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Evaluating oropharyngeal carcinoma with transcervical ultrasound, CT, and MRI

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ABSTRACT

Objective: To compare transcervical ultrasonography (US) to standard cross-sectional imaging for the visualization of human papillomavirus-related oropharyngeal cancer (HPV-OPC).
Materials and methods: Patients with HPV-OPC and available standard imaging (CT and/or MRI) were identified in clinic and prospectively enrolled. US was performed to visualize the oropharynx and lymph nodes. Tumor characteristics across imaging modalities were evaluated (CT versus MRI, and US versus standard imaging (SI)).
Results: Forty-three patients were included. The overall blinded detection rates for CT and MRI were 83% and 71%, respectively. The unblinded detection rate for US was 98%. Agreement of tumor anatomic subsite was moderate for both CT vs MRI ($\kappa = 0.59$) and US vs SI ($\kappa = 0.47$). Comparison of tumor size by CT and MRI showed statistically significant correlations in craniocaudal (CC), anteroposterior (AP), and mediolateral (ML) dimensions ($Rho_{CC} = 0.51$, $p_{CC} = 0.038$; $Rho_{AP} = 0.81$, $p_{AP} < 0.0001$; $Rho_{ML} = 0.57$, $p_{ML} = 0.012$). Tumor size estimates by US and SI showed statistically significant correlations in CC and AP, but not ML ($Rho_{CC} = 0.60$, $p_{CC} = 0.003$; $Rho_{AP} = 0.71$, $p_{AP} < 0.0001$; $Rho_{ML} = 0.30$, $p_{ML} = 0.08$). Tumor volume estimates improved correlations between US and SI (Rho = 0.66, $p < 0.0001$). Stratification of US patients into early and late imaging studies demonstrated an increase in correlation strength from early (Rho = 0.32, p = 0.32) to late groups (Rho = 0.77, $p < 0.0001$) demonstrating that ultrasound accuracy improved with experience.
Conclusions: Our findings suggest that transcervical ultrasonography is a sensitive and relatively accurate adjunct to standard imaging for the evaluation of oropharyngeal tumors. Its cost, portability, and potential for in-clinic and serial imaging render US an attractive modality to further develop for imaging oropharyngeal tumors.

Introduction

The incidence of oropharyngeal squamous cell carcinoma (OPC) has increased significantly worldwide [1]. Trends in OPC are attributed to increasing oral exposure to human papillomavirus (HPV) infection [2]. Indeed, approximately 70% of OPCs in the United States are attributable to HPV [3]. HPV-positive OPC (HPV-OPC) are typically small tumors that arise within lymphoid-associated epithelial crypts of the palatine and lingual tonsils [4], rendering clinical and radiographic imaging difficult [5–11].

While computed tomography (CT) represents the most commonly available modality for imaging OPC, it is limited by dental filling artifact and poor soft tissue contrast resolution. Despite superior soft tissue contrast resolution to CT, magnetic resonance imaging (MRI) can be susceptible to significant motion artifact [9]. Furthermore, while intravenous radiocontrast agents enhance tumor visualization relative to surrounding tissue at most head and neck sites, the normal lymphoid tissue of the oropharynx enhances to a similar extent and precludes clear delineation of tumors [10]. Oropharyngeal lymphoid tissue also exhibits basal metabolic activity resulting in diffuse, mild FDG uptake that can obscure positron emission tomography (PET) signal from small tumors [11]. As a result, neither CT, MRI, nor PET/CT independently serve as an optimal imaging modality for the evaluation of oropharyngeal tumors [12,13].

Our group has investigated the potential role of transcervical ultrasonography (US) in the evaluation of oropharyngeal tumors. We have shown that US can identify the primary tumor site of unknown primary head and neck carcinoma and visualize clinically relevant

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features of BOT tumors [14–16]. We recently reported an optimized US protocol implementing anatomic landmarks for high-confidence visualization of tonsillar and BOT tumors [17]. In the current report, we apply this optimized protocol to compare the performance of CT, MRI, and US in accurately identifying and evaluating the dimensions of 43 tonsillar and BOT tumors.

Materials and methods

Patient population

Patients with OPC and available cross-sectional imaging (CT and/or MRI) were identified in clinic and prospectively enrolled for pretreatment transcervical ultrasonography of the oropharynx and lymph nodes. Since all patients enrolled for US were HPV-positive, an additional set of patients with HPV-OPC who had both CT and MRI imaging available were selected retrospectively to compare the performance of CT and MRI in evaluating OPC. This latter group underwent primary surgical treatment at Johns Hopkins Hospital between 2009 and 2015 and had both CT and MRI imaging available. The Johns Hopkins Institutional Review Board approved all procedures described in this study.

