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Overall Survival Rate and Recurrence Free Survival Rate in Breast Sarcoma Patients: Single Center 5-Years Retrospective Study

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Authors' contributions

This work was carried out in collaboration among all authors. Author MRW designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author WS managed the analyses of the study. Author IBBSA managed the literature searches. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Background: Overall survival rates of breast sarcoma patient in 10 years was 62%. 5-years and 10-year recurrence-free survival was 47% and 42%, respectively. The differences survival rate of breast sarcoma patient depend on age, stage, chemotherapy history and radiotherapy history that correlates with the natural history of the disease or well known as prognostic factor of the patient. The purposes of this study is to identify different prognostic factors and their impact to overall survival rates and recurrence-free survival rates on breast sarcoma patient.
Methods: This study was conducted on all patients of all breast sarcoma patients in 2015 - 2016 who were treated by the Subdivision of Surgical Oncology at Dr. Moewardi General Hospital Surakarta (21 patients). The required data were retrieved from medical records. Overall survival rate and recurrent survival rate were analyzed using Kaplan Meier and bivariate analysis using log-rank analysis.

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Results: The results of the log-rank analysis of the prognostic factors of age, histopathology (phylloides tumor and angiosarcoma tumor), stage, chemotherapy (administration of doxorubicin), radiotherapy, systemic disease, herbal treatment, and duration of the patient before taking any medication. With the overall survival rate showed P-values of 0.681, 0.007, 0.037, 0.034, 0.505, 0.891, 0.012, and 0.903, respectively. The results of the log-rank analysis of the prognosis factors with the recurrence-free survival rate showed that the P-values were 0.962, < 0.001, 0.059, 0.097, 0.537, 0.596, 0.021, and 0.274, respectively.

Conclusions: There was a significant difference of patient's overall survival rate in prognostic factors of chemotherapy history, histopathology, use of herbal treatment, and stage of the sarcoma. Histopathology, herbal treatment, and duration of the patient before taking any medication.showed a significant patient's recurrence-free survival rate difference.

Keywords: Breast sarcoma; survival; recurrences.

1. INTRODUCTION

Breast sarcoma is a rare and diverse group of malignancies that arise from the mesenchymal tissue of the breast with various subtypes and can be challenging in diagnosis because it initially mimics benign breast disease or benign skin disease [1-2]. Breast sarcomas account for less than 1% of total breast malignancies and less than 5% of all soft tissue sarcomas [3].

A study by Al-Benna et al. [1] showed 5-year recurrence-free survival ranging from 44 to 66% and 5-year overall survival ranging from 49 to 67% [1]. Another study by Duncan and Lautner (2018) stated that the overall survival at 10 years of breast sarcoma was 62%, and the recurrence-free survival at 5 years and 10 years was 47% and 42% in breast sarcomas without distant metastases [2].

During 2002-2014 there were 4,279 deaths caused by breast sarcoma and the age standard rate (ASR) of 1.3 / 10^5. Deaths by age from sarcomas in men (1.5 / 10^5) were higher than in women (1.2 / 10^5) [4]. Men with breast sarcoma had a higher survival rates live 5 years by 84%. The stage of the disease when first diagnosed plays a major role in maintaining that survival rate. If the cancer is located only in the breast, the 5-year survival rates for men with breast cancer is 97%. About 47% of cases are diagnosed at this localized stage. If the cancer has spread to regional lymph species, the 5-year survival rate is 83%. If the cancer has spread to distant parts of the body, the 5-year survival rate is 22% [5].

Several differences in the survival rates found in breast sarcoma patients were seen based on the prognosis factors of patients. Yin et al. [3] said that there was a difference in survival rates in patients who underwent mastectomy and conservative surgery [3]. Likewise, in the research conducted by Siotos et al. [6] breast reconstruction did not increase the risk of death or disease recurrence among patients with breast cancer. It was also stated that the choice of treatment modality and staging of breast sarcoma affected the survival rate [6]. Meanwhile, in the study of Yin et al. [3] routine radiation has no effect on the survival rate of primary angiosarcomas and seems to be associated with a worse rate in secondary angiosarcomas [7]. Survival rates did not difference significantly between sarcoma patients with and without prior breast cancer [8].

The purposes of this study is to identify different prognostic factors and their impact to overall survival rates and recurrence-free survival rates on breast sarcoma patient at Dr. Moewardi General Hospital (RSDM) Surakarta.

