

The Utilization of Doppler Ultrasonography with Color Flow Mapping in the Diagnosis and Evaluation of Malignant Trophoblastic Tumors

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The Doppler ultrasound with color flow mapping image has been recently applied for the evaluation of gynecologic diseases, in particular, malignant trophoblastic tumors with the characteristic abundant blood flow. Doppler color flow mapping of uterine artery and intratumoral blood vessels was performed at a regular interval in all 26 patients including 3 cases of lost for follow up. Systolic/diastolic (S/D) ratio representing blood flow was measured in 19 cases of malignant trophoblastic tumors and 7 cases of hydatidiform mole diagnosed at the department of Obstetrics and Gynecology, Yonsei University, College of Medicine. The initial mean S/D ratio and standard deviation (SD) of uterine artery in 11 remitted and 5 non-remitted patients were 272 ± 1.31 and 2.69 ± 1.80 , respectively. No significant difference was noted between two groups. However, the final S/D ratio of uterine artery in remitted group showed significantly higher values than non-remitted group, of which values were 6.23 ± 2.38 and 3.08 ± 1.54 , respectively ($P < 0.05$). In aspect of blood flow changes in malignant trophoblastic tumors after chemotherapy, remitted group showed entirely disappeared blood flow, while non-remitted group had persistent blood flow. The mean S/D ratio and SD measured in hydatidiform mole patients were 5.43 ± 1.65 , of which value reflects higher resistance than malignant trophoblastic tumors. Also blood flow was not detected in all cases. This study suggests that color flow mapping Doppler ultrasound can be a useful method in diagnosing and monitoring the treatment in malignant trophoblastic tumors along with the conventional serum β -hCG titration.

Key Words: Doppler color flow mapping, systolic and diastolic ratio, malignant trophoblastic tumor

Since the accurate diagnosis of malignant trophoblastic tumors has been known to be difficult even with the combination of ultrasonography and serum β -hCG titration, sometimes pathologic diagnosis has been required

(Taylor *et al.* 1987).

The abundant vascular supply of malignant trophoblastic tumors is the crucial factor for applying color Doppler analysis for the evaluation of such tumors. The Doppler ultrasonogram with color flow mapping image has been employed in the diagnosis of suspicious malignant trophoblastic tumors by assessing the blood flow of the uterine artery and intratumoral vessels (Shimamoto *et al.* 1987; Long *et al.* 1990). In malignant trophoblastic tumors, the flow resistance of the uterine arteries and intratumoral vessels was ex-

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tremely low and therefore, the S/D ratio decreased. In the patients who has reached toward the remission after the appropriate anti-cancer chemotherapy the S/D ratio of the uterine artery and intratumoral vessels tended to increase in correlation with loss of color flow (Shimamoto *et al.* 1987). Therefore, color flow mapping along with serum β -hCG titrations is expected to be clinically applicable as a follow up parameter after the treatment.

This study was designed to observe the change in the blood flow of the uterine arteries and intratumoral vessels with respect to the response to the therapy by measuring the S/D ratio and to explore possible utilization of color flow mapping in the diagnosis and follow up of the patients with malignant trophoblastic tumors.

MATERIALS AND METHODS

The color flow mapping was performed in 26 patients, 19 with malignant trophoblastic tumors and 7 with hydatidiform moles at the Department of Obstetrics and Gynecology, Yonsei University, College of Medicine. Three cases were lost for follow up and were excluded from this study. In cases of malignant trophoblastic tumor, initial serum β -hCG level was above 40,000 IU/L or distant metastatic focus was noted. All patients were examined by an ATL UM-9 (Advanced Technology Laboratories, Bothell, Washington.) ultrasound scanner with color and pulsed Doppler capabilities. A frequency of 5 MHz transvaginal transducer was used for the ultrasound imaging. A high-pass filter was used to eliminate Doppler shifts of less than 100 Hz. A sample gate of 2.0 mm was used and located on each side of the cervix in the lateral wall of the myometrium for the uterine artery and intratumoral blood vessels. Care was taken to avoid the internal iliac artery, which has a characteristic waveform (Taylor *et al.* 1985). After visualization of blood flow by color flow mapping, a pulsed Doppler beam was placed over the uterine artery and blood flow velocity waveforms were recorded. The same method was used to get the blood flow velocity

waveforms of the intratumoral vessels. Velocity waveform analysis was performed by calculating the S/D ratio. In each patients, Doppler velocity waveform analysis and serum β -hCG measurements were performed with about three week interval during the treatment period. In remitted group, serum β -hCG level dropped below 5 IU/L at the end of the chemotherapy and it has not risen during the treatment period. The changes in uterine artery S/D ratios before and after the treatment were analyzed using the paired t-test at 5% significance level.

