

|     |                                                    |    |
|-----|----------------------------------------------------|----|
| 1   | Controversies in neck management<br>by Anil D'cruz | 1  |
| 2.  | Management of MVO neck                             | 9  |
| 3.  | Ca endometrium                                     | 14 |
| 4.  | Imaging of neck (video)                            | 32 |
| 5   | Ca Ovary                                           | 37 |
| 6   | Ca Cervix                                          | 58 |
| 7   | Classification of hysterectomy                     | 74 |
| 8   | Paper analysis of Gyn Onco                         | 79 |
| 9.  | Ca Penis [NCCN]                                    |    |
| 10. | IASO Webinar (tongue)                              |    |

## Current Controversies in Neck Management

- Dr Arif D'Souza

- \* Cervical mets is a single most important prognostic factor. 50% reduction in survival with positive lymph node (minimum Stage III).
- \* Neck dissection to be done if risk of nodal spread is  $> 20\%$ .

→ ASCO Clinical guidelines

- Controversies :-
- 1) No neck
  - 2) Extent of neck dissection / Role of SNB
  - 3) Neck in CRT setting
  - 4) Adjuvant treatment / imaging etc.

No neck Randomized controlled trial in 2004

T<sub>1</sub> / T<sub>2</sub> N<sub>0</sub> (n = 1281) screened

↓  
n = 596 randomized

↓  
n = 500 analyzed

243 INT

253 TND

81 relapses

146 relapses

DFS - 69.5%

45.9% [Significant]



12.5% diff. in OS bet<sup>n</sup> END & ND (80% vs 67.5%)  
25% diff in DFS too.

8 Meta-analysis done - All show improved DFS, OS

ASCO guidelines:- For cT<sub>2</sub>-T<sub>4</sub> N<sub>0</sub>, an ipsilateral  
Elective neck dissection should be performed.

For cT<sub>1</sub> N<sub>0</sub> ipsilateral END should be performed.  
Alternatively, close surveillance may be done with  
high quality USG.

SEND study

T<sub>1</sub>/T<sub>2</sub> N<sub>0</sub> with or without END  
(lesion upto 3cm)

250 randomized.

Occult neck disease in 19.1% (T<sub>1</sub>)

34.7% (T<sub>2</sub>)

54% intention to treat Hazard ratios were

OS HR = 0.71 (P=0.18)

DFS HR 0.66 (P=0.04)

Benefit seen in T<sub>1</sub> as well.

\*  $N_0$  = CT and/or MRI ( $< 1.1$  cm or upto  $1.5$  cm in level II & no atypical features)  $\pm$  US-FNA/C. 3

SENT trial  $\rightarrow$  14 European centres, 415 patients  
T<sub>1</sub>/T<sub>2</sub> N<sub>0</sub>

Extensive radiological criteria for N<sub>0</sub>\*

SNB  $\rightarrow$  3.2 nodes removed per patient

Positive SN  $\sim$  23% patients.

85% with positive SLN had no further metastatic nodes  
Contralateral node in 12.5% . the SLN significantly affected OS.

Could neck dissection be avoided in thinner ~~lesions~~ <sup>lesions</sup>?

|                      |                          |
|----------------------|--------------------------|
| Size of lesion (DOI) | Risk of mets (John Shah) |
| $< 2$ mm             | 7% (low)                 |
| 3-8 mm               | 26%                      |
| $> 8$ mm             | 41%                      |

Maybe avoided in DOI  $< 3$  mm. How to evaluate depth?

Correlation bet<sup>n</sup> clinical & MRI assessment of DOI in  
on tongue - H A Alsaffar et al.

Result  $\rightarrow$  strong correlation bet<sup>n</sup> pathological, radiological  
& clinical measurement in deep tumours ( $> 5$  mm).  
In superficial tumours, low correlation.

### Observational Studies for Wait & Watch

- 1) Van Breckel et al (wait & watch) - US guided FNA/C - 18% incidence of neck nodes.  
- 9/12 pt had EUS, 4 died
- 2) Flach et al (wait & scan) - US guided FNA/C - 27.8% incidence.  
- 89% pt needed MND



Conclusion - END should be standard of care for early stage node negative oral cancers.

- 1 death prevented for every 8 patients treated w/ END (OS difference of 12.5% in Anil D'Cruz Paper)
- 1 recurrence prevented for every 4 patients treated (DFS diff. of 23.6% in Anil D'Cruz Paper)

Cost effectiveness of END using a Markov model

End result - ↓ overall costs by 600 US\$ over lifetime of a pt.

- Improved effectiveness by 0.42 QALY

Benefit of END is likely by negation of costs associated with Salvage etc.

### Role of Sentinel node biopsy

Pooled Sensitivity - 95%

Pooled NPV - 96%

RCT of 16 institutions in Japan - 271 patients

134  
(SWB)

137  
(neck dissection)



Syng OS - 89% SNB  
- 86% END

34n RFS - 80% SNB  
81% ND

\* SLB vs END for stage I & II anal cancers  
- John (names et al.)

Retrospective cohort study

Group 1 240 only  
Underwent END SNB.

\* Completion neck dissection avoided in 63.8% pt undergoing SNB.

SNB has reduced perioperative morbidity

Similar OS with END.

Disadvantages of SNB - steep learning curve

- More cost
- Cumbersome
- 2 step procedure.
- Prevention of morbidity is not that high, as morbidity in MND is minimal.

## Extent of neck dissection

SOHND vs MND for No Oral SCC - Chien Bin Guo et al

- Similar DFS, OS & disease specific survival
- Fewer complications in SOHND

Prospective study of 583 neck dissections in oral cancer  
- Arif D'Cruz et al

Each level sent separately.

357 unilateral & 113 bilateral necks.

91% mets seen in level I-III

level IV → 4.8%

V → 3.3%

No skip mets at IV & V in absence of level I-III.

Skin mets at level III is 17% for tongue cancers.

Factors predicting level IV disease - IIA & IIB positive nodes

" " IIB disease → IIA positive.

- \* From renewed literature, SOHND is a valid option in patients with  $< N_1$  & selected  $< N_2$  disease (non fixed nodes, absence of palpable mets at level IV or V or  $> 3$  cm multiple nodes)



## Contralateral Neck

ASCO Guidelines  $\rightarrow$  Tumor of Oral tongue and/or FOM that is T3/T4 or approaches midline, do a contralateral neck dissection.

Ans

Ipsilateral neck nodal status as a predictor of contralateral nodal mets in La tongue crossing midline - Arif D'Cruz et al.

273 patients underwent B/L ND for La tongue crossing midline.

Contralateral nodal mets in 29%. But out of these, 97% had ipsilateral nodal mets.

So, in the absence of ipsilateral nodal mets, there is very low risk of contralateral node.

✓ Minimum no. of nodes  $\rightarrow$  18 (ASCO guideline).

## Organ Preservation - Management of N2/N3 neck.

Earlier, Planned neck dissection was done 8 weeks after completion of CT-RT. But it increased morbidity, and with advent of better imaging, it was unnecessary in pT c complete response.

PET CT surveillance vs neck dissection in  
advanced head & neck cancer  
(PET NECK trial).

Results - OS was equivalent in both arms.

(85% in Surveillance vs 81.5% in surgery)

PET CT was more cost effective !!!

Equivocal scan? - Structural node, but no uptake,  
or uptake but no node.

Almost 50% risk of neck nodal mets.

PET neck trial had ~ 85% patients with Ca Oropharynx  
~ 78% Pt had N2a or N2b disease.  
(17%) (61%)

lessen Patients = N2c (N3).

For complete responders, recurrence rates are < 5%.

NPV of PETCT is 95%. @

- Operating on a large node pre operatively results in ↑ morbidity.
- Tolerance to adjuvant CRT is poor
- Salvage surgery not found to be inferior to upfront surgery

~~Risks~~



## Management of Muo neck

\* Approx 10% Patients with Metastatic SCC do not have a clinically identifiable primary.

### \* NCCN guidelines

- Complete examination
- Scopy
- FNA / biopsy

↓  
SCC / Adenocarc / Anaplastic / undiff. epithelial tumor



- CT/MRI neck & thorax
- FDG PET if indicated
- HPV, EBV testing for squamous cell or undifferentiated histology
- Dental evaluation
- Nutrition, Smoking cessation



If primary not found



level I, II, III,  
upper level IV

level IV, lower level IV

(1)

(2)

(1) → EUA

→ Biopsy from areas of clinical concern

→ Tonsillectomy

→ DL scopy

Primary not found

Primary found

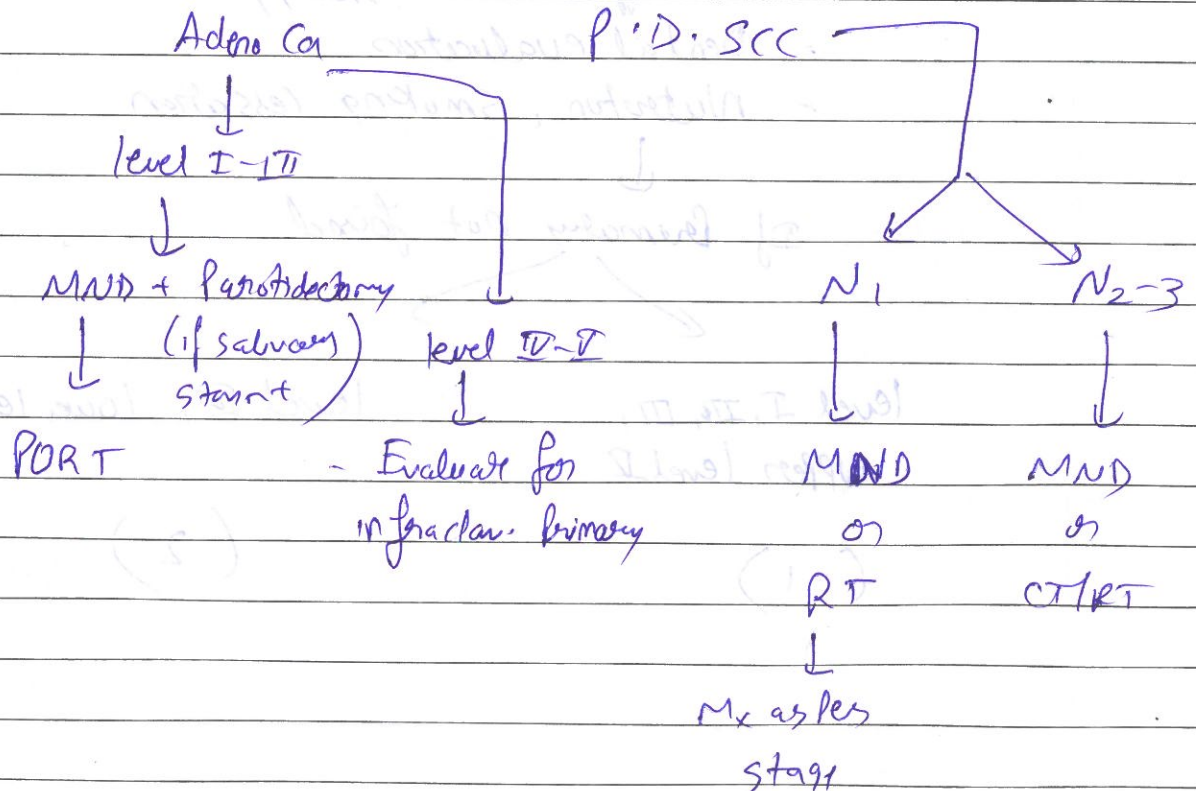
As per guidelines

(2) → EUA

→ DL scopy, UGI scopy, Bronchoscopy

→ Chest + Abdo + Pelvis / PET CT

Primary not found





\* Cystic nodal mets are seen in pt c Primary  
 SCC of tonsil & Palillary Ca thyroid

a For adeno ca lower neck, do thyroglobulin / calcitonin  
 stain for Ca thyroid.

After completion of CT-RS



Clinical assessment at 6 weeks



Disease Progression

Response (+)

Assess by CT/MRI



Unresectable

Resectable

Palate

Resect



PET-CT -ve

PET CT +ve

PET +ve

PET -ve

↓  
observe

↓  
 MND

↓  
 CT -ve  
 ↓  
 Observe on  
 Neck dissection

↓  
 CT +ve  
 ↓

- SND

- Excision B<sub>2</sub> &  
 MND

## Imaging of neck (Points from Myers)

\* Imaging modalities fail to detect mets in 14-28% cases.

\* Size is a radiological criterion used to detect nodal mets. Size  $>1.5$  cm in levels I & II & size  $>1$  cm in level III-IV are considered malignant.

But 33% of nodal mets are found in  $<1$  cm lymph node.

10% of cancer positive neck dissections contain mets  $\geq 3$  mm in size

25% of all clinically occult LN mets are too small to be detected by any imaging technique.

\* Sensitivity & specificity of PET CT is 80-98% resp. but it will miss subclinical mets in 20-50%.

\* USG - FNAC  $\rightarrow$  Highly operator dependant  
 $\rightarrow$  Outcomes of wait & watch after USG - FNAC have been disappointing.



## Possibility of Subclinical mes

I - low risk -  $< 20\%$

$T_1$  - Tongue

- FOM

- GBS

- BM

- RMT

- Hard Palate.

II - Intermediate risk  $\rightarrow 20-30\%$  -  $T_1$  - Soft Palate

- Pharyngeal wall

- Subglottic larynx

- Tonsil

$T_2 \rightarrow$  All from I

III  $\rightarrow$  High risk  $> 30\%$  -  $T_1$  - Nasopharynx

- PFS

- BOT

$T_2 - T_4$  - All from II

$T_3 - T_4$  - All from I.

## Endometrial Carcinoma

Risk factors - 1) Nullparity - due to ↑ anovulatory cycles

2) Meritally obese - Chronic hyperandrogenism, which is a key factor for ovarian hyperandrogenism, associated with anovulation & progesterone deficiency.

3) NIDDM & hypertension

4) Estrogen-only HRT & sequential OCP increase risk, while combined OC pills ↓ risk.

5) Tamoxifen has antiestrogenic effect in premenopausal women, but weak estrogenic in postmenopausal coz of ↑ receptors

No risk < 55 yrs, but 2.6% increased risk in 55-64 yrs.

