

Correlation between adjuvant radiotherapy and high-risk basal cell carcinoma patients at Dr. Soetomo Surabaya General State Hospital

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Abstract: Basal Cell Carcinoma (BCC) is a malignant epithelial neoplasm of the skin primarily affecting individuals with lighter skin tones. Patients with high-risk BCC often require more intensive treatment for proper management. This comparative study uses a descriptive-analytic design with a retrospective cohort study approach. The study sample consisted of all patients diagnosed with BCC who underwent wide excision at Dr. Soetomo General Hospital from 2019 to 2022, meeting the inclusion and exclusion criteria, selected through purposive sampling. The results showed that 58% of all BCC patients who experienced recurrence were female, with 56% of them having undergone radiotherapy. In the non-recurrent BCC group, 80% of patients received radiotherapy, with the majority being female. This study concludes a significant association between adjuvant radiotherapy and recurrence in high-risk BCC patients at Dr. Soetomo General Hospital, Surabaya.

Keywords: *Adjuvant radiotherapy, Basal cell carcinoma, Recurrent rate.*

1. Introduction

Basal Cell Carcinoma (BCC) is a malignant epithelial neoplasm of the skin that predominantly affects individuals with lighter skin tones. The prevalence of BCC is on the rise and represents about 70–80% of all skin cancers. A systematic review analyzing data from 38 countries from 1955 to 2007 revealed that Australia had the highest annual incidence rates of BCC (over 1,000 cases per 100,000 people), while some regions in Africa reported the lowest rates (fewer than 1 case per 100,000 people per year). In Asia, the incidence of BCC ranges from 1.5 to 15.57 per 100,000 population [1].

Basal cell carcinoma (BCC) rarely metastasizes, with a rate of less than 0.1%, but it can cause significant morbidity by infiltrating and destroying surrounding tissues. This can lead to disability, functional deficits, and, in rare cases, even death. Although BCC typically has a very low mortality rate, its ability to invade local structures can result in serious functional and cosmetic problems, particularly because most lesions develop on the face [1].

Surgical treatment is the most common strategy for managing both low-risk and high-risk basal cell carcinoma and is recognized as the most successful option for achieving a cure [2].

The risk of recurrence in BCC patients is divided into two categories: high risk and low risk. Low-risk BCC patients typically have tumors smaller than 2 cm, with well-defined margins, nodular or superficial BCC subtypes, and no evidence of perineural invasion. Conversely, high-risk BCC patients generally present with tumors ≥ 2 cm, located in high-risk areas such as the head, neck, or anogenital regions, with poorly defined margins, more aggressive and infiltrative pathological subtypes, and perineural invasion [3].

Basal cell carcinoma (BCC) can be treated through several methods, including radiotherapy, which can be used as either a primary treatment or as an additional therapy. However, radiotherapy is less ideal for tumors in areas with poor blood supply or those prone to injury, such as the pretibial region, since these areas are more vulnerable to trauma. In cases where there is microscopic residual disease following surgery and a higher risk of recurrence, adjuvant radiotherapy is more strongly advised [4].

In high-risk BCC patients, more aggressive therapy is required for effective management. Adjuvant radiotherapy is recommended for postoperative patients to minimize recurrence, particularly in high-risk BCC cases [5].

At Dr. Soetomo General Hospital, the impact of adjuvant radiotherapy on recurrence in high-risk BCC patients has not been extensively studied. Therefore, this study aims to further investigate the relationship between adjuvant radiotherapy and recurrence in high-risk BCC patients at Dr. Soetomo General Hospital, Surabaya.

The objective of this study is to determine whether there is a correlation between adjuvant radiotherapy and recurrence in high-risk BCC patients at Dr. Soetomo General Hospital, Surabaya.

2. Methods

This study is a comparative study using a descriptive-analytic research design with a retrospective cohort study approach. The study population includes all BCC patients who underwent wide excision at Dr. Soetomo General Hospital, Surabaya, from 2015 to 2022. The sampling technique used in this study was purposive sampling, resulting in a minimum of 30 samples that met the criteria, which included medical records of BCC patients who had undergone wide excision and were hospitalized in the Surgery Department of Dr. Soetomo General Hospital, as well as medical records of BCC patients who had received adjuvant radiotherapy.

