Research Report

Comparative of Pulsatile Index and Resistance Index of Vascularization Intratumoral in Operable and Non Operable Cervical Cancer (Cross Sectional Study)

Perbedaan Indeks Pulsatil dan Indeks Resistant Pembuluh Darah Intratumoral pada Kanker Serviks Operable dan Non Operable (Studi Potong Lintang)

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Abstract

Objective: A cross sectional study from 49 cases of cervical carcinoma, diagnosed by histopathology, early staged was done by Oncogynecologist at Gyneco-Oncology clinic of Sanglah Hospital. Doppler ultrasonography was used to compared the different Pulsatile Index (PI), Resistance Index (RI) from artery intratumoral with diameter mass of the tumor, including operable and non operable.

Method: This research was cross sectional study, present 49 samples established diagnosis with cervical cancer using anatomical patology analyzes and evaluation the staging by the supervisor in the policlinic of Oncology in Sanglah Hospital. Examination of intratumoral vascular cervical cancer Doppler ultrasonography was done at policlinic of Obstetrics Graha Amerta in Sanglah Hospital using Medison instrument, type Sonoace 8000 live prime. The data was analyzed using Kolmogorov Smirnov test normality, then the selected data with Independent Samples Test.

Result: Profile mean of age and parity between operable cervical cancer and non operable was not significant ($p > 0.05$). The mean Pulsatile Index (PI) in operable sample is 0.66 ± 0.9, non operable sample is 1.11 ± 0.84, $p=0.089$ ($p > 0.05$), RI for operable sample is 0.32 ± 0.36 and non operable sample is 0.49 ± 0.28 ($p > 0.05$).

Conclusion: There were no significant difference of PI and Resistance Index (RI) between operable and non operable on cervical cancer, but they were different in velocity mean.

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Keywords: pulsatile index, resistance index, cervical cancer

Abstrak

***Tujuan**: Telah dilakukan penelitian studi potong lintang terhadap 49 kasus kanker serviks yang telah tegak diagnosanya secara histopatologis. Evaluasi awal sudah dilakukan spesialis Onkoginekologi di poliklinik Obstetri dan Ginekologi Onkologi Rumah Sakit Umum Pusat Sanglah. Setiap kasus dilakukan pemeriksaan ultrasonografi Doppler untuk melihat Indeks Pulsatil (IP), Indeks Resistant (IR) dari arteri intratumoral dan diameter massa tumor kanker serviks yang operable maupun non operable.*

***Metode**: Pemeriksaan ultrasonografi Doppler pembuluh darah intratumoral dilakukan di poliklinik Obstetri Ginekologi Graha Amerta RSUP Sanglah dengan alat ultrasonografi merek Medison tipe Sonoace 8000 live prime. Analisis data dengan uji normalitas Kolmogorov Smirnov, kemudian dipilih untuk uji statistik Independent Samples Test.*

***Hasil**: Rerata usia dan paritas, antara kelompok kanker serviks operable dengan non operable tidak berbeda secara statistik ($p > 0,05$). Pada penelitian ini didapatkan rerata IP pada kelompok operable $0,66 \pm 0,9$ dan kelompok non operable $1,11 \pm 0,84$ dengan $p = 0,089$ ($p < 0,05$), sedangkan untuk IR pada kelompok operable $0,32 \pm 0,36$ dan kelompok non operable $0,49 \pm 0,28$ dengan $p = 0,118$ ($p > 0,05$).*

***Kesimpulan**: Tidak ada perbedaan yang bermakna IP dan IR pada kelompok kanker serviks operable dengan non operable, pada kecepatan rata-rata (velocity mean) didapatkan perbedaan.*

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***Kata kunci**: indeks pulsatil, indeks resistant, kankers serviks*

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INTRODUCTION

Cervical cancer is more invasive than endometrial and ovarian cancers. Surgery, radiation, chemotherapy and their combination are its therapies. The characteristics of its circulation have been histologically proven to be different from the normal cervical network. In addition, the parameter of cervical cancer blood circulation can be evaluated by using color Doppler ultrasonography and pulsatile Doppler ultrasonography. The mean of resistance index value has been found to be significantly different from the mean of pulsatile index concerning the patient and healthy control.[1-4]

