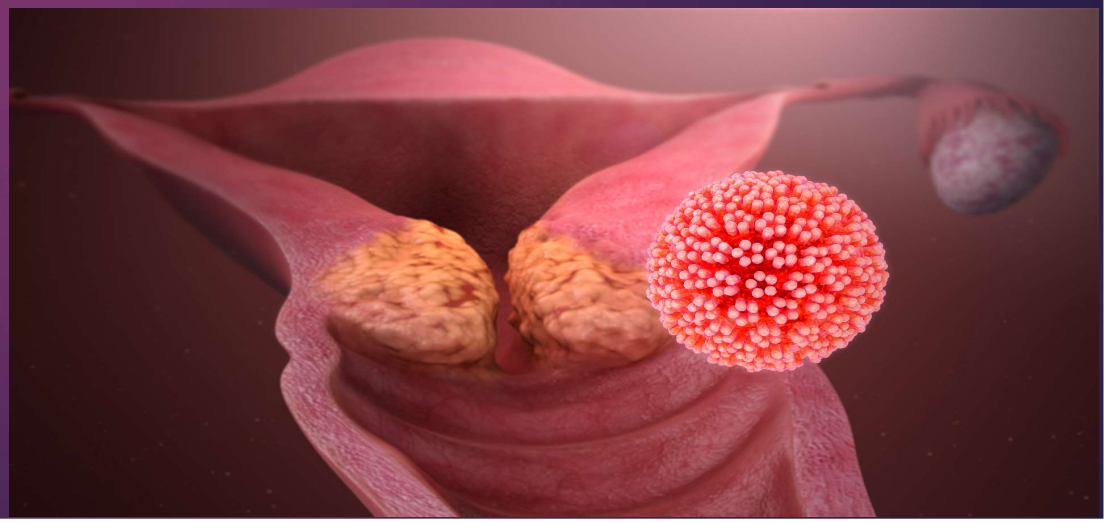
Guidelines for the management of patients with cervical cancer Update 2023

DR. EHAB AL-RAYYAN



ESGO/ESTRO/ESP Guidelines for the management of patients with cervical cancer — Update 2023*

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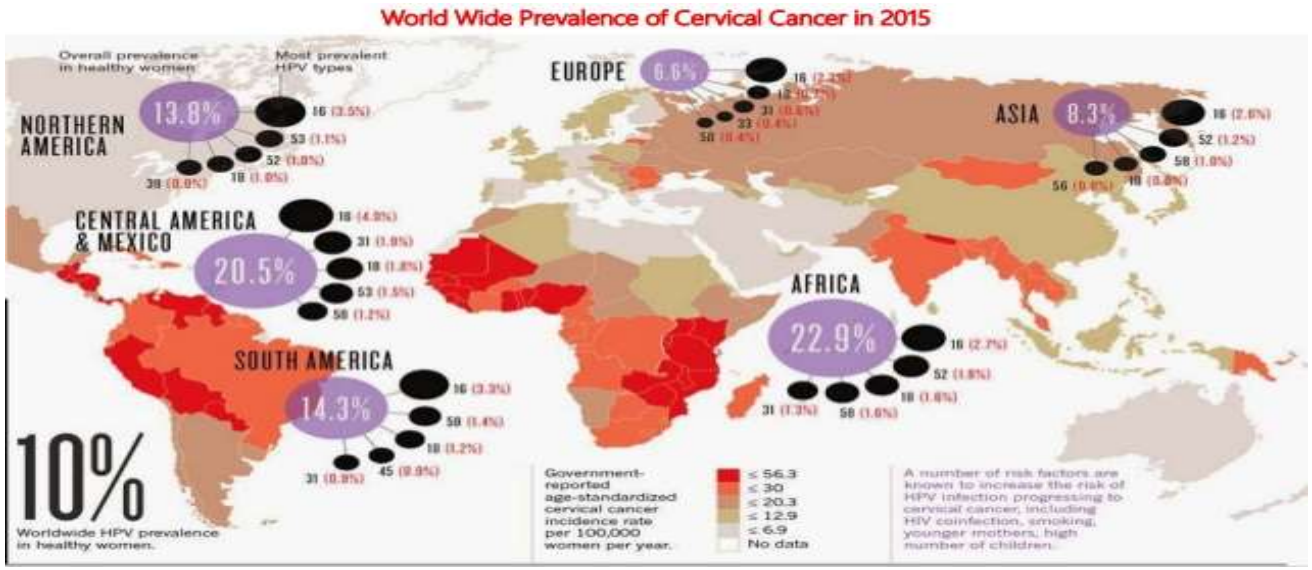
- **ESGO** European Society of Gynecological Oncology
- **ESTRO** European Society for Radiotherapy and Oncology
- **ESP** European Society of Pathology

Introduction

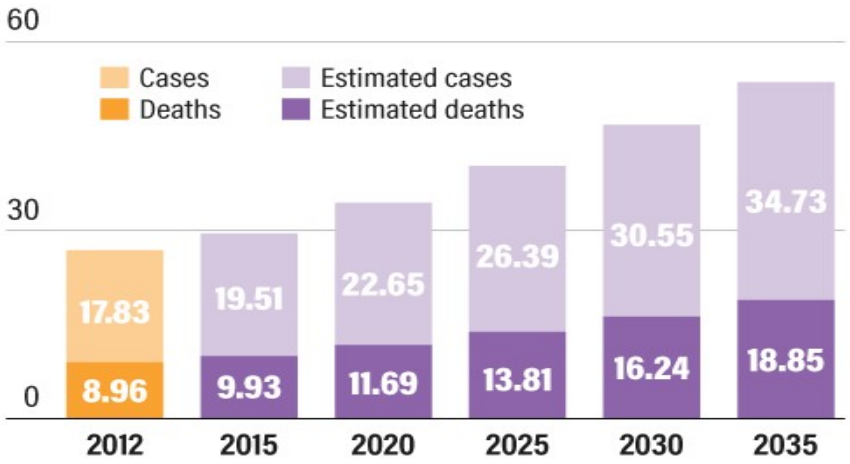
- Cervical cancer major public health problem
- 4th most common cause cancer incidence and mortality in women world-wide

- Geographical variation
- Prevalence HPV
- Coverage screening
- Adequate treatment



Prevalence

Cervical cancer deaths are expected to more than double between 2012 and 2035 (thousand)



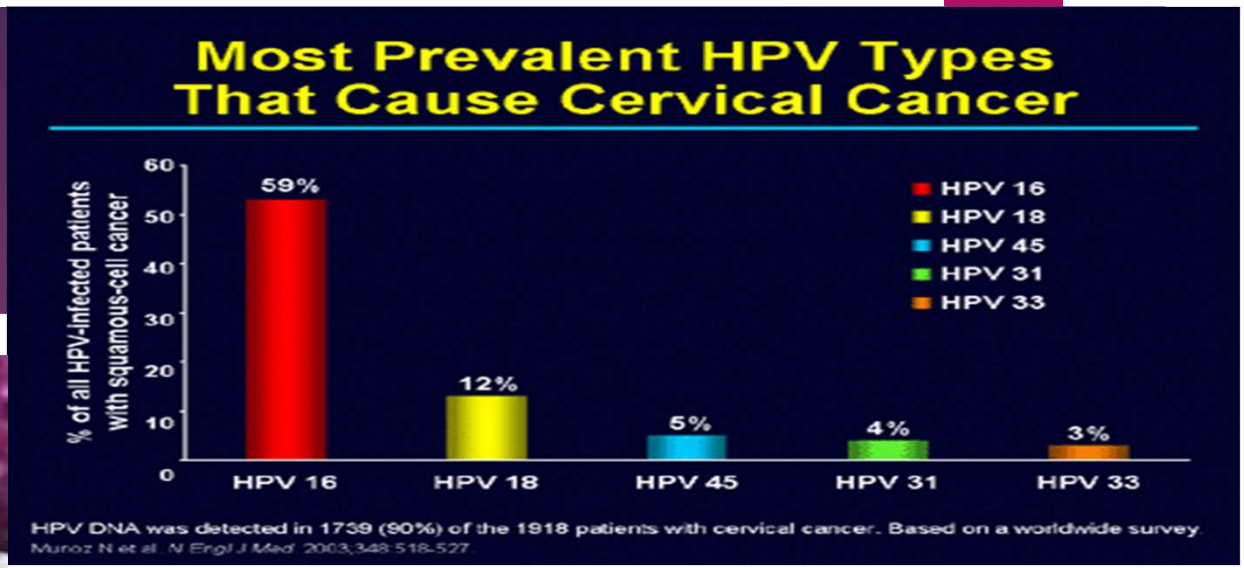
HPV rates, cervical cancer cases and deaths

