

# <sup>18</sup>F<sup>18</sup>FDG-PET/CT Specificity for the Detection of Lymphoma Recurrence in the Tonsils

OTO Open  
 2021, Vol. 5(4) 1–7  
 © The Authors 2021  
 Article reuse guidelines:  
[sagepub.com/journals-permissions](http://sagepub.com/journals-permissions)  
 DOI: 10.1177/2473974X211059081  
<http://oto-open.org>  


Jonathan D. West, MD<sup>1</sup>, Mary E. Kim<sup>1</sup> , Dorian M. Lapalma, MD<sup>2</sup>,  
 Maria Vergara-Lluri, MD<sup>3</sup>, Peter Conti, MD<sup>2</sup>, Tamara N. Chambers, MD<sup>4</sup>,  
 and Mark S. Swanson, MD<sup>4</sup>

## Abstract

**Objective.** In patients with a history of lymphoma who demonstrate palatine tonsil uptake on posttreatment PET/CT (positron emission tomography/computed tomography), tonsillectomy is often performed to evaluate for lymphoma recurrence. However, predictive clinical and imaging factors for true tonsil recurrence in this setting are not well established; this will be explored herein.

**Study Design.** Retrospective case series.

**Setting.** Patients treated at a tertiary medical center from January 2008 to May 2020.

**Methods.** Chart review was performed on all patients with a history of treated lymphoma in clinical remission who presented for evaluation of abnormal PET/CT imaging findings and subsequently underwent tonsillectomy.

**Results.** Among 15 patients who met inclusion criteria, 14 had benign findings on surgical pathology, yielding a false-positive rate of 93%. The patient with malignancy was identified on biopsy after inconclusive surgical pathology and is the only documented case of recurrence in this specific patient population throughout the literature. The patient presented with B symptoms, irregularly shaped tonsils, increased lymph node activity on PET/CT, and uptrending bilateral tonsil activity but with one of the lowest maximum standardized uptake values of the cohort. The singular distinguishing feature for the patient with recurrent disease was a prior tonsil biopsy suspicious for recurrence, which prompted the otolaryngology referral.

**Conclusion.** PET/CT lacks specificity in identifying lymphoma recurrence in the oropharynx. Clinical and radiographic features that were previously considered concerning for recurrence are most likely not indicative of malignancy in this patient population. Our findings call into question whether tonsillectomy should be routinely performed in this patient population.

## Keywords

PET/CT, lymphoma, tonsillectomy, pathology, recurrence

Received August 31, 2021; accepted October 15, 2021.

<sup>18</sup>F<sup>18</sup>fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) is a valuable tool during the diagnostic and treatment phases of lymphoma management. While the imaging modality is highly sensitive and can detect asymptomatic recurrences, it is recommended only for surveillance in symptomatic patients following complete metabolic response to treatment given its high false-positive rate.<sup>1–4</sup> The tonsils are a known lymphoma recurrence site, but they also have high baseline metabolic activity,<sup>5</sup> making it difficult to differentiate between benign and malignant findings on PET/CT imaging at this location. The risk of false positive is increased in patients with lymphoma, as chemotherapy exposure has been shown to increase tonsil fluorodeoxyglucose (FDG) uptake due to reactive enlargement of the lymphoid tissue.<sup>6,7</sup> Given these challenges, patients with a history of lymphoma and PET/CT imaging with signs of possible tonsil recurrence (eg, elevated standard uptake value [SUV], asymmetric SUV, and asymmetric tonsil volume) are routinely referred to otolaryngology for evaluation at our institution. The decision to observe with serial examinations and imaging or to obtain definitive pathology via tonsillectomy must be made with the patient; however,

<sup>1</sup>Keck School of Medicine, University of Southern California, Los Angeles, California, USA

<sup>2</sup>Division of Neuroradiology, Department of Radiology, Keck School of Medicine, University of Southern California, Los Angeles, California, USA

<sup>3</sup>Hematopathology Section, Department of Pathology, University of Southern California, Los Angeles, California, USA

<sup>4</sup>USC Caruso Department of Otolaryngology–Head and Neck Surgery, Keck School of Medicine, University of Southern California, Los Angeles, California, USA