RESULTS

Changes in S/D ratio of the uterine artery in the malignant trophoblastic tumors

The initial mean S/D ratio and SD of the uterine artery in the remitted group were 2.72 ± 1.31 and in the non-remitted group, 2.69 ± 1.80 , respectively. The difference between these two groups was not significant. After the completion of chemotherapy, the S/D ratio of the remitted group increased up to 6.23 ± 2.38 while the non-remitted group's S/D ratio showed 3.08 ± 1.54 , respectively. These differences were statistically significant ($P < 0.05$, Table 1).

Fig. 1. demonstrates an inverse relationship between uterine artery S/D ratio and serum β -hCG titration in case No. 1. As serum β -hCG titration regressed in response to chemotherapy, the S/D ratio gradually increased.

Table 1. Changes of uterine artery S/D ratio before and after treatment in malignant GTN

Group	Total number	Before treatment	After treatment
Remitted	11	2.72 ± 1.31	$6.23 \pm 2.38^*$
Non-remitted	5	2.69 ± 1.80	3.09 ± 1.54

*: $p < 0.05$

S/D: Systolic/Diastolic

GTN: Gestational Trophoblastic Neoplasm

Changes in S/D ratio of the intratu-moral blood vessel in the malignant trophoblastic tumors

The initial mean S/D ratio and SD of the

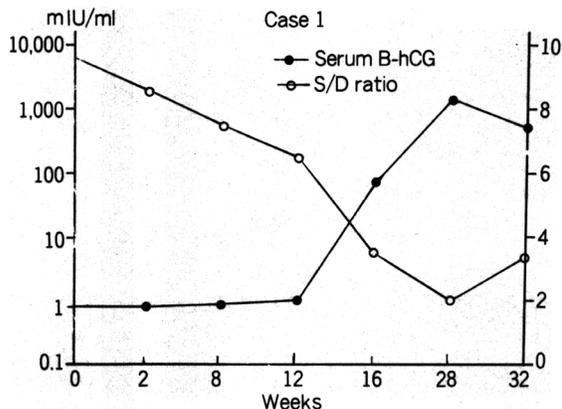


Fig. 1. An inverse relationship between uterine artery S/D ratio and serum β -hCG titration in case No. 1.

Table 2. Changes of tumoral blood flow before and after treatment in Malignant GTN

Case	Age	Initial S/D ratio	Response of treatment	Blood flow after treatment
	27	1.57	remitted	absent
2	33	1.60	remitted	absent
3	27	1.33	remitted	absent
4	25	1.80	remitted	absent
5	54	1.44	remitted	absent
6	25	2.07	remitted	absent
7	26	3.30	remitted	absent
8	30	1.81	remitted	absent
9	28	1.77	remitted	absent
10	32	1.71	remitted	TAH
11	33	1.71	remitted	TAH
13	24	1.33	non-remitted	present
15	30	1.88	non-remitted	present
16	27	1.94	non-remitted	present
18	43	1.63	non-remitted	present
19	24	2.13	non-remitted	present

Mean \pm SD of initial S/D ratio: 1.81 ± 0.44

GTN: Gestational trophoblastic neoplasm

TAH: Total abdominal hysterectomy(3 cases of Case No. 12, 14, 17 were excluded due to lost to follow up)

