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Sonologic features of vulvar cancer and lymph node status among patients at a tertiary hospital – A 10-year review

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Abstract:

CONTEXT: Vulvar cancers are rare gynecologic tumors. Ultrasound can characterize primary tumors and guide the biopsy of suspicious nodes. Currently, there are no studies on the sonologic features of different vulvar cancer types.

AIMS: The aim is to determine the sonologic features of different vulvar malignancies. To compare the accuracy of ultrasound in identifying lymph node status.

SETTINGS AND DESIGN: This is a retrospective descriptive study.

SUBJECTS AND METHODS: Patient records, ultrasound images, and reports of vulvar cancer with long- and short-axis (L/S) ratio of inguinal nodes were reviewed from the year 2010 to 2019.

STATISTICAL ANALYSIS USED: The accuracy of ultrasound to detect lymph nodes and the correlation of L/S ratio to histopathology were done.

RESULTS: The study included 49 patients. The most common histopathologies were squamous cell carcinoma (SCCA), vulvar melanoma (VM), and adenocarcinoma (ADCA). Most tumors were > 4 cm, unifocal, and lateral in location. SCCA, verrucous carcinoma, VM, ADCA, adenosquamous carcinoma (ASCA), eccrine carcinoma (ECCA), and carcinosarcoma (CS) were irregular heterogeneous masses. Leiomyosarcoma (LMS) and proximal-type epithelioid sarcoma (PES) were regular, heterogeneous masses. Paget's disease of the vulva (PDV) was hypoechogenic with regular borders. Vascularities were absent in PDV and LMS, minimal in ECCA, moderate in ASCA and PES, moderate to abundant in CS, and variable in VM. The accuracy of ultrasound in detecting lymph nodes was 78%; the accuracy of the L/S ratio was 75%. Tumor border and FIGO stage showed significant association with histopathologic type.

CONCLUSIONS: Sonologic features and accuracy of ultrasound in predicting lymph node status help prognostication in vulvar cancer. Nodal morphometric studies are recommended for future researches.

Keywords:

Long- and short-axis ratio, lymph node status, ultrasound, vulvar cancer

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Introduction

Vulvar cancer, a rare gynecologic malignancy, has varying incidence rates (2.5 per 100,000 women worldwide, 0.9 in Asia, and 0.2–0.3 in the Philippines).[1,2] Imaging techniques such as magnetic resonance imaging (MRI) and computed tomography (CT) with or without positron emission tomography (PET) aid in staging but are not always accessible due to cost.[3,4] Ultrasound offers a safe, cost-effective alternative guiding biopsies and accurately identifying inguinal lymph node metastasis (86.0% accuracy).[5] Long- and short-axis (L/S) ratio of <2 indicates malignancy. A combination of ultrasound and FNAC may prevent unnecessary groin dissection and potential surgical morbidities.[6] Limited studies exist on vulvar cancer's sonologic features.

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Objectives

General objective

To determine the different sonographic features of vulvar malignancies.

Specific objectives

1. To describe sonographic features of primary tumors based on their histologic subtype
2. To compare the accuracy of ultrasound in identifying lymph node status in those who underwent biopsy of inguinofemoral lymph nodes or inguinofemoral lymphadenectomy
3. To identify demographic features and clinical presentations of Filipino vulvar cancer patients
4. To identify surgical and histopathologic features of vulvar cancer, if any.

Subjects and Methods

Study design

This is a retrospective descriptive study.

Subjects

Patients included are: vulvar cancer patients seen in the institution from the year 2010 to 2019 who underwent ultrasound with histopathologically proven biopsy or surgical staging with or without inguinofemoral lymphadenectomy. Patients who were excluded are: those with metastatic vulvar malignancies, and those with incomplete records (either ultrasound or histopathologic reports). Other imaging procedures were not correlated.

Description of study procedure

Patient selection was from a review of patient records, histopathology, ultrasound reports, and images from 2010 to 2019.

