Prognostic value of PET/CT and MR-based baseline radiomics among patients with Nasopharyngeal Carcinoma

Roshini Kulanthaivelu (roshini.kulanthaivelu@uhn.ca)
University Health Network https://orcid.org/0000-0002-2279-8346
Andres Kohan
University Health Network
Ricarda Hinzpeter
University Health Network
Zhihui Amy Liu
Princess Margaret Hospital Cancer Centre
Andrew Hope
University Health Network
Shao Hui Huang
University Health Network
John Waldron
University Health Network
Brian O'Sullivan
University Health Network
Claudia Ortega
University Health Network
Ur Metser
University Health Network
Patrick Veit-Haibach
University Health Network

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Abstract

Purpose

Radiomics is an emerging imaging assessment technique, which has shown promise predicting survival among nasopharyngeal carcinoma (NPC) patients. Studies so far have focused on MR-based radiomic analysis. The aim of our study was to evaluate the prognostic value of clinical and radiomic parameters derived from both PET/CT and MR.

Methods

Retrospective evaluation of 124 NPC patients with PET/CT and radiotherapy planning MR (RP-MR). Primary tumors were segmented using dedicated software (LIFEx .version 6.1) from PET, CT, contrast enhanced T1-weighted (T1-w), and T2-weighted (T2-w) MR sequences with 376 radiomic features extracted. Summary statistics described patient, disease and treatment characteristics. Kaplan Meier (KM) method estimated overall survival (OS) and progression free survival (PFS). Clinical factors selected based on univariate analysis and multivariate Cox model were subsequently constructed with radiomic features added.

Results

The final models comparing clinical, clinical + RP-MR, clinical + PET/CT and clinical + RP-MR + PET/CT for OS and PFS demonstrated that combined radiomics signatures were significantly associated with improved survival prognostication (AUC 0.62 vs 0.81 vs 0.75 vs 0.86 at 21 months for PFS and 0.56 vs 0.85 vs 0.79 vs 0.96 at 24 months for OS). Clinical + RP-MR features initially outperform clinical + PET/CT for both OS and PFS (< 18 months), and later in the clinical course for PFS (> 42 months).

Conclusion

Our study demonstrated that PET/CT-based radiomic features may improve survival prognostication among NPC patients when combined with baseline clinical and MR-based radiomic features.

Background

Nasopharyngeal carcinoma (NPC) is an epithelial malignancy arising from the mucosa of the nasopharynx and accounting for 0.7% of all malignancies [1]. NPC affects less than 1 person per 100 000 in North America [2], however is endemic in Southern China, the Middle East and North Africa [2]. Although the prognosis of NPC is largely good, with 5 year survival rates reaching up to 80% [3], 20–30% of patients experience treatment failure from locoregional recurrence or distant metastasis [4].

Radiotherapy with or without concurrent chemotherapy is regarded as standard of care for NPC, and accurate staging, including optimized imaging, is crucial for appropriate treatment stratification [5]. MR assessment is performed due to superior soft tissue contrast resolution compared with CT, and ^{18}Fluoride-Fluorodeoxyglucose-Position Emission Tomography/Computed Tomography (PET/CT) is utilized to evaluate for both the presence of a primary lesion in cases of diagnostic uncertainty, and for the presence of local lymph node and distant metastatic disease. Increasing stage has been demonstrated to be associated with poorer prognosis [3, 6], however if these patients are identified early, escalated therapy strategies can be employed.

Outside of conventional TNM staging, there is no consensus on specific prognostic biomarkers that can potentially improve survival among NPC patients [4]. Various clinical factors such as EBV tire, hemoglobin, LDH, CRP, neutrophil to lymphocyte ratio and platelet counts have been identified as factors potentially associated with poor survival [6, 7], however the clinical utility of these parameters, outside of EBV titer [4], is limited and new tools are required to identify patients at risk of poor prognosis. In recent years, radiomics has emerged as a promising field which can potentially provide a means of improved prognostication.

Radiomics is an extension of computer aided diagnosis and detection and relies upon the concept that ‘medical images contain information about disease specific processes that are imperceptible to the human eye’ [8]. Images are converted to mineable data that are analyzed using computer algorithms both quantitatively, in terms of spatial distribution of signal intensities and pixel interrelationships, and qualitatively, in terms of differences in intensity, shape or texture [8–10].

Multiple studies dating as far back as 2017 have demonstrated that multiparametric MR-based radiomic parameters can be utilized to predict prognosis, progression/progression free survival (PFS) and recurrence in patients with advanced NPC [6, 11–19] and non-metastatic NPC [20, 21] with superior prognostic performance over TNM staging [17, 22].

Metabolic parameters derived from PET/CT have revolutionized oncological imaging [7]. In terms of radiomic analysis, more recent studies have utilized radiomic features from baseline PET/CT to quantitatively characterise intra-tumoral heterogeneity and provide prognostic information among patients with NPC, with prediction of locoregional recurrence and distant metastasis in advanced NPC [7, 23, 24].

There have not however been any studies in the literature so far that have evaluated the association between radiomic signatures on both PET/CT and MR and clinical parameters among patients with NPC. The aim of this study was to therefore evaluate and compare the prognostic value of clinical data, radiomic features extracted from PET/CT and MR both separately and combined.

