Webinar GISCi

Adenocarcinoma della cervice uterina: quale prevenzione oggi?

Venerdì 9 Aprile 2021 – ore 17.00 – 19.30

Classificazione istologica WHO 2020 delle lesioni ghiandolari cervicali e correlazione con HPV

Galliano Tinacci

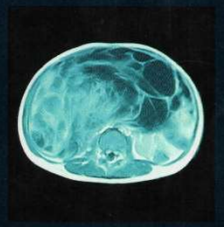
Il sottoscritto Dott. Galliano Tinacci
ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato-Regione del 5 novembre 2009,

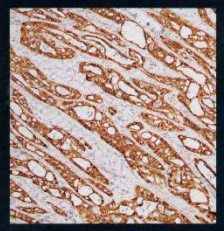
dichiara

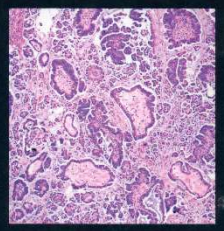
che negli ultimi due anni NON ha avuto rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario

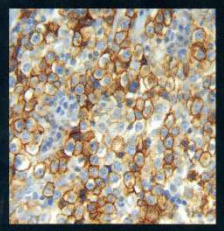
WHO Classification of Tumours of Female Reproductive Organs

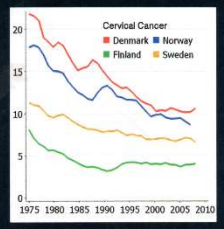
Edited by Robert J. Kurman, Maria Luisa Carcangiu, C. Simon Herrington, Robert H. Young

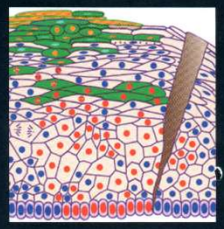


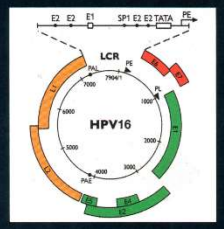












WHO

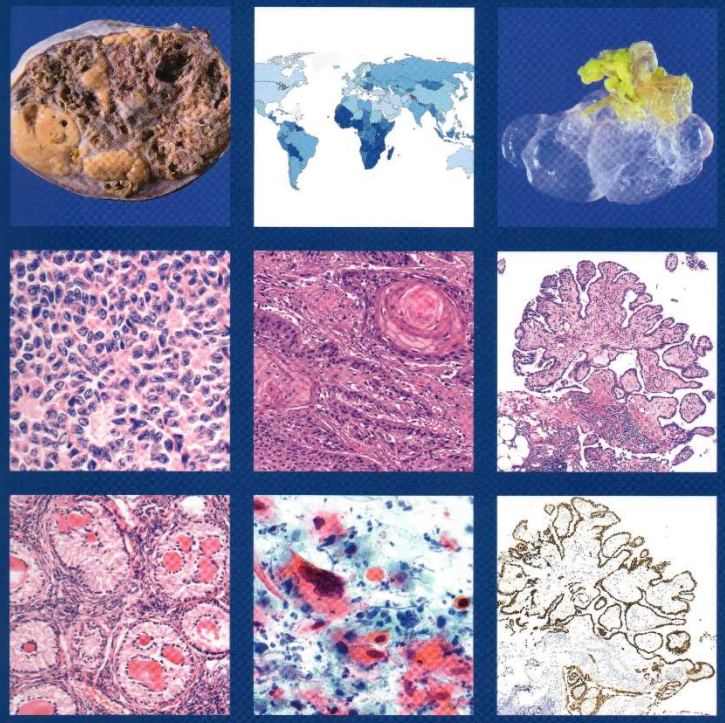
WHO Classification of tumours of the uterine cervix[a,b]

Epithelial tumours	
Squamous cell tumours and precursors	
Squamous intraepithelial lesions	
Low-grade squamous intraepithelial lesion	8077/0
High-grade squamous intraepithelial lesion	8077/2
Squamous cell carcinoma, NOS	8070/3
Keratinizing	8071/3
Non-keratinizing	8072/3
Papillary	8052/3
Basaloid	8083/3
Warty	8051/3
Verrucous	8051/3
Squamotransitional	8120/3
Lymphoepithelioma-like	8082/3
Benign squamous cell lesions	
Squamous metaplasia	
Condyloma acuminatum	
Squamous papilloma	8052/0
Transitional metaplasia	
Glandular tumours and precursors	
Adenocarcinoma in situ	8140/2
Adenocarcinoma	8140/3
Endocervical adenocarcinoma, usual type	8140/3
Mucinous carcinoma, NOS	8480/3
Gastric type	8482/3
Intestinal type	8144/3
Signet-ring cell type	8490/3
Villoglandular carcinoma	8263/3
Endometrioid carcinoma	8380/3
Clear cell carcinoma	8310/3
Serous carcinoma	8441/3
Mesonephric carcinoma	9110/3
Adenocarcinoma admixed with neuroendocrine carcinoma	8574/3
Benign glandular tumours and tumour-like lesions	
Endocervical polyp	
Müllerian papilloma	
Nabothian cyst	
Tunnel clusters	
Microglandular hyperplasia	
Lobular endocervical glandular hyperplasia	
Diffuse laminar endocervical hyperplasia	
Mesonephric remnants and hyperplasia	
Arias Stella reaction	
Endocervicosis	
Endometriosis	
Tuboendometrioid metaplasia	
Ectopic prostate tissue	
Other epithelial tumours	
Adenosquamous carcinoma	8560/3
Glassy cell carcinoma	8015/3
Adenoid basal carcinoma	8098/3
Adenoid cystic carcinoma	8200/3
Undifferentiated carcinoma	8020/3
Neuroendocrine tumours	
Low-grade neuroendocrine tumour	
Carcinoid tumour	8240/3
Atypical carcinoid tumour	8249/3
High-grade neuroendocrine carcinoma	
Small cell neuroendocrine carcinoma	8041/3
Large cell neuroendocrine carcinoma	8013/3
Mesenchymal tumours and tumour-like lesions	
Benign	
Leiomyoma	8890/0
Rhabdomyoma	8905/0
Others	
Malignant	
Leiomyosarcoma	8890/3
Rhabdomyosarcoma	8910/3
Alveolar soft-part sarcoma	9581/3
Angiosarcoma	9120/3
Malignant peripheral nerve sheath tumour	9540/3
Other sarcomas	
Liposarcoma	8850/3
Undifferentiated endocervical sarcoma	8805/3
Ewing sarcoma	9364/3
Tumour-like lesions	
Postoperative spindle-cell nodule	
Lymphoma-like lesion	
Mixed epithelial and mesenchymal tumours	
Adenomyoma	8932/0
Adenosarcoma	8933/3
Carcinosarcoma	8980/3
Melanocytic tumours	
Blue naevus	8780/0
Malignant melanoma	8720/3
Germ cell tumours	
Yolk sac tumour	
Lymphoid and myeloid tumours	
Lymphomas	
Myeloid neoplasms	