Ultrasound images and reports of the primary tumor and of the inguinal lymph nodes were retrospectively reviewed by a senior sonologist with more than 10 years' of experience in gynecologic ultrasound. Dimensional parameters were reviewed: L/S of the dominant lymph node (lymph node with most suspicious morphology or largest one in case of similar morphology), and L/S ratio, considering as suspicious when the value is <2.[6] Inguinal lymph nodes were recorded as positive and negative, according to original reports. Final histology was considered a reference standard.

Ethical approval was obtained from review ethics board.

Description of analysis

All information was manually entered into an electronic spreadsheet after data extraction. Processing and analysis were carried out using Microsoft Excel.

Results were presented as percentages for nominal variables and as median for continuous variables. Accuracy of ultrasound to detect lymph nodes and correlation of L/S ratio to histopathology were done.

Results

Forty-nine patients met the inclusion criteria. Demographic data and clinical characteristics of vulvar cancer patients in terms of age, tumor site, focality, maximum tumor diameter, type of vulvar surgery, inguinofemoral surgery, histopathologic type, lymphovascular space invasion (LVSI), and staging are presented below.

Majority of cases were postmenopausal, accounting for 85.7% (n = 42) of the total study population. Premenopausal patients accounted for 14.3% (n = 7). The median age at diagnosis was 65 years old.

The most common site of tumor was lateral (42.9%), followed by anterior (26.5%), posterior (16.3%), and extensive (14.3%). Most tumors were unifocal (77.6%), with multifocal tumors comprising 22.4%. Based on the widest tumor diameter, most belong to more than or equal to 4 cm (69.4%), followed by 2–4 cm (26.5%) and <2 cm (4.1%).

Thirty-three (63.3%) patients underwent vulvar biopsy only. 16 (34.7%) patients underwent radical vulvectomy and only two patients had partial vulvectomy. 22 (44.9%) patients underwent inguinofemoral surgery, 14 (63.6%) underwent inguinofemoral lymphadenectomy, and 8 (36.4%) underwent sentinel node biopsy.

The most common histologic type was squamous cell carcinoma (SCCA) at 55.1%; LVSI was absent for most tumors (82.4%) and present in only 17.8% of cases. Most tumors belong to FIGO Stage II or III (each with 34.1%), followed by Stage I (22.7%) and Stage IV (9.1%). Vulvar melanomas (VM) cases were detected at advanced stages: stage V (80.0%) and stage IV (20.0%).

Ninety-six percent of SCCA had irregular borders and only 3.7% had regular borders. Tumor echo pattern was heterogeneous in 77.8%, hypoechogenic in 18.5%, and isoechogenic 3.7% of cases. On color flow mapping, 33.3% had moderate flow, 25.9% had minimal flow, and 7.4% had no color flow. Verrucous carcinoma, a subtype of squamous carcinoma, had irregular borders with heterogeneous echo pattern and minimal vascularity [Figures 1 and 2].

Sonologically, VMs all appeared as tumors with irregular borders. Eighty percent was heterogeneous, while 20% was hypoechogenic. Color flow mapping showed 1 case (20.0%) each for absent, minimal, moderate,

and abundant vascularity. One report did not include Doppler studies.

Glandular tumors of the vulva appeared on ultrasound as follows: 1 case of Paget's disease of the vulva had regular tumor borders with hypoechogenic echo pattern and absent color flow. Adenocarcinomas (ADCAs) appeared as heterogeneous masses with irregular borders in three cases (75.0%), while 1 case (25.0%) appeared as a hypoechogenic mass with regular tumor borders. Doppler studies showed absent and minimal color flow, each comprising 25.0%. Adenosquamous carcinoma (ASCA) and eccrine carcinoma (ECCA) had irregular tumor borders with heterogeneous echo pattern. ASCA had moderate vascularity, while ECCA had minimal vascularity.