The variables in this study consist of independent and dependent variables. The independent variable is adjuvant radiotherapy, and the dependent variable is the recurrence of high-risk BCC.

Data processing was carried out descriptively and through comparative analysis. The researcher used SPSS version 23.0 for Windows for data processing. Descriptive data of research variables will be presented in the form of tables, diagrams, and cross-tabulations. The analysis of independent and dependent variables will be statistically tested using the Chi-Square Test and the Spearman Test. Analysis of confounding variables will be conducted descriptively to assess differences between the sample groups. Furthermore, to determine the strength of the relationship, the Odds Ratio (OR) will be used as the measure of association.

This study complies with research ethical standards and has obtained approval from the ethics committee.

3. Results and Discussion

From this study, 18 samples were obtained in the case group, consisting of patients with recurrence, and 20 samples were obtained in the control group, consisting of patients without recurrence..

Table 1.
Sociodemographic characteristics of recidive BCC.

| | Frequency(N=64) | Percentage (%) |
|--------------------|-----------------|----------------|
| Radiotherapy | | |
| Radiotherapy | 10 | 56% |
| Tidak Radiotherapy | 8 | 44% |
| Gender | | |
| | 8 | 44% |
| Female | 10 | 56% |
| Age | | |
| <60 Years | 4 | 22% |
| >60 Years | 14 | 78% |
| Regio | | |
| H | 15 | 83,3% |
| M | 3 | 16,7% |
| L | 0 | 0% |
| Size | | |
| ≤ 2 cm | 3 | 17% |
| >2 cm | 15 | 83% |

At the table of BCC recurrence characteristics, a total of 18 samples were identified, with 56% of patients having undergone radiotherapy and 44% not undergoing radiotherapy. In the age category cases of recurrent BCC, the highest occurrence was found in patients aged > 60 years, with a prevalence of 78%. The most affected region group was recurrent BCC in the H region, with a prevalence of 83.3%. In the size category, the majority had a size of more than 2 centimeters was 83%.

Table 2.
Sociodemographic characteristics of recurrent BCC.

| | Freq. (N=64) | Perc. (%) |
|------------------|--------------|-----------|
| Radiotherapy | | |
| Radiotherapy | 16 | 80% |
| Non radiotherapy | 4 | 20% |
| Gender | | |
| Male | 8 | 40% |
| Female | 12 | 60% |
| Age | | |
| <60 years | 3 | 15% |
| >60 years | 17 | 85% |
| Regio | | |
| H | 12 | 60% |
| M | 8 | 40% |
| L | 0 | 0% |
| Size | | |
| ≤ 2 cm | 5 | 25% |
| >2 cm | 15 | 75% |

In the Non-Recurrent BCC characteristics table, there were 20 samples, with 80% of patients having undergone radiotherapy and 44% not having received radiotherapy. In the recurrent BCC group, the majority of cases were in patients aged over 60 years, accounting for 85%. For the anatomical region, the most affected area was the H region in recurrent BCC cases, comprising 60% of the samples. Regarding tumor size, the most common size was greater than 2 centimeters, observed in 75% of the cases.

3.1. The Analysis of the Relationship Between Recurrence and Adjuvant Radiotherapy

The relationship between recurrence and adjuvant radiotherapy was analyzed. The Chi-Square Test was performed to assess this relationship because both the independent and dependent variables are categorical data. Table 5.4 below shows the relationship between recurrence and adjuvant radiotherapy.

Table 3.

Correlation between radiotherapy and adjuvant radiotherapy.

| | Radiotherapy | | | | p | OR (CI 95%) |
|-------------|---------------------|----|-------------------------|----|--------|-------------|
| | Radiotherapy (N=26) | % | Non Radiotherapy (N=12) | % | | |
| Recurrent | | | | | | |
| Recurrent + | 10 | 56 | 8 | 44 | <0.023 | 5 (1,2-21%) |
| Recurrent - | 16 | 80 | 4 | 20 | | |

Based on Table 3 above, a significant relationship was found between recurrence and adjuvant radiotherapy. Among high-risk BCC patients who received adjuvant radiotherapy, the recurrence rate was 56%, while among those who did not receive adjuvant radiotherapy, the recurrence rate was 44%.