Data collection

CT and MRI images were read by a neuroradiologist (N.A.) blinded to diagnosis and with more than 15 years of experience. Separate standardized CT/MRI data collection forms documented imaging modality and quality, anatomic subsite, lesion size in craniocaudal (CC), anteroposterior (AP), and mediolateral (ML) dimensions, number of radiologically suspicious lymph nodes, and CC, AP, and ML dimensions of the largest radiologically suspicious lymph node.

Prospectively enrolled patients underwent ultrasonography per standardized protocol for imaging oropharyngeal structures as previously described [17]. Prior to ultrasound, the study coordinator and sonographer reviewed patient clinical records, including standard imaging, biopsy, and medical history. Sonographic imaging included transverse, sagittal, and parasagittal still images and cine clips of the BOT, bilateral tonsils, and largest suspicious lymph node. Ultrasonography was performed by trained sonographers (M.B.W., E.S.P., and D.B.) with at least 5 years of experience in general ultrasound. The sonographers received specialized training in oropharyngeal transcervical ultrasound imaging. The Philips iU22 or Philips EPIQ7 (Koninklijke Philips N.V., Amsterdam, Netherlands) ultrasound systems were used with the C5-1, C8-5, L12-5, and X6-1 transducers. Data was collected on standardized US data collection forms. During ultrasound imaging, the sonographer provided relevant information to the study coordinator (F.F.), who completed the standardized data collection form.

Clinical data including patient age, sex, race, clinical tumor and lymph node stage, primary treatment modality, greatest tumor dimension on pathological inspection were abstracted from patient electronic medical records.

Statistical analysis

Statistical analyses were performed with GraphPad Prism® 6.0 g. Scatterplots were generated for cross-modality comparisons of tumor sizes and volumes. Tumor volumes were calculated assuming ellipsoid shape: $Volume = \frac{4}{3}\pi(\mathrm{CC})(\mathrm{AP})(\mathrm{ML})$. Correlation analyses were performed with Spearman's test. Anatomic subsite concordance was defined as the reliability of identifying the same anatomic subsite with different imaging modalities and was determined by generating contingency tables to calculate Cohen's kappa for inter-imaging-modality agreement [18]. Strength of agreement is indicated by the following ranges of kappa values: < 0 (poor), 0–0.20 (slight), 0.21–0.4 (fair), 0.41–0.6 (moderate), 0.61–0.80 (substantial), 0.81–1.00 (near perfect) [19].

Table 1
Patient characteristics.

		n	%
Age	Median	59	
	Mean	59.6	
	Range	42–81	
Sex	Male	60	90
	Female	7	10
Race	White	61	91
	Non-white	6	9
Anatomic subsite	Base of tongue	37	55
	Tonsil	24	36
	Overlap	2	3
	Unknown	4	6
cT category	cTx	4	6
	cT1	30	45
	cT2	24	36
	cT3	4	6
	cT4a	4	6
	cT4b	1	1
AJCC8 cN category	cN0	6	9
	cN1	56	84
	cN2	4	6
	cN3	1	1
AJCC8 stage group	I	56	84
	II	5	7
	III	6	9
Primary treatment	Surgery	43	64
	RT ± chemo	24	36

Results

Patient characteristics

The study population (n = 67) included 43 patients prospectively enrolled for ultrasonography and an additional 24 patients with available CT and MRI. The study population included 60 (90%) men and 61 (91%) white patients ranging from 42 to 81 years in age (Table 1). Diagnostic biopsies confirmed 37 (55%) base of tongue (BOT) tumors, 24 (36%) tonsil tumors, and 2 (3%) tumors involving both the BOT and tonsil (overlapping lesions). Four primary tumors (6%) were not clinically identified and considered tumors of unknown primary origin. All tumors were HPV-positive. Most primary tumors were cT1 (45%) or cT2 (36%). Forty-three patients (64%) were treated with primary surgery and 24 (36%) with primary radiotherapy.

Standard imaging characteristics

Sixty-three patients had available CT imaging (Table 2). Eighty-six percent of CT studies were good (54%) or fair (32%) quality. The 5 (8%) CT studies performed without intravenous contrast were considered poor or fair quality. CT failed to identify 11 primary lesions, resulting in an 82.5% overall detection rate. Excluding non-contrast CT studies (of poor or fair quality), the detection rate was 82.8% (48 of 58).

Gadolinium-based contrast-enhanced MRIs were available for 36 patients, of which 65% were good quality (Table 2). The single non-contrast enhanced MRI was considered fair quality. The primary tumor detection rate by MRI was 71.4% (25 of 35).