中 山 醫 學 大 學 附 設 醫 院

卵 巢 癌 診 療 指 引

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2011/02/21 Version 2.0
2010/07/12 Version 1.0

臨床指引參考台灣國家衛生研究院、與美國 NCCN 版本
再依據中山醫學大學附設醫院婦癌小組經驗作編修
婦癌醫療小組

癌症委員會主任委員	癌症委員會執行長	癌症中心主任	團隊負責人

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建議進行遺傳學檢查(如果以往都沒做過，建議檢查)</td></tr>
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五、 分期、分期手術與減積手術
<table><tr><th colspan="2">FIGO 分期</th><th>TNM Categories</th></tr><tr><td>I</td><td>Tumor confined to ovaries
(癌症只限在卵巢)</td><td>T1</td></tr><tr><td>IA</td><td>Tumor limited to 1 ovary; capsule intact, no tumor on surface, negative washings.
(癌症只限在一側的卵巢；沒有腹水；卵巢的表面完整，且表面沒有癌病變)</td><td>T1a</td></tr><tr><td>IB</td><td>Tumor involves both ovaries otherwise like IA.
(癌症只限在兩側的卵巢；沒有腹水；卵巢的表面完整，且表面沒有癌病變)</td><td>T1b</td></tr><tr><td>IC</td><td>Tumor limited to 1 or both ovaries or fallopian tubes
(腫瘤限於單側或雙側卵巢、輸卵管)</td><td>T1c</td></tr><tr><td>IC1</td><td>Surgical spill
(手術破裂)</td><td>T1c</td></tr><tr><td>IC2</td><td>Capsule rupture before surgery or tumor on ovarian surface
(卵巢前囊膜或腫瘤於手術前破裂)</td><td>T1c</td></tr><tr><td>IC3</td><td>Malignant cells in the ascites or peritoneal washings
(腹水或腹腔沖洗有惡性細胞)</td><td>T1c</td></tr><tr><td>II</td><td>Tumor involves 1 or both ovaries with pelvic extension (below the pelvic brim)
or primary peritoneal cancer
(單側或兩側卵巢癌，並且有骨盆腔擴散，或原發性腹膜癌)</td><td>T2</td></tr><tr><td>IIA</td><td>Extension and/or implant on uterus and/or Fallopian tubes
(擴散只限於子宮或輸卵管)</td><td>T2a</td></tr><tr><td>IIB</td><td>Extension to other pelvic intraperitoneal tissues.
(擴散至骨盆腔內的其他組織)</td><td>T2b</td></tr></table></td><td>五、 分期、分期手術、減積手術及保留生育手術：修訂為-
五、 分期、分期手術、減積手術及保留生育手術
<table><tr><th colspan="2">FIGO 分期</th><th>TNM Categories</th></tr><tr><td>N/A</td><td>Primary tumor cannot be assessed
原發腫瘤無法評估</td><td>TX</td></tr><tr><td>N/A</td><td>No evidence of primary tumor
沒有原發腫瘤的證據</td><td>T0</td></tr><tr><td>I</td><td>Tumor limited to ovaries (one or both) or fallopian tube(s)
腫瘤限於卵巢（一個或兩個）或輸卵管（S）</td><td>T1</td></tr><tr><td>IA</td><td>Tumor limited to one ovary (capsule intact) or fallopian tube, no tumor on ovarian or fallopian tube surface; no malignant cells in ascites or peritoneal washings
腫瘤限於一個卵巢（表面完整）或輸卵管，卵巢或輸卵管表面無腫瘤;腹水或腹腔沖洗液中無惡性細胞</td><td>T1a</td></tr><tr><td>IB</td><td>Tumor limited to both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in ascites or peritoneal washings
腫瘤局限於兩個卵巢（表面完整）或輸卵管;卵巢或輸卵管表面無腫瘤;腹水或腹腔沖洗液中無惡性細胞</td><td>T1b</td></tr><tr><td>IC</td><td>Tumor limited to one or both ovaries or fallopian tubes, with any of the following:
腫瘤限於一個或兩個卵巢或輸卵管，具有以下任何一種：</td><td>T1c</td></tr><tr><td>IC1</td><td>Surgical spill
(手術破裂)</td><td>T1c</td></tr><tr><td>IC2</td><td>Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface
手術前囊膜或卵巢或輸卵管表面腫瘤破裂</td><td>T1c</td></tr><tr><td>IC3</td><td>Malignant cells in the ascites or peritoneal washings
(腹水或腹腔沖洗有惡性細胞)</td><td>T1c</td></tr><tr><td>II</td><td>Tumor involves one or both ovaries or fallopian tubes with pelvic extension below pelvic brim or primary peritoneal cancer</td><td>T2</td></tr></table></td></tr>
</table>

