# CORRELATIONS BETWEEN STAGING AND CHEMOTHERAPHY RESPONSE WITH TESTICULAR CARCINOMA NON-SEMINOMA AT DR. SOETOMO HOSPITAL, SURABAYA, INDONESIA

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## ABSTRACT

*The purpose of this study was to describe patients' characteristics, correlation between staging non-seminoma cancer and chemotherapy response. Data on age, location of tumor, staging, serum levels of the tumor marker post operative, adjuvant therapy, chemotherapy side effects, and response of patient to chemotherapy were gained from medical records in Soetomo Hospital Surabaya from January 2012 to December 2015, and analyzed with SPSS. Correlation between staging and chemotherapy response, correlation primary tumor staging (pT) and Metastasis (M), correlation regional lymph nodes staging (N) and metastasis (M), correlation serum tumor marker and chemotherapy response was proccessed by Spearman correlation test. There were no significant correlation between pT staging and M and no significant correlation between N and M staging. Based on tumor markers (S), mostly patients were S2. There were no significant correlation between the response to chemotherapy and serum tumor marker levels. In category of staging group, the most are 14 patients stage III. BEP was the most adjuvant Chemotherapy. Nausea and vomiting were The most complained during chemotherapy. Anemia were the most hematologic side effects of chemotherapy. There are no significant correlation between the staging of non-seminoma and the response to chemotherapy. Conclusion: Non seminoma mostly happened in young males. Non-seminoma responses to chemotherapy. Patients in early stage would give a good response to chemotherapy compared to those with advanced stage. After chemotherapy, evaluation should be done to the patients' complaints and complete blood count to detect side effects.*

***Keywords**: Germ cell tumor; non-seminoma; chemotherapeutic response*

## ABSTRAK

*Tujuan penelitian untuk mengetahui karakteristik pasien, hubungan antara staging Non seminoma testis dan respon kemoterapi. Usia, lokasi tumor, staging, kadar serum tumor marker setelah operasi, adjuvant terapi, efek samping kemoterapi, dan respon kemoterapi pasien yang didapatkan dari rekam medis di RSUD dr Soetomo Surabaya dari Januari 2012 sampai Desember 2015 dianalis menggunakan SPSS. Analisis data antara hubungan staging dan respon kemoterapi, staging primary tumor (pT) dan metastasis (M), staging regional lymph nodes (N) dan metastasis (M) dan respon kemoterapi dan kadar serum tumor marker di uji dengan uji korelasi Spearman. Didapatkan korelasi yang tidak signifikan antara staging pT dan M dan didapatkan hubungan korelasi yang tidak signifikan antara staging N dan M. Kadar serum tumor marker (S) yang paling banyak adalah S2. Tidak didapatkan korelasi yang signifikan antara respon kemoterapi dan kadar serum tumor marker. Berdasarkan pembagian staging non seminoma testis, terbanyak 14 pasien dengan stage III. Adjuvan terapi yang paling banyak diterima adalah kemoterapi BEP. Keluhan paling banyak akibat pemberian kemoterapi adalah mual dan muntah. Efek samping hematologi yang sering timbul pasca kemoterapi adalah anemia. Penelitian ini menunjukan korelasi yang tidak signifikan antara staging Non seminoma testis, dan respon kemoterapi. Pasien Non seminoma testis paling sering muncul pada laki laki usia muda. Non seminoma testis bersifat kemosensitif, pasien yang datang pada stadium dini akan memberikan respon kemoterapi yang lebih baik jika dibandingkan dengan pasien yang datang dengan stadium lanjut. Setelah pemberian kemoterapi harus dilakukan evaluasi terhadap keluhan pasien dan laboratorium darah, untuk mencegah efek samping yang ditimbulkan.*

***Kata kunci**: Tumor sel germinal; testis non seminoma; respon kemoterapi*

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## INTRODUCTION

Testicular cancer includes 1% malignancy in men and 5% malignancy in the field of urology with 3-10 new cases per 100,000 men per year in Western countries. The number of incidents increased surprisingly on the last 10 years, especially in developed countries. The Surveillance Epidemiology and End Results Program (1992 to 2011) data show an increased risk of developing seminomas in male caucasian races. The highest incidence on non-seminoma occurs at the age of third and fourth decade for pure seminoma.(Albers et al 2014) . Testicular cancer incidence varies depends on the geographical area. The incidence is highest in Switzerland, Scandinavia, New Zealand and Germany. The incidence rate is intermediate in the North America and the England and lowest in Asia Africa. The incidence of testicular cancer in the North America is five times higher than African-Americans, four times higher than in Asia, and 78% higher than that of Hispanics (Andrew Cramer and Mike B Siroky, 2004)

