Compositional Changes of the Uterine Arteries in Japanese and Thai with Aging

Pasuk Mahakkanukrauh[1], Setsuko Tohno[1,2], Takeshi Minami[3], Apichat Sinthubua[1], Patipath Suwannahoy[1], Takashi Naganuma[2], Cho Azuma[2] and Yoshiyuki Tohno[1,2,*]

[1]Department of Anatomy, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand
[2]Department of Anatomy, Nara Medical University School of Medicine, Kashihara, Nara 634-8521, Japan
[3]Laboratory of Environmental Biology, Department of Life Science, Faculty of Science and Engineering, Kinki University, Higashi-Osaka, Osaka 577-8502, Japan

**Corresponding author. E-mail: ytohno@med.cmu.ac.th*

ABSTRACT

To elucidate compositional changes of the uterine artery with aging, the authors investigated age-related changes of elements in the uterine arteries of Japanese and Thai by direct chemical analysis. After ordinary dissections at Nara Medical University and Chiang Mai University were finished, the uterine arteries were resected from the subjects. After ashing of arteries with nitric acid and perchloric acid, element contents were determined by inductively coupled plasma-atomic emission spectrometry. It was found that a higher accumulation of Ca occurred in the uterine artery with aging in comparison with other three branches of the internal iliac artery. In the uterine arteries of both Japanese and Thai, the Ca, P and Na content increased significantly with aging. In the uterine artery of Thai, the Ca content began to increase in the forties and increased up to the seventies. As far as the uterine arteries in the subjects more than 60 years of age, the extent of Ca accumulation in the uterine arteries of Thai was one half of that in the uterine arteries of Japanese. It should be noted that the Ca accumulation occurred in the uterine artery independently of other arteries, such as the thoracic and abdominal aortas and the coronary, common carotid, splenic and common iliac arteries.

Key words: Uterine artery, Internal iliac artery, Calcium, Phosphorus, Atherosclerosis, Aging

INTRODUCTION

There are several reports (Camiel et al., 1967; Fisher and Hamm, 1975; Kadziolka et al., 1985; Punnonen et al., 1995; Crawford et al., 1997) on calcification or atherosclerosis of the uterine artery. Histological and pathologic studies

(Crawford et al., 1997) revealed that atherosclerosis of the uterine artery occurred more frequently in postmenopausal women than in premenopausal women. However, few studies had been conducted on the element contents in the uterine artery by direct chemical analysis. Therefore, the authors investigated first whether the extent of Ca accumulation was different between the branches of the internal iliac arteries. Next, the authors focused on the uterine artery and investigated age-related changes of elements in the uterine arteries of both Japanese and Thai. It was found that a higher accumulation of Ca occurred in the uterine artery in comparison with other branches of the internal iliac artery and that there was a significant difference in age-related changes of the Ca content between the uterine arteries of Japanese and Thai.

MATERIALS AND METHODS

Sampling of Arteries

Japanese cadavers were treated by injection of a mixture of 36% ethanol, 13% glycerin, 6% phenol, and 6% formalin through the femoral artery (Tohno, Y. et al, 1985). Thai cadavers were treated by injection of a mixture of 26% methanol, 14% glycerin, 3% phenol, 14% formalin, 0.34 M potassium nitrate, and 14 mM arsenic oxide through the femoral artery (Tohno, Y. et al., 2001a). After ordinary dissections by medical students at Nara Medical University and Chiang Mai University were finished, the uterine arteries were resected from the subjects. The distal sites of the uterine arteries were used in the present study.

Determination of Elements

The samples of arteries were washed thoroughly with distilled water and were dried at 80°C for 16 h. After 1 mL conc. nitric acid was added to the dry samples, the mixtures were heated at 100°C for 2 h. After the addition of 0.5 mL conc. perchloric acid, they were heated at 100°C for an additional 2 h. The samples were adjusted to a volume of 10 mL by adding ultrapure water and were filtered through filter paper (No. 7; Toyo Roshi, Osaka, Japan). The resulting filtrates were analyzed with an inductively coupled plasma-atomic emission spectrometer (ICPS-7510; Shimadzu, Kyoto, Japan) (Tohno, Y. et al., 1996). The conditions were 1.2 kW of power from a radio-frequency generator, a plasma argon flow rate of 1.2 L/min, a cooling gas flow of 14 L/min, a carrier gas flow of 1.0 L/min, an entrance slit of 20 μm, an exit slit of 30 μm, a height of observation of 15 mm, and an integration time lapse of 5 s. The element amount was expressed on a dry-weight basis.

