# Prognostic Value of $^{18}$F-FDG PET/CT Assessment After Radiotherapy of Squamous Cell Carcinoma of the Anus in Patients from the National Multicentric Cohort FFCD-ANABASE

Virginie Combet-Curt[1], Chloé Buchalet[2], Karine Le Malicot[3], Claire Lemanski[2], Emmanuel Deshayes[4], Nathalie Bonichon-Lamichhane[5], Astrid Lièvre[6], Florence Huguet[7], Ghoufrane Tlili[8], and Véronique Vendrely[1]

[1]*Radiotherapy, CHU Bordeaux, Bordeaux, France;* [2]*Radiotherapy, ICM–Montpellier, Montpellier, France;* [3]*Biostatistics, University of Burgundy, FFCD, Dijon, France;* [4]*Nuclear Medicine, ICM–Montpellier, Montpellier, France;* [5]*Radiotherapy, Clinique Bordeaux Tivoli-Ducos, Bordeaux, France;* [6]*Hepatogastroenterology Department, CHU Rennes, Rennes, France;* [7]*Radiotherapy, Hôpital Tenon AP-HP, Paris, France; and* [8]*Nuclear Medicine, CHU Bordeaux, Bordeaux, France*

This study aimed to evaluate the prognostic value of $^{18}$F-FDG PET/CT qualitative assessment in terms of recurrence-free survival (RFS), colostomy-free survival (CFS), and overall survival (OS) after radiation therapy (RT) of squamous cell carcinoma of the anus (SCCA). Secondary objectives were to evaluate the prognostic value of baseline and posttherapeutic quantitative $^{18}$F-FDG PET/CT parameters in terms of RFS, CFS, and OS. **Methods:** We included all consecutive patients from the French multicentric cohort FFCD-ANABASE who had undergone $^{18}$F-FDG PET/CT at baseline and 4–6 mo after RT or chemoradiotherapy for a localized SCCA. Qualitative assessments separated patients with complete metabolic response (CMR) and non-CMR. Quantitative parameters were measured on baseline and posttreatment $^{18}$F-FDG PET/CT. RFS, CFS, and OS were analyzed using the Kaplan–Meier method. Associations among qualitative assessments, quantitative parameters, and RFS, CFS, and OS were analyzed using univariate and multivariate Cox regression. **Results:** Among 1,015 patients treated between January 2015 and April 2020, 388 patients (300 women and 88 men) from 36 centers had undergone $^{18}$F-FDG PET/CT at diagnosis and after treatment. The median age was 65 y (range, 32–90 y); 147 patients (37.9%) had an early-stage tumor and 241 patients (62.1%) had a locally advanced-stage tumor; 59 patients (15.2%) received RT, and 329 (84.8%) received chemoradiotherapy. The median follow-up was 35.5 mo (95% CI, 32.8–36.6 mo). Patients with CMR had better 3-y RFS, CFS, and OS, at 84.2% (95% CI, 77.8%–88.9%), 84.7% (95% CI, 77.2%–89.3%), and 88.6% (95% CI, 82.5%–92.7%), respectively, than did non-CMR patients, at 42.1% (95% CI, 33.4%–50.6%), 47.9% (95% CI, 38.1%–56.8%), and 63.5 (95% CI, 53.2%–72.1%), respectively ($P < 0.0001$). Quantitative parameters were available for 154 patients from 3 centers. The following parameters were statistically significantly associated with 3-y RFS: baseline $SUV_{max}$ (primitive tumor [T]) (hazard ratio [HR], 1.05 [95% CI, 1.01–1.1; $P = 0.018$]), $SUV_{peak}$ (T) (HR, 1.09 [95% CI, 1.02–1.15; $P = 0.007$]), MTV 41% (T) (HR, 1.02 [95% CI, 1–1.03; $P = 0.023$]), MTV 41% (lymph node [N]) (HR, 1.06 [95% CI, 1.03–1.1; $P < 0.001$]), MTV 41% (T + N) (HR, 1.02 [95% CI, 1–1.03; $P = 0.005$]), and posttreatment $SUV_{max}$ (HR, 1.21 [95% CI, 1.09–1.34; $P < 0.001$]). **Conclusion:** Treatment response assessed by $^{18}$F-FDG PET/CT after RT for SCCA has a significant prognostic value. $^{18}$F-FDG PET/CT could be useful for adapting follow-up, especially for patients with locally advanced-stage tumors. Quantitative parameters could permit identification of patients with a worse prognosis but should be evaluated in further trials.

**Key Words:** anal cancer; squamous cell carcinoma of the anus; chemoradiotherapy; $^{18}$F-FDG PET/CT; PET

**J Nucl Med 2024; 65:1194–1201**
DOI: 10.2967/jnumed.124.267626

Squamous cell carcinoma of the anus (SCCA) is considered a rare tumor, accounting for about 2,000 new cases per year in France (*1*). Its incidence is rising, but the age at diagnosis is decreasing, allowing for an earlier diagnosis, mostly at a localized stage. Only 5% of cases are diagnosed at a metastatic stage (*2*).

The standard of care for patients with localized disease is radiation therapy (RT) associated with chemotherapy, including mitomycin C and 5-fluorouracil with curative intent (*3*). Surgery is a salvage treatment in cases of locoregional relapse.

