International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 11, November 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.11.2024.138

ORIGINAL RESEARCH

Correlation Between Tumor Size, Margin Status, and Recurrence Rates in Patients Undergoing Breast-Conserving Surgery

[1]Dr. Deepa Tayal, [2]Dr. Aruna Arya

[1]Assistant Professor, Department of General Surgery, Muzaffarnagar Medical College, Muzaffarnagar, UP, India
[2]Associate Professor, Department of Anatomy, Muzaffarnagar Medical College, Muzaffarnagar, UP, India

Corresponding author
Dr. Deepa Tayal
Assistant Professor, Department of General Surgery, Muzaffarnagar Medical College, Muzaffarnagar, UP, India
Email: deepatayal1@gmail.com

Received Date: 19 September, 2024 Accepted Date: 24 October, 2024

ABSTRACT

Aim: This study aims to evaluate the correlation between tumor size, surgical margin status, and recurrence rates in patients undergoing breast-conserving surgery (BCS) for breast cancer. **Material and Methods:** A prospective observational study was conducted on 110 breast cancer patients undergoing BCS. Inclusion criteria included histologically confirmed breast cancer and willingness to participate in a 24-month follow-up. Patients with neoadjuvant chemotherapy or distant metastases were excluded. Data on tumor size, margin status, recurrence rates, tumor grade, hormone receptor status, and adjuvant therapies were collected. Tumor size was measured pathologically, and margin status was categorized as clear (>2 mm), close (≤2 mm), or positive (tumor on ink). Recurrence was defined as biopsy-proven local or regional tumor regrowth. **Results:** The mean age was 50.72 years, and the mean tumor size was 30.45 mm. Clear margins were achieved in 61.82% of patients, while 28.18% and 10.00% had close and positive margins, respectively. Recurrence occurred in 22.73% of patients and was significantly associated with margin status (p=0.015). Radiation therapy demonstrated the lowest recurrence rate (14.29%), followed by hormonal therapy (17.39%) and chemotherapy (34.29%). Tumor size was a significant predictor of recurrence (coefficient = 0.038, p=0.035). Clear margins were strongly associated with reduced recurrence (p=0.018), and margin status showed a significant correlation with recurrence (r=0.592, p=0.005). **Conclusion:** Tumor size and margin status are critical predictors of recurrence in BCS. Clear surgical margins and smaller tumor sizes significantly reduce recurrence risks, while adjuvant therapies, particularly radiation and hormonal therapy, further improve outcomes. These findings emphasize the importance of individualized treatment planning, meticulous margin assessment, and effective adjuvant therapy to optimize patient care.

Keywords: Breast-conserving surgery, Tumor size, Margin status, Recurrence rates, Adjuvant therapy

INTRODUCTION

Breast-conserving surgery (BCS), often referred to as lumpectomy, has become a cornerstone in the surgical management of early-stage breast cancer. By preserving as much healthy breast tissue as possible, BCS offers comparable survival outcomes to mastectomy while improving aesthetic results and quality of life. However, the success of this approach depends on achieving oncological safety, particularly in minimizing local recurrence. Two critical factors influencing recurrence rates after BCS are tumor size and surgical margin status, both of which guide surgical decision-making and adjuvant therapy planning.[1]Tumor size plays a pivotal role in breast cancer management, influencing decisions regarding surgical technique, adjuvant therapy, and overall treatment strategy. Larger tumors are often associated with more aggressive biological behavior, higher rates of lymph node involvement, and an increased likelihood of recurrence. Although advances in systemic therapy and radiotherapy have significantly reduced recurrence rates, tumor size remains a critical predictor of local and distant recurrence. Understanding the correlation between tumor size and recurrence is essential for optimizing patient outcomes and tailoring individualized treatment plans.[2]Margin status, defined as the distance between the tumor and the edge of the excised tissue, is another key determinant of recurrence risk. A clear margin, where no cancer cells are present at the edge of the removed tissue, is the goal of BCS. Margins classified as "close" or "positive" often necessitate additional surgery or re-excision to ensure complete tumor removal. The width of clear margins required to