Based on the odds ratio calculation from the chi-square test, it was found that high-risk BCC patients who did not receive adjuvant radiotherapy had a 5 times (1.2-21%) higher likelihood of recurrence compared to high-risk BCC patients who received adjuvant radiotherapy. Additionally, the p-value was found to be <0.023.

Table 4.

Correlation between recurrent and gender.

| | Subtype | | % | P |
|-------------|-------------|---------------|----|-------|
| | Male (N=16) | Female (N=22) | | |
| Recurrent | | | | |
| Recurrent + | 8 | 10 | 45 | 0.789 |
| Recurrent - | 8 | 12 | 55 | |

3.2. Correlation Between Recurrent and Gender

Based on Table 4 above, it was found that there is no significant relationship between Recurrent and Gender. Patients experiencing Recurrent have a Gender proportion of Male 50% and Female 45% with a p-value of 0.789.

Table 5.

Correlation Between Recurrent and Age

| | Subtype | | % | P |
|-------------|-----------------|------------------|----|-------|
| | <60 years (N=7) | >60 years (N=31) | | |
| Recurrent | | | | |
| Recurrent + | 4 | 14 | 45 | 0.579 |
| Recurrent - | 3 | 17 | 55 | |

3.3. Correlation Between Recurrent and Age

Based on Table 5 above, it was found that there is no significant relationship between recurrence and age. Patients who experienced recurrence showed no significant difference in percentages between those aged >60 years (45%) and those aged <60 years (57%), with a p-value greater than 0.05.

Table 6.
Correlation between BCC with size.

| | Subtype | | % | P |
|-------------|------------|-------------|----|-------|
| | <2cm (N=8) | >2cm (N=30) | | |
| Recurrent | | | | |
| Recurrent + | 5 | 15 | 50 | 0.542 |
| Recurrent - | 3 | 15 | 50 | |

3.4. Correlation Between BCC with Size

Based on Table 6 above, it was found that there is no significant relationship between recurrence and tumor size. Among patients with tumor size >2 cm, 50% experienced recurrence, while 62.5% of patients with tumor size <2 cm had recurrence, with a p-value of 0.542.

Table 7.
Correlation between recurrent with Regio.

| | Subtype | | % | L (N=) | % | p |
|-------------|----------|----------|----|--------|---|-------|
| | H (N=27) | M (N=11) | | | | |
| Recurrent | | | | | | |
| Recurrent + | 15 | 3 | 27 | 0 | 0 | 0.119 |
| Recurrent - | 12 | 8 | 73 | 0 | 0 | |

3.5. Correlation Between Recurrent with Regio

Based on Table 7 above, it was found that there is no significant relationship between recurrence and region. Patients with recurrence in the H region had a percentage of 44.5%, while those in the M region had 27%, with a p-value of 0.119.

BCC on the head and neck can behave more aggressively and lead to greater morbidity and mortality. Aggressive characteristics include histological subtypes, large primary tumor size, location in the "H-zone" (the central face, eyes, and ears), and extracutaneous extension; additionally, disrupted surgical resection margins and recurrent disease, especially after previous definitive therapy, also carry a higher risk [6].

In an analysis using a large BCC patient database (N = 3381), an increase in the percentage of BCC with aggressive histological growth patterns was observed in younger patients. On the other hand, another analysis with a large number of subjects (N = 1000 to >10,000) showed that patients with BCC at a younger age were more likely to have superficial subtypes [5]. In this study, most patients were over 60 years old, but no significant relationship was found.

BCC developing in the head and neck area, including the "H-zone" or "mask area" on the face, has a higher likelihood of recurrence compared to those growing on the body and extremities. According to a retrospective review of 5755 BCC cases over 27 years, recurrences were significantly more frequent in tumors located in high-risk areas (central face, eyebrows, nose, lips, chin, ears, temples, genitalia, nipples/areolas, hands, feet, ankles, and nail units) with a diameter of 6 mm or greater. When tumors occurred in moderate-risk areas (cheeks, forehead, scalp, neck, jawline, pretibial surfaces) with a diameter of 10 mm or greater, recurrence was also more frequent [6]. Another study noted that recurrence risk depends on tumor size, localization, choice of treatment modality, and the clinician's experience [6]. In this study, the recurrence rate in the H region was highest at 44.5%, followed by the M region at 27%, but no significant value was found (p-value 0.119).