Statistical Analysis

Statistical analyses were performed using the GraphPad Prism version 3.0 (GraphPad Software Inc., San Diego, CA, USA). Pearson's correlation was used to investigate the association between parameters. A two-tailed unpaired Student's *t* test was used to compare differences between groups. A *p*-value of less than 0.05 was considered to be statistically significant. Data were expressed as the

mean±standard deviation.

RESULTS

Ca Content in Four Branches of the Internal Iliac Arteries

To examine whether the extent of Ca accumulation with aging was different between the branches of the internal iliac artery, the authors investigated the Ca content of four branches of the internal iliac artery, such as the uterine, internal pudendal, umbilical, and obturator arteries in ten Japanese women subjects. The Japanese women subjects ranged in age from 52 to 96 years (average age=77.4±13.1 years). Table 1 indicates the average content of Ca in the four branches of the internal iliac artery. The average content of Ca was highest in the uterine arteries and decreased in order of the internal pudendal, umbilical and obturator arteries. A significant difference in the average content of Ca was found between the uterine and either umbilical or obturator arteries, but it was not found between the uterine and internal pudendal arteries. The average content of Ca in the uterine arteries corresponded to 46-fold the amount of that in the obturator arteries. This result indicated clearly that the extent of Ca accumulation was different among the four branches of the internal iliac artery at old age.

Table 1. Comparison of the Average Content of Ca in the Branches of the Internal Iliac Arteries.

Artery	Average Content of Ca (mg/g)
Uterine	68.74±84.81
Internal Pudendal	26.02±56.69
Umbilical	3.40±2.29*
Obturator	1.48±2.16*

Note: *A p value between the uterine and either umbilical or obturator arteries was < 0.05.

Age-Related Changes of Elements in the Uterine Arteries of Japanese and Thai

To elucidate compositional changes of the uterine artery with aging, the authors investigated age-related changes of elements in the uterine arteries of 27 Japanese and 28 Thai women subjects. Japanese women subjects ranged in age from 58 to 99 years (average age=82.7±10.1 years). Thai women subjects ranged in age from 27 to 86 years (average age=63.3±17.7 years).

Figure 1 shows age-related changes of the Ca, P and Na contents in the uterine arteries of both Japanese and Thai. In the uterine arteries of Japanese, the correlation coefficients between age and element contents were estimated to be 0.430 (p=0.025) for Ca, 0.425 (p=0.027) for P and 0.526 (p=0.005) for Na. Significant direct correlations were found between age and either Ca or P content and a very significant direct correlation was found between age and Na content in

the uterine arteries of Japanese. However, no significant correlations were found between age and element contents, such as Mg, Zn and Fe in the uterine arteries of Japanese.

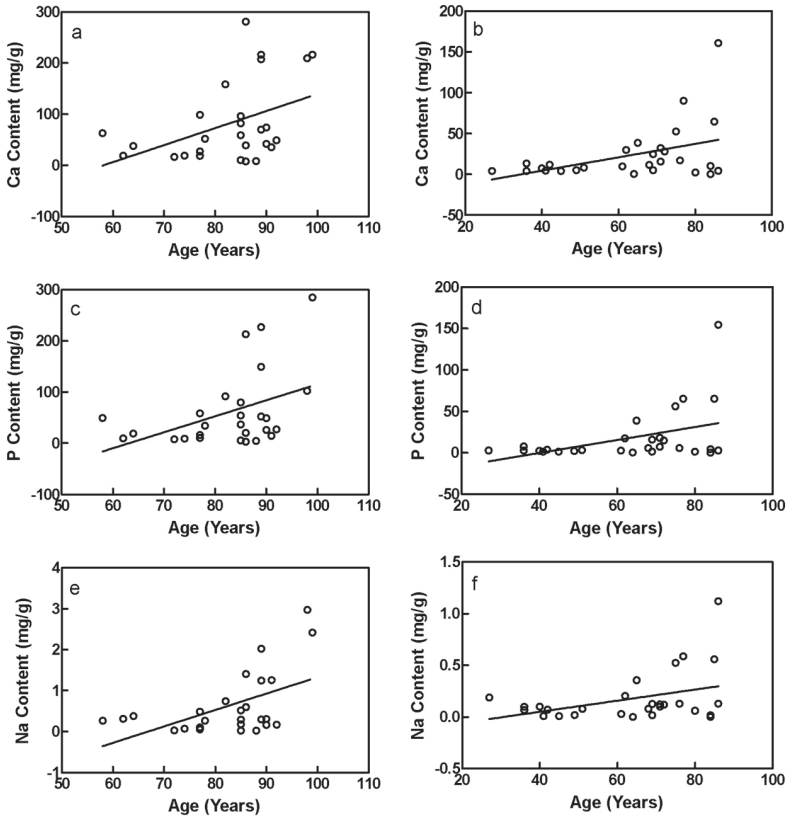

Figure 1. Age-related changes of the Ca (a), P (c) and Na (e) contents in the uterine arteries of Japanese and of the Ca (b), P (d) and Na (f) contents in the uterine arteries of Thai.

