外陰與陰道表皮內癌前病變之診斷與處置

Diagnosis and Management of Pre-invasive Vulvar and Vaginal Lesions

新竹市立馬偕兒童醫院婦產部
陳子健

感謝

顏明賢教授

惠予指導

VIN
(Vulvar Intraepithelial Neoplasia)

OPEN ACCESS

The European Society of Gynaecological Oncology (ESGO), the International Society for the Study of Vulvovaginal Disease (ISSVD), the European College for the Study of Vulval Disease (ECSVD) and the European Federation for Colposcopy (EFC) consensus statements on pre-invasive vulvar lesions

Mario Preti ,[1] Elmar Joura,[2] Pedro Vieira-Baptista ,[3,4] Marc Van Beurden,[5] Federica Bevilacqua,[1] Maaike C G Bleeker ,[6] Jacob Bornstein ,[7] Xavier Carcopino,[8] Cyrus Chargari ,[9] Margaret E Cruickshank,[10] Bilal Emre Erzeneoglu,[11] Niccolò Gallio ,[1] Debra Heller,[12] Vesna Kesic,[13] Olaf Reich,[14] Colleen K Stockdale ,[15] Bilal Esat Temiz,[11] Linn Woelber ,[16,17] François Planchamp,[18] Jana Zodzika,[19] Denis Querleu ,[20,21] Murat Gultekin [22]

Int J Gynecol Cancer 2022;32:830-845.

2020 WHO VIN Terminology

- **HPV-associated squamous intraepithelial lesions**
  - low-grade squamous intraepithelial lesion of the vulva (LSIL)
  - *high-grade squamous intraepithelial lesion of the vulva (HSIL)*
- **HPV-independent VIN**
  - *differentiated vulvar intraepithelial neoplasia (dVIN)*
  - differentiated exophytic vulvar intraepithelial lesion (DEVIL)
  - vulvar acanthosis with altered differentiation (VAAD)

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Etiology of VIN

- VHSIL
  - HPV16 in > 70% of cases
  - Additional risk factors include smoking and immunosuppression
- dVIN
  - HPV-independent
  - Arise mostly in a field of lichen sclerosus or lichen planus, chronic inflammatory lymphocyte-mediated skin diseases

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VIN Epidemiology

- **Incidence**
  - **VHSIL: 2.5-8.8 per 100 000 women/year**
  - **dVIN: less than 10% of VHSIL**
- **Median age**
  - **VHSIL: 47.8 years**
  - **dVIN: 67 years**

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VIN Clinical Presentation

- No single pathognomonic clinical feature
  - Visible various vulvar lesion
    - Maybe papular, raised, sharp bordered, keratotic roughened surface
    - Maybe white, red, gray, blue, brown, etc
  - Itching, irritation, pain
  - Bleeding

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HPV (+)

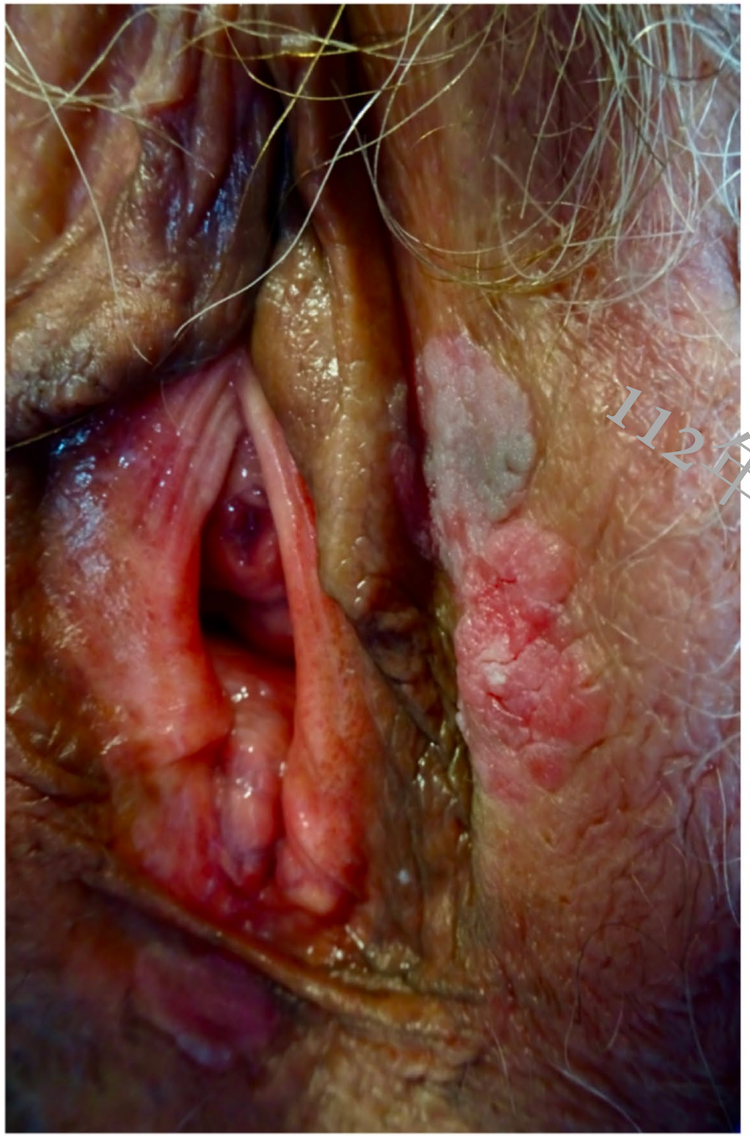

Figure 1 Vulvar high grade squamous intraepithelial lesion; brownish and erythematous poorly marginated plaques on the inner side of left labium.

HPV (-)

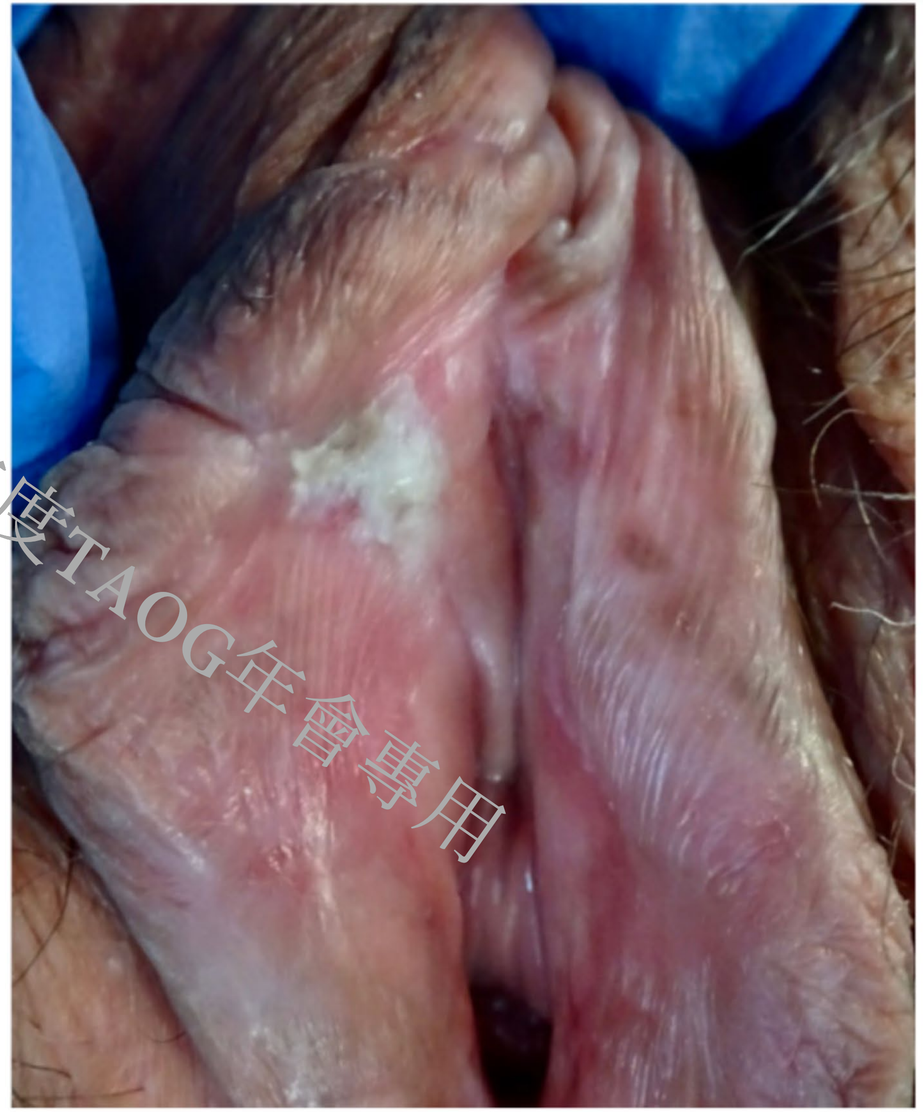

Figure 2 Differentiated vulvar intraepithelial neoplasia; whitish poorly marginated plaque on internal side of right labium minus in a field of lichen sclerosus.