Tamoxifen Lens - Early Stage

- Favourable features
- Increasing rates of Serious. (Clear cell Carcino sarcoma & sarcoma)

6) Lynch Syndrome → 5% pt of Ca Endometrium have Lynch, but 40-60% of Lynch syndrome pt have Ca endometrium.  
Highest risk = MCH1 gene.



A) Kluver Syndrome - Ca Breast, thyroid, endometrium & macrocephaly.

Two types of Ca endometrium

Type I → Older

→ Signs of hyperestrogenism

(early menarche

late menopause

Infertility

Anovulatory bleeding)

→ Endometrial hyperplasia

→ Well diff., minimal invasive

→ Good Prognosis

Genes - PTEN, AKT (PI3K)

- MSI

Type II → Older patients

→ Not associated with hyperestrogenism

→ Deep myometrial invasion

→ Poorly differentiated

→ Worse Prognosis

→ Genes - p53

p16

## Routes of Spread

Lymphatic  $\rightarrow$  Body of uterus drains into lymphatics that coalesce into parametrium & end up in pelvic nodes

Superior part of fundus & fundal uterine serosa parallels ovarian vessels to drain into para aortic nodes.

Distant spread - lung, liver, bone.

## Clinical features

- 1) Post menopausal bleeding, seen in 80-90% patients of Ca endometrium, BUT in patients preserving  $\pm$  PMB, only 10-15% have Ca endometrium
- 2) Pelvic fullness/pain - Simpson's Pain
- 3) Abnormal vaginal discharge
- 4) If cervical stenosis occurs, symptoms of pyometra.

## Genes involved

- 1) MMR genes - M.C. due to MLH1
- 2) PTEN gene - 10q - Tumor suppressor gene
- 3)  $\beta$ -catenin - gain of function mutation.



## Diagnosis

- 1) Office endometrial biopsy is the preferred approach.  
Sensitivity is 99% in postmenopausal  
91% in premenopausal.  
Specificity > 98% in both.  
It is performed using Pipelle device
- 2) Pap Smear - It is positive in only 50% cases.  
So, biopsy is recommended.
- 3) If symptoms persist & pt is being considered for fertility sparing approaches, dilation & curettage / functional curettage is done.
- 4) TV-USG → Endometrial thickness  $\geq 5$  mm is abnormal. Risk of  $M_x$  is minimal if thickness  $< 5$  mm. False neg. here is 4%.
- 5) CT Scan - Useful for higher grade histology & high grade disease subtypes.
- 6) MRI - Accuracy of 85-93% in detecting myometrial invasion.  
- In pt w/ suspected cervical involvement, MRI can be used to define the lower extent of disease
- 7) PET/CT to look for distant mets, not for nodal mets.

- 8) CA125 - Independent risk factor for pelvic & Para-aortic lymph node mets.  
- Also useful for post treatment surveillance.

### Pathology

- \* Endometrial hyperplasia is a precursor lesion for endometrial adenocarcinoma

WHO Classification :-

- 1) Simple hyperplasia  $\rightarrow$  1% risk
- 2) Simple  $\bar{c}$  atypia
- 3) Complex hyperplasia
- 4) "  $\bar{c}$  atypia - 29% risk.

Risk of concurrent underlying carcinoma in atypical hyperplasia - 42.6%.

So, standard tlt for atypical hyperplasia is hysterectomy.

### Grading of endometroid Ca

- Grade 1  $\rightarrow$   $< 5\%$  tumor growth in solid sheets  
2  $\rightarrow$  5-50%  
3  $\rightarrow$   $> 50\%$



## Pathological Classification [End SCUMS Trm M]

- 1) Endometrioid - NOS
  - Adeno + sq. differentiation
  - Secretory
  - Ciliated
  - Villoglandular
- 2) Squamous
- 3) Clear cell
- 4) Undifferentiated
- 5) Mucinous
- 6) Serous ~ 10% . Aggressive subtype.
- 7) Transitional cell
- 8) Mixed type.

### Prognostic factors

- 1) Age → Increased age leads to poorer prognosis
  - More aggressive histology
  - More advanced disease.
- 2) Race - African Americans & Hispanics have worse outcomes.
- 3) Grade 3 has worse outcomes compared to Grade 1 & 2 [PORTEC 1 trial]
- 4) Histology - Survival & recurrence rate for patients with Clear cell carcinoma are similar to endometrioid grade 3, but

better than serous.

5) LVI is associated with metastasis.

GOG 210 Study - ~~2270~~ Rate of 20 mets in

pt w/ LVI  $\rightarrow$  37.5%.

& LVI  $\rightarrow$  4.1%.

6) Thickness of myometrial involvement, adnexal involvement, cervical stromal involvement.

### Prognostic factors in MSKCC nomogram

1) Age

2) Grade

3) Histologic type

4) Number of lymph nodes removed

5) FIGO staging.

### Molecular Classification

1) POLE ultramutated - Good prognosis

2) MSI hypermutated -

3) Copy number low - 52% had  $\beta$  catenin mutations

4) Copy number high - Worst prognosis

- Serous histology

- Grade 3 endometrioid.



## FIGO Staging

|                                                                    |            |
|--------------------------------------------------------------------|------------|
|                                                                    | 54% OS     |
| I <sub>A</sub> - <50% myometrial invasion                          | } - 80-90% |
| I <sub>B</sub> - >50% myometrial invasion                          |            |
| II - Endocervical stromal invasion                                 | 70-80%     |
| II <sub>A</sub> - Invades serosa of corpus uteri<br>and/or adnexa. | } - 30-60% |
| II <sub>B</sub> - Vaginal or parametrial involvement               |            |
| II <sub>C1</sub> - Pelvic LN                                       |            |
| II <sub>C2</sub> - Para-aortic LN                                  |            |
| IV <sub>A</sub> - Invasion of bowel/bladder                        | 10%        |
| IV <sub>B</sub> - Distant mets                                     |            |

Role of Positive Peritoneal Cytology - No role in Staging.

It has prognostic impact in Stage III & above, but not in early stage disease [Milgrom et al].

Treatment → Surgery - Hysterectomy + BSO +  
Peritoneal cytology + Lymph node  
assessment

→ Radiation - IMRT / IORT ± CT

→ Chemo - Adjuvant settings

Surgery - Salpingo-oophorectomy is recommended  
because 8.8% of the endometrium may have  
adnexal involvement

~ 5% of pt have may synchronous Ca Ovary  
The rate is 10% in women < 50 yrs.

### Technique of hysterectomy

~ Can be done by laparotomy or laparoscopy -  
\* In a prospective GOG trial (LAP2), patients  
of stage I & IIa were randomized to  
laparotomy & lap-scopy.

Lap is associated with fewer adverse events,  
lower rates of extended hospitalization.

Conversion rate to open  $\rightarrow$  25.8%.

Minimally invasive Preferred.

### Management of lymph nodes

\* Lymph node involvement depends on histology  
& depth of myometrial involvement

GOG 120  $\rightarrow$  0.8% for Grade I without invasion  
44.3% for high grade & serous  
histology & > 50% myometrial  
invasion.

Two randomized trials demonstrate no role of  
pelvic LNectomy in Stage I. worst OS.



\* "Berry picking" of ~~nodes~~ suspicious nodes can also be done, but it is not accurate enough.

\* SLNB  $\rightarrow$  Successful mapping achieved in 86-89% cases with sensitivity of 84-97.2% & NPV of 97%

If mapping fails, then side specific Lymphectomy including iliac & obturator nodes.

Rate of positive SLN  $\rightarrow$  23% } In a Prospective  
Detection rate - 89% } Study of grade 3  
Sensitivity - 95% } disease.

## Radiation

| Stage                          | Grade 1/2                                                          | Grade 3              |
|--------------------------------|--------------------------------------------------------------------|----------------------|
| I <sub>A</sub>                 | Observation,<br>If Age $\geq 60$ yr, LVI $\oplus$<br>Consider IVRT | Observation vs IVRT  |
| I <sub>B</sub>                 | IVRT                                                               | IMRT                 |
| II (<50%<br>Cervical invasion) | IVRT                                                               | IMRT vs IVRT + Chemo |
| II (>50%)                      | IMRT                                                               | "                    |

\* M.C. site of recurrence is vaginal. So, aim of RT is to reduce the risk of local recurrence.

↑ risk of relapse seen in - Shows / clear cell histology  
 - Grade III  
 - LVI, Age > 60  
 - > 50% myometrial invasion.

1) Swedish trial → 645 pt of Stage IA randomised after surgery (TAH/BSO + pelvic washing + LNectomy) to observation vs IVRT

No use of RT in Stage Ia G1

No statistically significant diff. in rates of recurrence for G1/G2.

High risk → Age > 60, LVI ⊕

2) PORTEC 1 trial → 715 pt, Stage I (excluding pt  $\bar{c}$  < 50% myometrial invasion + G1; and > 50% invasion + G3)

↓  
TAH + BSO

Observation      Pelvic RT

IA Stage, G2,3  
 IA G1,2  
 IB G1,2

Result → ↓ vaginal recurrence in < 50% invasion + G3.  
 ∴ RT has advantage in Stage Ia G3.

→ Stage IB G1, G2 also benefits from RT.  
 (Recurrence rate 1% vs 10% for G1  
 2% vs 13% for G2)



3) PORTEC 2 trial → 427 patients

Inclusion - Stage I IF Age > 60

G<sub>3</sub> + < 50% invasion

~~IURT can be given in  
Place of IURT in  
Ia G<sub>3</sub>, Ib G<sub>1</sub>, G<sub>2</sub>~~

Stage Ia G<sub>1</sub>, G<sub>2</sub>

↓  
TAH + BSO

Pelvic RT IURT

Syn. recurrence → 1.6% 1.8% (not significant)

Similar OS & DFS.

∴ Omission of Pelvic RT in favor of IURT does not increase risk of recurrence.

Routine LNHectomy and Pelvic RT not recommended in Stage I

1) Neither has been shown to ↑ survival

2) Most pt in PORTEC 2 with pelvic recurrence also had distant mets. At MSKCC, Stage Ib, G<sub>1</sub>/G<sub>2</sub> undergo SLNB. If negative, they receive only IURT.

4) G<sub>1</sub>/G<sub>2</sub> 99 → 190 pt & Stage I/II disease

~~High intermediate~~

↓  
TAH/BSO + Pelvic washing + Pelvic/Pan-aortic node sampling

Observation

Pelvic RT

2yr relapse

12%

3%

(significant)

4yr OS

86%

92%

(N.S.)

Benefit of Pelvic RT seen in a "high intermediate risk"

→ Advanced age

→ Grade 2/3

→ LVI

→ Outer  $\frac{1}{3}$  myometrial invasion.

For Stage II disease, IVRT alone can be considered in

1)  $< 50\%$  Cervical stromal invasion

2) Grade 1/2

3) Adequate hysterectomy / SN mapping.

For the rest → Pelvic RT

\* Pelvic RT has poorer quality of life in PORTEC 2 trial

- Fecal leakage, diarrhea

- Urinary urgency, bowel urgency.

Chemotherapy - Adjuvant chemo not routinely recommended

1) PORTEC 3 → High risk early stage & Stage III

Pelvic RT

Pelvic RT + cisplatin

No OS/DFS benefit for stage I & II.

✓ But, there was an RFS advantage for serious & clear cell adenoca (stage I-III).

2) GOG 249 → 602 pt. Stage I/II HIR endometrial adenoca, serious or clear cell

Pelvic RT

IVRT + 30 Paclitaxel

No diff. in RFS or OS.

Chemo arm had HIGH recurrence & toxicity.



## Stage III

Randomized trials for adjuvant chemo

1) GOG 122 → Stage III

Whole abdo RT

Doxo + Cisplatin × 8 cycles.



Better PFS & OS

2) PORTEC 3 - Showed PFS advantage for Chemoradiation (versus EBRT) for Stage III. But no diff. in OS.

3) MANGO ILTADP-III → No significant improvement in outcome with chemo RT.

4) GOG 258 → Chemo RT Vs Chemo alone  
Stage I, II (serous/clear cell), Stage III, IV

Cisplatin based RT

6 OP+C

plu 4 OP+C

lowers Vaginal & nodal recurrence in chemo RT  
but more distant mets. No diff in DFS/OS.

3 risk factors as independent predictors of relapse.

- 1) >50% Myometrial invasion
- 2) Positive Peritoneal cytology
- 3) Aggressive histology (Grade 3 endometrioid; serous, clear cell, undifferentiated)

Stage III pt  $\geq 2$  risk factors  $\rightarrow$  60 Pacl + carb  
Only 1 risk factor  $\rightarrow$  Chemo RT as given in PORTEC 3.

Preferred form of RT is IMRT - 50.4 Gy / 28#.

Positive peritoneal cytology  $\rightarrow$  60 Pacl + carb.

### Treatment of distant recurrence

#### Endocrine

- 1) Alternating tamoxifen & Medroxyprogesterone acetate or megestrol acetate is based on hypothesis that anti estrogen therapy could upregulate PR.  
Response rate 30% in Chemo naive pt.

- 2) Randomized Phase II trial comparing mTOR inhibitor sirolimus to progestin therapy showed a response rate of 4.3% only for progestin therapy.

• Serous histology  $\rightarrow$  Lack of response  
Endometrioid wth CTNNB1 mutation  $\rightarrow$  Good response.

~~Endocrine~~ Endocrine therapy  $\rightarrow$  low grade ER+ve tumours  
 $\rightarrow$  long interval from Dx to recurrence

Regimen  $\rightarrow$  MA 80mg BD

MA 80mg BD  $\times$  3 weeks alternating  $\rightarrow$

Tamoxifen 20mg BD  $\times$  3 weeks



## Cytotoxic Chemo - TAP [Paclitaxel, Doxo, Cisplatin]

is the only treatment proven to produce a response in Stage IV or recurrent endometrial Ca.

• Higher toxicity  $\pm$  TAP, median OS 13 months.

- 1<sup>st</sup> line treatment is Paclit + Carbo every 3 weeks.  
Liposomal doxo + Carbo can be a reasonable alternative.

2<sup>nd</sup> line chemo  $\rightarrow$  limited efficacy.

$\rightarrow$  If there is prolonged time interval from 1<sup>st</sup> line platinum based chemo, they can be re-treated with platinum. (12 months).

