Prognostic Value of Pre-treatment F-18 FDG PET Metabolic Metrics in Patients with Locally Advanced Carcinoma of the Anus with and without HIV Infection

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Keywords

F-18 FDG PET, SUV_{max}, MTV, TLG, HIV, carcinoma of the anus

Summary

Aim: To investigate the prognostic value of F-18 FDG PET metabolic parameters in patients with anal carcinoma with and without human immunodeficiency virus infection (HIV). **Methods:** Maximum standardized uptake value (SUV_{max}), mean standardized uptake value (SUV_{mean}), metabolic tumor volume (MTV) and total lesion glycolysis (TLG) were obtained on F-18 FDG PET/CT images of treatment-naïve patients with locally advanced anal squamous cell carcinoma (ASSC). We compared patients' characteristics and F-18 FDG PET metabolic metrics between the HIV-infected patients and the HIV-uninfected patients. We did a simple Cox regression analysis followed by a multiple Cox regression analysis to determine factors predictive of death. **Results:** We studied 33 patients including 21 HIV-infected individ-

uals, mean age = 46.06 ± 12.59, female = 16, males = 17. Median CD4 count among HIV-infected patients was 400.50 cells/mm³ (IQR: 304.0–642.25). HIV-infected patients were younger than the HIV-uninfected patients at the time of diagnosis; 38.71 ± 7.98 vs. 58.92 ± 7.88 respectively, p < 0.001. No significant difference in the TNM stage and F-18 FDG metabolic parameters between the two groups. In a simple Cox regression analysis, MTV and TLG were significant predictors of death. Following a multiple Cox regression analysis, MTV and SUV_{mean} were significant predictors of death. The median overall survival was 44.63 (95 % CI: 34.12–55.14) among HIV-infected patients versus 54.65 (95 % CI: 45.73–63.57) among HIV-uninfected patients, p = 0.415. **Conclusion:** HIV-infected patients are diagnosed with ASSC at a younger age compared with HIV-uninfected patients. F-18 FDG PET metabolic metrics especially MTV predicts overall survival in patients with ASSC. There is no difference in the

overall survival of HIV-infected and HIV-uninfected patients treated similarly for ASSC.

Schlüsselwörter

F-18 FDG PET, SUV_{max}, MTV, TLG, HIV, Analkarzinom

Zusammenfassung

Ziel: Die Untersuchung der prognostischen Bedeutung der F-18 FDG PET metabolischen Aktivität bei HIV-negativen und positiven Analkarzinom-Patienten. **Methoden:** Bestimmt wurden maximale standardisierten Uptake-Werte (SUV_{max}), mittlere standardisierte Uptake-Werte (SUV_{mean}), das metabolische Tumervolumen (MTV) sowie die gesamte Tumorlyse-Glukose (TLG) mittels F-18 FDG PET/CT bei behandlungsnaiven Patienten mit lokal fortgeschrittenem Anal-Plattenepithelkarzinom (ASSC). Die Patientencharakteristika und F-18 FDG PET metabolischen Ergebnisse der HIV-positiven und HIV-negativen Patienten wurden verglichen. Eine einfache Cox-Regressionsanalyse gefolgt von einer multiplen Cox-Regressionsanalyse diente der Bestimmung von Faktoren für Tod.

Ergebnisse: Wir untersuchten 33 Patienten, davon 21 HIV-Infizierte, mittleres Alter = 46,06 ± 12,59, Frauen = 16, Männer = 17. Die mediane CD4-Zahl unter den HIV-Patienten war 400,50 Zellen/mm³ (IRQ: 304,0–642,25). Die HIV-infizierten Patienten

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waren jünger als die HIV-negativen Patienten zum Zeitpunkt der Diagnose; $38,71 \pm 7,98$ vs. $58,92 \pm 7,88$, $p < 0,001$. Es gab keinen signifikanten Unterschied in der TNM-Klassifikation und in den F-18 FDG metabolischen Werten zwischen den beiden Gruppen. In einer einfachen Cox-Regressionsanalyse waren MTV und TLG signifikante Prädiktoren für Tod. Das

mediane Gesamtüberleben lag bei 44,63 (95 % CI: 34,12–55,14) unter den HIV-infizierten Patienten vs. 54,65 (95 % CI: 45,73–63,57) unter den HIV-negativen Patienten, $p = 0,415$.