$^{18}$F-FDG PET/CT is recommended for the initial staging of SCCA in the French guidelines (*4*,*5*) and is considered an option by the European Society of Medical Oncology (*6*). Indeed, prospective and retrospective studies have shown good performance for $^{18}$F-FDG PET/CT, especially in lymph node staging (*7*,*8*), modifying the TNM classification in 15%–40% of cases (*9*,*10*). Thus, identifying pathologic lymph nodes can modify the RT plan and can be useful for target volume delineation (*11*,*12*). Moreover, some metabolic parameters measured by baseline $^{18}$F-FDG PET/CT, such as metabolic tumor volume (MTV) or total lesion glycolysis (TLG), could have prognostic value (*13*–*16*). Studying these parameters could allow identification of patients with a high risk of relapse or treatment failure. During follow-up after treatment, the role of $^{18}$F-FDG PET/CT is not clearly defined. $^{18}$F-FDG PET/CT is recommended when relapse is suspected (*4*) but could also be useful to assess treatment response.

This study aimed to evaluate the prognostic value of $^{18}$F-FDG PET/CT assessment in terms of recurrence-free survival (RFS), colostomy-free survival (CFS), and overall survival (OS) after RT of SCCA. We studied the prognostic value of qualitative response on $^{18}$F-FDG PET/CT performed 4–6 mo after RT or chemoradiotherapy,

Received Feb. 20, 2024; revision accepted May 28, 2024.
For correspondence or reprints, contact Virginie Combet-Curt (virginie.combet-curt@chu-bordeaux.fr).
Published online Jun. 27, 2024.

and we identified prognostic factors among quantitative parameters measured on $^{18}$F-FDG PET/CT.

## MATERIALS AND METHODS

Patients treated for SCCA between January 2015 and April 2020 were included in the cohort for French Federation of Digestive Oncology (FFCD)-ANABASE, which is a prospective multicentric observational study conducted by the FFCD. This study aimed to evaluate clinical practice, treatments, and oncologic outcomes for SCCA in France, and the main results have been published (*17*). The ethics committee (CCTIRS-15.698) and the Commission National de l'Informatique et des Libertés (authorization 915622) approved this retrospective study, and the requirement to obtain written informed consent was waived. All patients received written information and provided oral informed consent.

Among the patients included in the FFCD-ANABASE cohort, we focused in this study on those who had undergone $^{18}$F-FDG PET/CT at baseline and again at 4–6 mo after the end of RT or chemoradiotherapy. The main objectives were to evaluate the prognostic value of $^{18}$F-FDG PET/CT qualitative response to treatment in terms of RFS, CFS, and OS. Secondary objectives were to identify prognostic factors among quantitative parameters measured on baseline and posttreatment $^{18}$F-FDG PET/CT in terms of RFS, CFS, and OS.

### Image Acquisition and Interpretation

The following data were collected prospectively and entered into the database by the physicians of each center: $SUV_{max}$ and presence of significant $^{18}$F-FDG uptake for baseline $^{18}$F-FDG PET/CT, and $SUV_{max}$ and global qualitative evaluation for posttreatment $^{18}$F-FDG PET/CT.

A complete metabolic response (CMR) was defined as the visual absence of residual $^{18}$F-FDG uptake or the presence of nonpathologic minimal residual uptake (left at the discretion of each nuclear medicine physician). A partial metabolic response was defined as any persistent pathologic uptake in the lesions visible on the baseline image. Stability was defined as findings similar to those on the baseline scan. Progressive disease was defined as an increase in uptake because of tumor growth or new pathologic uptake because of the development of a new site of disease.

Moreover, we decided to further analyze the $^{18}$F-FDG PET/CT data of patients from 3 large inclusion centers accredited by European Association Research Ltd., which is an accreditation program developed in collaboration with the European Organization for Research and Treatment of Cancer with the aim of providing a common standard for harmonizing the acquisition and interpretation of PET/CT.

Quantitative $^{18}$F-FDG PET/CT parameters were collected retrospectively by 2 pairs of physicians (an RT resident and a nuclear medicine senior) by reviewing the native $^{18}$F-FDG PET/CT images. These parameters were measured using a volume of interest placed by the physicians over the primary tumor and each involved lymph node. $SUV_{max}$ and $SUV_{peak}$ were, respectively, defined as the maximum voxel intensity and the average SUV within a 1 $cm^3$ volume of interest centered on the hottest area of the tumor or lymph node. Metabolic tumor volume (MTV) 41% was defined as the hypermetabolic tissue volume with a cutoff greater than 41% of $SUV_{max}$. $SUV_{mean}$ was defined as the mean of SUV of all voxels within the MTV.

The following data were collected on baseline $^{18}$F-FDG PET/CT (where T indicates primitive tumor and N indicates lymph nodes): $SUV_{max}$ (T), $SUV_{peak}$ (T), $SUV_{mean}$ (T), and MTV 41% (T). Total lesion glycolysis (TLG) (T) was calculated ($SUV_{mean}$ [T] × MTV 41% [T]). MTV 41% (N) and $SUV_{mean}$ (N) were collected for zero to 10 lymph nodes. TLG (N) was calculated for each lymph node ($SUV_{mean}$ [N] × MTV 41% [N]). Sums were realized to obtain MTV 41% ([total] N), TLG ([total] N), MTV 41% (T + N), and TLG (T + N).

A quantitative evaluation was realized on posttreatment $^{18}$F-FDG PET/CT with a measure of posttreatment $SUV_{max}$, allowing calculation of change in $SUV_{max}$ ([pretreatment $SUV_{max}$ − posttreatment $SUV_{max}$]/pretreatment $SUV_{max}$ × 100).

