International Journal of Research in Medical Sciences
Maulidan Y et al. Int J Res Med Sci. 2019 Jul;7(7):2595-2598
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20192884

Original Research Article

Correlation cyclooxygenase-2 expression and histopathological grading in locally advanced breast cancer

Yasser Maulidan[1]*, Salman A. Syamsu[1], Rudy Thabry[2], Zaenal Abidin[2]

[1]Department of Surgery, Hasanuddin University, Makassar, South Sulawesi, Indonesia
[2]Department of Surgery, Mulawarman University, Samarinda, East borneo, Indonesia

Received: 15 April 2019
Accepted: 13 May 2019

***Correspondence:**
Dr. Yasser Maulidan,
E-mail: surgeon1118@gmail.com

ABSTRACT

Background: Cyclooxygenase-2 (COX-2) is involved in the carcinogenesis process and tumor progression into cancer. It has been reported recently, there was a COX-2 expression at breast cancer. Patients with a high level of COX-2 expression can have a local recurrence and decrease life expectancy, and an increase of COX-2 expression in tissue likelihood has prognostic value. This study aims to correlation cyclooxygenase-2 (cox-2) expression and histopathological grading in locally advanced breast cancer patient in AW Sjahranie Hospital in Samarinda city.
Methods: This study was an observational study with crossectional design to analysis the correlation COX-2 expression and histopathological grading in patients with locally advanced breast cancer and using data analysis with the Chi-Square test.
Results: The results showed that the correlation was not significant (P>0.05), where there was no correlation of COX-2 expression with histopathological grading (P=0.221) and there was no correlation with the last condition of patients (P=0.61). Although patients with breast cancer high grade and moderate grade percentages were significantly higher in positive COX-2 than in COX-2 negative expression.
Conclusions: There were no correlation between COX-2 expression and histopathological grading and there was no significant relationship between COX-2 expression and the last condition, as evidenced by the statistical test results showing that the differences were not significant.

Keywords: Breast cancer, Cyclooxygenase-2, Histopathological grading

INTRODUCTION

Breast cancer is one of the malignancies in women that causes high mortality rates throughout the world. Based on data from the World Health Organization.[1]

In Indonesia (based on basic Health Research data in 2013), breast cancer is cancer with the highest prevalence in Indonesia in 2013, by 0.5% (61.682 sufferers). Where is the most in Central Java province 11.511 people with breast cancer.[2-4] Authors got data from the Dharmais Hospital in Jakarta on the period 2010-2013 breast cancer ranks first in the cancer incidence rate of 700-900 new cases.[5-7] Whereas in East Borneo in 2013 there were 1.879 breast cancer cases (1.0%).[3,8]

Based on the role of COX 2 in carcinogenesis of breast cancer at the molecular level.[9,10] That IHC COX-2 examination it is important in management strategies and to predict the prognosis of breast cancer patients. [9,11] The COX-2 expression studies on various parameters of breast cancer are still controversial.[12,13] The research data

about correlation COX-2 with the parameters of breast cancer histopathology grading in Samarinda has never been done. Therefore, a study is needed to determine the correlation of the expression of Cyclooxygenase-2 (COX-2) with histopathological grading in women with advanced-local breast cancer in Samarinda, East Borneo.

METHODS

This study was an observational study with cross-sectional design to assess the relationship between COX-2 expression and histopathological grading of advanced-local breast cancer patients in Abdul Wahab Hospital Sjahranie Samarinda. This research was held at the Installation of Sub-Division of Surgical Oncology Hospital RSUD. AW Sjahranie Samarinda, East borneo, Indonesia.

This study was done from January 2017 to January 2018 with a total of 50 samples. All affordable populations that meet the research criteria are obtained based on the order of admission to the hospital (sequential random sampling). Samples taken from tumor tissue in women with breast cancer who have been diagnosed as local advanced breast cancer who have not received prior treatment and who have undergone a mastectomy or biopsy surgery performed by COX-2 are included, whereas breast cancer patients are metastatic (as evidenced by chest x-ray and abdominal ultrasonography) and tissue samples or paraffin blocks that are not representative we will exclude.

The data which we obtained were recorded and grouped based on the purpose and type of data. The appropriate statistical method that we used was SPSS version 22. The statistical test used was the Chi-Square test and the significant results if the value was P<0.05.

RESULTS

The research was done from January 2017 until January 2018 in breast cancer patients who were treated in the Oncology surgery section of AW Sjahranie Hospital. Authors obtained 50 subjects who met the study inclusion criteria. The differences based on ages group subjects were <50 years 20 (40%) and >50 years as many as 30 patients (60%) as soon in Table 1.

Table 1: Distribution characteristics of research subjects.

Variable	N	%
Age (years)		
<50	20	40.0
≥50	30	60.0

*Range of age 30-82 years old, mean: 52 years old.

Based on the characteristics of the TNM Stadium from 50 patients, it was found that patients with stage IIIA were 13 patients (26%), stadium IIIB were 32 patients (64%) and stadium III C as many as 5 patients (10%) as soon in Table 2.