2. METHODS

This research was a retrospective cohort study conducted at the surgical oncology division of RSDM. This research was conducted from September until October 2020 by collecting medical records of all breast sarcoma patients in 2015-2016. We have received ethical approval from Moewardi General Hospital which can be proven by letter no: 1.103 / IX / HREC / 2020 issued by the Health Research Ethics Commission of Moewardi General Hospital. Patients with incomplete medical records and the patients who died from causes other than cancer were excluded. A total of 21 subjects were obtained as research samples.

Overall survival was defined as the duration from the date of diagnosis to death or last follow-up, without limitation on the cause of death. Recurrence free survival rate was defined as time interval from initial surgery to first

recurrence of breast sarcoma or death because of any cause. Prognostic factor was defined as factor affecting the prognosis of disease. In this study, the prognostic factors studied were age, stage, histopathology, history of chemotherapy (drug treatment that uses powerful chemicals to kill fast-growing cells in your body, this study using doxorubicin as single agent of chemotherapy), history of radiotherapy, history of systemic disease, herbal treatment (Herbal medicine is the study of pharmacognosy and the use of medicinal plants, which are a basis of traditional medicine), and duration of the patient before taking any medication.

The subject characteristics were analyzed using univariate analysis. The Kaplan Meier method was used for univariate survival rate analysis. The log-rank test was used to compare differences between groups of variables. Analyses were performed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.

3. RESULTS

3.1 Univariate Analysis

Based on Table 1, it was found that of the 21 subjects, the age with the highest proportion was subjects under 50 years of age at 61.9% (13 patients) while subjects over 50 years old were 38.1% (8 patients). In the histopathological characteristics, the greatest proportion was the type of malignant phyllodes tumor at 85.7% (18 patients) while the type of angiosarcoma was 14.3% (3 patients). The largest staging proportion was stage IV of 47.6% (10 patients), while stage IIIA was 28.6% (6 patients) and stage IIIB was 23.8% (5 patients).

In the history of chemotherapy, 28.6% (6 patients) underwent chemotherapy and 71.4% (15 patients) did not.

Other characteristics were obtained from the subjects. In the characteristics of systemic disease, 5 people (23%) had systemic disease and 16 (78.2%) had no systemic disease. In the herbal medicine category, 10 patients (47.6%) used herbal medicine and 11 (52.4%) did not. In the pre-treatment onset category, 18 patients (85.7%) had an onset less than 5 years and 3 patients (14.3%) had an onset more than 5 years.

Within 5 years of observation, from a total of 21 subjects, 14 patients (66.7%) were still alive while 7 patients (33.3%) were known to have died before the end of the observation period. Six patients (28.6%) experienced recurrence during the 5 years of observation and 15 patients (71.4%) had no recurrences.

Fig. 1 showed that out of 21 breast sarcoma patients, 7 patients died with an average overall survival rate of 4.095 years (95% CI 3.506 - 4.684). There were 6 patients who experienced recurrence during the observation with an average recurrence-free survival rate of 4.048 years (95% CI 3.395 - 4.701).

Table 1. Patient's characteristics (N = 21)

Variable	Category	N	(%)
Age	< 50 Years old	13	61.9
	≥ 50 Years old	8	38.1
Histopathology	Angiosarcoma	3	14.3
	Tumor Phyllodes Malign	18	85.7
Stage	IIIA	6	28.6
	IIIB	5	23.8
	IV	10	47.6
History of Chemotherapy	Chemotherapy	6	28.6
	No chemotherapy	15	71.4
History of Systemic Disease	Yes	5	23.8
	No	16	76.2
Herbal Treatment	Yes	10	47.6
	No	11	52.4
Onset before Treatment	< 5 years	18	85.7
	≥ 5 Years	3	14.3
Recurrence	Yes	6	28.6
	No	15	71.4
Alive		14	66.7
Dead		7	33.3