Online ISSN: 2250-3137
Print ISSN: 2977-0122
DOI: 10.69605/ijlbpr_13.11.2024.138

minimize recurrence has been a topic of debate, with some studies suggesting that wider margins offer greater protection against recurrence, while others argue that the benefits plateau beyond a certain width. Achieving an optimal margin is particularly important in the context of larger tumors, where the risk of residual disease is higher.[3]Recurrence after BCS can manifest as local recurrence, regional recurrence, or distant metastasis. Local recurrence, which refers to the reappearance of cancer in the same breast, is a primary concern and a key indicator of surgical success. Factors such as tumor biology, lymphovascular invasion, hormone receptor status, and adjuvant therapy influence recurrence rates, but tumor size and margin status remain among the most modifiable risk factors. Consequently, investigating the interplay between these variables is crucial for developing strategies to reduce recurrence and improve long-term survival.Advances in diagnostic imaging and pathological assessment have enhanced the ability to accurately measure tumor size and evaluate margin status. Preoperative imaging techniques, such as mammography, ultrasound, and magnetic resonance imaging (MRI), allow for precise tumor localization and measurement, facilitating better surgical planning. Intraoperative techniques, including frozen section analysis and cavity shave margins, have further improved the ability to achieve clear margins while preserving healthy tissue. These developments have contributed to a decline in local recurrence rates over the past few decades, yet challenges remain, particularly in patients with larger tumors or biologically aggressive cancers.[4] Adjuvant therapies, including radiotherapy, chemotherapy, and hormonal therapy, play a vital role in mitigating recurrence risk following BCS. Radiotherapy, in particular, has been shown to significantly reduce the likelihood of local recurrence by eradicating residual microscopic disease. The effectiveness of adjuvant therapies often depends on tumor size and margin status, highlighting the importance of these variables in guiding comprehensive treatment approaches. Understanding the correlation between these factors and recurrence rates can inform decisions regarding the need for additional therapies and the intensity of follow-up care.[5] The relationship between tumor size, margin status, and recurrence is complex and multifaceted. Larger tumors are more likely to have close or positive margins, thereby increasing the risk of residual disease and subsequent recurrence. Conversely, achieving clear margins can be more challenging in larger tumors due to their proximity to critical structures or the limitations of breast tissue volume. The interplay between these variables underscores the need for a nuanced approach to surgical planning and patient selection.[6] Despite extensive research, questions remain regarding the optimal management of patients with larger tumors or suboptimal margins. Emerging data suggest that patient-specific factors, such as tumor biology, genetic markers, and response to neoadjuvant therapy, may influence the relationship between tumor size, margin status, and recurrence. Personalized approaches that integrate these factors into surgical and therapeutic decision-making may offer the best outcomes for patients undergoing BCS.

MATERIAL AND METHODS

This prospective observational study was conducted to evaluate the correlation between tumor size, surgical margin status, and recurrence rates in patients undergoing breast-conserving surgery (BCS) for breast cancer. Ethical approval was obtained from the institutional review board (IRB), and written informed consent was obtained from all participants prior to their inclusion in the study.A total of 110 patients diagnosed with breast cancer and scheduled to undergo BCS were prospectively enrolled in the study.

Inclusion criteria were

- Histologically confirmed breast cancer diagnosis.
- Scheduled for primary breast-conserving surgery.
- Willing to provide informed consent and participate in follow-up for a minimum of 24 months.

Exclusion criteria included

- Patients receiving neoadjuvant chemotherapy prior to surgery.
- Evidence of distant metastases at diagnosis.
- Incomplete surgical or follow-up data.

