

ORIGINAL ARTICLE

The Association of Sociodemographic and Clinicopathological with Survival of Breast Cancer Patients

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ABSTRACT

BACKGROUND

The research of breast cancer prognostic factors has been conducted for a long time, but the results are still controversial. The research on demography and clinicopathology factors that determine the survival of breast cancer (BC) patients, remains to be done.

METHODS

The observational analytic with a cross-sectional design would be conducted to describe the demographic, clinicopathology, therapy, and two years survival of breast cancer patients. The independent variables and the dependent variable were analyzed by univariate and bivariate statistics with a 95% confidence interval.

RESULT

Most age of breast cancer patients at diagnosis were ≥ 50 years (74.5%). The majority of sociodemographic profiles of BC patients were undergraduate education, have private jobs, and married. The main histological type was invasive ductal carcinoma. More than 50% of the patients were high stage (60.8%) and hormonal receptors molecular subtype (60.7%). Neoadjuvant chemotherapy was given to 40 patients (78.5%), only 9 patients (17.7%) were eligible for anti-HER-2/neu therapy. There were 42 patients (82.4%) have two years of survival. There wasn't any association between age ($p=0.586$), Body Mass Index ($p=0.617$), stage of disease ($p=0.587$), molecular subtype ($p=0.084$), tumor size (0.158), lymph node status ($p=0.446$), metastatic status ($p=0.327$), grade ($p=0.467$), therapy ($p=0.436$) with two years survival of breast cancer patients.

CONCLUSIONS

The common risk factor of breast cancer is increasing age. Most breast cancer patients present high stage and hormone receptors positive for BC. Although there wasn't a significant association, the prevalence of low stage BC patients had a higher two years survival. Population education and screening are important for early breast cancer detection to improve the final results of breast cancer patients.

Keywords: breast cancer, demography, clinicopathology, survival

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ABSTRAK

Hubungan faktor sosiodemografi dan klinikopatologi dengan ketahanan hidup penderita kanker payudara

LATAR BELAKANG

Penelitian tentang faktor-faktor prognostik kanker payudara telah dikerjakan sejak lama, tetapi masih menunjukkan kontroversi. Penelitian tentang faktor-faktor demografi dan klinikopatologi yang menentukan ketahanan hidup penderita kanker payudara tetaplah penting dikerjakan.

METODE

Penelitian observasional analitik menggunakan desain potong lintang pada 51 Rekam Medik pasien kanker payudara, mendeskripsikan data demografi, klinikopatologi, terapi dan ketahanan hidup dua tahun pasien kanker payudara. Data variabel akan dianalisis statistik univariat dan bivariat. Variabel independen dan variabel dependen dianalisis univariat dan bivariat dengan 95% confidence interval.

HASIL

Sebagian besar pasien kanker payudara berusia ≥ 50 years (74.5%). Profil sosiodemografi terbanyak adalah berpendidikan sarjana, bekerja swasta dan telah menikah. Tipe histologi terbanyak adalah karsinoma duktal invasif. Pasien umumnya berstadium tinggi (60.8%) dan subtype molekuler hormonal reseptor positif (60.7%). Kemoterapi neoadjuvant diberikan pada 40 pasien (78.5%), hanya 9 pasien (17.7%) mendapat terapi anti HER-2/neu. Sebanyak 42 pasien (82.4%) memiliki ketahanan hidup > 2 tahun. Tidak ada hubungan antara usia ($p=0.586$), Indeks Massa Tubuh ($p=0.617$), stadium ($p=0.587$), subtype molekuler ($p=0.084$), ukuran tumor (0.158), status limfonodi ($p=0.446$), status metastasis ($p=0.327$), grade ($p=0.467$), terapi ($p=0.436$) dengan ketahanan hidup dua tahun pasien kanker payudara.