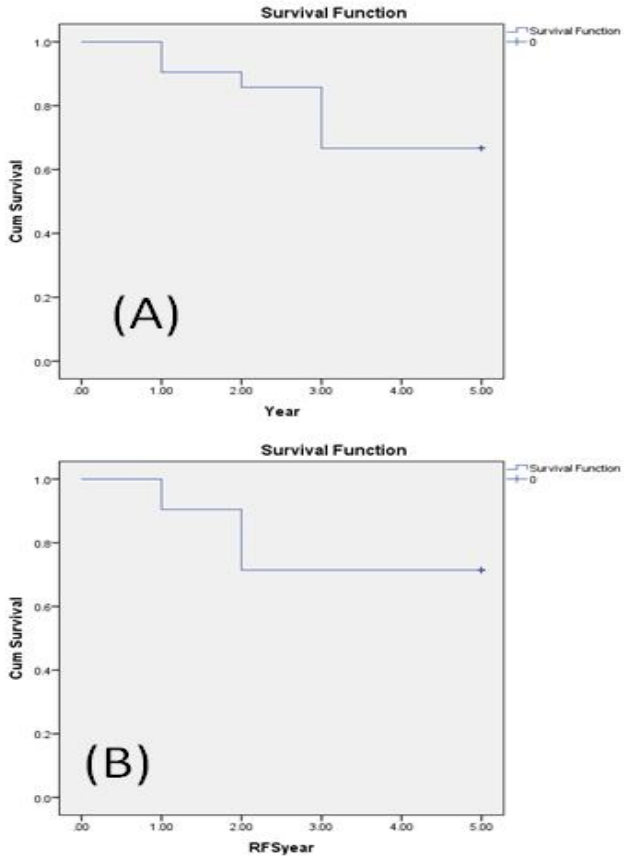

Fig. 1 (A). Overall survival and (B) recurrence-free survival rate of breast sarcoma patients

3.2 Bivariate Analysis

Log-rank analysis was used to determine the correlation of each prognostic factor variable with the overall survival rate (OS) and recurrence-free survival (RFS).

Fig. 2 showed an insignificant relationship between age and overall survival rate where p-value = 0.681 and an average overall survival of 4.3 years (95% CI 3.728 - 4.887) in patients aged < 50 years and 3.7 years (95% CI 2.562 - 4.938) in patients aged ≥ 50 years. The relationship between age and the recurrence-free survival rate (RFS) also showed insignificant (p = 0.962) with an average RFS of 4.5 years (95% CI 3.828 - 5.095) at < 50 years and 4.2 years (95% CI 3.219 - 5.198) at ≥ 50 years of age.

Fig. 3 showed a significant relationship between stage and OS with P-value = 0.037. Meanwhile, the relationship between stage and RFS did not have a significant value (p = 0.059). The average data analysis result was not obtained because all cases were censored in the Kaplan-Meier analysis.

Fig. 4 showed a significant relationship between chemotherapy history and OS with p-value = 0.034. The mean OS was 3.2 years (95% CI 1.996 - 4.337) in chemotherapy patients and 4.4 years (95% CI 3.886 - 5.047) in patients who did not undergo chemotherapy. There was an insignificant relationship between chemotherapy and RFS with p-value = 0.097 and a mean RFS of 3.6 years (95% CI 2.548 - 4.652) in chemotherapy patients and 4.6 years (95% CI 3.929 - 5.271) in patients without chemotherapy.

Fig. 5 showed a significant correlation between histopathology and OS with p-value = 0.007. The mean OS was 2.3 years (95% CI 1.027 - 3.640) in patients with angiosarcoma and 4.3 years (95% CI 3.831 - 4.947) in patients with phyllodes malignant tumors. The correlation between histopathology and RFS was also significant (p = < 0.001) with a mean RFS of 2.3 years (95% CI 1.027 - 3.640) in patients with angiosarcoma and

4.7 years (95% CI 4.226 - 5.185) in patients. with phyllodes malignant tumor.

Fig. 6 showed an insignificant relationship between systemic disease history and OS with p-value = 0.891. The mean OS was 4.2 years (95% CI 3.341 - 5.059) in patients with systemic disease and 4.1 years (95% CI 3.338 - 4.787) in patients without systemic disease. There was also no significant correlation between history of systemic disease and RFS (p = 0.596) with a mean RFS of 4.2 years (95% CI 3.570 - 4.993) in patients without a history of systemic disease and 4.6 years (95% CI 3.899-5.301) in patients with a history of systemic disease.

Fig. 7 showed a significant correlation between herbal treatment history and OS with p-value = 0.012. The mean OS was 3.3 years (95% CI 2.338 - 4.262) in the patients taking the herbal treatment and 4.8 years (95% CI 4.478 - 5.158) in those without herbal treatment. There was a significant correlation between herbal treatment and RFS with p-value = 0.021 and a mean RFS of 3.8 years (95% CI 2.772 - 4.853) in patients with herbal treatment and 4.8 years (95% CI 4.478 - 5.158) in patients without herbal treatment.