In the uterine arteries of Thai, the correlation coefficients between age and element contents were estimated to be 0.425 (p=0.024) for Ca, 0.419 (p=0.026) for P and 0.383 (p=0.045) for Na. Significant direct correlations were found between age and element contents, such as Ca, P and Na in the uterine arteries of Thai. However, no significant correlations were found between age and element contents, such as Mg, Zn and Fe in the uterine arteries of Thai. The common finding that there were significant direct correlations between age and element contents, such as Ca, P and Na was obtained in the uterine arteries of both Japanese and Thai.

Figure 2 shows age-related changes of the Ca content in the uterine arteries of both Japanese and Thai. The linear slopes drawn with the computer software were different between the uterine arteries of Japanese and Thai. The difference between the two slopes was significant, because a p value was 0.046.

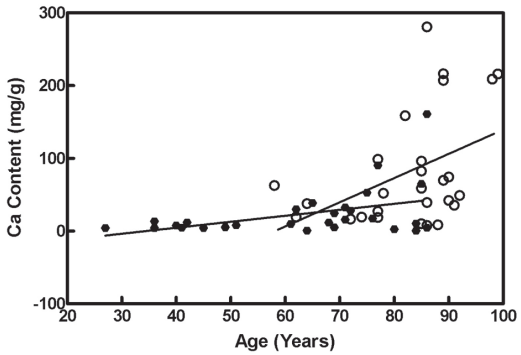

Figure 2. Age-related changes of the Ca content in the uterine arteries of both Japanese (open circle) and Thai (solid circle). The equation of Japanese, y=3.328x-193.4; the equation of Thai, y=0.805x-27.7. The difference between the two slopes in Fig. 2 was significant, because a p value was 0.046.

Comparison in the Average Content of Elements Between the Uterine Arteries of Japanese and Thai

Figure 3 shows the average content of Ca in the uterine arteries of Japanese and Thai by age group. In the uterine arteries of Japanese, the average content of Ca was significantly high in the seventies and increased remarkably in the eighties. The average content of Ca in the eighties corresponded to 2.7-fold the amount of that in the seventies. In the uterine arteries of Thai, the average content of Ca was significantly high in the sixties and increased remarkably in the seventies. The average content of Ca in the seventies corresponded to 6-fold the amount of that in the forties.

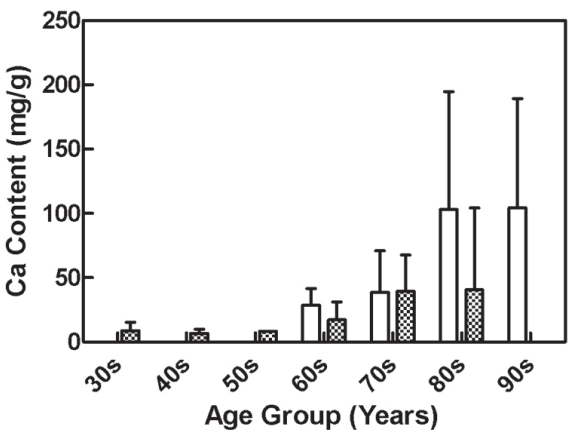

Figure 3. Comparison in the average content of Ca in the uterine arteries of Japanese and Thai by age group. The open and crossed bars indicate Japanese and Thai, respectively.

In comparison with the uterine arteries of Thai, the average content of Ca in the uterine arteries of Japanese was similar to in the seventies, but it was two times higher in the eighties. However, the difference between their average contents of Ca in the eighties was not statistically significant.

Table 2 indicates the incidence of the uterine arteries of Japanese and Thai with the Ca content more than 10 mg/g which is not contained in a normal artery. In Japanese, the incidence of the uterine artery with the high Ca content was 100% in the seventies, 83% in the eighties and 100% in the nineties. In Thai, the incidence of the uterine artery with the high Ca content was 57% in the sixties, 100% in the seventies and 50% in the eighties. It is interesting that in Thai, the incidence of the uterine artery with the high Ca content decreased from 100% in the seventies to 50% in the eighties.