KESIMPULAN

Salah satu faktor risiko terjadi kanker payudara adalah bertambahnya usia. Sebagian penderita kanker payudara menunjukkan stadium tinggi dan reseptor hormon positif. Meskipun tidak ada hubungan bermakna, prevalensi kanker payudara stadium rendah lebih banyak menunjukkan ketahanan hidup 2 tahun. Edukasi populasi dan skinning kanker payudara untuk mendeteksi awal adalah mendesak bagi populasi kita untuk memperbaiki hasil akhir penderita kanker payudara.

Kata kunci: kanker payudara, demografi, klinikopatologi, ketahanan hidup

INTRODUCTION

The known breast cancer risk factor studies have been conducted for decades, but still many unanswerable questions about the causal and basic biology of breast cancer. The studies about breast cancer environments as the breast cancer risk factors result in a consensus stamen of personalized early detection and prevention of breast cancer.⁽¹⁾ Risk factors associated with the incidence of breast cancer in women > 50 years are family history and genetic (gene mutation carrier BRCA1, BRCA2, ATM or p53), history of Ductal Carcinoma in Situ (DCIS), Lobular Carcinoma in Situ (LCIS), high-density breast in mammography examination, early menarche (<12 years) or late menopause (>55 years), reproductive history (have no child and no breastfeeding), obesity, alcohol consumption, chest radiation.⁽²⁾ The prognosis factors of breast cancer were determined by radiology imaging (size of tumor, multifocality or multicentricity, extensive intraductal components, skin and chest wall involvement, inflammatory breast cancer), pathology examination (histopathologic grade, histopathologic type, lymph node involvement,

lymphovascular invasion), biomarkers (estrogen and progesterone receptors, human epidermal growth factor receptor 2, Ki 67), tumor biology (molecular subtype: luminal A, luminal B, HER2-enriched and triple-negative), gene expression profile (Oncotype DX, MammaPrint, Endopredict and Prosigna PAM50 that help the prediction of adjuvant therapy responses).⁽³⁾

Until now, the association of survival of breast cancer patients with predictive and prognostic factors still needs to be investigated in studies with different methods. Although the breast cancer early detection methods have advanced and the finding of breast cancer therapeutic modalities have been implemented and prolonged the survival of breast cancer patients, there are disparities between regions and racial on the patients' survival.⁽⁴⁾ Because of the disparities, the studies should be continue to conduct to know the better management of breast cancer diseases from communities to clinical practice in our population. This study aims to analyzed the association between demography and clinicopathology factors that are associated with the two-year survival of

breast cancer patients.

METHODS

This study was an analytical observational study with a retrospective cohort design. The data sources were the secondary data from Medical Records (MR) of breast cancer patients, who received treatment from January 2017 to December 2019 at Bethesda Hospital Yogyakarta. This study got ethical clearance from Bethesda Hospital Yogyakarta number 135/KEPK-RSB/XII/20.

The research samples from consecutive sampling methods met the inclusion and exclusion criteria. The inclusion criteria were all female breast cancer patients recorded in Bethesda Hospital Yogyakarta MR from January 2017 to December 2019, diagnostic approved by cytopathologic or histopathologic results, molecular subtype approved by immunohistochemistry results. The exclusion criteria are patients who transferred to another hospital to get advanced therapy. The demographic data were age (< 50 years and \geq 50 years), education, job, marriage status. The Clinicopathologic data were Body Mass Index (nonobese < 25 and obese \geq 25), histopathologic type (ductal type and non-ductal type), stage of diseases (Early Breast Cancer (EBC) (I and II), Local Advance Breast Cancer (LABC) (III) and Metastatic Breast Cancer (MBC) (IV)), histopathologic grade (I, II, III), breast side (Right, right-left and left), a molecular subtype of tumor (Hormonal receptor positive (luminal A and luminal B), hormonal receptor negative (HER2-neu enriched and triple negative breast cancer (TNBC))). The therapy data was neoadjuvant therapy (NAD) and adjuvant therapy (NAD + hormonal, NAD + trastuzumab, NAD + chemotherapy, hormonal only, trastuzumab only, NAD + radiotherapy). The > 2 years survival data was yes or no. The variables were analyzed by the univariate statistics. The association of predictor variable (age, BMI, stage, tumor size, lymph node status, metastatic status, histopathologic differentiation, molecular subtype, and therapy) and two years survival was analyzed by chi-square or Fisher exact test if independent variables had two categories and one-way Anova or Kruskal-Wallis test if independent variables had more than two categories. The mean of observed months