## Targeted Rx

1) Anti angiogenic - Bevacizumab, Beva + TZ [no improved OS]

2) No benefit of mTOR inhibitors

3) No benefit of Trastuzumab even in Her2+ve disease

4) EGFR 2 inhibitor  $\rightarrow$  Dovitinib - 2<sup>nd</sup> line.

5) PARP inhibitor - Investigational group of Olaparib.

★ 6) Pembrolizumab - Response rate of 53%.

(PD-1 antibody).

FDA approved for any cancer  $\pm$  MSI.

## Locally recurrent disease

1) Surgery - For patients with recurrence in irradiated area.

At least R1 resection should be achieved.

Pelvic exenteration may be considered in women  $\pm$  pelvic recurrence.

2) Radiation - Mainstay for isolated vaginal recurrence.  
- Local control of 40-70% in isolated vaginal recurrence.

- For tumor size  $> 2\text{cm}$ , combined Pelvic + Brachy RT  
 $< 2\text{cm}$ , pelvic + IORT.

Dose is 45 Gy Pelvic RT + 20-30 Gy Brachy RT.

For nodal recurrence, EBRT is used. Poor results - 1 mR.

Chemo RT may be useful.



## Classification of hysterectomy [Piver, Rutledge & Smith]

Type I → Simple hysterectomy

Type II → Modified radical hysterectomy

Ureters dissected to the point of their entry into bladder.

Proximal uterosacral ligaments resected

Medial half of cardinal ligaments removed

1-2 cm of upper vagina removed.

Type III → Radical hysterectomy

Removal of as much uterosacral ligaments as possible

Entire width of parametria resected

Upper  $\frac{1}{3}$  vagina removed.

Type IV → Extended Radical

Same as III, but  $\frac{3}{4}$  vagina removed

& paravaginal tissue removed.

Type V → Partial exenteration

terminal ureters or a segment of bladder or rectum is removed along w uterus & parametria (supralevator)

Type II-V - Systemic Bilateral pelvic LNectomy,

half the way along common iliac artery, down till femoral ring.

Removal of tubes & ovaries NOT a part of it. per se.

## Imaging of the neck

Diff investigations - USG neck  
USG FNAB  
CT/MRI  
PET  
Diffusion weighted MRI

### Assessment of lymph node

Size cutoff - 1cm in the largest axial diameter  
88% sensitivity, 39% specificity

1.5 cm cutoff has 56% sensitivity, 84% specificity  
[Curtin et al].

Sonography of (n) LN - Oval, hypoechoic, echogenic hilus continuous  
with adjacent soft tissue.

Reactive LN  $\rightarrow$  Same as above, but has ↑ vascularity

Malignant  $\rightarrow$  Hypoechoic  
Round  
Echogenic hilus absent  
Ill defined borders  
Intranodal coag. necrosis / cystic necrosis

PCT lymph node - Hyperechoic, intranodal anechoic calcification



Arterial invasion - most sensitive sign - loss of fascial planes  
 Most specific  $\rightarrow$  narrowing or irregularity of artery.

CT neck - Fast, high quality imaging

- Easily reproducible
- less affected by breathing & swallowing artefacts.

\* Presence of necrotic / cystic area is highly predictive for mets.

PET CT -  $SUR \geq 3.16$  is more suggestive of LN mets.

NCCN guidelines for neck node evaluation

- 1) CT/MRI, whichever is used for evaluation of primary
- 2) Multistation LN  
 lower level neck node  
 high grade }  $\rightarrow$  CT thorax / PET CT

Other use of PET CT - For tumours approaching midline, to determine surgical approach to C/L neck.

- Identify involved lymph nodes in pt Planned for definitive RT.

de Bondt et al - Detection of LN mets in head & neck cancer - a meta-analysis

Max sensitivity  $\rightarrow$  USG (87%)

Max specificity  $\rightarrow$  USG FNAC (97%)

Morphological criteria in MRI (de Bondt)

- 1) Border irregularity
- 2) Heterogeneity of signal intensity
- 3) Size.

Magnetic resonance lymphography has a NPV of 90% but PPV is only 10%. So, limited use.

Liao et al - Comparison of USG/CT/MRI/PET

Sensitivity is similar in all four.

CT was superior to USG in specificity.

Role of FDG PET (Kyzas et al) -

sensitivity  $\sim$  50% (in No patients)  
specificity - 87%

So, it does not detect  $\sim$  50% of patients with mets & No.

| Liao et al  | CT  | MRI | PET | USG |
|-------------|-----|-----|-----|-----|
| Sensitivity | 52% | 65% | 66% | 66% |
| Specificity | 93% | 81% | 87% | 78% |



## Sonographic Classification of Vascular Resectability [Mann et al]

Stage I → Independent carotid pulsations & an obvious cleavage plane visible.

II → Residual independent mobility of artery & node but obvious plane not visible

III → loss of independent mobility of the carotid artery and luminal compression

IV → Gross invasion of carotid artery.

- \* Cross flow Circulation of the MIA by using Transcranial doppler, demonstrating >90% of flow velocity within 20 sec of external compression of the carotid artery allows safe resectability of the vessel.

## PET CT in Unknown Primary

Use first recognized by Reuthoven et al in 2004.

✓ DAHANCA 13 Study - overall detection rate of PET in CUP → 29%.

Therapeutic change of treatment in 25% by PET

PET before Penendoscopy demonstrated fewer false positive pathological foci.



## Post treatment surveillance

What to look for?

Stage I - 2-3 months after treatment & then annually  
Cervical smear every 6 months

II - 3-4 months after treatment & then annually  
but observe skin & not smear

III - 4-6 months after treatment & then annually  
and blood count & chest X-ray

IV - 6-12 months after treatment & then annually

For all stages, if the patient is not responding to treatment, then the patient should be referred to a specialist for further management. The patient should also be advised to avoid sexual intercourse until the infection is cleared.

For all stages, if the patient is not responding to treatment, then the patient should be referred to a specialist for further management.

Use of post treatment surveillance is essential for the early detection of relapse.

For all stages, if the patient is not responding to treatment, then the patient should be referred to a specialist for further management.

For all stages, if the patient is not responding to treatment, then the patient should be referred to a specialist for further management.

For all stages, if the patient is not responding to treatment, then the patient should be referred to a specialist for further management.



## Carcinoma Ovary

- \* Epithelial Ovarian cancers are the most common Ovarian Cancer, and the most common subtype is high grade serous lesion; most commonly arising from fimbriated end of fallopian tube and associated with BRCA 1/2 in 10-15% cases.

### Risk factors

- Age
- Family history
- Nulliparity, infertility
- DM, obesity
- Smoking (asso.  $\bar{c}$  mucinous adenoc.)

Incessant ovulation hypothesis - Higher rate of spontaneous mutations occurring with the repair of surface epithelium following each ovulatory cycle. So, early menarche, late menopause, nulliparity  $\uparrow$  the number of ovulation cycles.

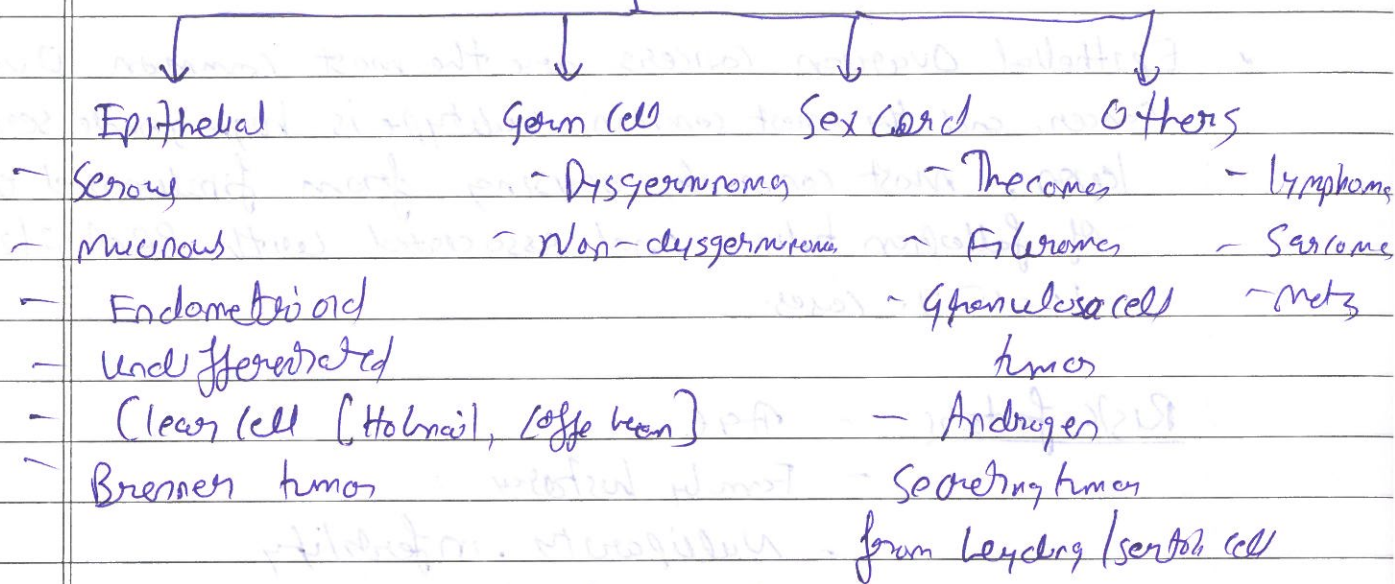
Gonadotropin hypothesis - LH & FSH may be directly involved in pathogenesis.

Protective factors -  $\uparrow$  Parity

- OCPs
- Salpingo-oophorectomy.

Role of family history - 1<sup>st</sup> degree relatives have 3-7x risk  
 Lifetime risk  $\bar{c}$  BRCA 1  $\rightarrow$  >50%  
 BRCA 2  $\rightarrow$  12-13%.

## Classification of Ovarian tumors



\* Risk of CA Ovary & HRT is conflicting. It produces gonadotropins, but also enhances estrogen induced proliferation.

\* Benign conditions implicated in CA Ovary

- PCOS
- Endometriosis
- Pelvic inflammatory disease.

Cancer And Steroid Hormone (CASH) study showed 1.5% pt of EOC had PCOS.

Hysterectomy & Tubal ligation reduce risk by 30-40%.

Risk reducing Salpingo-oophorectomy for BRCA1/2

does not entirely eliminate the risk as there is risk of 1.8-2% of having primary peritoneal cancer.



Other genes involved - DNA repair genes like  
BRIP1, RAD51C, RAD51D

- Lynch / HNPCC associated (MSH2, MSH6)

BRCA1 & 2 have early age of onset, higher response to chemo, longer DFS & achieve clinical remission.

WHO classification → Pg 1233, Denta.

M.C. subtype - Serous cystadenocarcinoma [psammoma bodies]  
↑ CA 125

2<sup>nd</sup> - mucinous [↑ CEA]

Serous carcinomas can be high grade or low grade & clear cell and undifferentiated tend to be most aggressive.

## Screening & Prevention

1) CA 125 - Only US FDA approved biomarker for cancer detection.

- Expressed only in 75%, that too serous subtype. Not expressed by mucinous & other subtypes

- Low sensitivity for detecting early stage disease, & abnormally high levels ~~for~~ in benign gynecological conditions

- Not used for screening in average risk pt

Uses - 1) TO determine if a pelvic mass is malignant (>35)

2) Assisting in diagnosis of Cancer of unknown Primary

3) Monitoring response to chemo

4) Screening in high risk pt (family history)  
BRCA

5) Follow up, Surveillance.

PLCO trial - 34 261 women

No screening

Annual TV USG + CEA

Total 90 patients detected in both arms, out of them, 60 were detected through screening.

BUT, 72% of screen detected were late stage (III/IV)  
15% of those who underwent surgery, had serious complications.

So, screening does NOT improve mortality.

2017 update → Histologic heterogeneity of the disease impacts detection & survival.

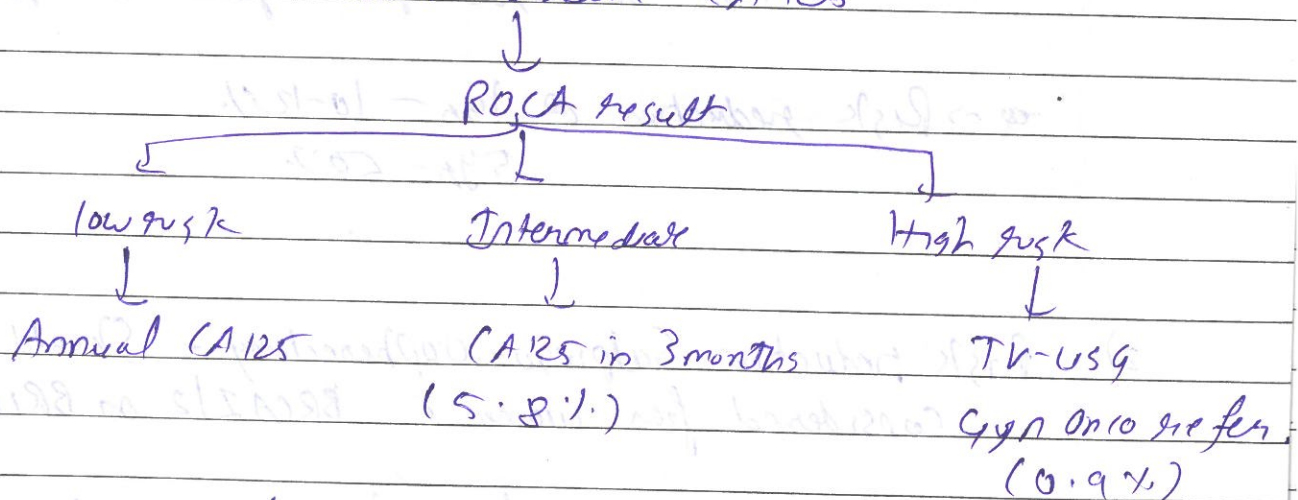


UK CTORS study  $\rightarrow$  CA125 + TV-US vs usual care. CA125 used as ROCA score. ASSO.  $\pm$  non significant mortality reduction at 41 1444

## Risk of Ovarian Cancer Algorithm (ROCA)

- \* Improves sensitivity of CA125 in Assat EOC.
- \* Base line CA125 is measured and is used as a yardstick, against which any fluctuations or changes over time can be measured.
- \* ROCA score is provided by inputting CA125 values into a mathematical model that includes age of the woman.
- \* Hypothesis is that CA125 levels should steadily increase in a woman who is to have an ovary.
- \* So, by monitoring the ROCA score, disease can be intercepted before it spreads.

i) US ROCA Study - 4051 women with no family h/o, Underwent baseline CA125



10 women underwent surgery. 4 pt had invasive cancer.  
PPV  $\rightarrow$  40%.  
Specificity  $\rightarrow$  99.9%.