All carcinosarcomas (CSs) had heterogeneous echo pattern with irregular tumor borders. Two cases had moderate and abundant flow (50.0% each). Leiomyosarcoma (LMS) and PES both showed regular borders with heterogeneous echo pattern. LMS had absent color flow, while PES had moderate color flow.

Other undifferentiated malignant tumors of the vulva are as follows: two cases of malignant round cell neoplasms had regular tumor borders and heterogeneous echo pattern. One case (50%) each had minimal and abundant color flow. Both malignant neoplastic neoplasm and poorly differentiated carcinoma had irregular tumor borders with heterogeneous echo pattern and minimal color flow.

Thirty-two inguinal areas were examined using ultrasound. Histopathologic results were correlated with ultrasound findings. Nine groins had histopathologically positive inguinal lymph nodes; 7 (77.8%) were detected

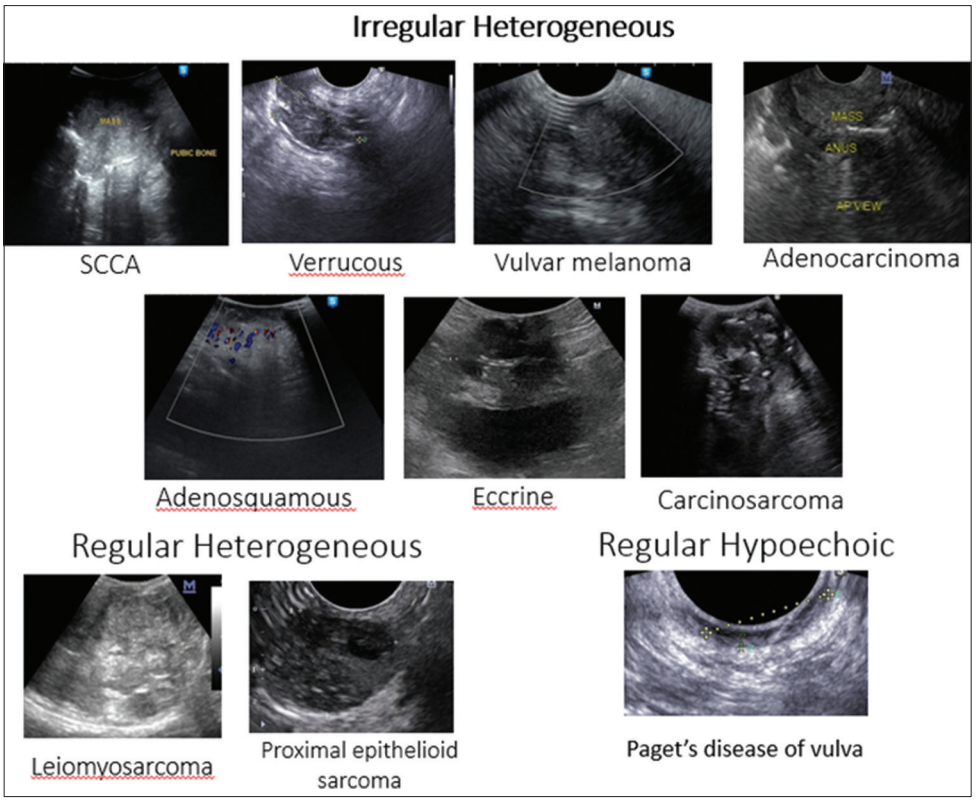

Figure 1: Sonologic features of different vulvar cancer types

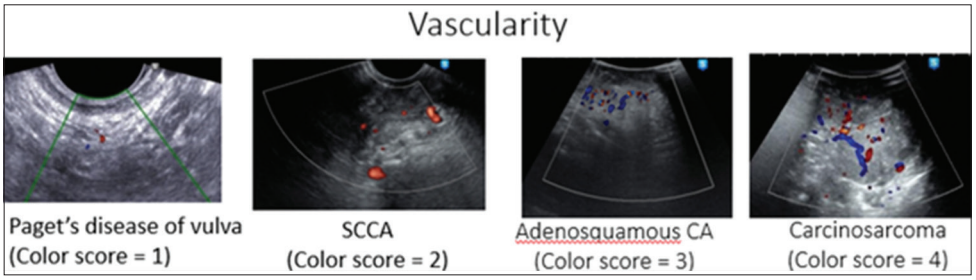

Figure 2: Doppler studies of different vulvar cancer types

preoperatively using ultrasound. Out of the nine nodes, 5 (55.6%) cases were unilateral and 2 (44.4%) cases were bilateral. Ultrasound correctly identified laterality in all (100%) node-positive cases. Out of 23 groins analyzed with histopathologically negative inguinal nodes, 18 (78.3%) were correctly diagnosed by ultrasound.

The L/S ratio was obtained for 12 lymph nodes. For those with an L/S ratio of <2, ultrasound was able to identify 7 out of 9 nodes (77.8%). For those with an L/S ratio >2, ultrasound was able to identify 2 out 3 (66.7%) nonmalignant lymph nodes. Both tumor border and FIGO stage showed significant association with histopathologic type.

Seventeen patients (34.7%) had no ultrasound reports of inguinal lymph nodes. Of 17 patients, 5 had positive lymph nodes and 2 had negative lymph nodes on histopathology. The remaining 10 patients had no histopathology reports.

Discussion

Vulvar cancer is diagnosed by vulvar biopsy and is frequently seen among 65–74 years old, with a median age of 69 years old. Prognosis is related to stage of disease, tumor size, and inguinal node status.[7] The median age in our study was 65 years old. All patients underwent vulvar biopsy for diagnosis.