## Corresponding Author:

Mark S. Swanson, MD, USC Caruso Department of Otolaryngology–Head and Neck Surgery, Center for Health Professionals Office 204M, 1540 Alcazar St, Los Angeles, CA 90033, USA.  
 Email: [mark.swanson@med.usc.edu](mailto:mark.swanson@med.usc.edu)



there are very limited data to guide this decision making. In our experience, patients who undergo tonsillectomy based on our recommendation often have benign findings on surgical pathology. Consistent with our observations, there are 2 case reports, an abstract, and a retrospective cohort study that each describe a phenomenon in which patients with a history of lymphoma in remission following systemic chemotherapy undergo tonsillectomy or biopsy due to concerning findings on a follow-up PET/CT yet demonstrate benign surgical pathology.<sup>7-10</sup> To our knowledge, no publication to date has identified a patient in this clinical context who demonstrates malignant pathology on tonsillectomy or biopsy, nor has any study established risk factors for true recurrence in this patient population.

Given the limited data in the literature, we designed a retrospective case series to investigate the surgical pathology findings of patients with a history of lymphoma in remission following chemotherapy treatment who underwent tonsillectomy for suspected recurrence based on follow-up PET/CT findings. We hypothesized that more aggressive and advanced primary lymphoma, presence of throat symptoms, higher tonsil maximum SUV ( $SUV_{max}$ ), asymmetric tonsil SUV and volume, and a counterpart lesion on CT scan would be associated with malignant findings on surgical pathology. We aimed to determine the rate of tonsil false positives on PET/CT imaging in this patient population and identify risk factors for malignant findings on surgical pathology. Our study has the potential to improve the ability to differentiate between malignant and benign tonsil findings on PET/CT scans and help guide treatment decisions for otolaryngologists presented with this specific clinical scenario.

## Materials and Methods

### Patient Selection

Following University of Southern California Institutional Review Board approval, we designed a retrospective case series. Patients were recruited by searching a *Current Procedural Terminology* code database from January 2008 to May 2020 at a tertiary medical center for tonsillectomy, tonsil biopsy, nasopharynx biopsy, and oropharynx biopsy (42820, 42821, 42825, 42826, 42804, 42806). Patients were included in this study if they had a history of lymphoma in clinical remission following definitive systemic treatment and subsequently underwent tonsillectomy to evaluate for recurrence based on abnormal PET/CT findings. Exclusion criteria were a concurrent or previously treated head and neck carcinoma or sarcoma. Of the 1762 tonsillectomies performed between 2008 and 2020 at our institution, 15 patients were included.

### Indication for Tonsillectomy

Patients with a history of lymphoma and PET/CT scan findings concerning for recurrence in the tonsils were referred to otolaryngology for evaluation. Following a head and neck examination and review of all relevant imaging, options presented to the patient included tonsillectomy for definitive diagnosis or serial clinical and radiographic examinations for surveillance. The decision to proceed with tonsillectomy was

based on patient preference and individual case characteristics. A strong recommendation for tonsillectomy was made in the presence of higher SUV values, throat symptoms, asymmetric tonsils on examination, or a primary head and neck lymphoma, each of which was thought to confer a presumed higher likelihood of true recurrence. Given the paucity of research on the subject and absence of guidelines for this clinical scenario, a strict tonsil SUV cutoff or other objective criteria could not be applied to the decision to pursue a tonsillectomy.

### PET Imaging

All PET/CT scans, performed with intravenous iodinated contrast, were read by an attending radiologist prior to patient referral to otolaryngology for evaluation of possible lymphoma recurrence. For this study, 1 head and neck radiologist reviewed the scans to verify prior findings, collect additional data as necessary, and limit variability. When original scans were not available, the data collection was limited to the radiology report within the electronic health record. Last, to characterize tonsil SUV and volume on PET/CT imaging following chemotherapy, we randomly selected a group of 15 patients with a history of a non-head and neck, non-lymphoma primary malignancy who underwent follow-up PET/CT imaging after definitive chemotherapy treatment, to act as a control group for tonsil SUV and volume.

### Data Collection

The medical records, radiology reports, and otolaryngology clinic notes of patients were subsequently reviewed for demographic, diagnostic, clinical, and postoperative information.

