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Prognostic Factor and Survival Rate Among Breast Cancer Patients' Post-Surgical Treatment

Memedeki Kanser Hastalarının Cerrahi Tedavi Sonrası Prognostik Faktörler ve Sağkalım Oranı

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ABSTRACT

Objective: The prognosis of breast cancer patients is affected by various types of factors, such as the present stage of illness during the initial diagnosis. The goal of this study is to evaluate the biological factors that can be assessed before breast cancer surgery to predict the outcome of breast cancer surgery for patients who have already undergone the procedure.

Methods: STATA was utilised for reviewing and analysing the data obtained from the retrospective review of the breast cancer records, which focused on post-surgical treatment patient outcomes. Patients who underwent breast cancer surgery were analysed using the "Cox proportional hazards regression model" to evaluate the factors that predict survival rates. The data analysis includes 482 of breast cancer patients after surgical procedures.

Results: A total of 482 patients with breast cancer had surgical procedures from 2016 to 2019. In terms of survival rate, prognostic factors were associated with a poor prognosis for higher-grade tumours, advanced-stage breast cancers, and invasive lobular carcinoma tumour types.

Conclusion: Several clinical and pathological factors influence the overall prognosis and treatment choices. Therefore, it is crucial to adopt the right screening programme to diagnose breast cancer at an early stage. Healthcare practitioners must be aware of various therapeutic methods in the management of cancer to enhance the percentage of survival breast cancer patients

Keywords: Prognostic factor, survival rate, breast cancer, post-surgical

ÖZ

Amaç: Meme kanseri hastalarının prognozu, ilk tanı sırasında hastalığın mevcut evresi gibi çeşitli faktörlerden etkilenmektedir. Bu çalışmanın amacı, meme kanseri cerrahisi öncesinde değerlendirilebilecek biyolojik faktörleri değerlendirerek, meme kanseri cerrahisi geçirmiş hastaların prognozunu tahmin etmektir.

Yöntemler: Cerrahi tedavi sonrası hasta sonuçlarına odaklanan meme kanseri kayıtlarının retrospektif incelemesinden elde edilen verilerin gözden geçirilmesi ve analizi için STATA kullanılmıştır. Meme kanseri ameliyatı geçiren hastalar, sağkalım oranlarını öngören faktörleri değerlendirmek için "Cox orantılı tehlikeler regresyon modeli" kullanılarak analiz edilmiştir. Veri analizi, cerrahi işlem sonrası 482 meme kanseri hastasını kapsamaktadır.

Bulgular: 2016-2019 yılları arasında meme kanseri olan 482 hastaya cerrahi prosedür uygulanmıştır. Sağkalım oranı açısından, prognostik faktörler yüksek dereceli tümörler, ileri evre meme kanserleri ve invaziv lobüler karsinom tümör tipleri için kötü prognoz ile ilişkilendirilmiştir.

Sonuç: Çeşitli klinik ve patolojik faktörler genel prognozu ve tedavi seçeneklerini etkilemektedir. Bu nedenle, meme kanserinin erken evrede teşhis edilmesi için doğru tarama programının benimsenmesi büyük önem taşımaktadır. Sağlık hizmeti uygulayıcıları, meme kanseri hastalarının hayatta kalma yüzdesini artırmak için kanser yönetiminde çeşitli terapötik yöntemlerin farkında olmalıdır.

Anahtar Sözcükler: Prognostik faktör, sağ kalım oranı, meme kanseri, ameliyat sonrası

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INTRODUCTION

Globally, breast cancer is the primary cause of mortality among cancers affecting women, with 685 thousand reported deaths among women in 2020 (1). The number of breast cancer cases worldwide increased to around 6,232,000 between 2008 and 2012, with this accounting for 15.8 percent of cancer-related fatalities, as reported by (2). The Global Cancer Burden Study, a recent comprehensive investigation, unveiled a substantial increase in the incidence of breast cancer, as an estimated 2.3 million individuals are anticipated by 2020 (3). Approximately 16.5 percent of all officially reported cancer cases in 2016 were female breast cancer cases and 4,621 cases were registered with the Malaysia National Cancer Registry. A Malaysian woman has a 50 percent lifetime potential of becoming a breast cancer patient (4). The incidence of cancer in Malaysia is projected to rise because of the growing life expectancy, improved socio-economic position, and evolving lifestyles. Malaysia recorded a total of 8,418 new cases and 3,503 fatalities in 2020 (5).