Fig. 8 showed an insignificant correlation between duration of the patient before taking any medication and OS with p-value = 0.903. The mean OS was 4.1 years (95% CI 3.394 - 4.717) in patients with an onset of less than 5 years and 4.3 years (95% CI 3.266 - 5.400) in patients with an onset greater than 5 years. There was no significant relationship between onset before treatment and RFS with p-value = 0.274.

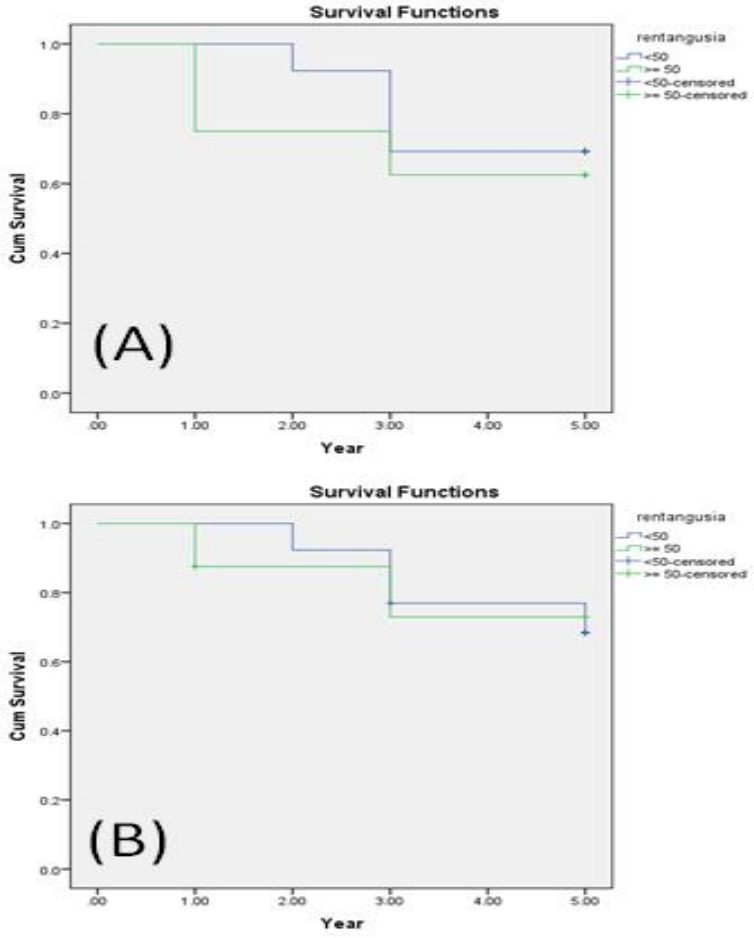

Fig. 2 (A). Log-rank analysis between age and overall survival and (B) recurrence-free survival rate of breast sarcoma patients

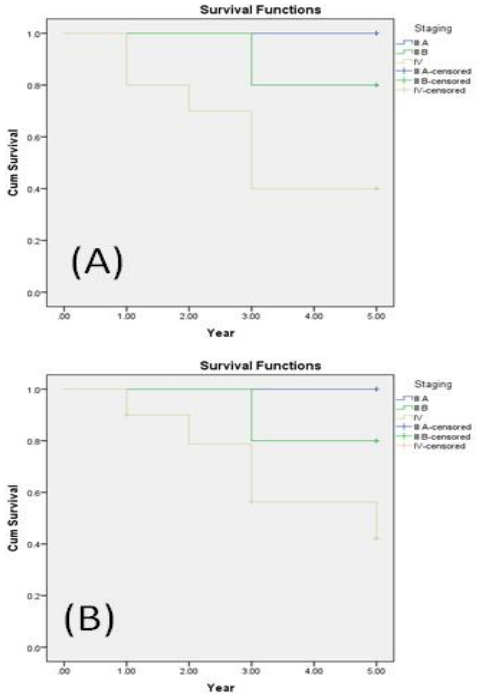

Fig. 3. Log-rank analysis between stage, (A) overall survival rate, and (B) recurrence-free survival rate