2) UKFOCSS included  $>10\%$  lifetime risk of ovarian cancer, age  $<35$  yrs and no hRSO.

→ Women ~~with~~ with high risk who decline hRSO, can be monitored using ROCA. Sensitivity - 94.7% & Significant Stage shift from I to II.

✓ USPTE recommended against Screening of (a) ovaries.

✓ NIH consensus panel advised annual pelvic exam, CA125 BTU in Prevention BRCA1/2 +ve females till 35th age.

1) OCP → Significant ↓ in risk of cancer.

→ Analysis of CASH data have indicated that formulations with high level of progestins are associated with lower risk.

→ SHARE study - No diff bet<sup>n</sup> androgenic & non-androgenic pills for cancer prevention.

→ Risk reduction @ 1yr - 10-12%  
5yr - 50%

2) Risk reduction Salpingo-oophorectomy - Should be considered for women with BRCA1/2 or BRIP mutations

- Women with strong family history who have not undergone genetic testing should also consider hRSO.

- hRSO reduces risk of (a) Breast by 30-75%



- RSO should be deferred until age 35 or older.
- Since pt of Lynch Syndrome are at risk for ovarian cancer, as well as endometrium, RSO + hysterectomy should be done.
- Risk of developing Primary Peritoneal carcinoma after RSO is 1.7-4.3%.

Technique of RSO should include - BIL Salpingo-oophorectomy with removal of entire fallopian tube.

- Cytological examination of peritoneal washings
- Random peritoneal & omental biopsies
- Serial sectioning of ovary & fallopian tube at 2mm intervals.

GOG 0199 → Non randomized trial for women at high risk to undergo RSO or TVUS + ROCA.

↓

Pathological review of 966 specimens revealed 4 pre-invasive & 20 invasive pelvic cancers.

3.2% pt w BRCA mutations had serious pelvic cancers.

- 3) HE4 → product of HE4 gene. Expressed in EOC.  
 ↑ HE4 correlated with advanced stage & serious histology.  
 It has prognostic significance.

## Diagnosis

### ① Benign vs Malignant pelvic mass

Suspicious features on TV USG  $\rightarrow$  BIL disease

- $\rightarrow$  Complex mass
- $\rightarrow$  Solid area / mural nodule
- $\rightarrow$   $>3$ mm thick septations
- $\rightarrow$  Persistent enlarged mass in postmenopausal women.

Premenopausal  $\rightarrow$  Refer to gyn-onco in case of:

1) Asites

2) CA 125  $>200$  U/ml

3) mets

4)  $>1$  first degree relative  $\in$  (a breast / Ovary).

Post menopausal  $\rightarrow$  CA 125  $>35$

$\rightarrow$  Asites

$\rightarrow$  Nodularity, limited mobility

$\rightarrow$  Mets, 1° relative -

DD of adnexal mass  $\rightarrow$  Hydrosalpinx & Paratubal cysts

$\rightarrow$  Ectopic pregnancy

$\rightarrow$  Tube - ovarian abscess

$\rightarrow$  Intra uterine pregnancy in bicornuate uterus

$\rightarrow$  Pedunculated uterine myoma

$\rightarrow$  Distended Sigmoid

$\rightarrow$  Distended bladder or hydroptic kidney.



\* TV USG can be used to detect the mass, ascertain its nature (solid/cystic).

\* USG can also determine if ascites is present.

\* CT or MRI can be done in case of high suspicion of malignancy.

\* If ascites (+), ascitic fluid for cytology.

ROMA → Risk of Malignancy algorithm.

\* Uses CA 125 & HE4.

\* Diagnostic for pt w/ a pelvic mass.

\* Sensitivity of 93.8%.

\* Should be used for preop triage of women w/ pelvic mass.

OVA1 22 - First FDA approved blood test for assisting with the triage of an adnexal mass.

Five biomarkers of OVA1 → CA 125 (↑)

apolipoprotein A2 (↓)

$\beta_2$  microglobulin (↑)

Transferrin (↓)

Prealbumin (↓)

It can detect different types of cancer, not just serous also performs well in detection of early & advanced cancers.

Scale of 1-10

Premenopausal - abn if > 5

Post menopausal - abn if > 4.4

OVA 2 → substitutes FSH & LH for P<sub>2</sub> microglobulin & preallum.

Single point cut off → 5

No need to check menstrual status.

### Clinical features

- Abdominal swelling
- Dyspepsia
- Urinary frequency
- Wt change
- Abdominal bloating
- Partial small bowel obstruction
- Shortness of breath due to malignant pleural effusion.

FIGO Staging — Pg 1237 Devita.

Broadly, I → Ovary & tube

II → Pelvis

III → Extrapelvic & node

IV → Distant mets

Surgical Staging → TAH + BSO

→ Total omentectomy

→ BIL Pelvic & Para-aortic LMPATHY

→ Multiple peritoneal biopsies

→ Four quadrant peritoneal washings

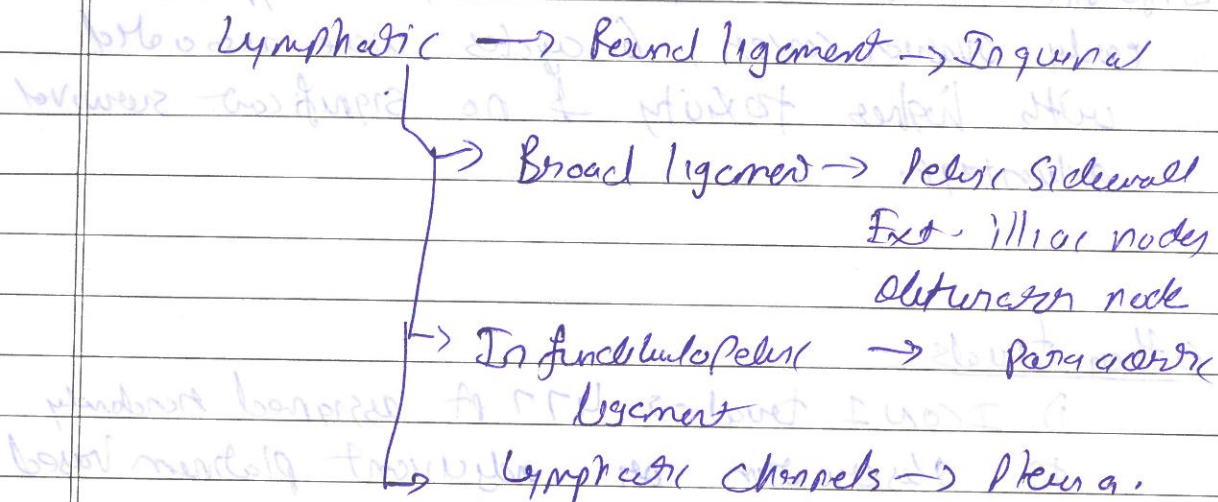
(BIL Pelvic & BIL subdiaphragmatic). It

leads to 30% upstaging. at stage I.



## Mode of Spread

M.C. is transcoelomic.



## Management

Stage I - Only 10% pt are diagnosed in Stage I.

Stage IA, IB, Grade 1/2 with non clear cell histology



Adequate Surgical staging

No adjuvant Chemo needed.

If Stage IC or Grade 3 or clear cell → Adjuvant Chemo

GOG 157 → 3 cycle Pacl + Carb vs 6 cycle

in women with early stage ovarian carcinoma who had undergone Comprehensive Surgical Staging



6.8yr follow up

RR was 24% lower in 6 cycle arm, but overall death rate similar.

- Higher toxicity in 6 cycle regimen.

Inference  $\rightarrow$  For Surgically staged high risk early ovarian cancer, 6 cycles were associated with higher toxicity & no significant survival advantage.

### Other trials

- 1) ICON1 trial  $\rightarrow$  477 pt assigned randomly to observation or adjuvant platinum based chemo



5yr OS - observation - 70%

Chemo - 79% (significant)

Recurrence free survival - Obs - 62%

Chemo - 73%



- 2) ACTION trial  $\rightarrow$  1448 pt assigned randomly to observation or chemo.

Chemo improves recurrence free survival but not OS (original analysis)

Long term follow up showed improved OS.

Non optimally staged pt showed significantly lower OS.





Q<sup>n</sup> - Role of Sx in ovarian malignancy  
Management of advanced Ca ovary.

44

Stage II - R →

Survival in stage II is 71.7% [SEER

Stage III → 27.4% database]

Traditional Paradigm is cytoreductive surgery & chemo.

- (1) Cytoreductive Surgery → Previous concept of optimal cytoreduction was  $\leq 1-2$  cm of gross tissue. Now, the concept is on R<sub>0</sub> resection.

- 1) Landmark Study by Griffiths → 20% 2yr survival in pt of advanced Ca ovary in whom residual tumor burden  $\leq 1.5$  cm, compared to 0% survival if residual disease is  $> 1.5$  cm.

- 2) Brustow et al meta-analysis - Most imp. determinant of survival was maximal cytoreduction. 10% increase in tumor resection associated with a 5.5% increase in median survival.

- 3) LION Study → For need of LNectomy in cNo Patients while doing CRS.

Total LNectomy → OS 66 month.

No LNectomy → OS 69 month.

∴ No need for LNectomy in cNo disease.

Post op morbidity & mortality higher in lymphadenectomy atm.



For primary disease → Upfront surgery or after 3-4 cycles of NACT

If patients cannot be cured with surgery then palliative surgery can be done.

### Interval debulking Surgery (IDS)

→ After 3-4 cycles NACT

→ Bulky disease

→ Doubtful operability

Post NACT, if remission (biological/biochemical/radiological)

↓  
Go for palliative debulking

Secondary cytoreductive Surgery → Patients in remission who experience recurrence may be candidates for additional CRS.

Criteria → DFS  $\geq$  12 months

→ Small volume / isolated disease

→ Medically optimized.

GOG <sup>0213</sup> ~~0213~~ → Pt with first recurrence & resectable disease randomized to secondary CRS + platinum based chemo vs platinum based chemo alone.

Minimum platinum free interval → 6 months

Chemo regimen - Pacl- (carb) / Gen- (carb)



Results- Complete gross resection achieved in 67% pt assigned to surgery arm.

\* No impact on OS with Surgery.

### Neoadjuvant Chemotherapy

\* NACT considered in patients with unresectable disease.

1/ Woche (logical) MRC - CHORUS trial → Non inferiority trial

→ No diff in PFS/OS bet<sup>n</sup> debulking Surgery vs Adju CT  
vs NACT → IDS → Adju CT

So, NACT is non inferior

2) EORTC trial by Vergote et al → No diff in PFS/OS  
bet<sup>n</sup> surgy → chemo vs NACT → surgy → chemo

Low, optimal cytoreduction rate is 80.6% ± NACT  
vs 41.6% ± upfront surgery. And, optimal  
cytoreduction is the strongest independent predictor  
of OS.

Post 3-4 @ NACT, IDS is done after 4 weeks,  
then adjuvant chemo started 2-3 weeks post op.

## Chemo regimens

1) Pacli + Cisplatin → GOG Protocol 6111  
[ Cisplatin + Cyclo 13 months OS 24  
Cis + Pacli 18 38 ]

2) Carbo ≥ Cisplatin → GOG 158

Better tolerance of Carbo, similar neurotoxicity,  
less myelosuppression, nephropathy.

3) Docetaxel = Pacli → ~~SCOTROC~~ SCOTROC study  
lower neurotoxicity.

Docet + Carbo can be given in pt c neuropathy.

1<sup>st</sup> line therapy → Pacli + Carbo

Pacli + Cis

Docet + Carbo.

## Intraperitoneal Chemotherapy

Post op intraperitoneal chemo & IV combination chemo  
for advanced ovarian cancer has been studied in 4  
trials

1) GOG 104 - IV Cisplatin + Cyclo OS  
IV Cyclo + IP Cisplatin 41 months  
IV Cyclo + IP Cisplatin 49 months.



2) GOG 114 → IV Pacli } Every 3 weeks x 6 cycle  
IV Cisplatin

VS

IV carbop (AUC 9)

IV Pacli

IP Cisplatin every 3 weeks x 6 cycle

new sub group (control) with a better level

OS → 52 vs 63 month

PFS → 22 vs 27 month.

3) GOG 0172 [EPIC] trial → m. Imp

415 pt, with no residual mass > 1cm after  
debulking

↓  
IV Pacli + Cisplatin

VS

IV Pacli + IP Cisplatin

Treatment was repeated every 21 days for 6 cycles

Grade 3/4 pain, fatigue, hematological toxicity is  
higher in IP/IV arm.

Only 42% completed all 6 cycles in IP/IV arm, but

OS → 65 month vs 49 month

PFS → 23 month vs 18

∴ Significant OS/PFS benefit seen

Quality of life significantly worse in (PIV) arm.

- 4) GOG 252 → Bevacizumab added  
→ one arm tested 1P carboplatin  
→ weekly dose dense pack added.

Trial lacked a definitive control and data were not interpretable.

HIPEC - Combines the pharmacokinetic advantage of intracavitary chemo to direct cytotoxicity of increased temperature.

- Chemo agents should have cell cycle non specific action & heat-synergistic cytotoxic action.

Technique ← Open Coliseum technique  
closed technique

- 1) Fagotti et al → 1<sup>st</sup> studied HIPEC following Secondary cytoreductive surgery in recurrent platinum sensitive ovarian cancer.

Sec. CRS + HIPEC Vs Sec. CRS + systemic Chemo

38 months OS vs 24 months



2) OVHIPEC Trial by Von Minckwitz et al

FIGO stage III, PS = 2



3ONACT [Pacli + Carb]



Stable disease



IDS

IP cisplatin

IV Pacli + Carb

PFS → 14 months

10 months

OS → 45 m

33 m.