Life expectancy for testicular cancer patients has increased dramatically with the discovery of effective combination chemotherapy. New cases of testicular cancer in the North America is 8,000 in 2005, a mortality rate of less than 400 patients was reported. New cases are reported 6.7 per 100,000 men per year in Scandinavian countries, in Japan there are 0.8 new cases per 100,000 men per year. White people in the United States reported four times the incidence of blacks (Houldsworth et al 2006; Albers et al 2014; Ade IM, 2015).

In the United States, The incidence of Germ Cell Tumors is increasing, patients aged 15 to 49 years rise from 2.9 in 1975 to 5.1 in 2004 per 100,000. Testicular tumor incidence rates due to seminomas increased when compared to NSGCT. The testicular cancer incidence increased from 55% in 1973 to 73% of cases in 2001. As many as 10% to 30% of cases will come with conditions of distant metastases. In Germ Cell Tumor, seminoma was the most case, approximately 52 - 56% of cases (Andrew Cramer and Mike B Siroky, 2004).

According to the Global Cancer Statistic in 2011, the testicular cancer incidence in developing countries was 4.6 per 100,000 (Ahmedin 2011) Based on research at RSUD Dr. Soetomo from 2008 to 2013 regarding testicular cancer, 37 cases (80%) were testicular seminomas, 4 cases (9%) were yolk sac tumors, 1 patient (2%) with embryonal tumors, 1 patients (2%) with teratomas and 3 patients (7%) with mixed germ cell tumors.(Ade IM, 2015).

This aims of study to determine the characteristics non-seminoma testicular tumor patients in RSUD DR. Soetomo Surabaya based on patient identity, age, history of previous testicular undescence, levels of tumor markers, knowing the relationship between non-seminoma staging and chemotherapy response taking from Soetomo Hospital Surabaya from January 2012 to December 2015.

## MATERIALS AND METHODS

The design study was a retrospective analytic study, where Non-Seminoma Testis patients underwent treatment at Soetomo Hospital from January 1st, 2012 to December 31st, 2015 will be the sample in this study. There is no special treatment in the sample, because the research is retrospective. The study was conducted on medical records of inpatient and outpatient care at Dr. Soetomo Surabaya from 1 January 2012 until 31 December 2015. Inclusion criteria: Non-seminoma testis patients, which are established based on the results of Anatomical Pathology. Exclusion criteria: patients with testicular cancer with PA results are not a non-seminoma testis and incomplete medical record data. Patients with non-seminoma testis will be noted regarding age, tumor location, serum tumor marker level, TNM staging of testicular seminoma, given therapeutic adjuvant, chemotherapy regimen and chemotherapy cycle given, chemotherapy response, chemotherapy side effects and current patient condition. We assessed the correlation between staging and chemotherapy response from non-seminoma testis. For intervals and ratios, data will be displayed in the form of averages and standard deviations, for data that is nominal and ordinal, the data will be displayed in percentages. Interval and ratio data, with normal distribution of data analysis using Annova test and Pearson correlation test, if the abnormal data distribution will be used Wilcoxon test with Spearman correlation test, for nominal and ordinal data, data analysis using Wilcoxon test with the Spearman correlation test. Data is processed and analyzed using SPSS 22.0 for Windows computer software

## RESULTS

The results from January 1, 2012 to December 31, 2015 showed that there were 16 Nonseminoma testicular patients with an average age of stage I patients was 15.5 ± 16.26 years and metastases 20.85 ± 9.73 years. The location of the tumor is more often in the left testis as many as 9 patients (56.25%), right testicles 5 patients (31.25%) and 2 patients (12.5%) with testicular intraabdominal tumors. A total of 3 patients (18.75%)