### Statistical Analysis

RFS was defined as the time between the start of treatment and the first recurrence or death (from any cause). CFS was defined as the time between the start of treatment and the first colostomy or death (from any cause). Alive patients without recurrence or colostomy were censored at the date of the last follow-up. OS was defined as the time between the start of treatment and death (from any cause). Alive patients were censored at the date of the last follow-up.

Descriptive analyses were performed for each $^{18}$F-FDG PET/CT parameter. RFS, CFS, and OS were analyzed using the Kaplan–Meier method and described using medians with 2-sided 95% CIs. Log-rank tests were used to compare rates and event-time distributions with a 95% CI. Univariate and multivariate analyses were done to evaluate the association between qualitative response to treatment on $^{18}$F-FDG PET/CT; other parameters linked to $^{18}$F-FDG PET/CT and clinical parameters; and RFS, CFS, and OS using Cox proportional hazards regression reporting hazard ratios (HRs) and 95% CI. A receiver operating characteristic curve was used to determine a discriminative threshold value of posttreatment $SUV_{max}$ in terms of RFS, CFS, and OS.

## RESULTS

### Patient Characteristics

Among 1,015 patients who received first-line RT or chemoradiotherapy for nonmetastatic SCCA between January 2015 and April 2020, 388 from 36 centers underwent $^{18}$F-FDG PET/CT at baseline and 4–6 mo after treatment (Fig. 1). There were 88 (22.7%) men and 300 (77.3%) women. The median age was 64 y (range, 32–90 y). Patient and tumor characteristics are presented in Table 1.

Fifty-nine patients (15.2%) received RT, and 329 (84.8%) received chemoradiotherapy, with concurrent mitomycin-5-fluorouracil for 286 patients (86.9%) and cisplatin-5-fluorouracil for 14 patients (4.3%). The median RT dose was 60 Gy on the tumor volume and 45 Gy on the pelvis. Among patients previously described, 154 patients from 3 main recruiter centers had a secondary analysis with quantitative evaluation of baseline and posttreatment $^{18}$F-FDG PET/CT.

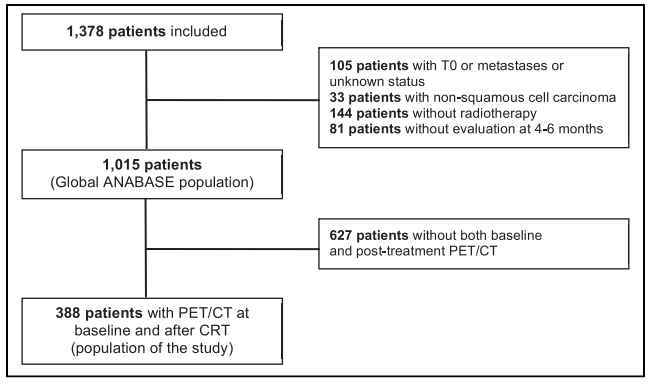


**FIGURE 1.** Flowchart. CRT = chemoradiotherapy.

**TABLE 1**
Patient and Tumor Characteristics

| Characteristic | Category | Data |
|---|---|---|
| Sex ($n$ = 388) | Male | 88 (22.7) |
| | Female | 300 (77.3) |
| Age (y) ($n$ = 388) | | 65 (32–90) |
| OMS status ($n$ = 383) | 0 | 258 (67.4) |
| | 1 | 112 (29.2) |
| | 2 | 9 (2.3) |
| | 3 | 4 (1) |
| | 4 | 0 (0) |
| Smoking ($n$ = 336) | Yes | 189 (56.3) |
| | No | 147 (43.8) |
| HIV status ($n$ = 385) | Positive | 33 (8.6) |
| | Negative | 178 (42.6) |
| | Unknown | 174 (45.2) |
| Tumor size (cm) ($n$ = 372) | | 4.16 (0.5–15.5) |
| T-stage ($n$ = 388) | T1 | 42 (10.8) |
| | T2 | 203 (52.3) |
| | T3 | 82 (21.1) |
| | T4 | 61 (15.7) |
| N-stage ($n$ = 388) | N0 | 177 (45.6) |
| | N1 | 211 (54.4) |
| Stage ($n$ = 388) | Early: T1–2, N0 | 147 (37.9) |
| | Locally advanced: T3–4 or N1 | 241 (62.1) |
| P16 staining* ($n$ = 384) | Positive | 225 (58.6) |
| | Negative | 12 (3.1) |
| | Unknown | 147 (38.3) |
| Baseline imaging ($n$ = 388) | | |
| CT | Yes | 212 (54.6) |
| | No | 176 (45.4) |
| MRI | Yes | 260 (67) |
| | No | 128 (33) |
| Echoendoscopy | Yes | 111 (28.6) |
| | No | 277 (71.4) |

OMS = Organisation Mondiale de la Santé.
Qualitative data are number and percentage; continuous data are median and range.

**Outcomes**

Median follow-up was 35.5 mo (95% CI, 32.8–36.6). The 3-y RFS, CFS, and OS for the whole population were 68.0% (95% CI, 62.5–72.9), 70.5% (95% CI, 64.8–75.5), and 79.2% (95% CI, 73.8–83.7), respectively. Among the 242 patients with CMR, 213 (88%) were free of recurrence at 3 y. Among the 146 patients with non-CMR, 77 (52.7%) had a recurrence at 3 y.

