American College of Radiology
ACR Appropriateness Criteria®
Staging and Follow-up of Anal Cancer

Variant: 1 Adult. Newly diagnosed squamous cell anal cancer. Locoregional assessment at initial staging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI pelvis without and with IV contrast	Usually Appropriate	O
FDG-PET/CT skull base to mid-thigh	Usually Appropriate	☢☢☢☢
MRI pelvis without IV contrast	May Be Appropriate	O
CT pelvis with IV contrast	May Be Appropriate	☢☢☢
FDG-PET/MRI whole body	May Be Appropriate	☢☢☢
US pelvis transrectal	Usually Not Appropriate	O
CT pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢

Variant: 2 Adult. Squamous cell anal cancer. Assessment for metastatic disease at initial staging or surveillance.

Procedure	Appropriateness Category	Relative Radiation Level
CT abdomen and pelvis with IV contrast	Usually Appropriate	☢☢☢
CT chest with IV contrast	Usually Appropriate	☢☢☢
CT chest without IV contrast	Usually Appropriate	☢☢☢
FDG-PET/CT skull base to mid-thigh	Usually Appropriate	☢☢☢☢
MRI abdomen and pelvis without and with IV contrast	May Be Appropriate	O
CT abdomen and pelvis without IV contrast	May Be Appropriate	☢☢☢
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	O
CT chest without and with IV contrast	Usually Not Appropriate	☢☢☢
FDG-PET/MRI whole body	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢

Variant: 3 Adult. Squamous cell anal cancer. Posttreatment locoregional assessment.

Procedure	Appropriateness Category	Relative Radiation Level
MRI pelvis without and with IV contrast	Usually Appropriate	O
FDG-PET/CT skull base to mid-thigh	Usually Appropriate	☢☢☢☢
MRI pelvis without IV contrast	May Be Appropriate	O
CT pelvis with IV contrast	May Be Appropriate	☢☢☢
FDG-PET/MRI whole body	May Be Appropriate	☢☢☢
US pelvis transrectal	Usually Not Appropriate	O
CT pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢

Panel Members

Natally Horvat,

[a], Peter S. Liu, MD[b], Kathryn J. Fowler, MD[c], James H. Birkholz, MD[d], Brooks D. Cash, MD[e], Bari Dane, MD[f], Cathy Eng, MD[g], Avinash R. Kambadakone, MD[h], Elena K. Korngold, MD[i], Jason A. Pietryga, MD[j], Tamer Refaat, MD, PhD, MS[k], Cynthia S. Santillan, MD[l], Devaki Shilpa Surasi, MD[m], Sarah Woolsey, MD, MPH[n], David H. Kim, MD[o]

Summary of Literature Review

Introduction/Background

Anal cancer is a relatively uncommon malignancy, with squamous cell carcinoma being the most prevalent histological type [1]. Over the past few decades, the incidence of anal cancer has been steadily rising. In 2023, it is estimated that there will be 9,760 new cases in the United States, with 6,580 cases in women and 3,180 cases in men. Additionally, approximately 1,870 deaths are expected to occur due to this disease [2]. There are risk factors associated with anal cancer including human papillomavirus (HPV) infection, immunosuppression after solid organ transplantation or human immunodeficiency virus (HIV), smoking, and history of cervical, vulvar, or vaginal cancer [3,4]. Individuals with HIV infection have a 30-fold higher risk of developing anal cancer compared to the general population, and transplant recipients have a 10-fold higher risk [4]. Most patients with anal cancer are asymptomatic during the initial stages of the disease; if symptomatic, the most frequent symptoms are anal pain, itching, anal discomfort, rectal bleeding, and sensation of rectal mass, which are often attributed to hemorrhoidal conditions and can contribute to a delayed diagnosis [3-6].

The diagnosis, staging, and surveillance of patients with anal cancer involve a combination of physical examination, imaging tests, and biopsy. The initial staging of anal cancer provides prognostic information and guides treatment planning. Local staging involves assessing the size of the primary tumor on its longest diameter and determining the involvement of locoregional organs, as follows: T1, tumor <2.0 cm; T2, tumor between 2.1 and 5.0 cm; T3, tumor >5.1 cm; and T4, tumor of any size invading adjacent organs, except sphincter, rectal wall, perianal skin, and subcutaneous tissues. With regard to the nodal local staging, it depends on the site of involved lymph nodes, as follows: N1a, inguinal, mesorectal, superior rectal, obturator, and/or internal iliac; N1b, external iliac, and N1c, N1b (external iliac) with any N1a [5,7]. With regard to overall American Joint Committee on Cancer staging, anal cancer can be classified as follows: stage I (T1N0M0), stage IIA (T2N0M0), stage IIB (T1-T2N1M0), stage IIIA (T3N0M0 or T3N1M0), stage IIIB (T4N0M), stage IIIC (T4N1M0), and stage IV (any T, any N, and M1) [8]. Usually, early-stage anal cancer has a favorable prognosis, however, advanced-stage or metastatic disease has a poorer prognosis and requires a more aggressive treatment approach.

