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Demographic, Clinical, and Treatment Factors That Affect the Five Years Survival of Thyroid Cancer Patients

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Abstract

Thyroid cancer is the most common malignancy of the endocrine glands, the incidence of thyroid cancer in Indonesia ranks ninth after other types of cancer, it is known that the survival rate of thyroid cancer is better when compared to other types of cancer because thyroid cancer has a slow growth rate. Several demographic factors such as age and gender, clinical factors and treatments factors can affect the survival rate of thyroid cancer patients. This study was conducted to analyze the influence of demographic, clinical, and management factors on thyroid cancer survival rates at Dr. M. Djamil Padang Hospital. This study is an observational analytic study with a retrospective cross-sectional design. Sampling was done by total sampling technique. Data collection is done through patient medical record data. The results showed a five-year survival rate for thyroid cancer of 86.7%. Age, histopathological type, metastases, tumor extension, and management were significantly related to survival (p=0.013) (p=0.000), (p=0.001), (p=0.000) and (p=0.001). Factors that have a significant relationship with survival rate are age, histopathological type, tumor extension, treatment, and metastases, and those that most influence survival rate are non-operative management and regional extension

Keywords: *Survival rate, thyroid cancer, treatments, tumor extension.*

INTRODUCTION

Thyroid cancer is the most common malignancy of the endocrine glands. Thyroid cancer is the ninth ranks in all types of new cases of cancer, which is as much as 3.8% of all cases. The American Cancer Society in 2016 conducted a study that found 62,450 cases of thyroid cancer in the United States, through a comparison of the numbers for the two sexes the ratio was 3:1.[1] From data in 2018, it is estimated that there are 893,094 people living with thyroid cancer in America United States. [2] According to data from the Global Burden of Cancer (GLOBOCAN), the incidence of thyroid cancer in Indonesia ranks ninth after other types of cancer, accounting for 586,202 new cases of thyroid cancer or a total of 3% of all cancer cases in 2020. [3]

Several factors influence the incidence of thyroid cancer, namely low iodine consumption, race, frequency of radiation exposure, height, weight, gender, and age. 54 years. [5] The incidence of thyroid cancer in the elderly group over the age of sixty years has a higher rate. [6] Most thyroid cancers are formed from follicular cells and some can originate from parafollicular cells, lymphoid tissue and other tissues.[7] Based on the description and type of histopathology, thyroid cancer can be divided into several types, namely anaplastic type, medullary type, follicular type, and papillary type. The highest incidence of thyroid cancer is papillary type thyroid cancer, which is 85% of all types of thyroid cancer then follicular type thyroid cancer as much as 11%, medullary type thyroid cancer 3-5%, and anaplastic type thyroid cancer 2-5%.

Judging from its aggressiveness, anaplastic thyroid cancer has the worst prognosis compared to other types with a mortality rate of almost 100%, then medullary types also appear with a mortality rate of 35% in 10 years, meanwhile papillary and follicular types have a better prognosis. The mortality rate for follicular type thyroid cancer is only 15%, while papillary type thyroid cancer is 6%.[8] Generally, thyroid cancer is a single hard nodule with uneven edges and has poorer function than the surrounding tissue. 7 Based on the data from the European Journal of Clinical Investigation, almost all of the thyroid nodules found in patients are benign nodules while only 5% are malignant.

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Based on information from the National Cancer Institute, it is shown that thyroid cancer has a better survival rate than uterine cancer and breast cancer. The survival rate for thyroid cancer reaches 94%, while uterine cancer only reaches 82%, followed by skin cancer 82%, and breast cancer. 78%. [2] Thyroid cancer survival rate is influenced by the stage of cancer at diagnosis and the determination of treatment has a major influence on the length of thyroid cancer survival rate. In general, if the cancer is first found in a localized part of the body, the prognosis and survival rate will be better than for cancer that has metastasized far.