The 3-y RFS was 84.2% (95% CI, 77.8–88.9) for patients with CMR, compared with 42.1% (95% CI, 33.4–50.6) for patients without CMR ($P < 0.0001$) (Fig. 2). Similarly, the 3-y CFS was 84.7% (95% CI, 78.2–89.3) for patients with CMR and 47.9% (95% CI, 38.1–56.8) for patients without CMR ($P < 0.0001$) (Fig. 3). The 3-y OS was 88.6% (95% CI, 82.5–92.7) for patients with CMR and 63.5 (95% CI, 53.2–72.1) for patients without CMR ($P < 0.0001$) (Fig. 4).

Qualitative response to treatment on $^{18}$F-FDG PET/CT was statistically significantly associated with better RFS, CFS, and OS on both univariate and multivariate analysis (Table 2). A descriptive analysis of quantitative $^{18}$F-FDG PET/CT parameters analyzed on 154 patients is presented in Table 3.

The results of univariate analysis between $^{18}$F-FDG PET/CT parameters and RFS, CFS, and OS are presented in Table 4. An

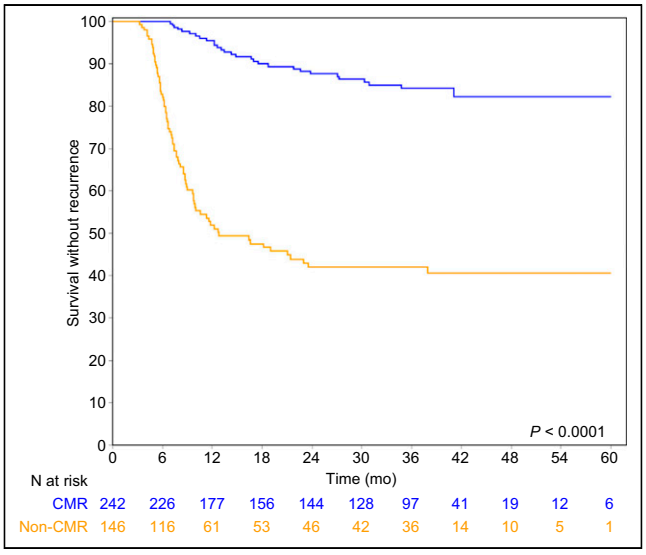


**FIGURE 2.** RFS curves of CMR patients and non-CMR patients.

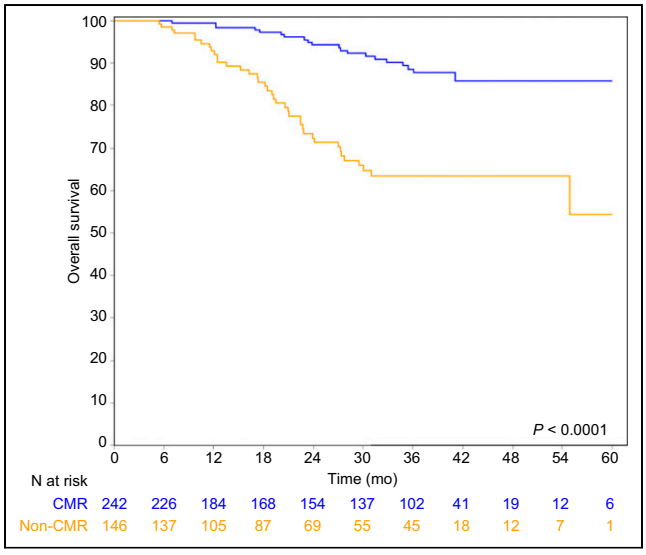


**FIGURE 4.** OS curves of CMR patients and non-CMR patients.

increase of 1 unit of baseline $SUV_{max}$ (T), $SUV_{peak}$ (T), MTV 41% (T), MTV 41% (N), MTV 41% (T + N), and posttreatment $SUV_{max}$ was significantly associated with a poor RFS, CFS, and OS. There was no statistically significant prognostic impact of TLG and change in $SUV_{max}$.

By using a receiver operating characteristic curve, we found that a threshold of 5 for posttreatment $SUV_{max}$ separates patients into prognostic groups. The recurrence rate was 35% for patients with a posttreatment $SUV_{max}$ of more than 5 and 18.4% for patients with a posttreatment $SUV_{max}$ 5 or less (HR, 0.44 [95% CI, 0.22–0.87]; $P = 0.018$). Similarly, the colostomy rate was 35% for patients with a posttreatment $SUV_{max}$ of more than 5 and 14.68% for patients with a posttreatment $SUV_{max}$ of 5 or less (HR, 0.30 [95% CI, 0.14–0.61]; $P = 0.001$). OS did not significantly differ between these 2 groups (HR, 0.47 [95% CI, 0.2–1.08]; $P = 0.075$).

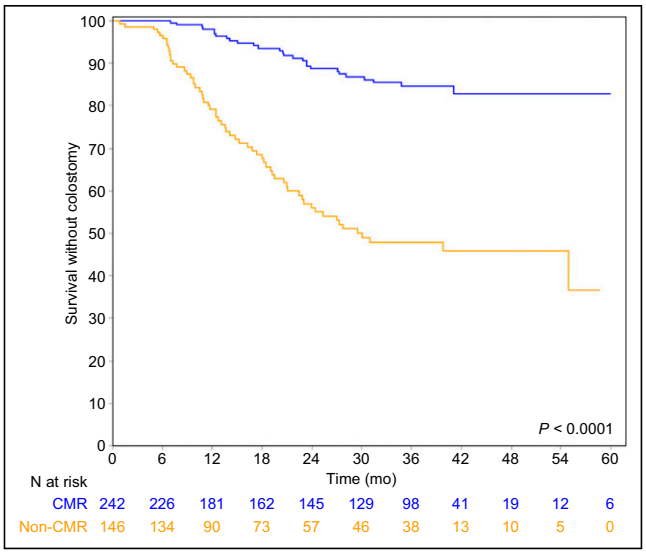


**FIGURE 3.** CFS curves of CMR patients and non-CMR patients.

## DISCUSSION

The purpose of this study was to determine the prognostic value of posttreatment $^{18}$F-FDG PET/CT in patients treated with RT or chemoradiotherapy for nonmetastatic SCCA. To our knowledge, our study, with a population of 388 patients, is one of the largest that aimed to assess the predictive value of $^{18}$F-FDG PET/CT response to treatment. We confirmed the significant prognostic value of $^{18}$F-FDG PET/CT qualitative response to treatment in terms of RFS, CFS, and OS.

