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子宮惡性肉瘤診療指引

2018年05月15日 第一版

婦癌醫療團隊擬訂

注意事項：這個診療原則主要作為醫師和其他保健專家診療癌症病人參考之用。假如你是一個癌症病人，直接引用這個診療原則並不恰當，只有你的醫師才能決定給你最恰當的治療。

修訂指引

- 本共識依下列參考資料修改版本
  - NCCN Clinical Practical Guidelines in Oncology ™ Uterine Sarcoma Cancer（Version 1.2018 — October 13, 2017）
  - 婦癌研究委員會，子宮惡性肉瘤癌篩檢臨床指引（2011）：國家衛生研究院
  - 其他相關子宮惡性肉瘤臨床指引

會議討論

上次會議：2017/05/16

本共識與上一版的差異

上一版	新版
1. 陳列分期為AJCC 7th版分期。(p. 5, 6) 2. 無陳列治療子宮惡性肉瘤診療指引相關之主要檢查。(p. 9) 3. 流程圖一:初步臨床發現，額外檢查手術後，病理組織無額外增加ER/PR檢查的選項。(p. 10) 4. 流程圖一:初步臨床發現，手術後，有殘留輸卵管/卵巢殘留情況下，初級處理方式考慮再次切除，尤其是低度子宮內膜基質惡性肉瘤。(p. 10) 5. 流程圖一備註第c點敘述為:卵巢摘除手術會因病人是否為已進入更年期而考慮。(p. 10) 6. 流程圖二:低度子宮內膜基質惡性肉瘤分期I的病人，可考慮觀察無備註。(p. 11) 7. 流程圖二:分期 II, III, IVA及IVB手術後輔助治療有觀察選項。(p. 11)	1. 刪除AJCC 7th版分期，更改為AJCC 8th版分期。(p. 5-8) 2. 增加治療子宮惡性肉瘤診療指引相關之主要檢查。(p. 9) 3. 流程圖一:初步臨床發現，額外檢查手術後，病理組織須額外增加ER/PR檢查。(p. 10) 4. 流程圖一:初步臨床發現，手術後，有殘留輸卵管/卵巢殘留情況下，初級處理方式考慮再次切除，尤其是低度子宮內膜基質惡性肉瘤，更改為考慮再次切除輸卵管/卵巢殘留。尤其是低度子宮內膜基質惡性肉瘤或ER (+)的病患。(p. 10) 5. 流程圖一備註第c點:卵巢摘除手術會因病人是否為已進入更年期而考慮。增加但如果ER/PR(+)則建議 BSO。(p. 10) 6. 流程圖二:低度子宮內膜基質惡性肉瘤分期I的病人，可考慮觀察，增加備註處尤其停經或BSO或使用雌激素抑制劑的病人。(p. 11) 7. 流程圖二:分期 II, III, IVA及IVB手術後輔助治療刪除觀察選項。(p. 11)

會議討論

上次會議：2017/05/16

本共識與上一版的差異

上一版	新版
8. 流程圖二:荷爾蒙治療僅為此字眼。(p. 11) 9. 流程圖一~五:全身治療及化學治療僅為此字眼。(p10, 12, 13, 14) 10. 流程圖五:局部復發之前從未接受放射線治療情形下，治療方式無±化學治療或全身系統性治療(化療/標靶/荷爾)。(p. 14) 11. 化療未加註輔助、轉移。(p. 16)	8. 流程圖二:荷爾蒙治療改為雌激素抑制劑。(p. 11) 9. 流程圖一~五:全身治療及化學治療字眼，更改成全身系統性治療(化療/標靶/荷爾)字眼。(p10, 12, 13, 14) 10. 流程圖五:局部復發之前從未接受放射線治療情形下，治療方式增加±化學治療或全身系統性治療(化療/標靶/荷爾)。(p. 14) 11. 化療加註輔助、轉移。(p. 16)