Schlussfolgerungen: HIV-infizierte Patienten werden in jüngeren Jahren mit ASCC diagnostiziert im Vergleich zu HIV-negativen Patienten.

F-18 FDG PET metabolische Aktivität, insbesondere MTV, kann das Gesamtüberleben von Patienten mit ASCC vorhersagen. Es gibt keinen Unterschied im Gesamtüberleben von HIV-infizierten und HIV-negativen Patienten bei gleicher Therapie des ASCC.

Introduction

Anal cancer is a rare malignancy of the gastrointestinal tract with a rising incidence. In the United States, it is projected to account for 0.49 % of new cancer cases in 2018 (1). Squamous cell carcinoma (SCC) accounts for the majority of anal cancers. Factors attributed to the rising incidence of SCC of the anus include human immunodeficiency virus (HIV) infection, human papillomavirus (HPV) infection, smoking, men having sex with men, multiple sexual partners, among others. Immunodeficiency syndrome associated with HIV infection leads to an increase in the incidence and persistence of HPV infection among HIV-infected individuals (2). Infection with high-risk strains of HPV is associated with the presence of high-grade squamous intraepithelial lesions, the precursor lesion for anal squamous cell carcinoma (ASCC) (3).

ASCC is the commonest type of non-acquired immunodeficiency syndrome (AIDS)-defining malignancies (4). There is, however, no consensus yet on the impact of HIV infection on the occurrence of treatment-related toxicities and survival among patients with ASCC. Some studies have reported a higher incidence of toxicity and shorter overall survival with 5-fluorouracil/mitomycin-C (MMC)-based concurrent chemoradiotherapy among HIV-infected patients (5, 6), others have reported no difference between HIV-infected and uninfected patients (7–10). Similar overall survival between HIV-infected and HIV-uninfected patients with ASCC but higher chemoradiotherapy-related toxicity has also been reported (11).

Positron emission tomography (PET)/computed tomography (CT) with F-18 flu-

orodeoxyglucose (F-18 FDG) has been shown to demonstrate high diagnostic performance in the staging and re-staging of various malignancies (12–14). In a recent meta-analysis, F-18 FDG PET/CT was found to outperform standalone CT in the evaluation of the primary tumor in patients with anal cancer (15). F-18 FDG PET/CT was found to lead to change in nodal staging in 21 % of patients. F-18 FDG PET metabolic parameters such as maximum standardized uptake value (SUV_{max}), mean standardized uptake value (SUV_{mean}), metabolic tumor volume (MTV) and total lesion glycolysis are a measure of tumor metabolic rate and its biology. They reflect tumor aggressiveness and have been found to predict therapy response and survival in different malignant diseases (16–18). These metabolic parameters have recently been reported in the assessment of the differences in tumor bulk in HIV-infected versus uninfected patients with Hodgkin lymphoma (19). The aim of this study was to determine the prognostic value of SUV_{max} , SUV_{mean} , MTV and TLG obtained at initial staging in a mixed group of HIV-infected and HIV-uninfected patients with locally advanced squamous cell carcinoma of the anus.

Material and Methods

Patients

Patients ≥ 18 years with histologically confirmed locally advanced (T3/4, or N1a/N1b/N1c or M disease) squamous cell carcinoma were included in this study. The staging was done using the American Joint Committee on Cancer (AJCC) TNM classification and staging system, 8th Edition (2018). All patients had a baseline F-18

FDG PET/CT before commencing chemotherapy. Patients with T1 /T2 disease without nodal or visceral metastasis were excluded. Other patients who were excluded include patients with histological variants other than squamous cell carcinoma, patients without baseline F-18 FDG PET/CT before commencing chemoradiotherapy, patients with a second malignancy, and patients with missing medical records in whom survival analysis could not be done.

