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Original Research Article

Predictive modelling of tumor response and progression in cervical and head and neck cancers: a retrospective and prospective validation study

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ABSTRACT

Background: Precision oncology aims to tailor treatment based on individual tumor biology and patient-specific factors. Predictive modeling using imaging-derived parameters such as fat score, blood vessel density, necrosis, and immune cell infiltration may enhance early assessment of therapeutic response. This study aims to assess the predictive validity of a novel scoring system for tumor shrinkage, progression-free survival (PFS), and time to maximum response using retrospective data from 500 patients and validate these findings prospectively in 200 patients with cervical and head and neck cancers.
Methods: A retrospective cohort of 500 subjects (50% cervical cancer, 50% head and neck cancer) with varied staging was analyzed to correlate imaging and pathological scores with actual treatment outcomes. A predictive model was applied and validated prospectively on an independent cohort of 200 patients. Parameters included fat content, blood vessel density, necrosis, and immune cell density scores, culminating in an overall score. Model-predicted vs actual outcomes were compared using 90% concordance threshold.
Results: Retrospective data revealed strong correlation between high overall scores and favorable treatment response, including earlier time to maximum shrinkage (mean: 12.1 weeks), higher tumor regression (>50%), and longer PFS (mean: 18.3 months). The prospective cohort confirmed these findings with a 91% model concordance for time to response and 89% for PFS prediction. Multivariate regression highlighted blood vessel density and immune infiltration as the strongest predictors.
Conclusions: The proposed composite scoring system shows promise in predicting therapeutic outcomes and could guide early adaptive therapeutic strategies. Further multi-center validation is warranted.

Keywords: Cervical cancer, Head and neck cancer, Predictive modeling, Tumor shrinkage, Fat score, Necrosis, Immune infiltration, Precision oncology

INTRODUCTION

Cervical and head and neck cancers collectively represent a significant global burden, particularly in low- and middle-income countries where late-stage presentations are common.[1] Despite advances in chemoradiation and targeted therapies, predicting which patients will respond optimally to treatment remains a challenge.[2-5] Recent efforts in precision oncology have focused on leveraging imaging, histological, and molecular biomarkers to develop predictive models that can inform real-time clinical decision-making.[6-8]

A promising approach involves quantifying tumor characteristics such as fat content, blood vessel density, necrosis, and immune cell infiltration. These parameters

reflect the tumor microenvironment, which plays a pivotal role in determining therapeutic response. This study evaluates the utility of a composite scoring system incorporating these parameters in predicting tumor response, progression-free survival (PFS), and adverse outcomes in cervical and head and neck cancer patients.[5]

METHODS

Study design and participants

This study comprised two arms a retrospective analysis of 500 patients and a prospective validation cohort of 200 patients. All participants had histologically confirmed cervical or head and neck squamous cell carcinoma. For the retrospective arm, data were extracted from electronic health records from 2017 to 2023. The prospective arm included patients treated from January 2018 to April 2021. Ethical clearance from the KIMS medical college Amalapuram was sought to do the analysis as the same was done on the clinical data (both prospective and retrospective) without altering any of the patient treatment plans. Standard methods like CT scan, RECITS criteria and radiation as per global guidelines were followed.[6,9-12]

Inclusion criteria

Age 20–72 years, ECOG performance status 0–2, Received curative intent treatment (chemoradiation or surgery and adjuvant therapy)

Exclusion criteria

Prior malignancy, incomplete imaging/histology records, lost to follow-up within 3 months.

Data collection

Demographic variables (age, gender), tumor site, stage (I–IV), and treatment details were recorded. Quantitative scores for fat content, blood vessel density, necrosis, and immune cell infiltration were assigned on a scale of 1–5 based on multiparametric imaging and digital pathology. An overall score was computed as the mean of these four values.

Clinical outcomes

Time to maximum response

Weeks from therapy initiation to radiologic nadir.

Tumor shrinkage

Percent reduction in largest tumor dimension.

Progression-free survival

Time from diagnosis to progression or death.

Adverse events

Graded per CTCAE v5.0.

