www.bircu-journal.com/index.php/birci
Budapest International Research and Critics Institute-Journal (BIRCI-Journal)
Humanities and Social Sciences
ISSN 2615-3076 Online)
ISSN 2615-1715 (Print)
Budapest Institute

Prognostic Factor of H-Zone Area in Basal Cell Carcinoma

Prasetyadi Mawardi[1], Irfany Arafiasetyanto Prihadi[2], Muhammad Eko Irawanto[3]
[1,2,3]Department Dermatology AND Venereology, Faculty of Medicine, Universitas Sebelas Maret/Dr. Moewardi Regional Hospital, Surakarta, Indonesia
prasetyadi_m@staff.uns.ac.id, irfany4a@gmail.com, ekokepik@gmail.com

Abstract

The study data were taken from secondary data obtained from medical records of BCC patients in Dr. Moewardi Hospital. The data were categorized based on gender, age, occupation, predilection/ location of tumor based on Baxter criteria, which divided the area into H-zone dan non-H-zone. H-zone was described to cover temporal, auricular, orbital, nasal, upper mandibular. Whereas the tumor size was divided into two, less than 2 cm and more than 2 cm. H-zone is a predilection with a high risk toward tumor biological characteristics, such as recurrence risk, aggressivity risk, and tumor infiltrative. The study obtained an ethics clearance from Health Research Ethics Committee of Dr. Moewardi Hospital with number 762/VIII/HREC/2021. The analysis was conducted to test whether there was a correlation or effect between two variables or more. In the study, the researcher also conducted statistics test to measure the correlation intensity of two variables or more by using Chi-square (X2), statistics test was conducted by using SPSS 22 for Windows. 99 patients were obtained from the medical records however only 70 patients who met the study requirements, who were subsequently categorized based on gender, age, occupation, BCC location and size, disease duration. 29 patients were excluded due to incomplete medical records (BCC location, BCC size, and treatment history were not found) non-primary BCC, data duplication, patients with more than one medical records, the result of histopathological test did not indicate seborrheic keratosis and Squamosa Cell Carcinoma. Based on the study there were more female patients compared to male patients. it discovered 45 female patients and 25 male patients (64,3% compared to 35,7%), with the age range was from 22-90 years, the BCC tumor was endured for more than 2 years, based on the education most of the patients had primary education background (elementary school and junior high school), the majority occupation of the patients was farmer (30%), followed by housewife (28,57%).

Keywords
prognostic factor; H-Zone area; basal cell carcinoma

I. Introduction

Basal Cell Carcinoma (BCC) is a non-melanoma skin cancer generated from the basal layer of epidermis and non-keratinized cell. BCC is locally invasive, aggressive, and destructive; however, the metastasis is very low. The cause of BCC is not yet clearly discovered (Carucci, 2008; Tilli, 2005). Epidemiologically, in the last two decades there have been increasing incidences rate of BCC worldwide. There are estimated nearly 5 million skin cancer patients in the USA (Guy, 2015). Increasing number of skin cancer cases also occurs in Indonesia. More than 72 % of skin cancer cases in Cipto Mangunkusumo Hospital are

Basal Cell Carcinoma. The other data indicate BCC also top the list in Dr. Moewardi Regional Hospital Surakarta among all skin cancer (Cipto, 2016; Mawardi, 2016).

The increasing prevalence is affected by various factors, especially genetic, environmental, and immunological factors. Exposure to ultraviolet (UV) light is considered as the major factor in BCC pathophysiology. UV light is a carcinogen absorbed and directly damages DNA, by developing cyclobutene pyrimidine dimmers (CPD) and 6-4 photoproduct, which inflicts gene mutation that is responsible for the carcinogenesis process. Continuous release of proinflammatory cytokines such as TNFα, Interleukin (Il) 6, Il-8 and basic Fibroblast Growth Factor, is responsible for the process of carcinogenesis (Gambichler, 2006; Ouhtit, 2001). The imbalance Il-6 is closely related to various types of solid tumor, in which cytokines play an important role in regulating apoptosis process and various types of cells (Shimizu, 2010). UV irradiation may inflict inflammation response over the skin by stimulating epidermal keratinocytes to express potential biological cytokines such as IL-1, IL-6 and TNF-α. The expressed TNF-α will affect various types of cell. Tumor Necrosis Factor (TNF)-α will increase the expression of class 1 Major Histocompatibility Complex (MHC) in endothelia cell and skin fibroblast, induce the production of IL-1α, increase the expression of adhesion molecule, including Intercellular Adhesion Molecule (ICAM-1, Vascular Cell Adhesion Molecule (VCAM-1) and E-selectin, as well as stimulate the development of sunburn cells. In addition, cytokines are not only involved in the mediation of local inflammation reaction, but also playing a different role in stimulating tumor development (Shimizu, 2010). The most common clinical descriptions of BCC are tumor indicates fragile lesion, never recover, often found on the areas easily exposed to the sun, such as neck and face, however it may happen on any part of the body. It is often accompanied by lesions which are easily to bleed, recover, and recurrent. The discovered descriptions are the occurrence of translucent lesion, ulceration, telangiectasia, and the occurrence of rising edges/induration. The typical descriptions may vary based on the various clinical variants (Tang, 2019).