Several studies have previously examined the value of treatment response assessed by $^{18}$F-FDG PET/CT and showed that a CMR is highly associated with better progression-free survival, OS (*18*,*19*), and cause-specific survival (*20*). Interestingly, metabolic response to treatment has even been found to be a more significant predictor factor of progression-free survival than pretreatment tumor size (based on physical examination) and nodal status in a study of 53 patients (*21*). Finally, it has also been shown that posttreatment $^{18}$F-FDG PET/CT has a high negative predictive value and could be used to rule out residual or recurrent disease (*22*).

Regarding quantitative $^{18}$F-FDG PET/CT parameters, we identified several significant prognostic factors: MTV, pretreatment $SUV_{peak}$ and $SUV_{max}$, and posttreatment $SUV_{max}$. These results are consistent with literature regarding MTV, assessed in 6 different studies (*13*–*16*,*23*,*24*), but also regarding pretreatment $SUV_{peak}$ and posttreatment $SUV_{max}$, which have not been frequently assessed (*16*,*25*). Literature regarding pretreatment $SUV_{max}$ showed more conflicting results, with a study of 77 patients showing its prognostic value (*26*) but also studies showing negative results (*13*,*23*,*24*,*27*).

By using thresholds to separate patients into prognostic groups, we found that a posttreatment $SUV_{max}$ of 5 or less was predictive of better RFS. A posttreatment $SUV_{max}$ of less than 6.1 has already been shown to be associated with reduced local recurrence and increased OS (*25*). In the literature, an MTV 35% threshold at 40 $cm^3$ was shown to be the best cutoff to discriminate a low from a high risk of recurrence (*15*).

In this study, we have shown $^{18}$F-FDG PET/CT to have major prognostic value regarding qualitative treatment response. Even if

**TABLE 2**
Association Between $^{18}$F-FDG PET/CT Qualitative Treatment Response and RFS, CFS, and OS

| | Event | | HR | |
|---|---|---|---|---|
| Response | *n* | % | Univariate analysis | Multivariate analysis* |
| RFS | | | | |
| CMR | 29/242 | 11.98 | Reference | Reference |
| PMR | 27/91 | 29.67 | 2.85 (1.69–4.82), $P < 0.001$ | 2.64 (1.51–4.62), $P = 0.001$ |
| Stability | 7/12 | 58.33 | 6.80 (2.97–15.54), $P < 0.001$ | 5.97 (2.42–14.68), $P < 0.001$ |
| Progression | 43/43 | 100 | 68.09 (37.69–122.99), $P < 0.001$ | 56.46 (29.62–107.61), $P < 0.001$ |
| CFS | | | | |
| CMR | 27/242 | 11.16 | Reference | Reference |
| PMR | 28/91 | 30.77 | 3.13 (1.84–5.31), $P < 0.001$ | 3.03 (1.73–5.32), $P < 0.001$ |
| Stability | 6/12 | 50.00 | 6.12 (2.52–14.87), $P < 0.001$ | 5.71 (2.09–15.63), $P = 0.001$ |
| Progression | 28/43 | 65.12 | 11.23 (6.53–19.31), $P < 0.001$ | 7.69 (4.18–14.14), $P < 0.001$ |
| OS | | | | |
| CMR | 20/242 | 8.26 | Reference | Reference |
| PMR | 13/91 | 14.29 | 1.83 (0.91–3.68), $P = 0.090$ | 1.49 (0.73–3.06), $P = 0.278$ |
| Stability | 4/12 | 33.33 | 5.41 (1.84–15.9), $P = 0.002$ | 3.53 (1.11–11.8622), $P = 0.032$ |
| Progression | 22/43 | 51.16 | 11.27 (6.06–20.96), $P < 0.001$ | 8.03 (4.18–15.4), $P < 0.001$ |

*Analysis with sex, OMS status, tumor stage.
PMR = partial metabolic response.
Data in parentheses are 95% CIs.

qualitative evaluation is subjective and is physician-dependent, this study still proves its reliability. Moreover, this study included patients from 36 centers in France with as many physicians, showing reproducibility and confidence in this evaluation.

Finally, we have shown that posttreatment $SUV_{max}$ was significantly associated with RFS, CFS, and OS. It is the main parameter used in $^{18}$F-FDG PET/CT interpretation and analysis and is easy to measure.