Furthermore, based on the GLOBOCAN cancer tomorrow prediction tool, there may be a global increase of over 46 percent in incident cases by 2040 (6). Incredible progress has already been made in the past twenty years in refining subatomic cluster formation and enhancing the prognosis for malignant breast growth to improve survival (7). Additional endeavours to combat worldwide breast cancer encompass prevention, timely identification, diagnosis and treatment, rehabilitation, and palliative care (8). Prevention and early detection, such as promoting breast cancer awareness, is paramount in reducing mortality. Our facility in Kota Kinabalu, Sabah, has a long-standing surgical programme for treating breast cancer, and we have maintained a population-based cancer registry. However, there is no publication on evaluating prognostic factors for breast cancer post-surgery. Therefore, this study seeks to evaluate the prognostic biological factors affecting the outcomes in breast cancer patients with post-surgical procedures.

MATERIALS AND METHODS

This study was conducted at the Breast Pink Ribbon Clinic in a tertiary hospital located in the west coast of Kota Kinabalu, Land Below the Wind. It was carried out as a retrospective cohort analysis. This study involved women who were diagnosed with breast cancer and had undergone breast surgery procedures, including wide local excision, mastectomy with axillary clearance, mastectomy, mastectomy with reconstruction, and mastectomy conserving, between 1 January 2016 and 31 December 2019, who were the only participants. The tumour types were invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC), and others. There was no sampling strategy applied because all patients who satisfied the inclusion criteria and had breast cancer surgery during the study period were included. We excluded participants who failed to adhere to the treatment, had missing medical records, or declined surgical intervention. The data collection form was created to document the demographic features of patients the prognostic variables influencing the survival rate, and the prognosis of breast cancer patients.

The sample size needed for this study has been determined to apply a multivariable model through the "Cox proportional hazard regression model". The objective was to evaluate the prognostic influences affecting the survival rate of patients with breast cancer who had undergone surgery procedures. To determine these sample size, the "rule of thumb" approach, requires a minimum of ten occurrences per predictor parameter (9). The total sample size was determined to be 482. A Microsoft Excel spreadsheet was used to document the data initially, and then STATA/SE12.0 was applied to conduct additional statistical analysis.

The "Cox proportional hazard regression analysis" was applied to evaluate the prognostic variables that influence the rates of post-operative survival among breast cancer patients. The main aim was to construct a mathematical representation of the time until an event occurs and its connection to a group of explanatory factors while accounting for instances where the event did not occur within the observed period. The multivariable Cox proportional hazard regression analysis considered additional variables that were identified as potential factors influencing the dependent variable. The automated variable selection approach was used to perform the best subset selection and determine the components that would create the most concise model, given the available data. The results of the assumption tests for the "Cox proportional hazard regression model" were displayed simultaneously with each model. The probability values were two-tailed. A p-value below 0.05 was considered statistically significant. The studies were authorised by the Malaysian Research Ethics Committee and certified by the National Malaysian Research Registry Medical Review and Ethical Committee from the National Institute of Health, Ministry of Health [approval number: NMRR-20-27-52650 (IIR), date: 12.02.2020].

RESULT

Table 1 presents a concise overview of the participants' key demographic characteristics and clinical classifications, highlighting their outcomes and associated p-values for understanding the findings. Our study engaged a diverse group of 482 participants, yielding a mean age of 52.1 years (standard deviation =11.7). The age distribution provided valuable insights, revealing that over half of the participants, specifically 53.1%, were aged over 50 years, indicative of a mature cohort. Meanwhile, 29.7% fell within the 41 to 50-year range, while 15.4% were aged between 30 and 40 years. Only 1.9% of the participants were younger than 30 years. The participants exhibited a range of body mass index (BMI) values, with an average BMI of 26.4 kg/m² and a standard deviation of 5.2. The categorization of participants by BMI highlighted distinct weight profiles: 2.7% were classified as underweight (BMI <18.5 kg/m²), a substantial 41.1% maintained a normal weight (BMI 18.5-24.9 kg/m²), while 34.2% were identified as overweight (BMI 25-29.9 kg/m²). Lastly, 21.9% of participants fell into the obese category (BMI ≥30 kg/m²).