The current standard treatment for patients with anal cancer is definitive chemoradiation (CRT), which entails the use of a combination chemotherapy along with external beam radiotherapy. Most patients with anal cancer achieve clinical complete response after CRT; considering that, surgical procedures are considered only in the setting of small lesions at the anal margin without lymph node metastases or as a salvage strategy for persistent or recurrent disease [4,5]. In the context of viable disease following the completion of chemoradiotherapy, in which surgical intervention is being considered, imaging plays a crucial role in guiding the surgical plan [9]. In the setting of metastatic disease, systemic therapy with or without CRT for primary site disease control are the therapy of choice. Finally, surveillance is essential for monitoring recurrence and long-term side effects of treatment [10].

Discussion of Procedures by Variant

Variant 1: Adult. Newly diagnosed squamous cell anal cancer. Locoregional assessment at initial staging.

In a newly diagnosed anal cancer with squamous cell histology, the goal of locoregional assessment is to determine the extent of the primary anal tumor, including involvement of surrounding organs and suspicious pelvic lymph nodes. Based on this information, the multidisciplinary team would be able to select appropriate treatment, particularly the radiation therapy plan.

Variant 1: Adult. Newly diagnosed squamous cell anal cancer. Locoregional assessment at initial staging.
A. CT pelvis with IV contrast

CT pelvis is commonly used to guide target delineation for radiation therapy in anal cancer, however, there is limited evidence supporting its initial staging role for locoregional assessment. In a study by Bannas et al [11], which included 22 patients, the authors compared the effectiveness of fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET and contrast-enhanced CT images both individually and in combination (FDG-PET/CT). The results showed that CT failed to identify T1 tumors, correctly identified 30% of T2 tumors, and accurately detected all T3 tumors. However, the study did not include any T4 tumors. Regarding nodal staging, CT identified 3 mesorectal and 2 iliac lymph nodes, all of which were negative on FDG-PET/CT. CT also detected 9 inguinal lymph nodes, with 5 confirmed as positive on FDG-PET/CT. In CT scans, the criteria for identifying lymph node metastases included a width-to-length ratio >0.8 cm or a single dimension measuring >1.5 cm; while FDG-PET/CT considered FDG uptake higher than the regional background the criteria for defining nodal metastases. Another study by Mistrangelo et al [12] involving 35 patients who underwent contrast-enhanced CT demonstrated that contrast-enhanced CT successfully detected 33% of T1 lesions, 78% of T2 lesions, and 100% of T3 and T4 lesions. The study also showed that mesorectal and pelvic nodes were detected in 18% of patients on contrast-enhanced CT and 26% on FDG-PET/CT. In comparison to sentinel nodal biopsy, CT exhibited a false-positive rate of 12% and a false-negative rate of 12% for inguinal lymph nodes. Additionally, CT raised suspicion of vaginal invasion in 2 cases, although subsequent clinical assessment did not confirm it. A meta-analysis conducted by Jones et al [13] demonstrated that CT had a sensitivity of 60% (95% confidence interval [CI], 46%-75%) in detecting the primary tumor, whereas Mahmud et al [14] reported a pooled sensitivity of 67% (95% CI, 50%-82%).

Variant 1: Adult. Newly diagnosed squamous cell anal cancer. Locoregional assessment at initial staging.
B. CT pelvis without and with IV contrast

There is no relevant literature to support the use of CT pelvis without and with intravenous (IV) contrast for locoregional assessment in the initial staging of anal cancer.

Variant 1: Adult. Newly diagnosed squamous cell anal cancer. Locoregional assessment at initial staging.
C. CT pelvis without IV contrast

There is no relevant literature to support the use of CT pelvis without IV contrast for locoregional assessment in the initial staging of anal cancer.

Variant 1: Adult. Newly diagnosed squamous cell anal cancer. Locoregional assessment at

initial staging.
D. FDG-PET/CT skull base to mid-thigh

There is a growing body of data on the added value of FDG-PET/CT for the locoregional assessment of anal cancer during initial staging.

In a meta-analysis conducted by Albertsson et al [15], which reviewed data from 10 studies (including 3 prospective studies), it was found that PET/CT changed the target volume for nearly 1 in 4 patients with anal cancer. Caldarella et al [16], in their analysis of 12 studies, demonstrated a pooled sensitivity of 56% (95% CI, 45%-67%) and specificity of 90% (95% CI, 86%-93%) in detecting locoregional lymph node involvement in patients with anal cancer. However, the presence of heterogeneity among the studies may introduce potential bias.