In the patients included, their HIV status was determined and recorded. In the HIV-infected patients, the CD 4 count and HIV viral load were documented. We determined whether patients were alive or dead at the time of image analysis. We determined the overall survival (OS) of subjects which was the time from diagnosis to death (in patients who had died) or the time of image analysis.

F-18 FDG PET/CT scan

Patient preparation for F-18 FDG PET/CT was as done in accordance with international guidelines. All patients had a minimum of 4 hours of fasting. Blood sugar before F-18 FDG injection was less than 7.2 mmol/L in all cases. The injected activity of F-18 FDG was based on patients' weight using the formula:

$$[(\text{body weight} \div 10) + 1] \times 37 \text{ MBq.}$$

We imaged patients after an uptake period of 60 minutes on a Biograph 40 Truepoint PET/CT scanner (Siemens Medical Solution, IL, USA). Oral contrast: 30 mL of gastrografin (Bayers, Isando, South Africa) diluted in 1 liter of water was given orally over 1 hour before imaging. Intravenous

contrast: 100 mL of omnipaque 350 (GE Healthcare, WI, USA) was given intravenously with a scan delay of 80 s. We performed a vertex to mid-thigh CT scan with parameters adjusted for patients' weight (120 KeV, 40–150 mAs) with a section width of 5 mm and pitch of 0.8. PET imaging was acquired in 3D mode at 3 minutes per bed position. A separate pelvic image acquisition was done after patients have emptied their urinary bladder. We used CT data for attenuation correction and for delineation of lesions. We performed image reconstruction using ordered subset expectation maximization iterative reconstruction algorithm (4 iterations, eight subsets) followed by post-reconstruc-

tion filtering with a Gaussian filter at 5.0 mm FWHM.

Image analysis

Reconstructed images were displayed as maximum intensity projection image, PET, CT, and fused PET/CT in the axial, coronal and sagittal planes on a dedicated workstation equipped with a syngo software (Siemens Medical Solutions, IL, USA). A semi-automatic spherical volume of interest (VOI) was drawn encircling the primary lesion in the anus using an SUV threshold of 2.5 and a 3D isocontour of 41%. The VOI was manually adjusted to exclude physiologic areas of uptake adjacent to the primary lesion. The SUV_{max} , SUV_{mean} , and MTV of the primary lesion in each patient were recorded. TLG was manually computed by multiplying the MTV by SUV_{mean} .

Two Nuclear Medicine Physicians with about a decade experience interpreting F-18 FDG PET/CT each determined the presence of nodal and distant metastases in a prospective analysis of a retrospective set of data. Disagreements were resolved by consensus.

Statistical analyses

We used descriptive statistics (mean, median, standard deviation and interquartile range) to describe the baseline clinicopathologic characteristics of the study population. We used Chi-square test to determine if significant differences exist between the HIV-infected and HIV-uninfected patients with regards to age, gender, presence or absence of nodal or visceral metastasis, TNM stage of the disease, and the proportion of patients alive at the time of analysis. We used Mann Whitney U test to test for differences in SUV_{max} , SUV_{mean} , MTV, and TLG between the two groups. We performed a simple Cox regression to determine which of age, gender, the presence of nodal or visceral metastasis, TNM stage, presence or absence of HIV infection, SUV_{max} , SUV_{mean} , MTV, and TLG will predict overall survival. We performed a multiple Cox regression [backward stepwise (Likelihood Ratio) method] of selected variables with $p < 0.25$ on simple Cox

regression (nodal metastasis, SUV_{max} , SUV_{mean} , MTV, and TLG) and those with probable clinical significance (HIV infection, TNM stage). We constructed survival curves to plot the proportion of surviving patients during follow-up.