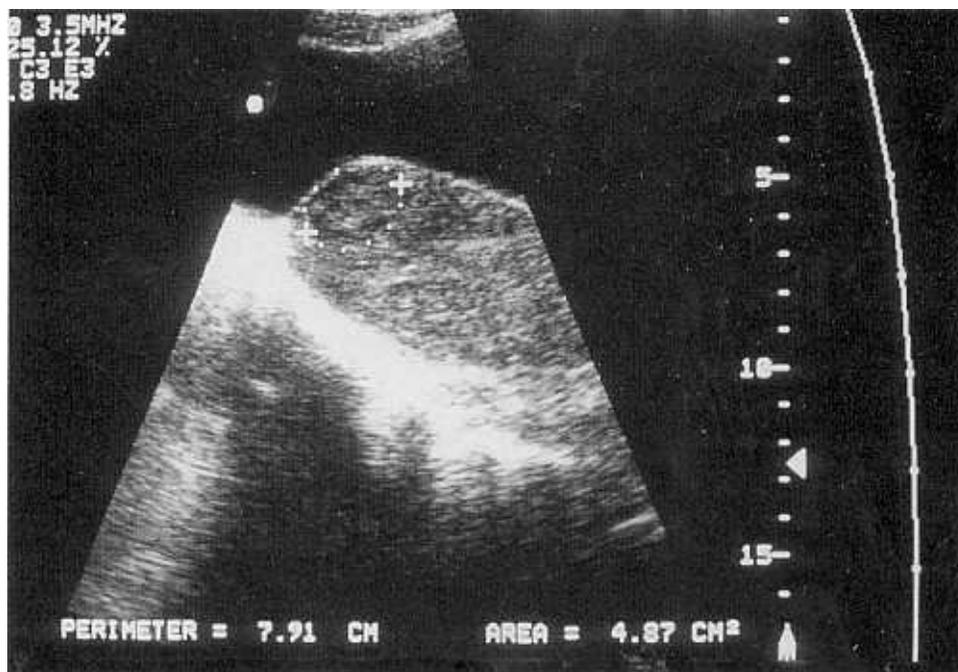


Fig. 2. An ill-defined hypochoic lesion is present in the uterine fundus.

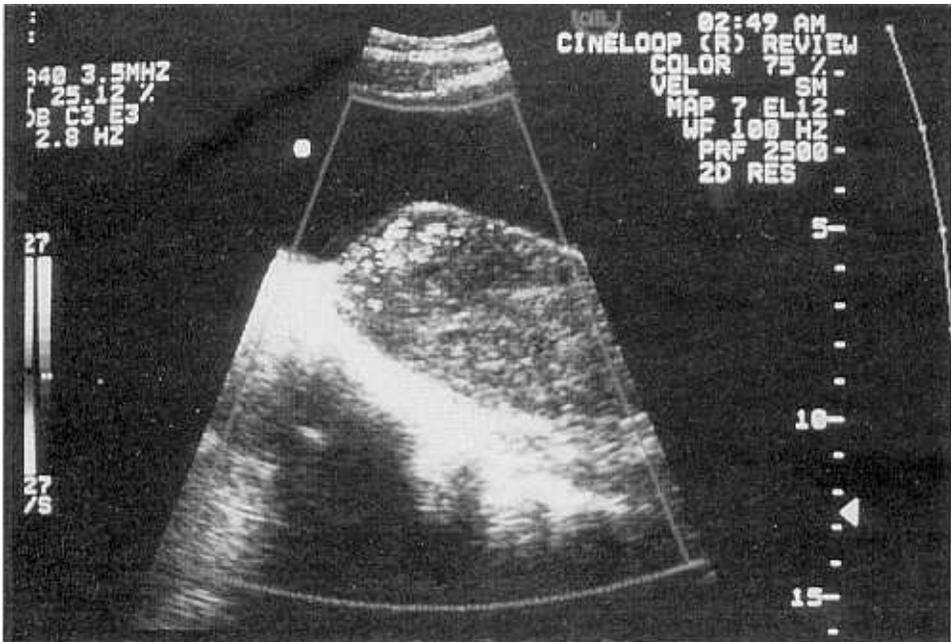


Fig. 3. The color flow mapping shows increased blood flow in the area of hypochoic lesion.