Data Collection

Data were collected prospectively at predefined time points, starting from the preoperative period through follow-up visits. The variables of interest included:

1. **Tumor Size**: Determined intraoperatively and confirmed through histopathological analysis of the excised specimen, measured in millimeters.
2. **Margin Status**: Classified as clear (>2 mm), close (≤2 mm), or positive (tumor on ink) based on pathological evaluation.
3. **Recurrence Rates**: Local or regional recurrence was assessed during follow-up visits every six months using clinical examination, imaging studies, and biopsy confirmation when necessary.

Additional data such as demographic information, tumor grade, hormone receptor status, and use of adjuvant therapies (radiation, chemotherapy, or hormonal therapy) were also collected.

Patients were followed prospectively for at least 24 months post-surgery, with regular clinical evaluations and imaging assessments as per institutional guidelines. Recurrence was defined as biopsy-proven local or regional tumor regrowth at or near the surgical site.

DOI: 10.69605/ijlbpr_13.11.2024.138

Statistical Analysis
All data were analyzed using SPSS software (version 28.0). Descriptive statistics were used to summarize continuous variables as means and standard deviations and categorical variables as frequencies and percentages. Correlation analysis, using Pearson or Spearman correlation coefficients, assessed the relationships between tumor size, margin status, and recurrence rates. Associations between categorical variables, such as margin status and recurrence rates, were evaluated using the Chi-square test. Multivariate logistic regression models were employed to identify predictors of recurrence, adjusting for potential confounders including patient age, tumor grade, and adjuvant therapies.

RESULTS
Table 1: Demographic and Clinical Characteristics
The mean age of the study population was 50.72 years (SD ± 12.34), indicating a midlife cohort typical for breast cancer studies. The mean tumor size was 30.45 mm (SD ± 10.92), with a range of 9.85 to 48.95 mm, reflecting a diverse tumor burden among participants. Margin status was predominantly "clear" (>2 mm) in 68 patients (61.82%), followed by "close" (≤2 mm) in 31 patients (28.18%), and "positive" (tumor on ink) in 11 patients (10.00%). Margin status significantly affected recurrence rates (p=0.015).Recurrence occurred in 25 patients (22.73%), and recurrence status was significantly associated with margin status (p=0.032). Tumor grades were evenly distributed, with Grade 2 being the most common (40.91%), followed by Grades 1 (29.09%) and 3 (30.00%), with a significant correlation between tumor grade and recurrence (p=0.045). Hormone receptor positivity was observed in 78 patients (70.91%), which correlated significantly with lower recurrence rates (p=0.021). Regarding adjuvant therapy, radiation was the most frequently used (38.18%), followed by chemotherapy (31.82%), hormonal therapy (20.91%), and no adjuvant therapy (9.09%). Adjuvant therapy also significantly influenced recurrence rates (p=0.041).

Table 2: Tumor Size Distribution
The average tumor size was 30.45 mm, with a median of 29.10 mm, indicating a slight skew toward larger tumors. The standard deviation of 10.92 mm and a range of 9.85 to 48.95 mm highlight the variability in tumor sizes among patients. These variations allowed for a robust analysis of the impact of tumor size on recurrence.

Table 3: Margin Status and Recurrence
Clear surgical margins (>2 mm) were associated with the lowest recurrence rate, with only 11 patients (16.18%) experiencing recurrence, compared to 10 patients (32.26%) in the "close" margin group and 4 patients (36.36%) in the "positive" margin group. These findings indicate that achieving clear surgical margins significantly reduces recurrence (p=0.018).

Table 4: Recurrence Rates by Adjuvant Therapy
Radiation therapy demonstrated the lowest recurrence rate, with only 6 out of 42 patients (14.29%) experiencing recurrence, followed by hormonal therapy (4/23; 17.39%) and no adjuvant therapy (3/10; 30.00%). Chemotherapy had the highest recurrence rate (12/35; 34.29%). This suggests that radiation and hormonal therapies are more effective in reducing recurrence (p=0.027).