As far as the subjects more than 60 years of age are concerned, the incidence of the uterine artery with the high Ca content was 92% in Japanese and 68% in Thai. The incidence of the uterine artery with the Ca content more than 10 mg/g was higher in Japanese than in Thai. Furthermore, as far as the subjects more than 60 years of age are concerned, the average content of Ca in the uterine arteries was 82.73±79.80 mg/g in Japanese and 31.57±39.32 mg/g in Thai. In the uterine arteries more than 60 years of age, both the incidence of the uterine artery with the Ca content more than 10 mg/g and the average content of Ca were higher in the Japanese than in the Thai.

Table 2. Incidence of the Uterine Arteries of Japanese and Thai with the Ca Content more than 10 mg/g.

Age Group (Years)	Incidence (%)	
	Japanese	Thai
30s	NA	50% (1/2)
40s	NA	20% (1/5)
50s	100% (1/1)	0 % (0/1)
60s	100% (2/2)	57% (4/7)
70s	100% (6/6)	100% (6/6)
80s	83% (10/12)	50% (3/6)
90s	100% (6/6)	NA

Note: The number of cases is indicated in parentheses.
NA indicates that the specimen was not analyzed.

Relationships Among Elements in the Uterine Arteries of Japanese and Thai

The relationships among element contents were examined in the uterine arteries of both Japanese and Thai. In the uterine arteries of Japanese, the correlation coefficients were estimated to be 0.922 (p<0.0001) between Ca and P contents, 0.860 (p<0.0001) between Ca and Mg contents and 0.973 (p<0.0001) between P and Mg contents (Table 3). In the uterine arteries of Thai, the correlation

coefficients were estimated to be 0.986 (p<0.0001) between Ca and P contents, 0.959 (p<0.0001) between Ca and Mg contents and 0.946 (p<0.0001) between P and Mg contents (Table 3). Extremely significant direct correlations were found between Ca and P contents, between Ca and Mg contents and between P and Mg contents in the uterine arteries of both Japanese and Thai. As shown in Table 3, extremely significant direct correlations were also found between Zn and element contents, such as Ca, P and Mg, and between Na and element contents, such as Ca, P, Mg and Zn. However, no significant correlations were found regarding Fe, except for a significant direct correlation between Zn and Fe contents. Therefore, extremely significant direct correlations were found among the contents of Ca, P, Mg, Zn and Na in the uterine arteries of both Japanese and Thai. This meant that as Ca increased in the uterine artery, P, Mg, Zn and Na also increased in the artery.

Table 3. Relationships Among Element Contents in the Uterine Arteries of Japanese and Thai.

Correlation Coefficient and p-Value					
Element	P	Mg	Zn	Fe	Na
Ca	0.922 (<0.0001) 0.986 *(<0.0001)*	0.860 (<0.0001) 0.959 *(<0.0001)*	0.805 (<0.0001) 0.657 *(<0.0001)*	0.125 (0.536) 0.209 *(0.286)*	0.804 (<0.0001) 0.967 *(<0.0001)*
P		0.973 (<0.0001) 0.946 *(<0.0001)*	0.793 (<0.0001) 0.667 *(0.0001)*	-0.014 (0.945) 0.235 *(0.228)*	0.773 (<0.0001) 0.982 *(<0.0001)*
Mg			0.778 (<0.0001) 0.759 *(<0.0001)*	-0.048 (0.813) 0.277 *(0.154)*	0.731 (<0.0001) 0.921 *(<0.0001)*
Zn				0.388 (0.046) 0.526 *(0.004)*	0.647 (0.0003) 0.651 *(0.0002)*
Fe					0.115 (0.569) 0.233 *(0.233)*

Note: The upper roman and lower italic numerals indicate Japanese and Thai, respectively. p-Values are indicated in parentheses.

Relationships in the Ca Content Between the Uterine Artery and Other Arteries

To examine whether there were significant correlations between the uterine artery and other arteries with regard to the Ca accumulation, the authors investigated age-related changes of the Ca content in the thoracic and abdominal aortas and the uterine, coronary, common carotid, splenic and common iliac arteries in 14 Japanese women subjects. The subjects ranged in age from 58 to 92 years (average age=82.1±9.2 years). The relationships between the uterine artery and other six arteries were examined with regard to the Ca content. The correlation coefficients between the uterine artery and other arteries in the Ca content were estimated to be 0.098 (p=0.738) for the thoracic aorta, 0.182 (p=0.534) for the abdominal aorta, -0.175 (p=0.549) for the coronary artery, 0.016 (p=0.956) for the common carotid artery, 0.030 (p=0.920) for the splenic artery and 0.271 (p=0.349) for the common iliac artery. No significant correlations were found between the uterine artery and the six arteries with regard to the Ca content. This result suggested that the Ca accumulation in the uterine artery occurred independently of that in the six arteries, such as the thoracic and abdominal aortas and the coronary, common carotid, splenic and common iliac arteries.