Another meta-analysis by Jones et al [13], which included 12 studies, aimed to compare the role of FDG-PET/CT or PET/CT with conventional imaging (CT or MRI) in detecting primary tumors and lymph node disease in patients with anal cancer. FDG-PET/CT exhibited a sensitivity of 99% (95% CI, 96%-100%) in detecting the primary tumor and altered the nodal stage in 28% (95% CI, 18%-38%) of the patients. However, nodal biopsy confirmation was performed in only a few cases. Overall, FDG-PET/CT up-staged 21% (95% CI, 13%-30%) of the patients and down-staged 17% (95% CI, 11%-23%) of the patients.

Mahmud et al [14] systematically reviewed the literature and summarized the evidence regarding FDG-PET/CT or PET use in patients with anal cancer (including 17 studies). The pooled sensitivity for assessing the primary tumor was also 99% (95% CI, 97%-100%), whereas the sensitivity for detecting suspicious inguinal lymph nodes including studies with biopsy confirmation was 93% (95% CI, 76%-99%) with a specificity of 76% (95% CI, 61%-87%). With regard to change in treatment planning, Mahmud et al [14] summarized 8 studies and FDG-PET/CT or PET changed the therapeutic plan in 13% to 59% of the patients, consisting mainly of radiotherapy dose or field changes. PET/CT has lower sensitivity than MRI in detecting mesorectal lymph nodes, but this does not change management because mesorectal nodes are routinely included in the radiation field.

The most recent meta-analysis led by Mirshahvalad et al [17] showed a pooled sensitivity and specificity for differentiating T3/T4 from T1/T2 of 91% (95% CI, 72%-97%) and 96% (95% CI,88%-98%), respectively. Regarding nodal staging, Mirshahvalad et al [17] demonstrated an estimated sensitivity and specificity for detecting lymph node metastases of 99% (95% CI, 80%-100%) and 93% (95% CI, 87%-96%), however, limiting the data only to cases with histopathology confirmation, the pooled sensitivity and specificity decreased to 86% (95% CI, 42%-98%) and 79% (95% CI, 69%-86%), respectively.

Variant 1: Adult. Newly diagnosed squamous cell anal cancer. Locoregional assessment at initial staging.
E. FDG-PET/MRI whole body

FDG-PET/MRI has potential advantages for local staging, taking into account studies that assessed FDG-PET/CT and MRI independently, however, there is no relevant literature evaluating FDG-PET/MRI for locoregional assessment in the initial staging of anal cancer.

Variant 1: Adult. Newly diagnosed squamous cell anal cancer. Locoregional assessment at initial staging.
F. MRI pelvis without and with IV contrast

Very few studies were published evaluating contrast-enhanced MRI for initial locoregional assessment in anal cancer, and some groups showed that the use of IV contrast may add value in imaging interpretation. Otto et al [18] compared contrast-enhanced MRI and transanal endoscopic ultrasound (US), showing comparable results, although endoscopic US was superior to small superficial lesions, and MRI was preferable to assess pelvic adenopathy. Golia Pernicka et al [19] showed in the survey and expert opinion that only 52% of expert panel considered contrast-enhanced T1-weighted sequence very helpful or extremely helpful; the majority of them used 2-D T2-weighted as the first-choice imaging sequence for the local assessment. There is no relevant literature to support the use of an endorectal coil when performing MRI pelvis without and with IV contrast in the staging of anal cancer.

Variant 1: Adult. Newly diagnosed squamous cell anal cancer. Locoregional assessment at initial staging.
G. MRI pelvis without IV contrast

Few studies have evaluated the use of pelvic MRI for locoregional assessment of anal cancer, and most of them did not use IV contrast. However, it is well known that MRI offers excellent contrast resolution, making it a valuable imaging modality for evaluating diseases of the anus and perianal region. Bhuva et al [20] showed concordance of 93% between MRI and FDG-PET/CT for primary tumor assessment. Min et al [21] reported good interobserver agreement among radiologists and radiation oncologists regarding gross tumor volume delineation on MRI using T2-weighted images and diffusion-weighted imaging (DWI), although reproducibility decreased in the presence of DWI artifacts. Prezzi et al [22] showed that DWI obtained higher interobserver agreement and higher tumor delineation confidence between a third year resident and a gastrointestinal radiology fellow. Additionally, Rusten et al [23] showed that the delineation based on PET and MRI were comparable. There is no relevant literature to support the use of an endorectal coil when performing MRI pelvis without IV contrast in the staging of anal cancer.