### Concept of dose dense Pacli

By TROG → Weekly administration of Paclitaxel has greater efficacy, sustained exposure to dividing cells.

↑ PFS

↑ OS

compared to standard 3 weekly chemo.

### Platinum Sensitive Recurrent Disease

ICON 4 study → Pacli + Platinum Vs conventional Platinum based in recurrent Platinum sensitive Ovary.

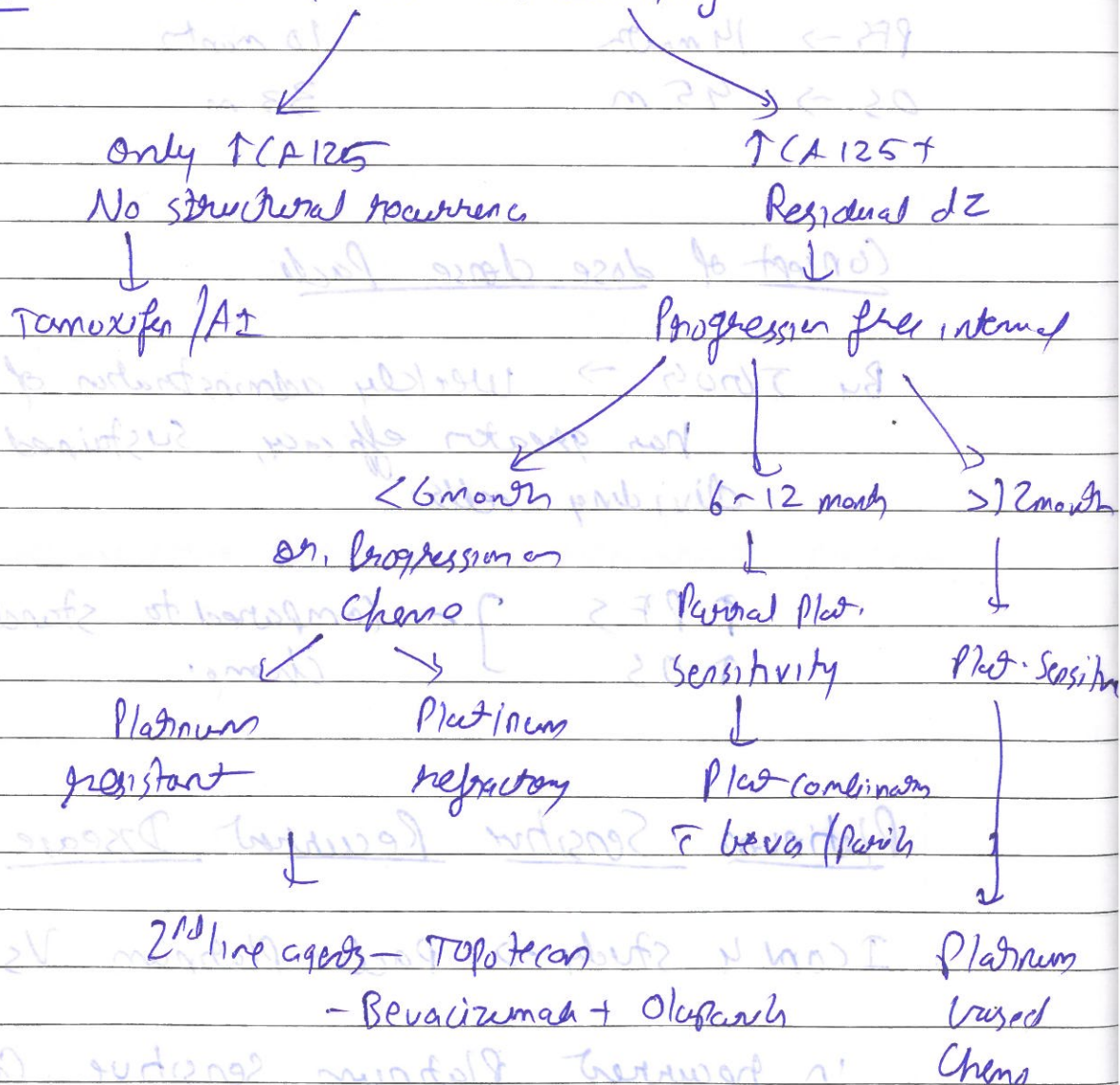
Significantly improved OS & PFS in FOLFIRI + Platinum group.

## Maintenance Chemo

- Up to 70% pt experience relapse
- Maintenance chemo has ↑ PFS, but no effect on OS.

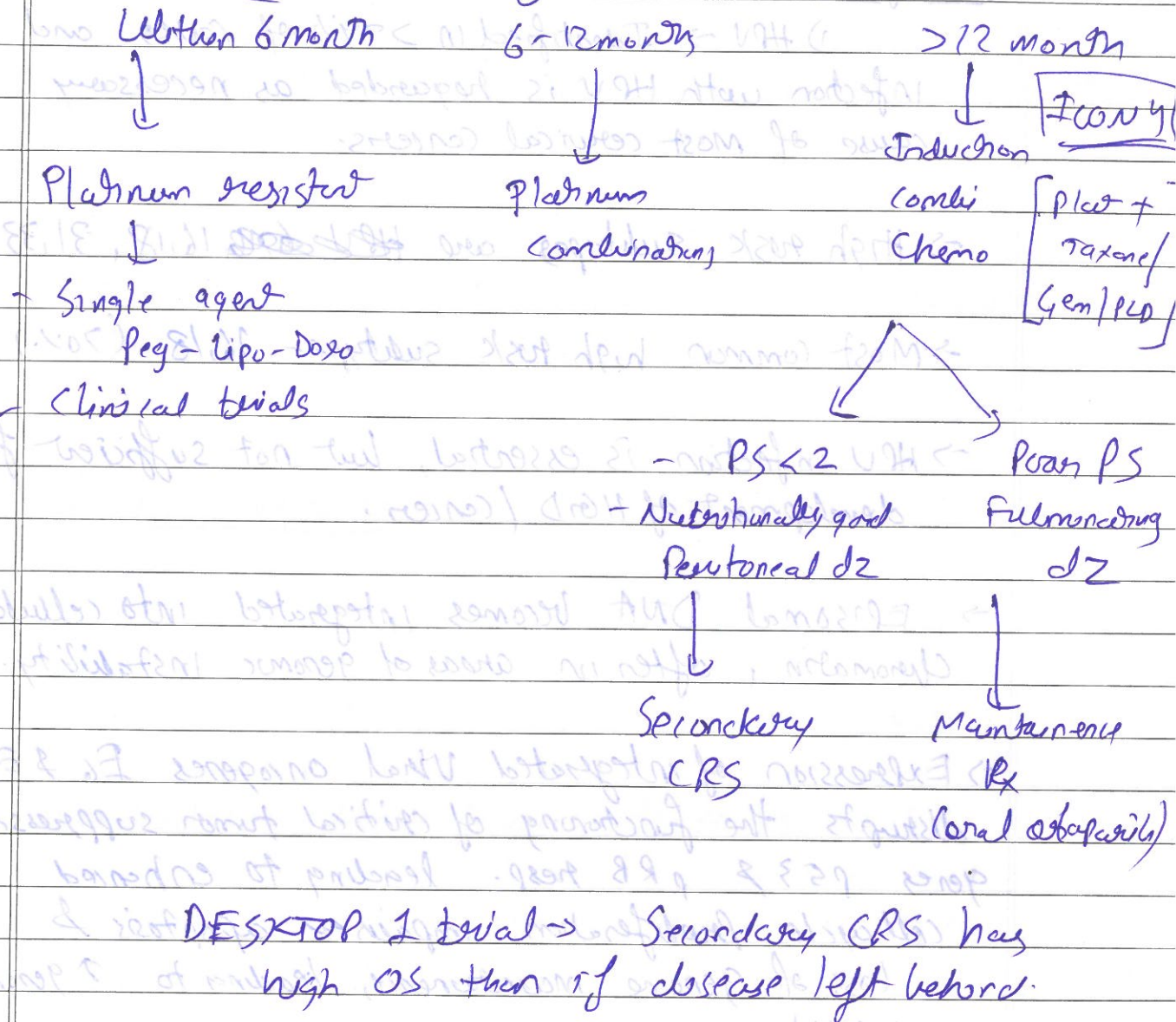
## Follow up

H&P, CA125, Imaging





# Recurrent disease (after 1<sup>st</sup> management)



## Cervix

### Risk factors

- 1) HPV → Identified in >99% of cases and infection with HPV is regarded as necessary cause of most cervical cancers.
  - High risk subtypes are ~~HPV 16, 18, 31, 33, 45~~ 16, 18, 31, 33, 45
  - Most common high risk subtype - 16, 18 (70%)
  - HPV infection is essential, but not sufficient for development of HGND / cancer.
  - Episomal DNA becomes integrated into cellular chromatin, often in areas of genomic instability.
  - Expression of integrated viral oncogenes E6 & E7, disrupts the functioning of critical tumor suppressor genes p53 & pRB resp. leading to enhanced cell cycle proliferation, impaired apoptosis & loss of genome maintenance, leading to ↑ genomic instability.
  - Co-factors -
    - Smoking
    - High parity
    - Co-infection w/ other STD

- 2) Coitus at young age, and have multiple sexual partners who have multiple sexual partners.



3) Circumcised males have lower incidence of HPV infection & lower risk of transmission to partners.

4) Cervix is an 'AIDS defining neoplasm'.  
HIV infected women have - higher incidence of HPV  
- More persistent infections  
- Faster rate of progression

ART does NOT affect HPV levels, or reduce rate of incidence of HSIL.

### Anti HPV Vaccines

1) Cervarix - Bivalent (HPV 16, 18)

2) Gardasil - Quadrivalent (HPV 16, 18, 31, 33)

3) Gardasil-9 - Above four + 31, 33, 45, 52, 58.

\* Vaccine composed of Viral-like particles (VLP) composed of 21 capsid protein assembled into highly immunogenic VLP form.

- Effect lasts for up to 5 years.

Can prevent 90-95% CIN in women who have no history of HPV infection.

\* WHO recommends two doses, 6 months apart, to girls < 15 years old.

- \* For persons vaccinated before 15<sup>th</sup> birthday, two-dose schedule is sufficient, administered 6-12 months after the first.

For older individuals, three dose schedule.

### Natural history & Pattern of Spread

- \* Most carcinomas arise at the junction between columnar epithelium of endocervix & squamous epithelium of ectocervix.
- \* This junction is a site of continuous metaplastic change, Maximum activity in utero  
 Puberty  
 1<sup>st</sup> Pregnancy.  
 Declines after menopause.
- \* Approx time interval bet<sup>n</sup> CIN & invasive cancer is 15 years.

### Spread

- 1) Exophytic growth into the cervix
- 2) Superiorly to lower uterine segment  
 Inferiorly to vagina  
 Laterally to broad ligaments where it may cause ureteral obstruction.  
 Posterolaterally to uterosacral ligament



### 3) Lymphatic Spread

Upper - Anterior & lateral chain, follow uterine artery & terminate in the uppermost hypogastric nodes.

Middle - Deeper hypogastric (obturator)

Lower - Posterior course to superior gluteal, common iliac, presacral & subaortic nodes.

Massive tumours, particularly those that involve rectovaginal septum can metastasize to perinectal nodes.

Lesions involving distal vagina goes to inguinal nodes.

For Stage I, Pelvic node involvement is 15-20%.

Para-aortic involvement is 1-5%.

Most accurate non invasive method of diagnosis of nodal mets  $\rightarrow$  FDG PET

Sensitivity - 82%. Specificity 95%.

\* Most frequent sites of mets follow hypogastric vessels

\* M.C. site of distant recurrence - Lung

- Left SC2 node

- Liver

- Bone

## Cytological Classification Systems

- Bethesda →
- 1) Within normal limits
  - 2) Infection
  - 3) Reactive & Reparative changes
  - 4) Atypical Squamous Cells of Undetermined Significance (ASCUS)
  - 5) Low grade Squamous intraepithelial lesion
  - 6) High grade
  - 7) Invasive Squamous carcinoma

Pap → I - normal

II - Infection / inflammation

~~III~~

III - Undefined - cytology suggestive but not conclusive for malignancy

IV - Cytology strongly suggestive of malignancy

V - Conclusive for malignancy

CIN → Cervical intra epithelial neoplasia are characterized by cellular immaturity, cellular disorganization, nuclear abnormalities and increased mitotic activity

If changes involve only lower third → CIN 1

Lower + middle → CIN 2

Upper third → CIN 3

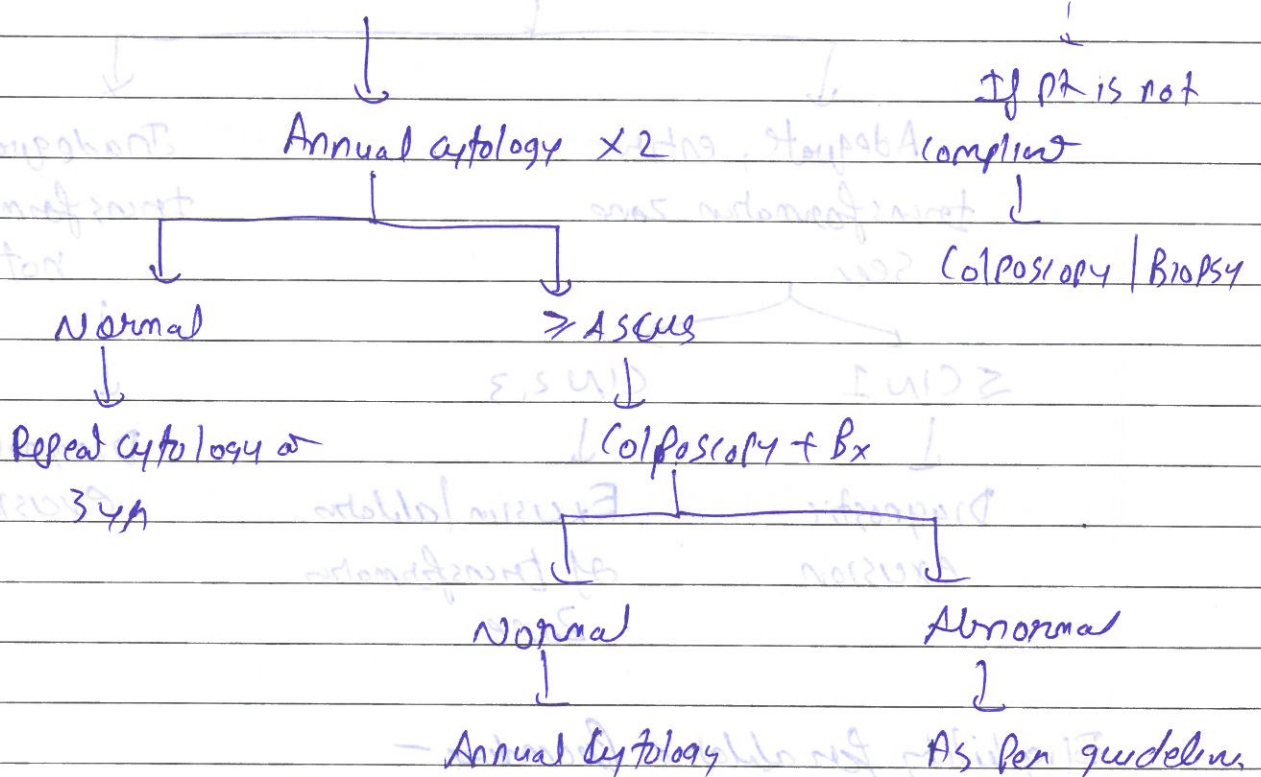


LSIL  $\rightarrow$  low grade dysplasia associated with HPV  
 $\rightarrow$  low likelihood of progressing to cancer  
 $\rightarrow$  low risk HPV types

HSIL  $\rightarrow$  High grade dysplasia  
 $\rightarrow$  High risk HPV types  
 $\rightarrow$  High likelihood of progressing to cancer.