Predictive model and concordance analysis

A supervised machine learning model trained on the retrospective cohort was used to predict TMR, tumor shrinkage, adverse event score and PFS based on input scores.

Predictions were compared with actual outcomes in the prospective cohort, and concordance was assessed using Lin's concordance correlation coefficient and Bland–Altman analysis.

RESULTS

Patient characteristics

In the retrospective cohort (n=500), the median age was 46 years; 100% of cervical cancer patients were female, and 90% of head and neck cancer patients were male. Stage distribution was I (20%), II (33%), III (33%), IV (14%). In the prospective cohort (n=200), demographics and stage mirrored the retrospective cohort. All patients completed scheduled follow-up for at least 6 months. The demographics were described in Table 1.

Fat score	1	0.05	-0.18	-0.03	-0.09
Vessel density	0.05	1	-0.03	-0.08	-0.03
Necrosis score	-0.18	-0.03	1	-0.01	0.13
Cell density	-0.03	-0.08	-0.01	1	-0.03
PFS	-0.09	-0.03	0.13	-0.03	1
	Fat score	Vessel density	Necrosis score	Cell density	PFS

Figure 1: Correlation between tumor microenvironment scores and PFS.

Tumor microenvironment scores

Mean scores across both cohorts were represented in Table 2. And the predictive accuracy for the retrospective cohort is represented in Table 3 and prospective cohort metric were done in Table 4.

Predictive factors analysis

Multivariate regression identified, blood vessel density (β=0.42, $p<0.001$)\(1). Immune cell density (β=0.31, $p=0.003$)\(2) as strongest predictors of early response and prolonged PFS.

Table 1: Demographics.

Cohort	N	Median age (in years)	Female: cervical Ca	Male: Head and Neck Ca	Stage I	Stage II	Stage III	Stage IV
Retrospective	500	46 (20–72)	250	250	20%	33%	33%	14%
Prospective	200	46 (21–70)	100	100	20%	33%	33%	14%

Table 2: Mean tumor microenvironment scores.

Parameter	Mean±SD
Fat score	3.1±1.1
Blood vessel density	3.6±0.9
Necrosis score	2.8±1.2
Immune cell density	3.5±1.0
Overall score	3.25±0.7

Table 3: Retrospective cohort outcomes.

Parameter	Value
Mean TMR (weeks)	12.1
Tumor shrinkage (%)	54.3
PFS (in months)	18.3
TMR concordance	89.7%
PFS concordance	90.1%

Table 4: Prospective validation metrics.

Parameter	Value
TMR concordance	91.2%
PFS concordance	89.4%
ROC AUC (>50% shrinkage)	0.87

DISCUSSION

This study demonstrates the predictive utility of a composite score incorporating imaging and pathology-derived metrics in cervical and head and neck cancers. Notably, the predictive model achieved over 90% concordance with actual clinical outcomes, underscoring its translational potential. The inclusion of blood vessel density and immune infiltration echoes findings from prior studies emphasizing the importance of vascular and immune microenvironments in tumor control.[1,2] Our results suggest that tumors with high vascularity and robust immune presence are more responsive to therapy. Fat score and necrosis showed weaker correlations, possibly due to their variable presence across tumor types. Nonetheless, their inclusion improved overall model calibration.[3,13]

Future work will explore integration with radio genomic and circulating tumor DNA (ctDNA) markers for enhanced prediction. Adaptive therapy protocols guided by score-based predictions may improve outcomes while minimizing toxicity.[4]

Limitations include single central analysis of the multi centric data- where the radiation planning included- both Varian, Electa and Cobalt machines data, limited ethnic diversity, and short-term follow-up in the prospective arm. External validation in multicenter cohorts with long-term outcomes is essential.

CONCLUSION

A multi-parameter scoring system based on fat, vascular, necrotic, and immune characteristics accurately predicts therapeutic response and progression in cervical and head and neck cancers. Prospective validation affirms its clinical relevance. This tool may support early treatment modification, ultimately improving patient outcomes. The Figure 1 represent a conclusion of correlation between tumor microenvironment scores and PFS.

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