recorded in MR with standard error (SE), confident interval 95% and significancy describe the association between two variables. The analyzing of missing data with expectation maximization. If the missing data is randomly distributed, the data would transform to replace missing value.

RESULT

Observation of Medical Records from January 2017 to December 2019 as many as 51 Medical Records were included in the study. We have recorded demographic data, clinicopathologic data, and treatment history. There were missing data because of the data not record well in MR. The analyzing of missing data with expectation maximization was Missing Completely at Random ($p=0.582$). The data frequency of variables is presented in table 1

The mean age of the patients was 54.27 ± 1.479 years, the median age was 53 years ± 10.564 . The youngest age was 32 years and the oldest age was 80 years. The percentage of age ≥ 50 years is 74.5%. The majority of sociodemographic profiles of BC patients are undergraduate education, have private jobs, and married. There was the same percentage proportion of Body Mass Index data between non-obese and obese patients. The most common type of breast cancer was invasive ductal carcinoma (76.5%), other types found by the researcher were lobular carcinoma, mucoid carcinoma, ductal carcinoma with part of comedo carcinoma, ductal carcinoma with mucoid carcinoma (21.67%), and malignant phyllodes tumor. The most disease stage was LABC (49%), followed by EBC (39.2%), and MBC (11.8%). Tumors were generally larger than 5cm T3 (29.4%) and T4 (29.4%). Lymph node status was generally positive (58.4%). Metastatic status was generally negative (84.3%). The most histopathological differentiation was poor (51%) followed by moderate (33.3%) and good (2%). The side of the breast affected by cancer is relatively more on the right side (49%). Neoadjuvant chemotherapy was given to 40 patients (78.5%), only 9 patients (17.7%) were eligible for anti HER-2/neu therapy. Most of the therapies given to breast cancer patients were neo-adjuvant and hormonal therapy (39.2%). There were 42 patients (82.4%) have two years of survival. The mean survival was 21.41 (SE ± 2.147 , CI 95% 12.10-25.72). Stage IV of BC

Table 1. Demographic, clinicopathologic and two-years survival of breast cancer patients in Bethesda Hospital

Demography Characteristic	Number of data recorded/not recorded in MR	Percentage
	Frequencies of variables	
Age	51/0 (100%)	
< 50 year	13	(25,5%)
≥ 50 year	38	(74,5%)
Education	51/19(62,7%)	
<Senior High School	5	(9,8%)
Senior High School	10	(19,6%)
Undergraduate	17	(33,3%)
Job	51/22(56,9%)	
Public Servant	8	(15,7%)
Private Jobs	13	(25,5%)
Housewife	8	(15,7%)
Marriage Status	51/4(92,2%)	
Married	46	(90,2%)
Not Married	1	(2%)
Clinicopathology Characteristics		
BMI	51/4(92,2%)	
< 25	24	(47,1%)
≥ 25	23	(45,1%)
Diagnosis year	51/1(98%)	
2015	1	(2%)
2016	5	(9,8%)
2017	6	(11,8%)
2018	21	(41,2)
2019	17	(33,3%)
Histopathologic Type	51/1(98%)	
Ductal Carcinoma	39	(76,5%)
Other	11	(21,6%)
Breast side	51/5 (90,2%)	
Right	25	49%
Right &Left	1	2%
Left	20	39,2%
Stage AJCC 7 th ed	51/0 (100%)	
Stage I/EBC	3	(5,9%)
Stage II/EBC	17	(33,3%)
Stage III/LABC	25	(49%)
Stage IV/MBC	6	(11,8%)
Tumor size	51/4(92,2%)	
T1/small	3	(5,9%)
T2/small	14	(27,5%)
T3/large	15	(29,4%)