Results

A total of 33 patients with locally advanced squamous cell carcinoma met the inclusion criteria and were included in this study, mean age $\pm$ SD = 46.06 ± 12.59 years, male = 17 (51.5%), females = 16 (48.5%). Of these patients, 63.67% (21/33) were HIV-infected. All HIV-infected patients were on combination antiretroviral therapy (cART) at the time of diagnosis of ASCC with a median CD 4 count of 400.5 cells/mm³ (Interquartile range, IQR = 304.00–642.25). Out of 21 HIV-infected patients, 14 had no detectable HIV viremia. The median HIV viral load among seven patients with detected HIV viremia was 303.50 copies/mL (range = 74.00–533.00). More than half of the patients (54.5%) had AJCC stage IIIC disease. Distant metastasis was present in five patients (stage IV disease). ► Table 1 shows the clinic-pathologic distribution of the study population.

Comparison of clinical, pathologic and F-18 FDG PET metabolic parameters between HIV-infected and HIV-uninfected patients

The HIV-infected patients were significantly younger at the time of diagnosis of ASCC compared with the HIV-uninfected patients, median age at diagnosis HIV-infected versus uninfected of 37.00 years versus 56.50 years respectively, $p < 0.001$. We found no significant difference in the gender distribution between the two groups. Fifteen HIV-infected patients had nodal metastases compared with six patients without HIV infection ($p = 0.274$). Among the five patients with visceral metastases, two were HIV positive while three were not. The median SUV_{max} and SUV_{mean} were slightly higher among HIV-infected patients compared with HIV-uninfected patients, but the differences did not reach statistical significance. Con-

Tab. 1 Clinicopathologic characteristics of the patients

Variable	Frequency	Percent
Age (years)		
≤ 40	15	45.5
41 – 60	14	42.4
> 60	4	12.1
Mean ± SD	46.06 ± 12.59	
Range	29 – 78	
Gender		
Male	17	51.5
Female	16	48.5
HIV infection		
Yes	21	63.6
No	12	36.4
TNM stage		
IIB	7	21.2
IIIA	2	6.1
IIIB	1	6.1
IIIC	18	54.5
IV	5	12.1
CD4 count (cells/mm ³)		
Median (IQR)	400.50 (304.00 – 642.25)	
Range	76.00 – 978.00	
Viral load (copies/mL)		
LDL	14	42.4
Median (IQR)	303.50 (74.00 – 533.00)	
Range	74.00 – 533.00	

versely, median MTV and TLG were somewhat higher among HIV-uninfected compared with the HIV-infected patients ($p > 0.05$). ► Table 2 shows the differences in the clinicopathologic and F-18 FDG PET metabolic parameters between HIV-infected and HIV-uninfected patients with ASCC. ► Figures 1 and 2 show representative F-18 FDG PET/CT images of HIV-infected and HIV-uninfected patients with ASCC.

Predictors of mortality

We performed a simple cox regression analysis to determine the factors predictive of mortality among patients with ASCC (► Table 3) and found MTV (hazard ratio, HR=1.008; 95 % confidence interval, CI: 1.001–1.016; $p=0.031$) and TLG (HR=1.001; 95 % CI: 1.000–1.002; $p=0.021$) to significantly predict patients dying from their cancer. The other two F-18 FDG PET metabolic parameters were not significant predictors of mortality. Similarly, clinicopathologic factors such as age (HR=0.987; 95 % CI: 0.941–1.035), gender (HR=1.394; 95 % CI: 0.441–4.409), presence of nodal metastasis (HR=3.195; 95 % CI: 0.699–14.613), presence of visceral metastasis (HR=1.806; 95 % CI: 0.487–6.694), and presence of HIV infection (HR=1.626; 95 % CI: 0.487–5.430) were also not significant in predicting mortality, $p > 0.05$.

In our multiple Cox regression analysis (► Table 4), MTV remained a significant predictor mortality in patients with ASCC (HR=1.013, 95 % CI: 1.003–1.022), $p=0.010$. TLG was no longer a significant predictor of mortality. SUV_{mean} which was not a significant predictor of mortality in simple Cox regression analysis became significantly predictive of mortality following multiple Cox regression (HR=2.428, 95 % CI: 1.22–4.817), $p=0.011$. Other factors such age, gender, the presence of nodal metastasis, the presence of visceral metastasis and presence of HIV infection remained statistically not significant, $p > 0.05$.