Materials And Methods

This retrospective study was approved by the institutional review board and the need to obtain informed consent from patients was waived.

Patient Selection

146 patients with pathologically confirmed NPC (Stage I-IVC), underwent staging with PET/CT between December 2012 and July 2018 at University Hospital Network, Toronto. Of these, 130 patients had undergone MR for the purpose of radiotherapy planning (RP-MR). 6 patients with stage M1 (treated with palliative intent) were excluded. Subsequently 124 patients with curative therapeutic intent with both PET/CT and RP-MR scans were included for analysis.

Demographic details (age, sex), as well as multiple clinical parameters including ECOG, smoking history, pathology, EBER, EBV titer, HPV, TNM staging, date of diagnosis and last follow up, treatment intent and regimen, RT dates, dose, and follow up data including local, regional or distant failure, date and status at last follow up were collated and are summarized in Table 1. Staging was performed according to the American Joint Committee on Cancer TNM staging System Manual, 7th edition. Patient follow up was measured from date of diagnosis to day of last follow up. Overall Survival (OS) was defined as date of diagnosis to date of death/last follow up, with PFS defined from date of diagnosis to date of local, regional or distant failure.

Table 1
Population characteristics

	n = 124
Sex (n)	
Male	84% (104)
Female	16% (20)
Age in years (SD)	54.8 (11.6)
Smoking History (n)	
Current	21% (26)
Ex-Smoker	26% (32)
Never	50% (62)
Unknown	3% (4)
Primary (n)*	
NPC Type 1/2	25% (31)
NPC Type 3	75% (93)
Viral State (n)	
EBER +	89% (110)
HPV +	6% (8)
Non-Viral	3% (4)
Unknown	2% (2)
mean EBV Titer (IU/ml, SD)	30433.3 (175831.1)
T Stage (n) ‡	
1/2	43% (54)
3	31% (38)
4	26% (32)
N Stage (n) ‡	
0	15% (18)
1	32% (40)
2	43% (53)
3	10% (13)
M Stage (n) ‡	
0	100% (124)
Overall Stage (n) ‡	
I-III	66% (82)
IV	34% (42)
RT/CRT Regimen (n)	
CCRT - RT	36% (45)
CCRT + AC - IC + CCRT	64% (79)

*WHO classification ‡7th edition UICC/AJCC staging system

Image Acquisition

PET

Pretreatment whole body PET/CT was acquired on a Siemens mCT40 PET/CT scanner (Siemens Healthineers, Erlangen, Germany). Patients were positioned supine with images obtained from the top of the skull to the upper thighs. Iodinated oral contrast material was administered for bowel opacification; no intravenous iodinated contrast material was used. Patients were injected with 300-400MBq (4–5 MBq/kg) of ^{18}Fluoride-Fluorodeoxyglucose (^{18}F-FDG) after having fasted for 6 hours, and PET/CT scanning performed after approximately 60 minutes. Overall, 5–9 bed positions were obtained, depending on patient height, with an acquisition time of 2–3 min per bed position. CT parameters were 120 kV; 3.0 mm slice width, 2.0 mm collimation; 0.8 sec rotation time; 8.4 mm feed/rotation. A PET emission scan using time of flight with scatter correction was obtained covering the identical transverse field of view. PET parameters were as follows: image size: 2.6 pixels; slice: 3.27; and 5-mm full width at half maximum (FWHM) gaussian filter type [25] .

RP-MRI

All patients were examined on a 3.0T MRI scanner for radiotherapy planning (Siemens Magnetom Verio syngo MR B17, Siemens Healthineers, Erlangen, Germany). Post contrast T1-weighted (T1-w) and T2-weighted (T2-w) MR images were acquired with the following parameters: axial T1-w turbo spin-echo fat saturated images post contrast (TR 1240 ms/TE 11ms, ET 256 x 205, FOV 24 x 24cm, slice thickness 3 mm) and axial T2-w turbo spin-echo fat saturated images (TR 8290 ms, TE 117 ms, ET 22, FOV 24 x 24 cm, slice thickness 3mm).

Radiomic Feature Extraction

Radiomic features were extracted using LIFEx platform version 6.1 (IMIV/CEA, Orsay France)[26] from axial PET, low-dose unenhanced CT (acquired as part of the PET/CT), axial fat saturated and contrast enhanced T1-w and T2-w RP-MR Digital Imaging and Communications in Medicine (DICOM) images that had been archived in PACS. Semi-automatic segmentation of the PET component was performed using a thresholding method, with minor manual correction as required. Volumetric segmentation of the tumor on CT and MRI was carried out manually. To account for the impact of different resampling schemes in MR, a fixed bin width of 128 bins, which corresponded to absolute resampling was chosen after initial sampling of healthy normal tissue (masseter muscle) for reference)[27]. Segmentation was performed by one radiologist with 7 years experience (RK). Only primary lesions were considered in the study; lymph nodes or secondary lesions were not included. 94 radiomic features were obtained from each imaging sequence.

Statistical Analysis and Modelling

Summary statistics were used to describe patient, disease and treatment characteristics. Kaplan Meier (KM) method was used to estimate OS and PFS.

Preprocessing of the radiomic data included removing features with more than 50% missing observations, and removing features with little variation (those with < 4 unique values). The value of the 99.9 percentile was used to cap the upper extreme values for each feature. All features were standardized with a mean of zero and standard deviation of one.