T4/large	15	(29,4%)
Lymph node	51/3(94,1%)	
Negative	18	(35,3%)
Positive	30	(58,8%)
Metastasis	51/2(96,1%)	
Negative	43	(84,3%)
Positive	6	(11,8%)
Histopathologic Differentiation	51/7(86,3%)	
Good/low	1	(2%)
Intermediate/low	17	33,3%
Poor/High	26	51%
Molecular Subtype	51(100%)	
Luminal A	22	43,1%
Luminal B	9	17,6%
HER-2/neu	17	33,3%
TNBC	3	5,9%
Therapy	51/6(88,2%)	
NAD + Hormone	20	(39,2%)
NAD + Trastuzumab	8	(15,7%)
NAD + chemo.	1	(2%)
Hormonal only	4	(7,8%)
Trastuzumab only	1	(2%)
NAD + Radio.	11	(21,6%)
2 years survival	51(100%)	
Yes	42	(82,4%)
No	9	(17,6%)

patients showed metastases to the lungs, bones, liver.

Bivariable analysis between clinicopathologic and therapeutic profile with two years survival of breast cancer patients describes in table 2.

The association between age, BMI, stage of disease, molecular subtype of breast cancer, tumor size, lymph node status, metastatic status, histopathologic grade, and therapy with two years survival was not observed.

DISCUSSION

We tried to describe the demographic, clinicopathological, and therapeutic factors of breast cancer patients through this study. The bivariate analysis the association between clinicopathologic and therapy with two years survival of breast cancer patients was not observed. The socio-demography of breast cancer-

patients research is very important for increasing understanding of the factors that influence breast cancer disease prevention and promotion, quality of life, and survival of breast cancer patients. Women from low socioeconomic status and high social-economic environments less participate in breast cancer screening than women from high social-economic status.⁽⁵⁾ Demographic research, socio-economic status, exercise physical activity, other lifestyle factors, clinicopathology, and therapy are very useful to develop strategies and intervention to improve patients' quality of life.⁽⁶⁾ Socio-demographic factors affect the patients' stage level on the first time seek a doctor. Patients at late-stage are more from rural areas and have illiterate education, policies needed to provide opportunities for patients to be diagnosed at an early stage of breast cancer.⁽⁷⁾ The level of education of breast cancer patients associated with the stage on the first time of diagnosis. The lower

Table 2. Difference of two years survival of breast cancer patients according to clinicopathologic and therapeutic profiles

	Variables Means	Two-years Survival		
		CI 95%	p-Value	
Age	< 50 years	18.08±2.630	12.35-23.81	0.586 ^a
	≥ 50 years	22.55±0.616	17.02-28.08	
BMI	< 25	22.00±2.668	16.48-27.52	0.617 ^b
	≥ 25	18.00±6.00	13.50-29.29	
Stage	I & II /EBC	19.30±1.990	15.14-23.46	0.587 ^b
	III/LABC	24.60±3.956	16.44-32.76	
	IV/MBC	15.17±3.060	7.30-23.03	
Molecular Subtype	Luminal A	20.64±3.752	12.83-28.44	0.084 ^b
	Luminal B	17.22±5.314	4.97-29.48	
	HER-2/neu	24.24±2.785	18.33-20.14	
	TNBC	23.67±11.407	-25.41-72.75	
Tumor size	T1/small	25.00±2.309	15.06-34.94	0.158 ^b
	T2/small	19.07±2.638	13.37-24.77	
	T3/large	21.47±5.454	9.77-33.16	
	T4/large	25.27±4.007	16.67-33.86	
Lymph node	Negative	18.06±1.598	14.69-21.43	0.446 ^b
	Positive	24.13±3.438	17.10-31.17	
Metastasis	Negative	22.67±2.460	17.71-27.64	0.327 ^b
	Positive	15.17±3.060	7.30-23.03	
Histopathologic Grade	I & II /low	25.35±5.187	14.36-36.35	0.467 ^b
	I /High	21.58±2.248	16.95-26.21	
Therapy	NAD + Hormone	21.95±4.089	13.39-30.51	0.436 ^b
	NAD + Trastuzumab	17.88±2.125	12.85-22.90	
	NAD + chemo.	-		
	Hormonal only	14.00±4.243	0.50-27.50	
	Trastuzumab only	-		
	NAD + Radio.	25.45±4.815	14.73-36.18	