Therapy modalities for BCC consist of intervention therapy (surgical) and non-intervention therapy (non-surgical). Intervention therapy such as Electrodessication and curettage (EDC), excision, cryosurgery, and Mohs micrographic surgery, have a high level of 5-year healing rates, generally it is more than 95%. Yet, it generates potentially higher functional damage and scar tissues compared to non-invasive therapy. The existing technological and economical challenges has attracted the attention of researchers to this topic (Nikmanian, 2019). In certain population, such as elderly, immunosuppressive patients, metastatic patients, or cosmetic indication, non-intervention-therapy might be a more desirable therapy. Intervention therapy is required for basal cell carcinoma, particularly to prevent local recurrence generated by inadequate therapy. The comprehensive eradication is important since tumor recurrence is often bigger and more aggressive than the primary one. The therapy should be able to give maximum result both for functional and cosmetic sides (Tang, 2019; Lanoe, 2016). The objective of the study is to discover prognostic factor of H-zone area in BCC.

II. Research Methods

It was a retrospective descriptive observational study with total sampling as the sampling method. The target population was all BCC patients in Dr. Moewardi Hospital during the period of 2016-2019. The study data were taken from secondary data obtained from medical records of BCC patients in Dr. Moewardi Hospital. The data were categorized based on gender, age, occupation, predilection/location of tumor based on Baxter criteria

which divided the area into H-zone and non-H-zone. H-zone was described to cover temporal, auricular, orbital, nasal, upper mandibular. Whereas the tumor size was divided into two, less than 2 cm and more than 2 cm.11 H-zone is a predilection with a high risk toward tumor biological characteristics, such as recurrence risk, aggressivity risk, and tumor infiltrative. Inclusion criteria of the study were all patients who had been diagnosed with primary BCC in the medical records of Dr. Moewardi Hospital Surakarta during the period of 2016 – 2019. The exclusion criteria were patients with repeated BCC, metastasis, and the occurrence of multi-lesions, incomplete medical records, non-BCC histopathologic examination result. The study obtained an ethics clearance from Health Research Ethics Committee of Dr. Moewardi Hospital with number 762/VIII/HREC/2021. The analysis was conducted to test whether there was a correlation or effect between two variables or more. In the study, the researcher also conducted statistics test to measure the correlation intensity of two variables or more by using Chi-square (X2), statistics test was conducted by using SPSS 22 for Windows.

III. Discussion

99 patients were obtained from the medical records however only 70 patients who met the study requirements, who were subsequently categorized based on gender, age, occupation, BCC location and size, disease duration. 29 patients were excluded due to incomplete medical records (BCC location, BCC size, and treatment history were not found) non-primary BCC, data duplication, patients with more than one medical records, the result of histopathological test did not indicate seborrheic keratosis and Squamosa Cell Carcinoma. Based on the study there were more female patients compared to male patients. it discovered 45 female patients and 25 male patients (64,3% compared to 35,7%), with the age range was from 22-90 years, the BCC tumor was endured for more than 2 years, based on the education most of the patients had primary education background (elementary school and junior high school), the majority occupation of the patients was farmer (30%), followed by housewife (28,57%). Characteristics of demographic data and clinical data can be observed in table 1 dan 2.

Table 1. Patient's Characteristics Data

Gender Category		
Male	25	35,71
Female	45	64,29
Age (year)		
< 20	-	-
21-30	1	1,42
31-40	1	1,42
41-50	5	7,14

51-60	22	31,42
>60 years	41	58,6
Occupation		
Farmer	21	30
Hosuewife	20	28,57
Civil Servant	6	8,57
Private employee	16	22,87
University student	1	1,42
Others	6	8,57
Tumor size		
<2 cm	51	72,8
>2 cm	19	27,2
Risk-zone		
H-*zone*	49	70
Non-H-*zone*	21	30
Clinical Sub-type		
Nodular	26	37,1
Noduloulcerative	15	21,4
Micronodular	4	5,7
Sclerotic	14	20
Superficial	8	11,5
Mixed	3	4,3

Based on the study conducted the majority of BCCs were less than 2 cm (72.8%), however the majority of the tumors were located on H-zone area (70%). Based on the

histopathological examination it obtained that the majority of the tumors were in nodular shape or noduloulcerative (58.5%).