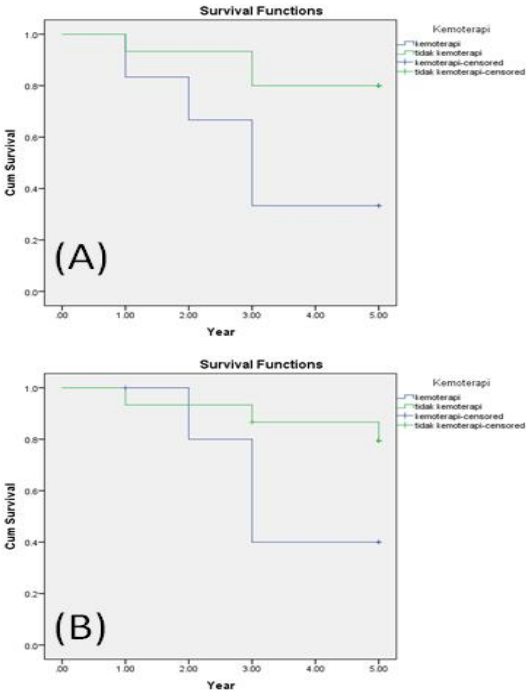

Fig. 4. Log-rank analysis between chemotherapy history and (A) overall survival rate and (B) recurrence-free survival rate

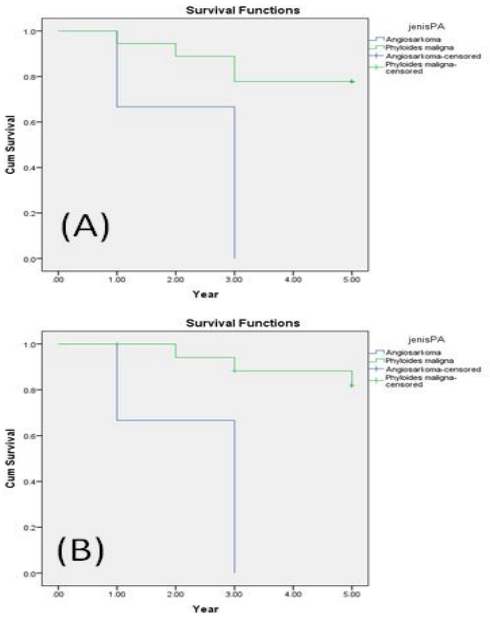

Fig. 5. Log-rank analysis between histopathology and (A) overall survival rate and (B) recurrence-free survival rate

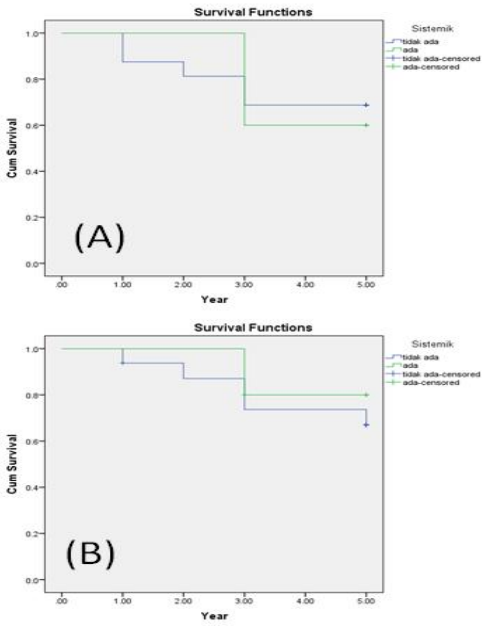

Fig. 6. Log-rank analysis between history of systemic disease and (A) overall survival rate and (B) recurrence-free survival rate