Clinical factors were selected based on clinical judgement and statistical significance i.e. with a p-value < 0.05 in the univariable analyses (UVA), to build a multivariable Cox proportional hazards model for OS and PFS respectively. Subsequently each radiomic feature was added to the clinical model. Features with a p-value < 0.01 were selected for correlation assessment. Highly correlated features (with a Pearson's correlation coefficient > 0.5) were filtered out. The final model included both clinical variables and radiomic features. Model performance was quantified and visualized using area under the time-dependent ROC curve (AUC), calculated using leave-one-out cross-validation.

Results

Population Characteristics

Out of the 124 patients analyzed, 84% (n = 104) were males, 50% (n = 62) had never smoked and 95% (n = 118) had had previous infection by either HPV or EBV, with a mean EBV titer of 30433.5 IU/ml. Mean age was 54.8y (± 11.6) and the majority had stage III disease or lower (66%, n = 82) (Table 1).

OS and PFS of our population can be seen in Figs. 1 and 2 respectively. Median follow up period was 50.3 months (range 4.5 to 88.3 months). Overall, 13 cancer related deaths and 28 patients with relapse of their index disease were noted during the follow up period. In both cases most of these events (100% for OS and 96% for PFS) happened before the 48 months.

Statistical analysis of prognostic factors

Univariate statistical analysis was performed for the clinical parameters, as demonstrated in Table 2. When assessing PFS, age was found to be significant while for OS, both age and treatment regimen (RT CRT Regimen) were found to be significant. Age was the only factor that remained significant in both cases when multivariate analysis was performed. However, given the number of events in each case, a decision was made to only include age in the final model for OS and to include both age and treatment regimen (RT CRT Regimen) into the model for PFS despite being non-significant in the multivariate analysis.

Table 2
Univariate analysis of clinical variables

Covariate	OS			PFS		
	HR (95% CI)	p-value	n	HR (95% CI)	p-value	n
Age	1.05 (1.00,1.10)	**0.043**	124	1.05 (1.01,1.08)	**0.0046**	124
Sex	Not Estimable	1	124	2.64 (0.63,11.11)	0.19	124
ECOG PS	2.70 (0.91,8.04)	0.074	124	1.46 (0.68,3.12)	0.33	124
Smoking PY	1.01 (0.98,1.05)	0.38	118	1.01 (0.99,1.03)	0.51	118
Hx Smoking	1.83(0.34,10.01)	0.92	124	2.05 (0.63,6.65)	0.67	124
Ex Smoker	1.40 (0.29,6.74)			1.46 (0.48,4.45)		
NOn-smoker	Not Estimable			1.91(0.21,17.14)		
Unknown						
Primary Pathology	1.40 (0.29,6.74)	0.55	124	0.98 (0.42,2.31)	0.97	124
EBER	Not Estimable	0.37	124	0.44 (0.17,1.16)	0.095	124
EBV Titer pre RT	1.00 (1.00,1.00)	0.59	120	1.00 (1.00,1.00)	0.59	120
HPV Status +	9.47(1.55,57.84)	**0.015**	124	2.61 (0.75,9.06)	0.31	124
TNM staging 7th						
T3	1.39 (0.35,5.56)	0.46	124	0.63 (0.24,1.66)	0.43	124
T4	2.28 (0.61, 8.48)			1.24 (0.53,2.91)		
N1	0.43 (0.09,2.11)	0.75	124	1.52 (0.42,5.54)	0.93	124
N2	0.69 (0.17,2.78)			1.44 (0.41,5.12)		
N3	0.46 (0.05,4.45)			1.59(0.32,7.87)		
Stage 7th	1.85 (0.62,5.50)	0.27	124	0.45 (0.21,0.95)	0.18	124
RT CRT Regimen	0.58 (0.19,1.72)	0.32	124	0.45 (0.21,0.95)	**0.035**	124

Statistically significant Radiomic feature were selected as described previously, resulting in the features listed in Table 3 for OS and Table 4 for PFS.

Table 3
Feature Selection for OS

Covariate	HR	95% CI lower BOUND	95% CI upper BOUND	p-value
PET_CONVENTIONAL_SUVbwQ1*	1.81	1.15	2.84	0.00981
PET_CONVENTIONAL_SUVbwQ2	1.83	1.17	2.86	0.00808
PET_CONVENTIONAL_TLG.mL..onlyForPETorNM.	1.72	1.15	2.59	0.00862
PET_DISCRETIZED_SUVbwQ1	1.88	1.20	2.96	0.00627
PET_DISCRETIZED_SUVbwQ2	1.82	1.17	2.85	0.00825
PET_DISCRETIZED_TLG.mL..onlyForPETorNM.	1.75	1.16	2.63	0.00781
PET40_CONVENTIONAL_TLG.mL..onlyForPETorNM.	1.77	1.18	2.64	0.00573
PET40_DISCRETIZED_TLG.mL..onlyForPETorNM.	1.80	1.20	2.71	0.00449
PET40_GLZLM_GLNU	1.76	1.18	2.62	0.00572
CT_GLZLM_ZLNU	1.69	1.13	2.53	0.00991
RP_T1_SHAPE_Volume.vx.	1.67	1.28	2.19	0.00019
RP_T1_GLRLM_LRE	1.57	1.14	2.18	0.00634
RP_T1_GLRLM_GLNU	1.83	1.38	2.43	0.00002
RP_T1_NGLDM_Busyness	1.60	1.18	2.17	0.00234
RP_T1_GLZLM_GLNU*	1.68	1.15	2.46	0.00688
*** Chosen variables for the model after correlation analysis.**				