were obtained with a history of UDT while a total of 13 patients (81.25%) had no known risk factors. From TNM staging, the most patients with pT3 stage were 6 patients (37.5%), then pT4 was 4 patients (25%), pT2 and pTx were 3 patients (18.25%) and 2 patients (12.5%) respectively. and pT1 as many as 1 patient (6.25%). From the regional (N) staging lymph nodes, there were 6 patients (37.5%), N0 4 patients (25%), N2 and Nos as many as 3 patients (18.25%) and N1 1 patients (6.25%). From the Staging Matastasis (M), the most abundant were M1a as many as 8 patients (50%), then M1b as many as 4 patients (25%) and M0 as many as 2 patients (20%), from the highest serum levels of tumor marker (S) is a master's degree, which is 7 patients (48.75%) followed by Sx, S3 and S1 respectively 3 patients (18.75%), 3 S3 patients (18.75%).

Table 1. Patients' characteristics

| | | (N) | | Percentage (%) | Distribution Data | Homogenity test |
|---|---|---|---|---|---|---|
| | | Stage I | Metastatic Non-Seminoma | | | |
| Age (Year) | | 15.5 ± 16.26 | 20.85 ± 9.73 | 100 | 0.560 | 0.364 |
| Location | Right Testicles | 1 | 4 | 31.25 | | |
| | Left Testicle | 0 | 9 | 56.25 | 0.000 | 0.898 |
| | Intraabdomen | 1 | 1 | 12.5 | | |
| Risk Factor | UDT | 1 | 2 | 18.75 | 0.000 | 0.229 |
| | Unknowned | 7 | 6 | 81.25 | | |
| Staging T | Tx | 0 | 2 | 12.5 | | |
| | pT 1 | 1 | 0 | 6.25 | | |
| | pT 2 | 1 | 2 | 18.75 | 0.041 | 0.881 |
| | pT 3 | 1 | 5 | 37.5 | | |
| | pT 4 | 0 | 4 | 25 | | |
| Staging N | Nx | 0 | 2 | 12.5 | | |
| | N0 | 2 | 2 | 25 | | |
| | N1 | 0 | 1 | 6.25 | 0.008 | 0.022 |
| | N2 | 1 | 2 | 18.75 | | |
| | N3 | 0 | 6 | 37.5 | | |
| Staging M | 0 | 2 | 2 | 25 | | |
| | 1a | 0 | 8 | 50 | 0.005 | 0.229 |
| | 1b | 0 | 4 | 25 | | |
| Tumor Marker Serum (S) | Sx | 0 | 3 | 18.75 | | |
| | S0 | 0 | 0 | 0 | | |
| | S1 | 2 | 1 | 18.75 | 0.005 | 0.067 |
| | S2 | 0 | 7 | 43.75 | | |
| | S3 | 0 | 3 | 18.75 | | |

Table 2. Characteristics of patients based on stage, adjuvant therapy and chemotherapy response

| Characteristics | | N | Percentage (%) |
|---|---|---|---|
| Stage | Stage I | 1 | 6.25 |
| | Stage II | 1 | 6.25 |
| | Stage III | 14 | 87.5 |
| Adjuvant terapy | BEP | 13 | 81.25 |
| | Lost | 3 | 18.75 |
| Chemotherapy response | Complete Response | 2 | 12.5 |
| | Partial Response | 9 | 56.25 |
| | No Response | 2 | 12.5 |
| | Lost | 3 | 18.75 |

Tabel 3. Therapy based on non-seminoma testis stage

| Stages | n | Adjuvant Therapy | N | Percentage (%) | Chemotherapy cycle |
|---|---|---|---|---|---|
| Stage I | 2 | BEP | 2 | 12.5 | 3 cycle |
| Stage IIA/B | 0 | - | - | - | - |
| Stage ≥ IIC | 14 | BEP 3 cycle | 4 | 25 | 3 cycle |
| | | BEP 4 cycle | 8 | 50 | 4 cycle |
| | | EP | 2 | 12.5 | 4 cycle |

Table 4. Average Increased Serum Tumor Marker Level (S) post operations

| Serum Tumor Marker | Category | Staging | | N | (%) | Mean | SD | Distribution | Homo-gene-ity |
|---|---|---|---|---|---|---|---|---|---|
| | | Stage I | Metastatic Seminoma | | | | | | |
| LDH | Normal | 1 | 0 | 1 | 9.09 | 898.58 | 1300.99 | 0.000 | 0.171 |
| | Increase | 1 | 10 | 11 | 90.9 | | | | |
| AFP | Normal | 2 | 2 | 4 | 33.33 | 1673.12 | 3440.05 | 0.000 | 0.005 |
| | Increase | 0 | 8 | 8 | 66.67 | | | | |
| β-Hcg | Normal | 2 | 5 | 7 | 58.33 | 2184.64 | 3906.65 | 0.000 | 0.047 |
| | Increase | 0 | 5 | 5 | 41.67 | | | | |