Golia Pernicka et al [19] led a survey and expert opinion from the Rectal and Anal Cancer Disease-Focused Panel of the Society of Abdominal Radiology, including 23 experts, 20 of 23 (87%) diagnostic radiologists, 2 of 23 (9%) nuclear medicine radiologists, and 1 of 23 (4%) both diagnostic and nuclear medicine radiologists, and 65% suggested MRI as the first-choice modality for primary local staging,

Variant 1: Adult. Newly diagnosed squamous cell anal cancer. Locoregional assessment at initial staging.
H. US pelvis transrectal

Few studies evaluated transrectal US for locoregional assessment of anal cancer. Reginelli et al [24] and Otto et al [18] both demonstrated that transrectal US is accurate for initial T-stage, but suboptimal to assess pelvic lymph nodes. Otto et al [18] prospectively compared transrectal US and MRI among 45 patients and showed comparable results in the evaluation of the primary tumor, with transrectal US performing better for assessment of small superficial lesions. However, transrectal US incompletely evaluated lymph nodes outside the sonographic field of view. Reginelli et al [24] retrospectively compared 58 patients who underwent physical examination, endoanal US, and MRI and demonstrated that transrectal US is more accurate to detect T1 anal cancers, whereas MRI provided better evaluation of the lymph nodes. The Golia Pernicka et al [19] survey showed that transrectal US is not routinely used at the participant's institutions.

Variant 2: Adult. Squamous cell anal cancer. Assessment for metastatic disease at initial staging or surveillance.

The National Comprehensive Cancer Network guidelines recommend assessing metastatic disease both at the initial presentation and during surveillance of patients with anal squamous cell carcinoma. Metastatic disease is rarely observed in patients during the initial presentation; it is more commonly associated with recurrence after treatment [4,5]. Typically, distant metastases manifest later in the course of the disease, with treatment failure often occurring at the primary tumor site [25]. The most frequent sites of metastases are the retroperitoneal lymph nodes, liver, and lungs. Accurate imaging assessment plays a critical role in diagnosing metastatic disease and guiding multidisciplinary treatment approaches, which frequently involve the addition of systemic therapy options [4].

Variant 2: Adult. Squamous cell anal cancer. Assessment for metastatic disease at initial staging or surveillance.
A. CT abdomen and pelvis with IV contrast

CT is frequently used for evaluation of distant metastatic disease in patients with cancer at initial presentation and surveillance, including in patients with anal cancer [13]. CT abdomen and pelvis with IV contrast is useful to evaluate for metastatic disease at primary staging and surveillance of oncological patients, including patients with anal squamous cell carcinoma [10].

Variant 2: Adult. Squamous cell anal cancer. Assessment for metastatic disease at initial staging or surveillance.
B. CT abdomen and pelvis without and with IV contrast

CT is frequently used for evaluation of distant metastatic disease in patients with cancer at initial presentation and surveillance, including in patients with anal cancer [13]. There are no studies evaluating the added benefit of noncontrast imaging in addition to postcontrast series at CT in metastatic anal cancer assessment.

Variant 2: Adult. Squamous cell anal cancer. Assessment for metastatic disease at initial staging or surveillance.
C. CT abdomen and pelvis without IV contrast

CT is frequently used for evaluation of distant metastatic disease in patients with cancer at initial presentation and surveillance, including in patients with anal cancer [13]. Assessment is typically done with IV contrast given the increased conspicuity of parenchymal lesions such as in the liver over noncontrast studies. There are no recent studies evaluating CT abdomen and pelvis without contrast in metastatic evaluation for anal cancer.

Variant 2: Adult. Squamous cell anal cancer. Assessment for metastatic disease at initial staging or surveillance.
D. CT chest with IV contrast

Body CT is frequently used for evaluation of distant metastatic disease in patients with cancer, including in patients with anal cancer. CT chest with IV contrast is usually useful to evaluate for metastatic disease at primary staging and surveillance of patients with anal squamous cell carcinoma. The use of IV contrast, although not mandatory for assessing lung metastases, can aid in nodal delineation. Because a CT chest is typically included in a CT abdomen and pelvis request, and IV contrast is suitable for abdominal and pelvic staging, a CT chest with IV contrast is also considered appropriate [10].

Variant 2: Adult. Squamous cell anal cancer. Assessment for metastatic disease at initial staging or surveillance.
E. CT chest without and with IV contrast

Body CT is frequently used for evaluation of distant metastatic disease in patients with cancer, including in patients with anal cancer. Similarly, CT chest with IV contrast is useful to evaluate for metastatic disease at primary staging and surveillance of patients with anal squamous cell carcinoma [10].

Variant 2: Adult. Squamous cell anal cancer. Assessment for metastatic disease at initial staging or surveillance.
F. CT chest without IV contrast

CT chest without IV contrast is useful to evaluate for metastatic disease at primary staging and surveillance of patients with anal squamous cell carcinoma [10], particularly when the abdomen and pelvis have already been staged.