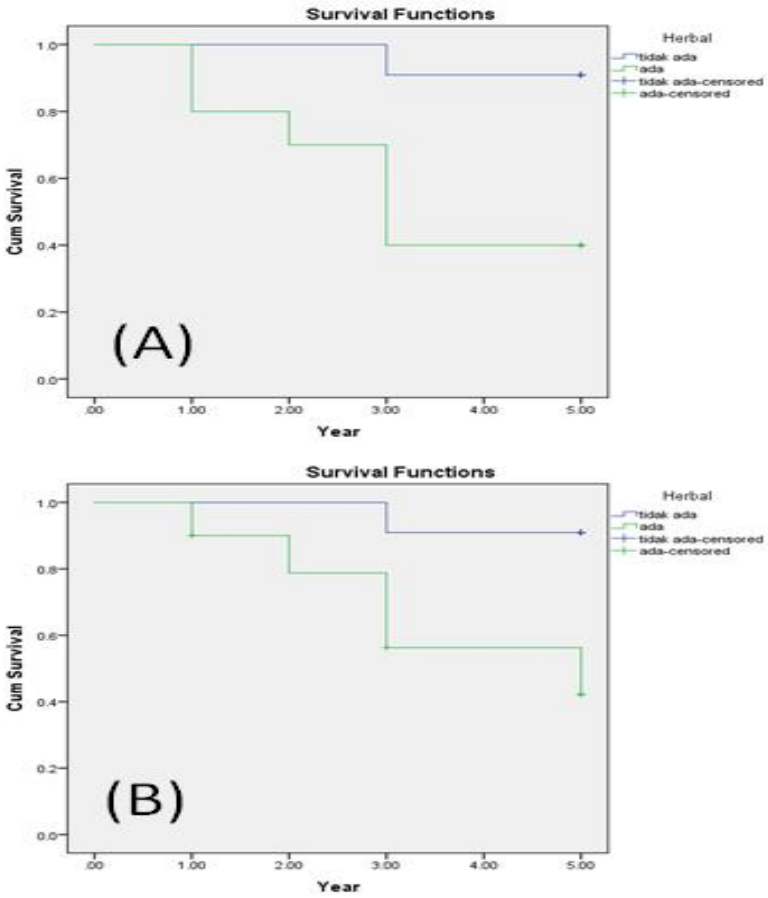

Fig. 7. Log-rank analysis between herbal treatment and (A) overall survival rate and (B) recurrence-free survival rate

4. DISCUSSION

Overall survival was defined as the duration from the date of diagnosis to death or last follow-up, without limitation on the cause of death [9]. In this study, it was found that the overall survival of breast sarcoma averaged 4.095 years (95% CI 3.506 - 4.684). Recurrence-free survival is the length of time after primary care for cancer ends until the patient survives without any signs or symptoms of the cancer. In clinical trials, assessing relapse-free survival is one way of seeing how well treatment is working. In this study, the average recurrence-free survival of breast sarcoma was 4.048 years (95% CI 3.395 - 4.701).

There was no significant relationship between overall survival and age (p = 0.681). Overall survival in patients aged < 50 years was better than in patients aged ≥ 50 years (4.308 vs 3.750 years). The relationship between age and recurrence-free survival rate (RFS) was not significant (p = 0.962) either with a mean RFS of 4.5 years (95% CI 3.828 - 5.095) at < 50 years and 4.2 years (95% CI 3.219 - 5.198) at ≥ 50 years of age. In the research of Yin M. et al. (2017), older people (age at diagnosis) have a higher risk of death than younger ages. Meanwhile, according to Sinaga et al. (2017), age of diagnosis is related to the 5-year survival of breast cancer patients, and the risk of death in breast cancer patients in the < 50-year age group is 3.64 times greater than in the age group ≥ 50 years [10].

There was a significant relationship between stage and OS with p-value = 0.037. Meanwhile, the relationship between stage and RFS did not have a significant value (p = 0.059). Research by Yin et al. (2016) showed that stage (GTNM) is highly correlated with OS results and cancer specific survival (CSS). Patients with G1 and G2 appear to have similar OS and CSF outcomes