Table 2: The distribution of breast cancer staging.

Diagnosis	N	%
Stadium		
III A	13	26.0
III B	32	64.0
III C	5	10.0

Based on the characteristics of the histopathological examination in 50 samples of the breast cancer case study, the histopathological examination results were higher in the moderate grade examination of 22 cases (44.0%) than with high grade 20 cases (40.0%) and low grade as many as 8 cases (16.0%) (Table 3).

Table 3: Distribution of histopathology grading.

Variable	N	%
Type of Histology		
Invasive Ductal Ca	39	78.0
Invasive Lobular Ca	9	18.0
Lobular Infiltrative Ca	2	4.0
Degree of differentiation		
Low Grade	8	16.0
Moderate Grade	22	58.0
High Grade	20	42.0

According on Table 4, The last patient's condition was mostly non-residual (82.0%) and there were two patients who died (4.0%).

The percentage of moderate and high-grade subjects was found to be higher in positive COX-2 expressions (45.7% and 39.1%) than in negative COX-2 expressions (25.0% respectively). While the percentage of subjects with low grade was found to be higher in negative COX-2 (50.0%) than in positive COX-2 (15.2%). However, the results of statistical tests show the difference is not significant (P>0.05) as soon in Table 5.

Table 4: The last patient's condition.

Last condition	N	%
Non-residual	41	82.0
Residual	7	14.0
Died	2	4.0
Total	50	100.0

According to Table 6 about four patients with negative COX-2, all were found to be non-residual (100%). Whereas in 46 patients with positive COX-2 found 7 patients (15.2%) were recidive and 2 patients (4.3%) died. But the results of statistical tests showed that the different is not significant.

Table 5: The correlation of COX-2 expression with histopathological grading.

COX-2 Expression			Histopathological Grading			Total	P
			Low	Moderate	High		
	Positive	N	7	21	18	46	0.221
		%	15.2%	45.7%	39.1%	100.0%	
	Negative	n	2	1	1	4	
		%	50.0%	25.0%	25.0%	100.0%	
Total		n	9	22	19	50	
		%	18.0%	44.0%	38.0%	100.0%	

Table 6. The correlation of COX-2 expression with the last patient's condition.

COX-2 Expression			The Last Patient's Condition			Total	P
			Non-Residual	Residual	Died		
	Positive	N	37	7	2	46	0.621
		%	80.4%	15.2%	4.3%	100.0%	
	Negative	N	4	0	0	4	
		%	100.0%	0.0%	0.0%	100.0%	
Total		N	41	7	2	50	
		%	82.0%	14.0%	4.0%	100.0%	

DISCUSSION

The research about biomarker of breast cancer is the main priority in our center. The recent study about KI-67, BCL-2, ERα as predictor of clinical response to chemotherapy in breast cancer have done in our center.[6,14]

The characteristics of this study, mostly breast cancer patients were found in the age group >50 years with 30 cases (60%) at least 30 years and a maximum of 82 cases. With an average of 52 years. Invasive breast cancer is very rare before the age of 25 years.[4,15] COX-2 were found significantly higher in patients aged >50 years in breast cancer.[16,17] This is in accordance with the characteristics of our research data.

In our study, we found patients with breast cancer with high grade 20 cases (42%), moderate grade 22 cases (58%), and low grade 8 cases (16%).The higher the degree of differentiation of the tumor the worse the prognosis and the results of its treatment.[17,18] The higher degree of differentiation, it has higher prognosis than that lower degree of differentiation.[19,20] COX-2 overexpression was obtained in moderate and high grade (45.7% and 39.1%) and there was no correlation between COX-2 expression and diagnosis. In Ristimaki's study of 1576 patients with ductal type invasive breast cancer who received COX-2 overexpression found that increased COX-2 expression was associated with an increase in the differential degrees of breast cancer.[21,22]

In our study, the last condition of 46 patients with positive COX-2 was found in 7 patients (15.2%) recidive and 2 patients (4.3%) died. But the results of statistical tests show that the difference is not significant. In Rosen's study examined the relationship between histopathological grading[18] and WHO-based prognostics for low-grade percentages for 5 and 10-year survival rates of 75% and 45%.[18,23]

At moderate grade, this number is 53% and 27% while for high grades 31% and 18% are obtained.[24] In our study, the correlation of COX-2 expression with histopathological grading (P=0.221) and COX-2 with the last condition (P=0.621) was proven by the results of statistical tests showing that the difference was not significant (P>0.05).

CONCLUSION

There are no correlation between cyclooxygenase-2 **(**COX-2) expression and histopathological grading and there is no significant relationship between cyclooxygenase-2 **(**COX-2) expression and the last patient's condition, as evidenced by the statistical test results showing that the difference is not significant.