Variant 2: Adult. Squamous cell anal cancer. Assessment for metastatic disease at initial staging or surveillance.
G. FDG-PET/CT skull base to mid-thigh

Several studies explored the added value of FDG-PET/CT in the evaluation of metastatic disease among patients with anal cancer, considering that the metastatic disease is usually highly FDG-avid. Jones et al [13] showed in the meta-analysis that FDG-PET/CT identified undetected distant metastases in 3% (95% CI, 1%-5%) of the patients, however, with lower specificity due to false-positive cases related to inflammatory nodal disease in HIV-positive patients, undetected synchronous tumors, and other conditions, such as sarcoidosis. Mahmud et al [14] in a meta-analysis also showed that FDG-PET/CT identified distant metastases in 2.4% to 4.7% of the patients, however, biopsy was not always performed.

For disease surveillance, the routine use of FDG-PET/CT is not clear. Wells et al [26] suggests to consider FDG-PET/CT in selected situations as a problem-solving tool or if salvage surgery is planned. Wells et al [26] showed that the M stage was changed in 21% (10 of 48) of the patients, up-stage occurred due to detection of distant lymph node metastases and new liver metastases, whereas down-stage occurred in suspected liver and bone lesions not FDG-avid.

Mirshahvalad et al [17] showed in a meta-analysis including 5 studies that assessed distant metastases a pooled specificity of 99% (95% CI, 97%-100%), with 3 false-positive cases (2 patients with mediastinal lymph nodes negative on biopsy and 1 patient demonstrated and FDG-avid osteoarthritis mimicking metastasis). Among the 4 studies that described sensitivity, all reported 100%.

Variant 2: Adult. Squamous cell anal cancer. Assessment for metastatic disease at initial staging or surveillance.
H. FDG-PET/MRI whole body

There is no relevant literature to support the use of FDG-PET/MRI whole body in the assessment for metastatic disease of anal cancer.

Variant 2: Adult. Squamous cell anal cancer. Assessment for metastatic disease at initial staging or surveillance.
I. MRI abdomen and pelvis without and with IV contrast

In specific scenarios including assessing small, indeterminate liver lesions, MRI plays a valuable problem-solving role. For guidance on liver lesion characterization, reference should be made to the ACR Appropriateness Criteria® topic on "Liver Lesion-Initial Characterization" [27].

Variant 2: Adult. Squamous cell anal cancer. Assessment for metastatic disease at initial staging or surveillance.
J. MRI abdomen and pelvis without IV contrast

The use of IV contrast in indicated to increase the diagnostic accuracy of MRI in assessing liver lesions. For guidance on liver lesion characterization, reference should be made to the ACR Appropriateness Criteria® topic on "Liver Lesion-Initial Characterization" [27].

Variant 3: Adult. Squamous cell anal cancer. Posttreatment locoregional assessment.

Most patients with anal squamous cell carcinoma typically achieve a clinical complete response after CRT, and surgery is considered only in cases of persistent disease or recurrence [4]. Traditionally, the assessment of locoregional treatment response has relied on clinical evaluation, and the role of imaging assessment is still a subject of debate. In the setting in which surgery is indicated, locoregional imaging assessment plays a role for surgical planning [3,5,6].

Variant 3: Adult. Squamous cell anal cancer. Posttreatment locoregional assessment.
A. CT pelvis with IV contrast

There is limited evidence supporting the use of CT pelvis on posttreatment locoregional assessment, anecdotally if the clinical question is related to distinguishing posttreatment changes from viable tumor, CT may lack sufficient anatomical resolution for effective differentiation. This procedure may be useful for assessing nodal size change and primary size change, however, CT might not offer the level of soft tissue detail necessary for thorough surgical decision-making.

Variant 3: Adult. Squamous cell anal cancer. Posttreatment locoregional assessment.
B. CT pelvis without and with IV contrast

There is no relevant literature to support the use of CT pelvis without and with IV contrast for posttreatment locoregional assessment.

Variant 3: Adult. Squamous cell anal cancer. Posttreatment locoregional assessment.
C. CT pelvis without IV contrast

There is no relevant literature to support the use of CT pelvis without IV contrast for posttreatment locoregional assessment.

