Vascular Ultrasound in Gynecology

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Abstract: The usefulness of the vascular ultrasound in the filed of gynecology is now well recognized. The intima-media thickness (IMT) and the elastic property of the common carotid artery are reported to be associated with the risk of cardiovascular diseases and are thought to be influenced by menopause. The assessment of the flow-mediated vasodilation (FMD) of the brachial artery is a noninvasive method for the evaluation of vascular endothelial function and is reported to be associated with menopause or hormone replacement therapy. Certain gynecological situations such as contraceptive use or hormone replacement therapy are reported to increase the risk of thrombosis. For the screening of deep vein thrombosis of the lower extremities in the gynecological diseases, compression ultrasonography (CUS) is useful.

Key words: Vascular ultrasound, carotid artery, radial artery, flow-mediated vasodilation, deep vein thrombosis.

INTRODUCTION

A great progress has been made in the noninvasive assessment of the blood vessels using ultrasound analysis in the clinical medicine, and the deaths due to cardiovascular diseases were reduced with the progress in diagnostic methods and management of atherosclerotic diseases. Since the risk of cardiovascular disease is high in perimenopausal and postmenopausal women, gynecologists may have to play important roles in the diagnosis and management of the disorders. Since the risks are high for venous thrombosis and pulmonary embolism in some gynecological diseases and situations, the screening of deep vein thrombosis is requested in such gynecological situations as postoperative conditions. We reviewed two topics of vascular ultrasound in gynecology in this article: (i) vascular ultrasound of atherosclerotic diseases in perimenopausal and postmenopausal women, and (ii) screening of deep vein thrombosis in gynecological diseases and surgeries. The results obtained by our own studies in these topics are also discussed in this report.

METHODS

Ultrasound techniques used in this study were realtime B-mode, color Doppler flow mapping and M-mode ultrasound. The devices of SONOLINE Antares with a 4 to 9 MHz electronic linear and a 2 to 5 MHz electronic compound scan transducer (Mochida Siemens Medical System, Tokyo), LOGIQ 500 MD with a 3.5 MHz electronic compound scan transducer (GE Yokogawa Medical System, Tokyo) and SSD-550 with a 30 MHz mechanical linear scan transducer (Aloka, Tokyo) were used in this study.

We assessed the intima-media thickness of the radial artery by realtime B-mode in 485 normotensive subjects (336 men and 27 women), and in 164 patients with hypertensive disorders (137 male and 27 female patients). The elastic property of the common carotid artery was assessed by M-mode ultrasound in 12 normotensive and 20 hypertensive women. The femoral and popliteal veins were studied by conventional B-mode and color flow duplex sonography in the supine position. Deep vein thrombosis was assessed by the technique of compression ultrasonography. We assessed 317 postoperative women consisting of 180 benign abdominal, 115 malignant abdominal and 22 benign vaginal surgeries.

RESULTS

Vascular Ultrasound of the Atherosclerotic Diseases in Perimenopausal and Postmenopausal Women

It is well known that the incidence of atherosclerotic disease is high in postmenopausal women. Although the mechanism of its increase has not been completely explained, the elevation of lipids, especially that of LDL cholesterol, is thought to be one of main factors for the developing mechanism. Although the diagnostic accuracy of atherosclerotic vascular disease was improved by the ultrasonography which has been playing an important role in the diagnosis by the combination of B-mode and Doppler ultrasound, we will review mainly the results obtained by B-mode ultrasonography in this report.

Menopause and the Arterial Wall Structure

The longitudinal image of the arterial wall represents three layers in the high-resolution ultrasound images (a) the innermost first

echogenic line adjacent to the vascular cavity, (b) the outer hypoechoic line and (c) the second echogenic line. The thickness of the innermost echogenic line does not represent any histological structure but mainly depends on the property of the ultrasound signal. In contrast to the histologic structure, ultrasound overestimates the thickness of the intima and adventitia, and underestimates the thickness of the media.[1] In 1986, Pignoli and colleagues reported that the distance from the leading edge of the first echogenic line to the leading edge of the hypoechoic line in the arterial wall showed a significant correlation with values of the combined thickness of the intimal and medial layers obtained by histological tissue examination.[2] This distance is called the intima-media thickness (IMT). Since then, many reports have been published about the arterial wall thickness assessment by high-resolution ultrasound. Most of the reports were made on the common carotid artery. It was reported that the increase of the IMT of the common carotid artery was related to the increased incidence of acute myocardial infarction (AMI) and other coronary artery diseases (CAD).[3,4] The IMT values of femoral artery[5] and radial artery[6] have been published.