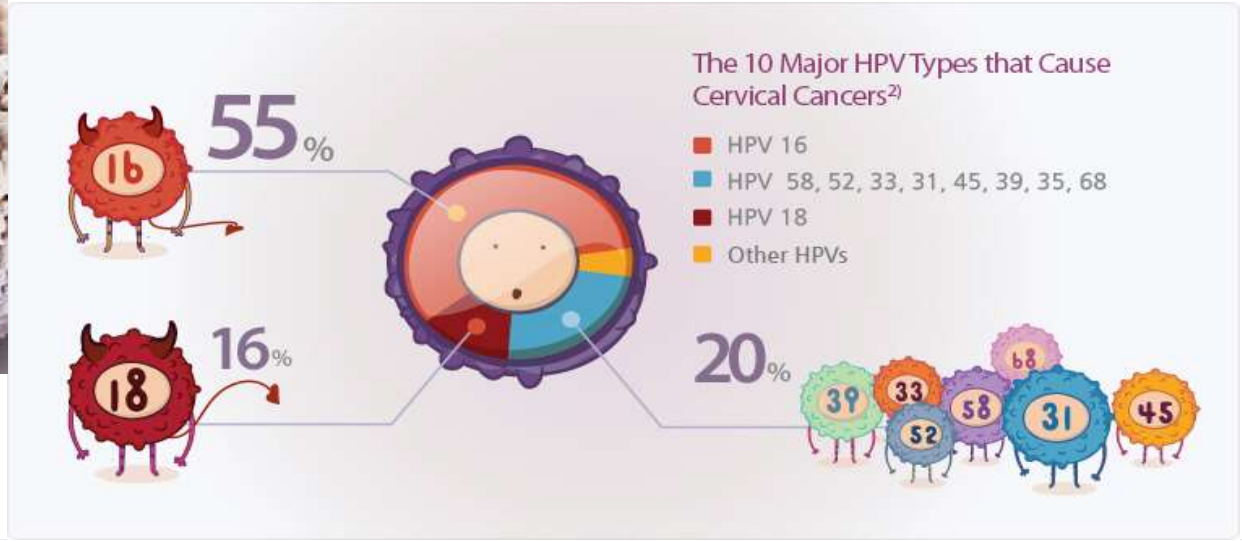
Country	HPV prevalence (%)	Cervical cancer cases	Cervical cancer deaths
Morocco	24.5	2,258	1,076
Turkey	13.2	1,686	663
Algeria	6.1	1,288	510
Iraq	15.65	291	142
Tunisia	14.6	265	103
Saudi Arabia	28.6	241	84
Libya	10.7	241	95
Lebanon	10.2	113	42
UAE	3.5	93	28

Sources: who.int, hpvcentre.net, cdc.gov

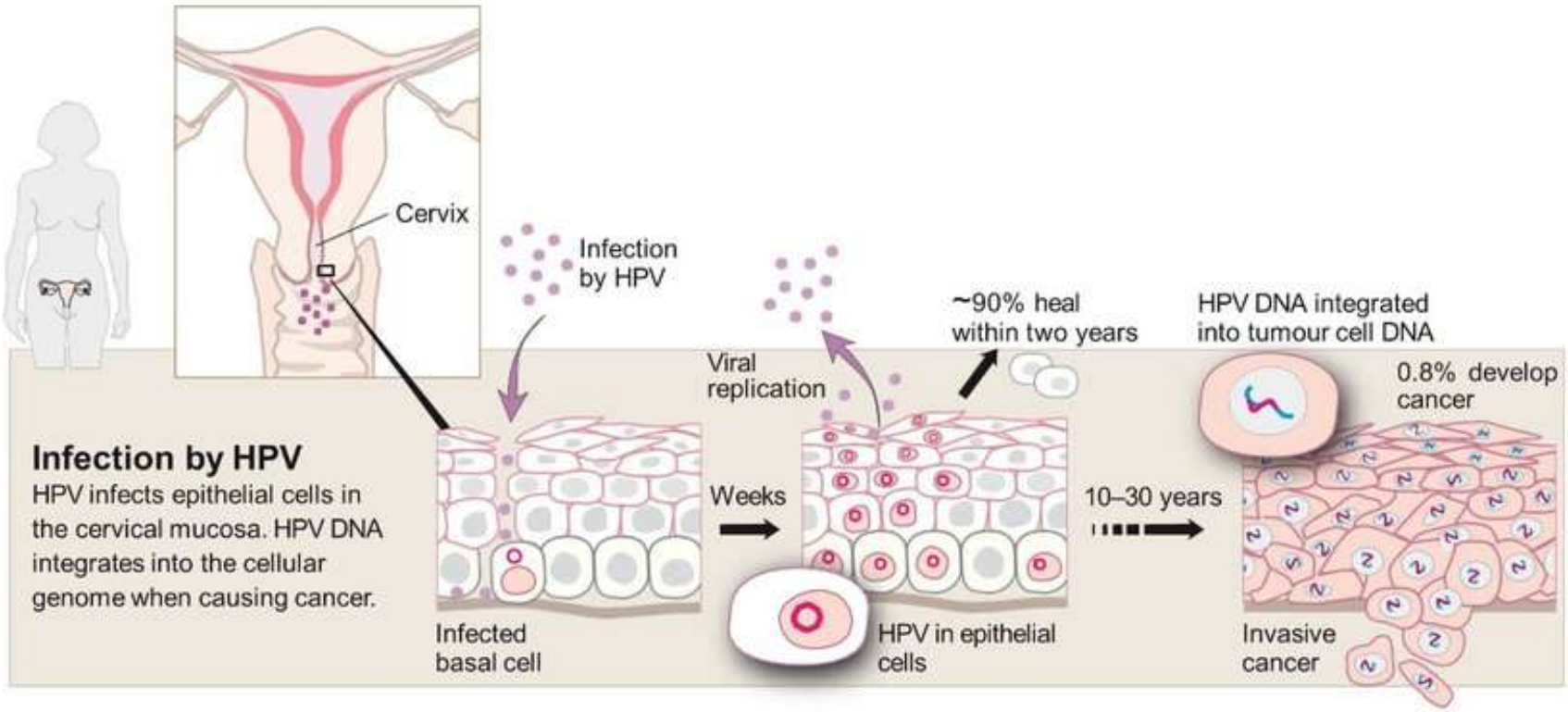
Cause


HPV
Cancer cell


Most Prevalent HPV Types That Cause Cervical Cancer
% of all HPV-infected patients with squamous-cell cancer
60
50
40
30
20
10
0
59%
12%
5%
4%
3%
HPV 16
HPV 18
HPV 45
HPV 31
HPV 33
HPV DNA was detected in 1739 (90%) of the 1918 patients with cervical cancer. Based on a worldwide survey.
Munoz N et al. N Engl J Med 2003;348:518-527


The 10 Major HPV Types that Cause Cervical Cancers2)
HPV 16
HPV 58, 52, 33, 31, 45, 39, 35, 68
HPV 18
Other HPVs
55%
16%
20%
16
18
39
33
52
58
68
31
45

Pathogenesis



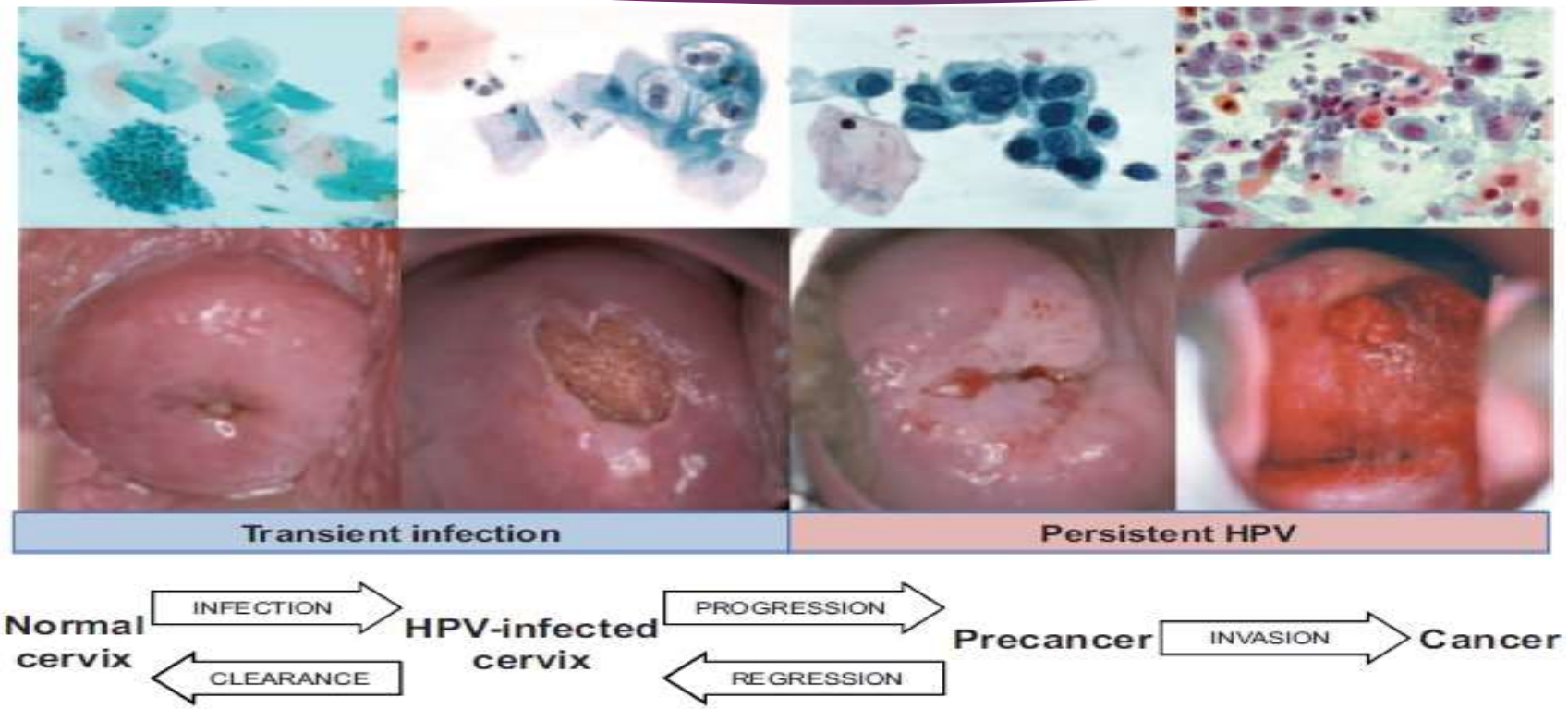
Risk factors

TABLE 1
Cervical Cancer Risk Factors

Human papillomavirus infection
First intercourse at an early age
Multiple sex partners
Lack of regular Pap tests
History of sexually transmitted infections
HIV/AIDS
Multiparity
Immunodeficiency
Long-term oral contraception use (> 5 years)
Smoking
Low socioeconomic status
Poor access to health care

Sources: Whyte. *Consultant*. 2012[2]; Leaver and Labonte. *Radiation Therapist*. 2010[7]; Lea and Lin. *Obstet Gynecol Clin North Am*. 2012.[9]

Pathogenesis



Old Staging become history

- **FIGO guidelines for cervical cancer staging include:**

- Invasive procedures (cystoscopy, recto-sigmoidoscopy)
- Plenty of time-consuming "old fashioned" imaging methods
  (barium enema, intravenous urography, lymphangiography, chest and skeletal radiographs)
- Today, rarely used in clinical practice.