### Statistical Analysis

Given our small sample size and single patient with malignant findings on postoperative pathology, we were unable to perform any univariate or multivariate statistical analyses to determine risk factors for malignancy. Mann-Whitney *U* tests were used to examine the relationships between the control and study cohorts with regard to tonsil SUVs and volumes. Statistical significance was set at  $P \leq .05$ . All *P* values were 2-sided. All statistical analysis was performed with Stata 15 (StataCorp).

## Results

### Patient Demographics and Diagnostic Characteristics

Among our cohort of 15 patients, the majority were diagnosed with non-Hodgkin B-cell lymphoma ( $n = 9$ ), followed by non-Hodgkin T-cell lymphoma ( $n = 5$ ) and classic Hodgkin lymphoma ( $n = 1$ ). Of the cases of non-Hodgkin lymphoma, 11 (79%) were considered clinically aggressive. Primary lymphoma treatment involved chemotherapy in all patients ( $N = 15$ ), with 3 also receiving radiation. All patients were determined to be in clinical remission following primary lymphoma treatment based on clinical hematology/oncology documentation. See **Table 1** and Supplemental Table S1 (available online) for detailed demographic and diagnostic information.

**Table 1.** Demographic and Diagnostic Characteristics.<sup>a</sup>

	No. (%) or median (range)
Age, y	47.0 (20.2-68.6)
Sex: male	9 (60)
Ethnicity	
Caucasian	3 (20)
Hispanic	11 (73)
Asian	1 (7)
ASA	
I	1 (7)
II	6 (40)
III	2 (1)
IV	0 (0)
Not available	6 (40)
Charlson comorbidity index	3 (2-8)
Exposure	
Tobacco	1 (7)
Alcohol	2 (13)
Primary lymphoma type and staging	
B-cell non-Hodgkin stage	9 (60)
I or IE	1 (11)
II or IIE	4 (44)
III or IIIE	2 (22)
IV	2 (22)
Classic Hodgkin lymphoma: stage IIA	1 (7)
T-cell non-Hodgkin stage	5 (33)
IE	2 (40)
IIB	1 (20)
IIIE	1 (20)
IV	1 (20)
Non-Hodgkin lymphoma: clinical classification	
Indolent	3 (21)
Aggressive	11 (79)
Primary lymphoma site	
Nodal involvement	7 (47)
Extranodal	8 (53)
Head and neck	7 (47)
Abdomen	3 (20)
Axilla	1 (7)
Lung	1 (7)
Retroperitoneum	1 (7)
Cutaneous	1 (7)
Diffuse	1 (7)
Treatment prior to tonsillectomy	
Chemotherapy	15 (100)
Radiation	3 (20)
Remission to recurrence time, mo	11.2 (0.5-168.1)
History	
Prior recurrence	6 (40)
Second primary	3 (20)
Follow-up, mo	27.3 (0.1-71.1)

Abbreviation: ASA, American Society of Anesthesiologists.

<sup>a</sup>N = 15, unless otherwise specified.**Table 2.** Baseline Tonsil PET/CT Characteristics (N = 15).

Characteristic	Median (range)
Tonsil SUV	
Maximum	4.3 (2.6-5.7)
Absolute difference	0.3 (0.1-1.0)
Ratio	1.1 (0.1-1.4)
Tonsil volume, cm <sup>3</sup>	
Maximum	1.7 (1.1-2.9)
Absolute difference	0.2 (0.1-1.2)
Ratio	1.2 (1.1-1.8)

Abbreviations: CT, computed tomography; PET, positron emission tomography; SUV, standard uptake value.

### PET/CT Imaging

**Descriptive Data.** On review of scans, 7 patients had an uptrending tonsil SUV. The majority (11 patients) also displayed increased uptake outside the palatine tonsils: in the cervical lymph nodes (n = 9); in the Waldeyer ring, nasopharynx, and adenoid region (n = 6); at other head and neck sites (n = 4); and outside the head and neck region (n = 4). Three patients had counterpart lesions on CT scan. Individual patient PET data, including indication for scan, are detailed in Supplemental Table S2 (available online).