Several factors are associated with the prognosis of thyroid cancer. Among them are patient factors and tumor factors. According to a study conducted in Europe, the survival rate of patients with thyroid cancer varies based on the underlying factors. Several factors have a considerable influence on thyroid cancer survival, namely tumor extension, presence of metastases, presence of multifocal disease, tumor size, and patient age. [11] Several factors greatly influence patient survival rates, for example, the type of invasive or non-invasive cancer that have differences in survival rates.[9] Thyroid cancer is more common in patients aged 41 to 60 years and those over 60 years. Then followed by patients aged 21 to 40 years and then patients aged 20 years and under.

This theory is supported by research by Pasaribu ET and Adiputra PAT which stated that adult and elderly patients are more susceptible to thyroid cancer, where patients with an age range of 40 to 65 years will experience an increase in developing this disease. The incidence of thyroid cancer increases with increasing patient age and is very present in the age range below 15 years.[11] Dr. Kariadi Hospital produced a study based on the results of an analysis of several clinical characteristics in thyroid cancer patients. Where thyroid nodules have diagnostic value for thyroid cancer, namely if there is a thyroid nodule size that is more than four centimeters in diameter, and this result was found in 88 of the 120 patients studied.[7]

The Research on the five-year survival rate of thyroid cancer at Dr. M Djamil Padang Hospital in 2007 to 2011 showed a survival rate for thyroid cancer reaching 92.3% while the same research was conducted in 2013-2017 and showed a decrease in the survival rate of thyroid cancer patients which only reached 87.1%. Changes in the results of this study are very likely to occur, this disease can be caused by a number of factors. Since the end of 2019 until now, there has been a Covid-19 pandemic which has caused changes to the health order. This also causes many patients to not have access to proper health care. In addition, the Covid-19 pandemic has also increased the morbidity and mortality rates for patients. Thus, researchers have an interest in understanding how demographic, clinical, and management factors affect the five-year survival rate of thyroid cancer patients in Dr. M. Djamil Padang Hospital.

METHODS

The type of research conducted was an analytic observational study and used a retrospective cross-sectional study design by utilizing data obtained from medical records of patients who had been diagnosed with thyroid cancer at Dr. M. Djamil Padang Hospital. The patient's medical record data was obtained from the Medical Record Installation of Dr. M Djamil Padang Hospital. This hospital was chosen as the location for data collection because Dr. M Djamil Padang Hospital is a type A hospital and is the main referral hospital for the West Sumatra region. The research is planned to start from May 2022, while the collection and processing of patient medical record data will be carried out from October 2022 to December 2022.

The population in this study were all patients with a diagnosis of thyroid cancer based on the results of histopathological examination at Dr. M Djamil Padang Hospital from 2017 to 2021. The sampling technique used is a total sampling technique where the sample used in this study is the entire population that fits the inclusion and exclusion criteria. The sample size is the number of patients diagnosed with thyroid cancer based on the patient's medical records at Dr. M. Djamil Padang Hospital in 2017-2021 according to the sample criteria. The data was taken from the medical records of patients who had been diagnosed with thyroid cancer at Dr. M. Djamil Padang Hospital from 1st January 2017 to 31th December 2021. The data required from the medical record

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is patient identity data, including age, gender, patient address, and results of investigations on the patient.

Data processing was carried out using a computerized program, with bivariate and univariate instruments. Survival analysis was carried out using the Kaplan-Meier-Product-Limit method. The resulting data will be presented in the form of tables or curves. The log-rank test aims to find differences between the subvariables studied. The difference is said to be significant if the p value <0.05. To identify the strength of the relationship between variables, logistic regression analysis is used by including all independent variables that have a p-value <0.25 and then assessing the Odds Ratio (OR) to see the level of risk in each variable studied.