Ultrasonography is one of imaging techniques used for evaluating the pathological process of cervical cancer. The absence of neovascularization and high pulsatile index indicate no invasive process take place on such a cancer. When the vascular resistance is low and the blood circulation is fast, the angiogenesis process takes place which is one of the characteristics of invasiveness.[2,4-15]

DOPPLER ULTRASONOGRAPHY UTERINE ARTERY VELOCIMETRY

Angiogenesis refers to the production of new blood vessels in a specific area. It has been indicated that neoangiogenesis is an incident needed by a cancer to grow and develop. The process of angiogenesis initiates the degradation of the basalis membrane of the capillary blood vessel. Through this process, the mi-

grating endothelial cell forms sprouts and proliferates to form new lumen and to further maturate the blood vessels.[1,4,7,12,14]

As far as cervical cancer is concerned, angiogenesis has been shown to be an independent prognostic factor and to predict recurrence. The tumoral angiogenesis is commonly evaluated from Vascular Endothelial Growth Factor (VEGF), by painting immunohistochemical. This means that a set of histological equipment is needed for evaluating. The angiogenesis evaluation in a vivo manner is made possible by the ultrasound Doppler, which can be adopted in several ways:[1,13,16-19]

- Pulsed Doppler
  The velocity of the blood circulation and its resistance in particular blood vessels can be evaluated at a particular time by analyzing what is referred to as Circulation Velocimetry Waveform, which is abbreviated to FVW, and by calculating the velocity of the blood circulation along the heart cycle which includes the Peak Systolic Velocity, which is abbreviated to PSV/cm/second, mean of the velocity and diastolic final velocity, and its resistance to the circulation by calculating a number of velocimetric index such as Resistance Index or Pulsatile Index. The higher the velocity, the lower RI or PI will be, meaning that the blood circulation will be getting higher.
- Color Doppler
  It has the same principles as the pulsatile Doppler (Doppler frequency shift). It makes possible to visualize the blood vessel by encoding the colors. This method is useful for determining the existence of the blood vessels and for preparing information on the number of the blood vessels, their distribution and composition.
- Power Doppler
  This method is based on the shift of the Doppler signal amplitude rather than on the shift of frequency. It has more strengths than the color Doppler, making it more proper for evaluating vascularity.

THE ULTRASONOGRAPHY OF COLOR DOPPLER ON THE CERVICAL CANCER

Evaluating the cancer vascularization non invasively on the cervical carcinoma is made possible by the color Doppler ultrasonography or Doppler power ultrasonography. Although most of the studies published are derived from two groups, they have indicated that the cancer vascularization, as that evaluated using this technique, is related to a number of individual cancer characteristics such as its volume, the involvement of lymph nodes and its staging. So far, there is no consensus pertaining to which Doppler parameters or which parameters are better related to the tumoral characteristics.[3,8,9,11-15]

The transvaginal ultrasonographic observation technique on the cervical cancer is that after the vaginal transducer or probe is softly inserted into the vagina, the uterus and adnexa regio are scanned. The size of the cervical cancer is estimated using the electronic caliper on the screen. After the size of the cervical cancer is estimated, the color Doppler ultrasonography is activated in order to identify the intratumor blood vessels.[3,8,9,11-16]

The peripheral blood vessels cannot be guaranted to be have neovascularizations or the blood vessels which have been already in existence before. Therefore, the only central blood vessels, especially those which are located at least 5 mm from the cancer boundaries, are evaluated. The number of vascularizations is subjectively stated to be few or not too many. After one blood vessel is identified, the sample volume of pulsed Doppler is activated in order to obtain the FVW, the pulsed index, the resistance index and the maximum velocity of the systolic circulation for the blood vessels as the branches of uterine artery.[3,4,9,11-16]

The ability of the color Doppler ultrasonography in evaluating the intratumor blood circulation on the cervical cancer, the velocimetric index and the color signal are related to a number of prognostic factors on the cervical cancer. The higher the vascular index (VI), the higher the cancer vascularization is. In addition, the stoma is getting more invaded as well. The vascular index is better related to the density of the micro intratumor blood vessels as evaluated immunohistochemically. In the early stage of the cervical cancer, in which the cancer angiogenesis is evaluated by the three-dimensional power Doppler, it has been found out that the cancer vascularization is related to the cancer volume. The vascular circulation, as that evaluated by velocimetric index (the lowest PI), is only related to the more than 10 mm invasion to the stoma.

