Radiotherapy Outcome in Stage IIB Cervical Cancer Patients Resistant to Neoadjuvant Chemotherapy at Dr. Soetomo Hospital2006 – 2010

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ABSTRACT

*Neoadjuvant chemotherapy for advanced cervical cancer is controversial. In dr. Soetomo Hospital, stage IIB cervical cancer received neoadjuvant chemoteraphy (NACT), while there was no data for radiotherapy response in these patients. This study was to investigate the outcome of post-radiotherapy in NACT-resistant patients stage IIB cervical cancer. This study used descriptive and analytic observational retrospective survival design. Statistical analysis used Kaplan Meier method. Data were from medical records of cervical cancer patients in oncology outpatient clinic and obstetric and gynecologic inpatients, dr. Soetomo Hospital 2006-2010 . Data were collected from July to August 2012. Most patients, 80 persons (50.3%), were 40-49 years old and 49 patients (30.8%) were 50-59 years. Most patients, 110 (69.2%) cases, had squamous cell carcinoma and adenocarcinoma in 41 (25.8%). Post NACT evaluation revealed 123 patients (77.4%) had tumor size <4 cm, while 36 (22.6%) had > 4 cm. Patients with cancer free space (CFS) > 50% were 129 (81.1%), CFS < 50% were 30 (18.9%). Patients with complete response were 47 (29.6%), while 112 patients (70.4%) had incomplete response. Cancer histopathology did not affect therapeutic response. Treatment response did not differ between patients with CFS > 50% and <50%. Difference was found in therapeutic response in patients with tumor size > 4 cm (16.7% complete response) and < 4 cm complete response (33.3%), although not statistically significant (p = 0.062). Median survival was 2.9 years with 2-year survival rate 39%. Lost of follow-up reached 45.9%. Conclusively, radiotherapy response in NACT-resistant IIB stage cervical cancer patients is low.**(MOG 2013;21:56-60)***

Keywords: *Cervical cancer stage IIB, NACT, radiotherapy, response to therapy, survival*

ABSTRAK

*Kemoterapi neoadjuvant untuk kanker serviks stadium lanjut masih kontroversial. Di RSUD dr. Soetomo, pasien kanker serviks stadium IIB menerima chemoteraphy neoadjuvant (NACT), sementara tidak ada data respon radioterapi pada pasien ini. Penelitian ini bertujuan mengetahui hasil pasca-radioterapi pada pasien kanker serviks stadium IIB resisten NACT. Penelitian ini menggunakan descriptive and analytic observational retrospective survival design. Analisis statistik menggunakan metode Kaplan Meier. Data berasal dari rekam medis penderita kanker serviks di klinik onkologi rawat jalan dan pasien rawat inap obstetri dan ginekologi, RSUD dr. Soetomo 2006-2010. Data dikumpulkan dari Juli hingga Agustus 2012. Sebagian besar pasien, 80 orang (50,3%), berusia 40-49 tahun dan 49 pasien (30,8%) 50-59 tahun. Sebagian besar pasien, 110 (69.2%) orang, memiliki karsinoma sel skuamosa dan adenokarsinoma pada 41 pasien (25,8%). NACT pasca evaluasi mengungkapkan 123 pasien (77,4%) memiliki ukuran tumor < 4 cm, sedangkan 36 (22,6%) > 4 cm. Pasien dengan cancer free space (CFS) > 50% sebanyak 129 (81,1%), CFS <50% adalah 30 (18,9%). Pasien dengan respon lengkap yang 47 (29,6%), sedangkan 112 pasien (70,4%) memiliki respon yang tidak lengkap. Histopatologi kanker tidak mempengaruhi respon terapi. Respon pengobatan tidak berbeda antara pasien dengan CFS > 50% dan < 50%. Perbedaan ditemukan pada respon terapi pada pasien dengan tumor > 4 cm (16,7% respons lengkap) dan < 4 cm respon lengkap (33,3%), meskipun tidak signifikan (p = 0,062). Kelangsungan hidup rata-rata 2,9 tahun dengan 2 tahun tingkat kelangsungan hidup 39%. Tidak mengikuti tindak lanjut mencapai 45,9%. Simpulan, respon radioterapi pada pasien kanker serviks stadium IIB resisten NACT rendah.**(MOG 2013;21:56-60)***

Kata kunci: *kanker serviks stadium IIB, NACT, radioterapi, respons terhadap terapi, survival*

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INTRODUCTION

Concurrent chemoradiation is recommended for advanced cervical cancer. Neoadjuvant chemotherapy for advanced cervical cancer is controversial. In Dr. Soetomo Hospital, any stage IIB cervical cancer performed neoadjuvant chemoteraphy (NACT). No data for radiotherapy response in cervical cancer stage IIB resistant to NACT.