分期AJCC 8th

Corpus Uteri – Carcinoma and Carcinosarcoma

Primary Tumor (T)		
T	**FIGO**	**T Criteria**
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor confined to the corpus uteri, including endocervical glandular involvement
T1a	IA	Tumor limited to the endometrium or invading less than half the myometrium
T1b	IB	Tumor invading one half or more of the myometrium
T2	II	Tumor invading the stromal connective tissue of the cervix but not extending beyond the uterus. Does NOT include endocervical glandular involvement.
T3	III	Tumor involving serosa, adnexa, vagina, or parametrium
T3a	IIIA	Tumor involving the serosa and/or adnexa (direct extension or metastasis)
T3b	IIIB	Vaginal involvement (direct extension or metastasis) or parametrial involvement
T4	IVA	Tumor invading the bladder mucosa and/or bowel mucosa (bullous edema is not sufficient to classify a tumor as T4)

Regional Lymph Node (N)		
N	**FIGO**	**N Criteria**
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N0 (i+)		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
N1	IIIC1	Regional lymph nodes metastasis to pelvic lymph nodes
N1mi	IIIC1	Regional lymph node metastasis (greater than 0.2 mm but not greater than 2.0 mm in diameter) to pelvic lymph nodes
N1a	IIIC1	Regional lymph node metastasis (greater than 2.0 mm in diameter) to pelvic lymph nodes
N2	IIIC2	Regional lymph node metastasis to para-aortic lymph nodes, with or without positive pelvic lymph nodes
N2mi	IIIC2	Regional lymph node metastasis (greater than 0.2 mm but not greater than 2.0 mm in diameter) to para-aortic lymph nodes, with or without positive pelvic lymph nodes
N2a	IIIC2	Regional lymph node metastasis (greater than 2.0 mm in diameter) to para-aortic lymph nodes, with or without positive pelvie lymph nodes

分期AJCC 8th

Corpus Uteri – Carcinoma and Carcinosarcoma

Distant Metastasis (M)		
M	**FIGO**	**M Criteria**
M0		No distant metastasis
M1	IVB	Distant metastasis (includes metastasis to inguinal lymph nodes, intraperitoneal disease, lung, liver, or bone). (It excludes metastasis to pelvic or para-aortic lymph nodes, vagina, uterine serosa, or adnexa).

STAGE GROUPS			
T	**N**	**M**	**stage**
T1	N0	M0	I
T1a	N0	M0	IA
T1b	N0	M0	IIB
T2	N0	M0	II
T3	N0	M0	III
T3a	N0	M0	IIIA
T3b	N0	M0	IIIB
T1-T3	N1/N1mi/N1a	M0	IIIC1
T1-T3	N2/N2mi/N2a	M0	IIIC2
T4	Any N	M0	IVA
Any T	Any N	M1	IVB

分期AJCC 8th

Corpus Uteri – Sarcoma

Leiomyosarcoma and Endometrial Stromal Sarcoma		
Primary Tumor (T)		
T	**FIGO**	**T Criteria**
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor limited to the uterus
T1a	IA	Tumor 5 cm or less in greatest dimension
T1b	IB	Tumor more than 5 cm
T2	II	Tumor extends beyond the uterus, within the pelvis
T2a	IIA	Tumor involves adnexa
T2b	IIB	Tumor involves other pelvic tissues
T3	III	Tumor infiltrates abdominal tissues
T3a	IIIA	One site
T3b	IIIB	More than one site
T4	IVA	Tumor invades bladder or rectum

Adenosarcoma		
Primary Tumor (T)		
T	**FIGO**	**T Criteria**
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor limited to the uterus
T1a	IA	Tumor limited to the endometrium/endocervix
T1b	IB	Tumor invades to less than half of the myometrium
T1c	IC	Tumor invades more than half of the myometrium
T2	II	Tumor extends beyond the uterus, within the pelvis
T2a	IIA	Tumor involves adnexa
T2b	IIB	Tumor involves other pelvic tissues
T3	III	Tumor infiltrates abdominal tissues
T3a	IIIA	One site
T3b	IIIB	More than one site
T4	IVA	Tumor invades bladder or rectum

Regional Lymph Node (N)		
All Uterine Sarcomas		
N	**FIGO**	**N Criteria**
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N0 (i+)		Isolated tumor cells in regional lymph node(s) node(s) no greater than 0.2 mm
N1	IIIC	Regional lymph nodes metastasis