The relationship between the cancer angiogenesis and prognostic factors for recurrence on the cervical cancer is the increased vascularization, and the lowest PI is related to the response and prognostic of the cervical cancer.[2,4,12]

METHOD

The research design adopted in this study is the cross sectional study. The data used in this study was the values of the pulsatile index (PI) and resistance index (RI) of the intratumoral blood vessels which were obtained from those who suffered from the cervical cancer whose stadium had already been identified based on the criteria of Federation Internationale Gynecologyque d'obstetricque (FIGO) 2000.

Population

The population of this study includes the women who suffered from the cervical cancer at the Sanglah General Hospital Denpasar and who were treated without being hospitalized at the Obstetrics policlinics (Poli 108) and hospitalized at IRNA Cempaka Timur, obstetrics ward starting from June 2009 until all of the samples were fulfilled.

Samples of the Study

The samples were those who suffered from the cervical cancer and fulfilled the criteria. The criteria of being included: The people with cervical cancer, who were voluntarily prepared to take part in this study. The criteria of being excluded: Those who suffered from the cervical cancer with pregnancy, in the purpureal period, and cervical cancer with grade 4 uterine prolaps.

Size of the Samples

The size of the samples were calculated from the cervical cancer prevalence in Indonesia. This study adopted a 95% level of confidence interval and a 20% erroneous prediction was accepted. The total samples in this study was 49.

Variable and Operating Definition

Variable

Free variable : Cervical cancer

Dependent variable: Cervical cancer stadium, Pulsatile Index (PI), Resistance Index (RI), and the Vascular Index of the cervical cancer intratumoral blood vessels.

Definition of the Operating Variable

Cervical cancer is an invasive disease of the cervix which might be derived from epithelial cells, fibrublast blood vessels, and lymph both individually and collectively. As far as the samples in this study are concerned, the cervical cancer was identified based on the biopsy result. The cervical cancer staging refers to what is stated in the Federation Internationale Gynecologyque d'obstetricque (FIGO) 2000.[19-27]

Doppler ultrasonography refers to the ultrasonography which adopts the Doppler waves for detecting the blood circulation which can be measured by Doppler, in which the values of S/D ratio, Pulsatile Index and Resistance Index are obtained.

Intratumoral blood vessel means the blood vessels which supply utery cervix and direct downward to the utery cervix. Doppler ultrasonography is used for examining the intratumoral blood vessels. The tumoral central blood vessels examined are the central ones which are located at least 5 mm from the tumor boundaries.

Tumor Mass Diameter refers to the measurement of the outmost upright distance of the cancer in the two-dimensional figure with an assumption that the tumoral mass is assumed to look like a ball so that the mass diameter of the tumor is obtained.

When and Where the Study was Conducted

This study was conducted at the policlinic and the obstetrics ward at Sanglah General Hospital. The study was conducted from June 2009 to the time when the number of samples was fulfilled (January 2010).

Procedure and Mechanism of the Study

Data Collection

The data was obtained from those has cervical cancer and prepared to take part in this study after explanation was provided and letter of approval was signed. Their identities, the results of observation and the stadium were recorded in the form prepared for the study or on the data collection sheet.

The Procedure of How the Samples Were Examined

Those who suffered from the cervical cancer were diagnosed and their stadium were determined by the obstetricians at the Sanglah General Hospital. The data and clinic information were not included when ultrasonographic examination was undertaken. The objective is to confirm the staging made by the doctor evaluating the ultrasonography. The ultrasonography used is Medison type sonoace 8000 live prime with transducer abdomen (intratumoral blood vessel) which supplies blood to the cervix.

RESULTS

The Characteristics of the Subjects of the Study

Table 1. The distribution of the subjects of the study based on age and parity.