DISCUSSION

The present study revealed that the extent of Ca accumulation was different among the four branches of the internal iliac artery and was greater in the uterine arteries in comparison with the other three branches.

There are several reports (Camiel et al., 1967; Fisher and Hamm, 1975; Kadziolka et al., 1985; Punnonen et al., 1995; Crawford et al., 1997) on calcification or atherosclerosis of the uterine artery. Crawford et al. (1997) investigated histological changes of the uterine arteries in both premenopausal and postmenopausal women and reported that 3.4% of the uterine arteries in the premenopausal women contained complex atheromas, whereas 40% of those in the postmenopausal women contained complex atheromas. They revealed that atherosclerosis of the uterine artery appeared to correlate with age. Our finding is consistent with the finding by Crawford et al., (1997).

The present study revealed that Ca accumulation began to occur in the uterine artery of Thai in the forties and increased up to the seventies. The authors (Tohno, Y. et al., 2001a; Tohno, S. et al., 2002) previously investigated age-related changes of elements in the common iliac, internal iliac and coronary arteries of Thai and reported that Ca accumulation began to occur in the common iliac, internal iliac and coronary arteries in the forties. The tendency of Ca accumulation in the uterine arteries of Thai was similar to that in the common iliac, internal iliac and coronary arteries of Thai. However, in Japanese, the uterine artery did not correlate with the thoracic and abdominal aortas and the coronary, common carotid, splenic and common iliac arteries with regard to the Ca content. These results suggested that Ca accumulation occurred in the uterine artery independently of that in the thoracic and abdominal aortas and the coronary, common carotid,

splenic and common iliac arteries. Furthermore, it is unclear whether the uterine artery correlates with the internal iliac artery with regard to the Ca content because it has not yet been investigated.

Regarding the relationships among elements, it was found that there were extremely significant direct correlations among the contents of Ca, P, Mg, Zn and Na in the uterine arteries of both Japanese and Thai. This finding is consistent with the foregoing results obtained in the thoracic aorta and the basilar, coronary, radial, common iliac and femoral arteries (Tohno, Y. et al., 2001b).

It was found that as for the uterine arteries in the subjects more than 60 years of age, the extent of Ca accumulation in the uterine arteries of Thai was one half of that in the uterine arteries of Japanese. The authors previously investigated the differences in age-related changes of elements between the coronary or renal arteries of Japanese and Thai and found that the Ca accumulation occurred at least 10 years earlier and higher in the coronary arteries of Thai in comparison with Japanese (Tohno, S. et al., 2002), whereas the higher Ca accumulation occurred in the renal arteries of Japanese in comparison with Thai at old age (Mahak-kanukrauh et al., 2005). These results indicated that the uterine artery was similar to the renal artery with regard to age-related changes of the Ca content, but was not similar to the coronary arteries.

Kadziolka et al., (1985) studied the occurrence and characteristics of sclerotic lesions in the uterine arteries of sterile and multiparous pigs and reported that the incidence and degree of sclerotic lesions increased with age and parity.

It is well known that cyclic changes in uterine blood flow occur in association with blood estrogen and progesterone concentrations, and uterine blood flow increases markedly during early pregnancy (Ford, 1982). Konje et al., (2003) investigated the diameter of the proximal uterine artery and uterine artery volume flow during pregnancy by color power angiography and reported that the diameter of the proximal uterine arteries was enlarged about twice during late pregnancy and uterine artery volume flow was increased to 2.5-fold volume.

The birth rate and total fertility rate were high in Japan and Thailand in the 1950's and 1960's, when the subjects were still young women. It was thought that the subjects had delivered many babies.

With regard to occurrence of calcification in the uterine artery, there are two possibilities: The first is that the increase of uterine artery blood flow during pregnancy causes mechanical stress for the uterine artery and results in calcification of the uterine artery. The second is that the calcification in the uterine artery occurs with aging, independently of pregnancy or parity. For solving this problem, the authors are planning the study for the analysis of element contents, using the uterine arteries from the subjects with clinical history.

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