<0.01$)。 2 ）去勢後 6 か月で肌年齢は有意に悪化したが、卵巣温存群では変化しなかった（肌加齢度の推移：+3.5±1.4 歳 vs.-0.2±0.8 歳、$p<0.05$）。 3 ）化学療法群の化学療法終了 12 か月後の肌年齢は、対照に比較して有意に悪化した（肌加齢度の推移：+10.5±3.3 歳 vs.- 3.8±3.4 歳、$p<0.05$）。化学療法により、肌年齢が 5 歳以上若い女性の割合も有意に減少した（5/6 から 1/6、$p<0.05$）。

結論：E 依存性疾患患者では肌年齢が若く、外科的去勢による低 E 状態は肌年齢にも悪い影響を及ぼす。一方、卵巣温存群では肌年齢は悪化しなかったため、有経期女性の予防的卵巣摘出術には慎重であるべきである。また、化学療法はより高度に肌年齢を悪化させることが判明したため、治療中のケアは重要である。