Cancer Association of South Africa (CANSA)

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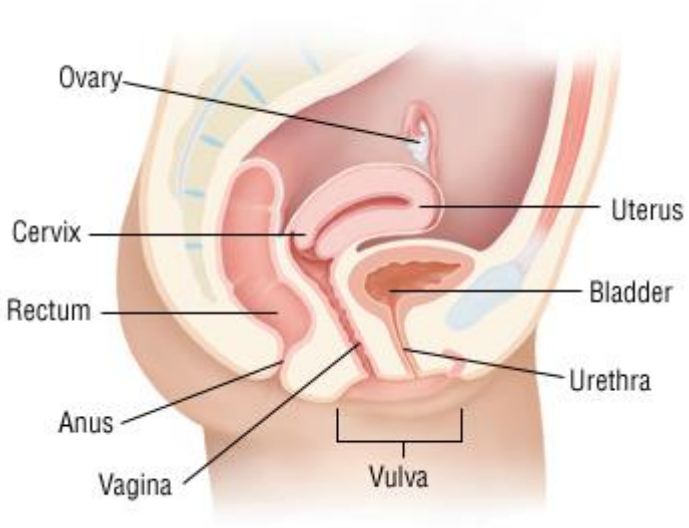
Fact Sheet
on
Melanoma of the Vulva and Vagina

Introduction

The vagina or birth canal is the opening through which menstrual fluid leaves a woman's body and babies are born. It is connected to the cervix, which is the opening of the uterus or womb, and the vulva (folds of skin around its opening).

Usually, the vagina is in a collapsed position with its walls touching. The walls have many folds that allow the vagina to open and expand during sexual intercourse and vaginal childbirth. The vaginal lining is kept moist by mucus released from glands in the cervix.



[Picture Credit: Female Genitalia]

The vaginal walls have a thin layer of cells called the epithelium, which contains cells called squamous epithelial cells. The vaginal wall, underneath the epithelium, is made up of connective tissue, involuntary muscle tissue, lymph vessels, and nerves.

Melanoma of Female Genitalia

Melanoma is a cancer that starts in cells called melanocytes. Melanocytes are pigment producing cells. They are mostly found in the skin. Most melanomas develop in parts of the body that are exposed to the sun. But one can get them anywhere, including in body organs, because there are melanocytes in those areas too. That is why one sometimes hears melanoma of the skin called cutaneous melanoma or melanoma of the skin. Cutaneous means of the skin. It is still not clear why melanomas can form in parts of the body that are not exposed to the sun.

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Even though some melanomas grow in parts of the body that is not exposed to the sun, it is still very important to remember that the best way to keep one's risk of melanoma or other skin cancers as low as possible is to avoid being in the sun too much.

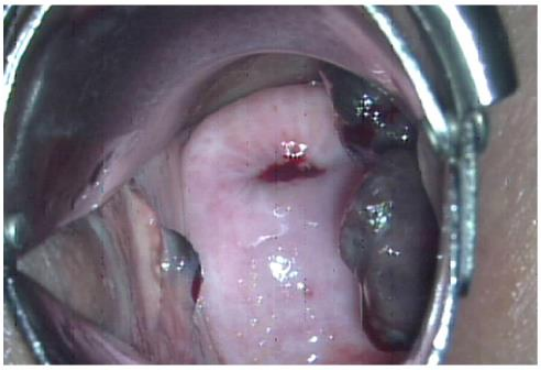
If someone has melanoma in an unusual site such as genital skin, the treatment should be planned by a multidisciplinary team (MDT). The team should include skin melanoma specialists and surgeons and oncologists who normally treat genital cancer.