Our study had some limitations. Patients were included from 36 centers, potentially leading to heterogeneity in patient management and $^{18}$F-FDG PET/CT assessment. The 36 centers could have different $^{18}$F-FDG PET/CT equipment. Assessment of CMR was left to the discretion of the nuclear medicine physician of each center. We selected patients with $^{18}$F-FDG PET/CT at baseline and 4–6 mo after treatment, but all centers did not have the same follow-up policy after RT or chemoradiotherapy of SCCA. $^{18}$F-FDG PET/CT could have been done systematically 4–6 mo after treatment or only when relapse was suspected. Concerning the quantitative parameter study, $^{18}$F-FDG PET/CT was performed at 3 different centers, and different PET/CT scanners can have variable quantification of $^{18}$F-FDG uptake. Moreover, the images were reviewed retrospectively by 2 physicians, and the analysis was univariate.

Currently, $^{18}$F-FDG PET/CT is recommended in cases of relapse or suspicion of treatment failure (*4*). By showing the major prognostic value of treatment response as assessed by $^{18}$F-FDG PET/CT, this study encourages a systematic evaluation by $^{18}$F-FDG PET/CT. We know that patients with early-stage tumors (T1–2, N0) and patients with locally advanced-stage tumors (T3–4 or N+) have different prognoses. Disease-free survival at 3 y is around 85% for patients with early-stage SCCA but 66% for patients with locally advanced SCCA (*17*,*28*). The 3-y CFS and OS are 86% and 92%, respectively, in the early-stage group compared with 67% and 78% in the locally advanced group (*17*). Present research about SCCA focuses on more personalized treatment and management according to tumoral stages. Modalities of evaluation and follow-up after treatment could be adapted too. Patients with early-stage tumors have a low risk of local or metastatic relapse. Most relapses are local and can be detected by clinical evaluation. Surveillance can rely on clinical examination, which seems to be reliable, whereas $^{18}$F-FDG PET/CT could be useful in suspected recurrence. On the other hand, patients with locally advanced-stage tumors still present a poor prognosis with a high risk of local and distant recurrence. Moreover, locally advanced tumors frequently involve adjacent organs or deep lymph nodes that cannot be accurately assessed by physical evaluation.

During follow-up, an evaluation by thoracoabdominopelvic CT is recommended once a year during the first 3 y according to the French and European guidelines (*4*,*6*). Pelvic MRI is recommended before salvage surgery (*4*). Despite past studies showing its value, $^{18}$F-FDG PET/CT is currently not included in guidelines for systematic follow-up of patients. By confirming its importance in this large-scale study, we suggest that $^{18}$F-FDG PET/CT could be recommended at 4–6 mo after the end of chemoradiotherapy for patients with locally advanced-stage tumors. Modalities of follow-up could be adapted according to the response on $^{18}$F-FDG PET/CT, since it is known that a CMR is highly predictive of a good outcome.

**TABLE 3**
Descriptive Analysis of $^{18}$F-FDG PET/CT Parameters

| Parameter | Category | Data |
|---|---|---|
| Baseline $^{18}$F-FDG PET/CT (total $n$ = 154) | | |
| $SUV_{max}$ (T) | $n$ | 150 |
| | Mean | 13.95 (SD, 6.00) |
| | Median | 12.87 |
| | Q1–Q3 | 10.08–16.35 |
| | Min–max | 3.22–41.36 |
| $SUV_{peak}$ (T) | $n$ | 130 |
| | Mean | 10.89 (SD, 5.14) |
| | Median | 9.94 |
| | Q1–Q3 | 7.41–13.70 |
| | Min–max | 2.36–28.35 |
| $SUV_{mean}$ (T) | $n$ | 132 |
| | Mean | 8.72 (SD, 5.98) |
| | Median | 7.67 |
| | Q1–Q3 | 5.86–9.99 |
| | min–max | 1.85–61.07 |
| MTV 41% (T) ($cm^3$) | $n$ | 131 |
| | Mean | 15.57 (SD, 19.42) |
| | Median | 8.63 |
| | Q1–Q3 | 4.06–17.29 |
| | Min–max | 1.83–115.80 |
| TLG (T) (g) | $n$ | 131 |
| | Mean | 143.68 (SD, 222.56) |
| | Median | 54.33 |
| | Q1–Q3 | 24.95–157.79 |
| | Min–max | 3.00–1,453.29 |
| MTV 41% (N) ($cm^3$) | $n$ | 134 |
| | Mean | 3.07 (SD, 5.94) |
| | Median | 0.00 |
| | Q1–Q3 | 0.00–4.00 |
| | Min–max | 0.00–38.00 |
| TLG (N) (g) | $n$ | 134 |
| | Mean | 15.69 (SD, 48.05) |
| | Median | 0.00 |
| | Q1–Q3 | 0.00–11.00 |
| | Min–max | 0.00–352.00 |
| MTV 41% (T + N) ($cm^3$) | $n$ | 134 |
| | Mean | 18.11 (SD, 21.55) |
| | Median | 10.00 |
| | Q1–Q3 | 4.11–21.90 |
| | Min–max | 0.93–125.29 |
| TLG (T + N) (g) | $n$ | 134 |
| | Mean | 156.16 (SD, 229.53) |
| | Median | 60.70 |
| | Q1–Q3 | 27.00–183.00 |
| | Min–max | 2.14–1,471.65 |

(*continued*)

**TABLE 3**
Descriptive Analysis of $^{18}$F-FDG PET/CT Parameters (cont.)

| Parameter | Category | Data |
|---|---|---|
| Posttreatment $^{18}$F-FDG PET/CT (total $n$ = 154) | | |
| $SUV_{max}$ | $n$ | 149 |
| | Mean | 4.77 (SD, 2.46) |
| | Median | 3.94 |
| | Q1–Q3 | 3.30–5.20 |
| | Min–max | 2.06–16.40 |
| Change in $SUV_{max}$ (%) | $n$ | 150 |
| | Mean | 62.07 (SD, 25.91) |
| | Median | 69.75 |
| | Q1–Q3 | 53.14–78.39 |
| | Min–max | −60.00–100.00 |

Min–max = minimum to maximum; Q1–Q3 = first quartile to third quartile.