Limitation FIGO clinical staging

- Lead to **under or over estimation** of the extent of disease at diagnosis,
  Adversely affecting patient optimal care.

- Literature data report clinical wrong staging in:

- *Up to 32%* *of patients with early disease (< FIGO ⅡB) and*
- *Up to 65%* *patients with advanced disease (FIGO Ⅱ-Ⅳ)*

Subak, Obstet Gynecol 1995, Bhosale ,*Comput Assist Tumor 2010*

Staging

- **Difficulties of clinical staging include assessment**
  - Endocervical tumor growth to the (not accessible)
  - Parametriam involvement (not accurate)
  - Lymph node involvement (impossible)

- currently, increased use of **cross sectional imaging modalities** (CT), (MRI), (PET-CT)

Staging 2022

TNM	FIGO	Description
Tx		Primary tumor cannot be assessed
T0		No evidence of primary tumor
Tis		Preinvasive carcinoma
T1	I	The carcinoma is strictly confined to the cervix (extension to the uterine corpus should be disregarded)
T1a	IA	Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion < 5 mm[a]
T1a1	IA1	Measured stromal invasion depth of < 3 mm
T1a2	IA2	Measured stromal invasion depth ≥ 3 mm and < 5 mm
T1b	IB	Invasive carcinoma with measured deepest invasion of ≥ 5 mm (greater than Stage IA), lesion limited to the cervix uteri[b]
T1b1	IB1	Invasive carcinoma with measured deepest stromal invasion of ≥ 5 mm, and greatest dimension of < 2 cm
T1b2	IB2	Invasive carcinoma with greatest dimension of ≥ 2 cm and < 4 cm
-	IB3[d]	Invasive carcinoma with greatest dimension of > 4 cm
T2	II	The carcinoma invades beyond the uterus, but has not extended into the lower third of the vagina or to the pelvic wall
T2a	IIA	Involvement limited to the upper two-thirds of the vagina without parametrial invasion
T2a1	IIA1	Invasive carcinoma with greatest dimension of < 4 cm
T2a2	IIA2	Invasive carcinoma with greatest dimension of ≥ 4 cm
T2b	IIB	With parametrial involvement but not up to the pelvic wall
T3	III	The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or nonfunctioning kidney and/or involves pelvic and/or para-aortic lymph nodes[c]
T3a	IIIA	The carcinoma involves the lower third of the vagina, with no extension to the pelvic wall
T3b	IIIB	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney (unless known to be due to another cause)
N[d]	IIIC[d]	Involvement of pelvic and/or para-aortic lymph nodes, irrespective of tumor size and extent (with r and p notations)[c]
	IIIC1[d]	Pelvic lymph node metastasis only
	IIIC2[d]	Para-aortic lymph nodes metastasis
T4	IV	The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum (the presence of bullous edema is not sufficient to classify a case as Stage IV)
	IVA	Spread to adjacent pelvic organs
M1	IVB	Spread to distant organs

Prognostic Factors

- Maximum tumor size
- Extracervical tumor extension
- LN involvement (number, location, size, metabolic activity)
- Pathological tumor type- HPV status
- Depth cervical stromal invasion
- Minimal thickness of uninvolved cervical stroma
- Margin status
- LVSI
- Presence distant metastases

Diagnostic Work-up

For Local disease - **Clinical and Radiological work-up**

- Pelvic exam and biopsy +- colposcopy >>>>> mandatory to diagnosis

- Pelvic MRI >>>>> mandatory for
  - Initial assessment
  - Guide treatment options

- ULS Endovaginal/transrectal >>>>> optional

- Cystoscopy or Proctoscopy >>>>> not routinely recommended

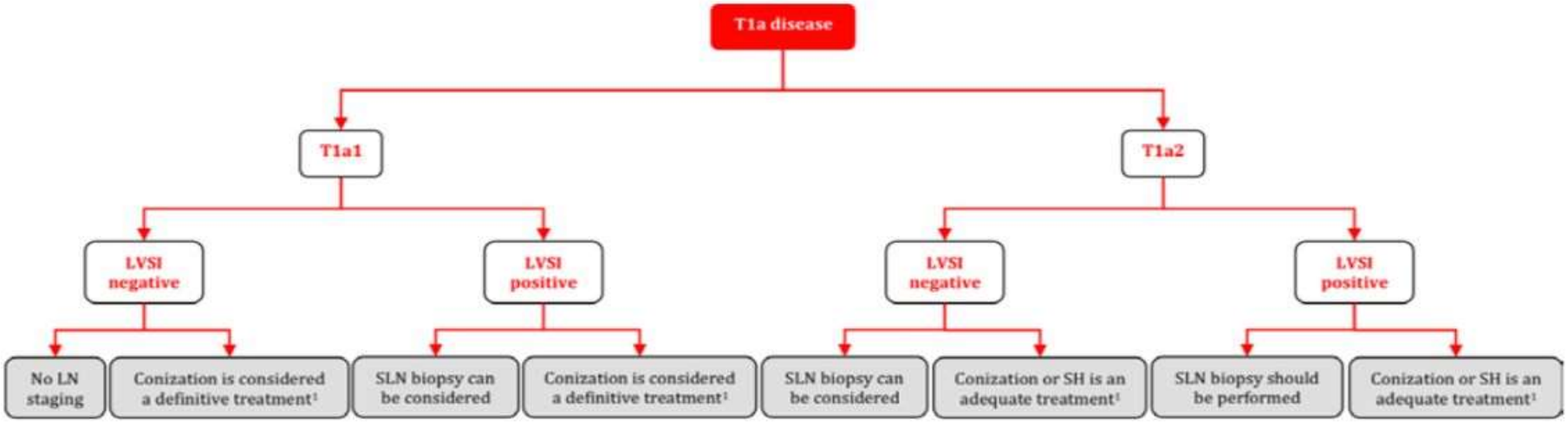
Diagnostic Work-up

For Nodal/Distant Diagnostic Work-up

- In early stages T1B1, T1B2, T2a1
  - Surgery PLND >>>>> standard treatment
  - Except for T1a1, T1a2 –ve LVSI

- In locally advanced stages T1b3 and higher (except T2a1)
  - PET CT recommended,
  - CT (if PET is not available)

Management of T1a Disease



LN lymph node; LVSI lymphovascular space involvement; SH simple hysterectomy; SLN sentinel lymph node

[1]Patients with adenocarcinoma who have completed childbearing should be offered simple hysterectomy

Management T1a1 disease (<3mm invasion)

- Diagnosis based on conization (depth invasion, margins, LVSI)
- Loop or Laser preferable to cold-knife for fertility preservation
- Surgical margins should be clear for invasion and preinvasion (except LSIL)
- If +ve margins >>>> repeat conization should be performed
- LN staging is not indicated when –ve LVSI
- Conization considered definitive treatment
- Hysterectomy dose not improve outcome in SCC
- SH should be offered adenocarcinoma who completed childbearing
- Radical surgery is overtreatment >>>>> should not be performed

Management T1a2 disease (3-5mm invasion)

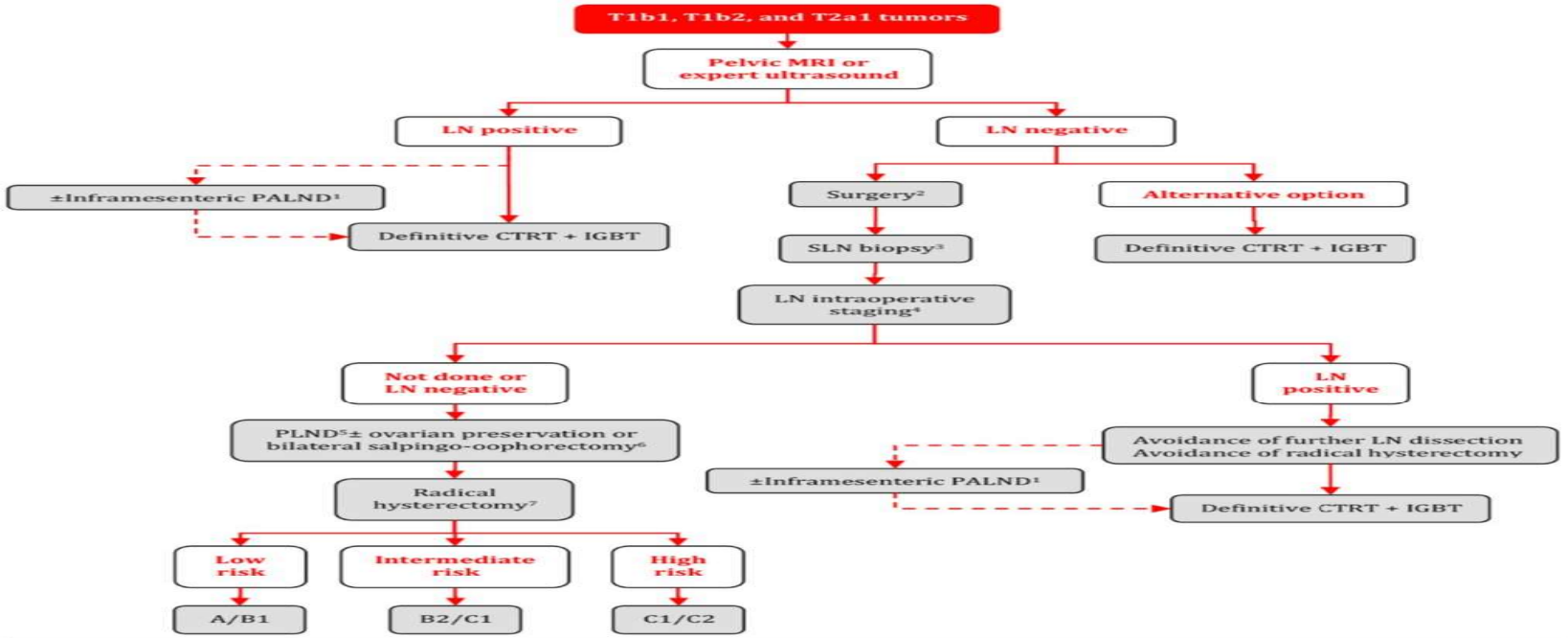
- Conization alone or SH is adequate treatment

- Parametrial resection is not indicated

- SLN biopsy
  - Can be considered –ve LVSI
  - Should be performed +ve LVSI

- SH should be offered adenocarcinoma for completed childbearing pt

Primary Treatment of T1b1, T1b2, and T2a1 Tumors



CTRT chemoradiotherapy; IGBT image-guided brachytherapy; LN lymph node; MRI magnetic resonance imaging; PALND paraaortic lymph node dissection; SLN sentinel lymph node.