**Differences Between Study and Control Cohorts.** When compared with our control group, our study cohort had a significantly higher tonsil SUV<sub>max</sub> (median [SD], 10.2 [6.94] vs 4.3 [1.12];  $P < .00001$ ), larger absolute intertonsil SUV difference (median [SD], 2.0 [1.05] vs 0.3 [0.45];  $P = .01$ ), larger maximum tonsil volume (median [SD], 8 [4.59] vs 1.7 [0.49];  $P = .001$ ), and larger absolute intertonsil volume difference (median [SD], 1.6 [1.91] vs 0.3 [0.38];  $P = .007$ ). Neither the intertonsillar SUV ratio nor the intertonsillar volume ratio was significantly different between the groups ( $P = .65$  and  $P = .46$ , respectively). See **Table 2** for details.

### Indication for Otolaryngology Referral and Clinical Evaluation

In all patients, the decision to refer for tonsillectomy evaluation was made for multiple reasons. PET imaging findings were a component of the referral rationale in all patients. Specific reasons were increased activity in the tonsils (n = 14), increased activity elsewhere in the head and neck region (n = 8), the presence of a tonsil mass/enlargement (n = 6), a history of a head and neck primary lymphoma (n = 2), and clinical signs and symptoms (n = 1). At the time of presentation to the otolaryngology service, the majority of patients had a noteworthy tonsil appearance on examination (n = 11), which included symmetrical enlargement (n = 7), asymmetrical enlargement (n = 4), and a visible mass (n = 2). Several patients displayed head and neck symptoms (n = 6) or B symptoms (n = 3; **Table 3**). Further information on the

**Table 3.** Diagnostic Characteristics and Surgical Pathology.<sup>a</sup>

	No. (%) or median (range)
<b>PET imaging</b>	
Posttreatment PET imaging: Lugano classification	
Complete response	9 (60)
Partial response	3 (20)
Information not available	3 (20)
Follow-up imaging indication	
Restaging or surveillance after treatment	5 (33)
Presenting symptoms	3 (20)
Findings on other imaging	3 (20)
Routine surveillance	2 (13)
Unspecified	1 (7)
Findings on biopsy for other clinical indication	1 (7)
Tonsil SUV	
Maximum	10.2 (4.6-33)
Uptrending (n = 9)	7 (78)
Asymmetric uptake	6 (40)
Absolute difference (n = 9)	2 (0.2-3.0)
Ratio (n = 9)	1.1 (1.0-1.3)
Tonsil volume, cm <sup>3</sup> (n = 6)	
Maximum	8 (1.9-15)
Absolute difference	1.6 (0.4-5.2)
Ratio	1.3 (1.2-2.1)
Other increased FDG uptake	
Waldeyer ring, nasopharynx, adenoid region	6 (40)
Cervical lymph nodes	9 (60)
Other head and neck site	4 (27)
Outside the head and neck region	4 (27)
Counterpart lesion on CT scan	3 (20)
<b>Clinical evaluation</b>	
Indication for otolaryngology referral	
Increased tonsillar activity	14 (93)
Asymmetrical increased tonsillar activity	6 (40)
Bilateral increased tonsillar activity	10 (67)
Uptrending tonsillar activity	7 (47)
Persistent tonsillar activity	3 (20)
Tonsillar mass/enlargement	6 (40)
Increased nasopharyngeal/adenoid activity	6 (40)
Increased cervical lymph node activity	2 (13)
Head and neck or B symptoms	1 (7)
Abnormal physical examination	1 (7)
Biopsy findings	1 (7)
Head and neck primary lymphoma	2 (13)
Any head and neck symptom	6 (40)
B symptoms	3 (20)
Abnormal tonsillar appearance	
Symmetrically enlarged	7
Asymmetrically enlarged	4
Visible mass	2
Other lymphoid tissue hypertrophy	6 (40)

(continued)

**Table 3.** (continued)

	No. (%) or median (range)
<b>Surgical pathology</b>	
Diagnosis	
Lymphoma of T-follicular helper cell origin: malignant	1 (7)
Atypical lymphoid hyperplasia: benign	1 (7)
Reactive lymphoid hyperplasia	12 (80)
Tonsillitis	1 (7)
False-positive rate	93%

Abbreviations: CT, computed tomography; FDG, fluorodeoxyglucose; PET, positron emission tomography; SUV, standard uptake value.