## CONCLUSION

Metabolic treatment response assessed by $^{18}$F-FDG PET/CT after RT or chemoradiotherapy for nonmetastatic SCCA has significant prognostic value in terms of RFS, CFS, and OS. $^{18}$F-FDG PET/CT could be useful to assess treatment response and adapt follow-up, especially for patients with locally advanced-stage tumors. Quantitative parameters measured on $^{18}$F-FDG PET/CT could permit identification of patients with the worst prognosis but should be evaluated in further trials.

**TABLE 4**
Association Between $^{18}$F-FDG PET/CT Parameters and OS, RFS, and CFS (Univariate Analysis)

| | | HR | | |
|---|---|---|---|---|
| Parameter | Category | OS | RFS | CFS |
| Baseline $^{18}$F-FDG PET/CT | $SUV_{max}$ (T) | 1.06 (1–1.12), $P$ = 0.038 | 1.05 (1.01–1.1), $P$ = 0.018 | 1.06 (1.01–1.11), $P$ = 0.019 |
| | $SUV_{peak}$ (T) | 1.09 (1.01–1.17), $P$ = 0.022 | 1.09 (1.02–1.15), $P$ = 0.007 | 1.09 (1.02–1.16), $P$ = 0.010 |
| | $SUV_{mean}$ (T) | 1.02 (0.97–1.07), $P$ = 0.385 | 1.02 (0.98–1.06), $P$ = 0.333 | 1.02 (0.98–1.06), $P$ = 0.342 |
| | MTV 41% (T) | 1.03 (1.01–1.05), $P$ = 0.001 | 1.02 (1–1.03), $P$ = 0.023 | 1.02 (1.01–1.04), $P$ = 0.002 |
| | TLG (T) | 1.00 (1–1), $P$ < 0.001 | 1.00 (1–1), $P$ = 0.009 | 1.00 (1–1), $P$ = 0.001 |
| | MTV 41% (N) | 1.06 (1.02–1.1), $P$ = 0.002 | 1.06 (1.03–1.1), $P$ < 0.001 | 1.06 (1.02–1.1), $P$ = 0.001 |
| | MTV 41% (T + N) | 1.03 (1.01–1.04), $P$ < 0.001 | 1.02 (1–1.03), $P$ = 0.005 | 1.02 (1.01–1.04), $P$ = 0.001 |
| | TLG (N) | 1.01 (1–1.01), $P$ = 0.025 | 1.01 (1–1.01), $P$ = 0.001 | 1.01 (1–1.01), $P$ = 0.029 |
| | TLG (T + N) | 1.00 (1–1), $P$ < 0.001 | 1.00 (1–1), $P$ = 0.004 | 1.00 (1–1), $P$ < 0.001 |
| Posttreatment $^{18}$F-FDG PET/CT | $SUV_{max}$ | 1.30 (1.14–1.49), $P$ < 0.001 | 1.21 (1.09–1.34), $P$ < 0.001 | 1.32 (1.19–1.48), $P$ < 0.001 |
| Both | Change in $SUV_{max}$ | 1.00 (0.98–1.02), $P$ = 0.889 | 1.00 (0.99–1.02), $P$ = 0.888 | 1.00 (0.98–1.01), $P$ = 0.487 |

Data in parentheses are 95% CIs.

## DISCLOSURE

Financial support was received from FFCD. No other potential conflict of interest relevant to this article was reported.

**KEY POINTS**

**QUESTION:** Could PET/CT be useful in assessing treatment response after RT of SCCA?

**PERTINENT FINDINGS:** This prospective cohort study showed PET/CT to have statistically significant prognostic value in assessing treatment response in terms of RFS, CFS, and OS.

**IMPLICATIONS FOR PATIENT CARE:** PET/CT could be useful to assess treatment response and to adapt follow-up, especially for patients with locally advanced-stage tumors.