It had been known that menopause was related to the increased risk of AMI or CAD and postmenopausal changes of the IMT were reported.[7] It was also reported that hormone replacement therapy (HRT) for postmenopausal women reduced the IMT,[8] but HRT did not affect IMT in later studies based on a large number of patients.[9,10] Elapsed years since bilateral oophorectomy was associated with increased IMT.[11]

We have reported the relationship between the IMT of the radial artery and aging.[12] We measured the IMT of radial artery in 649 patients using a 30 MHz mechanical linear transducer (Fig. 1). In the results obtained, the IMT of radial artery was significantly larger in postmenopausal cases than in premenopausal women (Figs 2 to 4). The association of increased IMT of radial artery and atherosclerotic diseases was suggested, because the IMT increase was related to the elapsed time after the menopause. It was suggested in our experience that the measurement of IMT in radial artery was useful in the management of postmenopausal women.

The attempt was reported to evaluate the arterial wall stiffness measuring the arterial diameter with high-resolution ultrasonography and the pulse pressure. Westendorp and colleagues[13] reported that the distensibility of the common carotid artery was negatively affected by menopause. However, HRT did not restore the distensibility of the common carotid artery.[14,15] Using high-resolution ultrasound, we also measured the elastic property of common carotid artery in normotensive and hypertensive women (Fig. 5). In our results obtained (Table 1), the elastic property in hypertensive women was larger than that in normotensive women. Further study, however, would be extended, because of small number of subjects who were not age-matched in the report.

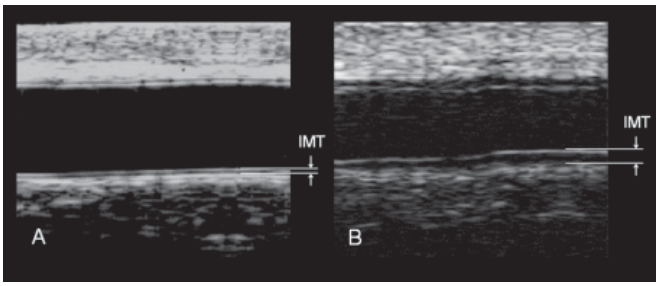

Fig. 1: Two cases of the IMT measurements in the radial artery: (A) 23 years old normotensive woman. IMT = 0.10 mm, (B) 46 years old hypertensive man. IMT = 0.30 mm

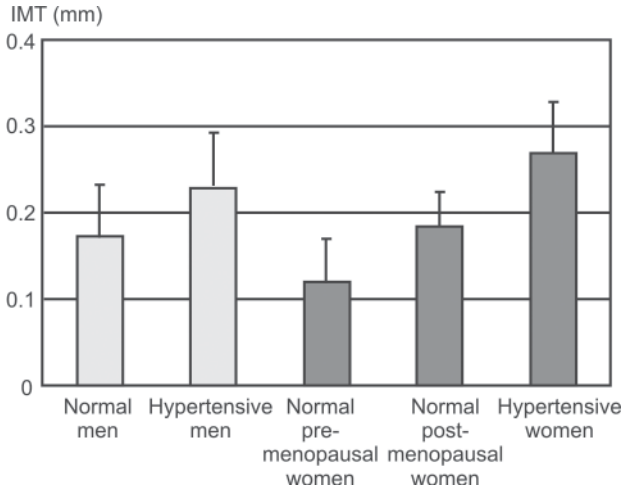

Fig. 2: The IMT of radial artery in the five groups. Vertical bars show the range of +1 SD in each group