RESULTS

a. Five Year Survival Rate of Thyroid Cancer Patients according to Kaplan – Meier

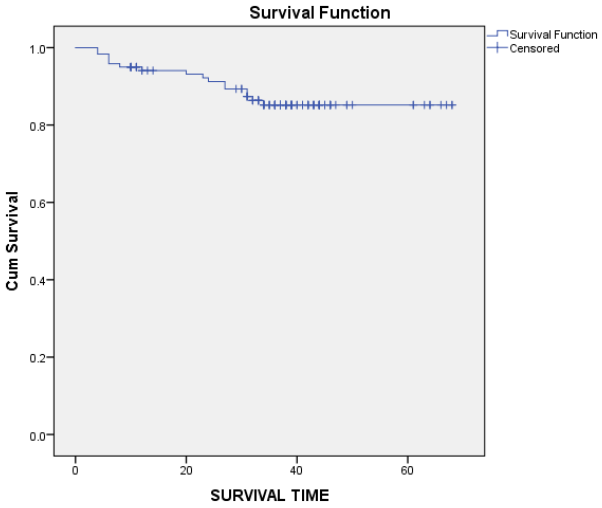

Figure 1. Graph of Thyroid Cancer Five-Year Survival Rate

Based on figure 1, the five-year survival rate for thyroid cancer patients in the 2017-2021 period is 86.7%. These results indicate that thyroid cancer has a higher survival rate compared to other types of cancer

b. Relationship of Age with Thyroid Cancer Five-Year Survival

Table 1. Relationship between Age and Survival of Thyroid Cancer Patients

Characteristic	Survive (%)	Died (%)	Total	P value
Age:				
1-18 Years	6 (100)	0 (0)	6	
19-44 Years	29 (100)	0 (0)	29	0.013
45-65 Years	51 (86.4)	8 (13.6)	59	
>65 Years	18 (69.2)	8 (30.8)	26	
Total	104 (86.7)	16 (13.3)	120	

In the analysis, the age of the patients in this study were categorized into four categories, they are patients aged 1-18 years, 19-44 years, 45-65 years, and patients over 65 years. Based on the results obtained through survival analysis using the Kaplan-Meier method, it turns out that patients with an age range of 44-65 years and over 65 years have lower survival rates, 86.4% for patients aged 45-65 years and 69.2% for patients over 65 years. While patients aged 1-18 years and 19-44 years the survival rate is very good, reaching 100%. Based on the results of log rank

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analysis on the age of the patients in this study, a p-value of 0.013 was obtained, which means that there was a significant difference in the age and survival rate of thyroid cancer patients.

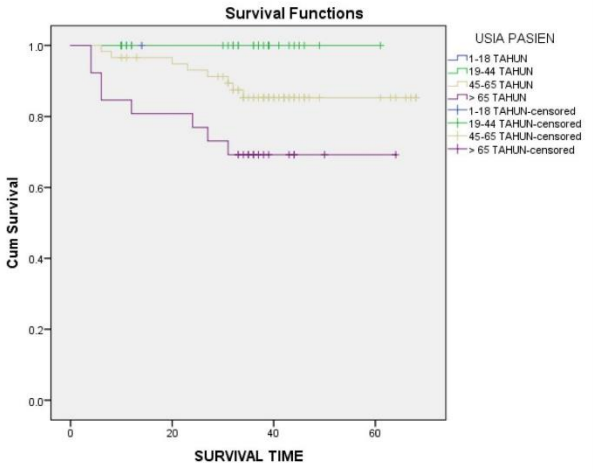

Figure 2. Graph of Thyroid Cancer Survival by Age

In Figure 2, it can be seen that patients aged 1-18 years and 19-44 years have a higher survival compared to patients aged 45-65 and >65 years and over.

c. Relationship of Gender with Five-Year Survival of Thyroid Cancer

Table 2. Relationship between Gender and Survival of Thyroid Cancer Patients

Characteristic	Survive (%)	Died (%)	Total	P value
Gender:				
Male	23 (82.1)	5 (17.9)	28	0.456
Female	81 (88)	11 (12)	92	
Total	104 (86.7)	16 (13.3)	120	

In this study, the survival rate for female patients was better than for male patients, with a five-year survival rate for female patients being 88% compared to only 82.1% for males. Based on **table 2,** it can be seen from the results of statistical tests using the log-rank test that there was no significant difference (p = 0.456) between the sexes on thyroid cancer survival.