WHO Classification of Tumours • 5th Edition

Female Genital Tumours

Edited by the WHO Classification of Tumours Editorial Board



International Agency for Research on Cancer
World Health Organization

WHO classification of tumours of the uterine cervix

Squamous epithelial tumours

- Squamous metaplasia
- Atrophy
- Condyloma acuminatum

8077/0 Low-grade squamous intraepithelial lesion
8077/0 Cervical intraepithelial neoplasia, grade 1
8077/2 High-grade squamous intraepithelial lesion
8077/2 Cervical intraepithelial neoplasia, grade 2
8077/2 Cervical intraepithelial neoplasia, grade 3
8085/3 Squamous cell carcinoma, HPV-associated
8086/3 Squamous cell carcinoma, HPV-independent
8070/3 Squamous cell carcinoma NOS

Glandular tumours and precursors

- Endocervical polyp
- Müllerian papilloma
- Nabothian cyst
- Tunnel clusters
- Microglandular hyperplasia
- Lobular endocervical glandular hyperplasia
- Diffuse laminar endocervical hyperplasia
- Mesonephric remnants and hyperplasia
- Arias-Stella reaction
- Endocervicosis
- Tuboendometrioid metaplasia
- Ectopic prostate tissue

8140/2 Adenocarcinoma in situ NOS
8483/2* Adenocarcinoma in situ, HPV-associated
8484/2* Adenocarcinoma in situ, HPV-independent

8140/3 Adenocarcinoma NOS
8483/3* Adenocarcinoma, HPV-associated
8482/3 Adenocarcinoma, HPV-independent, gastric type
8310/3 Adenocarcinoma, HPV-independent, clear cell type
9110/3 Adenocarcinoma, HPV-independent, mesonephric type
8484/3* Adenocarcinoma, HPV-independent, NOS
8380/3 Endometrioid adenocarcinoma NOS
8980/3 Carcinosarcoma NOS
8560/3 Adenosquamous carcinoma
8430/3 Mucoepidermoid carcinoma
8098/3 Adenoid basal carcinoma
8020/3 Carcinoma, undifferentiated, NOS

Mixed epithelial and mesenchymal tumours

8932/0 Adenomyoma NOS
- Mesonephric-type adenomyoma
- Endocervical-type adenomyoma

8933/3 Adenosarcoma

Germ cell tumours

9064/3 Germ cell tumour NOS
9080/0 Mature teratoma NOS
9084/0 Dermoid cyst NOS
9071/3 Endodermal sinus tumour
9071/3 Yolk sac tumour NOS
9100/3 Choriocarcinoma NOS

International Endocervical Adenocarcinoma Criteria and Classification (IECC): A new pathogenetic classification for invasive adenocarcinomas of the endocervix

Simona Stolnicu, MD[1], Iulia Barsan, MD[1], Lien Hoang, MD[2], Prusha Patel, MPH[9], Cristina Terinte, MD[3], Anna Pesci, MD[4], Sarit Aviel-Ronen, MD[5], Takako Kiyokawa, MD[6], Isabel Alvarado-Cabrero, MD[7], Malcolm C. Pike, PhD[9], Esther Oliva, MD[8], Kay J. Park, MD[9], and Robert A. Soslow, MD[9]

Am J Surg Pathol. 2018 February ; 42(2): 214–226.

HPV-associated adenocarcinoma (HPVA)

Apical mitotic figures and apoptotic bodies appreciable at scanning magnification. If those features were not seen at scanning magnification, a cursory exam at 200x was performed to detect additional cases. Those with easily-identified apical mitotic figures and apoptotic bodies were considered HPVA.
HPVA ECAs were further subcategorized, mostly based on cytoplasmic features, to provide continuity with pre-existing classification schemes, as follows:

Usual-type: 0–50% of cells with appreciable intracytoplasmic mucin, with or without benign-appearing squamous differentiation

Villoglandular: usual-type cytomorphology with exophytic long slender papillae

Mucinous, not otherwise specified (NOS): > 50% of cells with intracytoplasmic mucin in a background of usual-type

Mucinous, intestinal type: ≥ 50% of cells with goblet morphology in a background of usual adenocarcinoma

Mucinous, signet ring cell type: ≥ 50% of tumor cells with signet-ring morphology present in a background of usual adenocarcinoma