Joste, M., Dion, L., Brousse, S., Nyangoh Timoh, K., Rousseau, C., Reilhac, A., Laviolle, B., Lesimple, T., Lavoue, V. & Leveque, J. 2020.
Introduction: Mucosal melanomas (MM) of the female genital tract are rare a. We aimed to study the prognostic factors of vulvar and vaginal locations of MM.
Material and method: A multicenter, retrospective cohort study conducted between 01/01/2000 and 01/06/2019.
Result: Of the 33 patients included 25 (75.8 %) had vulvar (VuM) and eight (24.2 %) vaginal melanomas (VaM). VaMs were deeper: median Breslow index: 17.5mm [3.5-22] versus 4.3mm [0.35-18] (p=0.013). Average follow-up was 24.0±59.8 months. Twenty-six patients (78.8 %) experienced recurrence. Disease-free survival was 52.9 % at 1year (64.7 % for VuM and 14.3 % for VaM) and 8.4 % at 3 years (11 % for VuM and 0% for VaM) (p=0.002). Median time to the first recurrence was 9.01 months [CI95 %: 2.07-56.71]. VaM recurred earlier than VuM (3.12 months [CI95 %: 2.07-12.49] versus 17.72 [CI95 %: 3.58-56.71], p=0.011). VaM had a higher risk of recurrence (HR=5.64 [CI95 %: 2.01-15.82], p=0.001) in multivariate analysis. Overall survival was 88.5 % at 1year (100 % for VuM and 50 % for VaM), and 59.4 % at 3 years (69.3 % for VuM and 25 % for VaM). Women with VaM died earlier: median specific death occurrence of 8.76 months [CI95 %: 6.54-24.72] versus 39.61 [CI95 %: 21.89-209.21], p=0.013 (HR=5.08 [CI95 %: 1.39-18.60], p=0.014). A lesion size ≥3cm was associated with an increased risk of mortality (HR=8.45 [CI95 %: 1.60-44.52], p=0.012). In multivariate analysis, vaginal location remained an independent and predictive variable of a higher risk of specific death (HR=8.56 [CI95 %: 1.95-37.64], p=0.005).
Conclusion: A vaginal location of MM is associated with a poorer prognosis than a vulvar location.

Wohlmuth, C., Wohlmuth-Wieser, I., May, T., Vicus, D., Given, L.T. & Laframboise, S. 2020.
Background: Vulvar melanoma (VuM) and vaginal melanoma (VaM) represent a unique subgroup of malignant melanomas with important differences in biology and treatment.
Objective: The objective of this study was to describe the epidemiology and prognosis of VuM and VaM in a large representative cohort.
Methods: Women with invasive VuM or VaM were identified from the Surveillance, Epidemiology and End Results-18 population representing 27.8% of the US population. Data on age, ethnicity, stage, location, histopathology, primary surgery, and lymphadenectomy were collected. The Kaplan-Meier method was used to analyze disease-specific and overall survival. Univariate and multivariate regression models were used to identify factors with a significant association with disease-specific survival.
Results: A total of 1400 VuM and 463 VaM were included for further analysis; 78.6% and 49.7% of women with VuM and VaM underwent surgery, but only 52.9% of women with non-metastatic VuM and 42.9% of women with non-metastatic VaM undergoing surgery had lymph node assessment; one third of these had positive nodes. Superficial spreading was the most common subtype in VuM, and nodular melanoma in VaM ($p < 0.001$). The median disease-specific survival was 99 months (95% confidence interval 60-138) and 19 months (95% confidence interval 16-22), respectively. Survival was significantly associated with age at diagnosis, ethnicity, stage, surgery, lymph node metastases, histologic subtype, ulceration, mitotic count, and tumor thickness in VuM, and stage, surgery, and

lymph node involvement in VaM. In the Cox model, lymph node status and number of mitoses remained independent predictors of outcome in VuM; in VaM, only lymph node status remained significant.
Conclusions: The overall prognosis of VuM and VaM remains poor. The American Joint Committee on Cancer staging system is applicable and should be used for VuM; however, lymph node status and mitotic rate are the most important predictors of survival. Lymph node status should be assessed and patients with positive nodes may be candidates for adjuvant treatment.

Incidence of Melanoma of the Female Genitalia
The National Cancer Registry (2017) does not provide any information regarding melanoma of the female genitalia.



Melanoma of the Vagina and Vulva
In this Fact Sheet melanoma of the vagina and vulva will be discussed together under the heading of cancer of the vagina.

[Picture Credit: Vaginal melanoma]

It is not clear what causes vaginal cancers. In general, cancer begins when healthy cells acquire a genetic mutation that turns normal cells into abnormal cells.

Healthy cells grow and multiply at a set rate, eventually dying at a set time. Cancer cells, however, grow and multiply out of control, and they do not die. The accumulating abnormal cells form a mass (tumour).

Cancer cells invade nearby tissues and can break off from an initial tumour to spread elsewhere in the body (metastasise).

Vaginal cancer is divided into different types based on the type of cell where the cancer began.