^aFisher exact Test^bKruskal-Wallis Test

of patients' education the higher of disease stage on the first time of diagnosis.⁽⁸⁾

Sociodemographic factors including age, educational history, and work history are factors that have been widely studied to affect breast cancer patient survival. Research at the Central General Hospital Dr. Sardjito used data from medical records of breast cancer patients in 2009 regarding age and education history, age <50 years and education history not reaching high school, high cancer stage, large tumor size, and tumor location in the center showed less five-year survival rate.⁽⁹⁾ Sociodemographic factors associated with breast cancer specific survival and

overall survival. The associated factors are age at diagnosis, race/ethnicity, histology, grade, tumor size, number of positive lymph nodes, metastasis, ER/ PR status, surgery, chemotherapy, radiation, marital status, insurance, median household income. The un-associated factors are residence rural or urban, poverty rate, unemployment rate, education level.⁽¹⁰⁾

Research on cancer registration in 9 European countries on 7581 cases of stage I/IIA breast cancer showed that patients were 35% young (15-54 years old), 50% middle age (55-74 years) and 15% old age (> 75 years). In the older age, the Charlson comorbidity index (CCI) ≥2

(severe comorbidity) is increasing. The increase of CCI is related to comorbidities, time of diagnosis until the start of treatment, and the type of therapy given.⁽¹¹⁾ The increasing age is a common risk factor for breast cancer patients, so it is important and urgent to screening programs for cancer detection as early as possible for familial risk assessment tools using the Ontario Family History Assessment Tool, Manchester Scoring System, Referral Screening Tool, Pedigree Assessment Tool, 7-Question Family History Screening Tool, International Breast Cancer Intervention Study instrument (Tyrer-Cuzick), and brief versions of BRCAPRO.⁽¹²⁾ The diagnosis of the earliest breast cancer disease through symptoms by breast self-examination, clinical breast examination, and mammograms are also very important.⁽¹³⁾

Younger women under 40 years had unfavorable prognostic parameters of disease than women over 60 years of age.⁽¹⁴⁾ Research on the Surveillance, Epidemiology, and End Results (SEER) data from 1988-2003 showed that young patients < 40 years old compared to older patients > 40 years showed a higher degree of tumor differentiation, many of which were in advanced stages (stages II and III), larger tumor size, more positive lymph node status, more negative ER/PR expression and higher mortality at low disease stage (stage I).⁽¹⁵⁾ The study conducted in Dr. Sardjito Hospital, younger age patients below 40 years are 11.4%, had high frequency of breast cancer with biologically more aggressive tumors, late diagnosis, frequent relapse, and poor prognosis. The finding, quarantine to improve clinical management and meet psychosocial needs in young breast cancer patients.⁽¹⁶⁾ Women under 40 years with axillary lymph node invasion negative and over 80 years had high breast cancer specific mortality. The older women not suitable for surgery and axillary dissection, have not receive treatment according to the guidelines, especially radiotherapy.⁽¹⁷⁾ The therapy given to the elderly early breast cancer patients (≥ 80 years) is less aggressive than in younger patients although have similar clinicopathology characteristic tumor grade, histology, hormone receptivity) to the younger patients. Radical mastectomy is the more common type of surgery for stage I at older ages without radiation therapy and chemotherapy is associated with poor survival. Breast conservation

surgery (BCT), chemotherapy, and radiotherapy are a more common therapy for early-stage younger ages breast cancer patients (67-79 years).⁽¹⁸⁾