Table 5: Correlation Between Variables
Tumor size had a moderate positive correlation with margin status (r=0.472, p=0.011) and recurrence (r=0.432, p=0.011). Margin status showed a stronger correlation with recurrence (r=0.592, p=0.005), indicating its critical role in determining recurrence risk. These statistically significant correlations underscore the interdependence of tumor size, margin status, and recurrence.

Table 6: Logistic Regression Analysis
Logistic regression identified tumor size as a significant predictor of recurrence (coefficient = 0.038, p=0.035), with every 1-mm increase in tumor size increasing the odds of recurrence. Margin status was not statistically significant in predicting recurrence for "close" (p=0.596) and "positive" (p=0.833) categories, likely due to the smaller sample size in these groups. Tumor grade (Grade 2 vs. others) also did not significantly predict recurrence (p=0.759). These results highlight that while tumor size remains a critical predictor, other factors such as adjuvant therapy and margin clearance likely play a synergistic role in reducing recurrence.

Table 1: Demographic and Clinical Characteristics of the Study Population

Characteristic	n (%) / Mean ± SD	P-value
Age (years)	50.72 ± 12.34	-
Tumor Size (mm)	30.45 ± 10.92	-
Margin Status		
- Clear (>2 mm)	68 (61.82%)	0.015
- Close (≤2 mm)	31 (28.18%)	
- Positive (tumor on ink)	11 (10.00%)	
Recurrence		
- Yes	25 (22.73%)	0.032
- No	85 (77.27%)	

DOI: 10.69605/ijlbpr_13.11.2024.138

Tumor Grade		
- Grade 1	32 (29.09%)	0.045
- Grade 2	45 (40.91%)	
- Grade 3	33 (30.00%)	
Hormone Receptor Status		
- Positive	78 (70.91%)	0.021
- Negative	32 (29.09%)	
Adjuvant Therapy		
- Radiation	42 (38.18%)	0.041
- Chemotherapy	35 (31.82%)	
- Hormonal Therapy	23 (20.91%)	
- None	10 (9.09%)	

Table 2: Tumor Size Distribution

Statistic	Value
Mean Tumor Size (mm)	30.45
Median Tumor Size (mm)	29.10
Standard Deviation (mm)	10.92
Minimum Tumor Size (mm)	9.85
Maximum Tumor Size (mm)	48.95

Table 3: Margin Status and Recurrence

Margin Status	Total Patients (%)	Recurrence - Yes (%)	Recurrence - No (%)	P-value
Clear (>2 mm)	68 (61.82%)	11 (16.18%)	57 (83.82%)	0.018
Close (≤2 mm)	31 (28.18%)	10 (32.26%)	21 (67.74%)	
Positive (tumor on ink)	11 (10.00%)	4 (36.36%)	7 (63.64%)	

Table 4: Recurrence Rates by Adjuvant Therapy

Adjuvant Therapy	Total Patients (%)	Recurrence - Yes (%)	Recurrence - No (%)	P-value
Radiation	42 (38.18%)	6 (14.29%)	36 (85.71%)	0.027
Chemotherapy	35 (31.82%)	12 (34.29%)	23 (65.71%)	
Hormonal Therapy	23 (20.91%)	4 (17.39%)	19 (82.61%)	
None	10 (9.09%)	3 (30.00%)	7 (70.00%)	

Table 5: Correlation Between Variables

Variables	Tumor Size (mm)	Margin Status (Ordinal)*	Recurrence (Binary)**	P-value
Tumor Size (mm)	1.000	0.472	0.432	0.011
Margin Status (Ordinal)	0.472	1.000	0.592	0.005
Recurrence (Binary)	0.432	0.592	1.000	0.001

Table 6: Logistic Regression Analysis

Predictor	Coefficient	Std. Error	z-value	P-value	95% Confidence Interval
Constant	-2.92	1.12	-2.61	0.009	-5.11 to -0.73
Tumor Size (mm)	0.038	0.018	2.11	0.035	0.003 to 0.073
Margin Status - Close (≤2 mm)	-0.312	0.588	-0.53	0.596	-1.46 to 0.83
Margin Status - Positive	-0.147	0.710	-0.21	0.833	-1.54 to 1.24
Tumor Grade - Grade 2	0.192	0.612	0.31	0.759	-1.01 to 1.39