Vaginal cancer types include:
- Vaginal squamous cell carcinoma, which begins in the thin, flat cells (squamous cells) that line the surface of the vagina, is the most common type
- Vaginal adenocarcinoma, which begins in the glandular cells on the surface of your vagina
- Vaginal melanoma, which develops in the pigment-producing cells (melanocytes) of your vagina
- Vaginal sarcoma, which develops in the connective tissue cells or muscles cells in the walls of your vagina
- Clear cell adenocarcinoma, which occurs in women whose mothers took the drug diethylstilbestrol (DES) during pregnancy between the late 1940s and 1971. It is estimated that one woman out of 1 000 women exposed to DES will develop vaginal cancer.

Vaccari, S., Barisani, A., Salvini, C., Pirola, S., Preti, E.P., Pennacchioli, E., Iacobone, A.D., Patrizi, A. & Tosti, G. 2020.

Background: Vulvar melanoma (VM) is rare and is often diagnosed late. Dermoscopy may aid in its recognition, differentiating VM from other more common vulvar lesions, such as melanosis and naevi. However, little is known about the dermoscopic features of thin VM.

Aim: To retrospectively analyse a series of histopathologically diagnosed thin VMs and to highlight their most suggestive dermoscopic features.

Methods: A multicentre, retrospective study was conducted, including histopathologically proven thin VMs, either intraepidermal or with Breslow thickness ≤ 0.5 mm, diagnosed during the period 2016-2018. We particularly focused on their dermoscopic characteristics to highlight the most suggestive dermoscopic diagnostic clues.

Results: In total, 14 cases of early-stage VM were included, in women with a mean age at diagnosis of 64.86 years. The most frequently affected sites were the labia minora. Of these, 11 cases were unifocal. Dermoscopy most often revealed structureless areas, grey globules and areas, irregular black-brown dots, blue and white structures, and red areas.

Conclusions: In our experience, early-stage VM often exhibits dermoscopic features that are more typical of thicker cutaneous melanomas. Dermoscopy may provide useful clues for the prompt diagnosis of thin VM.

Signs and Symptoms of Vaginal Cancer

Women with vaginal cancer may experience the following symptoms or signs. Sometimes, women with vaginal cancer may not show any of these symptoms. Or, these symptoms may be caused by a medical condition that is not cancer.

The most common symptom of vaginal cancer may include abnormal vaginal bleeding. Vaginal bleeding, during or after menopause, is not normal and is a sign of a problem. Other symptoms of vaginal cancer may include:

- Abnormal vaginal discharge
- Difficulty or pain when urinating
- Pain during sexual intercourse
- Pain in the pelvic area (the lower part of the abdomen between the hip bones)
- Pain in the back or legs
- Swelling in the legs
- Unusual vaginal bleeding, for example, after intercourse or after menopause.
- Watery vaginal discharge.
- A lump or mass in the vagina.
- Painful urination.
- Constipation.
- Pelvic pain

If a woman is concerned about one or more of the symptoms or signs on this list, she should consult a physician. He/she will conduct a physical examination and also ask how long and how often the symptom(s) have been around, in addition to other questions.

If cancer is diagnosed, relieving symptoms remains an important part of cancer care and treatment. This may also be called symptom management, palliative care, or supportive care. Be sure to talk with the health care team about symptoms experienced, including any new symptoms or a change in symptoms.

Treatment of Melanoma of the Vagina

Surgery may be the best treatment regime that could possibley significantly improve longevity of patients.

Postoperative adjuvant therapy using chemotherapy, radiation therapy, topical creams immunotherapy, and targeted therapy may help prevent recurrence of the tumour

Wang, D., Xu, T., Zhu, H., Dong, J. & Fu, L. 2020.

"The female lower genital tract melanomas mainly include vulvar, vaginal and cervical melanoma. There is little clinical data on the melanomas thus making them highly lethal with their prognosis being worse than for cutaneous melanoma and other gynecological malignancies. Surgery is still the primary treatment for gynecological melanomas with wide local resection (WLE) of tumors with adequate margins being preferred for early-stage vulvar melanoma while complete resection of the primary tumor is the standard treatment for early-stage cervical and vaginal melanoma. Sentinel lymph node biopsy seems to avoid unnecessary complete regional lymphadenectomy. However, it should be chosen cautiously. Recently discovered molecular changes have provided new hopes for effective systemic treatment of female genital tract melanomas. In this review, we summarize the pathogenesis and clinicopathological characteristics of these rare melanomas with particular emphasis on new therapies and clinical management methods that may affect prognosis. The review aims to provide a viable direction for clinicians to diagnose and treat female lower genital tract melanomas."

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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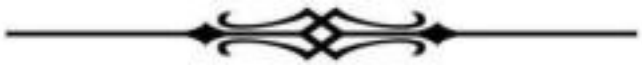

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