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VIN Histopathology

- **VHSIL**
  - Abnormal maturation and dysplastic features extending above the lower third of the epithelium
- **dVIN**
  - Basal atypia with abrupt maturation (hypereosinophilic keratinocyte), basal spongiosis, absence of granular layer, keratosis
  - Difficult diagnosis
    - Initially diagnosed as lichen sclerosus => 42% reclassified as dVIN after review

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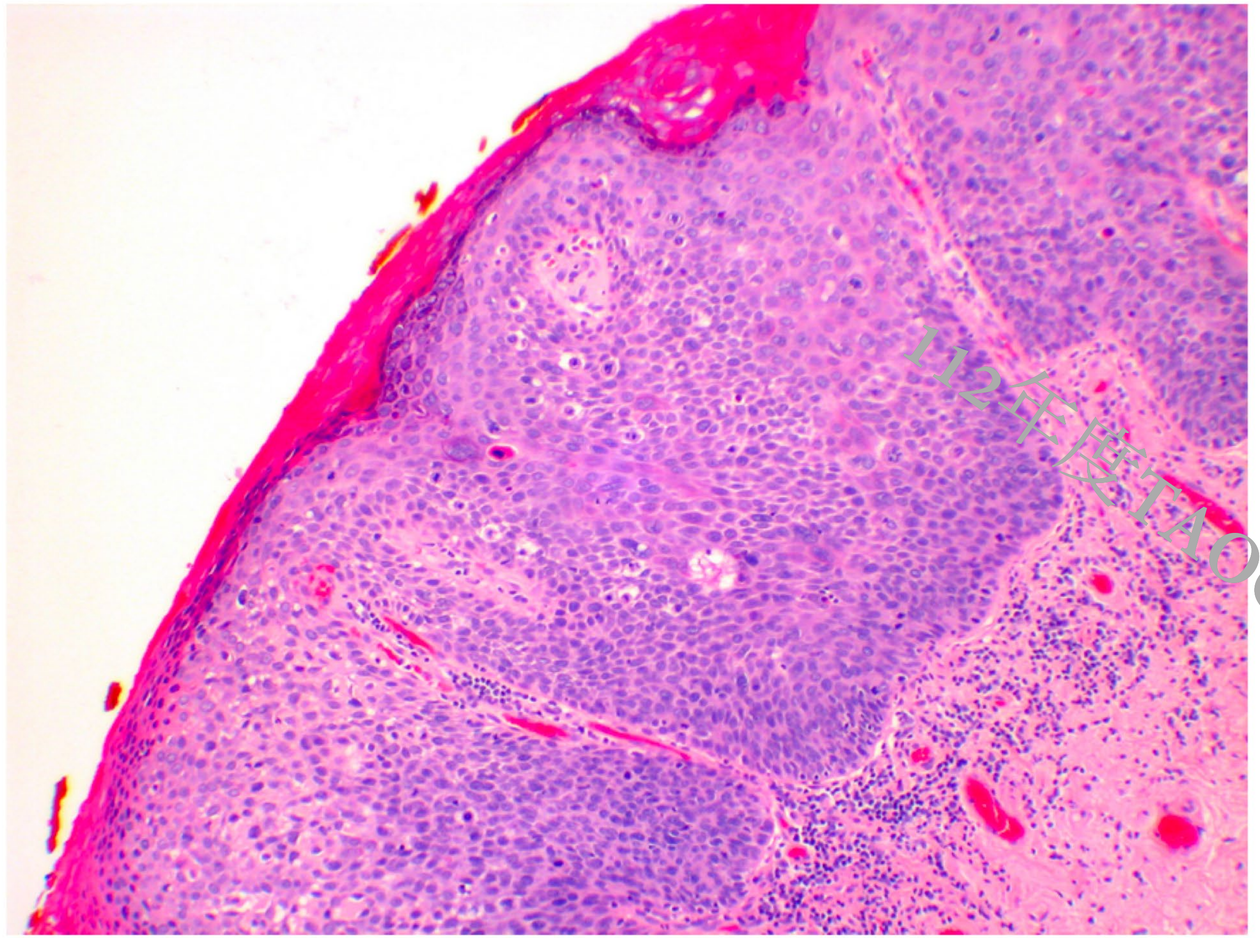

Figure 5 Vulvar high-grade squamous intraepithelial lesion; the lesion shows full thickness abnormality of maturation, and acanthosis (hematoxylin and eosin, x 10 magnification).

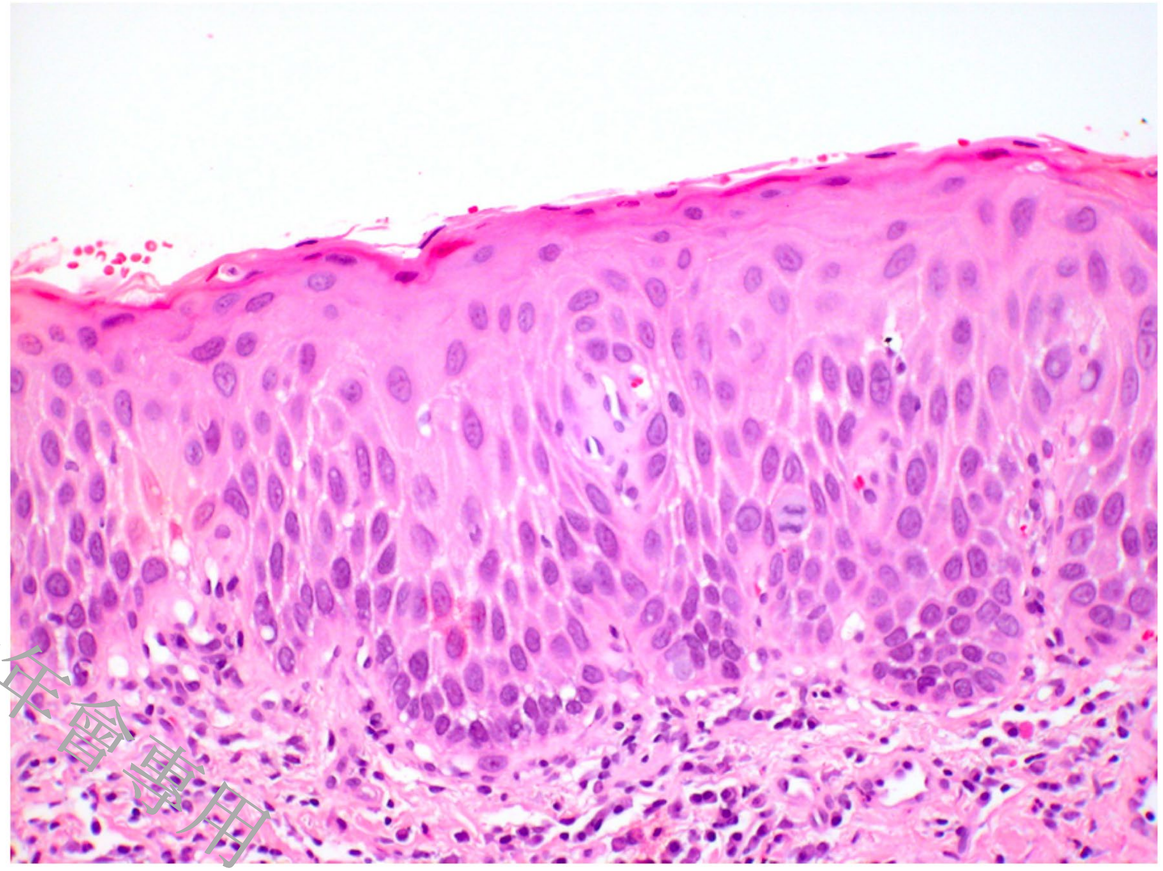

Figure 6 Differentiated vulvar intraepithelial neoplasia (dVIN). The histologic changes of dVIN are very subtle, and may be missed. Here there is basal atypia and acanthosis, but overall maturation is maintained. P53 and Ki-67 showed increased basal activity, and p16 was not block-positive, not shown (hematoxylin and eosin, x 20 magnification)

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Table 1 Immunohistochemistry in vulvar pre-invasive lesions

Lesion	Immunohistochemistry	Comment
VHSIL (VIN 2/3)	P16 block positivity, ki-67 extends above basal layers through entire epithelium	Ki-67 will stain above the basal layers in LSIL as well and cannot be used to distinguish LSIL from VHSIL. P16 is more useful in this distinction and can be occasionally positive in LSIL
dVIN	Aberrant p53 staining patterns. P16 not block positive. Ki-67 confined to basal layers	A panel of p53, p16, and ki-67 helpful in distinguishing VHSIL from dVIN
Vulvar Paget's disease	Cells contain mucine (PAS-D or alcian blue), mucicarmine, CK 7, GCDFP-15, GATA3[77]	Stains to distinguish secondary Paget's disease of urothelial (including uroplakin[200]) or anorectal origin (including CDX-2, CK20[201]) should be considered in appropriate cases
Melanoma in situ	Positivity with s100, Melan-A, and HMB 45[202]	A panel to distinguish melanoma in situ from Paget's disease can be helpful

dVIN, differentiated-type vulvar intraepithelial neoplasia; LSIL, low-grade squamous intraepithelial lesions; VHSIL, vulvar high-grade squamous intraepithelial lesions.

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VIN and Vulvar Cancer

- Potential for malignant transformation
  - 5.7% for VHSIL
  - 32.8% for dVIN
- Median progression time to cancer after VIN diagnosis
  - 4.1 years for VHSIL
  - 1.4 years for dVIN
- VHSIL
  - Underlying SCC in up to 20%
  - 15% of women treated surgically for VHSIL progression to SCC over a median of 71.5 months

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VIN and Anal SCC

- The HPV field infection

- VHSIL patients are at increased risk for anal squamous cell carcinoma and precursors

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Prevention of VHSIL

- HPV vaccine
  - VLSIL => the predominant HPV types are HPV 6 and 11
  - VHSIL => HPV 16
  - HPV-related vulvar cancer => HPV 16 and 33
  - 90% of related HPV genotypes are covered by Gardasil-9
- Treat lichen sclerosus
  - 3.5% risk of developing cancer
  - high-potency topical corticosteroid (e.g. clobetasol propionate ointment 0.05%, bid for 12wks, or qd for 4wks => then qod for 4wks => then biw for 4wks)

Int J Gynecol Cancer 2022;32:830-845. Am J Clin Dermatol 2013;14:27-47.