Table 4
Feature selection for PFS

Covariate	HR	95% CI lower BOUND	95% CI upper BOUND	p-value
PET_CONVENTIONAL_SUVbwmin	1.78	1.34	2.37	0.00008
PET_CONVENTIONAL_SUVbwQ1	1.90	1.38	2.61	0.00007
PET_CONVENTIONAL_SUVbwQ2	1.71	1.23	2.38	0.00157
PET_DISCRETIZED_SUVbwmin*	1.80	1.35	2.40	0.00006
PET_DISCRETIZED_SUVbwQ1	1.94	1.40	2.67	0.00006
PET_DISCRETIZED_SUVbwQ2	1.72	1.23	2.39	0.00133
PET_GLZLM_SZLGE	0.49	0.29	0.84	0.00884
RP_T1_CONVENTIONAL_Skewness*	1.64	1.16	2.31	0.00538
RP_T1_GLRLM_GLNU	1.49	1.14	1.94	0.00393
RP_T1_NGLDM_Busyness*	1.41	1.10	1.82	0.00766
*** Chosen variables for the model after correlation analysis.**				

The final model for OS included PET_CONVENTIONAL_SUVbwQ1 and RP_T1_GLZLM_GLNU, while for PFS a model was developed including PET DISCRETIZED SUVbwmin, RP T1 CONVENTIONAL Skewness and RP T1 NGLDM Busyness, as seen in Table 5.

Table 5
Final prognostic models for PFS and OS

Final Model for OS			RT MRI Model for PFS		
Covariate	**HR (95% CI)**	**p-value**	**Covariate**	**HR (95%CI)**	**p-value**
Age	1.06 (1.01,1.11)	**0.026**	**Age**	1.04 (1.00,1.08)	**0.06**
PET CONVENTIONAL SUVbwQ1	1.92 (1.18,3.13)	**0.0092**	**RT CRT Regimen**	0.63 (0.27,1.47)	0.28
RMP T1 GLZLM GLNU	1.70 (1.16,2.49)	**0.0062**	**PET DISCRETIZED SUVbwmin**	1.58 (1.14,2.19)	**0.0056**
			RP T1 CONVENTIONAL Skewness	1.38 (0.94,2.02)	0.097
			RP T1 NGLDM Busyness	1.31 (1.01,1.70)	**0.043**

Model performance

Performance of the following models was compared: clinical alone, clinical + PET/CT features, clinical + RP-MR and clinical + PET/CT + RP-MR, for both OS and in PFS, as shown in Figs. 3 and 4 respectively. In both situations, models considering clinical + PET/CT + RP-MR features outperformed those considering only clinical, clinical + PET/CT or clinical + RP-MR features (AUC 0.96 vs 0.56 vs 0.85 vs 0.79 at 24 months in OS and 0.86 vs 0.62 vs 0.81 vs 0.75 at 21 months in PFS), which suggests a synergy between PET/CT and RP-MR features. It is to note that in both the OS and PFS models, clinical + RP-MR features appear to initially outperform clinical + PET/CT features (AUC 0.87 vs 0.78 at 18 months in OS and AUC 0.82 vs 0.76 at 14 months in PFS). In the OS model, clinical + PET/CT outperformed clinical + RP-MR thereafter (AUC 0.89 vs 0.78 at 39 months), whilst in the PFS model clinical + PET/CT features outperformed clinical + RP-MR features from 18 to 39 months (AUC 0.81 vs 0.75 at 21 months), with clinical + RP-MR outperforming those of clinical + PET/CT features from 42 months thereafter (AUC 0.76 vs 0.74 at 45 months).

Discussion

To the best of our knowledge, no study so far has evaluated PET/CT combined with MR-based radiomics and baseline clinical parameters among patients with NPC. We identified that radiomic features from MR and PET/CT were associated with improved prediction of OS and PFS, particularly when combined (AUC 0.96 and 0.86 respectively). Clinical + MR features initially outperformed those of Clinical + PET/CT (< 18 months), with Clinical + PET/CT features then outperforming those of Clinical + RP-MR consistently in the OS model, whilst Clinical + RP-MR features subsequently outperformed those of Clinical + PET/CT (> 42 months) in the PFS model.

MRI

Our study confirms the findings of multiple studies in the literature that have demonstrated the pre-treatment prognostic value of MR-based radiomics among patients with NPC, consistently showing that MR-based radiomics outperform clinical features alone, when predicting either PFS or OS (4,6,11,12,14,16–18,20,22,28–30). The AUC for clinical + RP-MR in our study was as high as 0.84 for PFS and 0.87 for OS, which is comparable with the literature where AUC varies from 0.8 [18] to 0.886 [12], and the C-index from 0.72 [19] to 0.874 [20].