Variant 3: Adult. Squamous cell anal cancer. Posttreatment locoregional assessment.
D. FDG-PET/CT skull base to mid-thigh

Several studies have assessed the supplementary benefits of FDG-PET/CT in locoregional posttreatment evaluation. In a meta-analysis conducted by Jones et al [13], PET demonstrated complete response rates of 64% (95% CI, 10%-100%), 81% (95% CI, 71%-89%), 81% (95% CI, 51%-99%), and 80% (95% CI, 59%-93%) at 1, 2, 3, and 4 months after treatment, respectively. Mahmud et al [14] in a meta-analysis also demonstrated the heterogeneity regarding time of assessment after treatment, ranging from 1 to 8 months, with lower complete response rates in the study that used 1 month of posttreatment follow-up (33%). Among the studies that evaluated survival outcomes, patients with partial response or no response on posttreatment PET or FDG-PET/CT had significantly worse outcomes, including overall survival, disease-free survival, and progression-free survival. Susko et al [28] also demonstrated that higher metabolic tumor volume and total lesion glycolysis were associated with elevated rates of local recurrence and worse progression-free survival and overall survival. Adusumilli et al [29] in a retrospective study with 75 patients showed that FDG-PET/CT alone had accuracy of 69.3%, positive predictive value (PPV) of 36.7%, and a negative predictive value (NPV) of 91.1% in predicting complete response after CRT, however, when combined with MRI, it significantly increased the accuracy to 94.7%, PPV to 78.9%, and NPV

to 100%. Mirshahvalad et al [17] conducted a meta-analysis comprising 9 studies to evaluate response assessment after treatment on FDG-PET/CT; the pooled sensitivity and specificity were determined to be 96% (95% CI, 78%-99%) and 86% (95% CI, 75%-93%), respectively.

Variant 3: Adult. Squamous cell anal cancer. Posttreatment locoregional assessment. E. FDG-PET/MRI whole body

FDG-PET/MRI has potential advantages for local restaging, considering studies that assessed FDG-PET/CT and MRI independently, however, there is no relevant literature evaluating FDG-PET/MRI for posttreatment locoregional assessment in the restaging of anal cancer.

Variant 3: Adult. Squamous cell anal cancer. Posttreatment locoregional assessment. F. MRI pelvis without and with IV contrast

Few studies assessed the added value of postcontrast phases in the assessment of tumor response in patients with anal cancer. Reginelli et al [24] showed in a retrospective cohort of 58 patients that the time intensity curve on dynamic contrast-enhanced MRI were different in patients with complete response; the responders had significantly more type 2 curves, corresponding to slow sustained enhancement.

Variant 3: Adult. Squamous cell anal cancer. Posttreatment locoregional assessment. G. MRI pelvis without IV contrast

Some institutions follow similar rectal MRI protocols without IV contrast in the restaging of anal cancer. Kochhar et al [30] assessed tumor regression grade on T2-weighted image sequences in a prospective study of 74 patients 3 and 6 months after the CRT and showed that MRI-based tumor regression grade score was able to predict local disease relapse. All patients classified as tumor regression grade I or II did not have local disease relapse. Reginelli et al [24] showed in a retrospective cohort of 58 patients that DWI was significantly different between patients with complete response and incomplete response after CRT. Adusumilli et al [29] in a retrospective study with 75 patients showed that MRI alone using T2-weighted images and DWI findings had an accuracy of 76%, a PPV of 44.8%, an NPV of 95.7% in predicting complete response after CRT, however, when combined with FDG-PET/CT it significantly increased to accuracy to 94.7%, the PPV to 78.9%, and the NPV to 100%. Prezzi et al [31] demonstrated that DWI added value to T2-weighted by decreasing the indeterminate cases and increasing the radiologist's confidence in defining tumor response to treatment. Golia Pernicka et al [19] showed in their expert survey that MRI was the modality of choice with level of agreement between 52% and 60%, except for nodal staging in which PET/CT was selected as the modality of choice with 69% of agreement.

Variant 3: Adult. Squamous cell anal cancer. Posttreatment locoregional assessment. H. US pelvis transrectal

Few studies evaluated the added value of endoscopic US to digital rectal examination. Peterson et al [32] showed in a retrospective study that endoscopic US did not increase the accuracy in detecting recurrent anal cancer after CRT. In this study with 175 patients, no recurrence identified on endoscopic US were evident on digital rectal examination [32]. Additionally, Reginelli et al [24] found that endoscopic US was not able to differentiate residual tumor or fibrosis after CRT.

Summary of Highlights

This is a summary of the key recommendations from the variant tables. Refer to the complete narrative document for more information.

- **Variant 1**: For initial locoregional staging, MRI of the pelvis and FDG-PET/CT are usually appropriate to complement clinical and digital rectal examinations because they offer additional information regarding locoregional tumor invasion and nodal metastases.
- **Variant 2**: For metastatic disease assessment, which is rare in the initial presentation and commonly associated with recurrence, CT and FDG-PET/CT are usually appropriate for detecting distant nodal metastases and other sites of metastatic disease. MRI of the abdomen may be appropriate as a problem-solving tool, particularly in assessing small or indeterminate liver lesions.
- **Variant 3**: For patients who have completed locoregional treatment, the role of posttreatment imaging assessment is still debatable, however, in cases in which surgery is indicated, MRI and FDG-PET/CT are usually appropriate for assessing local tumor invasion and nodal metastases.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria.