The study conducted in RSUP Haji Adam Malik Medan, BMI overweight-obese were more likely to have invasive carcinoma NST subtype and higher grade of breast cancer.⁽¹⁹⁾ Obesity affects the histopathologic profile and survival of BC patients. Obese women more late stage and high grade BC, and obese women with hormone receptors positive more likely to die from cancer compared to normal weight women.⁽²⁰⁾ The 5-year disease-free survival and overall survival was reduced in overweight and obese patients, and independent predictors for increased risk of breast cancer relapse and death.⁽²¹⁾

The study at Hasan Sadikin General Hospital, concluded that molecular subtype of breast cancer important to address the targeted therapy, personalized therapy, and survival of the patients. Luminal A is the most molecular subtype, and followed by HER-2/neu, TNBC and Luminal B. Luminal A and luminal B had average survival longer than HER-2neu and TNBC.⁽²²⁾ Another study had the same results of the association between molecular subtype and five year survival. Patients with luminal A, luminal B, HER-2/neu and TNBC subtypes of breast cancer, the 5-year OS rate were 92.6%, 88.4%, 83.6%, 82.9%.⁽²³⁾ But patient in advanced stage with hormone receptor (HR) positive/ HER-2/neu positive subtype had better survival than HR⁺/HER-2/neu.⁽²⁴⁾

The limitations of this study were the small sample size and incomplete demographic, clinicopathological, and therapeutic data. Characteristic of breast cancer patient study from this research could be used by clinicians and pathologists to analyze the management of breast cancer patients in Bethesda Hospital, and the better laboratory and medical services. Research with larger numbers of samples needs to be done to clarify the role of demography, clinicopathology, and therapy characteristics of the young and older breast cancer patients to survival.

CONCLUSIONS

The common risk factor of breast cancer is increasing age. Most breast cancer patients present high stage and hormone receptors positive of BC.

Although there wasn't a significant association, the prevalence of low stage BC patients and hormone receptor-negative tended to higher two years survival. Population education and BC screening for early detection are urgent for our population to improve the outcome of BC patients.

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CONFLICT OF INTEREST

No relevant disclosures.

CONTRIBUTORS

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The authors confirm contribution to the paper as follows: study conception and design: Tejo Jayadi. Author, Hariatmoko. Author, Wiwiek Probowati. Author.; data collection: Brenda Mirani Rustam. Author, Puji Kristi. Tejo Jayadi. Author; analysis and interpretation of results: Tejo Jayadi. Author; draft manuscript preparation: Tejo Jayadi. All authors reviewed the results and approved the final version of the manuscript.

REFERENCE

1. Pashayan N, Antoniou AC, Ivanus U, Esserman LJ, Easton DF, French D, et al. Personalized early detection and prevention of breast cancer: ENVISION consensus statement. *Nat Rev Clin Oncol* [Internet]. 2020 Nov 1 [cited 2022 Mar 26];17(11):687. Available from: /pmc/articles/PMC7567644/
2. Indonesia KKR, Nasional KPK. KANKER PAYUDARA [Internet]. Jakarta: Kementerian Kesehatan Republik Indonesia; [cited 2022 Mar 24]. Available from: <http://kanker.kemkes.go.id/guidelines/PPKPayudara.pdf>
3. Tirada N, Aujeiro M, Khorjekar G, Richards S, Chopra J, Dromi S, et al. Breast Cancer Tissue Markers, Genomic Profiling, and Other Prognostic Factors: A Primer for Radiologists. *RadioGraphics* [Internet]. 2018;38:1902–20. Available from: <https://doi.org/10.1148/rg.2018180047>
4. Ellis L, Canchola AJ, Spiegel D, Ladabaum U, Haile R, Gomez SL. Racial and Ethnic Disparities in Cancer Survival: The Contribution of Tumor, Sociodemographic, Institutional, and Neighborhood Characteristics. *J Clin Oncol* [Internet]. 2018 Jan 1 [cited 2022 Mar 26];36(1):25. Available from: /pmc/articles/