The disease stage correlates to overall survival. Localized cancer (Stage I and II) confers a 5-year relative survival rate of 85.5%, regional involvement (Stage III) 50.6%, and distant metastasis 20.3%.[8] This study showed 57% of vulvar cancers were localized, 34% regional, and 9% metastatic; which were similar to the SEER cancer statistics review.[8]

Clark microstaging was used for staging VM because it was more predictive for recurrence and survival.[9] VM patients have an overall reported 5-year survival rate between 10% and 63%.[10] All our patients were diagnosed at later stages, which forebode a poorer prognosis.

Tumor size influences treatment.[11] Lesions <2 cm had a 19% risk of lymph node metastases and for >2 cm had a 42% risk.[12] Due to the initial delay in patient diagnosis before referral to our institution, 65% of tumors had sizes > 4 cm.

The most important prognostic and therapeutic factor is lymph node status. It is assessed either by sentinel lymph node biopsies or inguinal lymphadenectomies.[11] Risk factors for groin node metastases include clinically enlarged nodes, LVSI, tumor grade, age, and depth of invasion.[13]

The most common histologic type of vulvar malignancy is SCCA, which accounts for 90% of reported cases, followed by VM at 5%–10% and Bartholin's gland carcinoma at 2%–7%.[14] In the present study, SCCA was the most common histologic type, followed by melanoma and ADCA, similar to those seen in the literature.

MRI is the best imaging modality in vulvar cancer because of its excellent soft-tissue contrast for evaluation of tumor response, tumor recurrence, and posttreatment complications.[15] Most literature describe vulvar cancer lesions using MRI; however, there is a paucity of literature in describing each according to histopathologic type. In our setting, ultrasound was used as it was widely available and acceptable due to limited patient finances. We used ultrasound in the characterization of vulvar lesions and assessment of lymph node status.

SCCA was described as hypoechoic lesions with irregular borders using high-frequency ultrasound.[16] SCCA appeared as heterogeneous lesions in our study.

Verrucous carcinoma, a rare variant of SCCA, is a cauliflower-like lesion that is locally aggressive and possesses minimal or no risk of nodal metastasis.[17] Because of its rarity, there is a lack of literature on its imaging descriptions. To date, our study seems to be the first to describe sonographic features of this lesion. Pelvic lymph nodes appeared benign by ultrasound and by histopathology report, showing its low propensity for nodal metastasis.