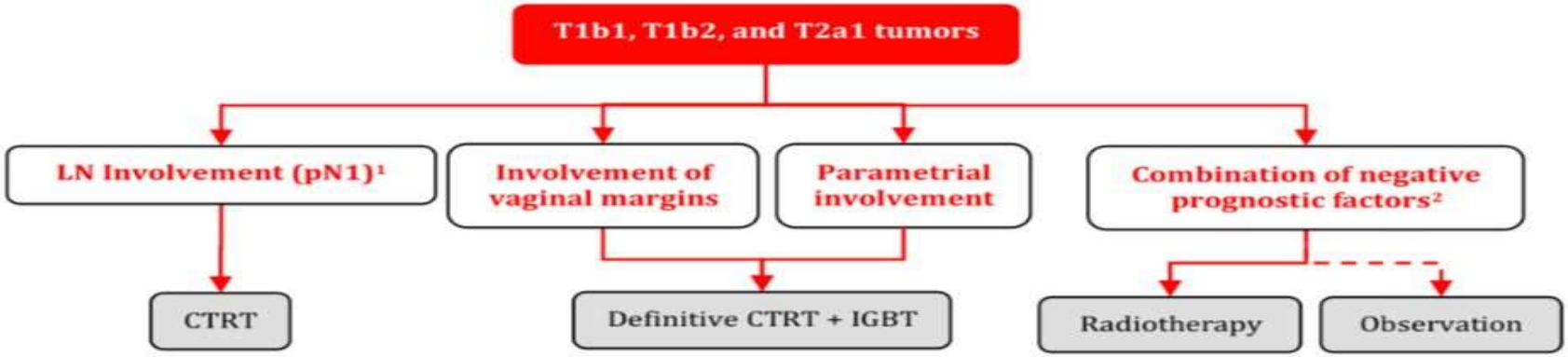
[1]PALND at least up to inferior mesenteric artery may be considered for staging purposes; [2]Laparotomy is the standard approach for all procedures which include radical parametrectomy. Minimally invasive surgery is an acceptable approach for LN staging; [3]SLN biopsy before pelvic lymphadenectomy should be performed. If SLN is not detected on either side, LN dissection should include on that particular pelvic side the removal of lymphatic tissue from all traditional regions including obturator fossa, external iliac regions, commoniliac regions, and presacral region; [4]Intra-operative assessment of LN status (evaluated by frozen section) is recommended. Sentinel nodes from both sides of the pelvis and/or any suspicious LN should be sent for intra-operative assessment; [5]If SLN are negative on frozen section, a systematic pelvic lymphadenectomy should be performed as the standard LN staging. If SLN is negative bilaterally in the pelvic level I area (below iliac bifurcation) LN dissection can be limited to level I; [6]Ovarian preservation should be discussed with women in reproductive age with squamous cell carcinoma, can be considered in HPV-associated adenocarcinoma and is not recommended for HPV-independent adenocarcinomas. Opportunistic bilateral salpingectomy should be performed if ovaries are preserved; [7]The type of radical hysterectomy (extent of parametrial resection, type A-C2) should be based on the presence of prognostic risk factors identified preoperatively such as tumor size, maximum stromal invasion, and lymphovascular space involvement, which are used to categorize patients at high, intermediate, and low risk of treatment failure. Complete description of the template used for radical hysterectomy should be present in the surgical report. The 2017 modification of the Querleu-Morrow classification is recommended as a tool.

Management T1b1,T1b2, T2a1 (5mm-4cm, upper vag.)

- Aim avoid combined radical surgery and radiotherapy
- Minimally invasive
  - should not be uses
  - may be considered low risk tumor (<2cm and free margin after conization)
- SLN first step of surgical management
- SLN using Indocyanine green >>> preferred

  Blue dye with radiocolloid >>> alternative
- Ovarian preservation
  - Squamous cell carcinoma
  - HPV-associated adenocarcinoma

Adjuvant Treatment of T1b1, T1b2, and T2a1 Tumors



CTRT chemoradiotherapy; IGBT image-guided brachytherapy.

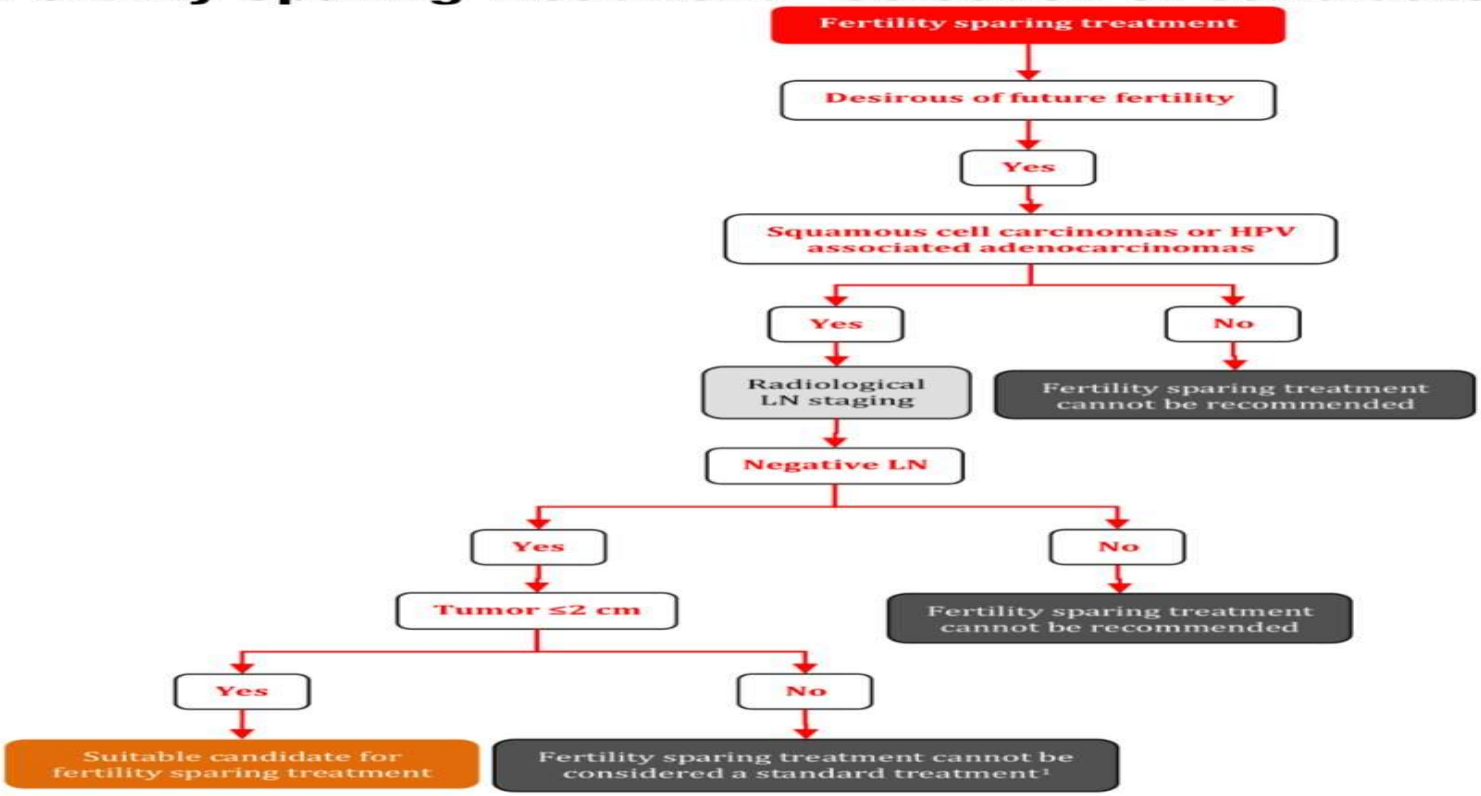
[1]Adjuvant CTRT is indicated in patients with metastatic involvement of pelvic lymph nodes (macrometastases pN1 or micrometastases pN1(mi)) on final pathologic assessment. It may also be considered if only isolated tumour cells are detected in sentinel lymph node, although its prognostic impact remains uncertain; [2]Adjuvant radiotherapy should be considered in the intermediate risk group (combination of risk factors at final pathology such as tumour size, lymphovascular space involvement, and depth of stromal invasion). When in these situations an adequate type of radical hysterectomy has been performed, observation is an alternative option, especially in teams experienced in this approach.