III	Tumor involves 1 or both ovaries or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes (腫瘤包括單側或雙側卵巢或輸卵管，或原發性腹膜癌，與細胞學或組織學上經實擴散到腹膜骨盆外和/或轉移至腹膜後淋巴結腫大)	T3
IIIA	Positive retroperitoneal lymph nodes and/or microscopic metastasis beyond the pelvis (陽性腹膜後淋巴結和/或超出骨盆微觀轉移)	T1 T 2T3a-N0/N1-M0
IIIA1	positive retroperitoneal lymph nodes(陽性腹膜後淋巴結腫大) *IIIA1(i)* metastasis≦10mm(轉移≦10 毫米) *IIIA1(ii)* metastasis＞10mm(轉移＞10 毫米)	T3a-N0/N1-M0
IIIA2	Microscopic, extrapelvic(above the brim) peritoneal involvement ± positive retro peritoneal lymph nodes (顯微鏡下，盆腔外（邊緣以上）腹膜轉移或後腹膜淋巴結轉移)	T3a-N0/N1-M0
IIIB	Macroscopic, extrapelvic, peritoneal metastasis ≤ 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen. (組織學檢查證實腹腔腹膜表面已經有了癌病變，但病變的最大徑並無超過兩公分者。淋巴沒有轉移)	T3b-N0/N1-M0
IIIC	Macroscopic, extrapelvic, peritoneal metastasis > 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen. (腹腔轉移病灶的最大徑已超過兩公分，或者有後腹腔或鼠蹊淋巴的轉移)	T3c-N0/N1-M0
IV	Distant metastasis excluding peritoneal metastasis (遠處轉移不包括腹膜轉移)	T4
IVA	Pleural effusion with positive cytology(胸腔積液細胞學陽性)	Any T, any N,M1
IVB	Hepatic and/or splenic parenchymal metastasis, metastasis to extra-abdominal organs(including inguinal lymph nodes and lymph nodes outside of the abdominal cavity) (肝和/或脾實質轉移，轉移到腹腔外臟器（包括腹股溝淋巴結和腹腔的外面淋巴結)	Any T, any N,M1