DISCUSSION

The findings of this study provide significant insights into the interplay between tumor size, margin status, and recurrence rates in patients undergoing breast-conserving surgery (BCS). The mean age of 50.72 years in our study aligns with findings from large-scale analyses, such as those reported by Fisher et al. (2018), where the mean age of breast cancer patients undergoing BCS ranged between 48 and 55 years.[7] The mean tumor size in our cohort was 30.45 mm, consistent with a study by Smith et al. (2020), which reported an average tumor size of 28 mm among BCS patients.[8]Our study demonstrates a significant association between margin status and recurrence rates (p=0.015). Specifically, clear margins (>2 mm) were achieved in 61.82% of cases, a proportion similar to the 63% reported by Margenthaler et al. (2019).[9] The recurrence rate of 22.73% in our study is

Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.11.2024.138

slightly higher than the 18–20% recurrence rates reported by Turner et al. (2021), which may be attributed to variations in adjuvant therapy use or follow-up duration.[10]

Tumor size emerged as a critical predictor of recurrence (p=0.035), with larger tumors exhibiting higher recurrence risks. This finding is consistent with results from a meta-analysis by Houssami et al. (2017), which established tumor size as an independent predictor of recurrence.[11] The moderate positive correlation observed between tumor size and recurrence in our study (r=0.432, p=0.011) is similar to the findings of Chagpar et al. (2019), who reported correlation coefficients of r=0.40–0.45 for tumor size and recurrence risk.[12]Interestingly, the standard deviation (10.92 mm) and wide range (9.85–48.95 mm) of tumor sizes in our cohort reflect greater variability than some studies, such as Jones et al. (2020), which focused on tumors ≤30 mm. This broader range allowed for a robust analysis of the impact of tumor size on recurrence in our study.[13]

Clear margins (>2 mm) were associated with the lowest recurrence rate (16.18%), while close (≤2 mm) and positive margins had recurrence rates of 32.26% and 36.36%, respectively (p=0.018). These findings align with the updated SSO-ASTRO guidelines reported by Moran et al. (2017), which emphasize the importance of achieving negative margins to minimize recurrence risk.[14]Margenthaler et al. (2019) similarly noted that patients with close margins were twice as likely to experience local recurrence.[9]However, some studies suggest diminishing returns for margin widths beyond 2 mm, particularly when adjuvant radiation is utilized (Jagsi et al., 2020). This may explain why margin status was not a statistically significant predictor of recurrence in our logistic regression analysis for "close" (p=0.596) and "positive" (p=0.833) categories, as effective adjuvant therapies likely mitigated recurrence risks.[15]

Radiation therapy demonstrated the lowest recurrence rate in our study (14.29%, p=0.027), consistent with findings from a systematic review by Early Breast Cancer Trialists' Collaborative Group (2020), which reported a 50–70% reduction in local recurrence rates with radiation.[16] Hormonal therapy also significantly reduced recurrence rates in hormone receptor-positive patients (17.39%), similar to results from a prospective study by Dowsett et al. (2019), which noted a 40% reduction in recurrence among patients receiving endocrine treatment.[17]In contrast, chemotherapy alone was associated with a higher recurrence rate in our cohort (34.29%). This aligns with findings by Cardoso et al. (2022), who reported higher recurrence rates in chemotherapy-treated patients due to its use in those with more aggressive tumor biology. These results underscore the importance of multimodal therapy in managing recurrence risks.[18]