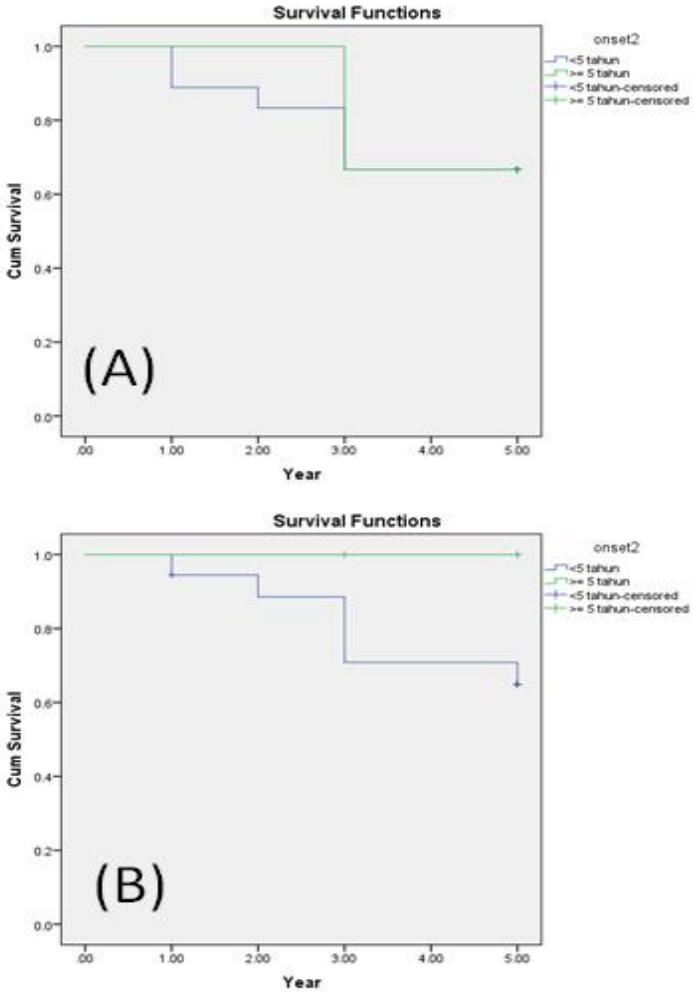

Fig. 8. Log-rank analysis between onset before treatment and (A) overall survival rate and (B) recurrence-free survival rate

while patients with Gx appear to have similar OS and relatively better CSF than patients with G3 [3]. Subjects in this study did not have complete data regarding histological grading (G), so the analysis used the stage of sarcoma. The stage of the sarcoma is divided into several levels, namely IA, IB, II, IIIA, IIIB, and IV, which are assessed from the primary tumor (T), regional lymph nodes (N), distant metastases (M), and histological grade (G) [11].

Chemotherapy had a significant relationship with OS ($p = 0.034$). Meanwhile, chemotherapy and RFS had an insignificant relationship with p-value = 0.097. In patients who received surgical therapy with chemotherapy and surgery alone, there was no difference in the average overall survival between the two groups [12]. This contrasts with the results of the randomized trial which stated that there was an increase in the benefits of OS and RFS in patients receiving neoadjuvant therapy [13]. OS in patients who did not receive chemotherapy was better than those who received chemotherapy (3.2 years vs. 4.4 years). This may be influenced by other factors such as the stage of the patient's sarcoma or the combination of therapy the patient is undergoing. Several study subjects mentioned that they stopped the recommended therapy program, for which the data was not recorded, so they could not be examined in this study.

The results showed that there was a significant relationship between histopathology and overall survival ($p = 0.007$). The relationship between histopathology and RFS was also significant ($p =$

< 0.001). The prognosis of breast angiosarcoma is usually poor, but phyllodes tumor does not cause shorter OS [6]. There was no significant relationship between systemic disease history and OS with p-value = 0.891. There was also no significant relationship between the history of systemic disease and RFS (p = 0.596). Cancer patients differ greatly from the general population in having important individual factors that can influence death from other causes (such as socioeconomic status, health status, and health behaviors such as smoking), biasing relative survival [14].

There was no significant relationship between onset before treatment and OS with p-value = 0.903. There was no significant relationship between onset before treatment and RFS with p-value = 0.274. Research by Rougraff et al. (2012) was unable to show a correlation between duration of symptoms before sarcoma diagnosis and tumor size, disease-free survival, overall survival, or stage at diagnosis. There was no evidence that patient or physician-related delays in treatment affected the oncological outcome of sarcomas [15].

There was a significant relationship between herbal medicine history and OS with p-value = 0.012. There was a significant relationship between herbal treatment and RFS with p-value = 0.021 where patients who used herbal medicine had lower OS and RFS. In contrast to a randomized controlled trial, there was a significant reduction in local breast sarcoma recurrence. However, no significant difference in metastasis or overall survival time could be demonstrated [16]. In the treatment of malignant bone and soft tissue tumors, intra-arterial chemotherapy combined with traditional Chinese medicine can reduce unwanted effects such as gastrointestinal reactions and myelosuppression, reduce damage to the heart, liver, kidneys, and urinary system, strengthen the immune system, and create a synergistic effect [17]. The result of this study might be affected by different types of herbal medicine used by the research subject and the subject's ignorance of the content of the herbal medicine being consumed. Each may influence the results other factor results, so it is necessary to conduct future research to determine the effect of these factors on the survival rate.

Although researchers have tried to contact the study subjects one by one, the information obtained is still limited due to the irregular follow-up of patients for the last 5 years. Future prospective studies are needed and patient follow-up can be better assessed. It may be possible to do future research with a larger sample size or it could be done in some surgical oncology centers in Indonesia. There are several factors that can cause bias in the results of the study; this is due to incomplete medical record data and several factors related to the personal factors of the research subject.