A significant proportion of these studies were only performed among patients with advanced (stage III-IV), non-metastatic NPC [4, 6, 11, 12, 14, 30], with the remainder performed among non-metastatic NPC patients of all stages, similar to our study [17–20, 22, 28].

Similar to the majority of MR-based radiomic studies, we included both contrast enhanced T1-w and T2-w MR sequences in our study (4,6,11,12,14,16–18,20,22,30); however, although both contrast enhanced T1-w, and T2-w MR sequences were evaluated, ultimately only radiomic features from the contrast enhanced T1-w sequences were found to be significant and included in our final OS and PFS models (RP_T1_GLZLM_GLNU, RP T1 CONVENTIONAL Skewness and RP T1 NGLDM Busyness). This is partly different when compared to other studies which have shown that joint contrast enhanced T1 and T2 radiomic features have a better prognostic performance than T1 or T2 features alone and may be the result of better performing PET-based radiomic features being incorporated into our model [11, 12].

Another differentiation compared to literature are the methods used for radiomic feature extraction (e.g. MATLAB), with only one other NPC radiomic study also using LIFEx software for radiomic feature extraction [14]. Despite utilization of the same MR sequences (contrast enhanced T1-w and T2-w sequences) and radiomic extraction software, different radiomic features were found to be significant (RP_T1_GLZLM_GLNU, RP T1 CONVENTIONAL Skewness and RP T1 NGLDM Busyness in our study, and GLCM_Energy, GLCM_Corre, and CONV_st in Yang et al. 2019 [14]). This may reflect our utilization of 3.0 T, fat-saturated MR sequences with different technical parameters. Similar to the majority of studies into NPC radiomics, our study evaluated radiomic parameters within the primary tumor; however, there are a number of studies that assess both the primary NPC tumor and adjacent locoregional lymph nodes, with similar findings, confirming the prognostic value of combined baseline clinical and MR-based radiomics [14, 19].

PET/CT

There are three studies in the literature exploring the performance of PET/CT based radiomic features among NPC patients. Similar to our study, they demonstrate that combined clinical with PET/CT features improved the prediction of PFS with a c-index of 0.77 [23], 0.69 [24] and AUC of 0.829 [7] compared with 0.81 in our study. The study from Peng et al. only examined patients with advanced NPC (stage II-IV) [7], compared with ours and the remaining PET/CT

radiomic studies. The study by Lv et al. identified age as a significant clinical parameter as in our study, in addition to IgA, N and M stage [23]. Our study identified PET_CONVENTIONAL_SUVbwQ1 and PET DISCRETIZED SUVbwmin as significant PET radiomic parameters; however, no PET features were retained following multivariate analysis in the study of Lv et al. 2019 [23]. By comparison, other parameters like PET-NGTDM-Complexity, CT-GLGLM-LGGE and PET-GLGLM-SGLGE were found to be significant in the study by Xu et al. 2019[24].

Our study evaluated both the PET and the CT component of the PET/CT study, however no CT parameters were found to have significant prognostic value in our study, unlike the remaining PET/CT-based radiomic studies [7, 23, 24]. We routinely evaluate the CT component in our radiomics studies since PET/CT is used clinically as a combined imaging modality. The complementary value of the CT component has previously been demonstrated in the literature [25], and if radiomics should ever make it into clinical routine decision making in the future, then the combined value of PET and CT radiomics would be beneficial per disease site.

There is currently only a single study examining the prognostic value between PET and MR in the existing literature [5]; however, this only utilizes T2-w MR and PET images. Our study is the first demonstrating the improved prognostic value of combined clinical + PET/CT + MR features compared with clinical, PET/CT or MR features individually for both OS and PFS (AUC 0.96 at 24 months in OS and 0.86 at 21 months in PFS). Since our results indicated that mainly PET and MR radiomics features seem to have a prognostic value, combined PET/MR imaging could be considered as a clinical tool for staging, prognostication and potentially surveillance of NPC. This may offer the patient (and the hospital) improved staging logistics (one combined exam compared to PET/CT and MR separately) as well as possibly a better prognostication tool in the future.

Interestingly, clinical + RP-MR features initially outperformed the clinical + PET/CT for both OS and PFS in the follow up period (< 18 months), and for PFS (> 42 months). Since MRI is used mostly for the local staging (because of its well documented superiority), one consideration is that the local tumor may potentially be the dominant driver and dictate short term tumoral behavior. PET however may provide improved overall prognostication, representing the overall pathophysiological behavior in a better way than morphological imaging procedures. Ultimately however, these findings remain indeterminate, and would need to be confirmed in similar studies.

Limitations

Our study had some limitations, predominantly in terms of methodology. This was a retrospective study with a moderate number of patients (124) (reported sample sizes in the literature range from 85–737 [3]), with mixed clinical stages of NPC (I-IV). Other prognostic molecular biomarkers, such as Haemoglobin, LDH, neutrophil-lymphocyte ration, c-Met, ERBB3 and MTDH were not available for inclusion in the study [21], as these were not routinely obtained at this time at our institute.

Although the PET/CT and RP-MR images were obtained from the same institution and scanners, maintaining uniformity in image acquisition, no image preprocessing was performed prior to segmentation. However, there is currently no general consensus available regarding if and which image preprocessing should be performed. Some researchers are opposed to image preprocessing, since it would be prohibitive to implement clinically on a large scale. Segmentation was also only performed manually, without reproducibility evaluation.