Table 5. Symptoms on chemotherapy

| No. | Symptoms | N | Percentage (%) |
|---|---|---|---|
| 1 | Nausea and vomiting | 9 | 56 % |
| 2 | Alopecia | 2 | 12.5 % |
| 3 | Neurotoxic, Ototoxic | 0 | 0 |
| 4 | No symptoms | 3 | 18.75 % |

From Table 3, 2 patients (12.5%) received BEP therapy in seminoma stage I. Four patients (25%) received BEP 3 cycle chemotherapy adjuvant therapy, eight patients (50%) received BEP 4 cycles, two patients received EP 4 cycle. From table 4, it was found that patients with elevated LDH levels were 10 patients (90.9%), and as many as 1 patient (9.09%) with normal LDH levels, with an average increase of 898.58 U/l ± 1300.99 U/l . There were 8 patients (66.67%) with elevated AFP levels while 4 patients (33.33%) with normal AFP levels. Average AFP increase is equal to 1673 mIU/mL ± 3440.05. B-hCG levels were increased in 5 patients (41.67%) and 7 patients (58.33%) had normal hCG levels with an average increase of 2184.64 ng/mL ± 3906.65 ng/ml.

From Table 2, there were 14 patients (87.5%) with stage III, 1 patient (6.25%) with stage I and stage II. With Adjuvant BEP chemotherapy therapy as many as 13 patients (81.25%), 3 patients (25%) did not receive chemotherapy because they refused medication. From the chemotherapy response, there were 9 patients (56.25%) with complete response, 2 patients (12.5%) with partial response, 2 patients (12.5%) with no response, 3 patients lost because they did not undergo chemo. There are no patients who experience progressive chemotherapy response.

From Table 4, it was found that patients with elevated LDH levels were 10 patients (90.9%), and as many as 1 patient (9.09%) with normal LDH levels, with an average increase of 898.58 U/l ± 1300.99 U/l. There were 8 patients (66.67%) with elevated AFP levels while 4 patients (33.33%) with normal AFP levels. Average AFP increase is equal to 1673 mIU/mL ± 3440.05. B-hCG levels were increased in 5 patients (41.67%) and 7 patients (58.33%) had normal hCG levels with an average increase of 2184.64 ng/mL ± 3906.65 ng/ml.

Table 6. Side effects of chemotherapy

| No | Side Effects | N | (%) |
|---|---|---|---|
| 1 | Lekopenia | 1 | 6.25% |
| 2 | Neutropenia | 1 | 6.25% |
| 3 | Trombocitopenia | - | |
| 4 | Anemia | 2 | 12.5% |

From Table 5. There were 9 patients (56%) with complaints of nausea and vomiting during chemotherapy, 2 patients (12.5%) with alopecia complaints. While as many as 3 patients (18.75%) did not experience complaints during the administration of chemotherapy drugs. From table 6. Obtained side effects of chemotherapy that most often appear are, anemia as much as 2 patients (12.5%), lekopenia occurred in 1 patient (6.25%) and neutropenia occurred in 1 patient (6.25%). From table 7. Spearman correlation test was conducted to assess the relationship between staging and chemotherapy response, obtained a negative correlation between the seminoma testis stages and chemotherapy response p = -0.304 (r = 0.253). From the table, there were 1 stage I seminoma testis patients giving complete chemotherapy response and 1 partial partial response, whereas in stage II there was 1 patient partial response. Stage III 2 patients complete chemotherapy response and 7 patients partial chemotherapy response and 2 patients no chemotherapy response.

From table 8 the correlation between pT and metastasis (M) staging, obtained rho (r) = 0.237 and p = 0.376, this means there is a weak correlation between pT staging and metastasis (M), and the relationship between pT and M is not significant.