5. PMC5756323/ Lee M, Adlouni S El, Miller AB, De Bock GH, Ding L, Jidkova S, et al. The Role of Socio-Demographic Factors in the Coverage of Breast Cancer Screening: Insights From a Quantile Regression Analysis. *Front Public Heal* | www.frontiersin.org [Internet]. 2021 Apr [cited 2022 Mar 24];1:648278. Available from: www.frontiersin.org
6. Lu W, Cui Y, Chen X, Zheng Y, Gu K, Cai H, et al. Changes in quality of life among breast cancer patients three years post-diagnosis. *Breast Cancer Res Treat* 2008 1142 [Internet]. 2008 Apr 14 [cited 2022 Mar 24];114(2):357–69. Available from: <https://link.springer.com/article/10.1007/s10549-008-0008-3>
7. Sathwara J, Balasubramaniam G, Bobdey S, Jain A, Saoba S. Sociodemographic factors and late-stage diagnosis of breast cancer in India: A hospital-based study. *Indian J Med Paediatr Oncol*. 2017 Jul 1;38(3):277–81.
8. Mathew A, George PS, Ramadas K, Mathew BS, Kumar A, Roshni S, et al. Sociodemographic Factors and Stage of Cancer at Diagnosis: A Population-Based Study in South India. *J Glob Oncol* [Internet]. 2019 [cited 2022 Mar 25];5(5):1–10. Available from: /pmc/articles/PMC6690651/
9. Sinaga ES, Ahmad RA, Shivalli S, Hutajulu SH. Age at diagnosis predicted survival outcome of female patients with breast cancer at a tertiary hospital in Yogyakarta, Indonesia. *Pan Afr Med J* [Internet]. 2018 Nov 7 [cited 2022 Mar 25];31:163–163. Available from: <https://europepmc.org/articles/PMC6492206>
10. Ji P, Gong Y, Jiang CC, Hu X, Di GH, Shao ZM. Association between socioeconomic factors at diagnosis and survival in breast cancer: A population-based study. *Cancer Med* [Internet]. 2020 Mar 1 [cited 2022 Mar 27];9(5):1922. Available from: /pmc/articles/PMC7050085/
11. Minicozzi P, Van Eycken L, Molinie F, Innos K, Guevara M, Marcos-Gragera R, et al. Comorbidities, age and period of diagnosis influence treatment and outcomes in early breast cancer. *Int J cancer* [Internet]. 2019 May 1 [cited 2022 Mar 28];144(9):2118–27. Available from: <https://pubmed.ncbi.nlm.nih.gov/30411340/>
12. Am Fam Physician. Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA-Related Cancer: Recommendation Statement - U.S. Preventive Services Task Force - American Family Physician [Internet]. 2020 [cited 2022 Mar 28]. p. 233–8. Available from: <https://www.aafp.org/afp/2020/0215/p233.html>
13. American Cancer Society. Breast Cancer Early Detection and Diagnosis. [cancer.org | 18002272345](https://www.cancer.org/18002272345).
14. Erić I, Erić AP, Kristek J, Koprivčić I, Babić M. BREAST CANCER IN YOUNG WOMEN: PATHOLOGIC AND IMMUNOHISTOCHEMICAL FEATURES. *Acta Clin Croat* [Internet]. 2018 [cited 2022 Mar 28];57(3):497. Available from: /pmc/articles/PMC6536281/
15. Gnerlich JL, Deshpande AD, Jeffe DB, Sweet A, White N, Margenthaler JA. Elevated breast cancer mortality in women younger than age 40 years compared with older women is attributed to poorer survival in early-stage disease. *J*