VIN diagnosis

- **Multiple biopsies**
  - **At multiple colors, at multi-centric lesions, at larger lesions**
- **Extent of biopsies**
  - **Hair-bearing skin**
    - **Biopsy width >= 4mm, depth >= 5mm**
  - **Hairless skin, mucosa**
    - **Biopsy depth >= 3mm**
  - **Ulcer, fissure**
    - **Biopsy include where there is intact epithelium**

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Colposcope (Vulvoscope) for VIN

- High false-positive rate
- dVIN => no acetowhite change
- VHSIL => acetowhite change
  - Maybe multi-centric
  - May also involve cervix, vagina, peri-anal

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Management of VIN

- dVIN => Excision (due to higher risk of progression)

- VHSIL
  - Excision (might impair function and anatomy)
  - Ablation (CO_2 laser, ABC, CUSA)
  - Medical (imiquimod, cidofovir)

- Before non-excisional management
  - Adequate representative biopsies to exclude malignancy

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Psychosexual impact of VIN Txs

- **Excision**
  - **Distorted anatomy**
  - **Impaired function**
- **Ablative or medical**
  - **Local irritation during treatment**

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Wide Local Excision for VIN

- Any size; remove the epidermis, dermis, and a small portion of underlying tissue
- Colposcopy and acetic acid to mark 1 cm margin
- Preserve as much normal anatomy as possible
- Depth of 3 mm or to the adipose tissue
- Incision with a scalpel to avoid coagulation artifact obscuring margin assessment
- Orient specimen for pathologic analysis

Te Linde's Operative Gynecology 2020 12th edi.

Vulvectomy

- **Simple vulvectomy (partial or total)**
  - **Skin grafting and constructive surgeon may be required**
- **Skinning vulvectomy**
  - **Rarely performed**
  - **Preserve the subcutaneous tissue**
  - **Split thickness skin graft**

UpToDate updated June 21, 2023

Positive margin after VIN excision

- Follow-up alone if no gross residual lesion
- Immediate re-excision not recommended

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CO2 Laser ablation for VIN

- Colposcopy with acetic acid
- Continuous setting of 10 W (but 5 W for atrophic tissue)
- Depth
  - 1-2 mm in non-hair-bearing areas
  - 3 mm in hair-bearing areas
- A margin of 1 cm
- Deep ablation => hypertrophic scar formation, loss of hair follicle

Te Linde's Operative Gynecology 2020 12th edi. UpToDate updated June 21, 2023.

Topical imiquimod versus surgery for vulvar intraepithelial neoplasia: a multicentre, randomised, phase 3, non-inferiority trial

Gerda Trutnovsky, Olaf Reich, Elmar A Joura, Magdalena Holter, Alexandra Ciresa-König, Andreas Widschwendter, Christian Schauer, Gerhard Bogner, Ziga Jan, Angelika Boandl, Martin S Kölbeis, Sigrid Regauer, Karl Tamussino

- Thin layer on the affected area
- Remain overnight without covering it
- Slowly escalating up to 3 times/week for 4-6 months
  - Once/week x 2, then twice/week x 2, then 3 times/week
  - Complete clinical response at 4 months => continue up to 6 months

Lancet 2022;399:1790-1798.

Imiquidmod vs. Surgery for VHSIL

- Complete clinical response at 6 months
  - Imiquimod group: 80%
  - Surgery group: 79%
- Complete clinical response at 12 months
  - Imiquimod group: 80%
  - Surgery group: 90%

Lancet 2022;399:1790-1798.

Imiquimod discontinued in 14%

	Imiquimod (n=46)	Surgery (n=52)
Number of clinical assessments	3·7 (0·9)	2·8 (1·3)
Symptoms assessed by study diary*		
Vulvar pruritus, NRS 0–10†	3·3 (1·3–4·7)	1·5 (0·4–2·8)
Days with pruritus	18·5 (8·0–30·5)	16·0 (11·0–27·0)
Vulvar pain, NRS 0–10†	3·2 (0–4·6)	3·0 (1·5–5·0)
Days with pain	13·5 (4·0–29·0)	21·0 (16·0–28·5)
Days with analgesic drug intake	1·5 (0–10·5)	3·5 (0–12·5)
Symptoms reported by the patient		
Fatigue		
None	16 (35%)	37 (71%)
Mild	7 (15%)	2 (4%)
Moderate	18 (39%)	12 (23%)
Severe	5 (11%)	1 (2%)
Headache		
None	18 (39%)	40 (77%)
Mild	10 (22%)	1 (2%)
Moderate	9 (20%)	7 (13%)
Severe	9 (20%)	4 (8%)
Muscle or joint pain		
None	30 (65%)	44 (85%)
Mild	5 (11%)	1 (2%)
Moderate	8 (17%)	7 (14%)
Severe	3 (7%)	NA

Symptoms reported by the investigator		
Erosion		
None	29 (63%)	38 (73%)
Grade 1 (mild)	12 (26%)	10 (19%)
Grade 2 (moderate)	5 (11%)	3 (6%)
Grade 3 (severe)	NA	1 (2%)
Erythema		
None	16 (35%)	28 (54%)
Grade 1 (mild)	17 (37%)	17 (33%)
Grade 2 (moderate)	9 (20%)	7 (14%)
Grade 3 (severe)	4 (9%)	NA

Lancet 2022;399:1790-1798.

Other Medical Managements for VIN

- 5% imiquimod cream vs. 1% cidofovir gel
  - Complete response => 46% vs. 46%
  - Recurrence among complete responders => 28.4% vs. 6%

- Photodynamic therapy
  - Topical photosensitizer 5-aminolevulinic acid + specific non-thermal light
  - Response rate 31.2~56%, recurrence rate 14.3~48%

- Therapeutic vaccine
  - Against HPV16 E6 E7 oncoprotein
  - Complete response in 47%, partial response in 32%

Int J Gynecol Cancer 2022;32:830-845.

VIN Recurrence after Treatment

- 6.8% at 6 months, 50% at 14 years
- 50% of recurrence occurred within 16.9 months => closer f/u during the first 2 years
- Immunosuppressant patients
  - More likely to recur
  - More likely to progression to cancer

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VIN Recurrence Rates by Treatments

- 0% by vulvectomy
- 15% by LEEP excision
- 9%~48.8% by cold knife wide local excision
- 34.9%~56% by laser ablation
- 48.3% by ABC (argon beam coagulation)
- 35% by CUSA (cavitational ultrasonic aspiration)
- 20% by imiquimod

Int J Gynecol Cancer 2022;32:830-845.

Follow-up for VIN

- On a long-term regular basis due to high recurrence rate
  - Pain, ulcer, etc => earlier evaluation
- Biopsy of any suspicious area
- Also check cervix, vagina, peri-anal
  - 4-25% of VIN patients also have lesion at other sites

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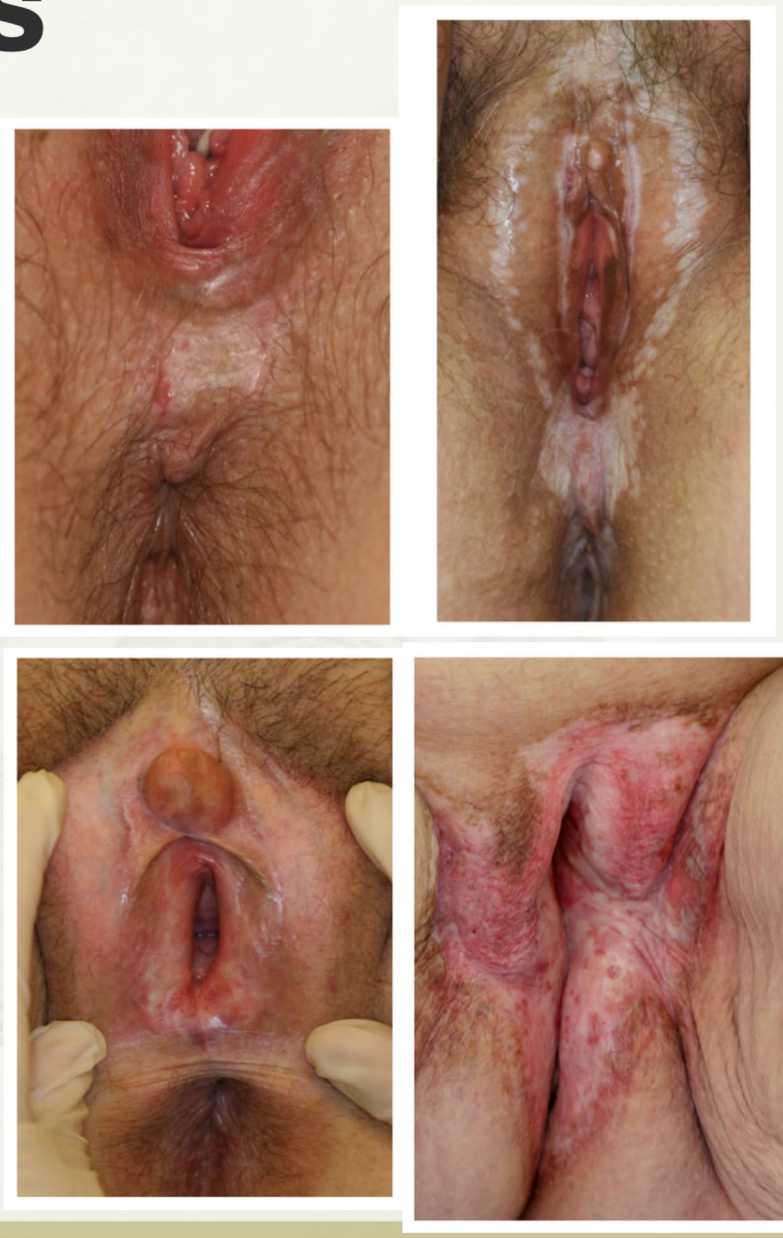
Lichen sclerosus

- Increased risk of vulvar SCC through a dVIN pathway
- Treatment => high-potency topical corticosteroid (e.g. clobetasol propionate ointment 0.05%)
  - bid for 12wks
  - or qd for 4wks => then qod for 4wks => then biw for 4wks



Am J Clin Dermatol 2013;14:27-47.