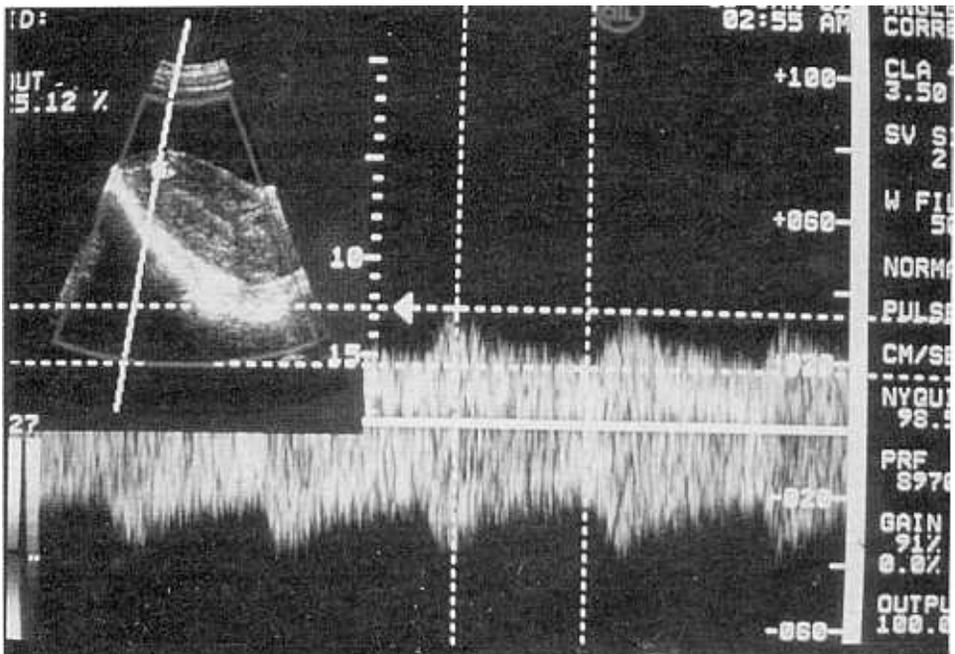


Fig. 4. Pulsed Doppler study shows Doppler waveform within the hypochoic area and the S/D ratio was obtained.

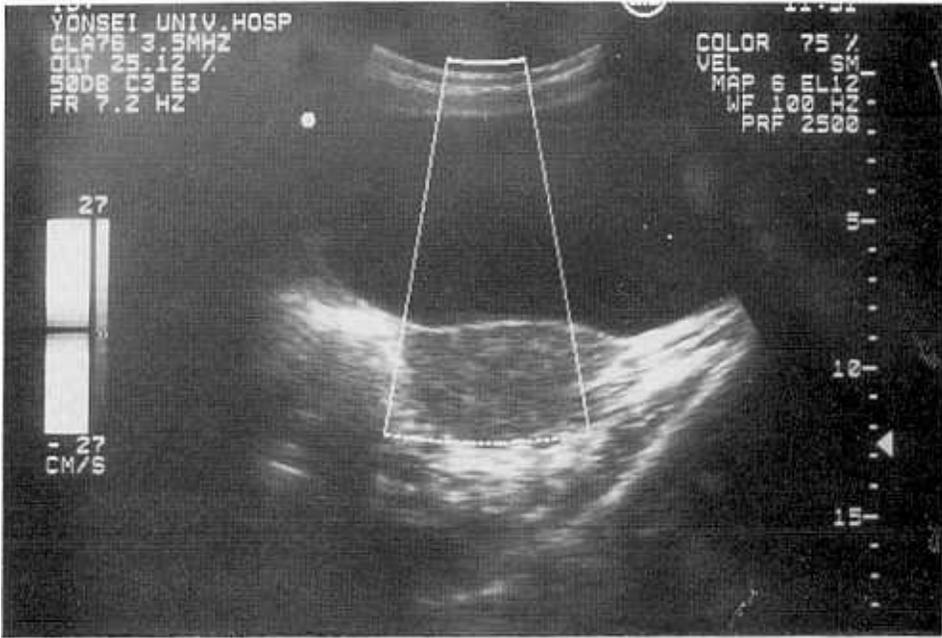


Fig. 5. The previously noted blood flow is absent after treatment.

Table 3. Uterine artery S/D ratio and blood flow in H-mole

Case	Age	Initial S/D	Uterine Artery S/D ratio	Blood flow in H-mole
1	32	complete	5.23	absent
2	24	complete	4.30	absent
	22	complete	6.20	absent
4	18	complete	3.53	absent
5	50	complete	4.50	absent
6	25	partial	5.43	absent
7	31	partial	9.00	absent

Mean \pm SD of S/D ratio: 5.43 ± 1.65

H-mole: Hydatidiform mole

intratumoral vessels were 1.81 ± 0.44 which reflects very low resistance of blood flow. After completion of chemotherapy, the remitted group showed loss of blood flow in all cases while in the non-remitted 5 cases showed persistent blood flow (Table 2).

Fig. 2. shows an ill-defined hypoechoic lesion

in the uterine fundus. Fig. 3 shows the color flow mapping of an increased blood flow and fig. 4 shows the Doppler waveform on pulsed Doppler in the same region. The S/D ratio of the intratumoral blood vessel was obtained. After completion of treatment, loss of blood flow was observed in that lesion (Fig. 5).