Invasive stratified mucin-producing carcinoma (iSMILE): invasive nests of stratified columnar cells with peripheral palisading and variable amounts of intracytoplasmic mucin, resembling its in-situ counterpart (SMILE)

Am J Surg Pathol. 2018 February ; 42(2): 214–226

Non-HPV-associated adenocarcinoma (NHPVA)

No easily identifiable apical mitotic activity and apoptotic bodies at scanning magnification. If focal or equivocal HPVA features were appreciable at 200x, tumors were considered to show “limited HPVA” features and tentatively classified as NHPVA adenocarcinoma.
NHPVA ECAs were subclassified based on established published criteria as follows:

Endometrioid adenocarcinoma: endometrioid morphology with “confirmatory endometrioid features” (at least focally identified low-grade endometrioid glands lined by columnar cells, with pseudostratified nuclei demonstrating no more than moderate atypia, with or without squamous differentiation and/or endometriosis present) and lacking HPVA features.

Gastric-type adenocarcinoma: tumor contains cells with abundant clear, foamy or pale eosinophilic cytoplasm, distinct cytoplasmic borders, generally low nuclear-cytoplasmic ratios and irregular basally-located nuclei, with no or limited HPVA-like features. Minimal deviation adenocarcinoma of mucinous type was considered part of the spectrum of gastric-type adenocarcinoma. Intestinal differentiation in the form of goblet cells and neuroendocrine-like eosinophilic granular cytoplasm was permitted.

Am J Surg Pathol. 2018 February ; 42(2): 214–226

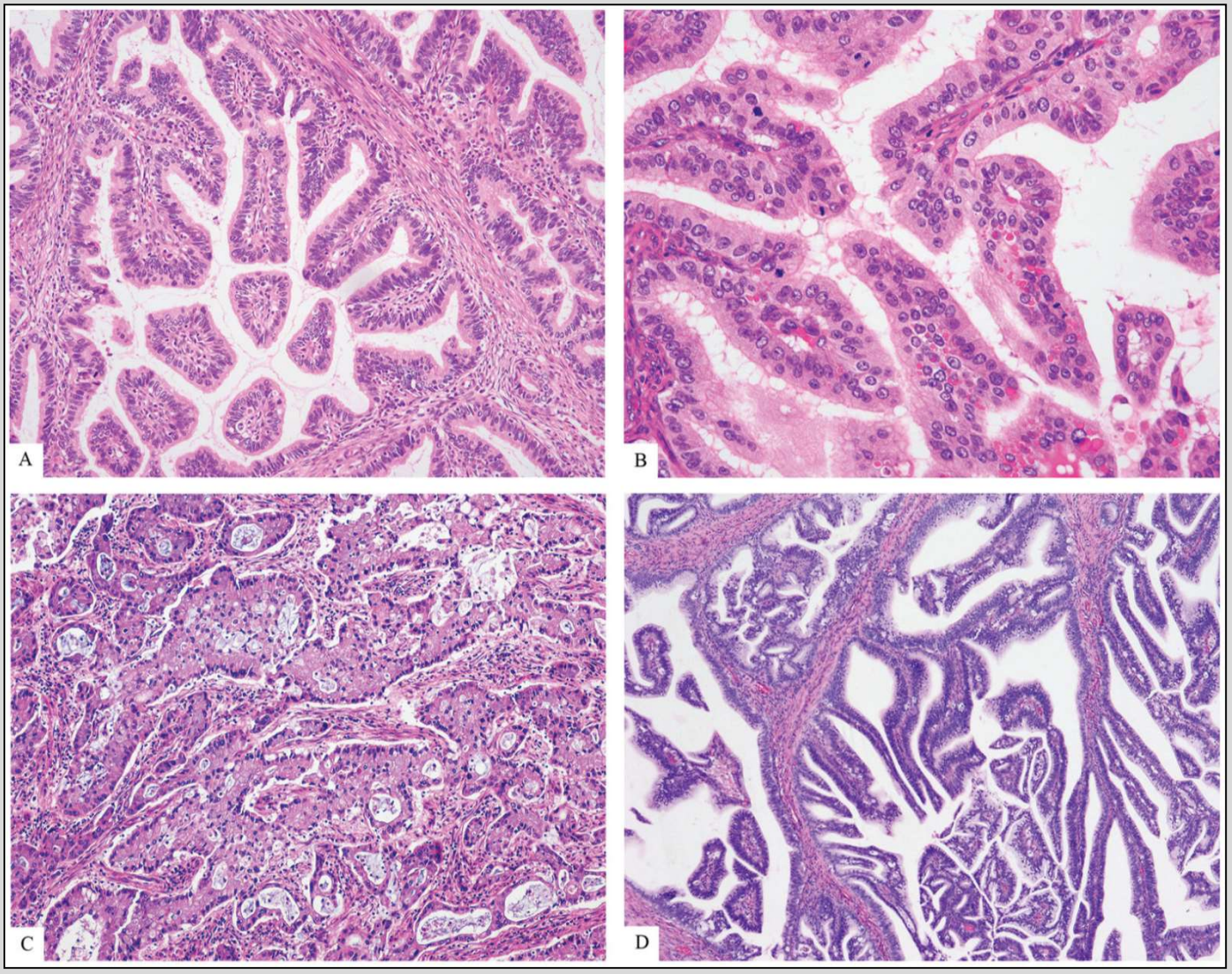
Serous adenocarcinoma: papillary and/or micropapillary architecture with cells showing diffusely distributed, highly atypical nuclei in stratified and pseudostratified cells with relative lack of intercellular adhesion. Mimics, such as drop metastases as well as other carcinomas with papillary architecture including usual-type, clear cell and mesonephric carcinoma were excluded

Clear cell adenocarcinoma: solid, papillary and/or tubulocystic architecture with polygonal cells and highly atypical, but uniform, nuclei.