Vulvar Paget's Disease

- **Surgery is the cornerstone**
  - The disease extension is usually wider than what is evident
  - **2-cm margin** is considered necessary
  - In cases with underlying adenocarcinoma => radical surgery

- **Positive surgical margin** but without gross lesion => follow-up

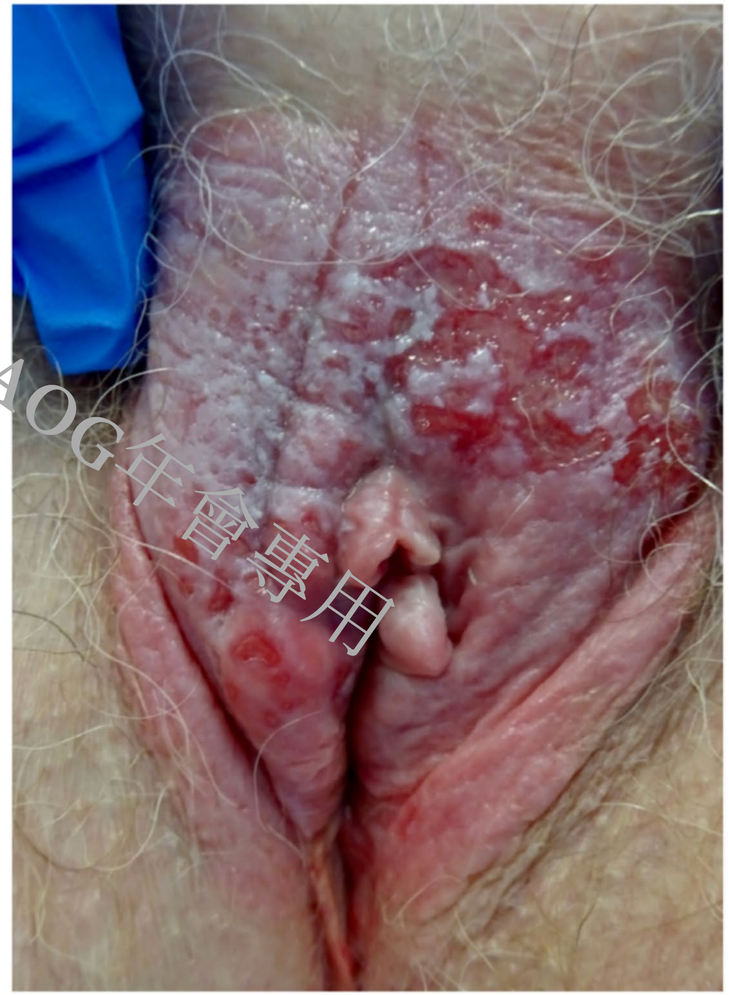


Figure 3 Vulvar Paget disease in situ; erythematous and white lesion involving whole vulva with superficial erosions.

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Imiquimod and Paget's Disease

- Recent studies favor an approach of imiquimod
  - Conservation of vulvar anatomy and function
  - 1~5 times a week; usually for 16 weeks
  - Complete response rates 22-90%

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Melanoma in situ

- **A wide local excision with 1-cm free margin**
- **No need for lymph node assessment**
- **5-year overall survival 74.4%**

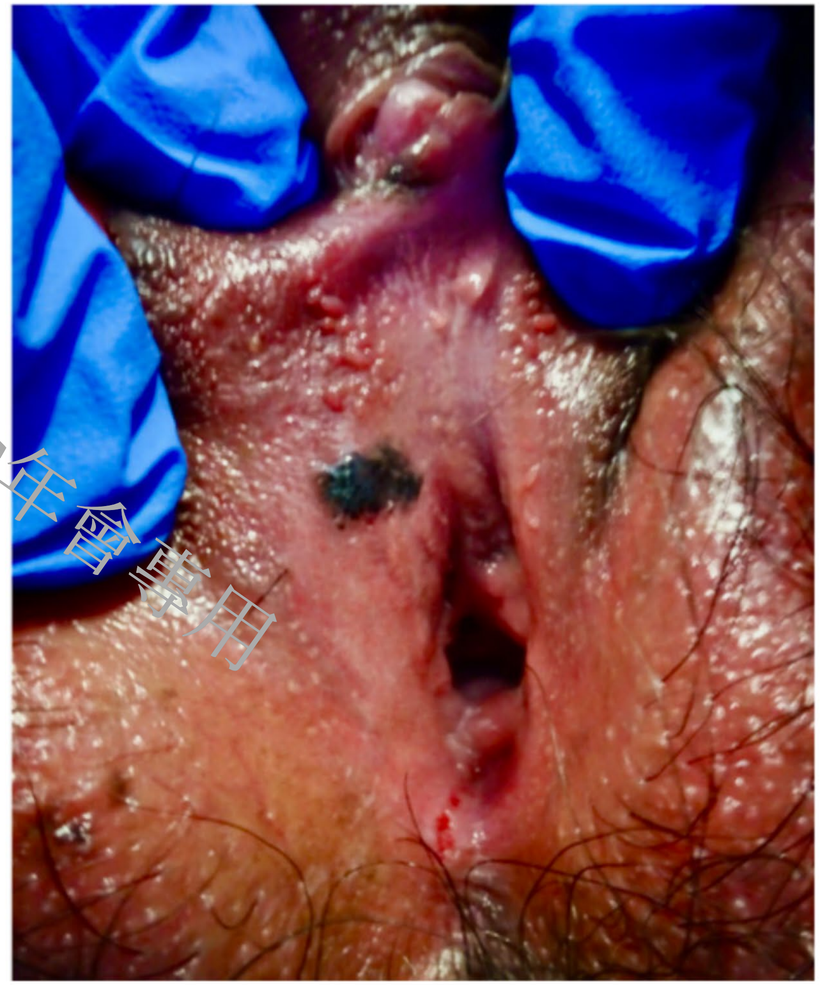

Figure 4 Melanoma in situ; black poorly marginated oval smooth lesion on the right superior vestibule.

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VaIN
(vaginal intraepithelial neoplasia)

Review

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The European Society of Gynaecological Oncology (ESGO), the International Society for the Study of Vulvovaginal Disease (ISSVD), the European College for the Study of Vulval Disease (ECSVD), and the European Federation for Colposcopy (EFC) consensus statement on the management of vaginal intraepithelial neoplasia

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VaIN Clinical Presentation

- **Absence of symptoms**
  - **often diagnosed by cytology +/- HPV test**
- **Rare**
  - **approximately 100 times less frequent than CIN**
  - **0.2-2 per 100,000 women/year**
  - **Incidence rate increased with advancing age**

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VaIN and Vaginal Cancer

- **Occult invasive** cancer
  - in 2.6-30% of VaIN
- **Progression rate** of VaIN towards vaginal cancer
  - in 1.4~20%
- Post-treatment progression to cancer
  - in 3.2~5.8% with mean intervals of 54.6~61 months

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VaIN Etiology

- **Usually HPV-related**
  - **VaIN 2/3 => High-risk types 16, 18, 33, 45, etc**
- **HPV-independent**
  - **vaginal adenosis might be the origin**

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Individuals at Higher Risk of VaIN

- **Most often associated with previous or current cervical neoplasia**
- **Immunosuppressed**
- **Previous irradiation for gynecologic malignancies**
- **Exposure to DES (diethylstilbestrol)**
- **Postmenopausal**

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Vaginal Microbiome

- The rate of a *Lactobacillus-depleted* microbiome
  - only 10% in healthy individuals
  - increases two-fold in patients with CIN1
  - increased three-fold in patients with CIN2/3
  - increased four-fold in patients with cervical cancer

- Patients with VaIN
  - increased abundance of several bacterial vaginosis-related bacteria (i.e., *Lactobacillus-depleted*)

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Prevention of VaIN

- HPV vaccination
- Avoid unsafe sex
- Cessation of cigarette smoking

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VaIN Diagnosis

- Histology obtained by biopsy is the gold standard for diagnosis before treatment
  - Sometimes difficult => mucosal lifting, shallow LEEP, etc
  - Risk of bleeding, accidental colpotomy, bowel injury, etc
- Vaginal cytology may be over-read due to vaginal atrophy
- Colposcopic assessment is not reliable enough

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Colposcopy for VaIN (1)

- **Less accurate than for cervix**
  - **The vaginal histopathology is frequently worse than what was anticipated by the colposcopic impressions**

- **Difficulties**
  - **Large field to be checked**
  - **Often multifocal lesions**
  - **Difficult to see all field at a right angle**
  - **Vaginal fold may hide lesions**
  - **Post-hysterectomy oversewn vaginal vault and "lateral dog ears"**

