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Effects of Combination of Cisplatin and Paclitaxel Chemotherapy on Tumor Mass in Nasopharyngeal Carcinoma Patients at Dr. Wahidin Sudirohusodo Hospital Makassar with the RECIST Method

(*Efek Kombinasi Kemoterapi Cisplatin dan Paclitaxel Terhadap Massa Tumor pada Pasien Karsinoma Nasofaring di RSUP Dr. Wahidin Sudirohusodo Makassar dengan Metode RECIST*)

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ABSTRACT

Background: Nasopharyngeal Carcinoma (NPC) is a malignant tumor that grows from epithelial cells that line the surface of the nasopharynx and has a tumor position close to the base of the skull, vital structures, and anatomical locations that are difficult to reach and various symptoms are the cause of increased patient mortality and morbidity rates. This research aims to identify the most effective chemotherapy effect on reducing tumor mass in nasopharyngeal cancer patients. **Methods:** This study was conducted retrospectively based on patient medical record data from January 2019 to December 2021 at Dr. Wahidin Sudirohusodo General Hospital. Inclusion criteria included NPC patients who received cisplatin, carboplatin, paclitaxel, and docetaxel chemotherapy and had complete data on tumor mass size before and after receiving chemotherapy from Series I to Series VI. The resulting assessment of tumor mass size was further categorized using RECIST. **Results:** A total of 166 NPC patients met the inclusion criteria. The results of the study obtained that NPC patients suffered more in men than women, most NPC patients were aged (41-50), Stage IVA had the highest percentage found in NPC patients, Histopathology based on WHO type III was most commonly found in 109 patients, 70 patients used the Cisplatin+Paclitaxel chemotherapy regimen, 55 patients used the Cisplatin+Paclitaxel chemotherapy regimen had a partial tumor mass response. **Conclusions:** The combination of Cisplatin + Paclitaxel has the most partial response to the tumor mass of NPC patients at Wahidin Sudirohusodo General Hospital, Makassar.

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INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a malignant tumor that grows from epithelial cells lining the surface of the nasopharynx and usually originates from the lateral wall of the nasopharynx, particularly the Rosonmuller fossa. This disease has rapid tumor growth, can infiltrate local tissues (Yusuf, 2020), metastasizes to cervical lymph nodes, and metastasizes deep into bones, lungs, and mediastinum (Farhat,, 2020). NPC has a poor prognosis because there are still frequent errors in diagnosis and delays in treatment, this is due to the position of the tumor adjacent to the base of the skull and vital structures and anatomical locations that are difficult to reach and the various symptoms cause the mortality and morbidity rates of patients to continue to increase and provide psychological and material burden for patients, families and the State (Farhat, 2020); (Yusuf, 2020).

One method of treating cancer is chemotherapy which has been proven to improve healing and improve the quality and survival of cancer sufferers (Noviyani, 2017). Treatment with chemotherapy provides effectiveness, especially in cancer patients, namely by inhibiting, destroying, and even stopping the life cycle of cancer cells that grow and develop abnormally, so that treatment can run optimally (Shead *et al.*, 2019);(Noviyani *et al.*, 2017), besides that, chemotherapy is due to other therapies are not enough to kill cancer cells and chemotherapy can prolong the survival of cancer patients (Farhat *et al.*, 2020). Based on The National Comprehensive Cancer Network (NCCN) the treatment of NPC is based on the patient's cancer stage, in the early stage (I) the patient receives radiation treatment, but in the advanced stage (II, III, and IV) the patient receives chemoradiation and chemotherapy treatment. Treatment with chemotherapy generally uses a combination of drugs namely, Cisplatin + paclitaxel, cisplatin + docetaxel, carboplatin + paclitaxel, and carboplatin + docetaxel. Treatment with this combination is the standard treatment for NPC patients (Shead *et al.*, 2019).

Currently, the assessment of the effectiveness of therapy in cancer patients can be determined by assessing the characteristics of the tumor mass (T), involved lymph nodes (N), and metastases to other organs (M) (Cai *et al.*, 2022). In addition to assessing the TNM system, the degree of tumor mass reduction has been reported to be a significant prognostic factor for some malignant tumors (Yang *et al.*, 2020). Reduction of a tumor mass can be used as a measure of the effectiveness of treatment because chemotherapy administration can cause tumor mass shrinkage (Noviyani *et al.*, 2017). To determine the response of chemotherapy to reducing tumor mass can be assessed objectively by measuring the mass after chemotherapy, namely by using RECIST (Response Evaluation Criteria in Solid Tumors). Assessment of chemotherapy response is used to predict patient survival rates and can be used as a guideline for further chemotherapy. Reduction in tumor size (objective response) according to RECIST is an important target in evaluating chemotherapy response (Rusli *et al.*, 2021). Based on this, the

purpose of this study was to identify the most effective chemotherapy effect on reducing tumor mass in nasopharyngeal cancer patients at Dr. Wahidin Sudirohusodo Makassar based on RECIST.