Tumour size was predominantly in the 2 to 5 cm range (55.8%), while 27.6% of participants had tumours larger than 5 cm and 16.6% had tumours smaller than 2 cm. Tumor staging revealed that 39.6% of cases were at stage 2, 28.8% at stage 4, 23.9% at stage 3, and 7.7% at stage 1. Tumor grading indicated that 19.9% of tumors were grade 1, 47.5% were grade 2, and 32.6% were grade 3. Regarding tumour type, 95.6% of cases were IDC, 1.8% were ILC, and 2.5% were categorized as other types.

Hormonal receptor statuses showed that 72.6% of participants were estrogen receptor-positive, while 27.4% were negative. Progesterone

Table 1. Demographic features & clinical states of the participants

Variable	Total: 482 n (%)	Mean (SD)	Outcome		p
			Alive n (%)	Dead n (%)	
Age (Years)		52.1 (11.7)	52.1 (11.7)	51.8 (13.5)	0.910
<30	9 (1.9)				
30-40	74 (15.4)				
41-50	143 (29.7)				
>50	256 (53.1)				
BMI (kg/m^2)		26.4 (5.2)	26.4 (5.1)	27.6 (6.4)	0.317
<18.5	13 (2.7)				
18.5-24.9	198 (41.1)				
25-29.9	165 (34.2)				
≥30	106 (21.9)				
Size of tumour (cm)					
<2	80 (16.6)		78 (16.8)	2 (11.1)	0.005
>2-5	269 (55.8)		264 (56.9)	5 (27.8)	
>5	133 (27.6)		122 (26.3)	11 (61.1)	
Stage					
1	37 (37.7)		37 (7.9)	0 (0.0)	0.001
2	191 (39.6)		190 (40.9)	1 (5.6)	
3	115 (23.9)		110 (23.7)	5 (27.8)	
4	139 (28.8)		127 (27.4)	12 (66.7)	
Grade of tumour					
1	96 (19.9)		96 (20.7)	0 (0.0)	0.013
2	229 (47.5)		222 (47.8)	7 (38.9)	
3	157 (32.6)		146 (31.5)	11 (61.1)	
Tumor type					
IDC	461 (95.6)		446 (96.1)	15 (83.3)	0.038
ILC	9 (1.8)		8 (1.7)	1 (5.6)	
Others	12 (2.5)		10 (2.2)	2 (11.1)	
Status of progesterone receptor					
Positive	289 (60)		227 (48.9)	9 (50)	0.929
Negative	193 (40)				
Status of estrogen receptor					
Positive	350 (72.6)		338 (72.8)	12 (66.7)	0.564
Negative	132 (27.4)				
Status of human epidermal growth factor receptor					
Positive	236 (49)		227 (48.9)	9 (50)	0.929
Negative	246 (51)				
Lymph node affected					
1 to 3	99 (46.1)		99 (47.8)	0 (0.0)	0.008
4 to 9	81 (37.7)		76 (36.7)	5 (62.5)	
≥10	35 (16.3)		32 (15.5)	3 (37.5)	
Lymph node ratio					
<0.20	340 (70.5)		330 (71.1)	10 (55.6)	0.137
0.20-0.65	93 (19.3)		89 (19.2)	4 (22.2)	
>0.65	49 (10.2)		45 (9.7)	4 (22.2)	

BMI: Body mass index, SD: Standard deviation

receptor positivity was observed in 60% of participants, with 40% being negative. Human epidermal growth factor receptor 2 (HER2) receptor status was positive in 49% of participants and negative in 51%. Lymph node involvement was categorized into three groups: 46.1% of participants had 1 to 3 lymph nodes affected, 37.7% had 4 to 9 lymph nodes affected, and 16.3% had 10 or more lymph nodes affected. The lymph node ratio was <0.20 in 70.5% of cases, 0.20-0.65 in 19.3%, and >0.65 in 10.2%.