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Colposcopy for VaIN (2)

- To overcome vaginal fold ==> rotate the speculum with the blades opened

- Schiller's test (application of Lugol's iodine solution)
  - VaIN may only present as iodine-negative epithelium

  - Difficult interpretation in markedly atrophic mucosa => recommend topical estrogen for 3-4 weeks before the exam

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Colposcopy for VaIN (3)

- **Abnormal cervical cytology, but no abnormal cervical pathology**

  ==> colposcopy for vagina

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Table 1 2011 IFCPC clinical/colposcopic terminology of the vagina

General assessment	Adequate or inadequate for the reason (ie, inflammation, bleeding, scar) Transformation zone	
Normal colposcopic findings	Squamous epithelium: Mature Atrophic	
Abnormal colposcopic findings	General principles	Upper third/lower two-thirds, anterior/posterior/lateral (right or left)
	Grade 1 (minor)	Thin aceto-white epithelium, fine punctuation, fine mosaic
	Grade 2 (major)	Dense aceto-white epithelium, coarse punctuation, coarse mosaic
	Suspicious for invasion	Atypical vessels Additional signs: fragile vessels, irregular surface, exophytic lesion, necrosis, ulceration (necrotic), tumor/gross neoplasm
	Non-specific	Columnar epithelium (adenosis) lesion staining by Lugol's solution (Schiller's test): stained/non-stained, leukoplakia
Miscellaneous findings		Erosion (traumatic), condyloma, polyp, cyst, endometriosis, inflammation, vaginal stenosis, congenital transformation zone

*Adapted from Bornstein et al.[6]
IFCPC, International Federation for Cervical Pathology and Colposcopy.

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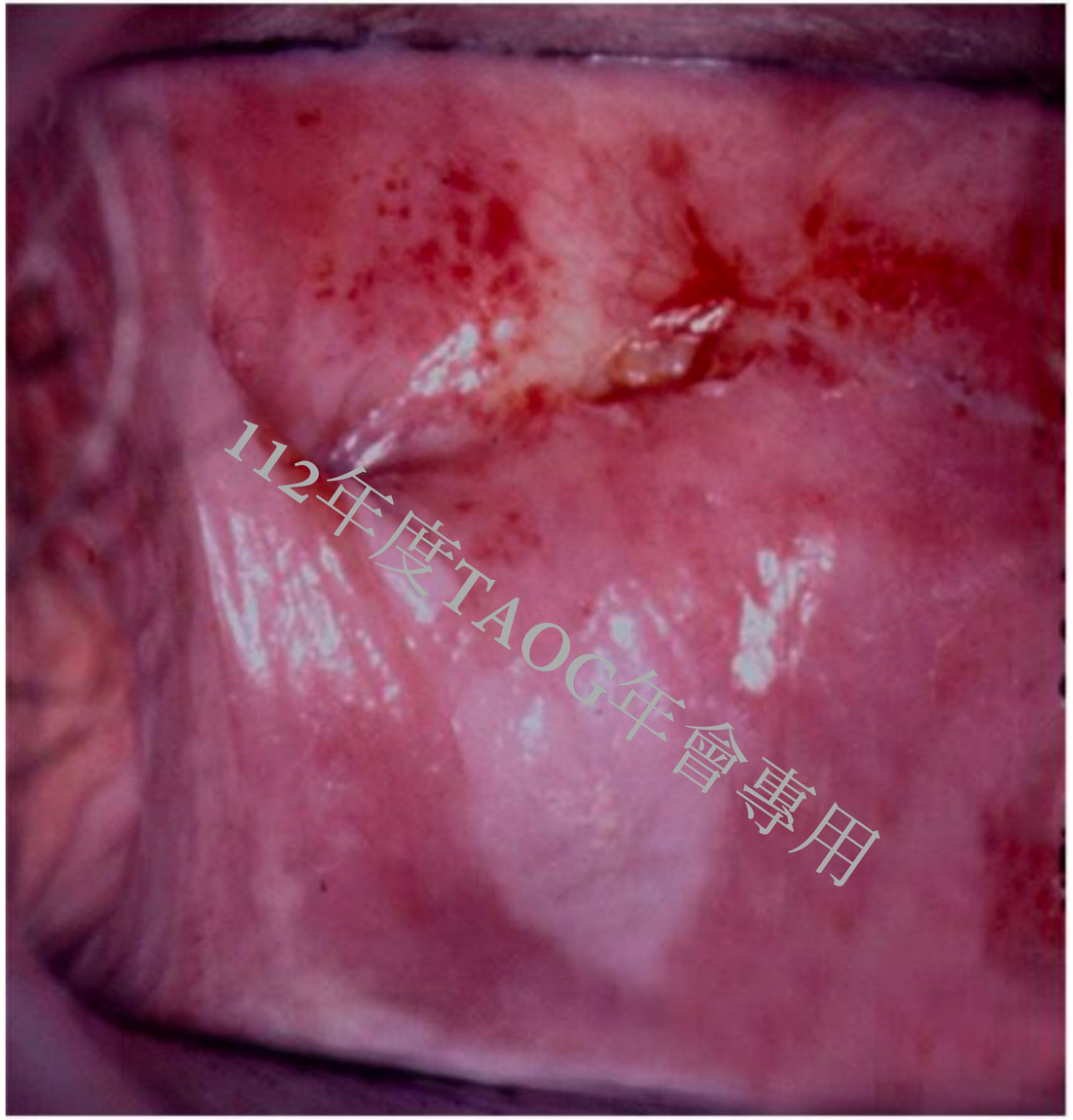

Figure 1 VaIN 3 (vaginal HSIL) on the posterior vaginal wall and between folds of the vaginal cuff. HSIL, high-grade squamous intraepithelial lesions; VaIN, vaginal intraepithelial neoplasia.

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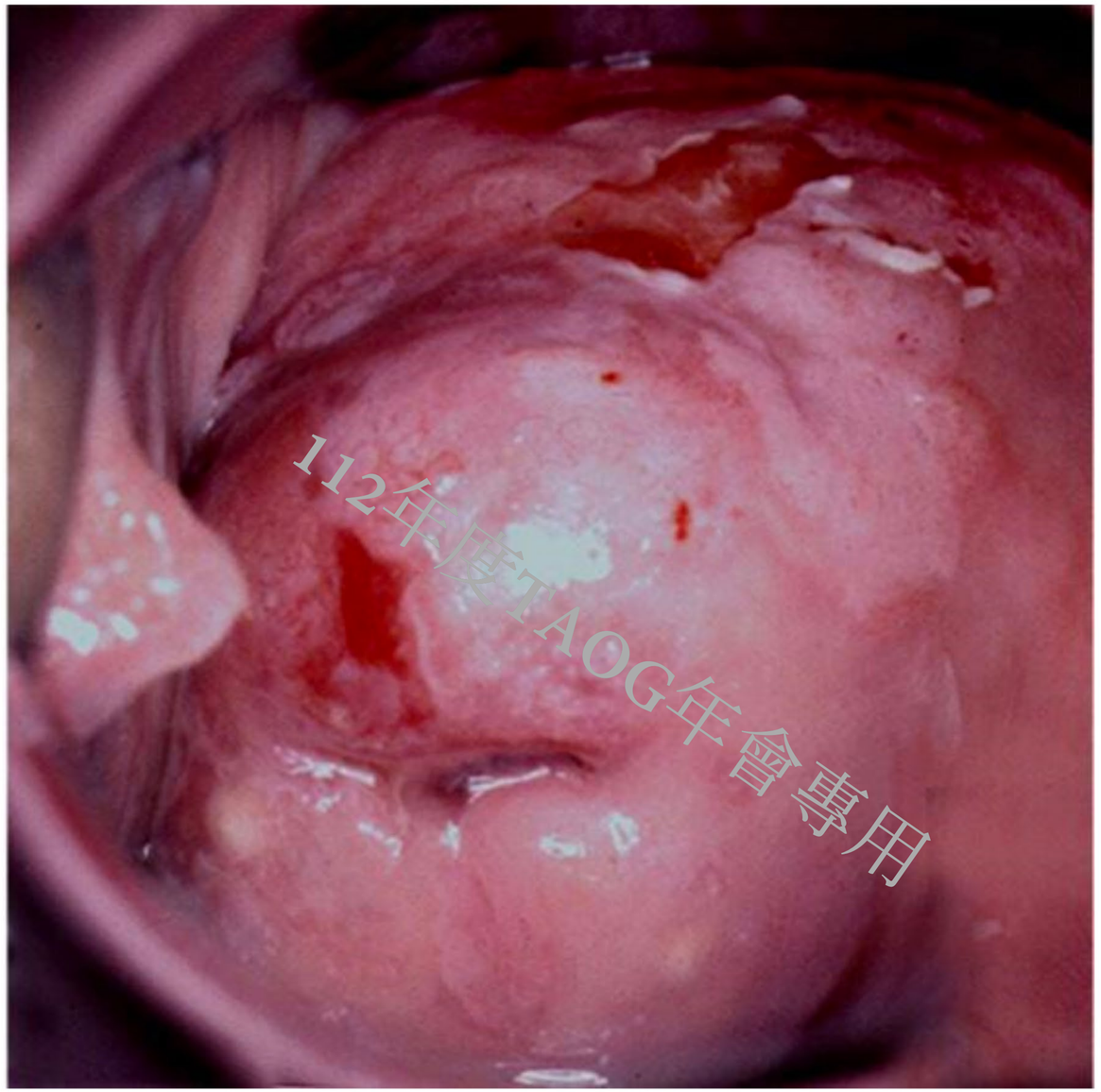

Figure 2 CIN3 (cervical HSIL) extending to anterior vaginal wall (VaIN 3/vaginal HSIL). CIN, cervical intraepithelial neoplasia; HSIL, high-grade squamous intraepithelial lesions; VaIN, vaginal intraepithelial neoplasia.