Characteristic	Mean Operable (n = 12)	Mean Non Operable (n = 37)	*p*
Age	44.08 ± 8.25	46.59 ± 11.67	0.494
Parity	2.25 ± 1.42	2.86 ± 1.83	0.293

Table 1 above shows that in the operable group the age ranges from 33 to 55 with 44.08 ± 8.25 years of age as the mean and that in the non operable group the age ranges from 25 to 73 with 46.59 ± 11.67 years of age as the mean. From the operable group, the parity obtained ranges from 0 to 5 with 2.25 ± 1.42 as the mean. In the non operable group, the parity obtained ranges from 0 to 7 with 2.86 ± 1.83 as the mean. Statistically, there is no significant difference between the operable group and non operable group with regard to age and parity, with $p > 0.05$.

The Difference of Pulsatile Index (PI) from Resistance Index (RI)

The data in this study was processed using software SPPS v 17. Before the data was analyzed, normality test was undertaken using Kolmogorov-Smirnov. Then the means variables were compared using Independent Samples Test.

Table 2. The average of Pulsatile Index (PI) and Resistance Index (RI) of the intratumoral blood vessels of the operable and non operable cervical cancer.

Cervical cancer	Mean Operable (n = 12)	Mean Non Operable (n = 37)	*p*
Pulsatile Index (PI)	0.66 ± 0.9	1.11 ± 0.84	0.118
Resistance Index (RI)	0.32 ± 0.36	0.49 ± 0.28	0.089

Statistically, there is no significant difference between the operable group and non operable one, with the p value is 0.118 (p > 0.05). As far as the Resistance Index (RI) is concerned, statistically there is no significant difference, the p value is 0.089 (p > 0.05).

Figure 1. The Doppler appears in the operable cervical cancer intratumoral vessels which are slightly seen.

Figure 2. The Doppler appears in the non operable cervical cancer intratumoral vessels which are excessively seen.

The other Results of the Ultrasonographic Doppler Examination

In this study, in the transabdominal ultrasonographic Doppler examination the tumoral mass diameter was also evaluated before identifying the intratumoral blood vessels. When measuring the pulsatile index and resistance index, the software of the Ultrasonography sonoace 8000 live prime also automatically evaluated the Peak Sistolic Velocity (PSV), End Diastolic Velocity (EDV), Velocity Mean, Gradient Mean and Gradient Peak of the cervical cancer intratumoral blood vessels.

Table 3. The results of the tumoral diameter and the characteristics of ultrasonograhic Doppler.

Characteristics of Ultrasonograhic Doppler	Mean Operable (n = 12)	Mean Non Operable (n = 37)	*p*
S/D ratio	2.43 ± 4.47	3.10 ± 2.51	0.069
Tumor diameter (cm)	2.71 ± 1.83	4.03 ± 2.05	0.053
PSV (cm/second)	14.29 ± 17.85	23.72 ± 14.16	0.067
EDV (cm/second)	4,16 ± 5.17	7.51 ± 5.06	0.054
V mean (cm/second)	7.34 ± 8.24	12.77 ± 7.52	0.039
G mean (mmHg)	0.06 ± 0.08	0.09 ± 0.08	0.173
G Peak (mmHg)	0.19 ± 0.32	0.30 ± 0.26	0.263

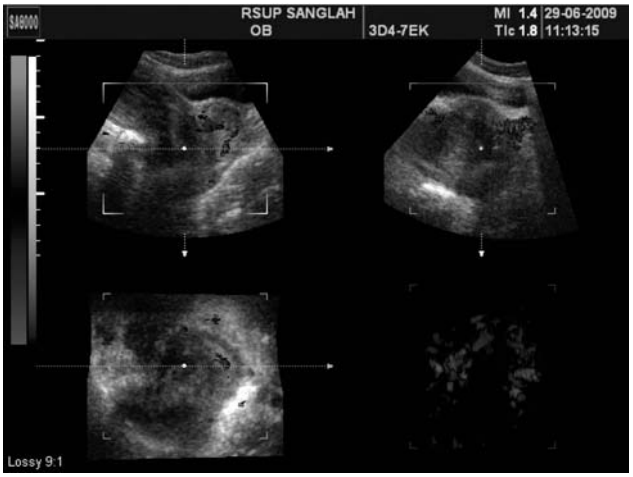

Figure 3. It can be seen from the figure above that after the tumoral mass was identified with transabdominal transducer, evaluation was conducted using the Doppler in order to identify the intratumoral blood vessels before the characteristics of the Doppler, S/D ratio, PI and RI were measured.