A comprehensive Cox proportional hazards regression analysis was conducted to rigorously evaluate how clinical and pathological factors influence patient outcomes (Table 2). In the simple regression analysis, tumour size greater than 5 cm (HR =3.57, p=0.009), stage 4 disease (HR =4.50, p=0.007), and grade 3 tumours (HR =3.20, p=0.016) were significantly associated with increased hazard. The cumulative hazard estimates for cancer stages as a prognostic factor for survival are shown in Figure 1. The cumulative hazard estimates for cancer tumour grade as a prognostic factor for survival are illustrated in Figure 2. Also, the cumulative hazard estimates for tumour type as a prognostic factor for survival are presented in Figure 3.

Table 2. Prognostic factor of breast cancer survival after surgical procedure by "Cox proportional hazard model" (n=482)

Variable	Regression Coefficient (b)	Simple Cox regression hazard ratio (95% CI)	Z statistic	p	Regression coefficient (b)	Multiple Cox regression adjusted hazard ratio (95% CI)	Z statistic	p
Age	0.01	1.00 (0.96,1.04)	0.04	0.966				
BMI	0.20	1.04 (0.97,1.12)	0.29	0.285				
Tumour Size (cm)								
≤5	0	1						
>5	1.27	3.57 (1.38,9.22)	2.63	0.009				
Stage								
1 to 3	0	1			0	1		
4	1.50	4.50 (1.69,12.00)	2.70	0.007	1.42	4.13 (1.54,11.11)	2.82	0.005
Grade of tumour								
1 to 2	0	1			0	1		
3	1.16	3.20 (1.24,8.27)	2.41	0.016	1.4	4.07 (1.50,11.01)	2.76	0.006
Tumour type								
IDC	0	1			0	1		
ILC and Others	1.38	3.97 (1.15,13.7)	2.18	0.029	1.86	6.43 (1.75,23.69)	2.8	0.005
Progesterone receptor								
Negative	0	1	-1.40	0.162				
Positive	-0.66	0.52 (0.20,1.31)						
Estrogen receptor status								
Negative	0	1						
Positive	-0.33	0.72 (0.27,1.92)	-0.66	0.51				
HER2 receptor								
Negative	0	1						
Positive	0.02	1.02 (0.41,2.57)	0.04	0.966				
Lymph node affected								
0	0	1						
≥1	0.01	1.01 (0.40,2.56)	0.02	0.980				
Lymph node ratio								
<0.20	0	1						
0.20-0.65	0.44	1.56 (0.49,4.97)	0.75					
>0.65	1.01	2.73 (0.86,8.71)	1.70	0.089				

BMI: Body mass index, SD: Standard deviation, HER2: Human epidermal growth factor receptor 2, IDC: Ductal carcinoma, ILC: Invasive lobular carcinoma, CI: Confidence interval

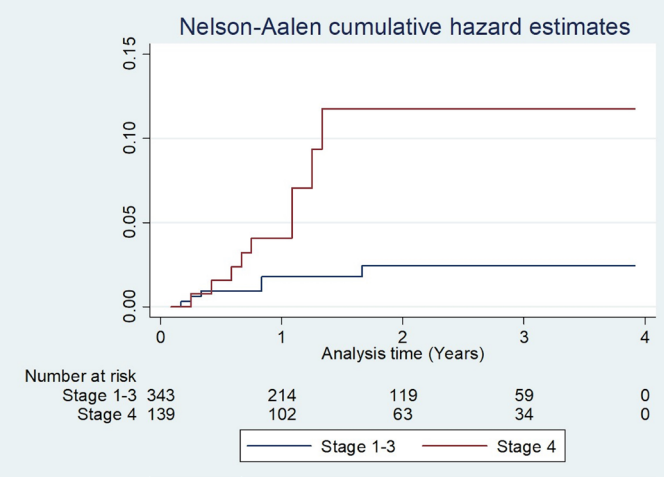

Figure 1. Cumulative hazard estimates for cancer stages as a prognostic factor for survival.