Melanomas may arise from the skin (cutaneous melanoma) or from mucosal epithelium (mucosal melanoma). Mucosal melanomas are rare and have a poorer prognosis than its cutaneous counterparts.[18] VM has classically been described as part of mucosal melanomas; however, a subset of VMs may share common risk factors with cutaneous melanoma.[19,20] Clinical presentation includes pruritus, vaginal bleeding, vaginal discharge, dyspareunia, or a mass with ulceration or necrosis.[21,22] Due to the metastasizing nature of VM, some advocate imaging as part of standard work-up for all cases. CT, MRI, or ultrasound of the groin and pelvis for loco-regional spread, and PET/CT for distant spread is recommended.[8] Using high frequency ultrasound, cutaneous melanomas appeared as hypoechoic, homogeneous, and well-defined lesions demonstrating 100% sensitivity in two studies with variable specificities of 33%–73%.[23] In another study, metastatic mucosal melanoma appeared as a heterogeneous nodular mass with minimal vascularity.[24] Most of the VM cases in our study also exhibited heterogeneous echo pattern, which may correspond to necrosis. Some tumors had hypoechogenic echo pattern, which suggests that there may be cutaneous manifestations. All tumor borders

were irregular, signifying possible tumor infiltration and aggressive behavior, though lymph node metastasis was not identified in the current study. Color flow mapping of the VM lesions was variable, which is comparable to the findings of Fernández *et al*.[25]

Glandular tumors of the vulva included in our study were Paget's disease of vulva (PDV), ADCA, adenosquamous carcinoma (ASC), and ECCAs.[26]

PDV presents as eczematoid weeping lesions with a high recurrence rate.[27] Until now, the role of imaging in PDV is indefinite. Migda *et al*. described it as a hypoechoic lesion with blurred, irregular outer margins, edematous, and enlarged blood vessels using high-frequency ultrasound.[16] Though their study and the present study both showed similar echo pattern of the mass, tumor borders were regular, and Doppler studies showed absent color flow in our study. Further studies are needed to further elucidate its sonologic characteristics. Ultrasound showed no inguinal nodes, and sentinel node biopsy was also negative in this case. Lymph node detection is influenced by the stage of the disease, specifically Stage III disease and above.

Primary ADCAs of the vulva mainly arise from Bartholin's glands.[28] ADCA histology and positive lymph node were correlated with a worse prognosis.[29] MRI of vulvar and vaginal ADCAs showed solid, homogeneously hyperintense masses on T2-weighted images, sometimes with central hyperintense areas corresponding to necrosis and isointense to muscle on T1-weighted images.[22,30] In our study, ADCAs mostly appeared as heterogeneous masses with irregular borders and sometimes appeared as hypoechogenic mass with regular tumor borders on ultrasound imaging.

ASC is thought to arise in Bartholin's glands.[31] Studies are limited in describing its sonographic features in the vulva. Lesions in other sites have been described as solid, hypoechoic masses with irregular borders.[32-34] In our case, ASC had heterogeneous echo pattern with irregular tumor borders and moderate vascularity.

Primary ADCA arising from eccrine sweat glands is very rare, representing approximately 0.005% of epithelial cutaneous neoplasms, with eccrine porocarcinoma (EPC) being the most common variant.[35] The two studies on imaging features of vulvar EPC described it as ulcerative lesions. MRI T2-weighted images showed intermediate to high signal intensity masses, ill-defined borders with high and nonhomogeneous enhancement after contrast medium administration with no lymph node involvement.[36,37] In our study, the tumor's sonologic appearance was comparable with gross and MRI findings of EPC.

Vulvar sarcomas account for 1%–3% of vulvar malignancies. LMS is the most common soft-tissue sarcoma at this site.[38] Tumors are well to poorly circumscribed and range in size from 5.5 to 13.5 cm.[39] Vulvar LMSs may be seen as large, heterogeneous masses with poor penetration of sound waves on ultrasound.[40] In our case, LMS presented as a 17.0 cm mass with similar ultrasound findings and behavior described in literature. The absence of color flow may be due to rapid enlargement, outgrowing its own blood supply.