## REFERENCES

1. Defossez G, Le Guyader-Peyrou S, Uhry Z, et al. *National Estimates of Cancer Incidence and Mortality in Metropolitan France Between 1990 and 2018.* Vol 1. French Public Health Service; 2019:372.
2. Bilimoria KY, Bentrem DJ, Rock CE, Stewart AK, Ko CY, Halverson A. Outcomes and prognostic factors for squamous-cell carcinoma of the anal canal: analysis of patients from the National Cancer Data Base. *Dis Colon Rectum.* 2009;52:624–631.
3. Gunderson LL, Winter KA, Ajani JA, et al. Long-term update of US GI intergroup RTOG 98-11 phase III trial for anal carcinoma: survival, relapse, and colostomy failure with concurrent chemoradiation involving fluorouracil/mitomycin versus fluorouracil/cisplatin. *J Clin Oncol.* 2012;30:4344–4351.
4. Moureau-Zabotto L, Vendrely V, Abramowitz L, et al. Anal cancer: French Intergroup Clinical Practice Guidelines for diagnosis, treatment and follow-up (SNFGE, FFCD, GERCOR, UNICANCER, SFCD, SFED, SFRO, SNFCP). *Dig Liver Dis.* 2017;49:831–840.
5. Salaün PY, Abgral R, Malard O, et al. Update of the recommendations of good clinical practice for the use of PET in oncology [in French]. *Bull Cancer.* 2019;106:262–274.
6. Rao S, Guren MG, Khan K, et al. Anal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2021;32:1087–1100.
7. Caldarella C, Annunziata S, Treglia G, Sadeghi R, Ayati N, Giovanella L. Diagnostic performance of positron emission tomography/computed tomography using fluorine-18 fluorodeoxyglucose in detecting locoregional nodal involvement in patients with anal canal cancer: a systematic review and meta-analysis. *ScientificWorldJournal.* 2014;2014:196068.
8. Cotter SE, Grigsby PW, Siegel BA, et al. FDG-PET/CT in the evaluation of anal carcinoma. *Int J Radiat Oncol Biol Phys.* 2006;65:720–725.
9. Jones M, Hruby G, Solomon M, Rutherford N, Martin J. The role of FDG-PET in the initial staging and response assessment of anal cancer: a systematic review and meta-analysis. *Ann Surg Oncol.* 2015;22:3574–3581.
10. Sveistrup J, Loft A, Berthelsen AK, Henriksen BM, Nielsen MB, Engelholm SA. Positron emission tomography/computed tomography in the staging and treatment of anal cancer. *Int J Radiat Oncol Biol Phys.* 2012;83:134–141.
11. Krengli M, Milia ME, Turri L, et al. FDG-PET/CT imaging for staging and target volume delineation in conformal radiotherapy of anal carcinoma. *Radiat Oncol.* 2010;5:10.
12. Mahmud A, Poon R, Jonker D. PET imaging in anal canal cancer: a systematic review and meta-analysis. *Br J Radiol.* 2017;90:20170370.
13. Bazan JG, Koong AC, Kapp DS, et al. Metabolic tumor volume predicts disease progression and survival in patients with squamous cell carcinoma of the anal canal. *J Nucl Med.* 2013;54:27–32.
14. Mohammadkhani Shali S, Schmitt V, Behrendt FF, et al. Metabolic tumour volume of anal carcinoma on $^{18}$FDG PET/CT before combined radiochemotherapy is the only independant determinant of recurrence free survival. *Eur J Radiol.* 2016;85:1390–1394.
15. Le Thiec M, Testard A, Ferrer L, et al. Prognostic impact of pretherapeutic FDG-PET in localized anal cancer. *Cancers (Basel).* 2020;12:1512.
16. Leccisotti L, Manfrida S, Barone R, et al. The prognostic role of FDG PET/CT before combined radio-chemotherapy in anal cancer patients. *Ann Nucl Med.* 2020;34:65–73.
17. Vendrely V, Lemanski C, Pommier P, et al. Treatment, outcome, and prognostic factors in non-metastatic anal cancer: the French nationwide cohort study FFCD-ANABASE. *Radiother Oncol.* 2023;183:109542.
18. Day FL, Link E, Ngan S, et al. FDG-PET metabolic response predicts outcomes in anal cancer managed with chemoradiotherapy. *Br J Cancer.* 2011;105:498–504.
19. Goldman KE, White EC, Rao AR, Kaptein JS, Lien WW. Post-treatment FDG-PET-CT response is predictive of tumor progression and survival in anal carcinoma. *Pract Radiat Oncol.* 2016;6:e149–e154.
20. Houard C, Pinaquy JB, Mesguich C, et al. Role of $^{18}$ F-FDG PET/CT in posttreatment evaluation of anal carcinoma. *J Nucl Med.* 2017;58:1414–1420.
21. Schwarz JK, Siegel BA, Dehdashti F, Myerson RJ, Fleshman JW, Grigsby PW. Tumor response and survival predicted by post-therapy FDG-PET/CT in anal cancer. *Int J Radiat Oncol Biol Phys.* 2008;71:180–186.
22. Teagle AR, Gilbert DC, Jones JR, Burkill GJ, McKinna F, Dizdarevic S. Negative $^{18}$F-FDG-PET-CT may exclude residual or recurrent disease in anal cancer. *Nucl Med Commun.* 2016;37:1038–1045.
23. Gauthé M, Richard-Molard M, Fayard J, Alberini JL, Cacheux W, Lièvre A. Prognostic impact of tumour burden assessed by metabolic tumour volume on FDG PET/CT in anal canal cancer. *Eur J Nucl Med Mol Imaging.* 2017;44:63–70.
24. Filippi L, Fontana A, Spinelli GP, Rossi L, Bagni O. Role of $^{18}$F-FDG PET-derived parameters for predicting complete response to chemoradiotherapy in squamous cell anal carcinoma. *Nucl Med Commun.* 2020;41:1089–1094.
25. Cardenas ML, Spencer CR, Markovina S, et al. Quantitative FDG-PET/CT predicts local recurrence and survival for squamous cell carcinoma of the anus. *Adv Radiat Oncol.* 2017;2:281–287.
26. Kidd EA, Dehdashti F, Siegel BA, Grigsby PW. Anal cancer maximum F-18 fluorodeoxyglucose uptake on positron emission tomography is correlated with prognosis. *Radiother Oncol.* 2010;95:288–291.
27. Deantonio L, Milia ME, Cena T, et al. Anal cancer FDG-PET standard uptake value: correlation with tumor characteristics, treatment response and survival. *Radiol Med (Torino).* 2016;121:54–59.
28. Martin D, Schreckenbach T, Ziegler P, et al. Evaluation of prognostic factors after primary chemoradiotherapy of anal cancer: a multicenter study of the German Cancer Consortium-Radiation Oncology Group (DKTK-ROG). *Radiother Oncol.* 2022;167:233–238.