Survival analysis

After a median follow-up period of 37 months (range: 5–66), 12 deaths had oc-

Tab. 2 Differences in clinic-pathologic and F-18 FDG PET parameters between HIV-infected and HIV-uninfected patients with anal squamous cell carcinoma

Variable	HIV infection			X ²	p value
	Positive n (%)	Negative n (%)	Total N (%)		
Age (years)					
≤ 40	15 (71.4)	0 (0.0)	15 (45.5)	13.384 ^Y	0.001
41 – 60	6 (28.6)	8 (66.7)	14 (42.4)		
> 60	0 (0.0)	4 (33.3)	4 (12.1)		
Mean ± SD	38.71 ± 7.98	58.92 ± 7.88			
Median (IQR)	37.00 (34.00 – 41.00)	56.50 (52.50 – 62.75)		15.000 ^U	<0.001*
Gender					
Male	11 (52.4)	6 (50.0)	17 (51.5)	0.017	0.895
Female	10 (47.6)	6 (50.0)	16 (48.5)		
Nodal metastasis					
Present	15 (71.4)	6 (50.0)	21 (63.6)	1.515	0.274
Absent	6 (28.6)	6 (50.0)	12 (36.4)		
Visceral metastasis					
Present	2 (9.5)	3 (25.0)	5 (15.2)	1.423	0.328
Absent	19 (90.5)	9 (95.0)	28 (84.8)		
TNM stage					
IV	2 (9.5)	3 (25.0)	4 (12.1)	1.344 ^Y	0.246
I-III	20 (90.5)	9 (75.0)	29 (87.9)		
Survival					
Alive	13 (61.9)	8 (66.7)	21 (63.6)	0.075	1.000
Dead	8 (38.1)	4 (33.3)	12 (36.4)		
SUV _{max}					
Media (IQR)	16.85 (13.38 – 25.11)	13.15 (8.28 – 19.31)		65.000 ^U	0.124
SUV _{mean}					
Median (IQR)	6.50 (4.90 – 8.08)	5.12 (3.36 – 6.99)		66.000 ^U	0.135
MTV					
Median (IQR)	153.48 (78.08 – 237.30)	172.27 (36.98 – 243.13)		93.000 ^U	0.758
TLG					
Median (IQR)	857.53 (513.34 – 1918.50)	1086.78 (106.42 – 1281.49)		82.000 ^U	0.551

X²: Chi-square test; Y: Yates Corrected Chi-square; U: Mann Whitney U test; HIV: Human Immunodeficiency Virus; SUV_{max}: maximum Standardized Uptake Value; SUV_{mean}: mean Standardized Uptake Value; MTV: Metabolic Tumor Volume; TLG: Total Lesion Glycolysis; *: p -value <0.05

curred while 21 patients were alive including 13 HIV-infected patients and 8 HIV-uninfected patients (► Table 2). We found

a lower median survival among HIV-infected patients compared with HIV-uninfected patients, 44.63 months (95 % CI:

Fig. 1 F-18 FDG PET/CT images of a 58-year-old HIV negative male with squamous cell carcinoma of the anus show a large anal mass with invasion into the adjacent left pelvic bone.

Fig. 2 F-18 FDG PET/CT images of a 32-year-old HIV positive female with squamous cell carcinoma show the primary anal mass with left inguinal and right iliac nodal metastases.

34.12–55.14) versus 54.65 months (95 % CI: 45.73–63.57), ► Table 5. This difference was however not statistically significant. ► Figure 3 shows the Kaplan-Meier survival curves demonstrating proportion of patients who remained alive during the follow-up period.