PES is an aggressive vulvar malignancy with <30 documented cases.[41] It appears as firm to fleshy nodular lesions with variable necrosis and hemorrhage.[26] Sonologic characterization and Color Doppler examination by Yue *et al*. showed a homogenous hypoechoic and ovoid solid mass with well-defined borders and moderate blood flow.[42] The presence of necrosis may be the reason the lesion was heterogeneous in our study, as seen in the case report by Rodrigues *et al*.[43]

CSs represent mixed mesodermal tumors that are extremely rarely in the vulva.[44] Sonographic findings of uterine CSs include: heterogeneous echo-texture masses with increased vascularity or large intracavitary mass with the expansion of the endometrial cavity and myometrial invasion.[45] There are only a few reported cases and to the best of our knowledge, ultrasound, and color Doppler findings of vulvar CSs have not been described to date. In this study, CS resembled sonographic findings of its uterine counterpart.

One of the round-cell tumors that appear similar to our study is rhabdomyosarcoma. It appears as well-defined, slightly hypoechoic to inhomogeneous mass that shows significantly increased flow.[46] However, it is still recommended to do further histopathological studies to ascertain the diagnosis.

Lymph node status is vital in management and monitoring after surgery or chemoradiation. Ultrasound can accurately identify lymph node's morphology, and changes in inner structure using grayscale mode and vascular pattern using power Doppler mode.[47] Combined ultrasound imaging and ultrasound-guided fine-needle aspiration biopsy was also the most reliable method for the evaluation of inguinofemoral lymph nodes with very high specificity (82%–100%) and sensitivity (80%–93%) when compared to other imaging modalities.[15]

Lymph nodes are evaluated mainly by transabdominal sonography using the convex-array probe for evaluating deep lymph nodes and the linear-array probe for peripheral lymph nodes. Infiltrated lymph nodes

are round with loss of fatty hilum, inhomogeneous echogenicity, irregular contour, and with peripheral or mixed perfusion.[47,48] Because of the shape of malignant nodes, their L/S diameter is distorted with a ratio of <2, indicating malignancy.[6]

The overall accuracy of ultrasound ranges from 86% to 89% in predicting the presence or absence of inguinal lymph node metastases.[5,49] Our result was lower compared to those in literature. The use of a curvilinear probe instead of a linear array probe may have contributed to a lower detection rate of lymph nodes. The current study was also limited by its small sample size and other missing information, hence making it impossible to compute for other factors such as sensitivity, specificity, and positive and negative predictive values. The overall accuracy of the L/S ratio in this study was higher compared to Abang *et al*.[49] Since values are too small to rule out coincidence or chance, authors recommend further studies with larger samples to look into this specifically.

Summary, Limitations and Recommendations

Ultrasound is safe, cost-effective, evaluates tumors in real time, and assesses tumoral blood flow. Technological advances have allowed ultrasound to be more sensitive in detecting smaller lesions. Sonologic features of vulvar malignancies and the overall accuracy of ultrasound in predicting lymph node status help in the prognostication of vulvar cancer patients. Since the study is retrospective, some clinical and histological information were incomplete. Digital images or video clips may not always have represented the most interesting areas of masses or dominant lymph nodes. This may have limited possibility to correctly describe ultrasound parameters of each dominant node. Further studies regarding lymph node morphology, vascularity, and L/S ratio are recommended.

Authorship contributions

Dr. Ma. Patricia Siao - Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data curation, Writing (original draft, review and editing) Visualization, Project administration, Funding acquisition.

Dr. Leovegildo Comia, Jr. Conceptualization, Methodology, Formal analysis, Investigation,, Writing (review and editing) Visualization, Supervision.

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Conflicts of interest

There are no conflicts of interest.

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