<sup>a</sup>N = 15, unless otherwise specified.

preoperative clinical evaluation of individual patients can be found in Supplemental Table S3 (available online).

### Surgical Pathology

Pathology findings of the tonsillectomy specimens were reported as benign in 14 patients and malignant in 1. The singular patient with malignant findings was initially diagnosed as having angioimmunoblastic T-cell lymphoma. However, the morphologic findings between the initial diagnostic nodal specimen and the subsequent extranodal tonsil lymphoproliferation appeared sufficiently dissimilar, raising the possibility of an unusual second malignancy. Follow-up excisional biopsy confirmed lymphoma recurrence by a T-cell lymphoma of follicular helper origin, which falls under an “umbrella” category of lymphomas that encompasses the patient’s original diagnosis of angioimmunoblastic T-cell lymphoma.<sup>11</sup> The rate of false positives on PET imaging among our patient cohort was 93% (**Table 3**; Supplemental Table S4, available online). The median follow-up was 27.3 months (range, 0.1-71.1) and resulted in no subsequent presentations for possible lymphoma recurrence.

### Risk Factors for Recurrence

The patient with recurrent disease was diagnosed with an advanced (stage IV) aggressive non-Hodgkin lymphoma, had a history of recurrence, and had a number of clinical symptoms and radiographic findings that traditionally raise suspicion for recurrence: B symptoms on presentation, abnormal tonsil appearance on physical examination, uptrending tonsil SUV resulting in a maximum value of 5.2 cm<sup>3</sup>, and increased FDG uptake at multiple other locations, including within the head and neck. However, all of these features were also seen in patients with benign pathology findings. The singular distinguishing feature for the patient with recurrent disease was the prior tonsil biopsy suspicious for recurrence, which prompted the otolaryngology referral. We were unable to determine absolute differences and ratios between individual

tonsil SUV and volume for this patient because the radiology report lacked necessary data and the original PET/CT files were unavailable for analysis.

## Discussion

Herein, we report a false-positive rate of 93% for PET/CT imaging correctly identifying tonsil recurrence in patients with a history of lymphoma in clinical remission following systemic chemotherapy. This study is unique because it is the first that investigated clinical and radiographic characteristics when trying to identify risk factors for recurrence. To our knowledge, we document the first patient with true recurrence in the literature that exists on this specific patient cohort, with the singular characteristic of this patient having a tonsil biopsy suspicious for recurrence prior to tonsillectomy.

The findings herein support our institution's observations and the existing literature on the topic, which together demonstrate that patients with a history of lymphoma in clinical remission following systemic chemotherapy who receive a tonsillectomy or biopsy due to concerning findings on PET/CT often have benign pathology results.<sup>7-10</sup> Prior case reports<sup>7,8</sup> and an abstract<sup>9</sup> document this false-positive phenomenon within the same patient population that we observe in our study, and in all 10 patients in these 3 previous works, abnormally elevated tonsil SUVs were attributed to prior chemotherapy exposure. The median tonsil SUV ratio (2.0; range, 0.2-3) and SUV<sub>max</sub> (10.3; range, 4.6-33.3) of the 14 patients with benign pathology reported here were comparable to the values presented in these studies: median tonsil SUV ratio (1.52, range, 1-2.53) and median SUV<sub>max</sub> (7.2, range, 4.2-11.3).<sup>9</sup> Rituximab, an agent used in the majority of our patients' chemotherapy regimens, has been associated with an especially high false-positive rate in patients with diffuse large cell lymphoma<sup>12</sup> and aggressive non-Hodgkin lymphoma.<sup>13</sup> However, it should be noted that the elevated SUVs in this specific patient population are likely due to a combination of factors, rather than just chemotherapy alone; this is supported by the significantly higher SUVs in our study cohort as compared with the control cohort, who completed chemotherapy but did not have a lymphoma diagnosis. In addition to chemotherapy, factors contributing to the elevated SUVs may include a history of lymphoma,<sup>3</sup> previous radiation treatment,<sup>2</sup> and the high avidity of the tonsils on PET/CT at baseline that leads to a high degree of SUV variability.<sup>5</sup>