Mesonephric carcinoma: tumors showing an admixture of growth patterns (ductal, tubular, papillary, cord-like and others), as well as intraluminal eosinophilic colloid-like material resembling mesonephric remnants.

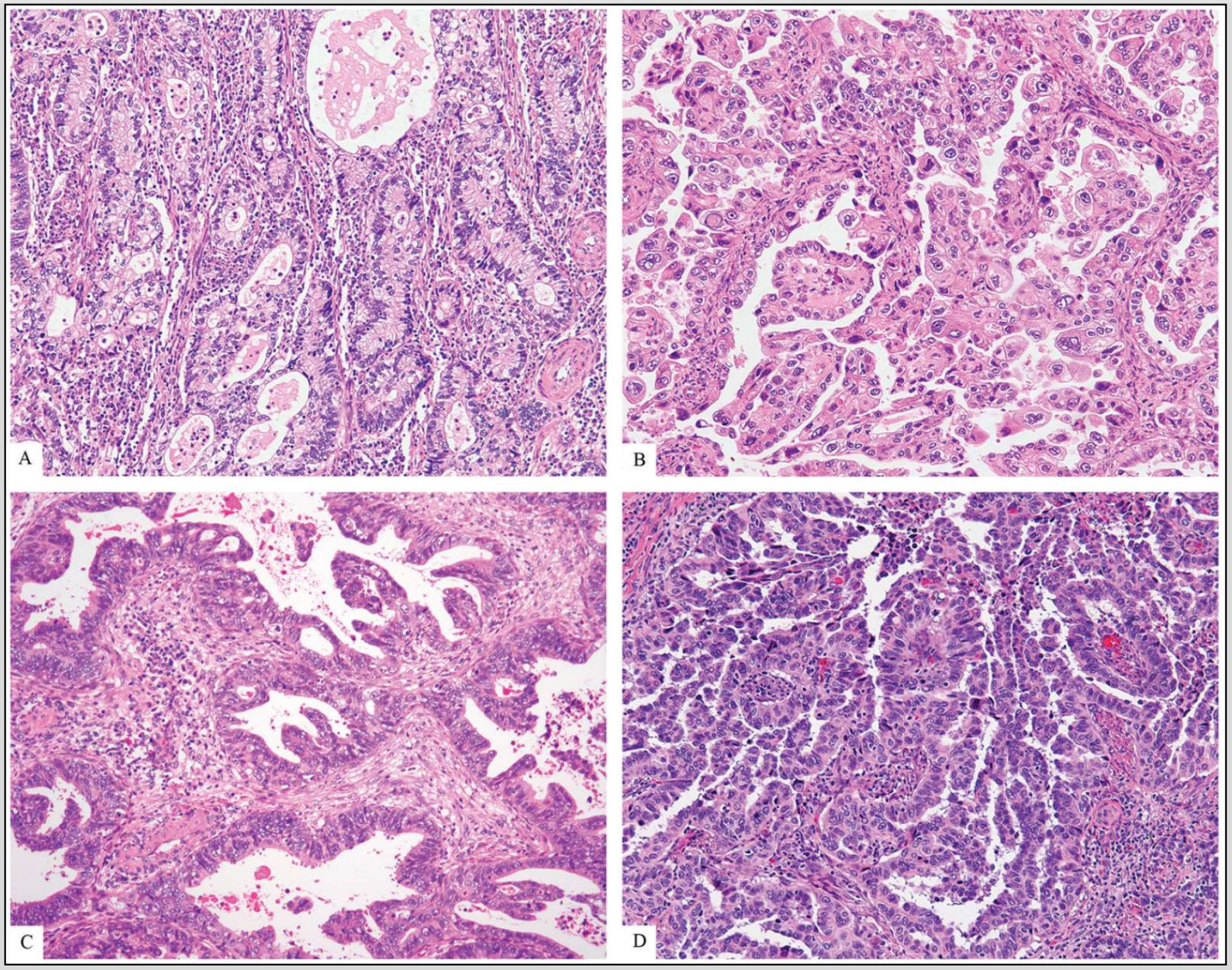
Invasive adenocarcinoma NOS: any tumor that could not be classified by WHO or IECC criteria.

Am J Surg Pathol. 2018 February ; 42(2): 214–226



HPV-associated adenocarcinomas (HPVA): Usual-type (A), mucinous (B), invasive adenocarcinoma with features reminiscent of stratified mucin-producing intraepithelial lesion (iSMILE) (C), villoglandular (D)

Am J Surg Pathol. 2018 February ; 42(2): 214–226



HPV-unassociated adenocarcinomas (NHPVA): Gastric-type (A), clear cell (B), endometrioid (C), serous (D)