Gender Equality and Inclusivity Clause

The ACR acknowledges the limitations in applying inclusive language when citing research studies that predates the use of the current understanding of language inclusive of diversity in sex, intersex, gender, and gender-diverse people. The data variables regarding sex and gender used in the cited literature will not be changed. However, this guideline will use the terminology and definitions as proposed by the National Institutes of Health.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.

Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document.

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as “Varies.”

References

1. Surabhi VR, Menias CO, Amer AM, et al. Tumors and Tumorlike Conditions of the Anal Canal and Perianal Region: MR Imaging Findings. [Review]. Radiographics. 36(5):1339-53, 2016 Sep-Oct.
2. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin 2023;73:17-48.
3. Ciombor KK, Ernst RD, Brown G. Diagnosis and Diagnostic Imaging of Anal Canal Cancer. [Review]. Surg Oncol Clin N Am. 26(1):45-55, 2017 01.
4. Eng C, Messick C, Glynne-Jones R. The Management and Prevention of Anal Squamous Cell Carcinoma. [Review]. Am. Soc. Clin. Oncol. educ. book. 39:216-225, 2019 Jan.
5. Golia Pernicka JS, Sheedy SP, Ernst RD, Minsky BD, Ganeshan D, Rauch GM. MR staging of anal cancer: what the radiologist needs to know. [Review]. Abdom Radiol. 44(11):3726-3739, 2019 11.
6. Hemachandran N, Goyal A, Bhattacharjee HK, Sharma R. Radiology of anal and lower rectal

cancers. [Review]. Clin Radiol. 76(12):871-878, 2021 12.

7. Gourtsoyianni S, Goh V. MRI of anal cancer: assessing response to definitive chemoradiotherapy. [Review]. Abdom Imaging. 39(1):2-17, 2014 Feb.

8. Amin MB, Edge S, Greene F, et al. AJCC Cancer Staging Manual. 8th ed. New York, NY: Springer; 2017.

9. Torkzad MR, Kamel I, Halappa VG, Beets-Tan RG. Magnetic resonance imaging of rectal and anal cancer. [Review]. Magn Reson Imaging Clin N Am. 22(1):85-112, 2014 Feb.

10. Maas M, Tielbeek JAW, Stoker J. Staging of Anal Cancer: Role of MR Imaging. [Review]. Magn Reson Imaging Clin N Am. 28(1):127-140, 2020 Feb.

11. Bannas P, Weber C, Adam G, et al. Contrast-enhanced [(18)F]fluorodeoxyglucose-positron emission tomography/computed tomography for staging and radiotherapy planning in patients with anal cancer. Int J Radiat Oncol Biol Phys. 81(2):445-51, 2011 Oct 01.

12. Mistrangelo M, Pelosi E, Bello M, et al. Role of positron emission tomography-computed tomography in the management of anal cancer. Int J Radiat Oncol Biol Phys. 84(1):66-72, 2012 Sep 01.

13. 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. [Review]. Ann Surg Oncol. 22(11):3574-81, 2015 Oct.

14. Mahmud A, Poon R, Jonker D. PET imaging in anal canal cancer: a systematic review and meta-analysis. [Review]. Br J Radiol. 90(1080):20170370, 2017 Dec.

15. Albertsson P, Alverbratt C, Liljegren A, et al. Positron emission tomography and computed tomographic (PET/CT) imaging for radiation therapy planning in anal cancer: A systematic review and meta-analysis. [Review]. Crit Rev Oncol Hematol. 126:6-12, 2018 Jun.

16. 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. [Review]. ScientificWorldJournal. 2014:196068, 2014.

17. Mirshahvalad SA, Mesci A, Murad V, et al. [18F]-FDG PET in anal canal cancer: a systematic review and meta-analysis. [Review]. European Journal of Nuclear Medicine & Molecular Imaging. 51(1):258-277, 2023 Dec.

18. Otto SD, Lee L, Buhr HJ, Frericks B, Hocht S, Kroesen AJ. Staging anal cancer: prospective comparison of transanal endoscopic ultrasound and magnetic resonance imaging. J Gastrointest Surg. 13(7):1292-8, 2009 Jul.

19. Golia Pernicka JS, Rauch GM, Gangai N, et al. Imaging of Anal Squamous Cell Carcinoma: Survey Results and Expert Opinion from the Rectal and Anal Cancer Disease-Focused Panel of the Society of Abdominal Radiology. [Review]. Abdominal Radiology. 48(9):3022-3032, 2023 09.