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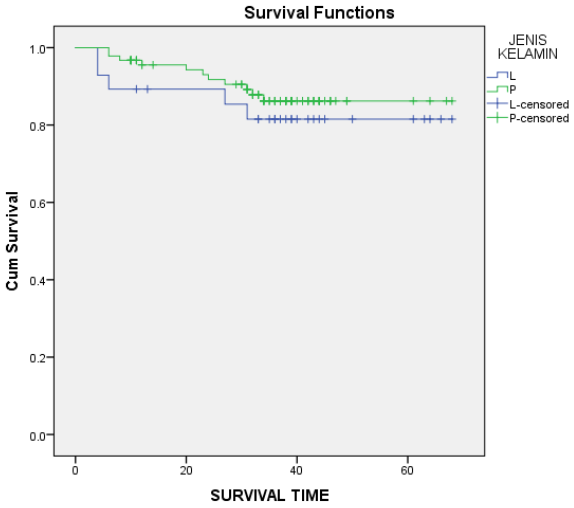

Figure 3. Graph of Thyroid Cancer Survival by Gender

In **Figure 3**, it can be seen that women have a higher average survival, which is around 61.56 months, while male patients are 58.18 months.

d. Relationship of Histopathological Type and Five-Year Survival of Thyroid Cancer

Table 3. Relationship between Histopathological Type and Survival of Thyroid Cancer Patients

Characteristic	Survive (%)	Died (%)	Total	P value
Histopatological Type:				
Papillar	82 (92.1)	5 (17.9)	28	0.456
Folikular	19 (90.5)	11 (12)	92	
Anaplastic	0 (0.0)	16 (13.3)	120	
Others	3 (75)			
Total	104 (86.7)	16 (13.3)	120	

Based on **table 3,** the five-year survival rate for patients with papillary thyroid cancer is very good, reaching 92.1%, followed by the follicular type at 90.5%, other types at 75% and the lowest is anaplastic at 0%. Based on the log rank test analysis, a p-value of 0.000 was obtained. This shows that statistically there is a significant difference between histopathological types on survival in thyroid cancer patients.

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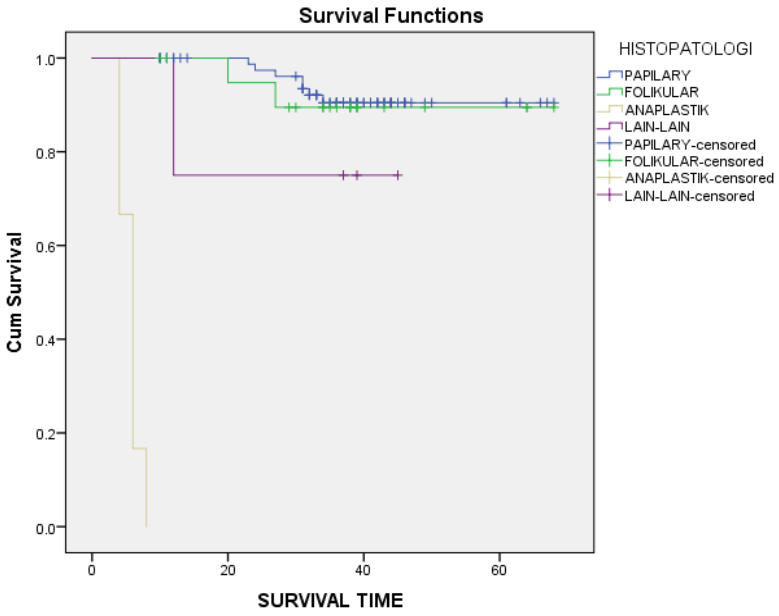