SEDLIS CRITERIA FOR EXTERNAL PELVIC RADIATION AFTER RADICAL HYSTERECTOMY IN NODE-NEGATIVE, MARGIN-NEGATIVE, PARAMETRIA-NEGATIVE CASES[1-4]

LVSI	Stromal Invasion	Tumor Size (cm) (determined by clinical palpation)
+	Deep 1/3	Any
+	Middle 1/3	≥2
+	Superficial 1/3	≥5
-	Middle or deep 1/3	≥4

LVSI: Lymphovascular space invasion

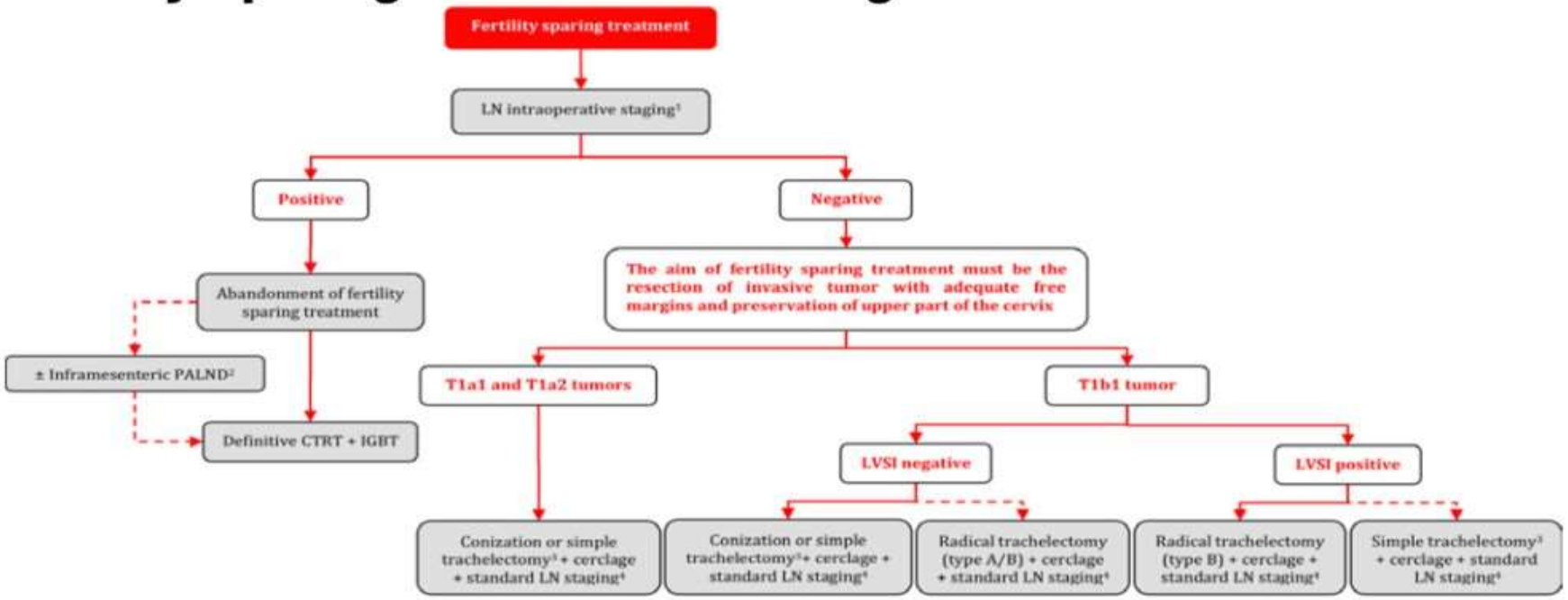
Fertility Sparing Treatment – Selection of Candidates



LN lymph node.

[1]Pelvic lymph node staging (sentinel lymph node) should always be the first step in each fertility sparing therapy procedure (except for T1a1 lymphovascular space involvement negative disease). All sentinel lymph nodes from both sides of the pelvis and any suspicious LN should be sent for frozen section. If sentinel lymph node cannot be detected on either pelvic side, a systematic pelvic lymphadenectomy should be performed on that side. Intraoperative assessment of LN status is highly recommended.

Fertility Sparing Treatment – Management



CTRT chemoradiotherapy; IGBT image-guided brachytherapy; LN lymph node; LVSI lymphovascular space involvement; PALND paraaortic lymph node dissection.

[1]Pelvic lymph node staging (sentinel lymph node) should always be the first step in each fertility sparing therapy procedure (except for T1a1 LVSI negative disease). All sentinel lymph nodes from both sides of the pelvis and any suspicious LN should be sent for frozen section. If sentinel lymph node cannot be detected on either pelvic side, a systematic pelvic lymphadenectomy should be performed on that side. Intraoperative assessment of LN status is highly recommended; [2]PALND at least up to inferior mesenteric artery may be considered for staging purposes; [3]In patients without deep stromal involvement and with a high probability of adequate endocervical tumour free margins, simple trachelectomy can be considered; [4]LN staging follows the principles of management of early stages.

Fertility-sparing treatment

- The aim of the fertility preservation should be to
- Offer the most efficient approach
- While not increasing the oncological risk
- Not be recommended for rare histological types including:
- Neuroendocrine carcinomas,
- HPV-independent adenocarcinomas and
- carcinosarcomas.

- Prognostic factors, clinical staging, and preoperative work-up do not differ from those not considering fertility sparing therapy.

Fertility sparing therapy

- Tumors >2 cm is significantly associated with a higher risk of recurrence
- Not be considered as a standard treatment.
- The risk of recurrence must be comprehensively discussed with the patient.
- NACT followed by radical trachelectomy or cone has been described.

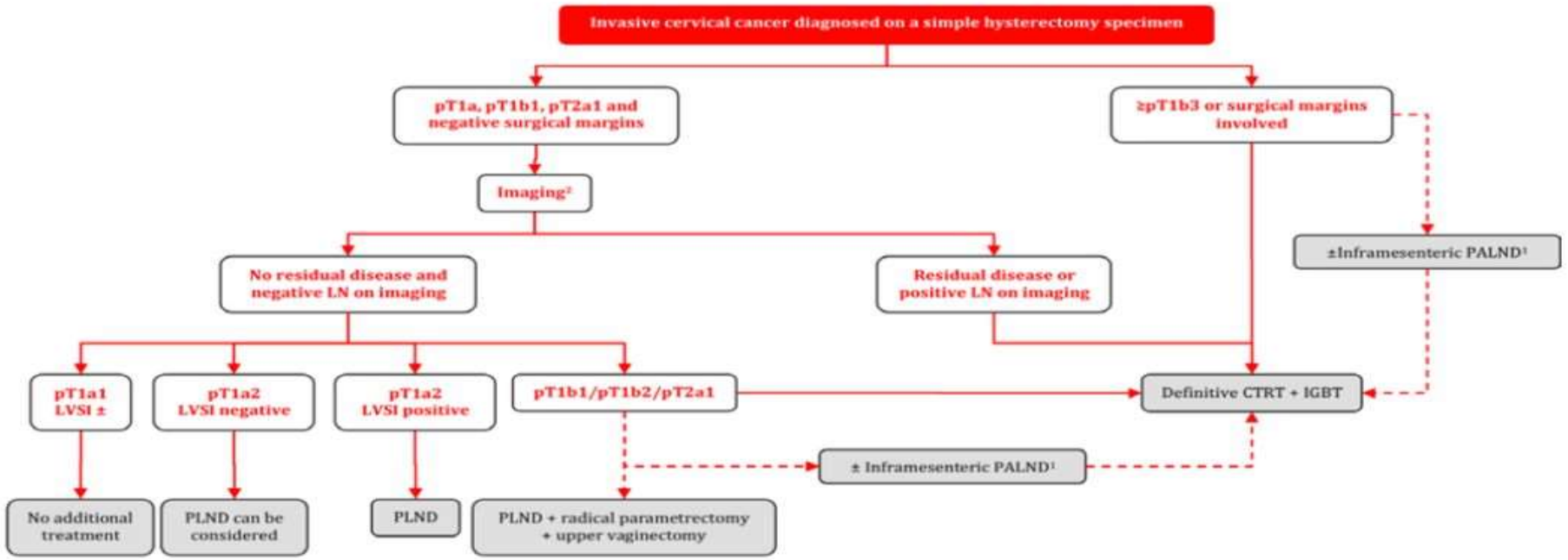
- Any pregnancy following fertility sparing therapy should be considered as a high-risk preg.
- Intraoperative placement of permanent cerclage should be performed during simple or radical trachelectomy.
- Following simple or radical trachelectomy with placement of a permanent cerclage, delivery can only be performed by cesarean section.

Fertility sparing therapy

- **Fertility sparing procedures:**
  - Conization, simple trachelectomy,
  - Radical trachelectomy, (abdominal or vaginal)
- **Other options**
  - Ovarian transposition
  - Oocyte, embryo, ovarian tissue preservation
  - Egg donation

- Routine hysterectomy after completing childbearing is not mandatory

Invasive Cervical Cancer Diagnosed on a Simple Hysterectomy Specimen



CTRT chemoradiotherapy; IGBT image-guided brachytherapy; LN lymph node; LVSI lymphovascular space involvement; PALND paraaortic lymph node dissection; PLND pelvic lymph node dissection.