	腫瘤包括一個或兩個卵巢或輸卵管，原發骨盆癌或原發性腹膜癌	
IIA	Extension and/or implants on the uterus and/or fallopian tube(s) and/or ovaries 擴散只限於子宮或輸卵管或卵巢	T2a
IIB	Extension to and/or implants on other pelvic tissues 擴散至骨盆腔內的其他組織	T2b
III	Tumor involves one or both ovaries or fallopian tubes, or primary peritoneal cancer, with microscopically confirmed peritoneal metastasis outside the pelvis and/or metastasis to the retroperitoneal (pelvic and/or para-aortic) lymph nodes 腫瘤包括卵巢或輸卵管或原發性腹膜癌中的一種或兩種，顯微鏡確認盆腔外的腹膜轉移和/或向腹膜後（盆腔和/或主動脈旁）淋巴結轉移	T3
IIIA1	Positive retroperitoneal lymph nodes only (histologically confirmed) 僅有腹膜後淋巴結陽性（組織學證實） *IIIA1(i)* metastasis≦10mm(轉移≦10 毫米) *IIIA1(ii)* metastasis＞10mm(轉移＞10 毫米)	T1/T2 N1-M0
IIIA2	Microscopic extrapelvic (above the pelvic brim) peritonealinvolvement with or without positive retroperitoneal lymph nodes 顯微鏡下外膜（盆骨邊緣以上）腹膜穿刺有或無腹膜後淋巴結陽性	T3a NX, N0, N1-M0
IIIB	Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension with or without metastasis to the retroperitonealLymph nodes 肉眼可見的腹膜轉移超過骨盆 2 厘米或以下的最大維度有或無腹膜後淋巴結轉移	T3b NX, N0, N1-M0
IIIC	Macroscopic peritoneal metastasis beyond the pelvis more than2 cm in greatest dimension with or without metastasis to the retroperitoneal lymph nodes (includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ) 最大尺寸超過 2 厘米的肉眼可見的腹膜轉移，有或沒有轉移到腹膜後淋巴結（包括腫瘤向肝和脾的囊膜延伸而沒有任何器官的實質累及）	T3c NX, N0, N1-M0
IV	Distant metastasis, including pleural effusion with positive cytology; liver or splenic parenchymal metastasis; metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity); and transmural involvement of intestine	T4Any T Any N-M1

	遠處轉移，包括伴有細胞學陽性的胸腔積液;肝或脾實質轉移;轉移到腹外器官（包括腹股溝淋巴結和腹腔外淋巴結）;和腸壁的透壁受累	
IVA	Pleural effusion with positive cytology 胸腔積液細胞學陽性	Any T, Any N,M1a
IVB	Liver or splenic parenchymal metastases; metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity); transmural involvement of intestine 肝或脾實質轉移;轉移到腹外器官（包括腹股溝淋巴結和腹腔外的淋巴結）;透壁涉及腸道	Any T, Any N,M1b

第 8 頁

完整的分期手術：

完整的分期手術

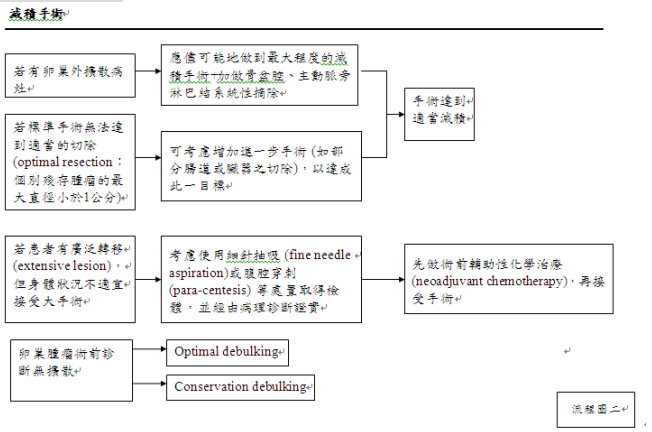
- 術前做腸道準備 (bowel preparation)
- 宜用中央垂直開腹切口
- 進入腹腔即抽取腹水或經由腹腔灌洗 (peritoneal lavage) 取得腹膜腔細胞學檢查的標本
- 盡可能完整地取出腫瘤
- 檢體常規性送冷凍切片 (frozen section)
- 全子宮及兩側卵巢輸卵管切除手術
- 儘量完整切除輸卵管漏斗部骨盆韌帶 (infundibulopelvic ligaments)
- 所有粘黏處需切片送檢
- 評估所有的腸道表面
- 若無明顯的卵巢外擴散病灶，則自子宮直腸陷窩 (cul-de-sac)、骨盆腔側壁、膀胱漿膜 (serosa)、兩側大腸側窩 (para-colic gutters)、橫膈膜下表面 (subdiaphragmatic surfaces) 等處隨機腹膜取樣
- 橫結腸下網膜切除手術 (infra-colic omentectomy)
- 取主動脈旁淋巴結 (para-aortic lymph nodes) 與骨盆淋巴結 (pelvic nodes) 送病理檢查。主動脈旁的淋巴結，至少需取樣至IMA之高度(建議儘量能拿到renal vein 之高度)。
- 若是黏液性 (mucinous) 卵巢癌，則應施行闌尾切除手術
- 若在卵巢癌的診斷過程中，曾使用腹腔鏡者，考慮切除腹腔鏡埠管路徑 (trocar tracks)
- 若首次紀錄需詳細記載殘存腫瘤(residual lesion)狀態及大小的比率。