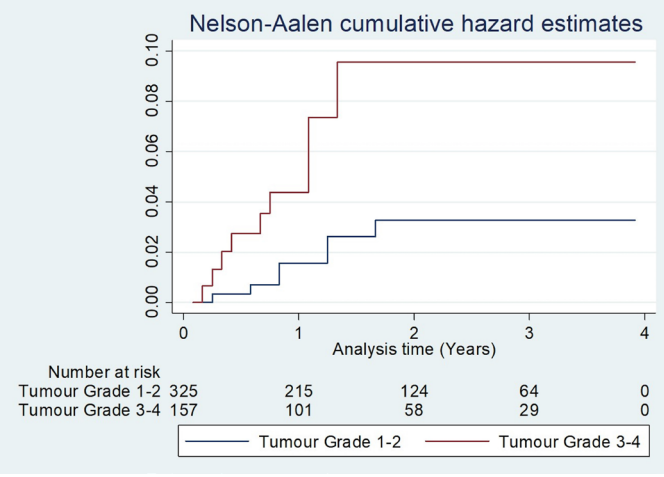

Figure 2. Cumulative hazard estimates for cancer tumour grade as a prognostic factor for survival.

Additionally, ILC and other tumour types showed a higher risk than IDC (HR =3.97, p=0.029). Hormone receptor status, HER2 positivity, and lymph node involvement were not significantly associated with hazard ratios. In the multiple regression analysis, stage 4 disease (Adjusted HR =4.13, p=0.005), grade 3 tumours (Adjusted HR =4.07, p=0.006), and ILC (Adjusted HR =6.43, p=0.005) remained significant predictors of poor outcomes.

DISCUSSION

The results from this study indicate that tumour size, stage, grade, and histological type significantly influence survival outcomes. These findings are consistent with previous studies demonstrating the prognostic importance of tumour characteristics in cancer progression. Tumour size greater than 5 cm was associated with a significantly increased hazard ratio, which is consistent with the study by (7), who reported that histologic grade remains a significant prognostic factor for overall survival, independent of tumour size. This finding emphasizes the necessity of early detection and intervention to improve patient prognosis. Advanced disease stage, especially stage 4, remained among the strongest predictors of poor outcomes. This is consistent with previous studies (8), which found that metastatic disease at the time of diagnosis drastically reduces survival rates. This emphasizes how crucial prompt staging and vigorous treatment are for advanced cases in clinical practice.

In our study, grade 3 tumours had considerably higher hazard ratios. Previous research, such as that conducted by (9), has designated the Nottingham histological grade as a key predictive indicator for breast cancer, vital for clinical decision-making. This emphasizes the importance of personalized treatment approaches, particularly for individuals with high-grade tumours who may benefit from intensive therapy. Histological tumour type was another key prognostic factor, with ILC and other variants exhibiting a significantly increased hazard compared to IDC. This aligns with previous studies indicating that ILC often presents with unique biological behaviour and a higher likelihood of late recurrences compared to IDC (10,11). These findings suggest that histological subtyping should be carefully considered when planning long-term patient management and follow-up strategies. Hormone receptor status, HER2 positivity,

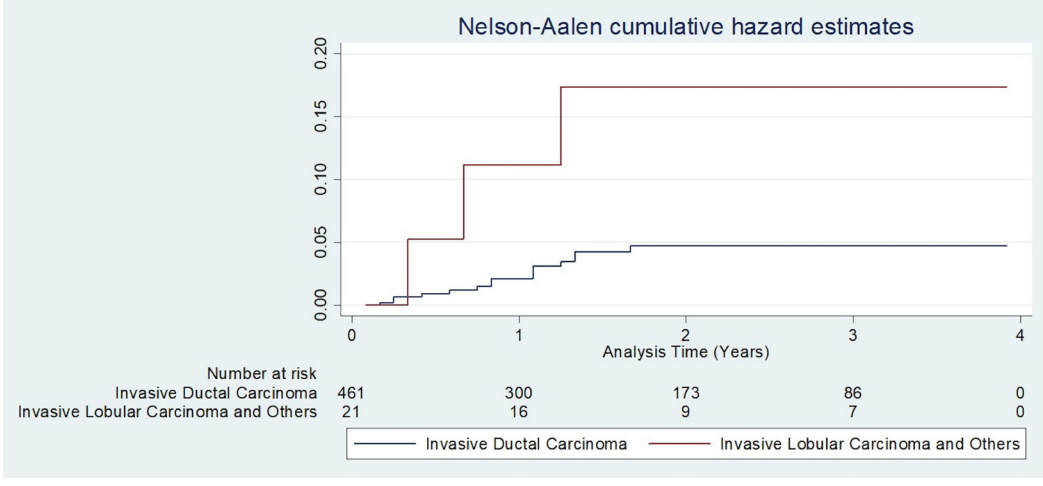

Figure 3. Cumulative hazard estimates for type of tumour as a prognostic factor for survival.

and lymph node involvement did not correlate significantly with hazard ratios. While prior research has demonstrated that hormone receptor-positive tumours generally have a more favourable prognosis (9,12), our study revealed no statistically significant difference, underscoring the robustness of our findings. This may be due to sample size limitations or differences in treatment modalities, suggesting the need for further investigation.