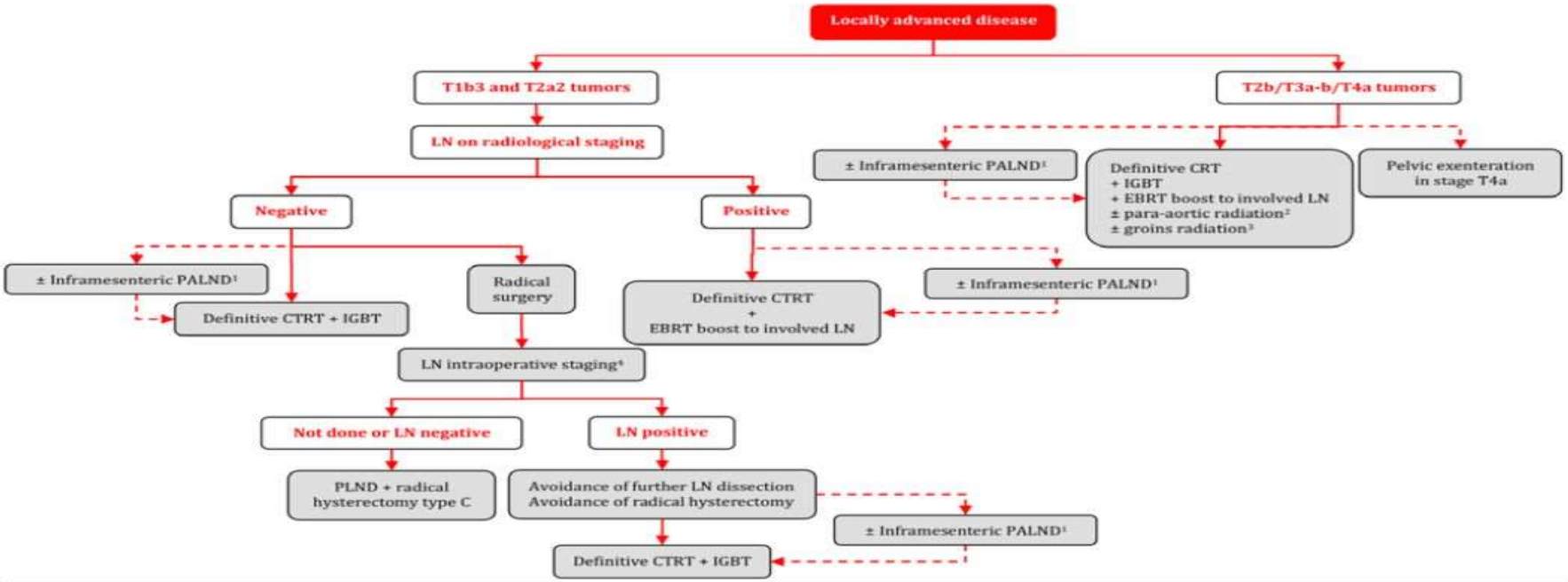
[1]PALND at least up to inferior mesenteric artery may be considered for staging purposes; [2]Optimal imaging follows the same recommendations as that for the standard management.

Diagnosed after SH

- In general, follows the principles of the standard management, and is based on pathologic findings, and clinical staging.
- Treatment strategy should aim to avoid combining further surgery and radiotherapy.

- Before making further management decisions, optimal imaging is necessary to evaluate the local and regional (nodal) disease status.
- Surgical staging of nodal disease considered as the first step of surgical management in radiologic node negative patients.
- Any suspicious LN should be sent for intraoperative assessment (frozen section).
- SLN biopsy cannot be performed in the absence of the uterus.

Management of Locally Advanced Disease



CTRT chemoradiotherapy; EBRT external beam radiotherapy; IGBT image-guided brachytherapy; LN lymph node; PALND paraaortic lymph node dissection; PLND pelvic lymph node dissection.

[1]PALND at least up to inferior mesenteric artery may be considered for staging purposes; [2]The indication for elective para-aortic irradiation can be based on the number of level 1 positive nodes (external iliac, interiliac, internal iliac) on imaging (e.g.>2 positive nodes). It should always be applied in patients who on imaging have even one positive node on imaging at level 2 (common iliac) and above. [3]The groins should also be included in the elective target for patients with tumour involvement of the lower third of the vagina; [4]LN staging should follow the same principles as in T1b1-2 tumors.

Management of locally advanced disease

- Definitive radiotherapy should include concomitant chemotherapy whenever possible.
- IGBT is an essential component of RT and should not be replaced with an external boost.
- (EBRT) with a dose of 45Gy/25 fractions or 46Gy/23 fractions
- Boosting of the **primary tumor** and/or the **parametria** by EBRT should be avoided.
- Additional dose of radiation should be applied to **pathological LN** on imaging,

- (60Gy EQD2, combined EBRT and estimated dose from IGBT).

- Concomitant weekly cisplatin is standard.

- However, weekly carboplatin can be considered as an alternative option
- Patients not suitable for cisplatin.

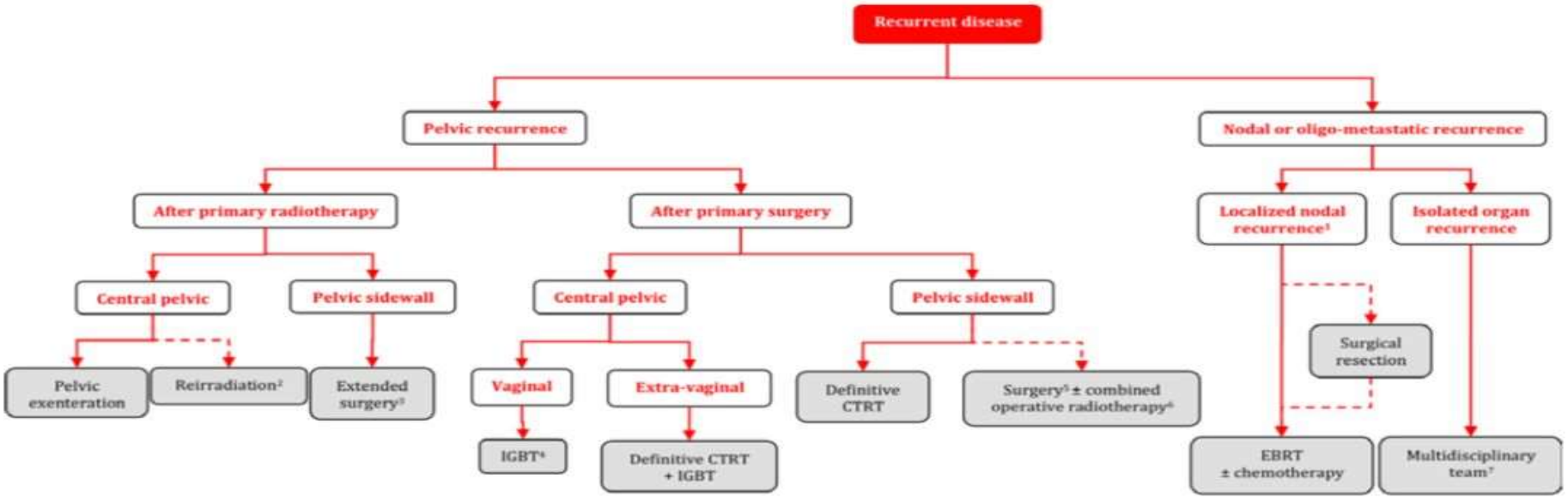
Management of locally advanced disease

- The overall treatment time including both CTRT and IGBT should not exceed 7 weeks.
- Surgical removal of large pathological PLN/PALN before CTRT is not routinely recommended.

- Not recommended outside of clinical trials:
- NACT in patients candidates for upfront definitive CTRT and IGBT
- Adjuvant CT following definitive CTRT does not improve survival and enhances toxicity
- Adjuvant hysterectomy after definitive CTRT should not be performed since it does not improve survival and is associated with increased morbidities.

- Patients with a persistent tumor 3–6 months after definitive CTRT and BT and without evidence of regional or metastatic disease should be referred salvage surgery.

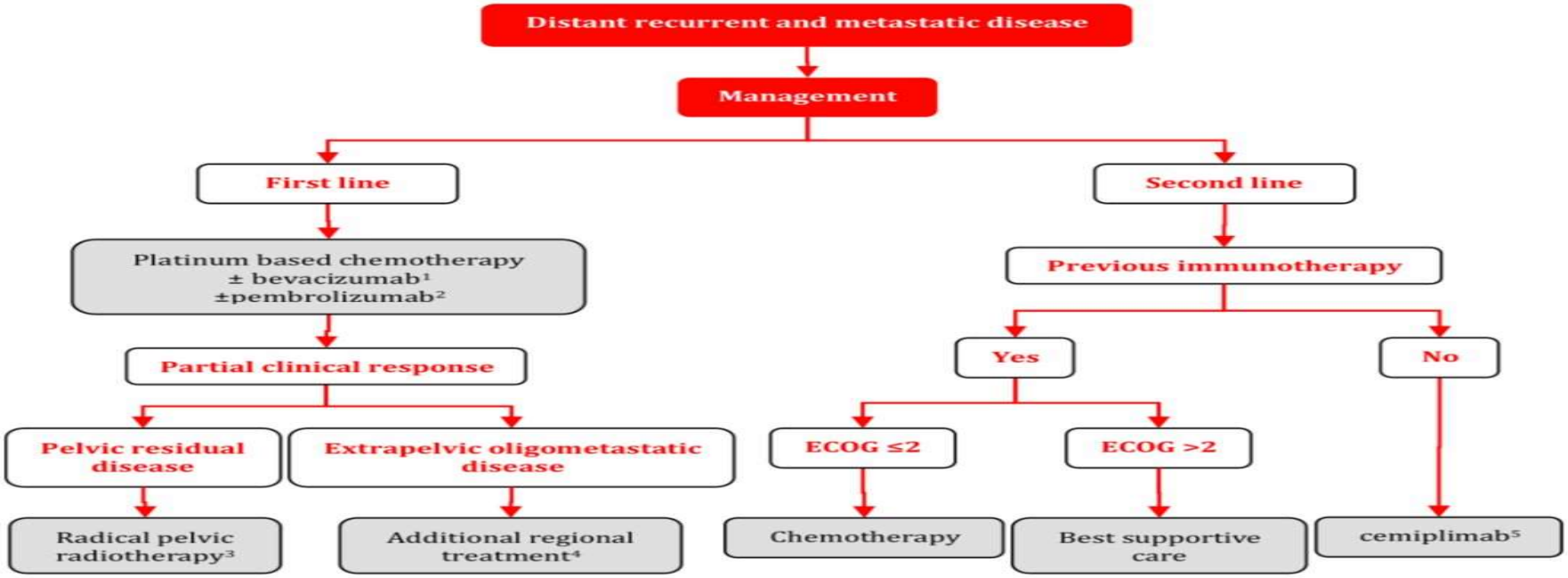
Recurrent Disease



CTRT chemoradiotherapy; EBRT external beam radiotherapy; IGBT image-guided brachytherapy.