分期AJCC 8th

Corpus Uteri – Sarcoma

Distant Metastasis (M)		
All Uterine Sarcomas		
M	**FIGO**	**M Criteria**
M0		No distant metastasis
M1	IVB	Distant metastasis (excluding adnexa, pelvic, and abdominal tissues)

Leiomyosarcoma and Endometrial Stromal Sarcoma			
STAGE GROUPS			
T	**N**	**M**	**stage**
T1	N0	M0	I
T1a	N0	M0	IA
T1b	N0	M0	IB
T1c	N0	M0	IC
T2	N0	M0	II
T3a	N0	M0	IIIA
T3b	N0	M0	IIIB
T1-3	N1	M0	IIIC
T4	Any N	M0	IVA
Any-T	Any N	M1	IVB

Adenosarcoma			
STAGE GROUPS			
T	**N**	**M**	**stage**
T1	N0	M0	I
T1a	N0	M0	IA
T1b	N0	M0	IB
T2	N0	M0	II
T3a	N0	M0	IIIA
T3b	N0	M0	IIIB
T1-3	N1	M0	IIIC
T4	Any N	M0	IVA
Any-T	Any N	M1	IVB

子宮惡性肉瘤診療指引相關之主要檢查

1.病史

2.理學檢查及一般婦科基本檢查:內診/抹片/婦科超音波

3.子宮鏡檢查、子宮內膜及子宮內頸切片檢查(報告)*

4.CXR, ECG

5.CBC/DC, SMA

6.Pelvic/Abdominal MRI or CT, Chest CT scan, Tumor markers ** :
LDH, Ca-125, Ca-199, CEA.

7.PET-CT**

8.Bone scan ***

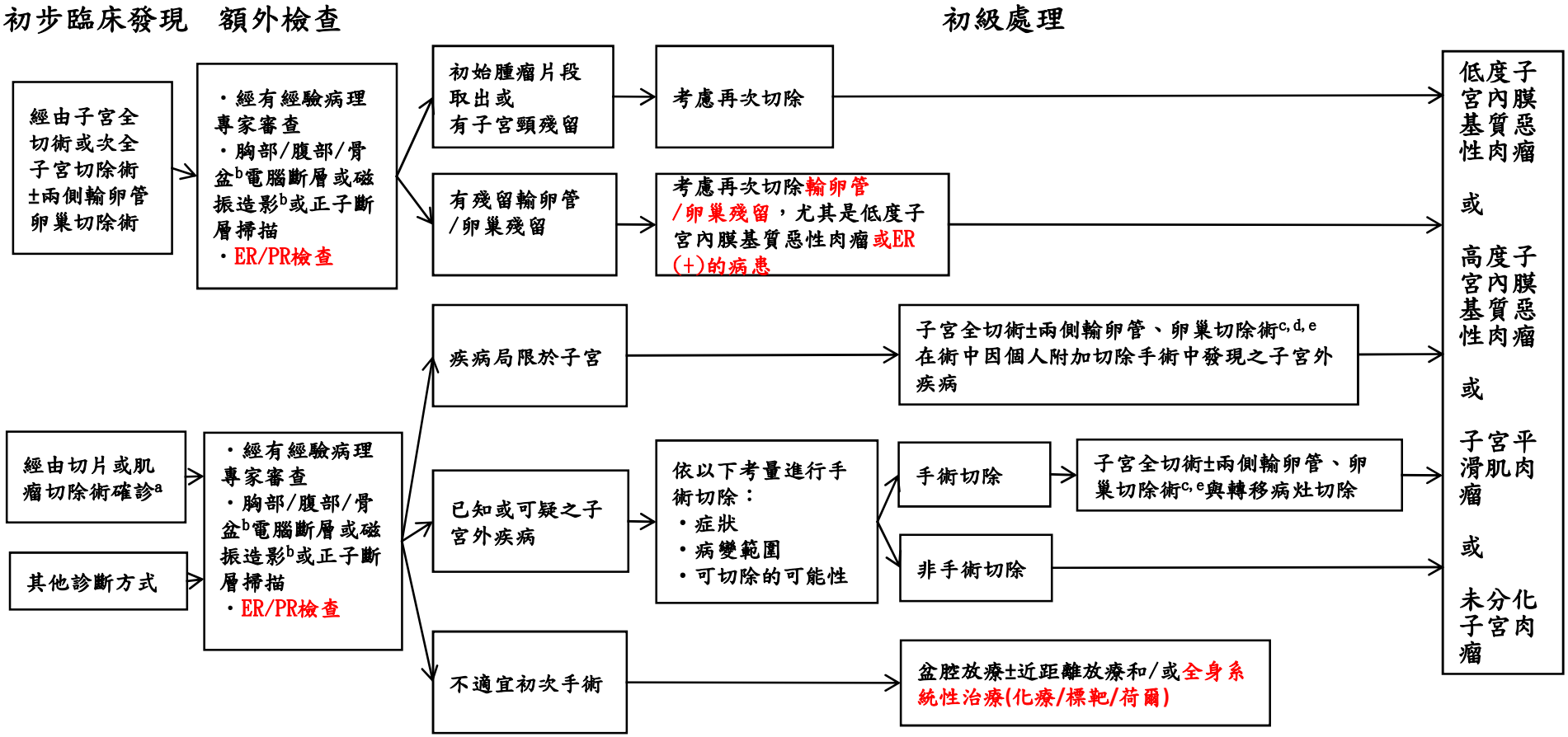
9. Pelvic CT scan, Chest CT scan, Bain CT/MRI***