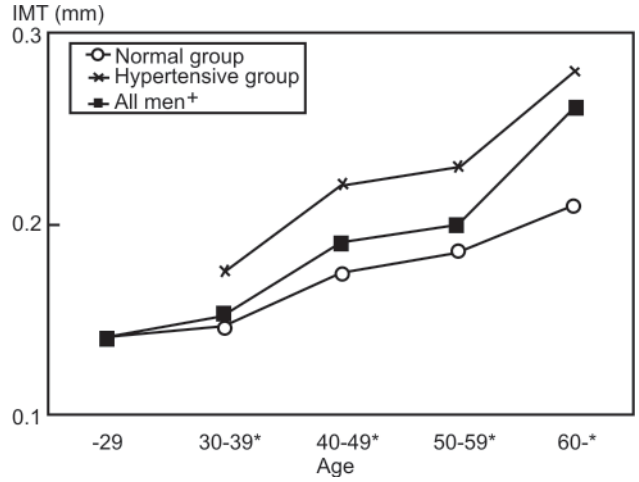

Fig. 3: The IMT of radial artery in 475 men
*Significant differences between normal and hypertensive groups ($p < 0.01$)
+ In all men, significant differences between 30-39 and 40-49, 50-59 and over 60 ($p < 0.01$)

Table 1: Maximum and mean IMT in each pregnant groups

	n	*Age (y/o)*	*Gestational age (w)*	*Maximum IMT (mm)*	*Mean IMT (mm)*
Normal pregnancy	35	30.5 ± 5.6	33.2 ± 2.3	0.54 + 0.10	0.50 ± 0.10
Chronic hypertension	22	32.3 ± 6.9	34.8 ± 3.5	0.74 + 0.18	0.68 ± 0.14
Pre-eclampsia	16	33.8 ± 8.5	33.0 ± 2.6	0.55 + 0.09	0.50 ± 0.09
Pregestational diabetes	22	31.5 ± 3.7	29.7 ± 5.3	0.86 + 0.36	0.81 ± 0.32
Gestational diabetes	18	30.8 ± 2.9	26.3 ± 12.1	0.67 + 0.31	0.60 ± 0.28

Data are expressed as mean ± SD

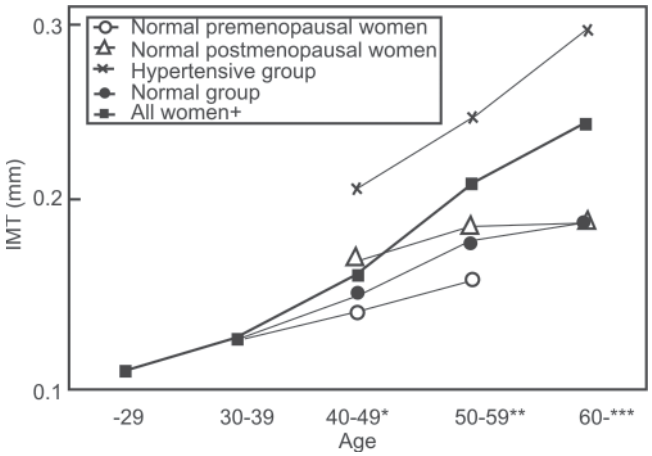

Fig. 4: The IMT of radial artery in 174 women.
All patients with hypertensive disorders was postmenopausal.
*Significant differences between normal premenopausal and hypertensive groups ($p < 0.01$) and between normal premenopausal and postmenopausal groups ($p < 0.01$).
**Significant differences between normal premenopausal and hypertensive groups ($p < 0.01$) and between normal postmenopausal and hypertensive groups ($p < 0.01$).
***Significant difference between normal and hypertensive groups ($p < 0.01$).
+In all women, significant differences between 30-39 and 40-49, 40-49 and 50-59 ($p < 0.01$)

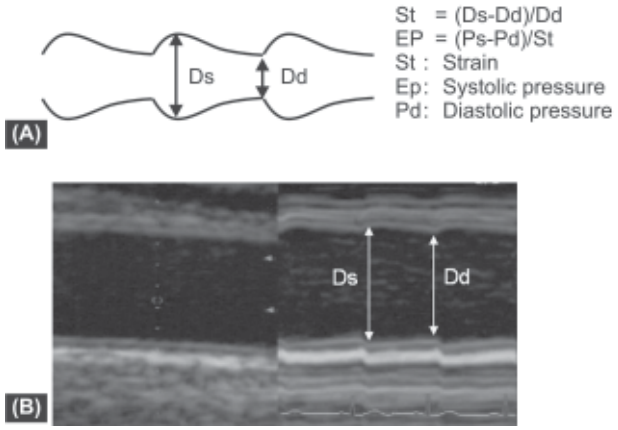

Fig. 5: Measuring methods of the elastic property in the common carotid artery.
M-mode image was recorded from the longitudinal section of common carotid artery. Systolic and diastolic internal diameters of the common carotid artery (Ds, Dd) were measured. The strain and the elastic property of the common carotid artery were calculated from Ds, Dd, systolic pressure (Ps) and diastolic pressure (Pd). An example of M-mode recording in common carotid artery is demonstrated (B)