Recommendations

Longitudinal research is needed about the role of COX-2 on risk factors and prognostics in breast cancer.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. IARC. Globocan: Estimated Cancer Incidence, Mortality and Prevalence Worldwide In 2012. Available at: http://Www-Dep.Iarc.Fr/. Accessed 9 July 2018.
2. American Cancer Society. Cancer Facts and Figures 2014, 2014. Available at: https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2014.html.
3. Kemenkes. Cancer situation: 4 February-world cancer day. 2015. Available at: http://www.depkes.go.id/resources/download/pusdatin/infodatin/infodatin-kanker.pdf. Accessed 13 August 2017.
4. Abidin Z. Correlation Cyclooxygenase-2 (COX-2) Expression and Histopathological Grading in a Breast cancer patient in Makassar, 2016.
5. Manuaba TW. Guideline for managing breast cancer. Solid cancer management guide. Peraboi. Jakarta: Sagung Seto; 2010: 17-48.
6. Prihantono P, Hatta M, Binekada C, Sampepajung D, Haryasena H, Nelwan B, et al. Ki-67 expression by immunohistochemistry and quantitative real-time polymerase chain reaction as predictor of clinical response to neoadjuvant chemotherapy in locally advanced breast cancer. J Oncol. 2017:6209849.
7. Panigoro S, Hernowo BS, Purwanto H, Handojo, Haryono SJ, Arif W, et al. Guideline for management of breast cancer, 2015. Available at: http://kanker.kemkes.go.id/guidelines/Breast_Cancer.pdf. Accessed 5 July 2018.
8. Suyatno, Pasaribu ET. Diagnosis and Oncology surgery and Therapy. Jakarta: Sagung Seto; 2014: 17-48.
9. Desen W. Textbook Clinical Onkologi. 2nd ed. Jakarta: Japaries; 2011: 50-62.
10. Deshayes F, Nahmias C. Angiotensin receptors: a new role in cancer?. Trends Endocrinol Metab. 2005;16(7):293-9.
11. Williams CS, Mann M, DuBois RN. The role of cyclooxygenases in inflammation, cancer, and development. Oncogene. 1999;18(55):7908-16.
12. Divvela AK, Challa SR, Tagaram IK. Pathogenic role of cyclooxygenase-2 in cancer. J Heal Sci. 2010;56(5):502-16.
13. Greenhough A, Smartt HJ, Moore AE, Roberts HR, Williams AC, Paraskeva C, et al. The COX-2/PGE2 pathway: key roles in the hallmarks of cancer and adaptation to the tumor microenvironment. Carcinogenesis: 2009;30(3):377-86.
14. Prihantono P, Binekada C, Hatta M, Sampepajung D, Islam AA. Correlation of BCL-2 and ERα mRNA expression with the clinical chemotherapeutic response in breast cancer. J Med Sci. 2017;17(1):31-7.
15. Lester SC, Bae JW, Woo SU, Kim H, Kim CH. The Breast. In: Kumar V, Abbas AK, Fausto N, Aster JC. Robbin and Cothran's Pathology Basic of Diseases. 3rd ed. Philadelphia: Elsevier Saunders; 2010: 63-78.
16. Yager JD, Davidson NE. Estrogen carcinogenesis in breast cancer. N Engl J Med. 2006;354(3):270-82.
17. Feig BW, Berger DH, Fuhrman GM. The MD Anderson surgical oncology handbook, Lippincott Williams & Wilkins. 4th ed. New England Journal of Medicine; 2006: 60-82.
18. Rosen P. Invasive ductal carcinoma assesment of prognosis, morphologic prognostic markers, and tumor growth rate. New Eng J Med. 2009;360(3):250-72.
19. Sobolewski C, Cerella C, Dicato M, Ghibelli L, Diederich M. The role of cyclooxygenase-2 in cell proliferation and cell death in human malignancies. Int J Cell Biol. 2010;2010:270-82.
20. Miglietta A, Toselli M, Ravarino N, Vencia W, Chiecchio A, Bozzo F, et al. COX-2 expression in human breast carcinomas: correlation with clinicopathological features and prognostic molecular markers. Expert Opin Ther Targets. 2010;14(7):655-64.
21. Ristimäki A, Sivula A, Lundin J, Lundin M, Salminen T, Haglund C, et al. Prognostic significance of elevated cyclooxygenase-2 expression in breast cancer. Cancer Res. 2002;62(3):632-5.
22. Ranger GS, Thomas V, Jewell A, Mokbel K. Elevated cyclooxygenase-2 expression correlates with distant metastases in breast cancer. Anticancer Res. 2004;24(4):2349-52.
23. Surowiak P, Materna V, Matkowski R, Szczuraszek K, Kornafel J, Wojnar A, et al. Relationship between the expression of cyclooxygenase 2 and MDR1/P-glycoprotein in invasive breast cancers and their prognostic significance. Breast Cancer Res. 2005;7(5):R862-70.
24. Rakha EA, Reis-Filho JS, Baehner F, Dabbs DJ, Decker T, Eusebi V, et al. Breast cancer prognostic classification in the molecular era: the role of histological grade. Breast Cancer Res. 2010;12(4):207.

Cite this article as: Maulidan Y, Syamsu SA, Thabry R, Abidin Z. Correlation cyclooxygenase-2 expression and histopathological grading in locally advanced breast cancer. Int J Res Med Sci 2019;7:2595-8.