A recent retrospective cohort study aimed to identify PET/CT characteristics that increase the risk of lymphoma recurrence at the tonsils.<sup>10</sup> To achieve this, Kurtoğlu and Göçer<sup>10</sup> compared 2 patient groups: (1) patients with a history of lymphoma and chemotherapy who had concerning Waldeyer ring/nasopharynx findings on follow-up PET/CT but benign tonsil biopsy results and (2) patients with concerning Waldeyer ring/nasopharynx PET/CT findings performed during workup for an unknown primary but with subsequent malignant biopsy findings. Note that, in contrast to our study, the patient cohort with malignant findings did not have a history of lymphoma or chemotherapy exposure,<sup>10</sup> 2 factors known to alter the reliability of PET/CT scans and

FDG uptake.<sup>2,3</sup> Therefore, the guidelines that Kurtoğlu and Göçer proposed are likely not applicable to the patient cohort described herein. Similar to previous studies,<sup>7-9</sup> Kurtoğlu and Göçer reported no cases of recurrence in patients who were referred for increased tonsil SUV on PET/CT imaging and had a history of lymphoma in remission following chemotherapy.

In addition to differences in study design, there are important dissimilarities between our findings and those of Kurtoğlu and Göçer<sup>10</sup> that challenge the applicability of their results to this specific patient cohort. Kurtoğlu and Göçer did not identify any patients with benign findings that had a counterpart Waldeyer ring/nasopharynx lesion on CT, thus prompting the authors to recommend using this radiographic feature as a risk factor for recurrence. In contrast, we identified 3 patients with a counterpart lesion on CT and benign pathology, calling into question this recommendation. Kurtoğlu and Göçer also postulated that higher SUV<sub>max</sub> may suggest recurrence. However, the findings herein contradict this: in our study, the patient with the highest tonsil SUV<sub>max</sub> (33.3) had benign findings, while the patient with one of the lowest (5.2) had a lymphoma recurrence. The final potential risk factor for recurrence that Kurtoğlu and Göçer cited was SUV asymmetry, reported in only 27% of patients with benign pathology as opposed to 90% of those with malignancy.<sup>10</sup> Although we were not able to determine tonsil asymmetry for our patient with lymphoma recurrence, as the scan was unavailable, tonsil SUV asymmetry was still noted in the radiology reports of 43% of our patients with benign pathology. Interestingly, studies in the setting of oropharyngeal squamous cell carcinoma have shown that tonsil SUV asymmetry can be used to successfully differentiate between physiologic tonsil activity and tonsil malignancy<sup>14,15</sup>; yet, this characteristic alone is unlikely to be predictive for recurrence in the patient cohort described here.

An important implication of our study is that clinical and radiographic features that have previously been considered concerning are most likely not indicative of malignancy in this patient population. Clinical characteristics were unreliable for predicting lymphoma recurrence in our study cohort. While the patient with malignant pathology did have abnormal tonsil appearance and B symptoms, these characteristics were present in other patients with benign findings. Additionally, although several patients presented with head and neck symptoms suggesting recurrence, these were all benign cases. Furthermore, it is clear that patients with a history of lymphoma and chemotherapy exposure have distinct PET/CT characteristics in the tonsil region. In particular, SUV<sub>max</sub>, intertonsil absolute SUV difference, tonsil volume, and intertonsil volume difference were all noted to be significantly greater in our study cohort when compared with a control cohort that underwent follow-up PET/CT after successful chemotherapy treatment of a non-head and neck, non-lymphoma primary malignancy. Given these unique radiographic characteristics, we advocate for future investigations to establish new baseline PET/CT values to better predict recurrence in this specific patient population.

Our findings and those of prior studies suggest the need for larger, multicenter studies to investigate risk factors for recurrence in this clinical setting. In the absence of such studies, one must rely on clinical judgment when deciding to pursue a tonsillectomy for these patients. We recommend that tonsillectomy in this setting be performed only in patients determined to be at an especially high risk of recurrence, given that the sole documented case of confirmed malignancy in the literature is described herein. While tonsillectomy is considered a safe procedure,<sup>16</sup> it still must be approached with caution. This is particularly important in the patient population under discussion, as rates of complication and reoperation are traditionally higher in patients with a history of malignancy, exposure to chemotherapy, and radiation.<sup>17-22</sup> Prior to pursuing surgical treatment, these high-risk patients should be counseled extensively on the inherent deficiencies of PET/CT imaging in this setting, the risks associated with performing a tonsillectomy, and the substantial likelihood of benign findings.