From table 9 the correlation between regional (N) and Metastasis (M) staging lymph nodes, obtained by the value of rho (r) = 0.08 and p = 0.769, this means that there is no correlation between staging N and M, and relationship N with M is not significant, which means that if there is an increase in staging N, it is not necessarily followed by an increase in staging M and this is not significantly related. From table 10 the correlation between chemotherapy response and serum tumor marker, obtained the value of rho (r) = -0.2244 and p = 0.363, this means there is a weak negative correlation between chemotherapy response and levels of serum tumor marker, and the relationship of chemotherapy response with levels serum tumor marker were not significant.

Table 7. Correlation between stage and chemotherapy response

| | Chemoterapy response | | | Total | R | P |
|---|---|---|---|---|---|---|
| | Complete | Partial | No Response | | | |
| Stage I | 1 | 1 | | 2 | | |
| Stage II | | 1 | | 1 | -0.304 | 0.253 |
| Stage III | 2 | 7 | 2 | 11 | | |

Table 8. Correlation between pT staging with Metastase (M)

| | | Staging pT | | | | | R | P |
|---|---|---|---|---|---|---|---|---|
| | | PTx | pT1 | pT2 | pT3 | pT4 | | |
| Metastasis (M) | M0 | 0 | 1 | 2 | 1 | 0 | 0.237 | 0.376 |
| | M1a | 1 | 0 | 1 | 4 | 2 | | |
| | M1b | 1 | 0 | 1 | 0 | 2 | | |

Table 9. Correlation between staging nodules (N) with Staging Metastase (M)

| | | Staging regional lymph nodes (N) | | | | | R | P |
|---|---|---|---|---|---|---|---|---|
| | | Nx | N0 | N1 | N2 | N3 | | |
| Staging | M0 | 0 | 2 | 0 | 1 | 1 | | |
| Metastasis (M) | M1a | 1 | 2 | 0 | 2 | 3 | 0.08 | 0.769 |
| | M1b | 1 | 0 | 1 | 0 | 2 | | |

Table 10. Correlation between chemotherapy response and increased serum tumor marker

| | | Chemotherapy response | | | R | P |
|---|---|---|---|---|---|---|
| | | Complete | Partial | No Response | | |
| Serum Tumor Marker (S) | S0 | 0 | 1 | 0 | -0.244 | 0.363 |
| | S1 | 1 | 2 | 0 | | |
| | S2 | 1 | 4 | 1 | | |
| | S3 | 0 | 2 | 1 | | |

## DISCUSSION

Testicular cancer is the most common cancer in men between 15 - 35 years.(Andrew Cramer and Mike B Siroky, 2004) Rarely in the age under 15 years or above the age of 60 years.(Merzenich et al 2000) The incidence in children is only 0.5 - 2.0 per 100,000 population, age distribution at children are also different from adults.(Srivastava & Kreiger 2004) Testicular seminoma patients most often appear in the 4th decade of life, whereas in non-seminomas most often occur in the 3rd decade of life (Albers et al 2014). From the results of the study, there were 16 patients with non-seminoma testis from January 1, 2012 to December 31, 2015. The average age of patients was 19.88 ± 10.651 years.

Testicular cancer is more common on the right side than the left side, as is the case with cryptorchidismus. The strongest factor suspected of testicular cancer is the previous history of cryptorchidismus testis, about 7-10% testicular cancer patients have a background of cryptorchidismus. Cryptorchidismus increases the risk of 4-6 times higher for testicular cancer. The risk of being higher in the testes in the abdominal cavity (1 in 20 events), and significantly lower in the testicular location in the inguinal (1 of 80 events).(Jerome et al 2012) From the results of the study found the location of the tumor more often on the left testis, namely 9 patients (56.25%), right testes 5 patients (31.25%) and 2 patients (12.5%) with intraabdominal testicular tumors. A total of 3 patients (18.75%) were obtained with a history of UDT while a total of 13 patients (81.25%) were not known for risk factors. There are 4 factors that are generally known as the cause of testicular cancer, including cryptorchismus, testicular cancer history of the family, testicular cancer history, and intra tubular germ cell neoplasia (ITGCN).(Jerome et al 2012) In this study, no four risk factors were obtained from 16 patients. Research conducted by Mersenich, et al showed that there was no correlation between a history of trauma to the testes as a risk factor for testicular cancer. (Merzenich et al 2000) Srivastava et al argued that there was no correlation between the time to start smoking and there was no reduction in the risk of stopping smoking. It is possible that the carcinogenic content in cigarettes and/or the influence of sexual hormones contribute to an increased risk among smokers. no exposure was found from these substances. John Guo's study, et al. Concluded that textile dust, pesticides and some organic content might be associated with risk of testicular seminoma. (Guo et al 2005) In this study no exposure was found.