5. CONCLUSIONS

There was a significant difference of patient's overall survival rate in prognostic factors of chemotherapy history, histopathology, use of herbal treatment, and stage of the sarcoma. Histopathology, herbal treatment, and onset before treatment showed a significant patient's recurrence-free survival rate difference. Each factor may influence other factor results; therefore, future studies need to be carried out to see the effect of prognostic factors on survival rates using prospective research methods with a longer duration both at the surgical oncology center and at other centers.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

Author have received ethical approval from Moewardi General Hospital which can be proven by letter no: 1.103 / IX / HREC / 2020 issued by the Health Research Ethics Commission of Moewardi General Hospital.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Al-Benna S, Poggemann K, Steinau H-U, Steinstraesser L. Diagnosis and

management of primary breast sarcoma. Breast Cancer Res Treat. 2010;122 (3):619–26.
2. Duncan MA, Lautner MA. Sarcomas of the Breast. Surg Clin North Am. 2018;98 (4):869–76.
3. Yin M, Mackley HB, Drabick JJ, Harvey HA. Primary female breast sarcoma: Clinicopathological features, treatment and prognosis. Sci Rep. 2016;6: 31497.
4. Pingping B, Yuhong Z, Weiqi L, Chunxiao W, Chunfang W, Yuanjue S, et al. Incidence and Mortality of Sarcomas in Shanghai, China, During 2002–2014. Front Oncol. 2019;9.
5. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA Cancer J Clin [Internet]. 2021;71(1):7–33. Available:https://doi.org/10.3322/caac.21654
6. Siotos C, Naska A, Bello RJ, Uzosike A, Orfanos P, Euhus DM, et al. Survival and Disease Recurrence Rates among Breast Cancer Patients following Mastectomy with or without Breast Reconstruction. Plast Reconstr Surg. 2019;144(2):169e-177e.
7. Yin M, Wang W, Drabick JJ, Harold HA. Prognosis and treatment of non-metastatic primary and secondary breast angio-sarcoma: A comparative study. BMC Cancer. 2017;17(1):295.
8. Karlsson F, Granath F, Smedby KE, Zedenius J, Bränström R, Nilsson IL. Sarcoma of the breast: breast cancer history as etiologic and prognostic factor-A population-based case-control study. Breast Cancer Res Treat. 2020;183 (3):669–75.
9. He C, Zhang Y, Cai Z, Lin X, Li S. Overall survival and cancer-specific survival in patients with surgically resected pancreatic head adenocarcinoma: A competing risk nomogram analysis. J Cancer. 2018;9(17):3156–67.
10. Sinaga ES, Ahmad RA, Hutajulu SH. Analisis ketahanan hidup 5 tahun pada pasien kanker payudara di RS Sardjito provinsi Yogyakarta, Indonesia. Ber Kedokt Masy. 2017;33(2):67.
11. Dickie C, Sullivan BO. Target Volume Delineation and Field Setup. Target Vol Delin F Setup. 2013;D:277–86.
12. Sheth GR, Cranmer LD, Smith BD, Grasso-Lebeau L, Lang JE. Radiation-induced sarcoma of the breast: A systematic review. Oncologist. 2012;17 (3):405–18.
13. Gronchi A, Ferrari S, Quagliuolo V, Broto JM, Lopez-Pousa A, Grignani G, et al. sarcoma Full-dose neoadjuvant anthracycline ifosfamide chemotherapy is associated with a relapse free survival (RFS) and overall survival (OS) benefit in localized high-risk adult soft tissue sarcomas (STS) of the extremities and trunk wall: Interim ana. Ann Oncol [Internet]. 2016;27(Supplement 6):vi587. Available:http://dx.doi.org/10.1093/annonc/mdw435.52
14. Mariotto AB, Noone AM, Howlader N, Cho H, Keel GE, Garshell J, et al. Cancer survival: An overview of measures, uses, and interpretation. J Natl Cancer Inst Monogr. 2014;(49):145–86.
15. Rougraff BT, Lawrence J, Davis K. Length of symptoms before referral: prognostic variable for high-grade soft tissue sarcoma? Clin Orthop Relat Res. 2012; 470(3):706–11.
16. Gerber B, Scholz C, Reimer T, Briese V, Janni W. Complementary and alternative therapeutic approaches in patients with early breast cancer: a systematic review. Breast Cancer Res Treat. 2006;95(3):199–209.
17. Feng Li D. Combination of western medicine and traditional chinese medicine for treatment of malignant bone and soft tissue tumors. Orthop Rheumatol Open Access J. 2018;10(4).

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