Our study was limited by its design and small sample size. Its retrospective nature restricted the data that were available for collection, specifically regarding PET/CT imaging and clinical evaluation prior to tonsillectomy. This also inhibited our ability to control for confounding variables, including criteria used for recommending otolaryngology evaluation and clinical judgment related to the decision to recommend a tonsillectomy. Establishing these objective measures is relevant in this clinical setting, given the variety of factors discussed here that contribute to tonsil SUV variability. Last, our study utilized *Current Procedural Terminology* codes for tonsillectomy and tonsil biopsy to identify potential patients. This approach was necessary to facilitate patient recruitment; despite this, it inevitably excluded patients who were referred to otolaryngology for evaluation but did not undergo biopsy or tonsillectomy. This limited our ability to fully investigate what characteristics prompted otolaryngologists to recommend biopsy or tonsillectomy in the study cohort, as compared with patients who were recommended observation only.

## Conclusion

Our study is the first to formally investigate clinical and post-treatment PET/CT radiographic characteristics that may be indicative of tonsil recurrence in patients with a history of lymphoma treated with systemic chemotherapy, adding to the existing literature that indicates a high likelihood for benign pathology.<sup>7-10</sup> We demonstrated a high risk of false-positive PET/CT findings in our patient cohort, suggesting that tonsillectomy should be recommended more selectively by otolaryngologists in this clinical setting. Last, our study revealed that this patient population has distinct PET/CT characteristics in the tonsil region that should be considered when utilizing this imaging modality to direct clinical decision making.

## Author Contributions

**Jonathan D. West**, conceptualization, data collection, original draft preparation, editing, submission; **Mary E. Kim**, conceptualization, data collection, original draft preparation, editing, submission;

**Dorian M. Lapalma**, conceptualization, data collection, editing; **Maria Vergara-Lluri**, conceptualization, data collection, editing; **Peter Conti**, conceptualization, editing; **Tamara N. Chambers**, conceptualization, data collection, editing; **Mark S. Swanson**, conceptualization, data collection, original draft preparation, editing, submission


## Disclosures

**Competing interests:** None.

**Sponsorships:** None.

**Funding source:** None.

## ORCID iD

Mary E. Kim  <https://orcid.org/0000-0002-7986-6119>

## Supplemental Material

Additional supporting information is available at <http://journals.sagepub.com/doi/suppl/10.1177/2473974X211059081>

## References

1. El-Galaly TC, Villa D, Gormsen LC, Baech J, Lo A, Cheah CY. FDG-PET/CT in the management of lymphomas: current status and future directions. *J Intern Med*. 2018;284(4):358-376. doi:10.1111/joim.12813
2. Long NM, Smith CS. Causes and imaging features of false positives and false negatives on F-PET/CT in oncologic imaging. *Insights Imaging*. 2011;2(6):679-698. doi:10.1007/s13244-010-0062-3
3. García Vicente AM, Bellón Guardia M, Soriano Castrejón A, et al. 18F-FDG-PET/CT in the surveillance of patients with lymphoma: detection of asymptomatic recurrences. *Rev Esp Med Nucl Imagen Mol*. 2012;31(1):22-27. doi:10.1016/j.remnm.2011.04.009
4. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *J Clin Oncol*. 2014;32(27):3059-3068. doi:10.1200/JCO.2013.54.8800
5. Nakamoto Y, Tatsumi M, Hammoud D, Cohade C, Osman MM, Wahl RL. Normal FDG distribution patterns in the head and neck: PET/CT evaluation. *Radiology*. 2005;234(3):879-885. doi:10.1148/radiol.2343030301
6. Okuyama C, Matsushima S, Nishimura M, Yamada K. Increased <sup>18</sup>F-FDG accumulation in the tonsils after chemotherapy for pediatric lymphoma: a common physiological phenomenon. *Ann Nucl Med*. 2019;33(5):368-373. doi:10.1007/s12149-019-01337-w
7. Hosokai R, Imai C, Takachi T, et al. Reactive tonsillar enlargement with strong 18F-FDG uptake after chemotherapy for tonsillar diffuse large B-cell lymphoma. *J Pediatr Hematol Oncol*. 2011;33(2):e87-e88. doi:10.1097/MPH.0b013e3181f69205
8. Feio POS, Gomes CB, Nogueira AS, et al. Reactive tonsillar enlargement showing strong 18F-FDG uptake during the follow-up of follicular lymphoma. *Head Neck Pathol*. 2013;7(3):258-262. doi:10.1007/s12105-012-0400-5
9. Munoz J, Arango B, Schering J, et al. The relevance of increased tonsil uptake when restaging lymphoma with positron emission