*當手術後意外發現(診斷)時無需檢查或外院病理複閱

**可做為首次/追蹤/複發檢查

***做為追蹤/複發檢查

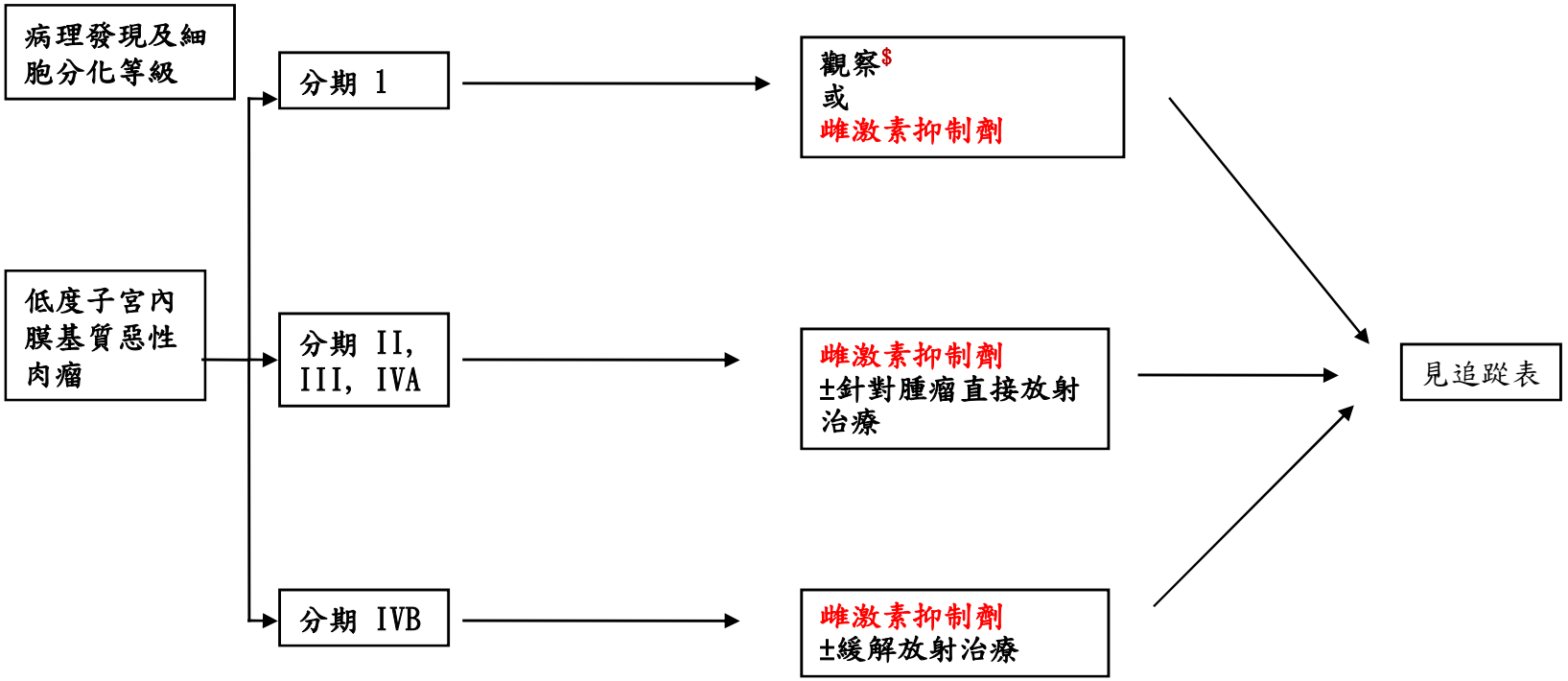
高雄榮總婦癌團隊子宮惡性肉瘤臨床診療指引



a. 術前影像學和切片可能有助於確定子宮肉瘤，雖然切片靈敏度小於子宮內膜癌。如果有基質惡性肉瘤的嫌疑，腫瘤片段取出應該避免。
b. 除非有禁忌，電腦斷層或磁振造影的對比要遵循準則。
c. 卵巢摘除會因病人是否為已進入更年期而考慮。但如果ER/PR positive則建議 BSO。
d. 對於經TH/ BSO或切片標本後發現子宮肉瘤：建議依個人狀態進行影像及額外的手術切除
e. 子宮惡性肉瘤應該整塊移除以獲取最佳結果；取出時應避免分碎組織

流程圖一

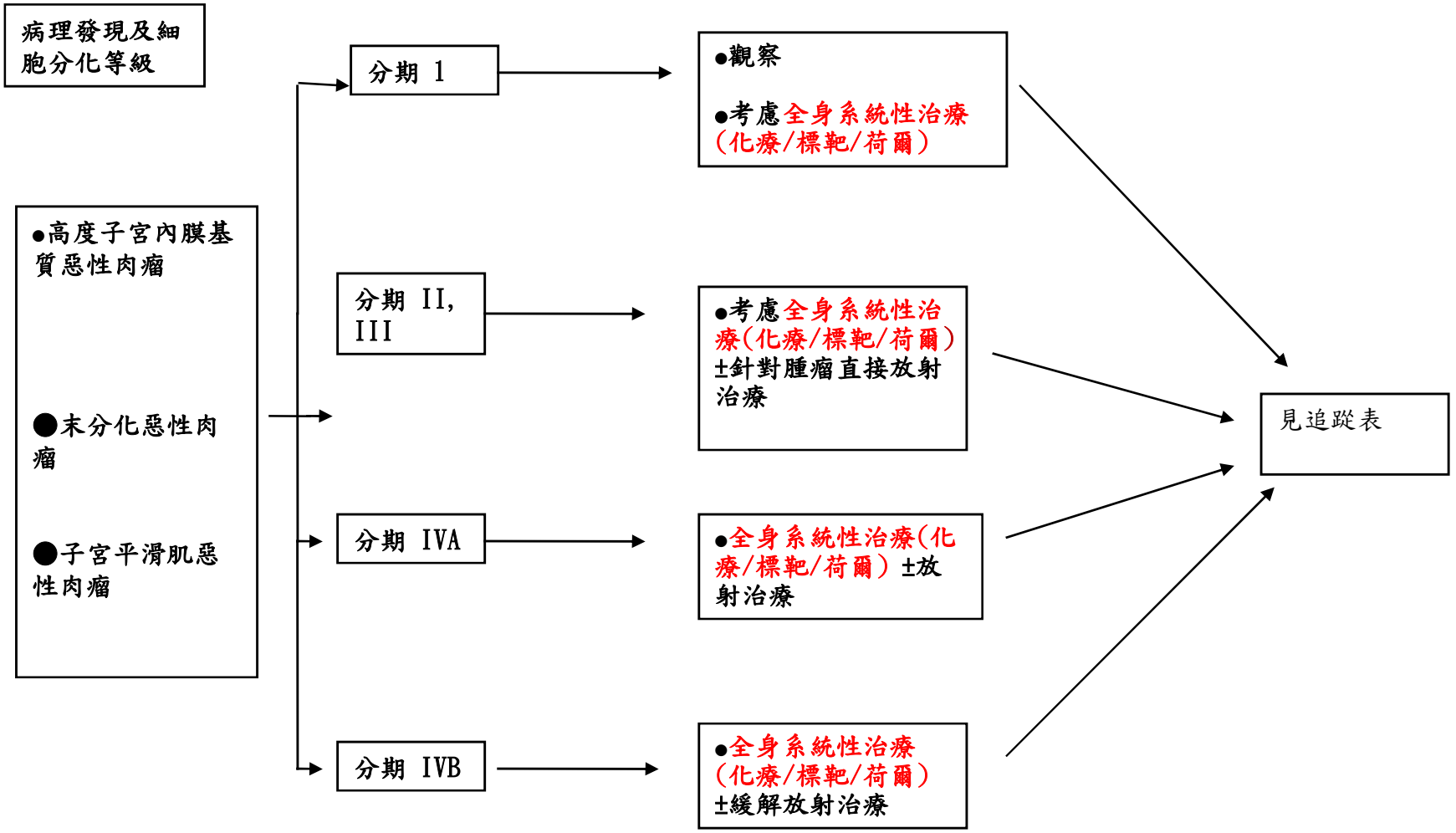
高雄榮總婦癌團隊子宮惡性肉瘤臨床診療指引



$尤其停經或BSO或使用雌激素抑制劑

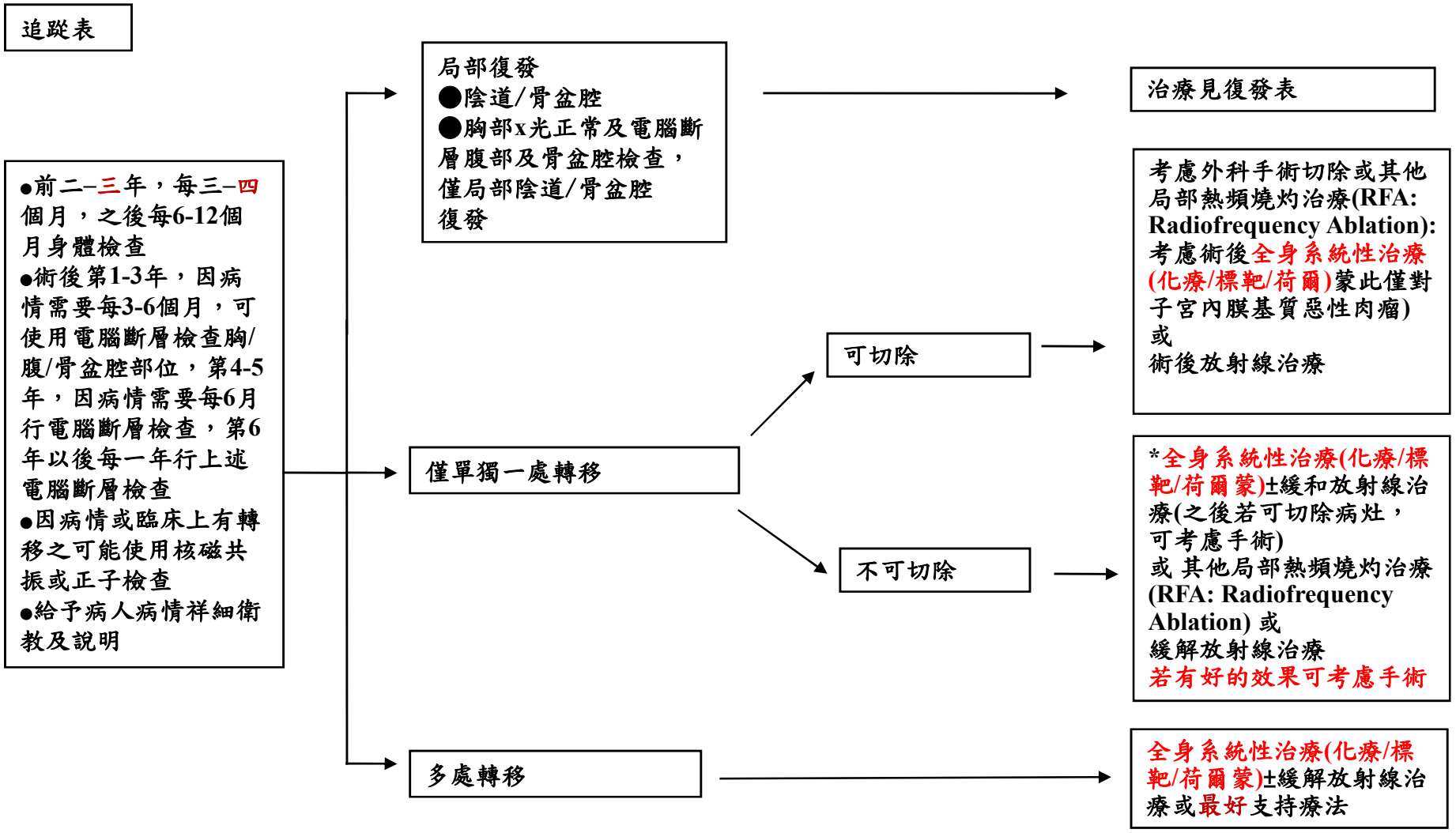
流程圖二

高雄榮總婦癌團隊子宮惡性肉瘤臨床診療指引



流程圖三

高雄榮總婦癌團隊子宮惡性肉瘤臨床診療指引



流程圖四

高雄榮總婦癌團隊子宮惡性肉瘤臨床診療指引

復發及治療

局部復發
●陰道
●胸部x光正常及電腦斷層腹部及骨盆腔檢查，僅局部陰道/骨盆腔復發

之前從未接受放射線治療

外科手術切除 ±手術中行病灶放射線治療*考慮術前體外放射線治療±化學治療或全身系統性治療(化療/標靶/荷爾)

病灶還是僅位於陰道內

針對腫瘤直接放射治療+陰道近接放射治療

已轉移至陰道外

若僅位於骨盆腔內:針對腫瘤直接放射治療

若位於骨盆腔外:
全身系統性治療(化療/標靶/荷爾)

或
針對腫瘤直接放射治療±陰道近接治療±化學治療或全身系統性治療(化療/標靶/荷爾)

接受過放射線治療

外科手術切除 ±手術中行病灶放射線治療*±全身系統性治療(化療/標靶/荷爾)

或其他局部熱頻燒灼手術(RFA: Radiofrequency Ablation)

或全身系統性治療(化療/標靶/荷爾)
或
針對腫瘤直接(再)放射治療±陰道近接治療

*手術中行病灶放射線治療(IORT)目前在本科未有此項服務。

流程圖五

子宮惡性肉瘤分類

UTERINE SARCOMA CLASSIFICATION[1]

- Low-grade endometrial stromal sarcoma (ESS)[2]
- High-grade ESS[3]
- Undifferentiated uterine sarcoma (UUS)[4]
- Uterine leiomyosarcoma (uLMS)[5]

Other Rare Uterine Mesenchymal Sarcoma Subtypes:
(see the NCCN Guidelines for Soft Tissue Sarcoma)

- Adenosarcomas
- PEComas
- Rhabdomyosarcoma

Adjuvant /or Salvage 化學治療(輔助或轉移)		
protocol	劑量	時程
DTIC (Decarbazine, Epirubicin, Platinum, Ifosfamide)	Dacarbazine 200mg qd x 5 days Epirubicin 50mg/m^2 st Carboplatin AUC x5mg st, CCR＜60 （Cisplatin 50mg/m^2 st, CCR≧60） Ifosfamide 4mg/m^2 st	Q3W x 6 cycles
Gemcitabine+Docetaxel	D1/D8 Gemcitabine 675-900 mg/m^2 D8 Docetaxel 75-100 mg/m^2	Q4W x 6 cycles
Paclitaxel+Cisplatin	Paclitaxel 175 mg/m^2 Cisplatin 50 mg/m^2	Q3W x 6 cycles
Paclitaxel+Carboplatin	Paclitaxel 175 mg/m^2 Carboplatin AUC(5MG)	Q3W x 6 cycles

PRINCIPLES OF IMAGING
(References)

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PRINCIPLES OF RADIATION THERAPY FOR UTERINE NEOPLASMS

- RT is directed at sites of known or suspected tumor involvement and may include external beam RT (EBRT) and/or brachytherapy. Imaging is required to assess locoregional extent and to rule out distant metastases before administration of RT. In general, EBRT is directed to the pelvis with or without the para-aortic region. Brachytherapy can be delivered: 1) to an intact uterus, either preoperatively or definitively; or 2) more commonly, to the vagina after hysterectomy. For the purposes of these guidelines, whole abdominal radiotherapy is not considered to be tumor-directed RT.
- For neoadjuvant radiation or radiation after resection of gross disease, doses of 45-50 Gy are typically used. One could consider adding 1-2 high does rate (HDR) insertions to a total dose of 75 to 80 Gy low-dose-rate equivalent. For neoadjuvant treatment to minimize risk of positive or close margins at hysterectomy.
- Pelvic radiotherapy should target the gross disease (if present), the lower common iliacs, external iliacs, internal iliacs, parametria, upper vagina/para-vaginal tissue, and presacral lymph nodes (in patients with cervical involvement). Extended-field radiotherapy should include the pelvic volume and also target the entire common iliac chain and para-aortic lymph node region. The upper border of the extended field depends on the clinical situation but should at least be 1-2 cm above the level of the renal vessels. External-beam doses for microscopic disease should be 45 to 50 Gy. Multiple conformal fields based on CT-treatment planning should be utilized, and consideration for IMRT for normal tissue sparing may be considered, with appropriate attention to QA and tissue interfraction mobility.
- Initiate brachytherapy as soon as the vaginal cuff is healed, preferably 6- 8 weeks after surgery but in general initiation of brachytherapy should not exceed 12 weeks. For vaginal brachytherapy, the dose should be prescribed to the vaginal surface or at a depth of 0.5 cm from the vaginal surface; the dose depends on the use of EBRT. The target for vaginal brachytherapy after hysterectomy should be no more than the upper two-thirds of the vagina; in cases of extensive LVSI or positive margins, a longer segment of the vagina may be treated.
  - For postoperative high-dose-rate vaginal brachytherapy preferred regimens include 6 Gy X 5 fractions prescribed to the vaginal surface, or 5.5 Gy X 4 prescribed to 5 mm below the vaginal surface. While 7 Gy x 3 prescribed at a depth of 0.5 cm from the vaginal surface is a regimen used by many, studies suggest there may be increased toxicity.
  - When high-dose-rate brachytherapy is used as a boost to EBRT, doses of 4 to 6 Gy x 2 to 3 fractions prescribed to the vaginal mucosa are commonly used.
- For medically inoperable uterine cancer, risk of extrauterine spread determines the combination of external beam plus brachytherapy or brachytherapy alone. Brachytherapy doses for definitive therapy are individualized based on the clinical situation. When available, image-guided therapy should be used. Based on the best available evidence, an EQD2 D90 of at least 48 Gy should be delivered to the uterus, cervix and upper 1-2 cm of vagina if brachytherapy alone is used, and should be increased to 65 Gy for the combination of external beam and brachytherapy. If an MRI is used as part of planning, the target dose for the GTV would be an EQD2 of ≥ 80 Gy.
- Evidence supports the use of combined modality radiation and chemotherapy as adjuvant treatment for patients with extrauterine disease.

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