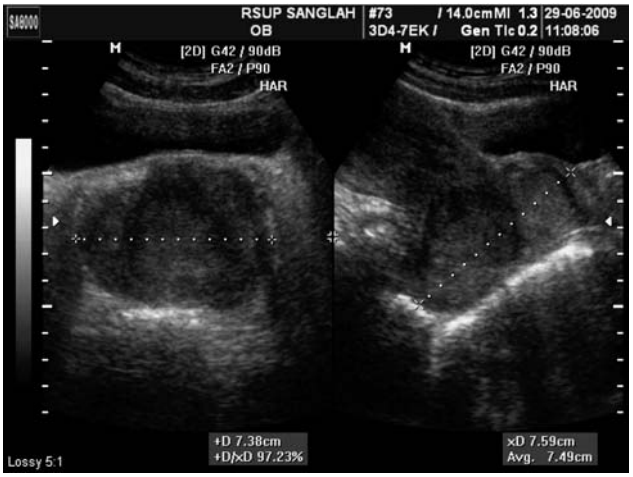

Figure 4. The figure above shows that after the tumoral mass was identified with transabdominal transducer, the tumoral mass diameter was measured.

When the S/D ratio of the operable and non operable groups were tested, no significant difference were discovered, the p value was 0.069 ($p > 0.05$). Statistically, as far as the tumoral mass diameter is concerned, no significant difference was found out; the p value was 0.053 ($p > 0.05$). There was no significant difference in the Peak Sistolic Velocity (PSV); the p value was 0.067 ($p > 0.05$). Similarly, no significant difference was found in End Diastolic Velocity (EDV); the p value was 0.054 ($p > 0.05$).

DISCUSSION

Not many researchers have investigated whether the characteristics of the intratumoral blood vessels of the operable cervical cancer are different from those of the non operable one. However, some stated that they are not different and others stated that they are different.

The Characteristics of the Subjects under Study

As far as the samples of the operable cervical cancer are concerned, the age was found out to be 44.08 ± 8.25 and as far as the samples of the non operable cervical cancer are concerned, the age was found out to be 46.59 ± 11.67. In some references the cervical cancer is stated to average 47 years of age. Furthermore, it is also stated that there are two bimodals of the range in which the cervical cancer takes place; one ranges from 35 to 39 years of age and the other ranges from 60 to 64 years of age. As far as the samples of this study are concerned, the age of the operable and non operable groups was found out to average 45.98 ± 10.90. The average age of the samples of this study is not much different from that of the samples stated in the literature.

The parity of the operable group was found out to be 2.25 ± 1.42 and that of the non operable group was found out to be 2.86 ± 1.83. While in some references it is stated that the occurrence of the cervical cancer is related to the number of parities. In this study, the operable group was found out not to differ from the non operable group with regard to the number of parities ($p < 0.05$).

This study revealed that the operable group was significantly different from the non operable regarding the age and parity. Therefore, it can be inferred that in this study the characteristics of the operable group and the non operable one are similar with regard to age and parity.

The Differences of the Pulsatile Index (PI) from the Resistance Index (RI)

When the ultrasonographic Doppler was conducted the tumoral mass of three samples from the operable group and five samples from the non operable one was not found out. As a result, the intratumoral blood vessels could not be measured. The same condition was also reported in the studies previously conducted, in which it was stated that the tumoral mass could not be found out in every cervical cancer. Therefore, the characteristics of the intratumoral blood vessels could not be evaluated; however, cervical ramus uterine artery of the blood vessels could be evaluated.

The three samples out of the five from the non operable group, whose tumoral mass could not be found out was treated with a four-series chemotherapy; one was treated with a combined chemotherapy referred to as BOMP (Bleocyn, Oncovin, Mitocyn, Paclitaxel) and two were treated with a combined chemotherapy of Paclitaxel-Cisplatin. This condition might be a good chemotherapy response but could not be inferred as such as the Doppler characteristics of the intratumoral blood vessels had not been evaluated before chemotherapy was conducted.