MATERIALS AND METHODS

This study is a descriptive survey using analytic observational retrospective survival design. Statistical analysis was performed using Kaplan Meier method. Data were retrieved from medical records of patients with cervical cancer recorded at oncology outpatient clinic and the inpatient wards, Department of Obstetrics and Gynecology, Dr. Soetomo hospital 2006-2010. Data collection was conducted from July to August 2012. Inclusion criteria when cervical cancer patients stage IIB who have received NACT and was declared inoperable and undergo a whole series of treatment. Analysis of survival was only performed on patients who wre still alive.

RESULTS AND DISCUSSION

Number of cervical cancer patients stage IIB were tracked from medical records in years 2006-2010. As many as 159 medical records met the inclusion criteria.Most cases were in the age of 40-49 years and 50-59 years, respectively 80 patients (50.3%) and 49 patients (30.8%). Most histopathological types was squamous cell carcinoma, which were found in 110 (69.2%) cases, and adenocarcinoma type 41 (25.8%) cases. In evaluation performed after NACT, there were 123 patients (77.4%) with a tumor size of <4cm, while the rest, 36 patients (22.6%) had tumor size of> 4cm. Rectal examination results obtained by cancer patients revealed free space (CFS)> 50% as many as 129 (81.1%), CFS <50% by 30 patients (18.9%) (Table 1).

In patients with squamous cell carcinoma pathology results, from 110 patients, found 35 patients (31.8%) who experienced a complete response to therapy and 75 patients (68.2%) experienced an incomplete response to therapy. Patients with adenosquamous pathology, amounting to 8 people, with 2 patients (25%) had a complete response to therapy, 6 patients (75%) had incomplete treatment response. Obtained 41 patients with adenocarcinoma pathology, with a complete response to therapy by 10 patients (24.4%) and 31 patients (75.6%) had incomplete responses. (Table 3).

Patients with tumor size larger or equal to 4 cm were 36 patients, with 6 patients (16.7%) had a complete response and 30 patients (83.3%) had incomplete responses. Patients with tumor size less than 4 cm, totally 123 patients, 41 (33.3%) of them experienced a complete response to therapy, and 82 patients (66.7%) had incomplete treatment response. (Table 4). Total 30 patients with CFS was less than or equal to 50%, with 7 patients (23.3%) who experienced a complete response and 23 patients (76.7%) who experienced incomplete responses.

Table 1. Patient characteristic of cervical cancer IIB resistant to neoadjuvant chemotherapy

Characteristic	N	%
Age		
30-39	21	13.2
40-49	80	50.3
50-59	49	30.8
≥ 60	9	5.7
Histopathology		
Squamous cell ca	110	69.2
Adenocarcinoma	41	25.8
Adenosquamous cell	8	5.0
Size of tumor		
< 4 cm	123	77.4
>or = 4 cm	36	22.6
Cancer free space		
≤ 50 %	30	18.9
> 50 %	129	81.1
Total	159	100

Table 2. The frequency distribution of IIB cervical cancer patients who are resistant NACT according to response after radiotherapy

Response	N	%
Complete response	47	29.6
Incomplete response	112	70.4
Total	159	100

Table 3. The frequency distribution of radiotherapy response in IIB cervical cancer patients who are NACT resistant on the basis of histopathological findings

Histopathology	Complete response	Incomplete response	N
Squamous cell ca	35	75	110
Adenocarcinoma	10	31	41
Adenosquamous cell ca	2	6	8
Total	47	112	59

Table 4. The frequency distribution of radiotherapy response in stage IIB cervical cancer patients who are resistant NACT based on tumor size

Size of tumor (cm)	Complete response	Incomplete response	N
< 4	41	82	123
≥ 4	6	30	36
Total	47	112	159