Menopause and Vascular Endothelial Function

Increased blood flow exerts the shear-stress on the endothelium and causes the release of endothelium-derived relaxing factor (EDRF) which is mainly nitric oxide. The EDRF acts on the vascular smooth muscle, increasing the vascular diameter, and decreased response to increased flow may reflect the impaired vascular endothelial function. Thus, we are able to assess the endothelial function noninvasively by measuring the vascular diameter change as a response to increased flow using high-resolution ultrasound. The vascular response was called the flow-mediated vasodilation (FMD) and this method was introduced by Celermajer and colleagues,[16] and a number of reports were published on the usefulness of this method in the assessment of endothelial function. Decreased FMD was reported to be associated with various diseases or situations complicated by such endothelial dysfunction as CAD, hypertension or diabetes mellitus.

The relationship between menopause and FMD was first reported by Celermajer and colleagues.[17] In their report, FMD in women was stable until the early 50s, after which it gradually declined, and this decline was considered to be the effect of menopause. Subsequently many reports were published on the association between menopause and the decreased FMD.[18,19]

A number of reports have been published on the relationship between HRT and FMD. McCrohon and colleagues[20] reported that long-term HRT is associated with improved arterial endothelial function in healthy postmenopausal women. Lieberman and colleagues[21] reported that even short-term estrogen replacement therapy improves FMD in postmenopausal women. Significant relationship between estrogen replacement therapy and FMD was reported by many researchers, but progesterone was reported to exert no effects on FMD.[22] Manolio and colleagues[23] reported that HRT actually reduces CAD, but most of recent reports have shown that HRT did not reduce the incidence of CAD.[24-26]

The FMD was also reported to be influenced by certain gynecological diseases. Hashimoto and colleagues[27] reported that FMD varied with the menstrual phase in premenopausal women. Kravariti and colleagues[28] reported that FMD was decreased in women with polycystic ovary syndrome.

Deep Vein Thrombosis in Gynecological Diseases and Surgeries

Table 2 outlines clinical risk factors which are associated with the increased risk for deep vein thrombosis.[29] Some gynecological situations as well as these factors are reported to increase the risk of thrombosis. These situations include prolonged surgery in the lithotomy position, large myoma or ovarian tumor, oral contraceptive, HRT and chemotherapy. At present, compression ultrasonography (CUS) is considered to be the most useful initial imaging test for the screening of venous thrombosis. Some of these gynecological factors are discussed below.

Oral Contraceptive, HRT and Thrombosis

The association between the oral contraceptive and venous thrombosis was first reported by Jordan in 1961[30] and later epidemiological surveys supported the association. The overall risk for thrombosis in oral contraceptive users is reported to be increased threefold over that for nonusers and the risk is higher during early use.[31] The risk is reported to be related to the dose of estrogen[32] and the effort to reduce the estrogen dose had been made in order to minimize the risk for thrombosis. However, oral contraceptives of the latest generation (third generation) are reported to have a higher risk of thrombosis than those of second generation, despite their lowered androgenic effects.[33]

The HRT is also thought to increase the risk for venous thrombosis. Recent studies reported that HRT is associated with about twofold to fourfold higher risk for venous thrombosis.[34,35] The epidemiological trial by the Women's Health Initiative (WHI) in the United States was initially planned to make a double-blind randomized study between the combined estrogen and progestin group and the placebo group for 8.5 years. However, the trial was discontinued earlier at the point of 5.2 years, as recommended by the data and safety monitoring board because of the health risks that exceeded health benefits.[36] The WHI reported that the estimated hazard ratio of venous thromboembolic disease was 2.11.

It is not clearly shown that routine check-up for venous thrombosis by CUS is useful in oral contraceptive users or patients on HRT, but CUS may be useful for early detection of venous thrombosis in contraceptive users and HRT patients. We have recently started the routine check-up of CUS in the femoral and popliteal veins for outpatients on oral contraceptives or HRT in our Nishisaitama-Chuo National Hospital, where the number of subjects is small and we have had no case of thrombosis detected by CUS.