In this study the pulsatile index (PI) for the operable group was 0.66 ± 0.9 and the non operable group was 1.11 ± 0.84. Statistically, no significant difference in pulsatile index with $p < 0.05$. (Table 2)

In some references it is stated that $PI < 0.82$ means the cut off point of the cervical cancer which has bad prognosis, meaning that the response to chemotherapy is insufficient and that the tumoral neovascularization is invasive. In another study it is stated that $PI > 0.45$ serves as the predictor that the treatment of the cervical cancer with chemotherapy is successful.[1,4,13]

Statistically, this study did not show a significant difference between the PI of the operable group and that of the non operable one; however, if the average of the non operable group is compared to that of the operable one, a great difference was shown, the average PI for the operable group and non operable group were 0.66 and 1.11 respectively. In some references it is stated that if the $PI < 0.82$ has bad prognosis, then this theory is in line with the study conducted, in which while the mean for the non operable group was 0.66 ($PI < 0.82$), the mean for the operable group was 1.11 ($PI > 0.82$).

In this study the resistance index (RI) for the operable group was 0.32 ± 0.36 and that for the non operable group was 0.49 ± 0.28. When the Pulsatile Index was statistically tested, it was found out that there was no significant difference; $p > 0.05$. (Table 2)

Some references stated that there is no significant difference with regard to the characteristics the RI of the intratumoral blood vessels between the early stage and the late stage of the cervical cancer. In one study, the average RI of the intratumoral blood vessels of the cervical cancer was found out to be 0.54 ± 0.13 and the average RI of the healthy cervix was 0.93 ± 0.09. Another study found that the cut off point of the RI was 0.573. The mean of both the operable group and non operable one was discovered to be 0.45 ± 0.31. In this study, the operable group did not differ from the non operable one in terms of the RI value. However, compared to the previous study the RI of the intratumoral blood vessels of the cervical cancer was < 0.54, meaning what was discovered in this study, in which the average RI of the operable group was 0.32 and that in the non operable one was 0.9, was supported.

The Doppler Characteristics of the Intratumoral Blood Vessels of the Cervical Cancer

When the pulsatile index and resistance index were measured, the software of the ultrasonography sono-

ace 8000 live prime also automatically evaluated the Peak Sistolic Velosity (PSV), End Diastolic Velocity (EDV), Velocity Mean (VM), Gradient Mean (GM) and Gradient Peak (GP) of the intratumoral blood vessels of the cervical cancer.

For the operable group the S/D ratio 2.43 ± 4.47 and for the non operable group 3.10 ± 2.51. When the S/D ratio of both the operable and non operable groups were examined, no significant difference was discovered; the p value was 0.087 ($p < 0.05$).

For the operable group, the tumoral mass diameter was 2.71 ± 1.83 and for the non operable one was 4.03 ± 2.05. When the tumoral mass diameter was examined, no significant difference was found out; the p value was 0.053 ($p < 0.05$). In another study it was stated that if the tumoral mass diameter was > 1.75 cm, then the cervical cancer would spread to the parametrial area. The tumoral mass diameter which is more than 4 cm is directly related to the increase in the intratumoral blood pressure, in which the PI and RI are found out to be low.

The Peak Sistolic Velocity (PSV) or the Maximum Systolic Circulation Velocity of the operable group was 14.29 ± 17.85 and that of the non operable one was 23.72 ± 14.16. When the PSV diameter was examined, it was found out that the operable group did not significantly differ from the non operable one, in which the p value was 0.067 ($p < 0.05$). While in another study the PSV of the cervical cancer sufferers were obtained to be 12.62 ± 0.61, in this study the PSV of all the samples were found out to be 21.40 ± 15.05.

The End Diastolic Velocity (EDV) of the operable group was 4.16 ± 5.17 and that of the non operable one was 7.51 ± 5.06. When the EDV was statistically examined, the two groups were found out not to be significantly different; the p value was 0.054 ($p < 0.05$). The average EDV of the operable group appeared to be bigger, indicating that the blood vessel circulation of the non operable group was bigger.