Statistical methodology, in terms of feature selection and modelling, is highly variable between radiomic studies (LASSO, RFE, univariate analysis; RS, CR and nomogram, Chi-squared test, SFFS and SVM). We performed univariate analysis followed by construction of a multivariate Cox regression model into which radiomic features were then added. The major difference between our studies and those in the literature is that the majority of studies use both training and validation cohorts to estimate model performance, with only one other study utilizing internal cross-validation [19]. Leave-one-out cross-validation is considered a robust statistical analysis, especially for study populations like ours. Although this is associated with the benefit of requiring a smaller sample size, because of the absence of an independent validation cohort, this study can however only be classified as explorative [19]. An independent dataset would therefore still be required for validation of the models presented.

Conclusions

In conclusion, our study demonstrated that PET/CT-based radiomic features may improve survival prognostication when combined with baseline clinical and MR-based radiomic features among NPC patients.

Declarations

Conflicts of Interest: None.

Disclaimers: None.

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Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical Approval: This retrospective study was approved by the institutional review board at University Health Network, Toronto, and the need to obtain informed consent from patients was waived.

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Figures

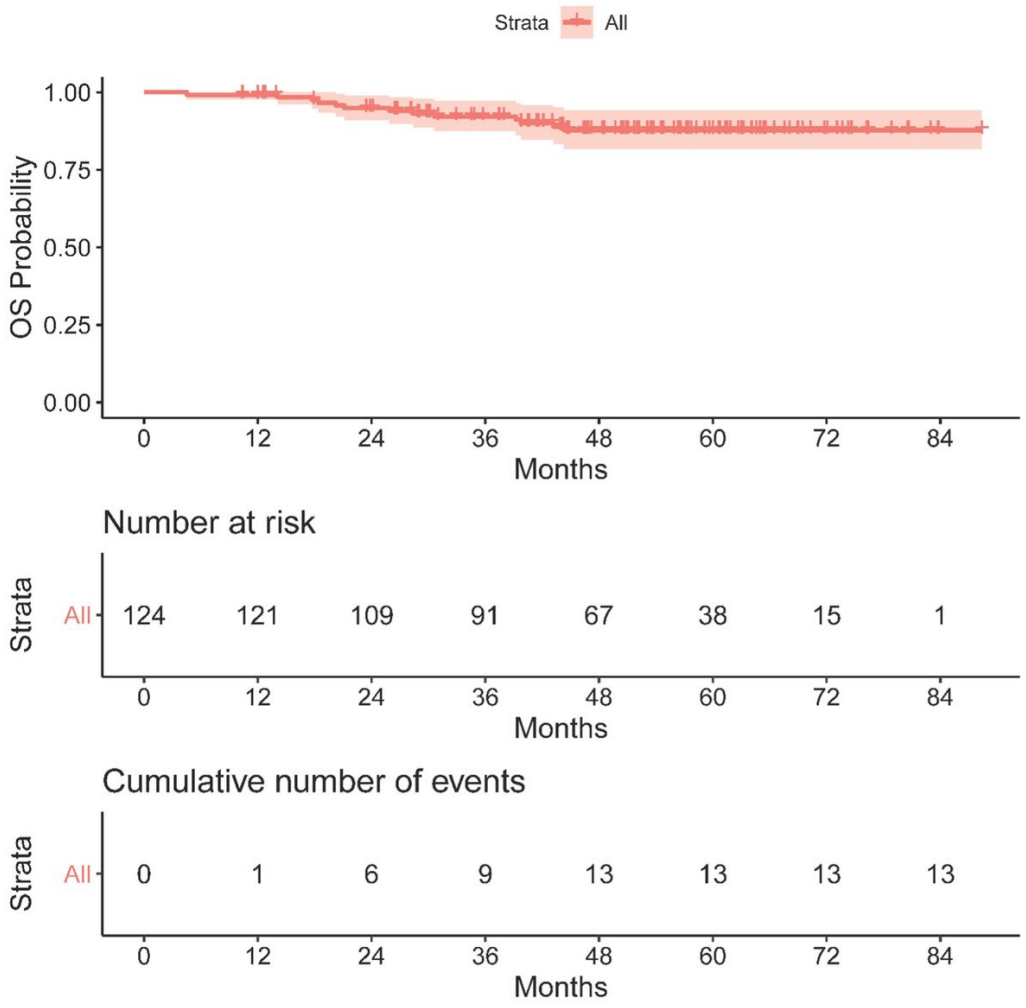

Figure 1

Overall Survival

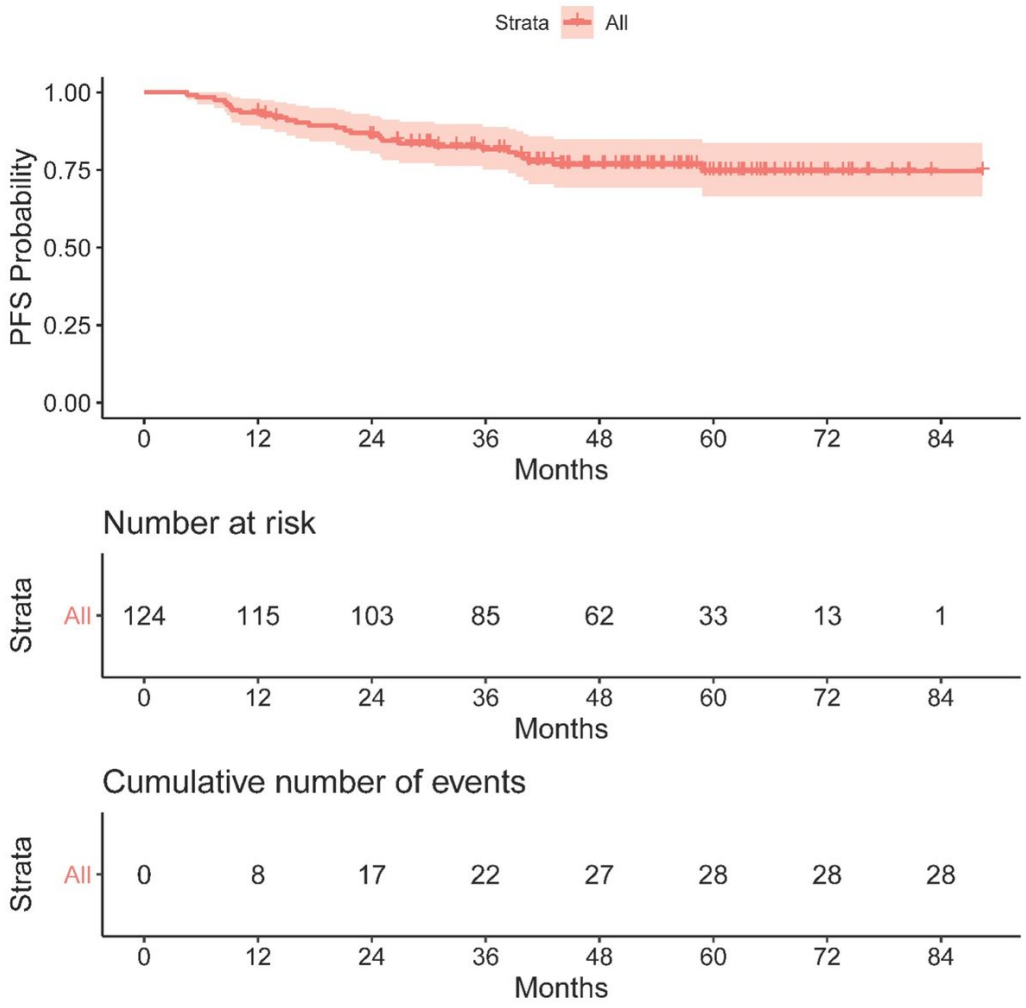

Figure 2

Progression Free Survival

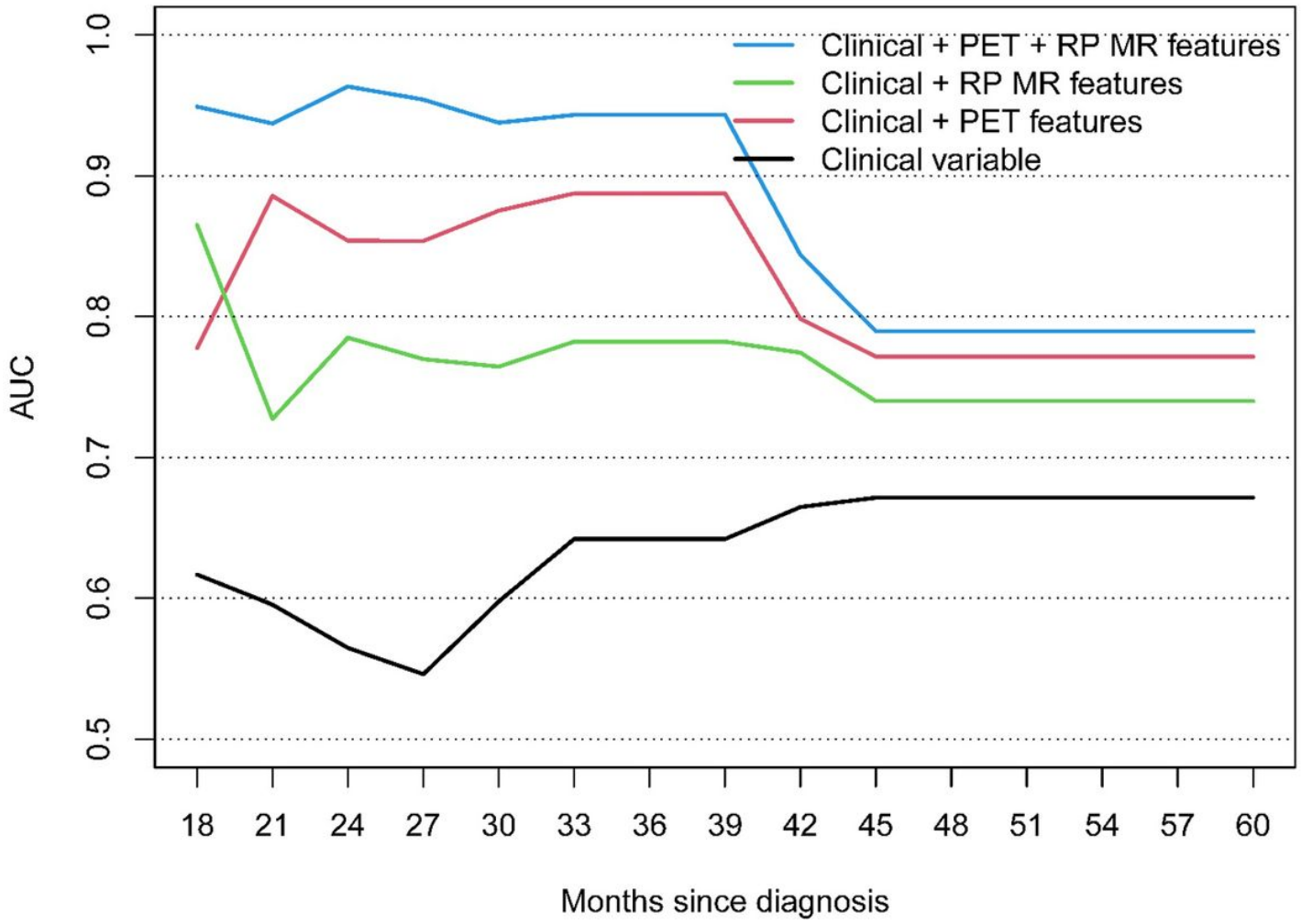

Figure 3

OS prediction models performance

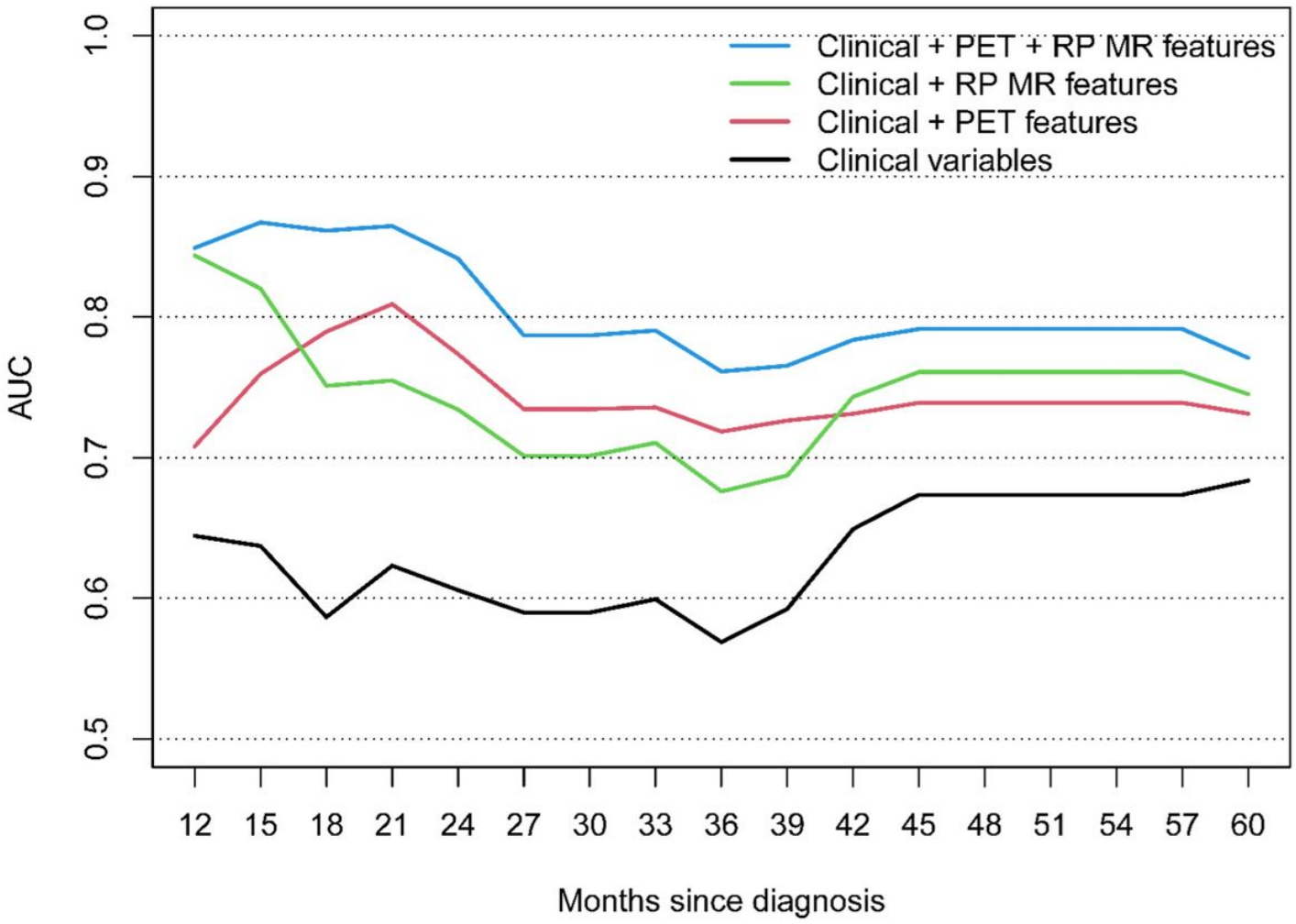

Figure 4

PFS prediction models performance

Supplementary Files

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