- tomography. *Blood*. 2010;116(21):3133. doi:10.1182/blood.V116.21.3133.3133
10. Kurtoğlu E, Göçer M. Clinical significance of increased FDG uptake in the Waldeyer ring and the nasopharynx region identified by PET-CT in postchemotherapy follow-up in patients with lymphoma: when should we perform biopsy? *Clin Lymphoma Myeloma Leuk*. 2020;20(12):830-835. doi:10.1016/j.clml.2020.08.004
  11. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood*. 2016;127(20):2375-2390. doi:10.1182/blood-2016-01-643569
  12. Avivi I, Zilberlicht A, Dann EJ, et al. Strikingly high false positivity of surveillance FDG-PET/CT scanning among patients with diffuse large cell lymphoma in the rituximab era. *Am J Hematol*. 2013;88(5):400-405. doi:10.1002/ajh.23423
  13. Han HS, Escalón MP, Hsiao B, Serafini A, Lossos IS. High incidence of false-positive PET scans in patients with aggressive non-Hodgkin's lymphoma treated with rituximab-containing regimens. *Ann Oncol*. 2009;20(2):309-318. doi:10.1093/annonc/mdn629
  14. Pencharz D, Dunn J, Connor S, et al. Palatine tonsil SUVmax on FDG PET-CT as a discriminator between benign and malignant tonsils in patients with and without head and neck squamous cell carcinoma of unknown primary. *Clin Radiol*. 2019;74(2):165.e17-165.e23. doi:10.1016/j.crad.2018.10.007
  15. Wong WL, Gibson D, Sanghera B, Goodchild K, Saunders M. Evaluation of normal FDG uptake in palatine tonsil and its potential value for detecting occult head and neck cancers: a PET CT study. *Nucl Med Commun*. 2007;28(9):675-680. doi:10.1097/MNM.0b013e32829152b1
  16. Chen MM, Roman SA, Sosa JA, Judson BL. Safety of adult tonsillectomy: a population-level analysis of 5968 patients. *JAMA Otolaryngol Head Neck Surg*. 2014;140(3):197-202. doi:10.1001/jamaoto.2013.6215
  17. Yamashita K, Makino T, Miyata H, et al. Postoperative infectious complications are associated with adverse oncologic outcomes in esophageal cancer patients undergoing preoperative chemotherapy. *Ann Surg Oncol*. 2016;23(6):2106-2114.
  18. Peled AW, Itakura K, Foster RD, et al. Impact of chemotherapy on postoperative complications after mastectomy and immediate breast reconstruction. *Arch Surg*. 2010;145(9):880-885.
  19. Roberts JR, Eustis C, Devore R, Carbone D, Choy H, Johnson D. Induction chemotherapy increases perioperative complications in patients undergoing resection for non-small cell lung cancer. *Ann Thorac Surg*. 2001;72(3):885-888.
  20. Bullard KM, Trudel JL, Baxter NN, Rothenberger DA. Primary perineal wound closure after preoperative radiotherapy and abdominoperineal resection has a high incidence of wound failure. *Dis Colon Rectum*. 2005;48(3):438-443.
  21. Girod DA, McCulloch TM, Tsue TT, Weymuller EA Jr. Risk factors for complications in clean-contaminated head and neck surgical procedures. *Head Neck*. 1995;17(1):7-13.
  22. Fracol ME, Basta MN, Nelson JA, et al. Bilateral free flap breast reconstruction after unilateral radiation: comparing intraoperative vascular complications and postoperative outcomes in radiated versus nonradiated breasts. *Ann Plast Surg*. 2016;76(3):311-314.