Figure 4. Graph of Thyroid Cancer Survival Based on Histopathology Type

In **Figure 4**, the average survival rate is highest for the papillary type, which is 64.28 months, follicular 63.31 months, and other types, 36.7 months. The anaplastic type was obtained at 5.6 months.

e. Relationship of Tumor Size to Five-Year Survival of Thyroid Cancer

Table 4. Relationship of Tumor Size to Five-Year Survival of Thyroid Cancer

Characteristic	Survive (%)	Died (%)	Total	P value
Tumor Size:				
≤5cm	41 (93.2)	3	44	
>5cm	63	13	76	0.154
Total	(82.9) 104	16	120	

In this study, tumor size was categorized into two, namely ≤5cm and >5cm. It was found that the survival of tumor size ≤5cm was 93.2%, which was very good, while the tumor size was > 5cm, the survival for 5 years was 82.9%.

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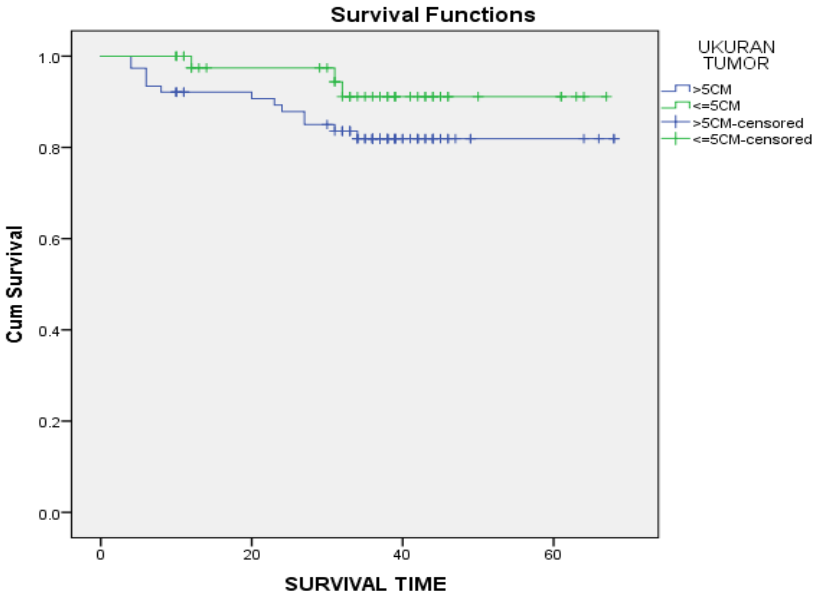

Figure 5. Graph of thyroid cancer survival based on tumor size

In Figure 5, it is found that the average survival of patients with tumor size ≤5cm is higher (63.35 months) compared to >5cm (58.87 months).

F. Relationship of Tumor Extension with Five-Year Survival of Thyroid Cancer

Table 5. Relationship of Tumor Extension and Survival of Thyroid Cancer Patients

Characteristic	Survive (%)	Died (%)	Total	P value
Ekstension				
Local	67 (97.1)	2 (2.9)	69	
Regional	37 (72.5)	14 (27.5)	51	0,000
Total	104	16	120	

In this study, tumor extension was categorized into two, namely local and regional. As shown in **Table 5**, the 5-year survival of local tumor extensions is better than regional, namely 97.1% for local extensions and 72.5% for regional ones.