Discussion

This study evaluated the predictive role of F-18 FDG PET metabolic parameters in a mixed group of HIV-infected and HIV-uninfected patients with locally advanced squamous cell carcinoma of the anus on the overall survival and found that HIV-infected patients are diagnosed at much earlier age compared with HIV-uninfected pa-

tients, by an average of almost 20 years. HIV infection causes with chronic immunosuppression which predisposes patients to persistent infection with HPV, an oncogenic virus which predisposes to the development of high grade squamous intraepithelial lesions, the precursor lesion of ASCC (2). Factors which predisposes to HPV infection or are themselves associated with ASCC are prevalent among HIV-infected individuals. Such factors include men having sex with men and smoking (20, 21). Lokko et al. also found HIV-infected patients in their study cohorts significantly younger than HIV-uninfected patients by an average of about 14 years (8). Others have similarly reported the diagnosis of ASCC at a younger age in HIV-infected patients (6, 9, 11).

In our cohort of patients, we did not find any significant difference between HIV-infected and HIV-uninfected patients regarding SUV_{max} , SUV_{mean} , MTV, and TLG. This may suggest that HIV infection does not impact on disease burden in patients with ASCC. Since these F-18 FDG PET metabolic parameters have been reported to have implications on therapy outcome and survival, our findings appear to support findings from a study that has reported no difference in the treatment outcome and overall survival between HIV-uninfected patients and other patients with ASCC without HIV infection (8). Similarly, HIV-infected patients were not significantly different from the HIV-uninfected group in our study with regards gender and the TNM stage of the disease.

F-18 FDG PET metabolic parameters are a measure of tumor biology which reflects tumor metabolism. These parameters have been found to predict therapy outcome and impact on survival in different malignancies (22–24). In a simple Cox regression analysis, we found MTV and TLG to significantly predict mortality among patients with ASCC. These volumetric metrics assess the viable volume of a tumor bulk rather than the whole tumor burden which may include regions of necrosis and fibrosis, especially in large tumor mass. They are therefore better metrics to predict tumor biology than anatomic measurement of gross tumor volume. MTV remained a significant predictor of mortality

after a multiple Cox regression analysis while TLG was not. Bazan et al., in a retrospective review of 39 patients with ASSC, also found MTV as a significant predictor of survival (25). SUV_{max} is the pixel with the highest F-18 FDG uptake within the tumor volume and may not reflect the global metabolic status of the tumor. We did not find SUV_{max} as a significant predictor of mortality. This is in agreement with the finding of a recent larger study that also did not find pre-treatment SUV_{max} as a significant predictor of survival in a multivariate analysis (26). Kidd et al. however reported SUV_{max} as a significant predictor of lymph node metastasis and survival (27).

The impact of HIV infection on treatment outcome and survival has been a subject of great interest. It is important to determine if the presence of HIV infection impact negatively on the outcome of treatment or mortality among patients with HIV-associated malignancies. The interest in this subject is geared to select optimum treatment strategy for these cancers. We found no difference in the overall survival of HIV-infected patients and patients without the infection in our cohorts. This is in agreement with the more recent studies in the literature reporting an absence of any negative impact of HIV infection on the overall survival of patients with ASSC (7–11). Based on these, patients with ASSC are now being treated similarly regardless of their HIV status. A similar finding has been demonstrated in other non-AIDS defining cancers including as Hodgkin lymphoma which is now considered to have the prognosis irrespective of the patient's HIV status (28–30).

Our study has many the limitations, the most significant of which is the modest study population. This is related to the rarity of anal cancer and the strict inclusion criteria. We only studied patients with locally advanced disease and excluded patients with a small primary lesion. This was done believing that the impact of partial volume effect will have a more significant effect on the F-18 FDG PET metabolic parameters in small tumors. We also excluded patients with other histological variants of carcinoma of the anus other than squamous cell cancer. We only evaluated for the impact on F-18 FDG PET metabolic met-

Fig. 3 Kaplan-Meier curves showing the proportion of surviving patients during follow-up.