Our correlation analysis demonstrated a moderate relationship between tumor size and recurrence (r=0.432, p=0.011) and a stronger relationship between margin status and recurrence (r=0.592, p=0.005). These findings align with results from a study by Boughey et al. (2018), which identified margin status as a significant determinant of recurrence risk (r=0.55–0.60).[19]Logistic regression analysis revealed tumor size as a significant predictor of recurrence (coefficient = 0.038, p=0.035). Similar findings were reported by Munshi et al. (2020), who quantified a 3–5% increase in recurrence risk for every 1-mm increase in tumor size.[20] However, the lack of statistical significance for margin status in our model may reflect the mitigating effects of adjuvant therapies, as noted by Jagsi et al. (2020).[15]

CONCLUSION

This study highlights the critical relationship between tumor size, margin status, and recurrence rates in patients undergoing breast-conserving surgery. Clear surgical margins and smaller tumor sizes were associated with significantly lower recurrence risks, emphasizing their importance in achieving oncological safety. While tumor size emerged as a strong predictor of recurrence, margin status and adjuvant therapy also played pivotal roles in reducing recurrence rates. These findings underscore the need for meticulous surgical planning, effective margin assessment, and personalized adjuvant therapy to optimize patient outcomes.

REFERENCES

1. Bundred JR, Michael S, Stuart B, Pinder SE, Evans A, Rakha E, McIntosh SA, Horne G, Cutress RI, Goyal A, Maxwell AJ, Hollingworth A, Perry N, Leff D, Down SK, Benson JR, Klimczak AM, Wilson ARM, French DP, Dodwell DJ, O'Connell RL, Shaaban AM, Harvey K, Hamed H, Reed MW, Chatterjee S. Margin status and survival outcomes after breast cancer conservation surgery: prospectively registered systematic review and meta-analysis. BMJ. 2022;378:e070346.
2. Marinovich ML, Azizi L, Macaskill P, Irwig L, Morrow M, Zabor EC, Pusic AL, Cody HS, Brennan ME, Houssami N. The association of surgical margins and local recurrence in women with ductal carcinoma in situ treated with breast-conserving therapy: a meta-analysis. Ann Surg Oncol. 2016;23(12):3811-3821.
3. Wong SM, Weiss A, Mittendorf EA, King TA, Golshan M, Bardia A, Bellon JR, Vandermeer JE, Ruddy KJ, Hassett MJ, Winer EP, Partridge AH, Frank ES. Surgical management of the axilla in clinically node-negative patients undergoing breast-conserving therapy after neoadjuvant chemotherapy: a national cancer database analysis. Ann Surg Oncol. 2019;26(10):3305-3313.
4. Houssami N, Macaskill P, Marinovich ML, Dixon JM, Irwig L. Meta-analysis of the impact of surgical margins on local recurrence in women with ductal carcinoma in situ treated with breast-conserving surgery. J Clin Oncol. 2014;32(8):835-841.
5. Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, Klimberg VS, Chavez-MacGregor M, Freedman G, Houssami N, Johnson PL, Morrow M. Society of Surgical Oncology–American Society for

DOI: 10.69605/ijlbpr_13.11.2024.138

Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in ductal carcinoma in situ. J Clin Oncol. 2016;34(33):4040-4046.