Am J Surg Pathol. 2018 February ; 42(2): 214–226

WHO classification of tumours of the uterine cervix

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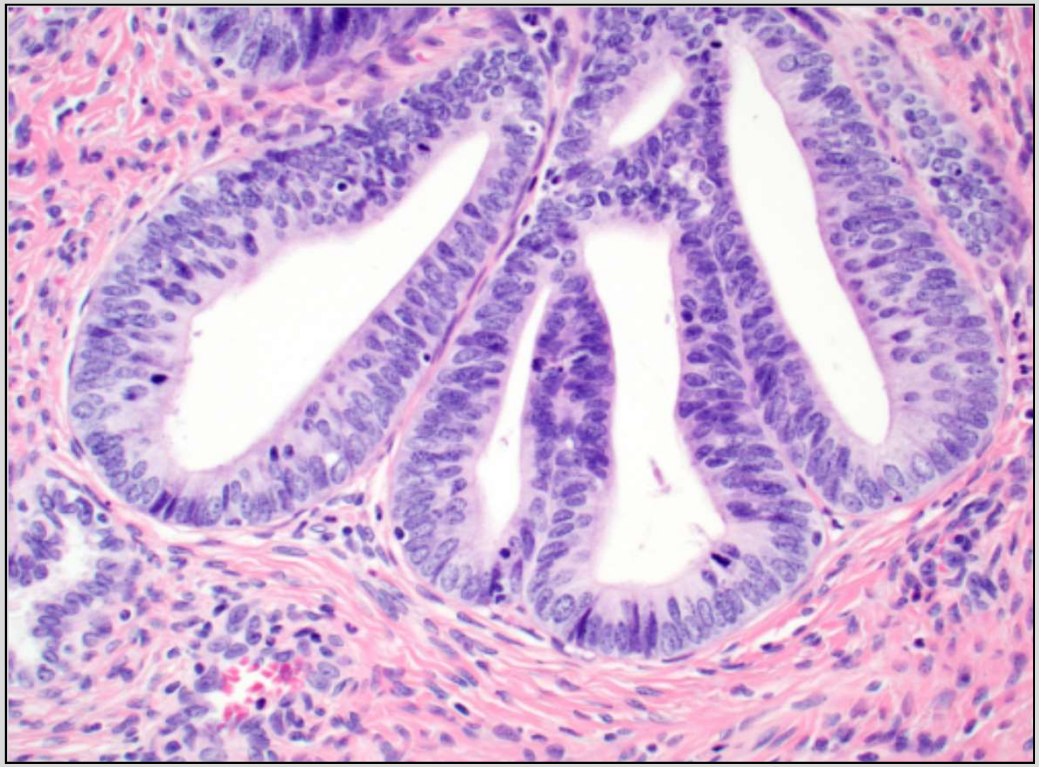
9080/0 Mature teratoma NOS
9084/0 Dermoid cyst NOS
9071/3 Endodermal sinus tumour
9071/3 Yolk sac tumour NOS
9100/3 Choriocarcinoma NOS

Adenocarcinoma in situ, HPV-associated, of the uterine cervix

Definition

Adenocarcinoma in situ (AIS), HPV-associated, is an HPV-associated glandular intraepithelial neoplasm.



WHO Classification of Tumours – 5° Edition

Adenocarcinoma in situ, HPV-associated, of the uterine cervix

Neoplasia intraepiteliale ghiandolare

Localizzata essenzialmente alla GSC

Età media nella 4° decade (circa 10 anni più giovane dell'adenocarcinoma invasivo)

HPV 16, 18, 45

HPV nel 99 % dei casi trovati con bio/colpo (90 % sono 16, 18)

Maggior importanza dell'HPV 18 rispetto alla controparte squamosa (anche nelle lesioni invasive)

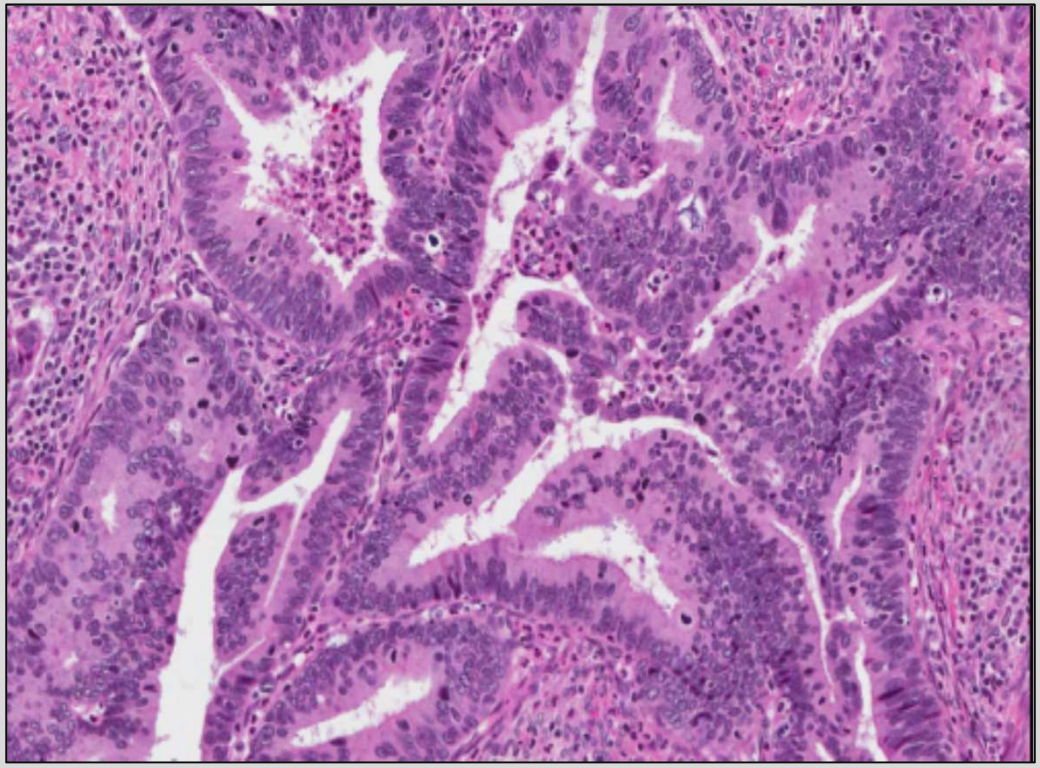
p16 in quasi tutti i casi

WHO Classification of Tumours – 5° Edition

Adenocarcinoma, HPV-associated, of the uterine cervix

Definition

Adenocarcinoma, HPV-associated, is a glandular tumour with stromal invasion and/or exophytic expansile-type invasion, associated with high-risk HPV (HR-HPV) infection.