Surgery is the primary treatment for BCC. Considerations such as function, patient preference, and other factors may lead to choosing radiotherapy (RT) as the primary treatment for non-surgical candidates with both low and high-risk BCC, as well as patients with advanced-stage BCC (locally advanced, nodal, and metastatic). Recommendations for RT include adjuvant treatment for low-risk BCC after positive margins with standard excision. RT is also recommended for high-risk BCC as adjuvant therapy after standard excision, Mohs, or other forms of PDEMA with positive margins and additional treatment after negative margins if there is extensive perineural or large nerve involvement.

For these patients, local control has been reported to range from 50% to 90% with post-operative RT. However, there are conflicting data regarding the value of adjuvant RT after negative surgical margins, particularly following Mohs surgery. For high-risk BCC patients who have undergone multiple resections and for whom further surgery is not an option, RT is recommended as part of a multidisciplinary consultation if residual disease remains. Although adjuvant radiotherapy has been recommended for high-risk BCC patients, there is still no research to definitively prove its benefits [6].

Two meta-analyses reported a 5-year recurrence rate of 8.7% and 9.8% after RT for primary and recurrent BCC, respectively. Retrospective analyses of BCC treated with RT have reported a 5-year local control, healing, or complete response rate ranging from 93% to 96%, with 5-year recurrence rates from 4% to 16%. RT efficacy is better for low-risk, primary BCC (compared to recurrent BCC) or tumors with smaller diameters or a nodular histological subtype. A randomized prospective study of 347 patients who received either surgery (standard excision with a free margin of ≥ 2 mm from the visible boundary) or RT as the primary treatment found that BCC recurrence rates were higher with RT compared to surgery (7.5% vs. 0.7%; $P = 0.003$), with worse cosmetic outcomes and more postoperative complications [6]. This study also found similar results, where high-risk BCC patients without radiotherapy had a 5-fold higher likelihood of recurrence compared to those with radiotherapy [3].

The etiopathogenesis of recurrent BCC is multifactorial. Previous studies have investigated the risk factors that increase local recurrence in BCC patients. Several clinical and histological features contribute to recurrence, such as larger tumor size, lesions in the head/neck region, unclear margins, positive margins, and perineural invasion. This study also reported a 5-year recurrence rate of 15% for BCC surgery aimed at lesions larger than 15 mm, considering tumor size as a significant predictor of recurrence when adjusted for lesions on the ears, eyes, scalp, nose, or face. BCC with large size has a recurrence risk of 9%, compared to a 0.8% recurrence risk for small BCC. However, this study found different results. In the analysis of recurrence with tumor size, no significant relationship was found between recurrence and size. Among patients with tumors >2 cm, 50% had recurrence, while 62.5% of patients with tumors <2 cm had recurrence, with a p-value of 0.542 [7].

4. Conclusion

Based on the research results, it can be concluded that there is a significant relationship between adjuvant radiotherapy and recurrence in high-risk BCC patients at Dr. Soetomo Hospital, Surabaya. High-risk BCC patients without radiotherapy are 5 times more likely to experience recurrence compared to those with radiotherapy. Additionally, no significant relationship was found between recurrence and the characteristics of high-risk BCC patients.

Transparency:

The authors confirm that the manuscript is an honest, accurate, and transparent account of the study; that no vital features of the study have been omitted; and that any discrepancies from the study as planned have been explained. This study followed all ethical practices during writing.

Acknowledgement:

The author would like to express gratitude to Dr. Sahudi, dr., Sp.B. Subsp.KL(K), and Dr. Marjono Dwi Wibowo, dr., Sp.B. Subsp.KL(K), as the supervising professors for this research. The author also extends thanks to the Director of Dr. Soetomo General Hospital, Surabaya, for providing the opportunity to conduct this study at Dr. Soetomo General Hospital, Surabaya.

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