Gynecological Cancer and Thrombosis

The association between cancer and venous thrombosis was well known and the risk was said to be about two- to threefold.[37,38] Ovarian cancer was reported to be one of the highest risks along with cancers of the liver, pancreas and brain.[38,39] Recently, the association between ovarian cancer and thrombosis was reported in some publications.[39,40] Gomes and colleagues[41] reported that CUS was the best initial imaging test for suspected DVT in cancer patients. However, Bernstein and colleagues[42] reported that CUS was not useful for the detection of DVT in asymptomatic cancer patients.

Gynecological surgery, especially surgery of malignant diseases is also one of risk factors of thrombosis. We are carrying out CUS of the femoral and popliteal veins for the screening of lower-extremity DVT in postoperative patients (Table 3). The incidence of DVT in our study is lower than that in previous reports, which may be the achievement of our prophylactic protocol (Fig. 6).

Table 2: Elastic property in each pregnant groups

	n	*Age (y/o)*	*Gestational age (w)*	*Elastic property (mmHg/m)*
Normal pregnancy	35	30.5 ± 5.6	33.2 ± 2.3	326 ± 97
Chronic hypertension	22	32.3 ± 6.9	34.8 ± 3.5	425 ± 59
Pre-eclampsia	16	33.8 ± 8.5	33.0 ± 2.6	366 ± 112

Data are expressed as mean ± SD

Table 3: FMD in each pregnant groups

	n	*Age (y/o)*	*Gestational age (w)*	*FMD (%)*
Normal pregnancy	38	30.8 ± 5.5	33.7 ± 2.3	18.2 ± 5.4
Chronic hypertension	16	32.3 ± 6.9	33.0 ± 2.6	7.8 ± 8.0
Pre-eclampsia	22	33.8 ± 8.5	34.8 ± 3.5	3.8 ± 1.4
Pregestational diabetes	25	31.5 ± 3.7	30.0 ± 4.5	5.8 ± 2.2
Gestational diabetes	10	30.8 ± 2.5	28.5 ± 7.0	7.0 ± 3.0

Data are expressed as mean ± SD

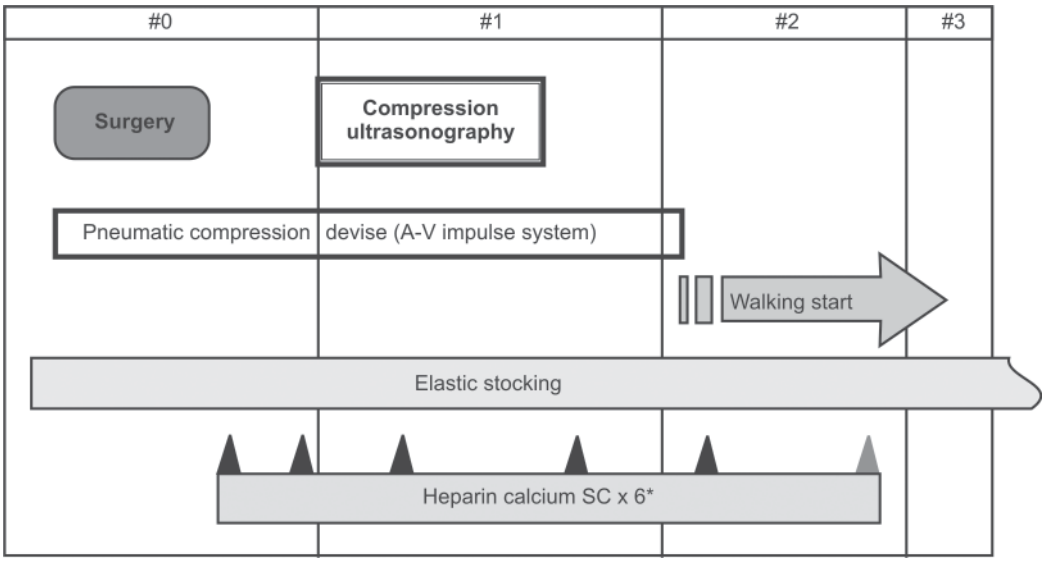

Fig. 6: Prevention protocol for deep vein thrombosis after gynecological surgery in Nishisaitama-Chuo National Hospital.
* The last heparin calcium administration is omitted in ambulatory patients

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