WHO Classification of Tumours – 5° Edition

Adenocarcinoma, HPV-associated, of the uterine cervix

Aumentato negli anni fino al 10 – 25 % dei casi (verosimilmente per diminuita proporzione delle lesioni squamose trovate e trattate con lo Screening)

Localizzata essenzialmente alla GSC

Età media 40 – 42 anni (più giovanile rispetto a quella delle corrispettive lesioni NON HPV correlate)

HPV 16, 18, 45 responsabili del 95 % dei casi

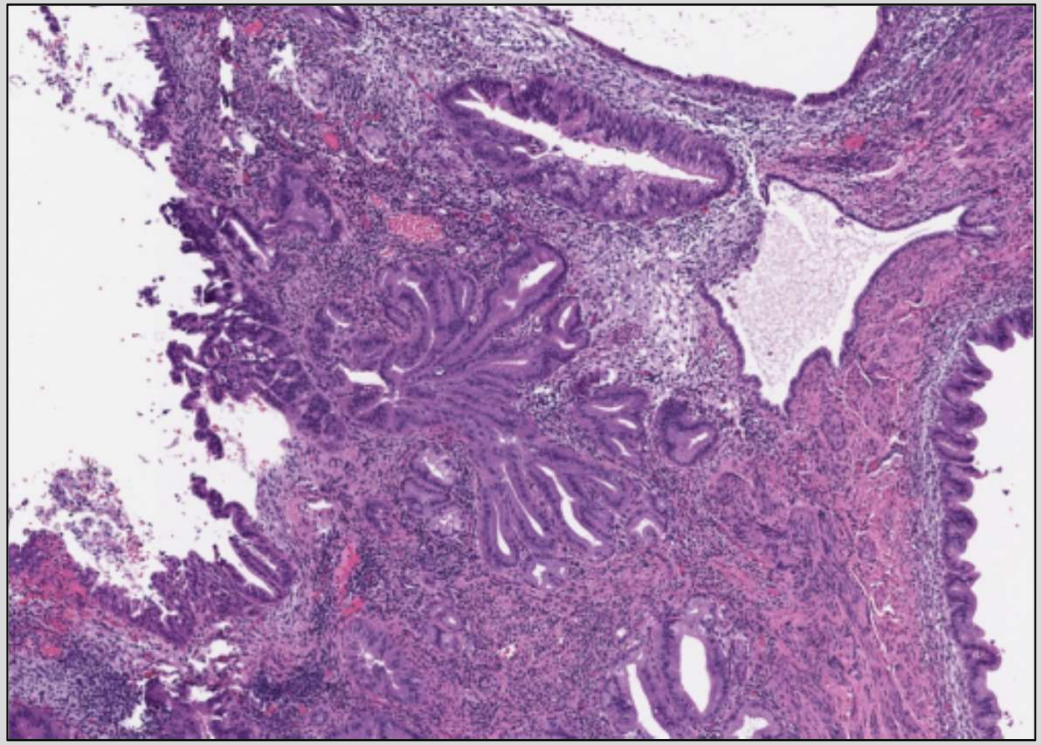
Infezione multipla da HPV nel 10 % circa dei casi

WHO Classification of Tumours – 5° Edition

Adenocarcinoma in situ, HPV-independent, of the uterine cervix

Definition

Adenocarcinoma in situ (AIS), HPV-independent, is a non-invasive glandular neoplasm unrelated to HPV. Gastric-type differentiation is characteristic.



WHO Classification of Tumours – 5° Edition

Adenocarcinoma in situ, HPV-independent, of the uterine cervix

Caratteristica la differenziazione «Gastric Type»

Età media 51 anni (25 – 74 anni)