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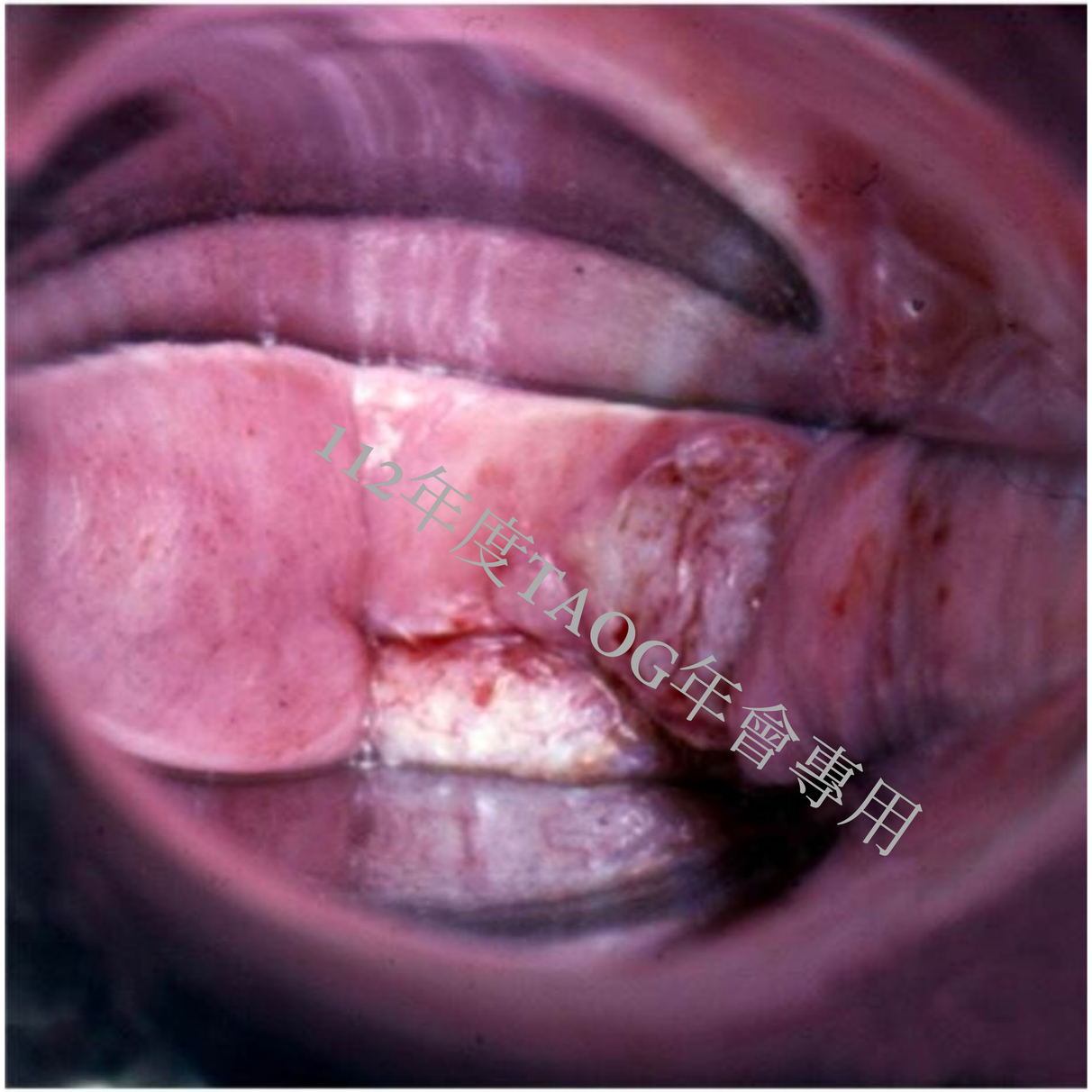

Figure 3 Invasive cancer at vaginal cuff after hysterectomy for cervical HSIL. HSIL, high-grade squamous intraepithelial lesions.

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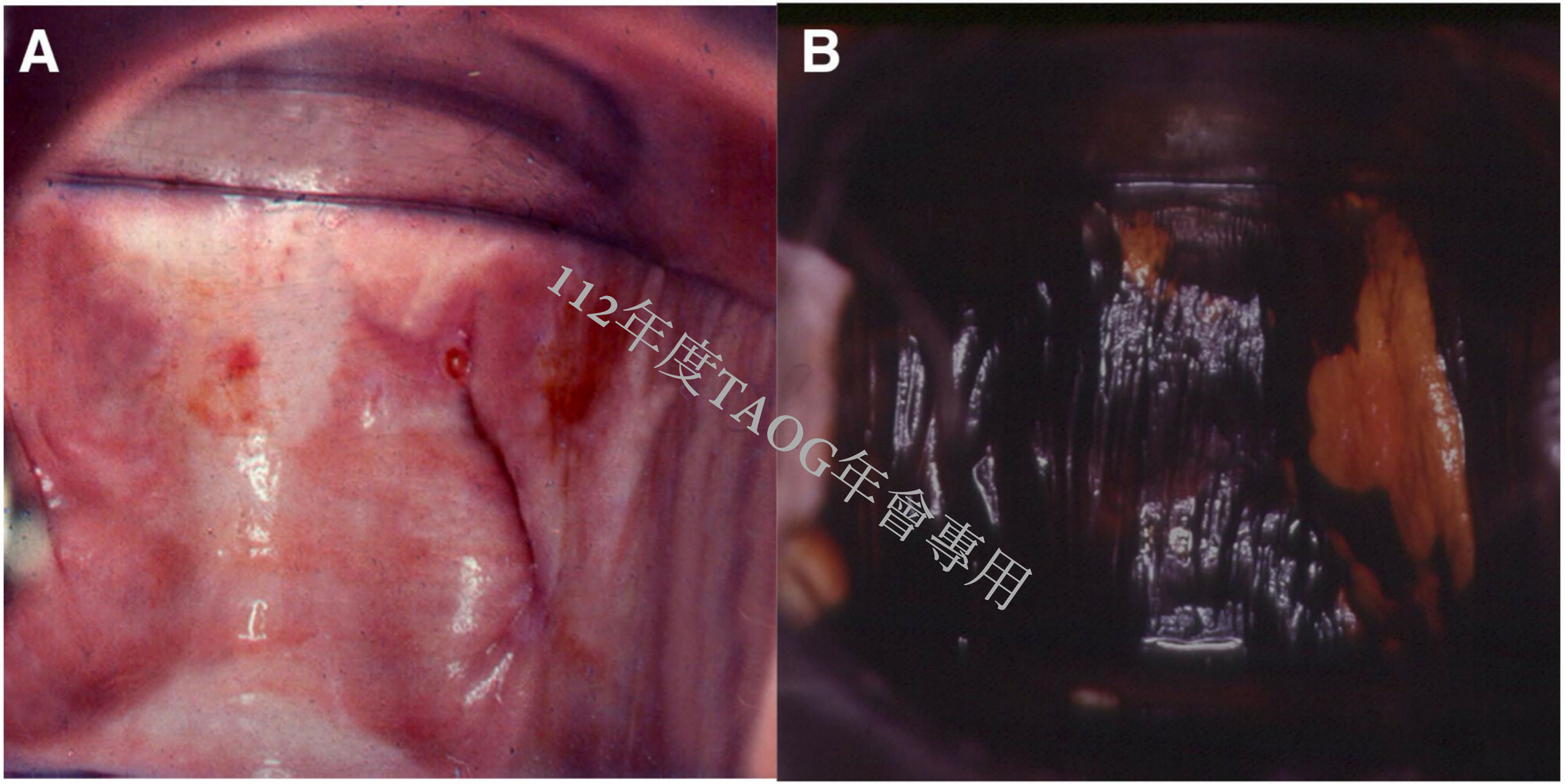

Figure 4 VaIN 3 (vaginal HSIL) (A) after the application of acetic acid, and (B) after staining with Lugol's solution. HSIL, high-grade squamous intraepithelial lesions; VaIN, vaginal intraepithelial neoplasia.