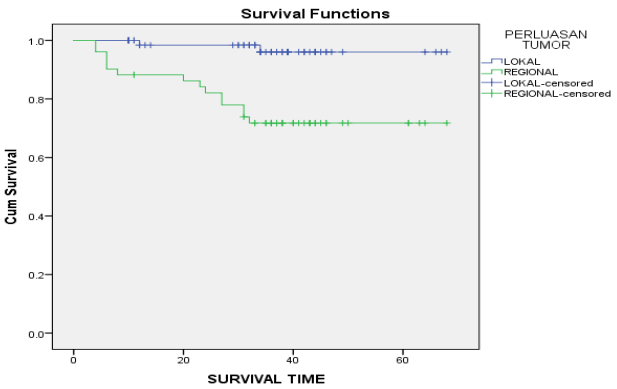

Figure 6 Graph of Thyroid Cancer Survival Based on Tumor Extension

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In **Figure 6,** it was found that the average survival of patients in local tumor extension was better than regional, namely at local 66.28 months and at regional 53.89 months**.**

g. Relationship of Tumor Extension with Five-Year Survival of Thyroid Cancer

Table 6. Relationship of Distant Metastases with Survival in Thyroid Cancer Patients

Characteristic	Survive (%)	Died (%)	Total	P value
Metastasis:				
Metastasis	27 (71.1)	11 (28.9)	38	
Not Metastasis	77 (93.9)	5 (6.1)	82	0.001
Total	104	16	120	

In this study distant metastases were categorized into two, namely metastases and no metastases. In **table 6**, five-year survival in cancers that do not metastasize is better, namely 93.9% compared to those with metastases, 71.1%. The results of the log rank test obtained a p-value of 0.001. This shows that there is a statistically significant difference between distant metastases on thyroid cancer survival.

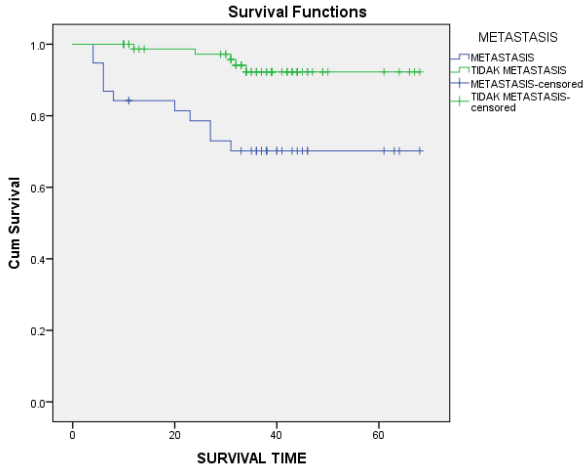

Figure 7. Graph of Thyroid Cancer Survival Based on Metastases

In **Figure 7**, the average survival in patients with metastases is 52 months, compared to those without metastases, the average survival is 64.85 months.

h. Relationship of Management with Thyroid Cancer Five-Year Survival

Table 7. Relationship between Management and Five-Year Survival of Thyroid Cancer

Characteristic	Survive (%)	Died (%)	Total	P value
Treatments:				
Surgical	103 (89.6)	12 (10.4)	115	
Non-Surgical	1 (20)	4 (80)	5	0.001
Total	104	16	120	

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In this study, treatment was categorized into two, namely operative and non-operative management. Treatment without surgery is carried out when thyroid cancer is inoperable (inoperable) or when the patient refuses to be operated on. In **table 7,** the 5-year survival in patients with operative management is better, namely 89.6% compared to those who do not have surgery, only 20%. The log rank test results obtained a p-value of 0.001. This shows that statistically there is a significant difference between the treatments given to patients on thyroid cancer survival.

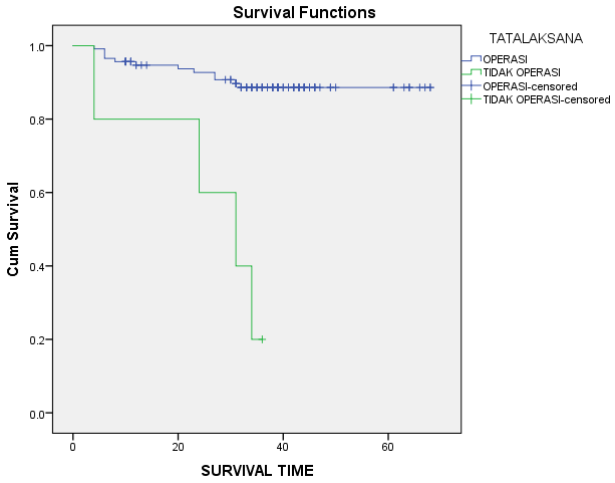

Figure 8. Graph of Thyroid Cancer Survival Based on Treatment

In **Figure 8**, it was found that the average survival in patients with operative management was 62.25 months, compared to those who did not have surgery, the average survival was 25.8 months.