五、 分期、分期手術、減積手術及保留生育手術- 完整的分期手術：修訂為-

五、 分期、分期手術、減積手術及保留生育手術- 完整的分期手術

- 術前做腸道準備 (bowel preparation)
- 宜用中央垂直開腹切口，評估新診斷或複發性卵巢癌患者是否可以達到最大化減瘤效果時，微創手術方法可能有用，如果臨床判斷表明最大減量不能達到，應考慮新輔助化療，並建議婦科腫瘤醫師進行適當的手術
- 進入腹腔即抽取腹水或經由腹腔灌洗 (peritoneal lavage) 取得腹膜腔細胞學檢查的標本
- 應盡可能採取BSO和子宮切除術，以在移除過程中保持腫瘤完整性
- 檢體常規性送冷凍切片 (frozen section)
- 全子宮及兩側卵巢輸卵管切除手術
- 儘量完整切除輸卵管漏斗部骨盆韌帶 (infundibulopelvic ligaments)
- 所有粘黏處需切片送檢
- 評估所有的腸道表面
- 若無明顯的卵巢外擴散病灶，則自子宮直腸陷窩 (cul-de-sac)、骨盆腔側壁、膀胱漿膜 (serosa)、兩側大腸側窩 (para-colic gutters)、橫膈膜下表面 (subdiaphragmatic surfaces) 等處隨機腹膜取樣
- 橫結腸下網膜切除手術 (infra-colic omentectomy)
- 取主動脈旁淋巴結 (para-aortic lymph nodes) 與骨盆淋巴結 (pelvic nodes) 送病理檢查，主動脈旁的淋巴結，至少需取樣至IMA之高度(建議儘量能拿到renal vein 之高度)，主動脈旁淋巴結清掃應邊緣腔靜脈和主動脈的淋巴結組織整側剝離到至少膀胱腹膜下動脈水平，最好達到腎血管水平
- 若是黏液性 (mucinous) 卵巢癌，則應施行闌尾切除手術
- 若在卵巢癌的診斷過程中，曾使用腹腔鏡者，考慮切除腹腔鏡埠管路徑 (trocar tracks)
- 若首次紀錄需詳細記載
  1.傷口長度範圍，
  2.腫瘤完整切除或不完整切除
  3.殘存腫瘤(residual lesion)狀態、及大小的比率。

流程圖一

<table>
<tr>
<td>第 9 頁</td>
<td>減積手術
 
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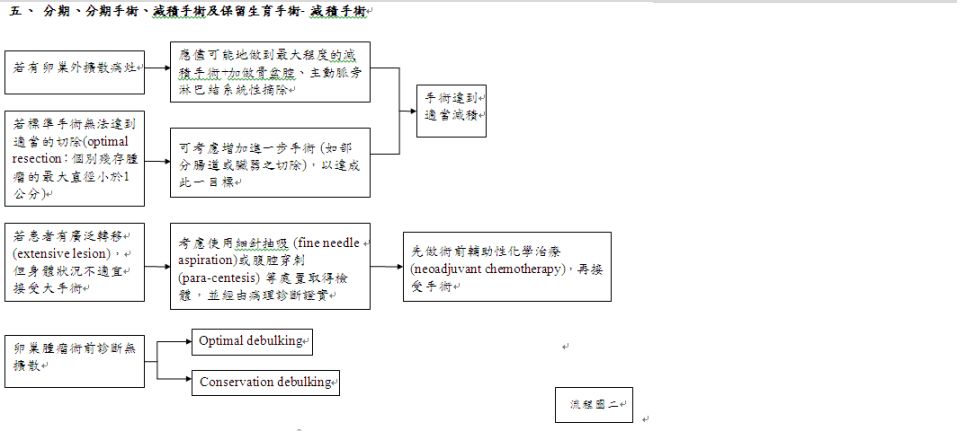
<td>五、 分期、分期手術、減積手術及保留生育手術- 減積手術：修訂為
 