20. Bhuva NJ, Glynne-Jones R, Sonoda L, Wong WL, Harrison MK. To PET or not to PET? That is the question. Staging in anal cancer. Ann Oncol. 23(8):2078-2082, 2012 Aug.

21. Min LA, Vacher YJL, Dewit L, et al. Gross tumour volume delineation in anal cancer on T2-weighted and diffusion-weighted MRI - Reproducibility between radiologists and radiation

oncologists and impact of reader experience level and DWI image quality. Radiother Oncol. 150:81-88, 2020 09.

22. Prezzi D, Mandegaran R, Gourtsoyianni S, et al. The impact of MRI sequence on tumour staging and gross tumour volume delineation in squamous cell carcinoma of the anal canal. Eur Radiol. 28(4):1512-1519, 2018 Apr.

23. Rusten E, Rekstad BL, Undseth C, et al. Target volume delineation of anal cancer based on magnetic resonance imaging or positron emission tomography. Radiat. oncol.. 12(1):147, 2017 Sep 06.

24. Reginelli A, Granata V, Fusco R, et al. Diagnostic performance of magnetic resonance imaging and 3D endoanal ultrasound in detection, staging and assessment post treatment, in anal cancer. Oncotarget. 8(14):22980-22990, 2017 Apr 04.

25. Glynne-Jones R, Tan D, Hughes R, Hoskin P. Squamous-cell carcinoma of the anus: progress in radiotherapy treatment. [Review]. Nat Rev Clin Oncol. 13(7):447-59, 2016 07.

26. Wells IT, Fox BM. PET/CT in anal cancer - is it worth doing?. Clin Radiol. 67(6):535-40, 2012 Jun.

27. Chernyak V, Horowitz JM, Kamel IR, et al. ACR Appropriateness Criteria® Liver Lesion-Initial Characterization. J Am Coll Radiol 2020;17:S429-S46.

28. Susko MS, Lazar AA, Wang CJ, et al. Use of advanced PET-volume metrics predicts risk of local recurrence and overall survival in anal cancer. PLoS ONE. 16(2):e0246535, 2021.

29. Adusumilli P, Elsayed N, Theophanous S, et al. Combined PET-CT and MRI for response evaluation in patients with squamous cell anal carcinoma treated with curative-intent chemoradiotherapy. Eur Radiol. 32(8):5086-5096, 2022 Aug.

30. Kochhar R, Renehan AG, Mullan D, Chakrabarty B, Saunders MP, Carrington BM. The assessment of local response using magnetic resonance imaging at 3- and 6-month post chemoradiotherapy in patients with anal cancer. Eur Radiol. 27(2):607-617, 2017 Feb.

31. Prezzi D, Muthuswamy K, Amlani A, et al. Diffusion-weighted imaging complements T2-weighted MRI for tumour response assessment in squamous anal carcinoma. European Radiology. 33(11):7575-7584, 2023 Nov.

32. Peterson CY, Weiser MR, Paty PB, et al. Does endoscopic ultrasound improve detection of locally recurrent anal squamous-cell cancer?. Dis Colon Rectum. 58(2):193-8, 2015 Feb.

33. Measuring Sex, Gender Identity, and Sexual Orientation.

34. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: https://edge.sitecorecloud.io/americancoldf5f-acrorgf92a-productioncb02-3650/media/ACR/Files/Clinical/Appropriateness-Criteria/ACR-Appropriateness-Criteria-Radiation-Dose-Assessment-Introduction.pdf.

Disclaimer

treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

[a] [b]Cleveland Clinic, Cleveland, Ohio. [c]Panel Chair, University of California San Diego, San Diego, California. [d]Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania. [e]University of Texas Health Science Center at Houston and McGovern Medical School, Houston, Texas; American Gastroenterological Association. [f]NYU Grossman School of Medicine, New York, New York. [g]Vanderbilt University Medical Center, Nashville, Tennessee; American Society of Clinical Oncology. [h]Massachusetts General Hospital, Boston, Massachusetts. [i]Oregon Health and Science University, Portland, Oregon. [j]University of North Carolina at Chapel Hill, Chapel Hill, North Carolina. [k]Loyola University Chicago, Stritch School of Medicine, Department of Radiation Oncology, Cardinal Bernardin Cancer Center, Maywood, Illinois; Commission on Radiation Oncology. [l]University of California San Diego, San Diego, California. [m]The University of Texas MD Anderson Cancer Center, Houston, Texas; Commission on Nuclear Medicine and Molecular Imaging. [n]Association for Utah Community Health, Salt Lake City, Utah; American Academy of Family Physicians. [o]Specialty Chair, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin.