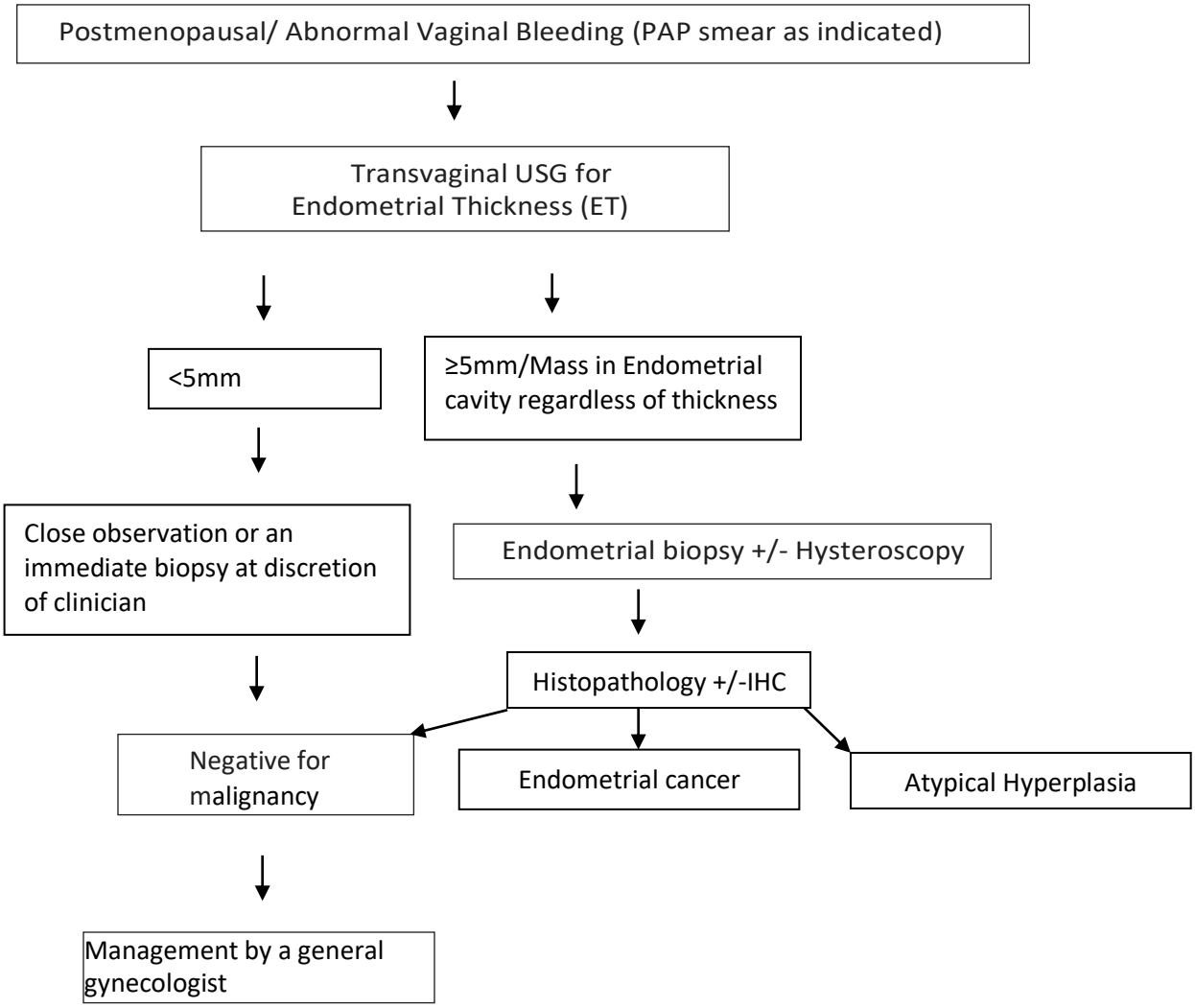
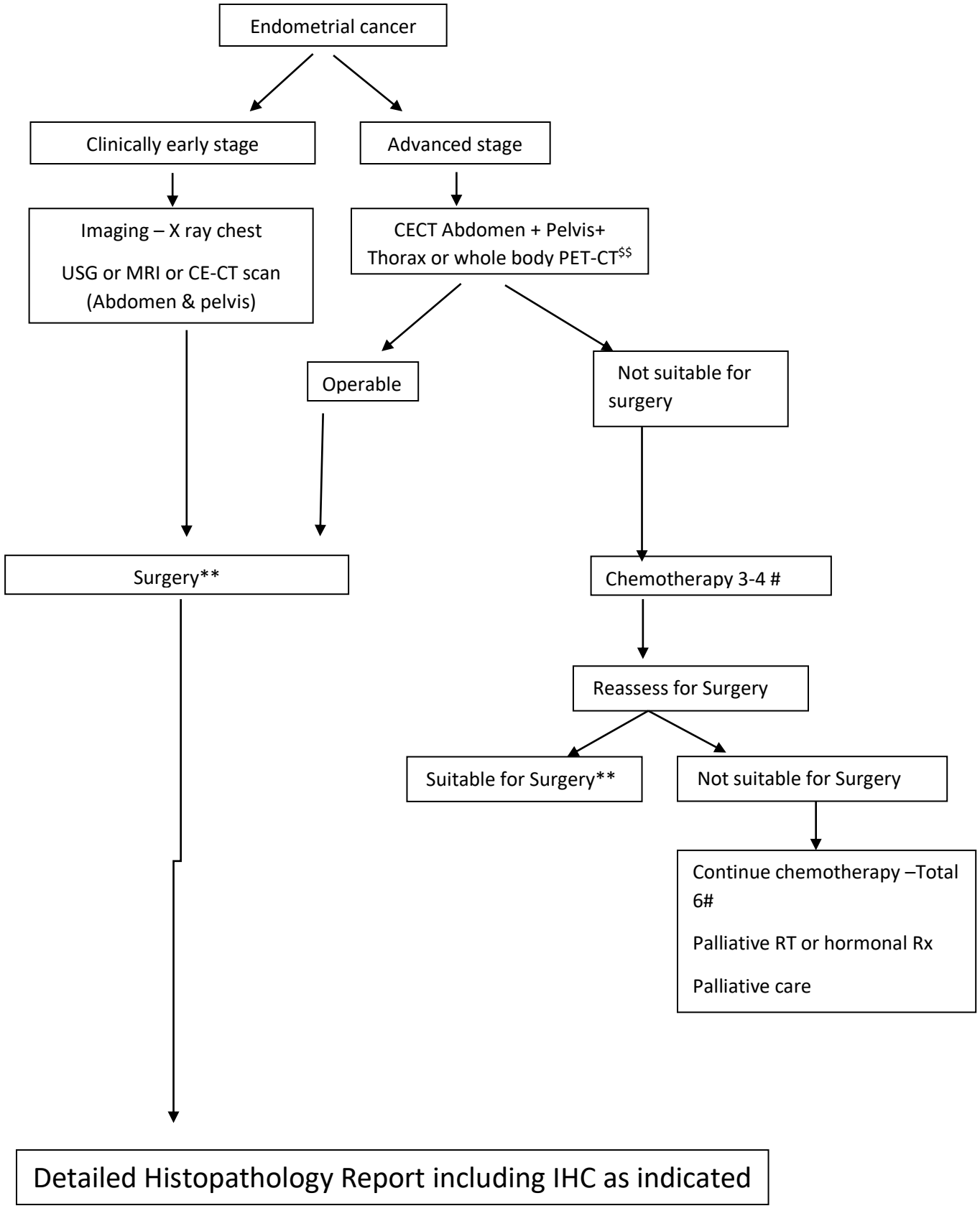
NCG GUIDELINES FOR ENDOMETRIAL CANCER

Treatment Algorithm: Endometrial Cancer





$$: PET-CT should not be done in early lesions.

* TH+ BSO is the minimum standard.
Lymph nodal dissection in patients with high risk features based on pre- or intra-operative assessment

** Table 1: Surgery

StageIA, G1	TH BSO[#]
Stage IA G2/3, IB G1	TH BSO +/-Pelvic Lymphadenectomy
Stage IB G2/3	TH BSO pelvic lymphadenectomy +/-paraaortic lymphadenectomy
Stage II	TH BSO/Type 2 Radical Hysterectomy &pelvic lymphadenectomy ± paraaortic lymphadenectomy
Serous histology	TH BSO + pelvic and paraaortic lymphadenectomy and infracolic omentectomy

[#]Normal appearing ovaries may be preserved in a young patient for fertility preservation after counselling and explaining associated risks.

Fertility preservation: In young patients, disease limited to endometrium, Grade I, endometriod histology, ER/PR Positive, and P53 negative. Counselling for the associated risks is mandatory.A pre-treatment MRI is mandatory to evaluate local extent of disease and status of ovaries. Treatment is done by high dose progesterone with frequent response monitoring at 2-3 monthly interval. The efficacy of progesterone containing IUDs alone is not proven in invasive endometrial cancer.

TH BSO: Total Hysterectomy Bilateral Salpingoophorectomy (Open/ Laparoscopic/ Robotic)

Post-operative Risk Group Stratification for Adjuvant Therapy ^^

Risk Group	**Description**
Low risk	Stage I endometrioid, grade 1–2, <50% myometrial invasion, LVSI negative
Intermediate risk	Stage I endometrioid, grade 1–2, ≥50% myometrial invasion, LVSI negative
High-Intermediate risk	Stage I endometrioid, grade 3, <50% myometrial invasion, regardless of LVSI status Stage I endometrioid, grade 1–2, LVSI unequivocally positive, regardless of depth of invasion
High Risk	Stage I endometrioid, grade 3, >50% myometrial invasion, regardless of LVSI status Stage II Stage III endometrioid, no residual disease Non endometrioid (serous or clear cell or undifferentiated carcinoma, or carcinosarcoma)
Advanced	Stage III residual disease and stage IVA
Metastatic	Stage IVB

^^: ESMO-ESGO-ESTRO Consensus Guidelines

FIGO 2009 Staging for Cancer Endometrium

Stage I	**Tumor confined to the corpus uteri**
IA	No or less than half myometrial invasion
IB	Invasion equal to or more than half of the myometrium
Stage II	**Tumor invades cervical stroma, but does not extend beyond the uterus**
Stage III	**Local and/or regional spread of the tumor**
IIIA	Tumor invades the serosa of the corpus uteri and/or adnexae#
IIIB	Vaginal and/or parametrial involvement#
IIIC	Metastases to pelvic and/or para-aortic lymph nodes#
IIIC1	Positive pelvic nodes
IIIC2	Positive para-aortic lymph nodes with or without positive pelvic lymph nodes
Stage IV	**Tumor invades bladder and/or bowel mucosa, and/or distant metastases**
Stage IVA	Tumor invasion of bladder and/or bowel mucosa
Stage IV B	Distant metastases, including intra-abdominal metastases and/or inguinal lymphnodes

Each Stage includes GI, G2, or G3 depending upon the histological grade of the tumor .

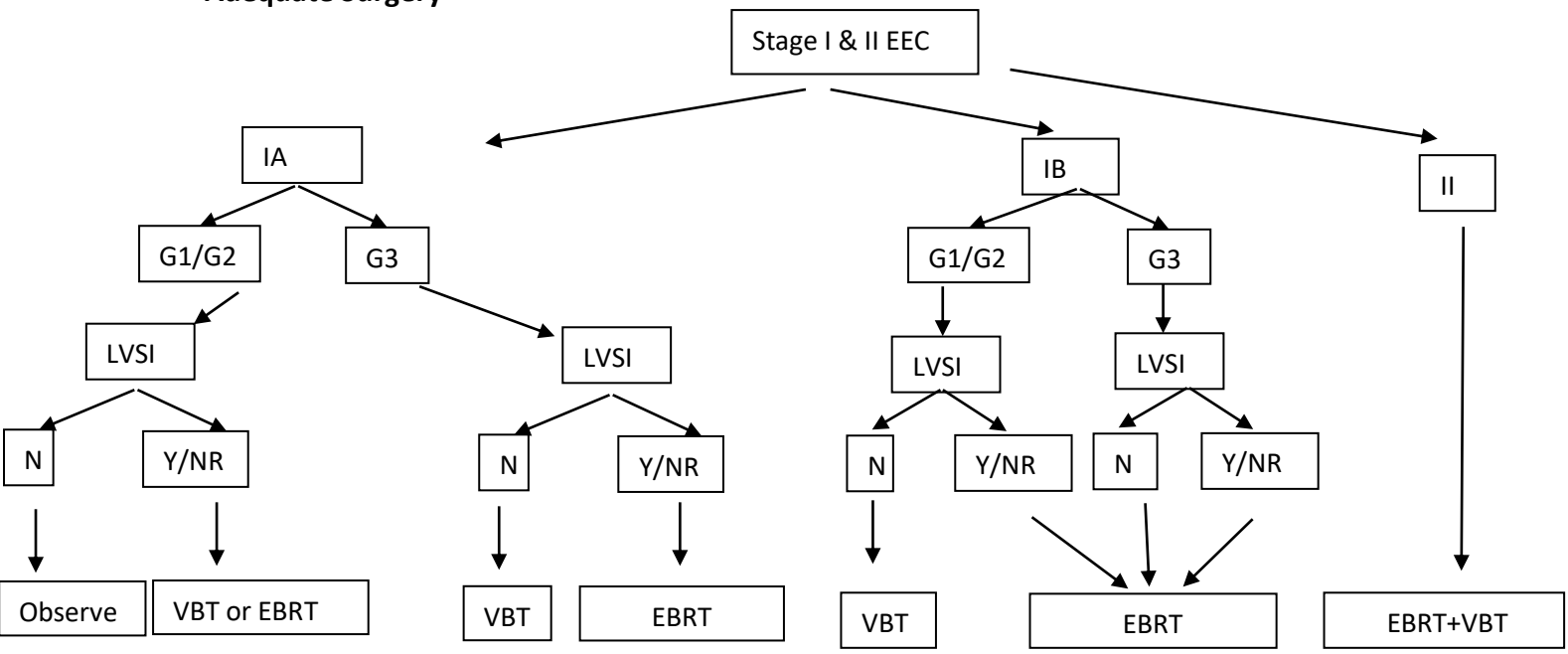
**Endocervical glandular involvement alone should be considered as Stage I*

 # Positive cytology has to be reported separately without changing the stage

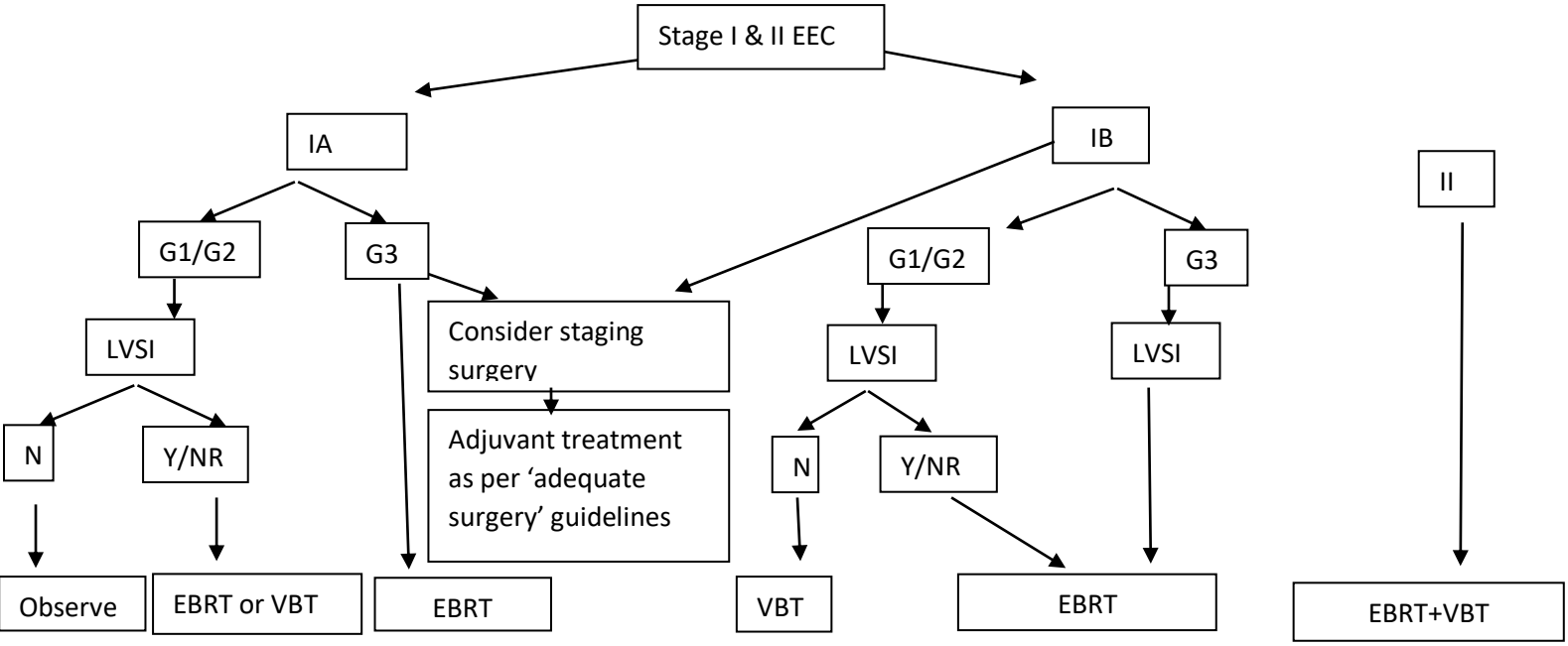
WHO Histological classification

Type I Histology	Endometrioid Adenocarcinoma
Type II Histology	Serous Mucinous Clear cell Carcinosarcoma Undifferentiated

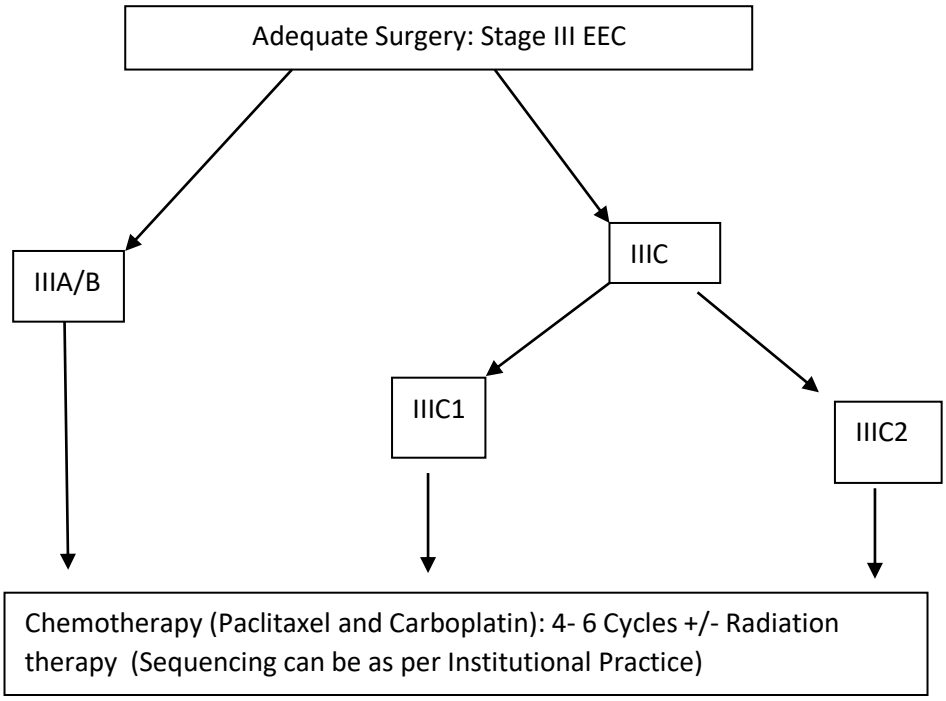
Adequate Surgery**

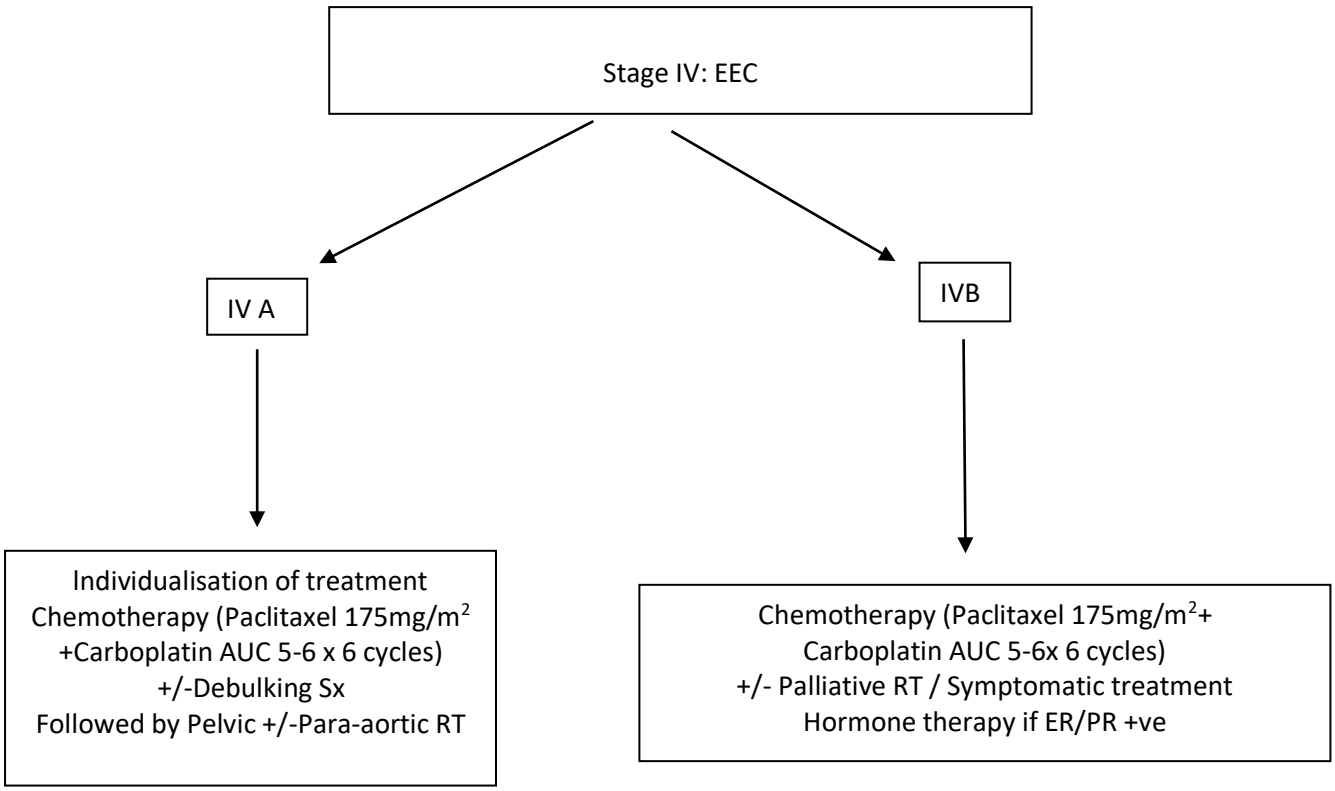


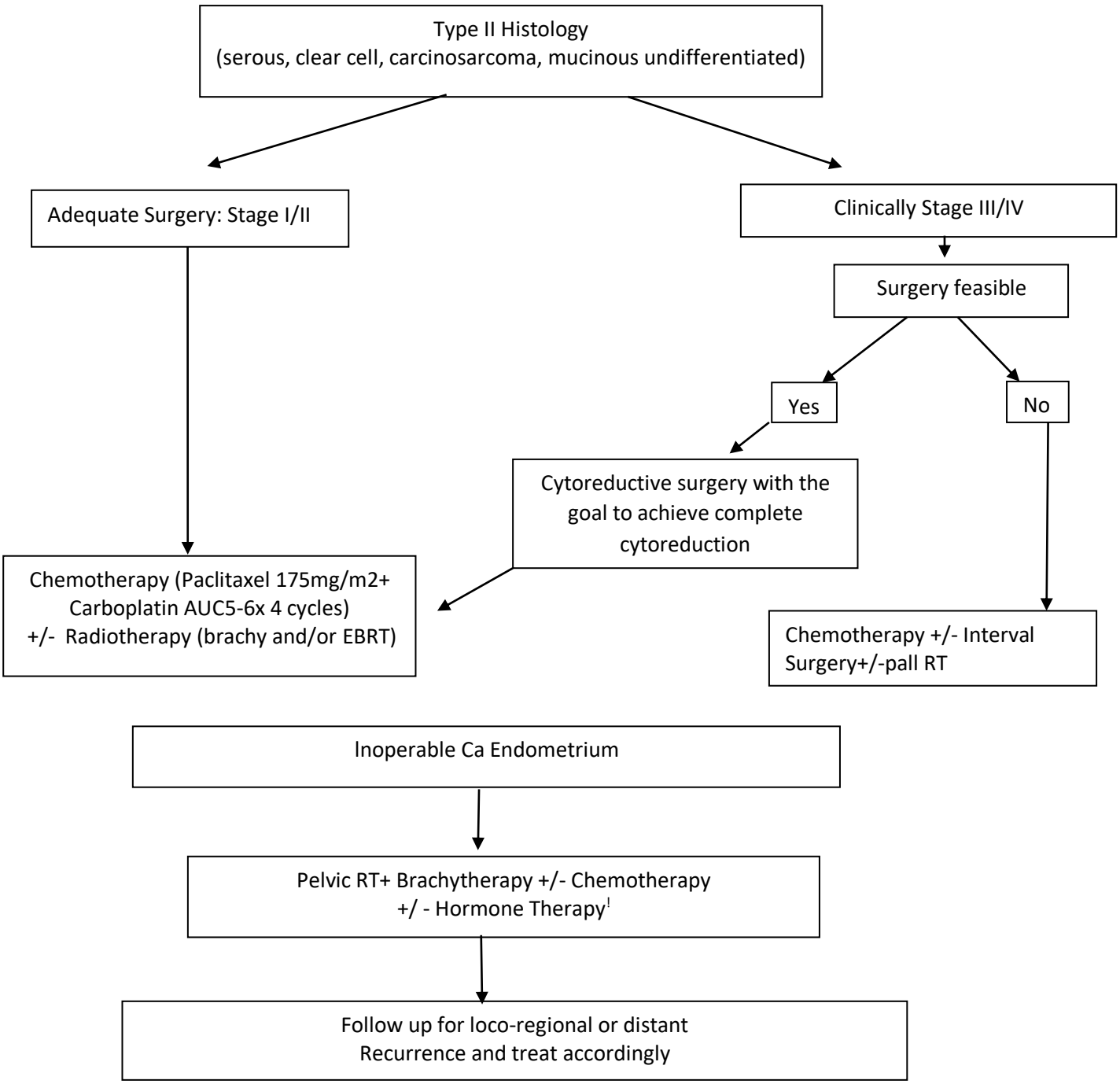
Inadequate Surgery ***



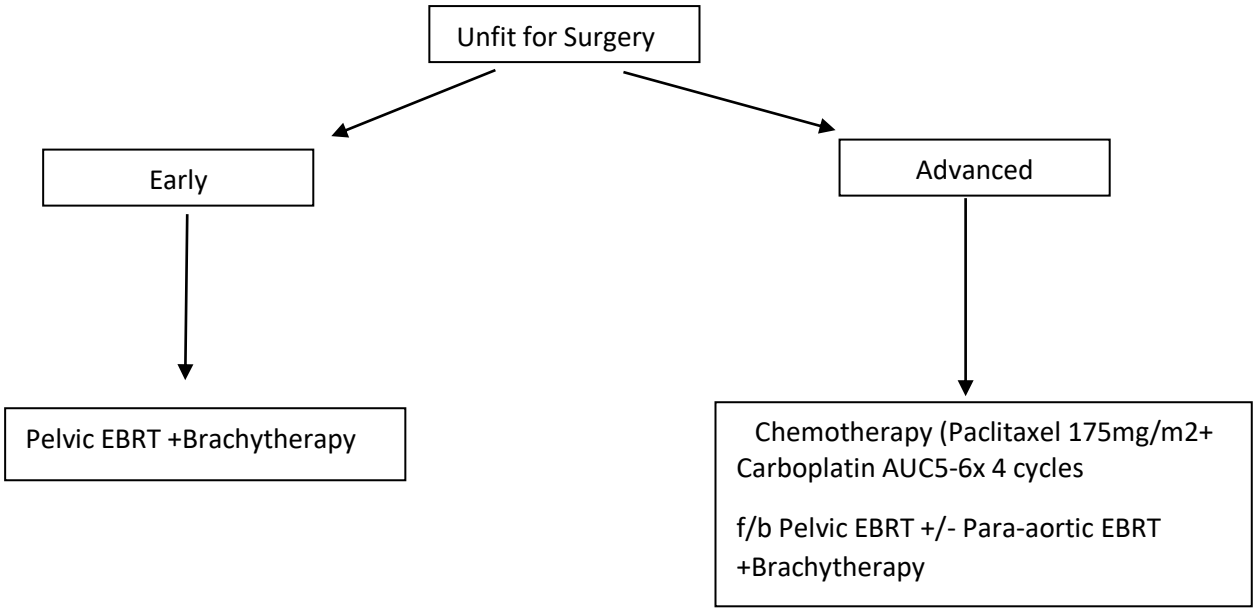
***Unilateral Salpingo-oophorectomy/ No Salpingo-oophorectomy/Lymph node dissection not done.

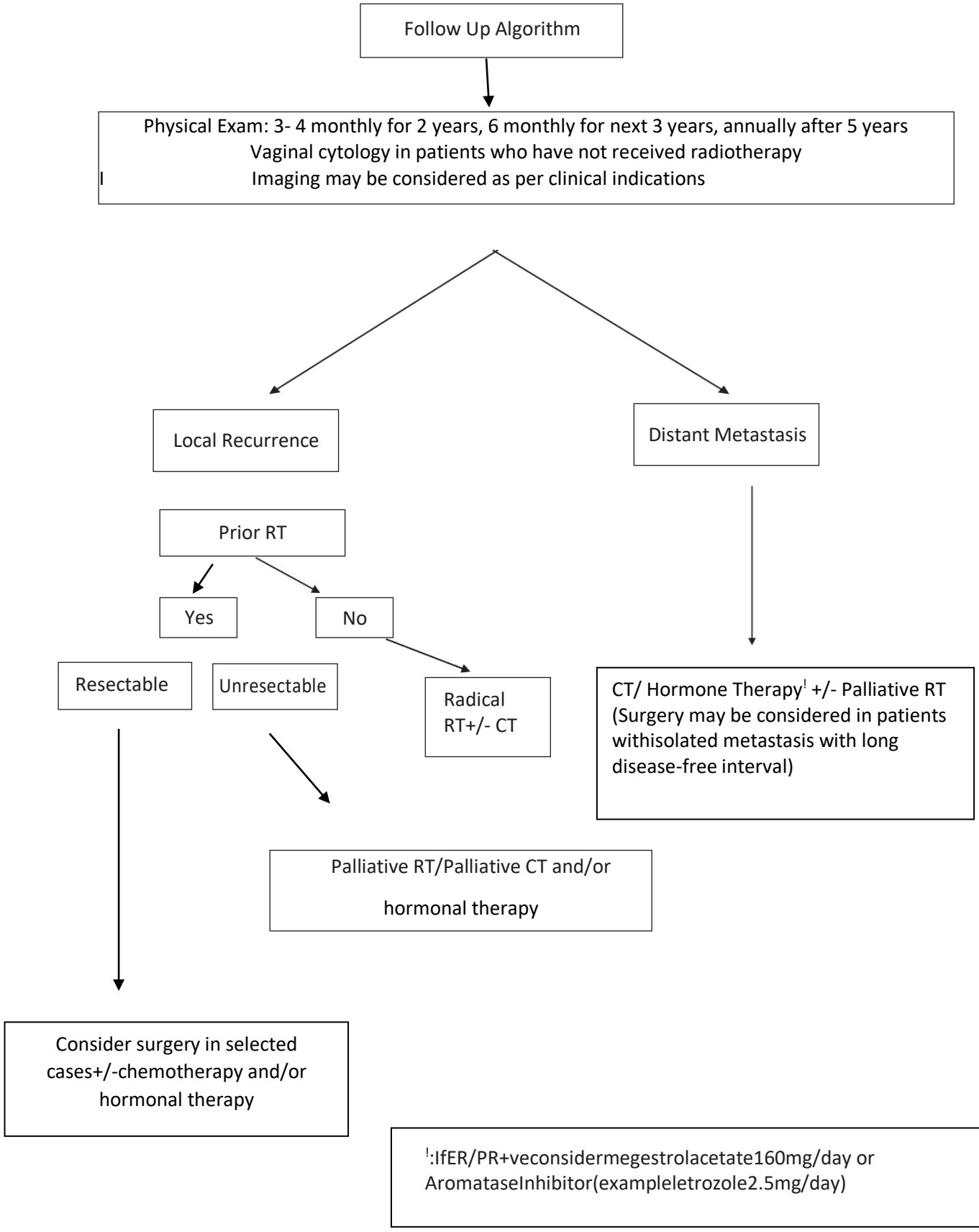



Stage IV: EEC
IV A
IVB
Individualisation of treatment
Chemotherapy (Paclitaxel 175mg/m2
+Carboplatin AUC 5-6 x 6 cycles)
+/-Debulking Sx
Followed by Pelvic +/-Para-aortic RT
Chemotherapy (Paclitaxel 175mg/m2+
Carboplatin AUC 5-6x 6 cycles)
+/- Palliative RT / Symptomatic treatment
Hormone therapy if ER/PR +ve



!: If ER/PR we consider megestrol acetate 160 mg/ day or Aromatase Inhibitor (example letrozole 2.5 mg /day)


Unfit for Surgery
Early
Advanced
Pelvic EBRT +Brachytherapy
Chemotherapy (Paclitaxel 175mg/m2+ Carboplatin AUC5-6x 4 cycles
f/b Pelvic EBRT +/- Para-aortic EBRT +Brachytherapy


Follow Up Algorithm
Physical Exam: 3- 4 monthly for 2 years, 6 monthly for next 3 years, annually after 5 years
Vaginal cytology in patients who have not received radiotherapy
Imaging may be considered as per clinical indications
Local Recurrence
Distant Metastasis
Prior RT
Yes
No
Resectable
Unresectable
Radical RT+/- CT
CT/ Hormone Therapy[!] +/- Palliative RT (Surgery may be considered in patients withisolated metastasis with long disease-free interval)
Palliative RT/Palliative CT and/or hormonal therapy
Consider surgery in selected cases+/-chemotherapy and/or hormonal therapy
[!]:IfER/PR+veconsidermegestrolacetate160mg/day or AromataseInhibitor(exampleletrozole2.5mg/day)

References

1. **Dijkhuizen FP, Brolmann HA, Potters AE, et al**. The accuracy of transvaginal ultrasonography in the diagnosis of endometrial abnormalities. Obstet Gyneco|1996;87:345—9.
2. Karlsson B, Granberg S, Wikland M, et al. Transvaginal ultrasonography of the endometrium in womenwith post-menopausal bleeding—a Nordic multicentre study. Am J of ObstetGynecol1995; 172:1488—94.
3. **Dijkhuizen FP, Mol BW, Brolmann HA &Heintz AP**. The accuracy of endometrial sampling in the diagnosis of patients with endometrial carcinoma and hyperplasia: a meta-analysis. Cancer 2000;89(8):1765—1772. (Level of Evidence: I).
4. **Connor JP, Andrews Jl, Anderson B, Buller RE**. Computed tomography in endometrial carcinoma. ObstetGynecol 2000; 95:692-696
5. HH, Kang S-B, Cho JY et al. Accuracy of MR imaging for the prediction of myometrial invasion of endometrial carcinoma. Gynecol Oncol 2007; 104:654—659.
6. **Nagar H, Dodds S, McClelland HR et al**. The diagnostic accuracy of magnetic resonance imaging in detecting cervical involvement in endometrialcancer.Gyneco|Oncol2006;103:431
7. **Selman TJ, Mann CH, Zamora J, Khan KS**. A systematic review of tests for lymph node status in primary endometrial cancer BMC Women's Health 2008 May 5; 8: 8 (Level of Evidence: 1)
8. **Creasman WT, Morrow CP, Bundy BN, Homesely HD**. Graham JE, Heller PB. Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Cancer Group Study. Cancer 1987; 60:2035-41.
9. **Ayhan A, Taskiran C, Celik C, Yuce K.** The Iong-term survival of women with surgical Stage II endometrioid type endometrial cancer. Gynecol Oncol 2004 Apr; 93(1): 9-13
10. **Lee TS, Kim DY, Kim YT, Lee KH et al**. Necessity of radical hysterectomy for endometrial cancer patients with cervical invasion. J of Korean Med Sci 2010 Apr; 25(4): 552-6
11. **Mariani A, Keeney GL, Aletti G, Webb MJ et al**. Endometrial carcinoma: para-aortic dissemination Gynecol Oncol 2004 March; 92(3): 833-38
12. **Mariani A, Dowdy SC, Cilby WA, Haddock MG et** al. Efficacy of systematic lymphadenectomy and adjuvant radiotherapy in node-positive endometrial cancer patients Gynecol Oncol 2006 May; 101 (2):191-93
13. **Mariani A, Dowdy SC, Cilby WA Gostout BS, Jones MB et al** Prospective assessment of lymphatic dissemination in endometrial cancer: a paradigm shift in surgical staging Gynecol Oncol 2008 Apr;109(1): 11-8

14. **ASTEC study group Kitchener H, SwartAM,et al**. Efficacy of systematic pelvic Lymphadenectomy in endometrial cancer: A randomized study Lancet 2009;373:125-136.
15. **BenedittiPanicciP,Basile S, ManeschiF,et al**. Systematic pelvic Lymphadenectomy vs No Lymphadenectomy in early stage endometrial cancer. A randomized controlled trial. J Nat Can|nst.2008;100:1707-1716.
16. **Creutzberg CL, van Putten WU, Koper PCM, Jobsen JJ et al**. Surgery and postoperative radiotherapy versus surgery alone for patients with stage 1 endometrial carcinoma: multicentre randomized trial.(PORTEC). Lancet 2000; 355:1404-11 **(Level of Evidence: I)**
17. **Nout RA, Creutzberg CL, van Putten WU, Jobsen JJ et al**. Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomized trial. Lancet 2010; 375:816-23 **(Level of Evidence: I)**
18. **Keys HM, Roberts JA, Spirtos NM, Brunetto VL et al**. A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. Gynecologic Oncology 92 (2004); 744-751 **(Level of Evidence: I)**
19. **Blake P, Swart AM, Orton J et al** Adjuvant external beam radiotherapy in the treatment of endometrial cancer (M RC ASTEC and NCIC CTG EN.5randomised trials): pooled trial results, systematic review, and meta-analysis Lancet 2009; 373: 137-46 **(Level of Evidence: I)**
20. **Johnson N, Bryant A, MilesTet al**. Adjuvant chemotherapy for endometrial cancers after hysterectomy. Cochrane Database Syst Rev.; (10): CD003175doi:10.1002/14651858.CD003175.pub2. **(Level of Evidence:I)**
21. **Colombo, Nicoletta, et al**. "ESMO-ESGO-ESTRO consensus conference on endometrial cancer: diagnosis, treatment and follow-up." *Annals of Oncology* 27.1 (2015): 16-41.