i. The Most Dominant Factors Affecting Survival

Table 8. Factors Affecting Survival Rates

No	Variable	P value
1	Age	0.013
2	Tumor Size	0.154
3	HistopatologicalType	0.000
4	Tumor Ekstension	0.000
5	Metastasis	0.001
6	Treatments	0.001

Table 8 is a variable that has a p-value of 0.005 will be eliminated so that what remains is a variable that has a p-value < 0.005.

Table 9. The Most Dominant Factors Influencing Survival

Variable	P value	Odd Ratio	95%CI
Tumor Ekstension : Regional	0.029	7.528	1.232-46.002
Treatments: Non-Surgical	0.04	52.289	3.468-788.460

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Table 9 is the final model of the logistic regression analysis. The variables with the highest degree of influence on the five-year survival of thyroid cancer are tumor extension and type of treatment. The p-value for regional tumor extension was 0.029 with OR=7.528 (95% CI: 1.232-46.002), meaning that regional tumor extensions had a 7,528 times greater risk of dying compared to local tumor extensions. The p-value for treatment without surgery was 0.04 with OR=52,289 (95% CI: 3,468-788,460), meaning that treatment without surgery had a 52,289 times greater risk of dying compared to surgery.

DISCUSSION

a. Thyroid Cancer Five-Year Survival Rate

The results obtained from this study were in the form of a five-year survival rate for thyroid cancer in 2017-2021 as much as 86.7%. 2017 as much as 87.1%. [4] Thyroid cancer is basically a type of cancer that has a high survival rate because thyroid cancer is a type of tumor that is slow in growth and has very low mortality and morbidity. In addition, the incidence of thyroid cancer that is well differentiated is higher than that which is not well differentiated. [9] According to the National Cancer Institute, survival for thyroid cancer is higher compared to other types of cancer such as uterine cancer (82%), skin cancer (82%), and breast cancer (78%). [2] Factors that influence thyroid cancer survival are tumor, clinical, and management factors. [11]

b. Effect of Age on Five-Year Survival of Thyroid Cancer

The highest incidence according to age from this study was found at the age of 41-60 years, namely 59 patients or 49.2%. The results of this study are the same as data from Surveillance, Epidemiology, and End Results (SEER). [2] Patients aged 40 or over have a greater risk of mortality than those aged 40 and under. This may happen because thyroid cancer that is well differentiated is more often found at a young age, while types of thyroid cancer that are not well differentiated (anaplastic) are often found in patients aged 60 years and over. [2] The incidence of thyroid cancer is also more frequent according to age increases and the figure drops greatly for those under the age of 15 years. [4] In addition, a decrease in the immune response with age can explain the worse prognosis in older patients. with elderly patients, namely survival in patients aged 45 years and under is 100% in patients aged 45-65 years (86.4%), and patients > 65 years (69.2%).

Then a log-rank test was carried out to compare the results statistically, and based on the test results it was found that there was a prominent difference between age and survival (p=0.013), this is the same as the study conducted by Oktahermoniza which found significant differences between ages. [11] However, these results are different from the research conducted by Mas Izatul, who did not find a significant difference between the ages of the patients in his research.

c. Effect of Gender on Five-Year Survival of Thyroid Cancer

Females were the most common sex of the 120 thyroid cancer patients studied with a total of 92 people (76.7%), while 28 people (23.3%) were male. This result is in accordance with the Grebe SK which states that the prevalence of thyroid cancer is more common among women than men. [13] This also applies to the theory given by Rahmadhani with the statement that women are more often affected by thyroid cancer due to the presence of hormones and the effects of estrogen on them. women themselves.[4] Although women are more frequently affected by thyroid cancer epidemiologically, men have a worse prognosis than women. Based on research conducted by Zhang in 2018, this is because women are more compliant with treatment and follow-up control with doctors compared to men. Thyroid cancer tends to be more aggressive towards men.