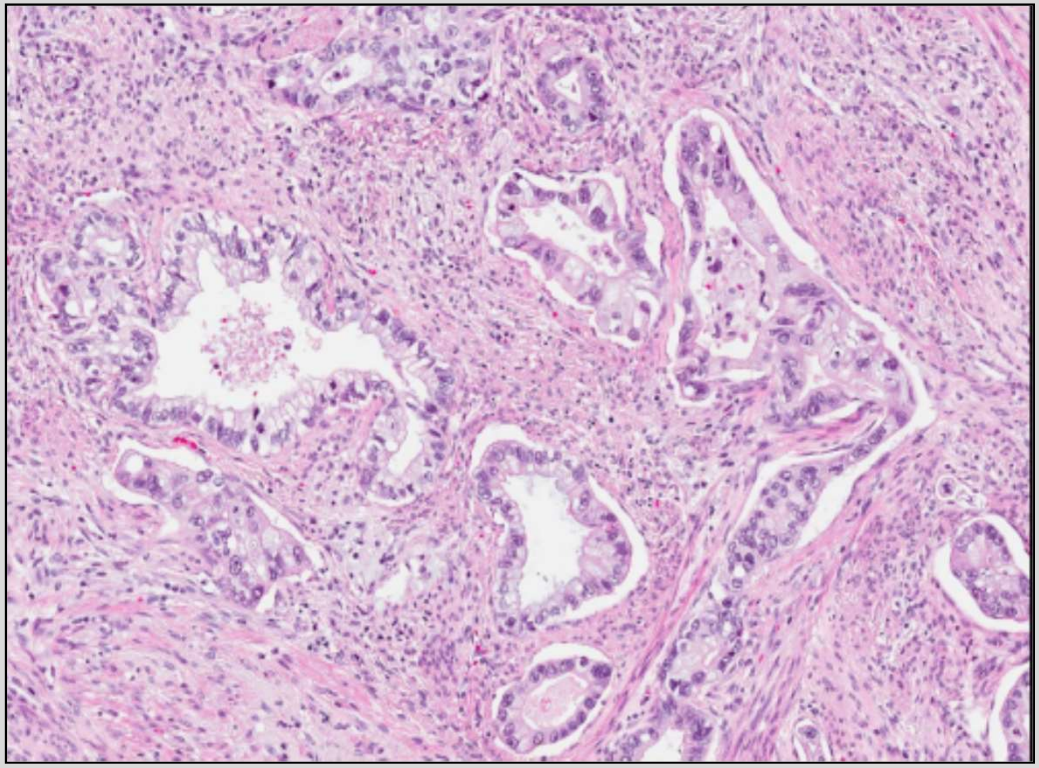
Riportati rari casi

WHO Classification of Tumours – 5° Edition

Adenocarcinoma, HPV-independent, gastric type, of the uterine cervix

Definition

Adenocarcinoma, HPV-independent, gastric type, is an invasive adenocarcinoma showing gastric (pyloric) differentiation, unrelated to HPV infection.



WHO Classification of Tumours – 5° Edition

Adenocarcinoma, HPV-independent, gastric type, of the uterine cervix

Differenziazione di tipo gastrico (Pilorico)

Localizzato essenzialmente nella parte superiore della cervice con frequente interessamento del corpo uterino

Rappresenta il 10 15 % circa degli Adenocarcinomi della cervice uterina (20 – 25 % in Giappone)

Età media 50 – 55 anni

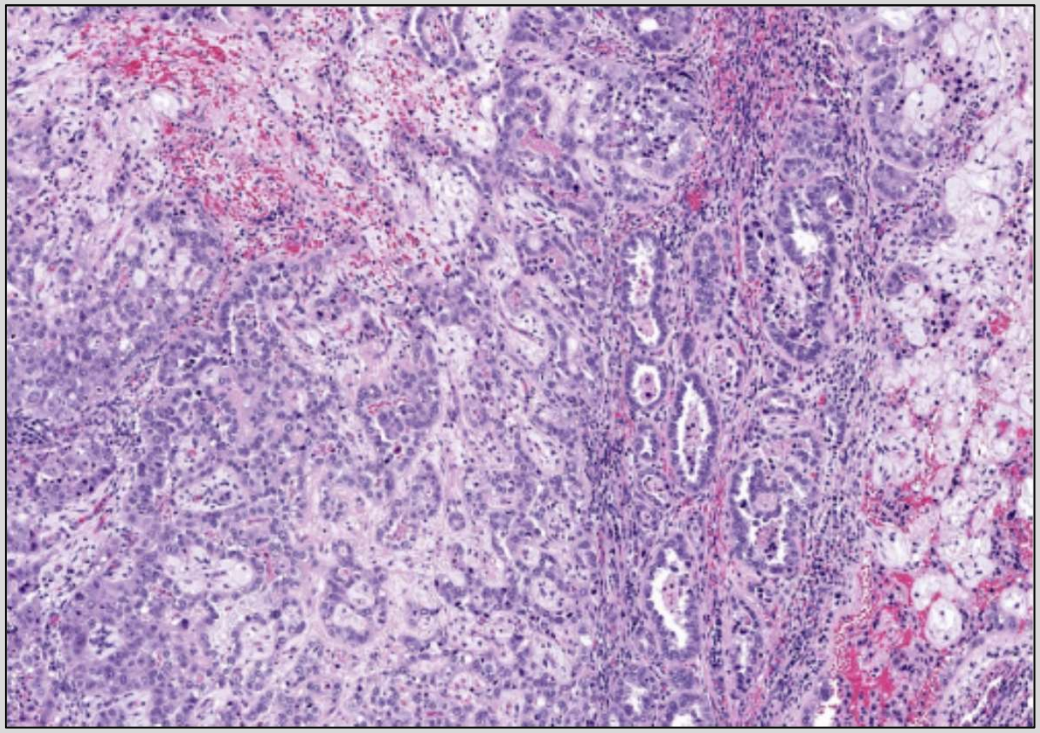
Alcuni casi correlati alla Sindrome di Peutz-Jeghers

WHO Classification of Tumours – 5° Edition

Adenocarcinoma, HPV-independent, clear cell type, of the uterine cervix

Definition

Clear cell carcinoma is a malignant glandular neoplasm composed of uniform, clear or eosinophilic, flat or cuboidal cells arranged in one or more patterns: tubulocystic, papillary, solid.