Of 129 patients with CFS, more than 50% obtained a complete response to therapy in 40 patients (31.0%) and 129 patients (89%) with incomplete response. Chi-square statistical tests revealed no statistically significant difference in the type of pathology with treatment response, with a P value of 0.407 (Table 5)

At this stage many patients lost of follow-up reached 73 (45.9%), those with follow-up <1year totally 39 (24.5%) patients, 29 (18.2%) patients lost of follow up between 1-2 years, 3 (1.9%) lost of follow-up of 2-3 years, 2 (1.3%) lost of follow-up of between 3-4 years. Eighty-one (50.9%) patients were still alive, 16 (10.1%) patients were alive in the range of <1 year, 62 (39.0%) patients in the follow-up of 1-2 years, 2 (1.3 %) of patients in the follow-up of 2-3 years, and only 1 (0.6%) patients who had been followed up 3-4 years. (Table 6).The number of medical records IIB cervical cancer neoadjuvant chemotherapy resistance that met the inclusion criteria of 2006-2010, as many as 159 cases.The age group mostlywas at the age of 40-49 years by 80 patients (50.3%), and 50-59 years in 49 patients (30.8%).[33,34]Most histopathologicaltypewas squamous cell carcinoma, in 110 (69.2%) cases, and adenocarcinoma in 41 (25.8%).

Tumor size measured is the amount of mass in the cervix, 123 (77.4%) measuring <4 cm, and a total of 36 (22.6%) with large tumors ≥ 4 cm. Cervical tumor infiltration into the parametrium was assessed by measuring cancer free space (CFS) through screening examination of the rectum (rectal toucher/RT). CFS obtained measurements were ≤ 50% by 30 (18.9%) patients, and> 50% in 129 (81.1%) patients.

Radiotherapy response to IIB cervical cancer patients with complete response was 47 patients (29.6%), whereas the remaining 112 patients (70.4%) had incomplete treatment response. This result is quite low when compared to the studies conducted earlier. Distance chemotherapy> 14 days will provide sufficient time for the chemotherapy-resistant cells to undergo repopulation, which in turn also reduces tumors response to radiotherapy.

Table 5. The frequency distribution of radiotherapy response in IIB cervical cancer NACT resistant base on tumor infiltration

Cancer free space (CFS)	Complete response	Incomplete response	N
≤ 50%	7	23	30
> 50%	40	89	129
Total	47	112	159

Complete response to the therapy pathology revealed squamous cell carcinoma, adenocarcinoma and adenosquamous of 31.8%, 24.4% and 25%. Incomplete therapeutic response to the pathology results squamous cell carcinoma, adenocarcinoma and adenosquamous by 68.2%, 75.6%, and 75%. We found that the histopathology of cancer does not affect the therapeutic response (p = not significant). Complete therapeutic response in CFS was less than or equal to 50% and more than 50% of CFS was 23.3% and 30%. Incomplete therapeutic response in CFS was less than or equal to 50% and over 50% of CFS, namely 76.7% and 89%. Treatment response did not differ between patients with CFS> 50% of patients with CFS and <50%.

Complete therapeutic response of patients with larger tumor size equal to 4 cm and less than 4 cm by 16.7% and 33.3%. Incomplete treatment response of patients with larger tumor size equal to 4 cm and less than 4 cm by 83.3% and 66.7%. There are differences in treatment response between larger tumor size equal to 4 cm and less than 4 cm, despite statistically insignificant. Survival of patients for 2.9 years with a survival rate of 39% for 2 years. Lost of follow-up were 45.9% achieved a constraint in the calculation of survival.

CONCLUSION

Response to radiotherapy in patients with NACT-resistant stage IIB cervical cancer is low.

Table 6. The frequency distribution of the last condition and time of follow up patients with stage IIB cervical cancer NACT resistant

Last condition		Length of follow up (years)					
		< 1	1 - 2	2 - 3	3 - 4	> 4	N
	Life	16 (10.1%)	62 (39.0%)	2 (1.3%)	1 (0.6%)	0	81 (50.9%)
	Death	0	2 (1.3%)	3 (1.9%)	0	0	5 (3,1%)
	Lost of follow up	39 (24.5%)	29 (18.2%)	3 (1.9%)	2 (1.3%)	0	73 (45.9%)
Total		55	93	8	3	0	159 (100%)

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