[1]Localized para-aortic, mediastinal, and/or peri-clavicular recurrences out of previously irradiated fields may be treated by radical EBRT with or without chemotherapy; [2]Reirradiation with image-guided adaptive brachytherapy for central recurrences could be considered in selected patients taking into account volume of the disease, or time from the primary radiotherapy and total dose administered initially; [3]In patients with pelvic sidewall involvement, extended pelvic surgery can be considered in specialized centres. Surgery must aim to a complete tumour resection (R = 0) also with the help of special techniques (extended endopelvic resection, out of box procedures), if required; [4]Small superficial lesions (ie, <5 mm thickness) in the vagina may be treated by IGBT; [5]When radical radiotherapy is not feasible, extended pelvic surgery can be considered. Surgery must aim to a complete tumour resection (R=0) also with the help of special techniques (extended endopelvic resection, out of box procedures), if required; [6]Combined operative-radiotherapy procedures using intra-operative radiotherapy or IGBT are an option if free surgical margins are not achievable; [7]Treatment options are represented by local resection, thermal ablation, interventional brachytherapy, or stereotactic ablative radiotherapy according to the size and localization.

Distant Recurrent and Metastatic Disease



ECOG: Eastern Cooperative Oncology Group

[1]The addition of bevacizumab to platinum-based chemotherapy is recommended when the risk of significant gastrointestinal/genitourinary toxicity has been carefully assessed and discussed with the patient; [2]The addition of pembrolizumab to platinum-based chemotherapy is recommended in patients with PD-L1 positive tumours, assessed as combined positive score of 1 or more; [3]The patients with distant metastatic disease at diagnosis, who have responded to systemic chemotherapy, could be considered for additional radical pelvic radiotherapy (including image-guided brachytherapy in selected cases); [4]Those with residual oligometastatic disease after systemic treatment could also be considered for additional regional treatment (surgery, thermal ablation, radiotherapy) to involved sites; [5]Patients who progressed after first-line platinum based chemotherapy should be offered anti PD-1 cemiplimab if they had not previously received immunotherapy).

Recurrence

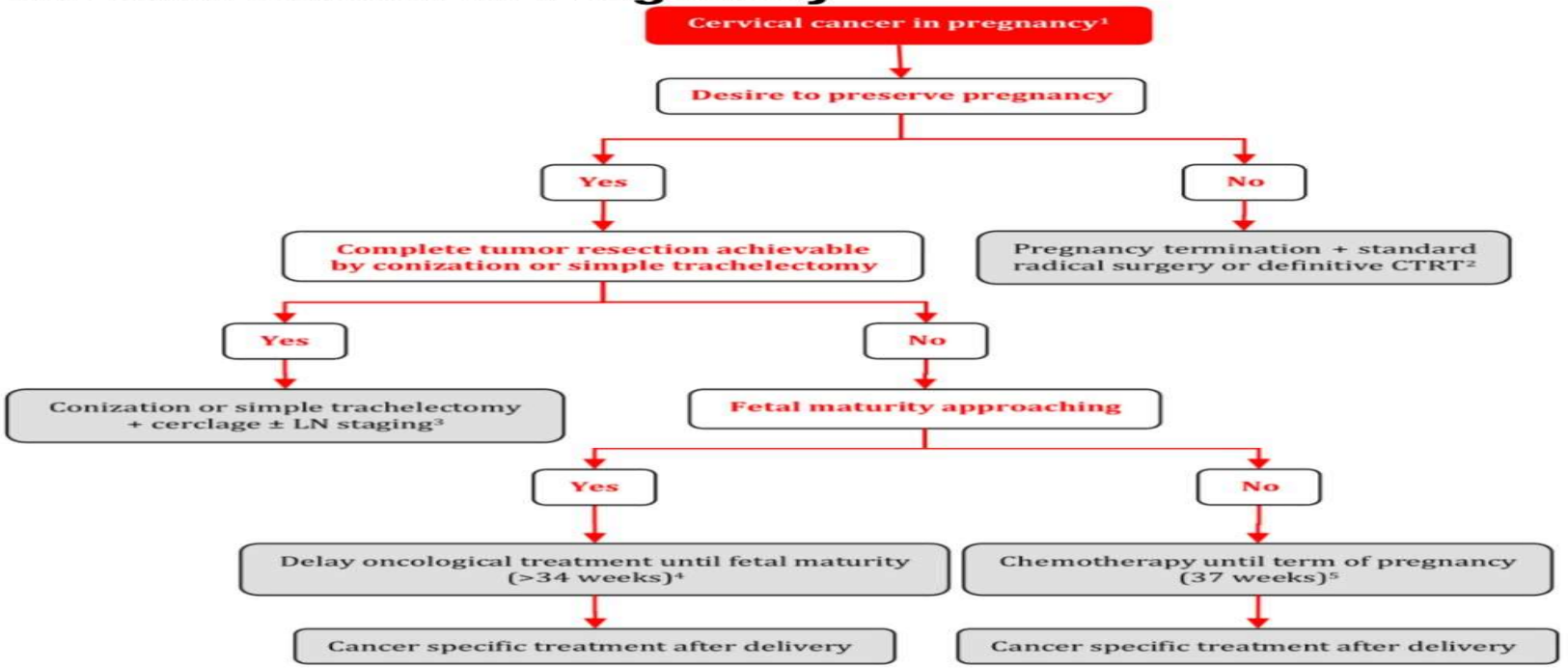
- The aim of the diagnostic work-up is to determine the extent of the locoregional and/or mets
- The recurrence should be confirmed by histological examination if feasible.

- **Should not be considered as candidates for radical treatment.**
  - Patients with multiple nodal/distant metastases or
  - Multifocal local disease
  - Extensive pelvic wall involvement
- **Should be considered for radical and potentially curative treatment options.**
  - Patients with oligometastatic or oligorecurrent disease
- Prognostic factors should be balanced in relation to the major morbidity caused by treatment.

Oncological follow-up

- Patients should be educated about symptoms and signs of potential recurrence.
- Appropriate imaging test (MRI, ultrasound, CT scan or PET-CT should be used in symptomatic women.
- In case of suspected tumor persistence, recurrence or second primary cancer, histological verification is strongly recommended.
- Vaginal vault cytology is not recommended.
- After fertility sparing treatment, follow-up should include HPV testing (at 6–12 and 24 months).

Cervical Cancer in Pregnancy



CTRT chemoradiotherapy; LN lymph node.

[1]Several treatment modalities are available and should be discussed with the patient taking into account the tumour stage, gestational week of pregnancy and patient´s preferences; [2]Standard treatment according to the disease stage as recommended outside pregnancy, if the woman decides not to preserve the pregnancy. Pregnancy termination is recommended before any treatment after the first trimester, and fetus evacuation before CTRT; [3]The aim is to completely remove the tumour, obtain free margins and perform nodal staging if needed, with the intention to preserve the pregnancy; [4]This option might be considered if the fetal maturity is approaching; Delay of oncological treatment until fetal maturity (if possible > 34 weeks of gestation) and initiate cancer-specific treatment immediately after delivery by cesarean section; [5]In patients with locally advanced disease or residual tumour after surgical procedure that cannot be completely removed (risk of premature rupture of amniotic membranes and/or cervical insufficiency), chemotherapy based on cisplatin or carboplatin can be considered starting after 14 weeks of pregnancy. Combination with taxanes is an option. Bevacizumab and checkpoint inhibitors are contraindicated. Before starting each cycle of chemotherapy, an assessment of treatment response should be made by clinical examination and transvaginal or transrectal ultrasound. If no response is achieved after 2 cycles of chemotherapy during pregnancy, treatment strategy should be re-evaluated. At least a two-week interval between chemotherapy and surgery is recommended.

Cervical Cancer in Pregnancy

- Every patient must be counseled by a multidisciplinary team.
- Gynecological oncology, neonatology, obstetrics, pathology, anesthesiology, radiation oncology, medical oncology, psycho-oncology, and, spiritual and ethical counseling.

- Recommend a treatment plan according to
- Patient's intention,
- Tumor stage, and
- Gestational age of pregnancy at the time of cancer diagnosis. T

Clinical and Imaging Diagnosis

- Pathological confirmation via colposcopy oriented biopsy or small cone
- Appropriate only during the first trimester of pregnancy,
- Endocervical curettage is contraindicated).

- Preferred imaging modalities for clinical staging include
- Pelvic MRI or expert ultrasound
- Gadolinium-based contrast agents should be avoided.
- If not available, chest CT scan with abdominal shielding is an alternative.
- PET-CT should be avoided during pregnancy.

Oncological Management

- Tumor involvement of suspicious nodes should be histologically confirmed.
- Minimally invasive approach could be considered before 14–16 weeks of gestation.
- Several treatment modalities are available and should be discussed with the patient.
- Conization or simple trachelectomy in order to
  - completely remove the tumor,
  - obtain free margins and
  - perform nodal staging if needed,
  - with the intention to preserve the pregnancy.