Tab. 3
Simple Cox regression
to determine the factors
predictive of mortality

Variables	b (SE)	Crude HR (95% CI)	p value
Age (years)	- 0.013 (0.024)	0.987 (0.941 – 1.035)	0.587
Gender			
Female		1	
Male	0.332 (0.588)	1.394 (0.441 – 4.409)	0.572
Nodal metastasis			
Absent		1	
Present	1.162 (0.776)	3.195 (0.699 – 14.613)	0.134
Visceral metastasis			
Absent		1	
Present	0.591 (0.668)	1.806 (0.487 – 6.694)	0.376
TNM stage			
I-III		1	
IV	0.591 (0.668)	1.806 (0.487 – 6.694)	0.376
HIV infection			
No		1	
Yes	0.486 (0.615)	1.626 (0.487 – 5.430)	0.429
SUV_{max}	0.046 (0.038)	1.047 (0.972 – 1.129)	0.228
SUV_{mean}	0.194 (0.125)	1.214 (0.951 – 1.552)	0.120
MTV	0.008 (0.004)	1.008 (1.001 – 1.016)	0.031 *
TLG	0.001 (0.000)	1.001 (1.000 – 1.002)	0.021 *

HR: Hazard Ratio; HIV: Human Immunodeficiency Virus; SUV_{max} : maximum Standardized Uptake Value; SUV_{mean} : mean Standardized Uptake Value; MTV: Metabolic Tumor Volume; TLG: Total Lesion Glycolysis; *: p value <0.05

Tab. 4 Multiple Cox regression analysis of predictors of survival

Variables	Crude HR ^a (95% CI)	p value	Adjusted HR ^b (95% CI)	p value
Age (years)	0.987 (0.941 – 1.035)	0.587		
Gender				
Female	1			
Male	1.394 (0.441 – 4.409)	0.572		
Nodal metastasis				
Absent	1			
Present	3.195 (0.699 – 14.613)	0.134		
Visceral metastasis				
Absent	1			
Present	1.806 (0.487 – 6.694)	0.376		
TNM stage				
I-III	1			
IV	1.806 (0.487 – 6.694)	0.376		
HIV infection				
No	1			
Yes	1.626 (0.487 – 5.430)	0.429		
SUV _{max}	1.047 (0.972 – 1.129)	0.228	0.800 (0.615 – 1.040)	0.096
SUV _{mean}	1.214 (0.951 – 1.552)	0.120	3.231 (1.207 – 8.648)	0.020*
MTV	1.008 (1.001 – 1.016)	0.031*	1.028 (1.003 – 1.054)	0.029*
TLG	1.001 (1.000 – 1.002)	0.021*	0.998 (0.994 – 1.001)	0.187

^a: Simple Cox proportional hazard regression; ^b: Multiple Cox proportional hazard ratio
 HR: Hazard risk of death; HIV: Human Immunodeficiency Virus; SUV_{max}: maximum Standardized Uptake Value; SUV_{mean}: mean Standardized Uptake Value; MTV: Metabolic Tumor Volume; TLG: Total Lesion Glycolysis; *: p value <0.05

Tab. 5 Difference between the median time of death of patients with carcinoma of anus based on HIV infection

Variable	n	Death (%)	Median (95% CI) (months)	Log Rank ^a (df)	p-value
HIV infection					
Yes	21	8 (38.1)	44.63 (34.12 – 55.14)	0.665 (1)	0.415
No	12	4 (33.3)	54.65 (45.73 – 63.57)		

^a Kaplan-Meier analysis; HIV: Human Immunodeficiency Virus

rics on overall survival. The impact of these metabolic metrics on other treatment outcomes such as treatment-related toxicity, event-free survival, etc. were not evaluated for in our study.

Conclusion

ASSC is diagnosed at a much younger age in HIV-infected patients. The burden of

disease is not different between HIV-infected and HIV-uninfected patients. F-18 FDG PET metabolic metrics especially MTV predicts overall survival in patients with ASSC. There is no difference in the overall survival of HIV-infected and HIV-uninfected patients treated similarly for ASSC.

Conflict of interest

The authors declare that they have no conflicts of interest.

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