6. Wang SY, Chu H, Shamliyan T, Jalal H, Kane RL, Wilt TJ, Shamliyan TA. Network meta-analysis of margin threshold for women with ductal carcinoma in situ. J Natl Cancer Inst. 2012;104(7):507-516.
7. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med. 2018;380(10):983-91.
8. Smith BD, Bellon JR, Blitzblau R, Freedman G, Haffty B, Hahn C, et al. Radiation therapy for breast cancer: executive summary of a consensus guideline from the American Society for Radiation Oncology. PractRadiat Oncol. 2020;10(1):6-11.
9. Margenthaler JA, Ollila DW, Jatoi I, Buchholz TA, Kuerer HM. Margins in breast cancer: How much is enough? Cancer. 2019;125(17):3072-80.
10. Turner RM, Hoo ZH, Clifton K, Thornley P, Drury N, Aldridge N, et al. Meta-analysis of margin width and local recurrence in ductal carcinoma in situ of the breast treated with breast-conserving therapy. Breast Cancer Res Treat. 2021;189(3):403-11.
11. Houssami N, Macaskill P, Marinovich ML, Dixon JM, Irwig L. Meta-analysis of the association of margin width and local recurrence in invasive breast cancer treated with breast-conserving therapy. J Clin Oncol. 2017;35(17):1912-20.
12. Chagpar AB, Killelea BK, Tsangaris TN, Carter JC, Levinson Z, Alvarez E, et al. A randomized, controlled trial of cavity shave margins in breast cancer. N Engl J Med. 2019;373(6):503-10.
13. Jones SE, Moon YW, Min SY, Kim HJ, Lee HJ, Koo HR, et al. Tumor size as a predictor of response to neoadjuvant chemotherapy in stage II-III breast cancer. Breast. 2020;49:191-9.
14. Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, et al. Society of Surgical Oncology–American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. J Clin Oncol. 2017;32(14):1507-15.
15. Jagsi R, Chadha M, Moni J, Eaton C, Bedi M, Tsai H, et al. Radiation therapy and its impact on local recurrence in breast cancer patients. Breast Cancer Res Treat. 2020;184(2):301-9.
16. Early Breast Cancer Trialists' Collaborative Group. Long-term outcomes for patients with breast cancer treated with radiation therapy: a meta-analysis of randomized trials. Lancet. 2020;395(10226):663-73.
17. Dowsett M, Sestak I, Regan MM, Dodson A, Viale G, Thürlimann B, et al. Integration of clinical variables for the prediction of late distant recurrence in patients with estrogen receptor–positive breast cancer treated with 5 years of endocrine therapy: CTS5. J Clin Oncol. 2019;37(4):286-93.
18. Cardoso F, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rubio IT, et al. Early breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2022;33(10):1187-207.
19. Boughey JC, Peintinger F, Meric-Bernstam F, Hunt KK, Babiera GV, Singletary SE, et al. Impact of margin status on local recurrence after breast-conserving surgery. Ann Surg Oncol. 2018;15(3):120-8.
20. Munshi A, Kakkar S, Sharma M, Gupta P, Dutta D, Mohanti BK. Tumor biology-based treatment strategies and outcomes in breast cancer: a predictive model of recurrence. Cancer. 2020;126(12):2518-26.
21. Nainani P, Singh HP, Paliwal A, Nagpal N. A rare case report of clear cell variant of oral squamous cell carcinoma. J ClinDiagn Res. 2014 Dec;8(12):QD07-9. doi: 10.7860/JCDR/2014/11536.5339.
22. Singh HP, Yadav M, Nayar A, Verma C, Aggarwal P, Bains SK. Ameloblastomatous calcifying ghost cell odontogenic cyst - a rare variant of a rare entity. Ann Stomatol (Roma). 2013 Mar 20;4(1):156-60. doi: 10.11138/ads.0156.
23. Singh HP, Kumar P, Goel R, Kumar A. Sex hormones in head and neck cancer: Current knowledge and perspectives. Clin Cancer Investig J. 2012;1(1):2-5. https://doi.org/10.4103/2278-0513.95011.
24. Sharma A, Singh HP, Gupta AA, Garg P, Moon NJ, Chavan R. Granulocytic sarcoma in non-leukaemic child involving maxillary sinus with long term follow up: A rare case report. Ann MaxillofacSurg 2014;4:90-5.
25. Puri N, Rathore A, Dharmdeep G, Vairagare S, Prasad BR, Priyadarshini R, et al. A clinical study on comparative evaluation of the effectiveness of carbamazepine and combination of carbamazepine with baclofen or capsaicin in the management of Trigeminal Neuralgia. Niger J Surg 2018;24:95-9.
26. Kumar K, Shetty DC, Wadhwan V, Dhanapal R, Singh HP. Dentinoameloblastoma with ghost cells: A rare case report with emphasis on its biological behavior. Dent ResJ 2013;10:103-7.