WHO Classification of Tumours – 5° Edition

Adenocarcinoma, HPV-independent, clear cell type, of the uterine cervix

Localizzato all'endocervice

Raro 3 – 4 %

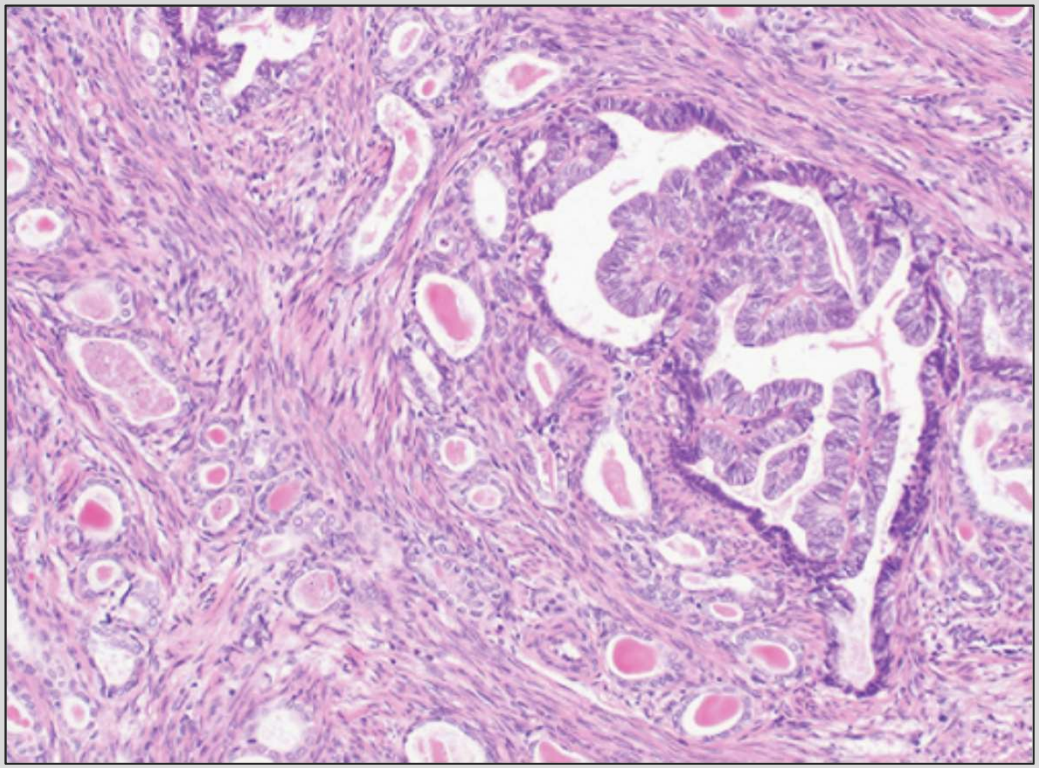
Due setting Sporadico
Associato alla esposizione in utero a DES

WHO Classification of Tumours – 5° Edition

Adenocarcinoma, HPV-independent, mesonephric type, of the uterine cervix

Definition

Adenocarcinoma, HPV-independent, mesonephric type, is a malignant neoplasm with mesonephric (Wolffian) differentiation.



WHO Classification of Tumours – 5° Edition

Adenocarcinoma, HPV-independent, mesonephric type, of the uterine cervix

Localizzato profondamente nella cervice, lungo il decorso del dotto Mesonefrico nelle pareti laterali, in sede di residui mesonefrici

Raro < 1 %

Età media 53 anni

WHO Classification of Tumours – 5° Edition

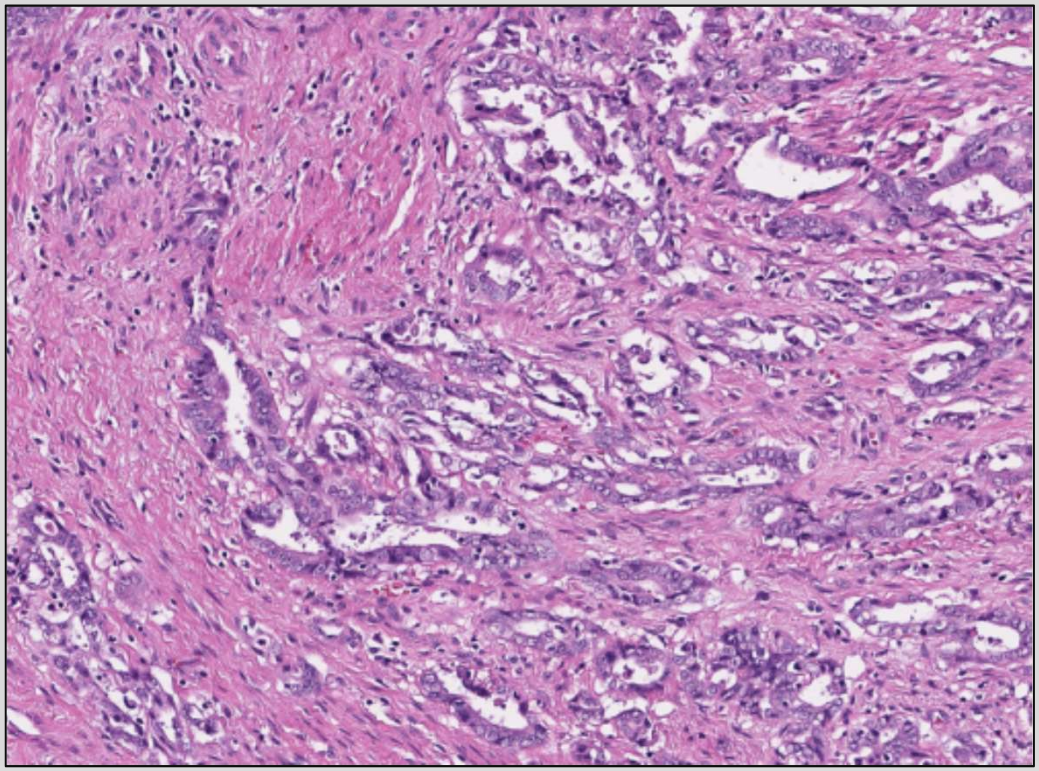
Other adenocarcinomas of the uterine cervix

Definition

Adenocarcinoma is a malignant glandular neoplasm involving endocervix.

Subtype(s)

Endometrioid adenocarcinoma NOS



WHO Classification of Tumours – 5° Edition

Other adenocarcinomas of the uterine cervix

Endometrioide

Raro < 1 %

Adeno del corpo ???

WHO Classification of Tumours – 5° Edition

Grazie