METHODS

This study was conducted retrospectively using secondary data derived from the medical records of NPC patients treated at RSUP Dr. Wahidin Sudirohusodo Makassar from January 2019 to December 2021. The research sample was all medical records of NPC patients who had undergone chemotherapy and met the inclusion and exclusion criteria. Inclusion criteria were NPC patients who had undergone complete chemotherapy (from chemotherapy I to chemotherapy VI to the 21-day schedule) without changing chemotherapy regimens, and complete patient medical record data including sex, age, stage, histopathology, chemotherapy regimen used, tumor mass size before chemotherapy, and tumor mass size after chemotherapy. The age group used is a 10-year interval (Yusuf and Foris, 2020), and the patient stage group uses the tumor node metastasis (TNM) classification system according to the 8th edition of AJCC, The tumor mass reduction group based on the type of treatment was classified by RECIST *(Respon Evaluation Criteria in Solid Tumor)* (Rouh *et al.*, 2017). Furthermore, the data were analyzed by Chi-Square Test to determine whether the type of chemotherapy treatment affects the tumor mass. If a p-value < 0.05 was obtained the correlation is confirmed. This research has received ethical approval issued by the research ethics committee of The Faculty of Public Health, Hasanuddin University on July 19, 2022, under number 8061/UN4.14.1/TP.01.02/2022.

RESULTS AND DISCUSSION

The total number of Nasopharyngeal Carcinoma patients at Wahidin Sudirohusodo Hospital Makassar for the 2019-2021 period was 166 patients who met the inclusion criteria. In table 1 the patient demographic data shows that there were more male patients (71.1%) than female patients (29.9%). This is in line with research that was conducted at Sun Yat-sen University Cancer Center (SYSUCC) from 2009-2015 with a total of 10,126 patients divided into 7,440 male patients and 2,686 female patients (Yao *et al.*, 2021), the high prevalence of NPC in males are associated with unhealthy lifestyles such as long-term tobacco use which is identical to males who are larger than females and frequent drinking of alcoholic beverages. Both of these are of risk factors for NPC, while the female hormone estrogen is the main trigger for NPC (Farhat *et al.*, 2020).

Table 1. Patient Demographics

Characteristics	Number of Patients	Percentage
Gender		
Man	118	71.1%
Woman	48	28.9%
Age		
21 – 30 Years	11	6.6 %
31 – 40 Years	45	27.1%
41 – 50 Years	49	29.5%
51 – 60 Years	45	27.1%
61 – 70 years	16	9.6%

Based on the results of the study (table 1) the average age of NPC patients ranges from 41-50 years (29.5%). This is in line with previous research conducted by Ji-Jin You which stated that out of 10,126 NPC patients, 3,492 NPC patients were aged 40-49 years (Yao *et al.*, 2021). Referring to the theory which says that the young age group of NPC sufferers is 15-19 years, the peak of NPC sufferers is most around the ages of 40-49 years and 50-59 years (Farhat *et al.*, 2020); (Yusuf, 2020), this is because NPC requires quite a long time to develop from pre-malignant cells into detectable solid tumors Thus, exposure to carcinogens early in life can have a substantial impact on the development of NPC (Farhat *et al.*, 2020).

Table 2. Clinical Characteristics of Patients

Characteristics	Number of Patients	Percentage
Stadium		
I	3	1.8%
II	17	10.2%
III	43	25.9%
IVA	66	39.8%
IVB	37	22.3%
Histopathology		
WHO Type 1	3	1.8%
WHO Type 2	54	32.5%
WHO Type 3	109	65.7%

Table 2 describes the clinical characteristics of the patients including stage I (1.8%), stage II (10.2%), stage III (25.9%), stage IVA (39.8%), and stage IVB (22.3%). Based on the results of the study, the most common stage was found in NPC patients at Wahidin Sudirohusodo Hospital, namely, stage IVA, this proved that most NPC patients were diagnosed at an advanced stage, namely stages III, IVA, and

IVB, this being the main cause of the poor NPC prognosis. Delays in treating NPC will worsen the patient's condition so it will increase the mortality and morbidity of NPC patients (Farhat *et al.*, 2020). The same thing has been reported in previous studies, namely patients in stage I have a better survival rate of 99.5% conversely, patients in stage IV are the most difficult to treat resulting in 25% of patients dying within 5 years (Yao *et al.*, 2021)

The histopathological characteristics group showed WHO type I (1.8%), WHO type II (32.5%), and WHO type III (65.7%). Based on research conducted by Ling-Quang Tang (2015) in NPC Endemic Areas, it was shown that out of 4,630 patients, 95.7% were patients with WHO type III criteria (Tang *et al.*, 2015). In WHO characteristics Type II and type III has a higher level of sensitivity to chemotherapy than type I, so this histopathological grouping can be used for therapeutic strategies and prediction of response to treatment (Yusuf and Foris, 2020).