From TNM staging, the most patients with pT3 stage were 6 patients (37.5%), then pT4 4 patients (25%), pT2 3 patients (18.75%) and pTx 2 patients (12.5%). From the regional (N) staging lymph nodes, there were 6 patients (37.5%), N2 3 patients (18.75%), N0 4 patients (25%), Nx 2 patients (12.5%) and N1 as many as 1 patient (6.25%). From Staging Matastasis (M), the most abundant were M1a as many as 8 patients (50%), then M1b as many as 4 patients (25%) and M0 as many as 4 patients (25%), from the highest serum levels of tumor marker (S) is a S2, which is 7 patients (43.75%) followed by Sx, S1 and S0, each with 3 patients (18.75%). From the results of the study, there were 14 patients (87.5%) with stage III, 1 patient (6.25%) with stage I and stage II. The most widely available adjunctive therapy was BEP chemotherapy as many as 13 patients (81.25%), as many as 3 patients (18.75%) medical record data were incomplete. From the chemotherapy response, 2 patients (12.5%) complete response, 9 patients (56.25%) partial response, as many as 2 patients (12.5%) with no response.

Although fetal serum AFP has a high level, after one year the number of AFP is very small (Jerome et al 2012). AFP will not increase in pure seminoma or choriocarcinoma.(Andrew Cramer and Mike B Siroky, 2004) Increased levels of β-hCG do not occur in pure embryonal cell carcinoma, these cancer cells do not contains syncytiotrophoblast, rarely increases AFP in pure embryonal cell carcinoma, and if this occurs usually in conjunction with yolk sac tumor.(Albers et al 2014) Mixed tumors occur in various combinations, often consisting of embryonal cell carcinoma, seminoma, yolk sac, teratoma or syncytiotrophoblast . Depending on the type of cell constituent, AFP increases usually when the cells compose yolk and tumor, and there is an increase in βHCG levels if there is an element of syncytiothropoblast. (Albers et al 2014) Serum tumor marker is an important for diagnosis and for prognosis. AFP increase in 50-70% and β-hCG in 40-60% of patients with non-seminomatous germ cell tumors (NSGCT). One or two serum tumor markers will increase in almost 90% NSGCT. Nearly 30% of patients with seminoma experience an increase in hCG. LDH is a less specific tumor marker which concentration increases proportional to tumor volume. 80% of patients with advanced testicular cancer, serum hCG usually increases. Patients with pure seminoma, Placenta alcali phosphatase (PLAP), a tumor marker serum that can be examined, smokers were not recommended for. (Albers et al 2014) The results showed that patients with elevated LDH levels after surgery were 11 patients (90.9%), and as many as 1 patient (9.09%) with normal LDH level, with an average increase of 898.58 ± 1300.99 U/l. There were 8 patients (66.67%) with elevated AFP levels while 4 patients (33.33%) with normal AFP levels. Average AFP increase is equal to 1673 mIU/mL ± 3440.05. B-hCG levels were increased

in 5 patients (41.67%) and 7 patients (58.33%) had normal hCG levels with an average increase of 2184.64 ng/mL ± 3906.65 ng/ml.

The risk of recurrence on Stage I NSGCT were 14-48% within 2 years after orchiectomy. Adjuvant chemotherapy BEP 2 cycles was introduced in 1996 by MRC. Chemotherapy is given especially in high-risk patients (vascular invasion) with no side effects on sexual activity or fertility. Side effects of BEP chemotherapy on longterm evaluation (>20 years) are unknown, especially the cardiovascular effects. This must be conveyed during the therapy selection consultation (Albers et al 2014). Ninety percent of advanced stage testicular cancer patients provide a good therapeutic response with chemotherapy (Jerome et al 2012). Compared to NSGCT, surveillance for testicular seminomas is slightly more complicated due to limited usefulness of serum tumor markers and the required time long to detect recurrence, because 10-20% of recurrences occur in the 4th year or more after being diagnosed with testicular cancer.