The velocity mean of the operable group was 7.34 ± 8.24 and that of the non operable one was 12.77 ± 7.52. When the VM of the two groups was statistically examined, significant difference was observed; the p value was 0.039 ($p < 0.05$). The VM mean of the operable group showed higher speed, indicating that the non operable group had a bigger blood vessel circulation.

The gradient mean (GM) of the operable group was 0.06 ± 0.08 and that of the non operable one was 0.09 ± 0.08. When the GM of the two group were statistically examined, no significant difference was found; the p value was 0.173 ($p < 0.05$). The GM of the operable group shows lower gradient.

The gradient peak of the operable group was 0.19 ± 0.032 and that of the non operable group was 0.30 ± 0.26. When the GP was statistically examined, both group showed no significant difference; the p value was 0.263 ($p < 0.05$). The GP mean shows that the operable group had lower gradient.

Weaknesses of the Study

One of the weaknesses of the study is that it has adopted the cross sectional method; as a result, the characteristics of the blood vessels of the cervical cancer sufferers already treated cannot be compared to the characteristics of their blood vessels after being treated. In addition, the samples in this cross sectional study that had been treated were not differentiated from those who had not been treated. In this study, the cervical cancer stadium was only clinically evaluated. In addition, the evaluation was done without any narcosis and was not followed by any other supporting evaluation.

CONCLUSION

This study does not show any differences in characteristics between the Pulsatile Index (PI) and Resistance Index (RI) as far as the intratumoral blood vessels of both the operable and non operable groups of the cervical cancer sufferers are concerned. No difference is shown by the operable and non operable groups with regard to the other Doppler parameter such as S/D ratio, tumoral mass diameter, PSV, EDV, GP. However, they are different with regard to VM.

SUGGESTIONS

From the literature, this is the first study that compares the Doppler characteristics of the intratumoral blood vessels of the cervical cancer with the transabdominal probe. This study also firstly compares the group with operable cervical cancer to that with non operable one. This means that this study prepares the initial data of the Doppler characteristics of the blood vessels of those who suffer from both the operable and non operable cervical cancer employing the transabdominal probe. Financially, it is not too expensive, and clinically, it is highly beneficial to use the transabdominal Doppler ultrasonography for evaluating cervical cancer.

The Doppler ultrasonography can be applied to copy with the cervical cancer which is already clinically identified. Hence, it should be so continuously used to identify the characteristics of the intratumoral blood vessel of the cervical cancer so that proper data can be obtained to be used for clinical application.

REFERENCES

1. Jurado M, Galvan R, Monge RM, Mazaira J, Alcazar JL. Research: neoangiogenesis in early cervical cancer: correlation between color Doppler and risk factor. A prospective observational study. Word J Surg Oncol 2008; 6: 126-32
2. Kerimoglu U, Akata D, Hazirolan T, Ergen FB, Kose F, Ozyar E. Evaluation of radiotherapy response of cervical carcinoma with gray scale and color Doppler ultrasonography: resistance index correlation with magnetic resonance findings. Diagnosis Intervensi Radiology 2006; 6: 155-60
3. Zalud I. Doppler ultrasonography for gynecologic malignancies, in: Maulik D (ed), Doppler ultrasound in obstetrics and Gynecology, 2nd resived and enlarged edition, Springer, Germany 2005: 599-608
4. Cheng WF, Lee CN, Chu JS, Chen CA, Shau WY, Hsieh CY. Vascularity Index as novel parameter for the in vivo assessment of angiogenesis in patient with cervical carcinoma. American Cancer Society 1999: 651-7
5. Aschoush S, Naggar E. The technique and value of Doppler Ultrasonography. ASJOG 2005: 403-6