The theory says that the hormone estrogen has a protective effect against thyroid cancer, so that thyroid cancer has a worse prognosis in an environment with low estrogen levels.[13] From the statistical analysis research, the results show that women have a five-year survival rate that is better (88%) compared to men (82.1%). But if it is assessed statistically, the results are not significant (p = 0.456).

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d. Effect of Histopathological Type on Thyroid Cancer Five-Year Survival

The types obtained are Squamous Cell Carcinoma and sarcoma. In this study, no medullary thyroid carcinoma was found. The results of this study are in accordance with data from SEER which says that papillary type thyroid cancer occupies 80-85% of all cases of thyroid cancer.[2] In addition, research has been conducted by Oktahermoniza which says that the most common type of thyroid cancer found is the papillary type. then followed by the follicular type in second order.

e. Effect of Metastases on Five-Year Survival of Thyroid Cancer

In this study, the results showed that the five-year survival rate for thyroid cancer without metastases was higher (93.9%) compared to those with metastases (71.7%). Statistically significant results where the value of p = 0.001. This is in line with research conducted by Sudoyo where in this study said that the incidence of metastases affected the five-year survival of patients, with the results obtained that metastatic events increased the risk of death three times greater than cancers that did not metastasize. The survival rate of patients with metastatic cancer is lower because the cancer cells have spread far throughout the body. In addition, thyroid cancer that has metastases will tend to be more difficult to treat when compared to cancer without metastases, so it requires more aggressive therapy to treat it. brain.

f. Effect of Treatment on Five-Year Survival of Thyroid Cancer

This study obtained the results of thyroid cancer that was managed by surgery. higher. (89.6%) compared to patients who could not be operated on or who refused surgery (20%). This is in line with research conducted by Nguyen et al in which in this study said that surgical management affects patient five-year survival, with the results obtained that surgical treatment increases survival rates and reduces recurrence rates. [14]

g. Factors Affecting Survival

The results of the study carried out by multivariate tests were age, histopathological type, tumor size, tumor extension, metastasis and the management given to patients. After multivariate logistic regression analysis was performed using the backward elimination method where p-values > 0.05 were eliminated one by one so that all that remained were p-values < 0.05. The final results of this analysis show that the variable that has the most dominant influence on the five-year survival rate of thyroid cancer is the type of tumor extension and its treatment.

CONCLUSIONS

Thyroid cancer patient at Dr. M. Djamil Padang Hospital is diverse, most of the patients are women with an age range of 45-65 years who have a tumor size of more than 5 cm with a papillary histopathological type and the presence of local tumors without metastases, and are managed by surgical management. The five-year survival rate for thyroid cancer patients was found in 104 out of 120 living patients, while 16 patients died or as much as 86.7% and it was found that age, histopathological type, tumor extension, metastasis, and management were factors that influenced the five-year survival rate. thyroid cancer patient.

DECLARATIONS

Competing interest

The authors declare no competing interest in this study

Ethics approval and consent to participate

This research ethics is intended to protect the rights and obligations of patients and researchers where researchers will guarantee the confidentiality of patient data from the time the data is collected until the results are obtained. Before carrying out data collection, researchers obtain permission from the ethics institution of Dr. M Djamil Padang Hospital. The campus will issue a research permit via a copy to the medical record installation Of Dr. M Djamil Padang hospital to obtain permission to collect medical record data for research purposes. Ethical permits

have been approved by Dr. M. Djamil Padang hospital with ethical number is LB.02.02/5.7/440/2022.

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