Uterine artery S/D ratio and intratumoral blood vessel blood flow in the hydatidiform mole patients

The mean \pm SD of uterine artery S/D ratio in the 7 hydatidiform mole patients were 5.43 ± 1.65 . None of these patients demonstrated any blood flow when color flow mapping was applied (Table 3).

DISCUSSION

Doppler analysis utilizing color flow mapping was developed to assist in the diagnosis of cardiovascular diseases, and this new meth-

od is being currently employed in the field of Obstetrics and Gynecology, today. Doppler color flow mapping is particularly useful in the early diagnosis for malignant tumors, in the evaluation of blood flow in the embryo and fetus to predict pregnancy outcomes and, finally, in the assessment of infertile women by measuring blood flow in the uterine and ovarian arteries (Kurjak *et al.* 1990; Kurjak and Zalud 1991). Color Doppler sonography encompasses structural analysis as well as functional evaluation of blood flow and, therefore, increases the knowledge regarding the nature of a disease and, moreover, contributes to establishing an adequate treatment plan.

Weiner *et al.* (1992) studied color Doppler analyses of patients with benign and malignant ovarian tumors and reported increased blood flow and low vascular resistance in ovarian cancers. Kawai *et al.* (1992) also reported the usefulness of the pulsatile index using color Doppler in diagnosing ovarian cancers. However, the best use of color Doppler analysis in gynecology is regarded to be in analyzing malignant trophoblastic tumors because of abundant vascularization within the tumor and also in offering accurate information with respect to residual cancer after treatment by serial serum β -hCG titrations (Shimamoto *et al.* 1987). Shimamoto *et al.* (1987) conducted color Doppler studies correlating the results with uterine imaging in one case with hydatidiform mole and five cases with invasive mole, and reported that there was an increase in intratumoral blood flow in patients with invasive mole, and that among them four patients showed loss of the blood flow after successful chemotherapy. Long *et al.* (1989) obtained the pulsatile index using Doppler analysis from patients diagnosed with invasive moles and malignant trophoblastic tumors and compared the results with the control group. They found that vascular resistance was significantly lower in the malignant trophoblastic tumor group. Taylor *et al.* (1987) reported that the S/D ratio obtained from the uterine artery in patients with malignant trophoblastic tumor was significantly lower compared to the control group, which suggested a clinical significance in distinguishing between malignant trophoblastic tumor

and hydatidiform mole, cystic changes of the placenta, and other benign uterine tumors.

The normal value for the uterine artery S/D ratio differs according to literature and also depends on the menstrual cycles (Taylor *et al.* 1985; Long *et al.* 1989). Schulman *et al.* (1986) reported that a value of 12.9 ± 4.4 in the proliferative phase, and 7.2 ± 3.2 in the secretory phase should be reasonably accepted. The results of this study show that initial mean \pm SD of S/D ratios of both remitted and non-remitted groups of malignant trophoblastic tumor were 2.72 ± 1.31 and 2.69 ± 1.80 , respectively. These values revealed a very low resistance of blood flow and this data agreed with the Long *et al.* (1990). After successful chemotherapy in remitted group, this S/D ratio increased significantly along with loss of blood flow on color flow mapping. This suggested that, color flow mapping Doppler ultrasound may be useful in evaluation of treatment outcome in malignant trophoblastic tumor patients. The mean \pm SD of uterine artery S/D ratio in patients with hydatidiform mole were 5.43 ± 1.65 , of which value was significantly higher than that of malignant trophoblastic tumors and there were no instances of increased blood flow in any patient. There were no false positive or false negative results when color Doppler analysis was used in patients with malignant trophoblastic tumor.

Color Doppler is also useful in distinguishing the type of a hypoechoic lesion in conventional ultrasonography, such as vesicle and hematoma, or a lesion with high blood flow can represent a hypoechoic lesion in conventional ultrasonography. But with aid from color Doppler ultrasound it can be easily diagnosed by simply measuring blood flow within a hypoechoic lesion. Before color flow mapping Doppler was introduced to study malignant trophoblastic tumors, invasive angiography was performed in order to observe the blood flow within the tumor, but now, it can be replaced by simple non-invasive color flow mapping Doppler ultrasound.

In conclusion, color flow mapping Doppler ultrasound can be a useful method in diagnosis and evaluation of treatment in malignant trophoblastic tumors along with conventional

serum β -hCG titration.

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