6. Mauklik D. Spectral Doppler: Basic principles and instrumentation, in: Maulik D (ed), Doppler ultrasound in obstetrics and Gynecology, 2nd resived and enlarged edition. Germany, Springer, 2005: 19-34
7. Maulik D. Spectral Doppler sonography: waveform analysis and hemodynamic interpretation, in: Maulik D (ed), Doppler ultrasound in obstetrics and Gynecology, 2nd resived and enlarged edition. Germany, Springer, 2005: 35-56
8. Chudleigh T, Thilaganathan B. The physic of Dopller ultrasound and Dopller equipment, in: Obstetric ultrasound how, why and when. United of Kingdom, Elsevier Churchill Livingstone, 2004: 209-22
9. Shung KK. Doppler Flow Measurements, in: Shung Kirk, Diagnostic ultrasound imaging and blood flow measurements. United States of America, Taylor and Francis, 2006: 103-17
10. Alcazar JL. Three dimensional ultrasound in gynecology: current status and future perspectives. Current Women's health reviews 2005; 1: 1-14
11. Schaberle W. Fundamental principles, in: Ultrasonography in vascular diagnosis, a therapy oriented textbook and atlas. Germany, Springer 2005: 1-26
12. Alcazar JL. Transvaginal color Doppler in the assessment of cervical carcinoma, review article. Cancer therapy 2005; 3: 139-46
13. Zalud I. Doppler ultrasonography for benign gynecologic disorders, ectopic pregnancy, and infertiliy, in: Maulik D (ed), Doppler ultrasound in obstetrics and Gynecology, 2nd resived and enlarged edition. Germany, Springer 2005: 569-94
14. Zalud I, Platt LD. Three dimensional Dopller ultrasound in gynecology, in: Maulik D (ed), Doppler ultrasound in obstetrics and Gynecology, 2nd resived and enlarged edition. Germany, Springer, 2005: 557-67
15. Erak M, Baucal M. 3-D planning for gynecological tumors (cervix uteri): procedure description. Archieve of Oncology 2005; 13 supl 1: 31-3
16. Breyer B. Physical Priciples of the Doppler Effect and its Application in medicine, in: Kurjaks A, Arenas JB (eds), Donald school text book of transvaginal sonograpgy. United States of America, Taylor and Francis, 2005: 343-54
17. Masciullo V, Giardano A. Moleculer genetic of cervical cancer. In: Giardano A, Bovicelli, Kurman JR, eds. Molecular Pathology of Gynecologic Cancer. United States of America, Humana Press, 2007: 113-20
18. Morris M, Levenback CS. Cervical cancer. in: Barakat R, Bevers MW, Gersherson GM. Handbook of Gynecologic Oncology. United Kingdom, Martin Dunitz 2001: 225-42
19. Suwiyoga K. Disertasi: Peran protein 53 (p53) dan protein Retinoblastoma (pRB) pada karsinogenesis kanker serviks terinfeksi Human Papilloma Virus tipe 16 dan 18: studi kasus kontrol. Denpasar, Program Doktor Ilmu Kedokteran Program Pascasarjana Universitas Udayana, 2006
20. Rock JA, Jones HW. Surgical of the anatomy pelvis, in: The Linde Operative gynecology 10th edition, United States of America, Lippincott Williams & Wilkins 2008: 84-113
21. Trush A, Hartshorne T. Blood flow and its appearance on color flow imaging, in: Peripheral vascular ultrasound how, why and when 2nd. China, Elsevier Churchill Livingstone 2005: 49-62
22. Bidus MA, Elkas JC. Cervical and vaginal cancer, in: Berek JS, Rinehart RD. Berek & Novaks Gynecology 14th edition. United Stated Of America, Churchill Livingstone, 2007: 1403-56
23. Edianto D. Kanker Serviks, dalam: Aziz FM, Andrijono, Saifuddin AB. Buku Acuan Nasional Onkologi Ginekologi, Jakarta. Yayasan Bina Pustaka Sarwono Prawirohardjo, 2006: 442-56
24. Hellweg GD, Doeberitz MK, Trunk MJ. Color atlas of histopathology of the cervix uteri 2nd. Berlin Germany, Springer Science 2006
25. Greene FL, Frizt AG, Winchester PD, Smith JR, Healy J, Priore GP. American Joint Committee on Cancer (AJCC) Cancer Staging Atlas: Cervix uteri. United States America, Springer Science, 2006: 249-57
26. Iyer R. Imaging Gynecologic Malignancies, in: Eifel PJ, Gershenson DM, Kavanagh JJ. Gynecologic Cancer. United stated of America, Springer 2006: 49-63
27. Lacombe JA, Priore GD, Hiller. Cervical cancer. In: Smith JL, Healy J, Priore. Atlas Of Staging In Gynecological Cancer. London, Springer Science 2008: 1-5