An analysis was conducted to test whether there was a correlation or an effect between the two variables or more. The result of statistics analysis can be observed in Table 2. The study indicated that there was no correlation between H-zone and gender, also occupation ($p>0.05$), however there was a correlation between H-zone and patients' age and tumor size.

Table 2. The Correlation between H-zone Risk Factor and Type of Occupation, Gender, Age, and Tumor Size

H-zone Risk Factor	Variables	P-*value*
H-zone	Occupation	0.398
H-zone	Gender category	0.091
H-zone	Age	0.030
H-zone	Size	0.039

In an effort to tackle cancer, the Indonesian government conducted an early cancer detection program for Indonesian women (Arysha, 2020). The study obtained more female patients than male patients (64.2% compared to 35.8%). It indicated an increase compared to the previous study, in which the study by Mawardi (2019) indicated a comparison of 55.3% compared to 44.7%. The other studies conveyed that men more easily suffer from BCC compared to women. The fundamental reason for the shifting of BCC prevalence to women is presumably because there are more women who work outdoor that they are easily exposed to UV light.13 BCC in the study was suffered more by people of above 50 years old (>90%). Skin cancer that significantly contributes in the burden of overall skin conditions among the population of elderly, significantly determines morbidity, mortality and cost related to health. Various studies mentioned that white old (65-79 years) – to very old (>80 years) individuals represents the sub-group of demography with the highest growth of BCC incidences level (Asgari, 2015). The elderly endures decreased capacity of immune system and inadequate DNA repair, which increases the risk of BCC development, particularly due to the cumulative effect of intensive and continuous sunlight exposure. As the result of the decreased response, number, and functions of T lymphocyte, the elderly often suffer from decreased cellular immune functions (Kasumagic, 2016). Based on the occupation, the majority occupation was farmer (30%). It is understood that the primary cause of BCC is UV light exposure. Farmers who exponentially receive UV light exposure, have higher risk for the occurrence of the skin cancer. Monoclonal antibodies have proven to be effective treatments for a growing range of human cancers (Sangy, 2021). Sunlight exposure during childhood and recreational sunlight exposure appears too important in the development of BCC during adulthood. Another study reports that the risk of BCC increases by 2 times risk of lower exposure (8.000-10.000 a lifetime cumulative hours) in the plateau and a slight risk decrease for high exposure (100.000 a lifetime cumulative hours) (Iannacone, 2012; Bauer, 2011). Clinicopathologically,

most patinets had tumor of less than 2 cm, however more than a half were found in H-zone. (70%). H-zone is a high risk area which indicates level of success and effectiveness of BCC management. Statistically there was a significant correlation of H-zone area with patient's age. Among elderly patients BCC is more likely to be found in H-zone area. There was also a significant correlation between the size of tumor and H-zone area. Despite the small size, tumor found in H-zone area has the risk of recurrency and aggressivity of BCC. Baxter et al, divides H-zone area into temporal area, auricular, orbital, nasal, upper mandibular (Baxter, 2012). the area anatomically has the structure of adnexa, subcutaneous dan perineural supporting stroma that consists of extremely complex series. Although it is not exactly similar, H-zone is almost similar to midface in the categorical facial division by Baker et al. (2007) Midface region is a line that starts from glabellar up to the lower part of the nose, above philtrum. Midface region consists of, orbital, auricula, nasal, cheeks, zygomaticus region. In the study conducted by Mawardi et al (2016), midface region was closely related to BCC agrresivity.

IV. Conclusion

The study discovers a shifting of BCC incidences which mostly found in women with the risk of tumor lesion over H-zone, which is a predilection with the risk of recurrency, infiltrative characteristics and high aggressivity compared to other locations.

References

Apalla, Z., Lallas, A., Sotiriou, E., Lazaridou, E. dan Ioannides, D. (2017). Epidemiological trends in skin cancer. Dermatology Practical & Conceptual [online] 7(2).https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5424654/.

Arysha, V.O., Santosa, H., and Sanusi, S.R. (2020). The Effect of Extrinsic Motivation on Housewife Actions in IVA Test in the Working Area of Community Health Center at Bandar Kalipah. Britain International of Exact Sciences (BIoEx) Journal Vol. 2 (1): 352-356.