Table 3. Treatment regimen profile for NPC patients at Wahidin Sudirohusodo Hospital

Variable	Number of Patients	Percentage
Cisplatin + Paclitaxel	70	42.2%
Cisplatin + Docetaxel	21	12.7%
Carboplatin + Paclitaxel	53	31.9%
Carboplatin + Docetaxel	22	13.3%

Chemotherapy is a treatment that can be used to treat NPC patients (Shead *et al.*, 2019) and chemotherapy treatment can be given before or simultaneously with radiotherapy or as an addition after radiotherapy (Zhu *et al.*, 2021). In this study (table 3) the results of the chemotherapy treatment regimens that were often used in NPC patients at Wahidin Sudirohusodo General Hospital consisted of four combinations including Cisplatin+Paclitaxel (42.2%), Cisplatin+Docetaxel (12.7%), Carboplatin+Paclitaxel (31.9%) and Carboplatin+Paclitaxel (13.3%). These four chemotherapy treatment regimens are the first line of chemotherapy in NPC patients (Shead *et al.*, 2019). Cisplatin+Paclitaxel has the highest percentage of use in NPC patients at Wahidin Sudirohusodo General Hospital compared to other treatments because this drug combination is an alternative to the cisplatin+5-FU treatment regimen for the treatment of recurrent or metastatic head and neck cancer, besides that the efficacy of cisplatin+paclitaxel has survival is better and also more practical. After all, it is only given for 1 day compared to cisplatin+5-FU (Farhat *et al.*, 2020). A similar study conducted by Yusuf (2020) stated that the choice of the Cisplatin + Paclitaxel regimen as first-line therapy was due to a lack of facilities and infrastructure in the inpatient room, considering the Cisplatin + 5-FU regimen requires

longer hospitalization compared to the Cisplatin+Paclitaxel regimen with a shorter length of stay (Yusuf, 2020).

Table 4. Decrease in tumor mass by type of treatment

Treatment Type	Partial Response (n)	Stable Disease (n)	Total	Chi-Squre Test	*p*-value
Cisplatin+Paclitaxel Persentage (%)	55 78.6%	15 21.4%	70 100%	Pearson Chi-Square	1,203[a]
Cisplatin+Docetaxel Persentage (%)	15 71.4%	6 28.6%	21 100%		
Karboplatin+Paclitaxel Persentage (%)	39 73.6%	14 26.4%	53 100%		
Karboplatin+Docetaxel Persentage (%)	15 74.7%	7 25.3%	22 100%		

In table 4. The decrease in patient tumor mass based on the type of treatment using the RECIST *(Response Evaluation Criteria in Solid Tumors)* assessment showed that the combination of Cisplatin + Paclitaxel (55 patients) had the most partial response to tumor mass in NPC patients compared to other regimens. Previous studies have suggested that NPC is highly sensitive to chemotherapy with reported response rates of up to 80% for cisplatin-based chemotherapy (Zhu *et al.*, 2021). Another similar study was conducted on cervical cancer patients using the Cisplatin + Paclitaxel regimen who were undergoing Neoadjuvant Chemotherapy with an assessment of mass reduction based on RECIST obtaining results of 91.8% of patients experiencing a decrease in tumor mass with the Complete Response and Partial Response categories (He *et al.*, 2018). Although based on statistical analysis with the chi-square test there is no significant relationship between the type of chemotherapy treatment on reducing tumor mass based on the RECIST category, the use of Cisplatin + paclitaxel chemotherapy can be recommended because it has the highest rate of reduction in tumor mass or with a partial response category in the RECIST method.

In NPC, chemotherapy and radiotherapy are the treatment options used to treat patients (Farhat *et al.*, 2020); (Shead *et al.*, 2019), because surgery is not a treatment option in NPC cases due to the location of the tumor adjacent to the neurovascular structure (Zhu *et al.*, 2021). Chemotherapy treatment can cause tumor mass shrinkage (Noviyani *et al.*, 2017) and if the use of chemotherapy does not cause an ideal change in tumor mass, it is advisable to change chemotherapy treatment regimens, increase Neodjuvan chemotherapy cycles, increase the dose of chemotherapy regimens or add immunological therapy to reduce volume tumor mass (Yang *et al.*, 2020). Currently, the tumor mass assessment can be used as an assessment of the effectiveness of the regimen used (Noviyani *et al.*, 2017). To determine the

response of chemotherapy to reducing tumor mass, can be assessed objectively by measuring the mass after chemotherapy, namely by using RECIST (Response Evaluation Criteria in Solid Tumors). Assessment of chemotherapy response is used to predict patient survival rates and can be used as a guideline for further chemotherapy. Reduction in tumor size (objective response) according to RECIST is an important target in evaluating chemotherapy response (Rusli *et al.*, 2021).

CONCLUSION

The effect of chemotherapy with the combination regimen of Cisplatin + Paclitaxel has the most partial response to the tumor mass of NPC patients at Wahidin Sudirohusodo General Hospital, Makassar.

CONFLICT OF INTEREST

We declare no conflict of interest

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