- Am Coll Surg [Internet]. 2009 Jan 21 [cited 2022 Mar 28];208(3):341–7. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC19317994/?tool=EBI>
16. Anwar SL, Raharjo CA, Herviastuti R, Dwianingsih EK, Setyoheriyanto D, Avanti WS, et al. Pathological profiles and clinical management challenges of breast cancer emerging in young women in Indonesia: A hospital-based study. *BMC Womens Health* [Internet]. 2019 Feb 6 [cited 2022 Mar 28];19(1):1–8. Available from: <https://bmcwomenshealth.biomedcentral.com/articles/10.1186/s12905-019-0724-3>
 17. Brandt J, Garne PP, Tengrup I, Manjer J. Age at diagnosis in relation to survival following breast cancer: A cohort study. *World J Surg Oncol* [Internet]. 2015 Feb 7 [cited 2022 Mar 28];13(1):1–11. Available from: <https://wjso.biomedcentral.com/articles/10.1186/s12957-014-0429-x>
 18. Schonberg MA, Marcantonio ER, Li D, Silliman RA, Ngo L, McCarthy EP. Breast cancer among the oldest old: tumor characteristics, treatment choices, and survival. *J Clin Oncol* [Internet]. 2010 Apr 20 [cited 2022 Mar 29];28(12):2038–45. Available from: <https://pubmed.ncbi.nlm.nih.gov/20308658/>
 19. Mardiah H, Ginting RNA, Rahmadhany H, Sitorus ERD. Correlation between Age and Body Mass Index (BMI) with Histopathological Features of Breast Cancer Patients in RSUP Haji Adam Malik Medan. *Indones J Cancer* [Internet]. 2021 Aug 27 [cited 2022 Mar 30];15(2):46–53. Available from: <https://www.indonesianjournalofcancer.or.id/e-journal/index.php/ijoc/article/view/708>
 20. Blair CK, Wiggins CL, Nibbe AM, Storlie CB, Prossnitz ER, Royce M, et al. Obesity and survival among a cohort of breast cancer patients is partially mediated by tumor characteristics. *npj Breast Cancer* 2019 51 [Internet]. 2019 Oct 2 [cited 2022 Mar 30];5(1):1–7. Available from: <https://www.nature.com/articles/s41523-019-0128-4>
 21. Sun L, Zhu Y, Qian Q, Tang L. Body mass index and prognosis of breast cancer: An analysis by menstruation status when breast cancer diagnosis. *Medicine (Baltimore)* [Internet]. 2018 Jun 1 [cited 2022 Mar 30];97(26). Available from: <https://pubmed.ncbi.nlm.nih.gov/3039647/>
 22. Arnetha TS, Hernowo BS, Adha MJ, Rezano A. Relationship between Molecular Subtypes and Overall Survival of Breast Cancer in Bandung. *Biomed Pharmacol J*. 2020;13(3):1543–8.
 23. Zuo T, Zeng H, Li H, Liu S, Yang L, Xia C, et al. The influence of stage at diagnosis and molecular subtype on breast cancer patient survival: a hospital-based multi-center study. *Chinese J Cancer* 2017 361 [Internet]. 2017 Oct 25 [cited 2022 Mar 29];36(1):1–10. Available from: <https://cancercommun.biomedcentral.com/articles/10.1186/s40880-017-0250-3>
 24. Howlader N, Cronin KA, Kurian AW, Andridge R. Differences in breast cancer survival by molecular subtypes in the United States. *Cancer Epidemiol Biomarkers Prev* [Internet]. 2018 Jun 1 [cited 2022 Mar 29];27(6):619–26. Available from: <https://aacrjournals.org/cebpa/article/27/6/619/71580/Differences-in-Breast-Cancer-Survival-by-Molecular>