### Management of Pre-invasive lesions

LSIL  $\rightarrow$  ASCUS in 25-29 years -

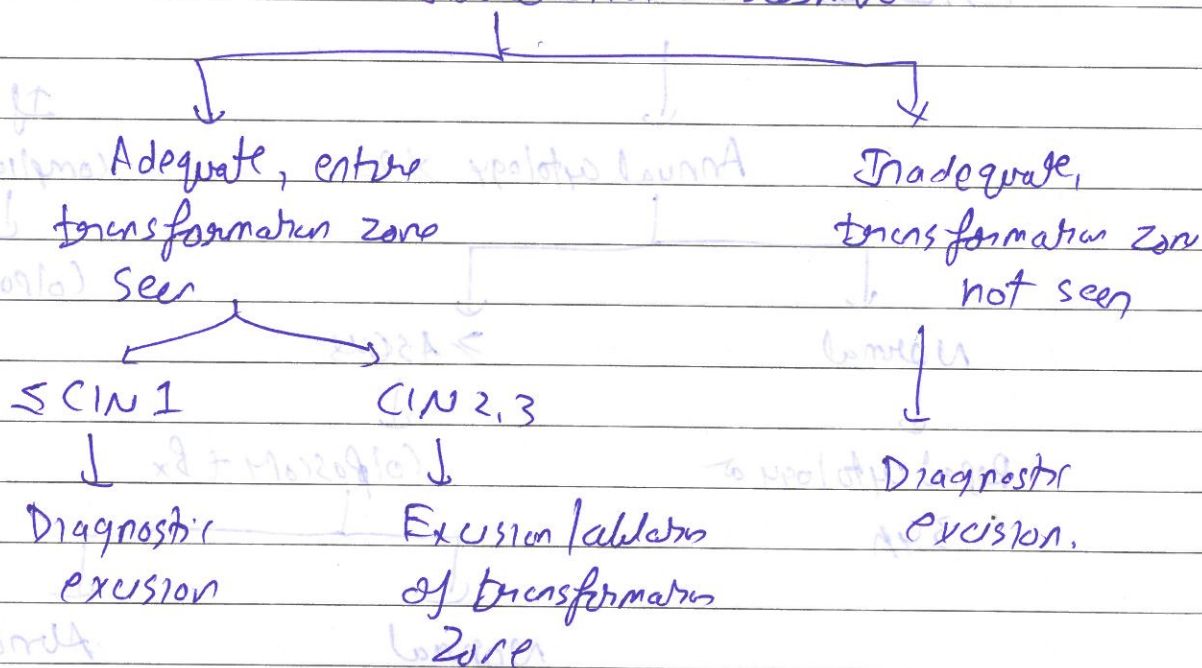


## LSIL in 30-64 years

- \* Women in this age group & LSIL have 80% HPV positivity & hence HPV testing not used as triage
- \* Colposcopic biopsy to be done initially

## HSIL

Colposcopy & cervical biopsy &  
endocervical assessment



## Eligibility for ablation procedure -

1) Lesion should be entirely visible and occupy not more than two quadrants of cervix

2) Entire lesion located on ectocervix. No vaginal involvement

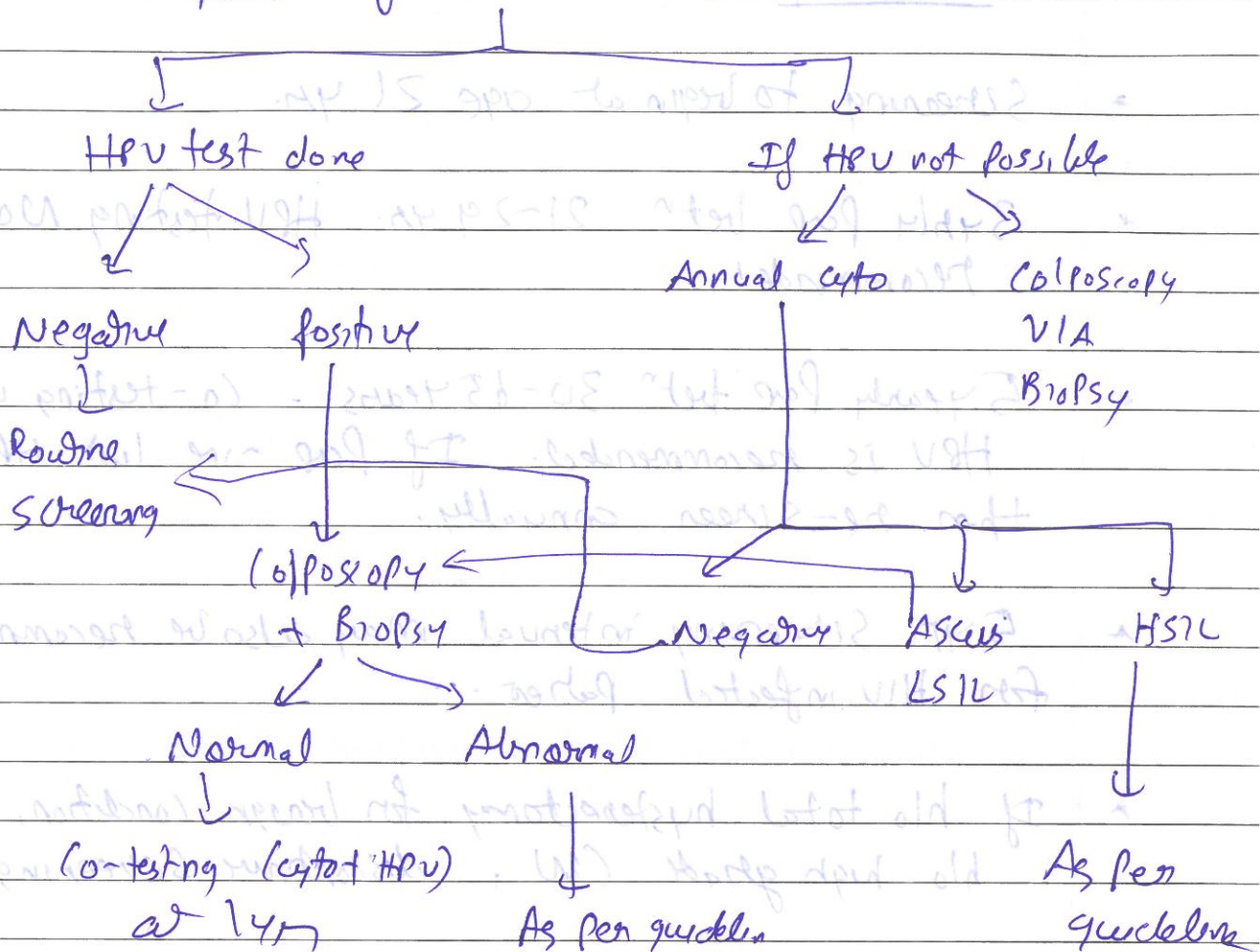
3) Lesion adequately covered by largest colposcope

4) No suspicion of cancer

5) No post coital or post menopausal bleeding.



## Management of ASCus in 30-64yr



ASCus-LSIL Triage Study (ALTS) compared three methods of management -

- immediate colposcopy
- cytologic follow up
- HPV DNA triage

In that HPV-triage was the effective method of triage.

## Screening

- \* Screening to begin at age 21 yrs.
- \* 3 yearly Pap bet<sup>n</sup> 21-29 yrs. HPV testing NOT recommended.
- \* 5 yearly Pap bet<sup>n</sup> 30-65 years - Co-testing with HPV is recommended. If Pap -ve but HPV +ve, then re-screen annually.
- \* 5 yr Screening interval may also be recommended for HIV infected patient.
- \* If h/o total hysterectomy for benign condition, and no h/o high grade CIN, discontinue screening.
- \* Discontinue screening at age 65-70 yrs.
- \* If E abnormal Pap, but not gross cervical lesion should undergo colposcopy + biopsy. Visualizing after applying 3% acetic acid can also be done.
- \* High grade Pap finding  $\rightarrow$  Additional endocervical sample to be collected. Rate of detection is higher when specimen is collected using a cytobrush, rather than by wetting.



## Cervical Cone Biopsy / LEEP

Indication - Squamo columnar Junction is poorly visualized on colposcopy and high grade lesion

- High grade dysplastic epithelium extends into endocervical canal

- Cytology slo HGD / carcinoma

- Microinvasive carcinoma

- Endocervical curettage shows CIN

- Cytology slo adenocarcinoma in situ

LEEP is the preferred treatment for HSIL.

In this technique, a charged electrode is used to excise the entire transformation zone.

It is an outpatient procedure that preserves fertility.

Should be performed when invasive or microinvasive disease is suspected with AIS.

### Prognostic factors

1) Lymph node mets

2) LVSI

3) Deep stromal invasion ( $>10\text{mm}$ )

4) Histologic type

(Adeno is worse)

5) Uterine body involvement associated with greater mets

6) Strong inflammatory response in cervix is good

prognosis

## Microinvasive disease (Stage 1A)

<1% lymph node involvement

LVI -ve

LVI +ve

Young

Old

Young

Old



Conization

Type II

Radical

Type II

hysterectomy

trachelectomy

± PLND

+ Pelvic LNectomy

IA2 → Lymph node involvement ~ 5%.

→ BIL PLND mandatory.

Young ft → Radical trachelectomy + BIL PLND

Family: complete → Type II hysterectomy

Radical trachelectomy - Removes Cervix & Parametrial tissue while retaining uterine corpus

- (Can be done in Stage IA2-IB1.

Complications - Dysmenorrhea

- Irregular menses

- Vaginal discharge

- Cervical suture problems

- Isthmic stenosis

- Prolonged amenorrhea

37% rate of Preterm delivery.



## Stage IB & IIA

\* Stage IB can be treated effectively with combined EBRT and brachy RT or with Radical (Type III) hysterectomy + BIL PLND.

\* Pt with high risk features benefit from PORT.

Young women, small, node -ve tumor → Surgery

(Londoni et al) → Type III hysterectomy Vs EBRT +  
(if high risk, then PORT) Intracavitary RT

↓

|                          |     |     |
|--------------------------|-----|-----|
| 54% OS<br>(≤ 4 cm tumor) | 80% | 82% |
|                          | 63% | 57% |
| (> 4 cm tumor)           |     |     |

IB1 < 2 cm, no comorbidity → Radical Trachelectomy  
Type C Hysterectomy

If > 4 cm, old age etc → CT-RT

IB2 is believed to be better treated by CT-RT,  
but no RCT to compare it to Surgery.

## Role of Adjuvant RT

1) GOG 92 → Tested the benefit of adjuvant pelvic irradiation in pt with intermediate risk of recurrence in Stage IB carcinoma.

Eligibility for study -  $> 1/3$  stromal invasion?  
- LUGI

Tumor diameter  $\geq 4$  cm

Exclusion - Involved nodes  
- Positive tumor margins.

46% reduction in risk of recurrence (significant)  
30% - " " death (not significant)

Benefit of PORT was more in pT  $\leq$  adenocarcinoma or  
adenosquamous (a).

2) SWOG 87-97  $\rightarrow$  Included pT  $\leq$  Parametral  
involvement, pelvic node & Positive margin

Adjuvant RT vs Adj. CT RT (cisplatin based)

46%  $\downarrow$  in Pelvic disease recurrence  
30% Survival advantage.

Definitive Radiotherapy

- Can be used for Stage IB-III patients,  
but for IB2 & IIA, concurrent CT-RT is  
better.



## Role of NART & hysterectomy?

GOG trial  $\rightarrow$  No improvement in survival  $\bar{c}$  surgery.

The only role is pt having uterine fibroids which may limit delivery of RT dose. In these pt, Type I hysterectomy can be done.

\* No role of NACT

## Stage IIb, III, IVA disease

- \* Bearing major medical contraindications, patients with locally advanced tumors should receive concurrent chemo - RT.
- \* Initial EBRT given to lesion & potential sites of regional spread. It shrinks the tumor, and that facilitates subsequent Brachy RT.
- \* Intracavitary Brachy RT should ~~be~~ follow EBRT.
- \* Total dose of EBRT + Brachy RT  $\rightarrow$  45-55 Gy
- \* With the use of IMRT, higher doses can be given. IMRT is particularly useful with ~~higher doses~~ para-aortic nodes, since they are near duodenum.
- \* No evidence that IMRT can safely be an alternative to Brachy RT.

## Pan-aortic Irradiation

\* Survival was poor in earlier days, but now with concurrent CT RT, survival is improving.

\* 5Y Disease Specific Survival is 47%.