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Management of VaIN 1

- Spontaneously regressed in 48.8-88%
- Treatment does not lead to better clinical outcome
- VaIN 1 is safely managed by observation alone

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Management of Vaginal HSIL (VaIN 2/3)

- **Should be treated**
  - **Though spontaneous regression in 46.2%**
  - **If not treated => risk of progression to cancer**

- **Treatment for vaginal HSIL**
  - **Excisional**
  - **Ablative**
  - **Medical**
  - **Radiotherapy**

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Psychosexual impact of VaIN Txs

- **Excisional** treatments => Higher risks of sexual dysfunction, persistent pain, scarring
- Topical treatments => Local burning/soreness => may interfere with usual activity
- **Radiotherapy** => vaginal narrowing, ovarian injury
- Vaginal dyspareunia => higher incidence of **depression**, anxiety

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Excisions for VaIN

- Excisional methods are preferred because they provide a specimen for a complete histopathological diagnosis
- Pre-excisional colposcopy to assess the extent of VaIN
- Excisional
  - Cold-knife
  - LEEP (loop electrosurgical excision procedure)
  - CO2 laser excision
  - CUSA (cavitational ultrasonic surgical aspiration)

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Wide Local Excision for VaIN

- **Lowest** risk of recurrence (success in 66-81%)
- **Limited** applicability because VaIN is frequently multifocal
- Residual disease rate after excision: 8.6-18.9%
- “vaginal stripping”
  - Combine sharp and blunt dissection
  - En bloc removal of the involved area, hemostasis by cauterization
  - May result in shortening or stenosis of vagina

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Vaginectomy (partial or total)

- **Upper partial vaginectomy**
  - Considered the treatment of choice in vaginal HSIL involving **vaginal cuff scar**
  - Cure rate 84-88%

- **Total vaginectomy**
  - Not advisable (because vaginal intercourse impossible)
  - Must be reserved for **exceptional** cases

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Vaginectomy (partial or total)

- Risk of bleeding, infection, scarring, stenosis, dyspareunia
  - At risk for injury: rectum, bladder, urethra
- Most can be accomplished transvaginally
- Some may require transperitoneal (laparoscopy or laparotomy)
  - Especially in cases of VaIN in vaginal vault rescesses after hysterectomy
- Colposcopy with acetic acid
- Goal
  - A margin of 1 cm
  - Excision of the full thickness of the epithelium
- Transvaginal approach
  - Consider hydrodissection (steric saline +/- local anesthetic +/- vasopressin)
- Transperitoneal approach
  - Vaginal manipulator with gauze on a ring forceps to facilitate dissection

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Other Excisions for VaIN (1)

- **CO2 Laser excision**
  - **Performed only by expert specialist**
  - **Overall complication rate: 7.8% (mostly vaginal bleeding)**
  - **Major complication rate: 0.8% (vaginal vault perforation)**
  - **Laser skinny vaginectomy**
  - **Excise in one piece with a depth of 2-3mm**
  - **Cure rate 87%**
  - **Moderate vaginal shortening in 6%, vaginal stenosis in 6%**

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Other Excisions for VaIN (2)

- **CUSA (Cavitational ultrasonic surgical aspiration)**
  - **Exact removal of epidermal or mucosal lesions without thermal or mechanical damage to the surrounding structures or underlying stroma**
  - **Cure rate 80.4% at 4.5 years**
  - **No reports of adverse events**

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Other Excisions for VaIN (3)

- Loop electrosurgical excision procedure
  - Not a treatment of choice
  - Difficult in controlling depth of excision
  - Deep necrosis reported

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Non-Excisional Management for VaIN

- Need adequate biopsies before Mx to decrease the risk of missing invasive cancer

- Inappropriate if
  - Buried lesion in post-hysterectomy vaginal scar can't be approached by non-excisional Mx
  - Abnormal epithelium can't be entirely visualized
  - Malignancy suspected

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CO2 Laser Vaporization for VaIN

- Epithelial destruction to a depth of 1~1.5 mm
- Full-thickness treatment: a depth of 3 mm
- Goal: a margin of 1 cm from the edges of the visible lesion
- Continuous setting of 10 W (less W for atrophic area)
- To avoid deep penetration
  - Larger spot size to avoid pinpoint settings
  - Superpulse mode
- Outcome
  - Relapse in 57%; 79.2% required multiple sessions, cure rate 69~86%

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Other Ablative Tx for VaIN

- Electrofuguration
  - Less precise than laser in depth
  - Primary remission rate of 25~87.62%

- Photodynamic therapy (PDT)
  - Photosensitizer ALA (5-aminolevulinic acid)
  - Activation by light at a specific wavelength
  - Maintain anatomical integrity
  - Complete remission rates 88.64~90.9%

- Plasma energy ablation
  - Reduce the risk of fire and retinal injury by laser
  - Recurrence rate (33.3%) similar to laser

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Imiquimod for VaIN

- At least 3 times a week, for 8 weeks
  - complete response rate 76%
  - overall response rate 89%

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HPV Clearance Rates after VaIN Tx

- Imiquimod => 63% cleared
- ALA-PDT => 38.1~61% cleared
- Laser ablation => 11% cleared
- Observation => 17.1% cleared

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Other Medical Tx for VaIN

- 5-Fluorouracil (5-FU)
  - Cure rates 46~86%
  - Highly uncomfortable side effects (16%): local irritation, ulcer, dyspareunia, discharge, etc

- Intravaginal estrogen therapy
  - Response rates 71.4~90%

Int J Gynecol Cancer 2023;33:446-461. J Low Genit Tract Dis 2014;18:115-121.

Radiotherapy for VaIN

- **Brachytherapy**
  - Effective with disease-free survival rate 86~93%
  - Last resort for repetitive treatment failure & surgical treatment not feasible
  - Vaginal fibrosis and stenosis, dyspareunia
  - Compromise the possibility of secondary surgery
  - Make subsequent colposcopy difficult

- **Before brachytherapy => first exclude cancer**
  - Multiple biopsies, pelvic MRI
  - If vaginal cancer diagnosed => chemoradiation + brachytherapy

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VaIN Follow-Up

- Similar to CIN f/u

- VaIN 1
  - [cytology+HPV co-testing at 12 months] x 1, or [cytology at 12 months] x 2
  - If all normal => stop follow-up

- VaIN 2/3 after treatment
  - [cytology + HPV co-testing at 6 months] x 2
  - If all normal => [annual cytology] or [q2-3yr co-testing]
  - Vulvar and anal checkup should be considered

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Recurrence Rates of VaIN Tx

- Medical => 61~62.5%
- Excision => 7.2~32.7%
- Ablative => 18.6~33%
- Laser ablation => 18.6~34%
- CUSA => 19.6~25%
- Radiotherapy => 0~13.6%

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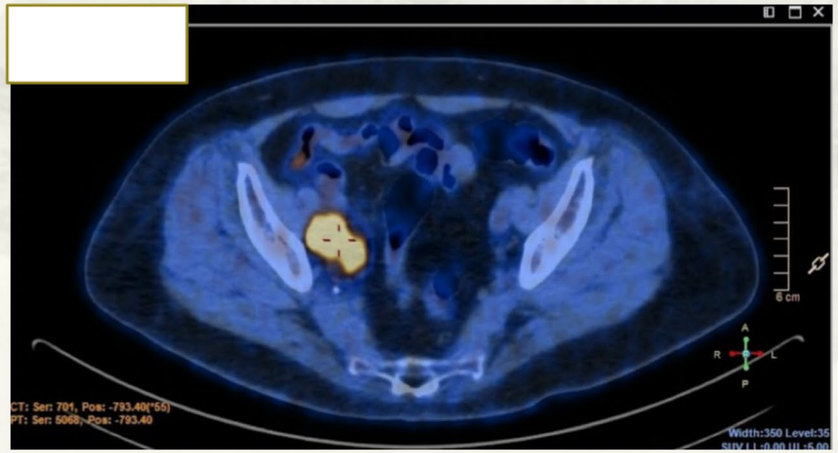
Case Sharing

- 71y/o, history of hysterectomy for stage IA1 cx ca
- Told to have Pap VaIN3 (but only chronic inflammation by biopsy)
- Told to have pelvic lymphadenopathy and elevated SCC (9.7 ng/ml) and CEA (6.2 ng/ml)
- Colposcopy => only mild erosion at right angle of vaginal stump (failed Schiller's test due to atrophic vaginal mucosa)



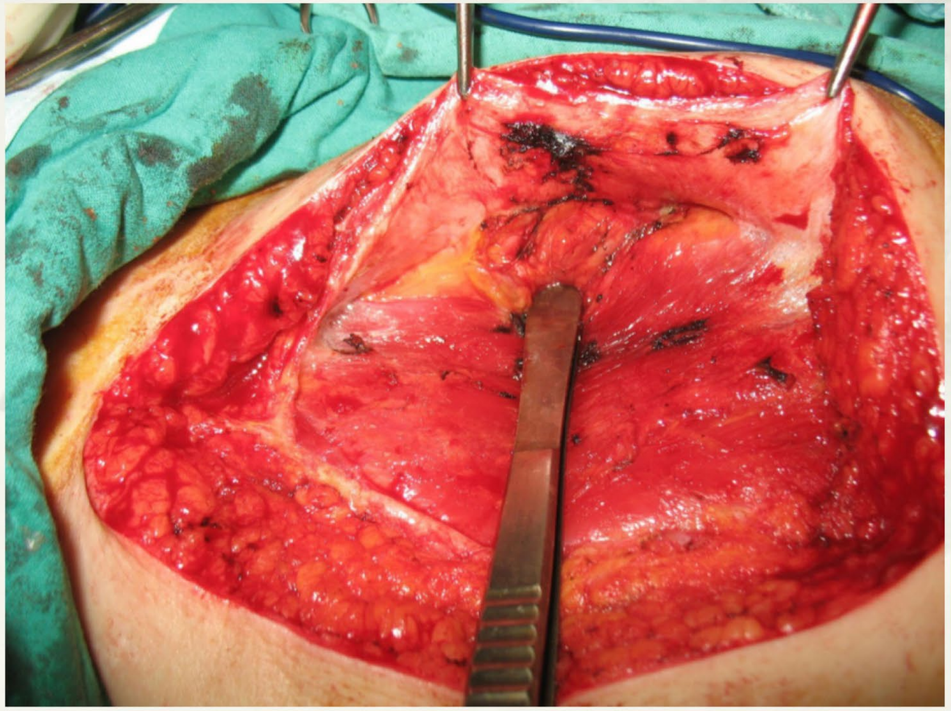
Impression:

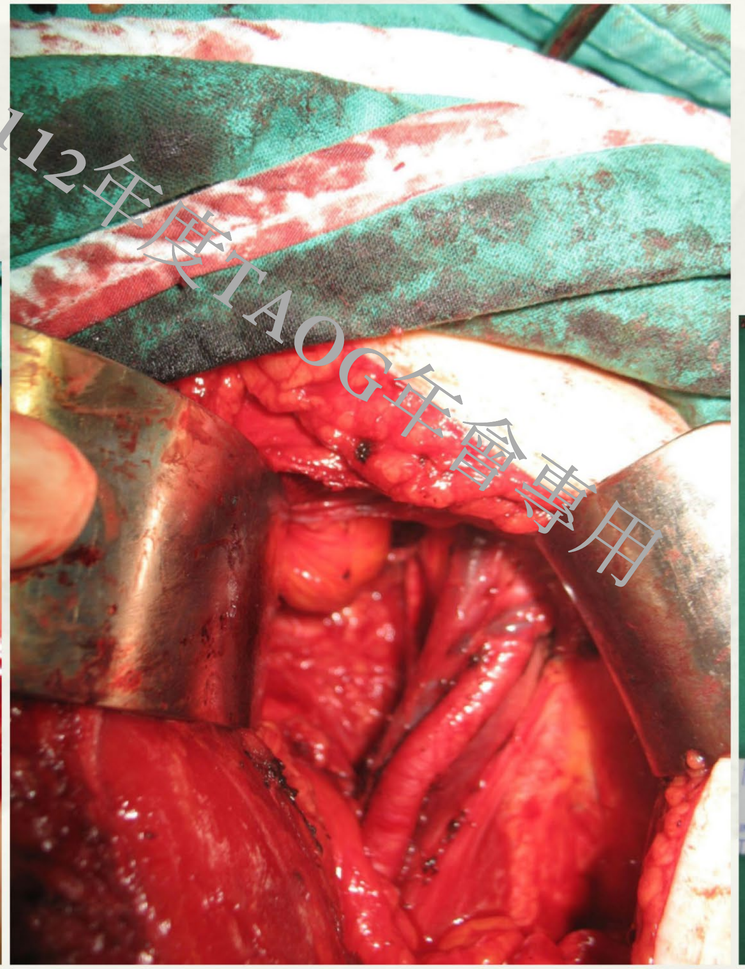
- VaIN3 with occult vaginal cancer and metastatic lymphadenopathy

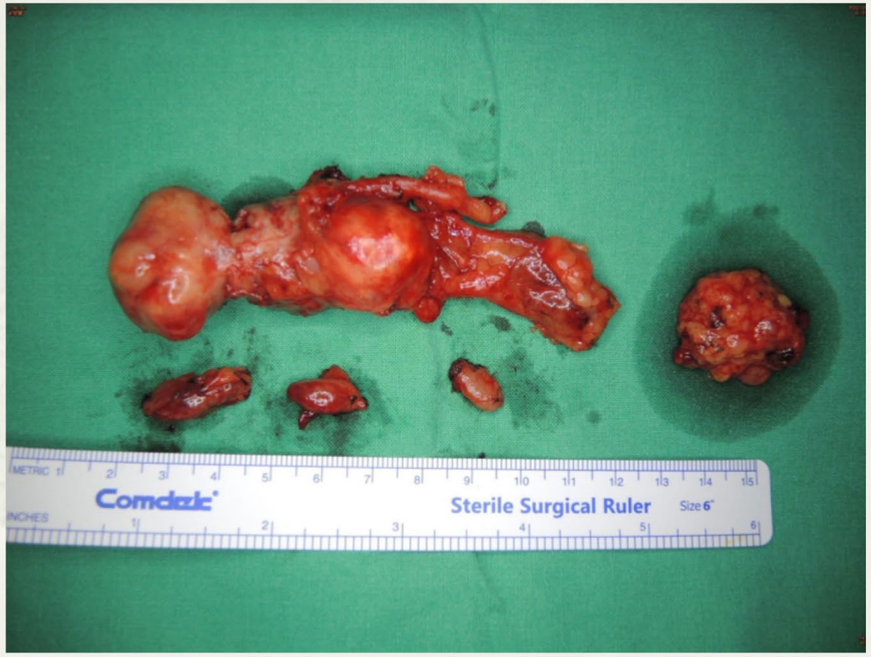
Plan:

- Arrange transvaginal upper vaginectomy + extraperitoneal lymphadenectomy
- CCRT if vaginal cancer confirmed

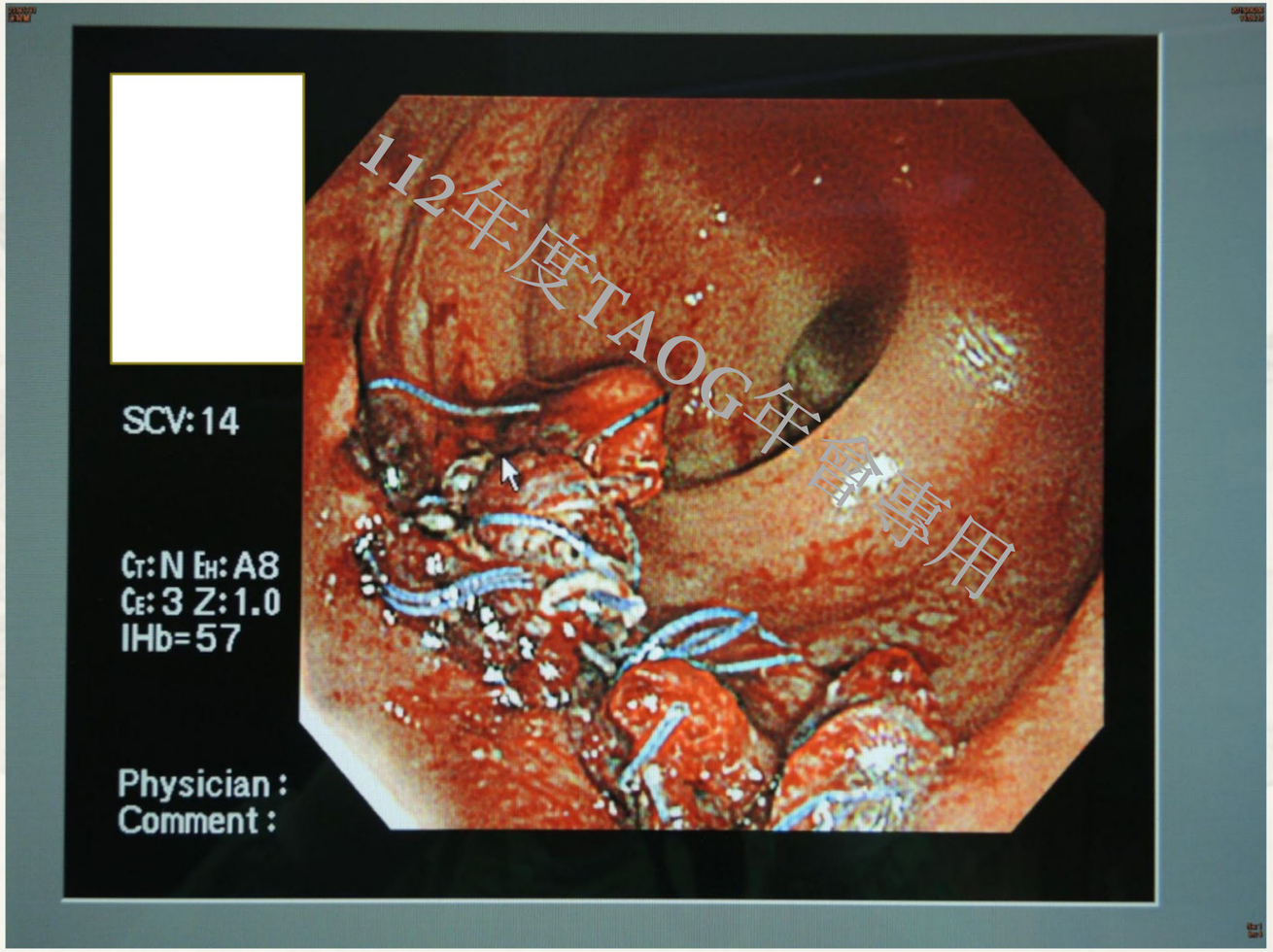
Case Sharing:
Extraperitoneal Right Pelvic Lymphadenectomy







Case Sharing:
Rectal Injury during Transvaginal Excision



Take-Home Message:

Psychosexual issue must be considered.
Adequate biopsies before non-excisional Tx.

- **Pre-invasive vulvar lesion**
  - VHSIL patients need multi-area colposcopy (cervix, vagina) and inspection (vulvar, per-anal, anal), and need life-long surveillance
  - Imiquimod can be used to preserve normal vulvar anatomy in VHSIL or Paget's disease
  - dVIN needs surgical excision
  - Topical high-potency corticosteroids (e.g., clobetasol) for dVIN-associated lichen sclerosus
  - F/U alone for positive surgical margin but no gross residual lesion in VIN or Paget's disease
- **Pre-invasive vaginal lesion**
  - Follow-up alone for VaIN1, while VaIN2 and VaIN3 need treatment
  - Surgical excision if invasion can't be excluded, or VaIN involving post-hysterectomy vaginal scar
  - Risk and complication of surgical excision
  - Topical agent (imiquimod best) for persistent multi-focal VaIN when surgery not OK
  - Brachytherapy reserved for poor surgical candidates with persistent multi-focal VaIN
  - Post-treatment follow-up mainly with cytology + HPV co-testing