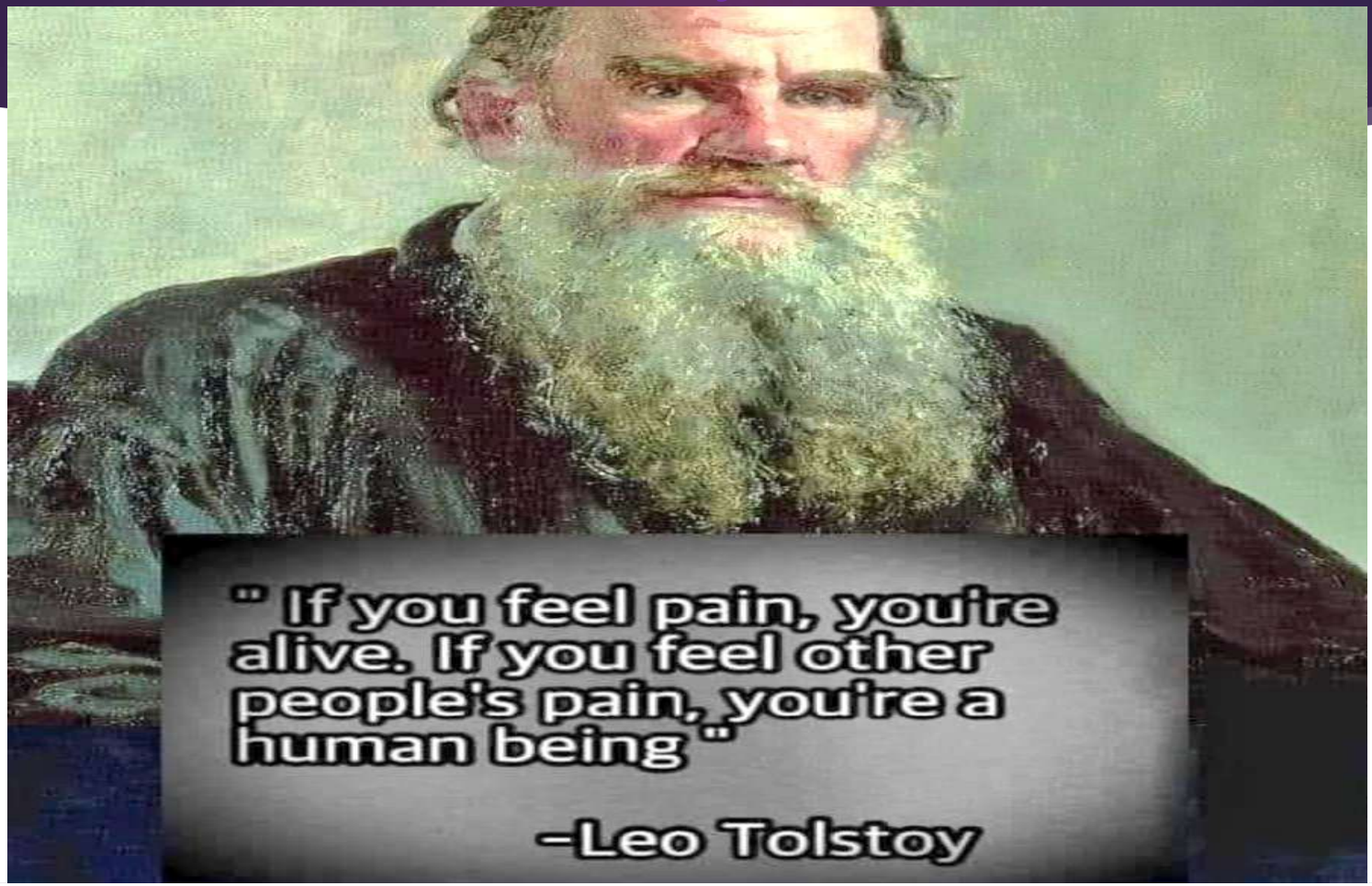
Oncological Management

- Radical surgery or definitive CTRT are recommended outside pregnancy.
- Chemotherapy until term of pregnancy (37 weeks of gestation)
- At least a 2week interval between chemotherapy and surgery is recommended.
- Chemotherapy based on cisplatin or carboplatin can be considered after 14 weeks
- Combination with taxanes is an option.
- Bevacizumab and checkpoint inhibitors are contraindicated.
- Before starting each cycle of CT, an assessment of treatment response should be made,
- If no response is achieved after 2 cycles of chemotherapy during pregnancy, treatment strategy should be re-evaluated.

Pregnancy Management

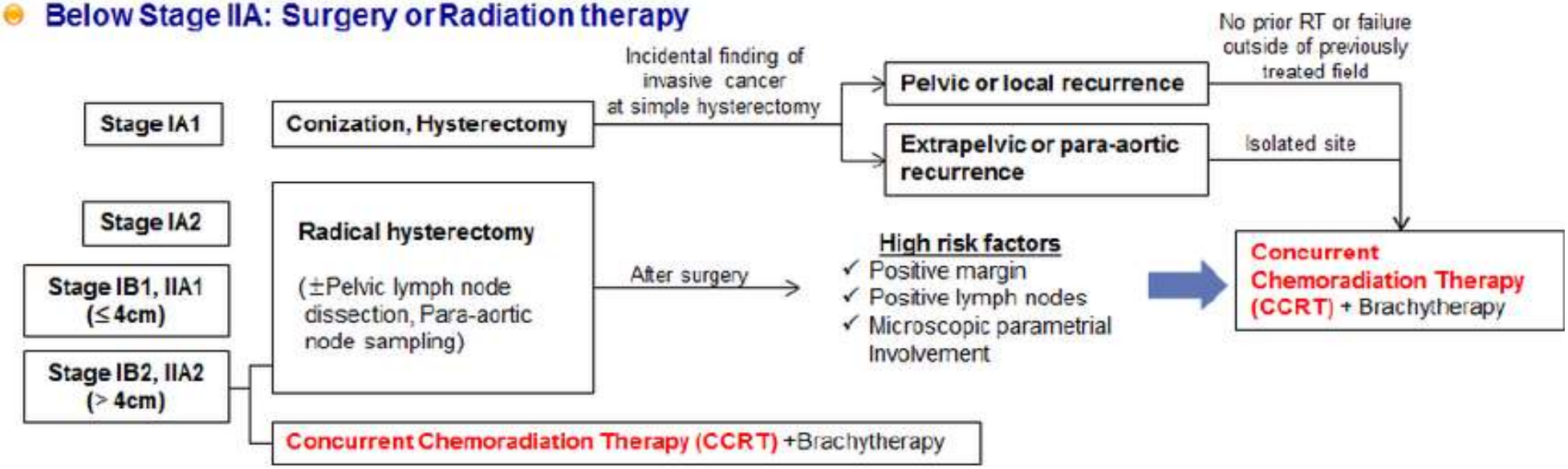
- Spontaneous delivery have negative prognostic impact in patients with cervical cancer in pregnancy.
- Thus, cesarean section is the recommended mode of delivery.
- At the time of cesarean section, definitive cancer specific treatment should be performed corresponding to that of nonpregnant women, taking into account the treatment that has already been given during pregnancy.

Thank you

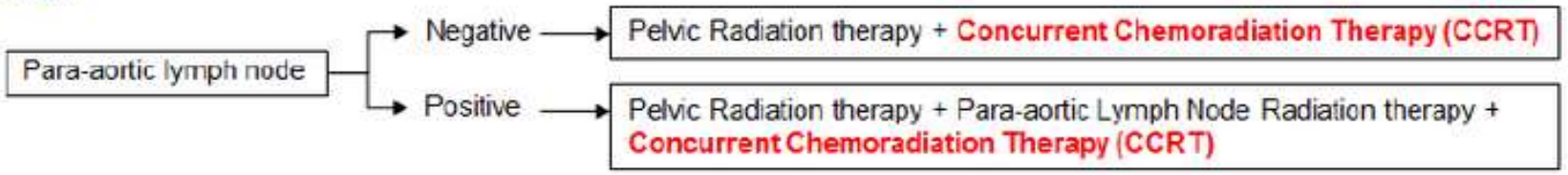

" If you feel pain, you're alive. If you feel other people's pain, you're a human being "
-Leo Tolstoy

Treatment - NCCN Guidelines

- **Below Stage IIA: Surgery or Radiation therapy**



- **Beyond Stage IIB:**



Radical surgery
Laparotomy vs laparoscopy

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 15, 2018 VOL. 379 NO. 20

Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer

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ABSTRACT

BACKGROUND

There are limited data from retrospective studies regarding whether survival outcomes after laparoscopic or robot-assisted radical hysterectomy (minimally invasive surgery) are equivalent to those after open abdominal radical hysterectomy (open surgery) among women with early-stage cervical cancer.

METHODS

In this trial involving patients with stage IA1 (lymphovascular invasion), IA2, or IB1 cervical cancer and a histologic subtype of squamous-cell carcinoma, adenocarcinoma, or adenosquamous carcinoma, we randomly assigned patients to undergo minimally invasive surgery or open surgery. The primary outcome was the rate of disease-free survival at 4.5 years, with noninferiority claimed if the lower boundary of the two-sided 95% confidence interval of the between-group difference (minimally invasive surgery minus open surgery) was greater than −7.2 percentage points (i.e., closer to zero).

RESULTS

A total of 319 patients were assigned to minimally invasive surgery and 312 to open surgery. Of the patients who were assigned to and underwent minimally invasive surgery, 84.4% underwent laparoscopy and 15.6% robot-assisted surgery. Overall, the mean age of the patients was 46.0 years. Most patients (91.9%) had stage IB1 disease. The two groups were similar with respect to histologic subtypes, the rate of lymphovascular invasion, rates of parametrial and lymph-node involvement, tumor size, tumor grade, and the rate of use of adjuvant therapy. The rate of disease-free survival at 4.5 years was 86.0% with minimally invasive surgery and 96.5% with open surgery, a difference of −10.6 percentage points (95% confidence interval [CI], −16.4 to −4.7). Minimally invasive surgery was associated with a lower rate of disease-free survival than open surgery (3-year rate, 91.2% vs. 97.1%; hazard ratio for disease recurrence or death from cervical cancer, 3.74; 95% CI, 1.63 to 8.58), a difference that remained after adjustment for age, body-mass index, stage of disease, lymphovascular invasion, and lymph-node involvement; minimally invasive surgery was also associated with a lower rate of overall survival (3-year rate, 93.8% vs. 99.0%; hazard ratio for death from any cause, 6.00; 95% CI, 1.77 to 20.30).

CONCLUSIONS

In this trial, minimally invasive radical hysterectomy was associated with lower rates of disease-free survival and overall survival than open abdominal radical hysterectomy among women with early-stage cervical cancer. (Funded by the University of Texas M.D. Anderson Cancer Center and Medtronic; LACC ClinicalTrials.gov number, NCT00614211.)

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This article was published on October 31, 2018, at NEJM.org.

N Engl J Med 2018;379:1895-904.
DOI: 10.1056/NEJMoa1806395