Our study reinforces the importance of tumour staging, grading, and histological classification in determining prognosis and guiding treatment decisions. Clinicians should prioritize early detection, as tumour size and stage are critical determinants of survival, which is in line with current guidelines from the American Joint Committee on Cancer (13). Staging at diagnosis significantly affects treatment options, with advanced-stage cancers requiring more aggressive and multimodal treatment strategies, including chemotherapy, targeted therapy, and radiotherapy (14). The observed differences in outcomes based on tumour grade and histology highlight the need for personalized treatment approaches. For instance, high-grade tumours and lobular carcinoma subtypes have been shown to exhibit aggressive behaviour and increased recurrence risk, necessitating more intensive follow-up and adjuvant therapy (15,16). Advances in molecular profiling and genomic testing now allow for a more individualized approach, helping to identify patients who may benefit from novel targeted therapies or immunotherapies (17).

Furthermore, the lack of significant findings for hormone receptor status and lymph node involvement suggests that additional prognostic markers may be required to refine risk stratification. Current guidelines emphasize the integration of genomic and molecular profiling, such as the Oncotype DX and MammaPrint assays, into clinical practice to improve patient selection for chemotherapy and endocrine therapy (18). The shift toward precision medicine could reduce overtreatment while ensuring high-risk patients receive appropriate interventions. Future research should focus on further integrating AI-driven risk assessment tools and biomarker-based therapies into routine oncology care (19).

Study Limitations

Preliminary research conducted in Kota Kinabalu; Sabah aimed to determine prognostic factors influencing postoperative survival rates in breast cancer patients. However, the study had limitations, including a brief time frame and incomplete data regarding breast cancer occurrence and death rates in Sabah. Therefore, certain prognostic factors and risk factors for breast cancer, such as clinical presentation, socio-economic status, and educational level, were not recorded or analysed due to missing or incorrectly written histopathology data. Future research should employ prospective, multicentre studies incorporating genetic profiling and molecular subtyping to provide a more holistic understanding of prognostic determinants. Additionally, addressing barriers to early detection, such as healthcare access disparities, remains a critical area for intervention.

CONCLUSION

Advanced breast cancer, higher tumour grade, and ILC tumour type are all associated with a poorer survival prognosis in patients. Identifying the risk factors for breast cancer recurrence is crucial as it can guide the selection of initial treatment strategy, assist in subsequent monitoring, and provide accurate information to patients. Our analysis of the results showed a higher proportion of younger patients were developing breast cancer. Thorough assessment of breast-conserving surgery is recommended for young patients with positive axillary lymph nodes. These women should receive rigorous post-surgical therapy and comprehensive follow-up. Prompt and accurate identification, along with timely access to appropriate therapy, is essential for reducing breast cancer mortality rates. Increasing awareness about breast cancer, instilling confidence in its manageability, and improving access to comprehensive primary healthcare, including skilled breast physical examinations, can potentially improve survival rates.

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Ethics

Ethics Committee Approval: The studies were authorised by the Malaysian Research Ethics Committee and certified by the National Malaysian Research Registry Medical Review and Ethical Committee from the National Institute of Health, Ministry of Health [approval number: NMRR-20-27-52650 (IIR), date: 12.02.2020].

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: F.H., N.A.S.N.L., Concept: F.H., R.K., Design: F.H., N.A.S.N.L., Supervision: F.H., N.A.S.N.L., S.Z.S., J.E.L., Resources: R.K., N.A.S.N.L., Material: S.Z.S., Data Collection or Processing: R.K., J.E.L., Analysis or Interpretation: R.K., J.E.L., Literature Search: R.K., D.L., D.C.C., Writing: R.K., D.C.C., D.L., Critical Review: R.K., D.C.C., D.L.

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