\* Even for PT  $\pm$  no clinically involved nodes, it is standard to extend radiation therapy field by 6cm above the highest involved node.

## Brachy RT - Details from Deurta.

### Complications of RT

- Mild fatigue
- mild to moderate diarrhea
- mild bladder irritation
- Nausea, Gastric irritation
- ovarian failure (if ovaries not transposed).

### Cx of intracavitary brachy RT

- Uterine perforation
- Fever
- Thromboembolism

Late Cx - Rectal - Bleeding, stricture, ulceration, fistula  
- Small bowel obstruction



### Concurrent CT RT

\* Weekly Cisplatin based RT is the most effective technique.

- CT RT is the standard for stage IB2 onwards, for patients  $\in$  IB1 undergoing definitive RT, the risks & benefits of concurrent chemo must be weighed against concurrent medical problems.

### ~~GOG trial compared~~

\* One trial compared concurrent weekly (Gem + Cis) based RT plus adjuvant Gem + Cis, with concurrent RT  $\in$  Cisplatin alone.

3yr PFS was 74% in combination group vs 60% in Cisplatin alone.

But higher toxicity, and incomplete followup.

\* ANZGOG 0902 - Outback trial - Ongoing trial for impact of adjuvant Paclitaxel following CT RT.

## Classification of hysterectomy

①

Piver, Rutledge & Smith

Class I - Extrafascial hysterectomy

- Deflection & retraction of uterus without dissection of uterine bed.

- Uterine artery, uterosacral ligaments & cardinal ligament are moved close to uterus

- No vaginal cuff removed

Class II - Modified Radical / Wertheim's

- Uterus are freed from parametrial position but not dissected out of the pubovesical ligament

- Uterine arteries divided just medial to uterus

- Uterosacral ligaments resected midway bet<sup>n</sup> uterus & sacral attachments.

- Medial half of cardinal ligaments removed

- Routine pelvic LNectomy



### Class III - Classical Meigs' Radical Hysterectomy

- Complete dissection of uterus from the Pubovesical ligament to entry into bladder, except a small lateral part, so that superior vesicle artery is conserved.
- Uterine vessels divided at origin
- Uterosacral ligaments resected at their sacral attachments.
- Cardinal ligaments resected at pelvic wall
- Upper half of vagina
- Routine Pelvic LNectomy.

### Class IV → Extended Radical

- Complete dissection of uterus from pubovesical ligament
- Superior vesical artery is sacrificed
- Upper  $\frac{3}{4}$  of vagina.

### Class V → Partial exenteration

- Excision of involved portion of distal uterus or bladder.

### Boundaries of Pelvic LN dissection

Lateral - Genitofemoral nerve

Medial - Internal iliac artery

Inferior - deep circumflex iliac vein

Superior - Bifurcation of common iliac

(2)

## Querleu & Morrow Classification

[extrafascial hysterectomy] Type A → Minimum resection of Parametrix, limited radical hysterectomy

- Parametrix transected medial to ureter but lateral to cervix
- Uterine artery, uterosacral ligament & cardinal ligament are ~~not~~ transected flush to uterus.
- Minimal vaginal cuff - < 1cm.

Done in → Microinvasive Cancer Stage IA2 & Stage IB1 < 2cm

- No nodes or LVI

→ completion surgery after CTR

Type B → Resection of Parametrix at the Ureter

[modified Radical]

- Ureter are unroofed & treated laterally
- Partial resection of uterosacral peritoneal folds
- Transection of Parametrix at the level of ureteric tumour
- At least 1cm Vaginal cuff removed

Type B1 - without removal of lateral Parametrial lymph node

B2 - with --



[Radical]

- Type C → ureters are completely mobilized
- Transection of uterosacral ligament at the bottom
  - vesicouterine ligament at bladder
  - Complete transection of parametrix
  - 15-20mm of vagina from cervix or tumor & corresponding para colpos.

(1 - Preservation of autonomic nerves  
(2 - Sacrifice)

(1 hysterectomy is associated with faster recovery of bladder function & less degree of bowel dysfunction.

### Steps of C1 hysterectomy

- Dissection of uterosacral ligament

Hypogastric nerves run 1-2cm dorsal to ureter. They are dissected & lateralized before cutting uterosacrals.

- Dissection of Parametrium

→ Inferior hypogastric plexus is situated in dorsal parametrium and caudal vesicouterine ligament. It must be preserved.

→ Preserved by dissecting only the parametrium above deep uterine vein. (located 1-2cm below uterine vessels)

### Type D → Extra-Radical

D1 - Resection of the entire parametrix at the pelvic side wall together with the hypogastric vessels, exposing the roots of sciatic nerve.

Corresponds to Palfalvi-Unger laterally extended parametrectomy. (for Stage IIB)



D<sub>2</sub> → D<sub>1</sub> + Entire Para-aorta with hypogastric vessels & adjacent fascial or muscular structures.  
aka LFER (laterally extended endopelvic resection).

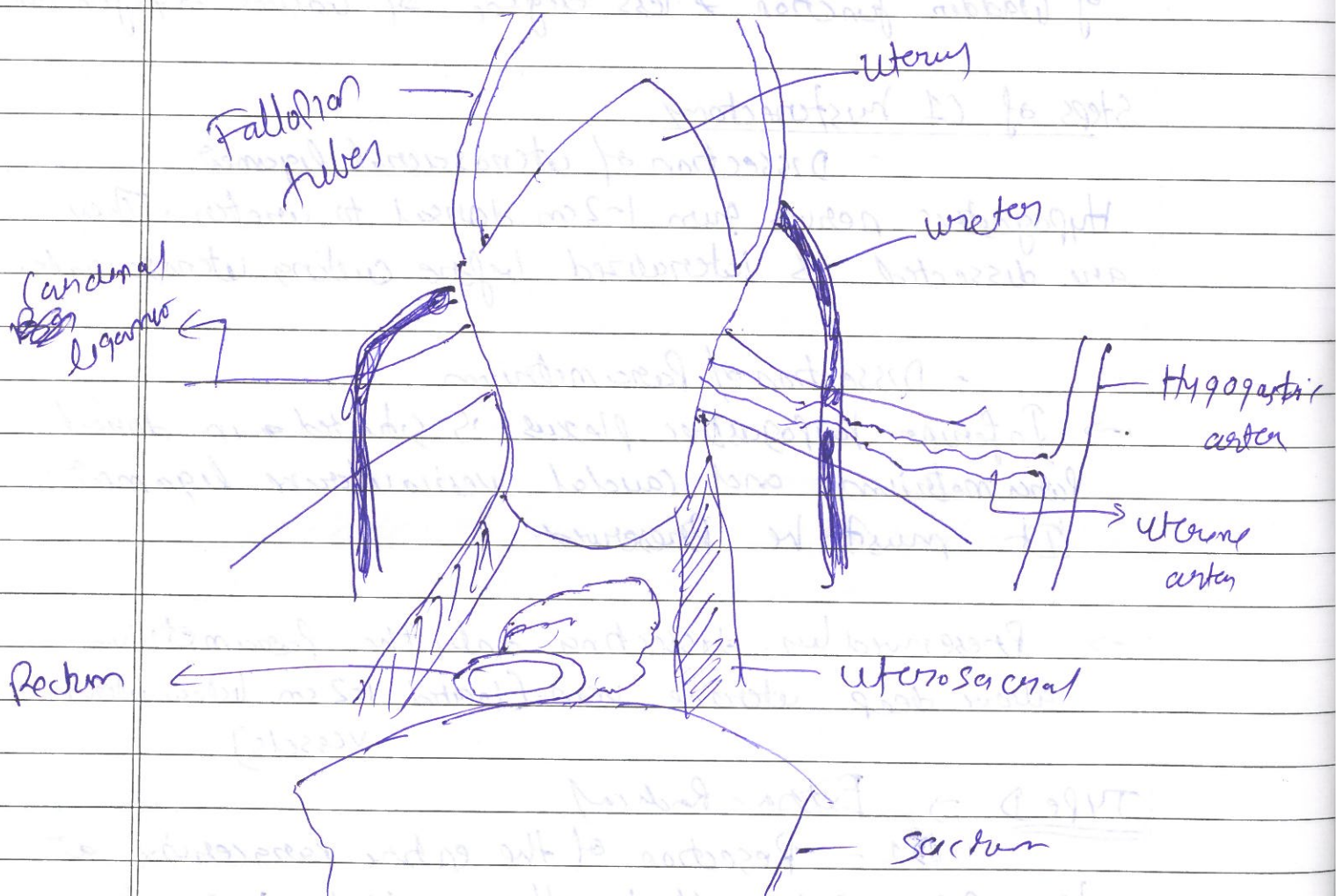
## Levels of lymph node dissection

Level 1 - Ext & Int iliac

2 - Common iliac (including presacral)

3 - Aortic, inframesenteric

4 - Aortic, infra renal





## Recent Question (Gyn Onco)

Fertility Sparing Surgeries in Ca Ovary → MSO

Mx of CIN type II

Uterine Sarcoma II

✓ Ca endometrium, types of hysterectomy

✓ Mx of adnexal mass

✓ LN mets in Ca endometrium

Trials of concurrent CRT in Ca Cervix

✓ Staging & Mx of Ca Ovary II

✓ Controversies in Mx of Stage I Ca endometrium

✓ Progesterone in Ca endometrium

✓ Radical Brachyectomy

GTN

Borderline tumour of ovary

✓ HPV vaccine

## Cervix [NCCN]

Tis or Ta → Attempt for Peric Preservation offered

- Topical therapy i.e. 5FU cream
- Watch local excision
- Laser
- Complete glossectomy
- Mohs micrographic Surgery

- ① Topical therapy → 1) Imiquimod 5%, apply at night 3 times per week x 4-16 weeks
- 2) 5FU 5% cream, apply twice daily x 2-6 weeks

② Laser therapy - CO<sub>2</sub> / Nd:YAG / KTP lasers can be used to treat Tis, Ta, T1 0.1-2 tumors

- Perioperative application of 3-5% acetic acid to potentially affected skin can be used to identify the suspected sites of HPV infection; which will turn acetowhite.
- A smoke evacuation should be used

CO<sub>2</sub> → wavelength - 10,600 nm  
Penetration → 0.1 mm

KTP → 532 nm  
→ 1-2 mm

Nd:YAG → λ → 1064 nm  
Penetration - 3-4 mm.



(3) Wide local excision for cancer confined to skin with little or no invasion ( $T_{is}$ ,  $T_a$ ,  $T_1$ )

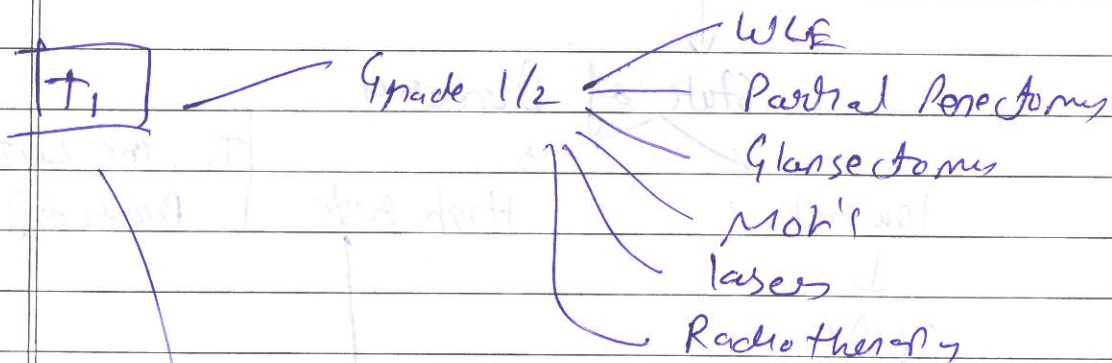
Circumcision alone may be sufficient for tumors of distal prepuce.

Reconstruction may be done by STSG or FTSG  
Glans resurfacing may be considered.

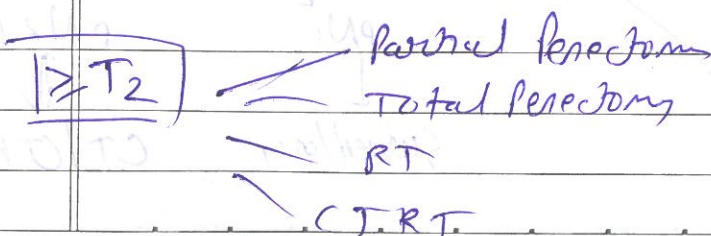
(4) Glossectomy  $\rightarrow$  Recommended only for  $T_a$  /  $T_{is}$  disease, as a cat. 2B recommendation.

$\rightarrow$  Not recommended for  $T_1$  G1-2.

(5) Moh's micrographic surgery - Small superficial lesion on proximal shaft.



Grade 3  $\rightarrow$  Moh's, Laser & Glossectomy NOT done.