In the United States, standard therapy for non-seminoma stage I is retroperitoneal lymph node dissection (RPLND). But because three-quarters of stage I patients with are only treated with orchidectomy, and morbidity due to RPLND is unavoidable, other alternatives are introduced, including modified surveillance and RPLND (Jerome et al 2012). Advanced non-seminoma patients with large retroperitoneal masses (nodules> 3 cm or 1 cm diameter nodules number 3 or more, seen from CT scan or spread NSGCT, treated with platinum-based combination chemotherapy after orchidectomy. If a marker of a normal tumor but from a radiological examination found the remaining tumor after chemotherapy, then the remaining tumor must be taken, because the remaining 20% will grow into tumors, 40% become teratomas, and 40% become fibrosis tissue (Joseph.& Presti 2013, Einhorn 2007, Daugaard et al 2014).

Based on IGCCCG, the initial therapy for non-seminoma metastases disease with a good progonist is BEP 3 cycle. If Bleomycin is contraindicated, EP 4 cycles can be given as therapy.(de Wit et al 1997, Horwich 1997). In patients with intermediate prognosis, with 5 years of 80% survival rate, 4 cycles of BEP therapy are recommended. (de Wit et al 1998) Patients with poor prognosis, IGCCCG standard therapy is BEP 4 cycle, 5 years progression free survival between 45-50%. Three Randomized studies show that there is no advantage of overall survival rate for the administration for patients with a poor prognosis category on giving high-dose chemotherapy (Motzer et al 2007, Daugaard et al 2011).

From the results of the study found 9 patients (56%) with complaints of nausea and during administration of chemotherapy, as many as 2 patients (12.5%) with complaints of alopecia, while as many as 3 patients (7.5%) had no complaints during the administration of chemotherapy drugs. The results of the study also found that the most frequent side effects of chemotherapy were 2 patients (12.50%) of anemia, then 1 patient (6.25%) and leukopenia in 1 patient (6.25%). The cause of neutropenia, leukopenia is the result of side effects of etoposide and cisplatin which causes bone marrow myelosuppression so that the production of white blood cells and platelets decrease (Li et al 1997) Alopecia is the most common side effect due to bleomycin and etoposide, this is due to chemotherapy drugs causing disruption of cellular absorption of hair follicles thus disrupting hair growth (Christian et al 2003).

In this study spearman correlation test was conducted, which assessed the relationship between stages of non-seminoma testis and chemotherapy responses that occurred, found that there was a negative correlation between stage and chemotherapy response. The higher the stage seminoma testis the chemotherapy response leads to a partial response and statistically not significant. P = -0,034 (r = 0,253). Negative correlation coefficient means that between stage variables and chemotherapy responses are not directly proportional, in this case not every stage increase is balanced with improvements in chemotherapy response. This is because the level of education of patients is still low for the disease, so that patients come for treatment under conditions that have metastases. From the table, there were 2 patients of stage I seminoma testis giving complete chemotherapy response 1 patient and 1 patient partial response, whereas in stage II there was 1 patient with partial response. Stage III with 2 patients complete chemotherapy response and 7 patients partial chemotherapy response and 2 patients no chemotherapy response.

## CONCLUSION

From the results of the study, there were 16 patients with non-seminoma testis from January 1, 2012 to December 31, 2015. The average age of patients was 19.88 ± 10.651 years. The location of tumor is more often in the left testis which is 9%, UDT risk factor is 18.75% while the unknown factor is 81.25%. From TNM staging, it was found that pT3 was the highest at 37.5%, from regional (N) staging lymph nodes, N3 was 37.5%, from Staging Metastasis (M), the most abundant was M1a by 50%, from levels The most common serum tumor marker (S) is S2, which is 43.75%. The most

patients who came to Dr. Soetomo Hospital were Stage III, which was 87.5%, Adjuvant therapy was obtained with BEP chemotherapy as much as 81.25%. From the chemotherapy response it was found that as many as 12.5% experienced complete response after giving chemotherapy, as much as 56.25% experienced a partial response and as many as 12.5% patients did not respond to the administration of chemotherapy. Based on the Spearman correlation test, obtained a weak correlation with negative correlation coefficient, this is not statistically significant. p = -0.304 (r = 0.253). Further research is needed, and better research designs to provide a clearer picture of non-seminoma testicular disease.

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