Asgari MM, Moffet HH, Ray GT, Quesenberry CP (2015). Trends in Basal Cell Carcinoma Incidence and Identification of High-Risk Subgroups, 1998-2012. JAMA Dermatol 2015, 151: 976-81

Baker, S.R. (2007). Reconstruction of the Nose. Baker Locals Flap in Facial Reconstruction. 2nd ed. British: Mosby Elsevier, pp.415–474.

Bauer A, Diepgen TL, Schmitt J. Is occupational solar ultraviolet irradiation a relevant risk factor for basal cell carcinoma? A systematic review and meta-analysis of the epidemiological literature. Br J Dermatol 2011; 165: 612-25.

Baxter, J.M., Patel, A.N. dan Varma, S. (2012). Facial basal cell carcinoma. BMJ, 345, pp.e5342–e5342.

Carucci JA & Leffel D. 2008. Basal Cell Carcinoma.In: Wolff K. Goldsmith, Katz, Paller A, Fitzpatric's dermatology in general medicine. 7th ed. New York: Mc Graw Hill: 1036-1041

Cipto H, Suriadiredja A. Tumor Kulit. Dalam: Menaldi SL, Bramono K, Indriatmi W, editor. Ilmu Penyakit Kulit Dan Kelamin. 7th ed. Jakarta: Badan Penerbit FK UI; 2016. .262–276.

Gambichler T, Skrygan M, Hyun J, Bechara F, Tumi S, Altmeyer P, Krenter A. 2006. Cytokine mRNA expression in basal cell carcinoma. Arch Dermatol Res: 218, 141

Guy GP, Machlin SR, Ekwueme DU, Yabroff KR. Prevalence and Costs of Skin Cancer Treatment in the U.S., 2002−2006 and 2007−2011. Am J Prev Med. 2015; 48(2):183–187.

Iannacone MR, Wang W, Stockwell HG, et al. Patterns and timing of sunlight exposure and risk of basal cell and squamous cell carcinomas of the skin–a case-control study. BMC Cancer 2012; 12: 417.

Kasumagic-Halilovic, E., Hasic, M. dan Ovcina-Kurtovic, N. (2019). A Clinical Study of Basal Cell Carcinoma. Medical Archives, [online] 73(6), pp.394– 398.

Lanoe J, Goldenberg G. Basal cell carcinoma: A comprehensive review of existing and emerging non surgical therapies. The journal of clinical aesthetic dermatology. 2016; 9 (51): 26- 37

Mawardi, P., Kalim, H., Kalim, K.H., Fitri, L.E., Mintarjo, K., Mudigdo, A. et al. (2016). Mid-face location of primary basal cell carcinoma related to cancer aggressivity. Asian Pac J Trop Dis 2016; 6(8): 650-653

Mawardi, P., Kalim, H., Kalim, K.H., Fitri, L.E., Mintarjo, K., Mudigdo A. et al. (2019). The role of protein-53 amyloid in determining the aggressiveness of basal cell carcinoma regulated by interleukin-6, myeloid cell leukemia-1 and basic fibroblast growth factor. Dermatology Reports, 11(11).

Mawardi P, Kalim H, Kalim KH, Fitri LE, Mintarjo K, Mudigdo A. Mid-face location of primary basal cell carcinoma related to cancer aggressivity=. Asian Pac J Trop Dis 2016. 2016; 6(8):650–3

Nikmanian, S. (2019). Investigation of Microstructure and Corrosion Resistance of Dissimilar Welded Joint between 304 Stainless Steel and Pure Copper. Budapest International Research in Exact Sciences (BirEx) Journal Vol 1 (3): 76-82.

Ouhtit A. 2001. A model for UV induction of skin cancer. J Biomed Biotechnol; 1:5-6.

Sangy, S., Ata, F.A.M., and Miryousefiata, F. (2021). Study of Thymus and T- cell Development and Tumor Immunology. Budapest International Research in Exact Sciences (BirEx) Journal Vol 3 (3): 162-170.

Shimizu T. 2010. The role of macrophage inhibitor factor (MIF) in ultraviolet radiation induced carcinogenesis. Cancer; 2:1555-1564.

Tang JY, Epstein, EH Jr., Oro AE. Basal Cell Carcinoma and Basal Cell Nevus Syndrome. Dalam: Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, McMichael AJ, Orringer AJ. Fitzpatric's dermatology in general medicine. 9th ed. New York: Mc Graw Hill: 2019: 1884-1897.

Tilli, CML, Steensel MAM, Krekels GAM, Neumann HAM, Ramaeker. 2005. Molecular aetiology and pathogenesis of basal cell carcinoma. Br J Dermatol; 152 (6):1108-1124.