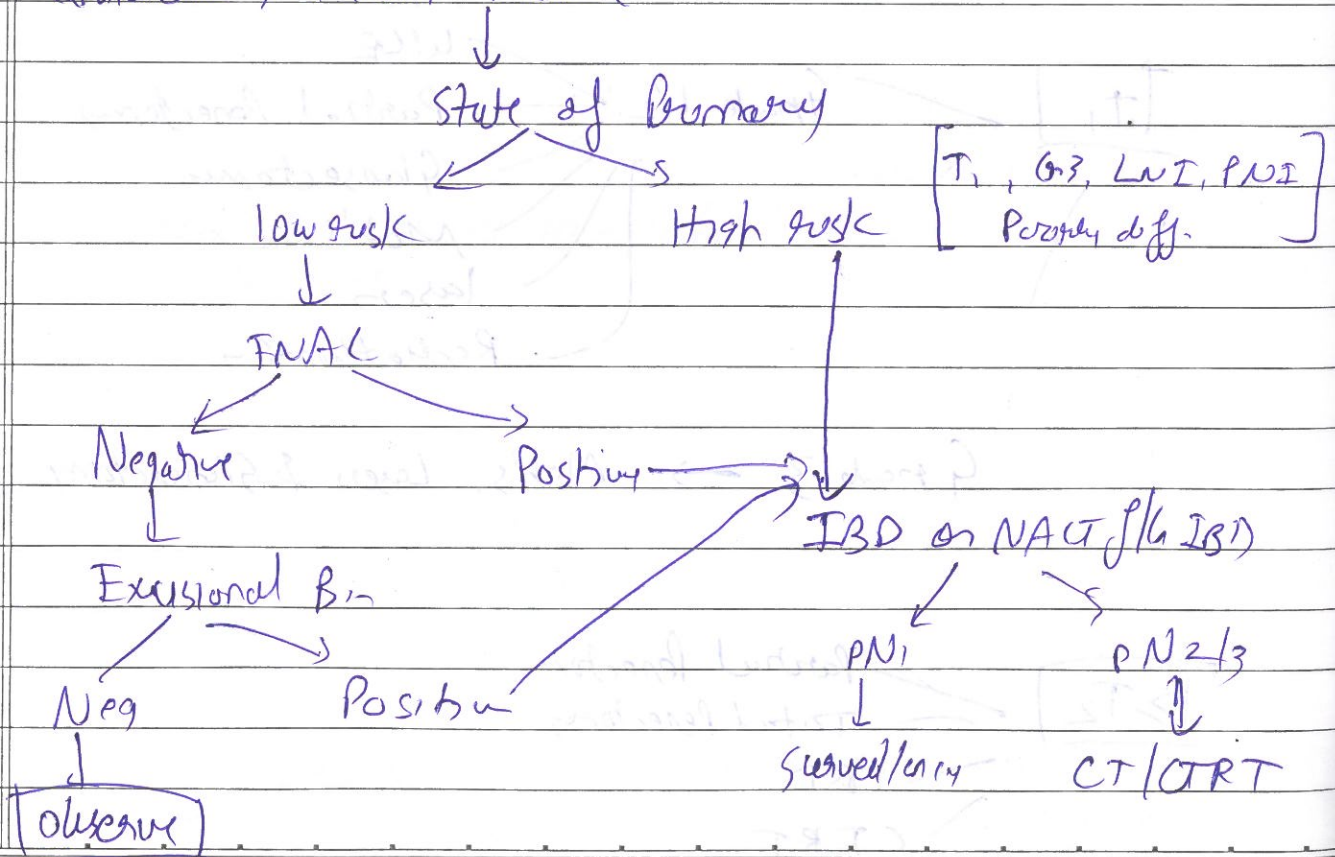
Non Palpable lymph node → These have 20% risk of being involved.

Low risk primary (Tis, Ta, T1a) → Surveillance  
(Clinical exam every 3 months for 2 years, then every 6 months for 3 years).

≥ T1c → CT(A+P) → Inguinal LN dissection  
→ Dynamic SLNB

### Palpable inguinal lymph nodes

① Unilateral, <4cm, mobile





②

Unilateral  $\geq 4$ cm (fixed or mobile)

Unilateral  $< 4$ cm (fixed)

Bilateral (fixed or mobile)

cN2/N3

$\geq 4$ cm, mobile

Others



FNAL

FNAL

Negative → Same as  
Positive → Various

Negative

Positive

Excisional Bx

NACT of IBD  
+ PLND

Negative

Positive

or  
RT / CRT

NACT

No response

Response / Not eligible for chemo

2<sup>nd</sup> line chemo

IBD + PLND

or  
RT / CRT

Adjuvant RT to be given if pelvic nodes ⊕. Otherwise  
adjuvant chemo only.

Chemo RT can also be considered.

(3)

Enlarged pelvic node

Pericuteaneous Leopsy, if feasible

Negative

Manage inguinals as described before

Positive

Surgical  
Candidate

Not a Surgical  
Candidate

NACT

CTRT

Repeat Imaging

Response?

Yes

Consolidation  
Surgery

NO

~~Next~~  
2nd line chemo

Radiotherapy in Penis → Commission should be done prior to initiation of radiotherapy.

T1-T2 No (Tumor < 4cm)

→ BrachyRT with interstitial implant

→ EBRT (65-70Gy) with 2cm margins

→ EBRT + concurrent chemo (65-70Gy) + 2cm margins.



> 4cm size → EBRT + chemo 45-50.4 Gy to whole  
Peri

Boost to primary  
(total dose 65-70 Gy)

→ Brachy RT in very select cases

T<sub>3</sub>-T<sub>4</sub> / N<sup>+</sup> (inoperable)

→ EBRT (same as above)

PORT given to primary site if margin free

45-60 Gy if  
no gross disease (+)

Like T<sub>3</sub>/T<sub>4</sub> if gross disease  
(+)

Adjuvant chemo RT - For inguinal and/or pelvic nodes (+)  
(pN<sub>2</sub>-N<sub>3</sub>)

- Inguinal & pelvic node EBRT to 45-50.4 Gy &  
boost to areas of nodes & ECE to a total dose  
of 65-70.

Choice of NACT → T-IP regimen [Erlotinib, ifosfamide,  
cisplatin]

Indication - Palpable node > 4cm, Positive on FNAC (mobile or fixed)  
- T<sub>4</sub> disease for down staging

If pt not eligible for T-IP, then they should undergo  
surgery up front.

- T<sub>1</sub> N<sub>2-3</sub> disease can receive upto 4 cycles TTP.

\* Cisplatin alone or with 5-FU can be given as radiosensitizer for CRT

### Inguinal node dissection

Anatomy \* Prepare & skin of the Penile shaft down into superficial lymphatic system

Glans & frenulum into deep lymphatic system

Lymphatics draining the penis traverse towards the base within Buck's fascia, & reach femoral triangle. It is possible for penile cancer to metastasize to contralateral nodes coz of this crossover in symphyseal region.

\* Femoral  $\Delta$  is bounded by  
Superiorly - Inguinal ligament  
Lateral - Sartorius muscle  
Medial - Adductor longus  
Floor - Pectineus medially  
Iliopsoas laterally.

Inguinal lymph nodes are divided into superficial & deep groups by fascia lata.



Superficial group  $\rightarrow$  4-25 nodes.

Divided into five groups

- Superolateral - sup. circumflex vein
- Inferolateral - lat. femoral cutaneous vein
- Superomedial - sup. ext. pudendal
- Inferomedial - Great Saphenous
- Central - SFS

Deep nodes are 1-3 in number & located medial to femoral vein.

The most cephalad of this group is LN of iliopect.

\* Blood supply to skin of inguinal region is derived from common femoral artery - Superficial external pudendal, sup. circumflex iliac & sup. epigastric artery.

\* Conventional open TBS sacrifices these branches.

### Investigations

US-FNAAC - Sensitivity - 50-100%

Specificity - 90-100%

CT & MFI are unreliable in staging non palpable nodes.

Sensitivity of PET CT with non palpable nodes is (57)%.

For palpable nodes, it is upto (96)%.

Not recommended for routine ~~staging~~ staging.



- \* Management of non palpable LN Pathy
- \* Approx 20% pt c non palpable nodes have cancer.
- \* LN mets are single most important predictor of Survival.

### Sentinel lymph node biopsy

\* Cabanas was first to introduce SLNB. But it did not achieve enough success because lymphatic anatomy is not static and it varies among patients.

- \* Subsequently, extended SN dissection proposed, where all tissue bounded by inguinal ligament superiorly, superficial external pudendal vein inferiorly & saphenous vein laterally is removed.

\* But it had false -ve rate of 25% - So discontinued.

Dynamic SLNB → Radioisotopes like  $Tc^{99m}$  or blue dye injected around tumor/resection site. & image guidance - lymphoscintigraphy is done to identify the sentinel node.

- \* US-FNA is done before the procedure. Characteristic of suspicious node → necrosis  
→ ↑ size  
→ longitudinal/transverse diameter ratio  $< 2$   
→ lack of echogenicity of hilum



- Technique → First, perform a groin ultrasound
- FNA C of any suspicious node. If +ve, straightaway B/L JBD.
  - The day before, or 4 hrs before the procedure,  $0.3-0.4\text{mCi}$   $\text{Tc}^{99\text{m}}$  is injected around the tumour or base of penis. and lymphoscintigraphy is performed.
  - Then 1ml blue dye is injected at the time of biopsy circumferentially around proximal penile shaft.
  - Small inguinal incision made & sentinel node isolated by gamma probe.
  - False negative results are due to lymph vessels re-routing to another ganglion or low uptake of tracer by the nodes.

### Superficial inguinal LN dissection

- Removal of lymph nodes superficial to fascial plane. & sent for frozen intra-op
- Pompea et al studied 50 cases & found no cases of deep compartment invasion in the event of a superficial compartment node negative disease.

Modified IBD - In 1988, Catalana proposed a modified IBD to provide proper diagnostic & therapeutic benefit while decreasing morbidity.

Modifications - Preserve Saphenous vein  
- Exclude areas lateral to femoral artery & caudal to fossa ovalis

Limits of dissection - Medially - Adductor longus  
Laterally - Femoral artery  
Superior - Inguinal ligament  
Inferior - Fossa ovalis

Endoscopic IBD -



## IASO Webinar (tongue)

H/O Salivation

Pronunciation of words.

D/D of tongue ulcer - Malignancy  
(with pain) - Aphthous ulcers.

Reason for salivation in tongue ulcer?

1) Deglutition is hindered due to pain, and as a result saliva is retained in the mouth.

2) Ulcer causes irritation of tongue, causing salivation.

Painless ulcers - Dental ulcers (chronic).

- Tuberculosis

- Syphilis

\* Pain in a tongue is a late disease.

Decrease in incidence of cancer after quitting tobacco, but over 5 years.

- Alcohol causes cancer by - formation of aldehyde

- local irritation

\* - Bacterial flora of oral cavity has alcohol dehydrogenase which produces acetaldehyde in oral cavity, which may cause cancer.

## Familial Cancers involving oral cavity Cancers

- Li Fraumeni
- ATM gene mutation
- Fanconi anemia

\* Relevance of Clubbing → Seen in Chronic Smokers.

Restriction of tongue movement indicates involvement of extrinsic muscles.

## \* Radiated Pain to ear

Sensory supply to ant  $\frac{2}{3}$  is by lingual nerve.

Taste sensation by chorda tympani

↓  
otic ganglion

↓  
auriculotemporal nerve → external ear.

Post tongue is supplied by glossopharyngeal nerve

↓  
Tympanic plexus

↓  
middle ear.



Improvement of neck imaging on MRI done by DWI

Support of STIR imaging.

Inoperability - Including pre-vertebral fascia

lesion reaching upto vallecula

- Carotid encasement

MRI for early tongue? - For DOI

neck node assessment

Induction chemo trials → Licitera et al

Zhong et al } for resectable lesions

For borderline resectable → Patel et al.

Margins in post NACT cases? - Some level of excision

★ Hypoglycemia in adjuvant RT? - It is useful for RT.

### Master class

Stage

5 yr survival

I

64-73%

II

55-60%

III

41-47%

IV

40-33%

Chances of having adverse pathological features, stage by stage, are worse in tongue.

EUA for operability 1) Mouth opening & tongue mobility

2) Anteriorly - involvement of TP

3) Posterior - Involvement of BOT & Tonsil

4) Medially - Crossing midline

5) Laterally - FOM / Mandible involvement (for reconstruction & resection extent)

~~6) Posterior~~

### Key MRI finding & Management implication

1) Tumor thickness  $> 4\text{mm}$   $\rightarrow$  Higher incidence of node mets  
 $\rightarrow$  Do elective neck dissection

2) DOI  $> 10\text{mm}$   $\rightarrow$  Poor prognostic marker

3) Lesion crossing midline  $\rightarrow$  Contralateral neck dissection & irradiation

4) Involvement of bilateral neurovascular bundle  $\rightarrow$  Total glossectomy may be needed.

5) Invasion limited to extrinsic muscle only versus invasion of FOM  $\rightarrow$  Recor by FRAFF vs ALT / PMMC flap



Extension to vallecular space → Relative contraindication to Surgery

→ Primary non surgical Ht

Extension to mastication space → Palliative Ht

Liao et al Metaanalysis for imaging No neck

|     | Sensitivity | Specificity |
|-----|-------------|-------------|
| CT  | 52%         | 93%         |
| MRI | 65%         | 81%         |
| PET | 66%         | 87%         |
| USG | 66%         | 78%         |

Molecular Markers → Overexpression of tumor suppression genes like p53, or oncogenes like EGFR, Her2 in free margins may result in recurrence & second primary tumors

- Significant practical & logistical limitations

Occult nodal mets in early tongue cancer → 24.8% (Choi et al).

\* Tongue has more nodal spread.

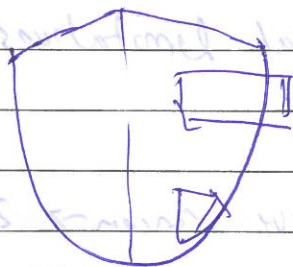
NACT in tongue.

- 1) Ant  $2/3$  disease extending upto or below hyoid bone
- 2) lesion extending upto vallecula
- 3) Extension of tumor into high ITF as defined by extension of tumor above an axial plane passing at the level of sigmoid notch
- 4) Extensive skin infiltration.

\* Role of NACT to convert inoperable to operable is NOT proven.

Zhong et al  $\rightarrow$  Improved DFS  $\pm$  NACT, not OS.

Tongue defect classification

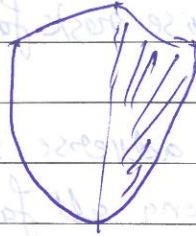


Type I [WLF]

$\rightarrow$  Primary closure or secondary intention.

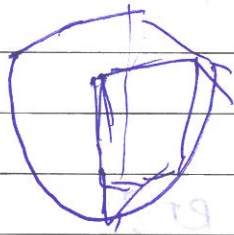


Type II



- HG
- Recon by FRAFF / ALT
- or pedicled flaps where free flap is contraindicated

Type III



- Anterolateral WLF
- Recon by ALT / FRAFF
- or PMMC

Type IV



- BOT resection + HG
- Recon by bulky flaps
- RAMFF / ALTFF / PMMC

Type V → Any resection  $\bar{c}$  floor of mouth involvement - Bone recon

Rehabilitation done by isometric & isotonic exercises

✓ Adjuvant Ht for single adverse risk factor?

→ ~~For~~ For single adverse risk factor, adjuvant Ht is not indicated, but among all factors, PNI has worse impact.

✓ Re-irradiation in case of unexpected local recurrence?  
54h.

✓ Salvage Surgery after CRT?

If operable, yes.

✓ No role of HPV DNA testing.