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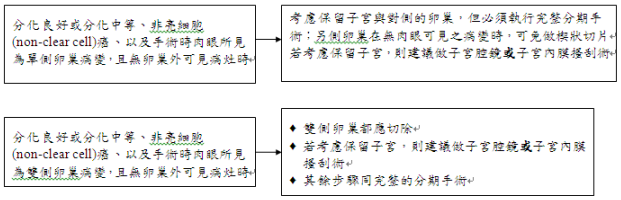
<td>第 10 頁</td>
<td>保留生育之完整分期手術 (仍強烈想要懷孕的患者)
 
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 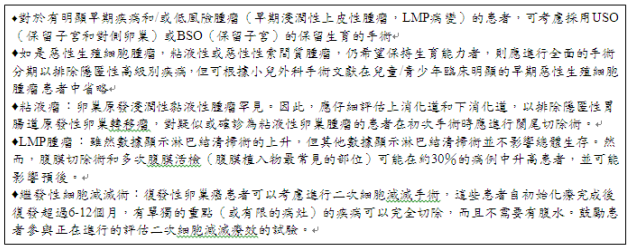
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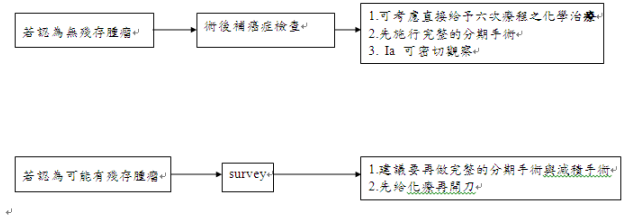
<td>第 11 頁</td>
<td>未接受完整手術的患者
 
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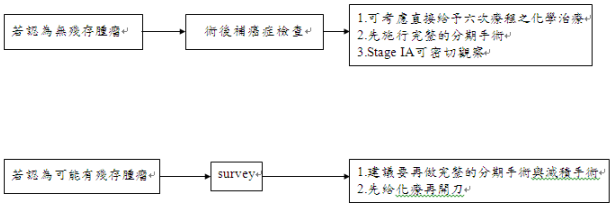
<td>五、 分期、分期手術、減積手術及保留生育手術 - 未接受完整手術的患者：修訂為
 
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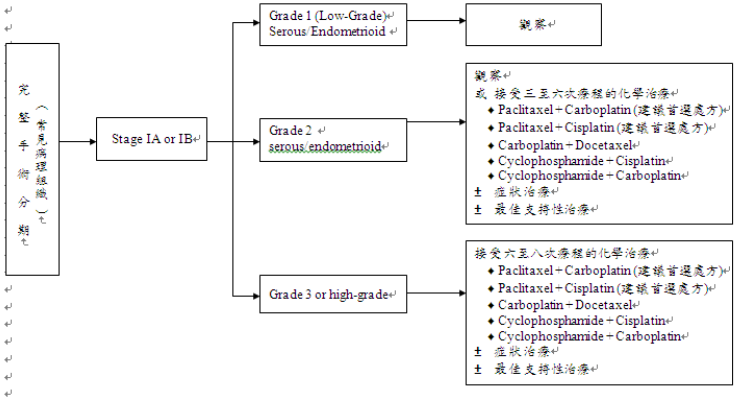
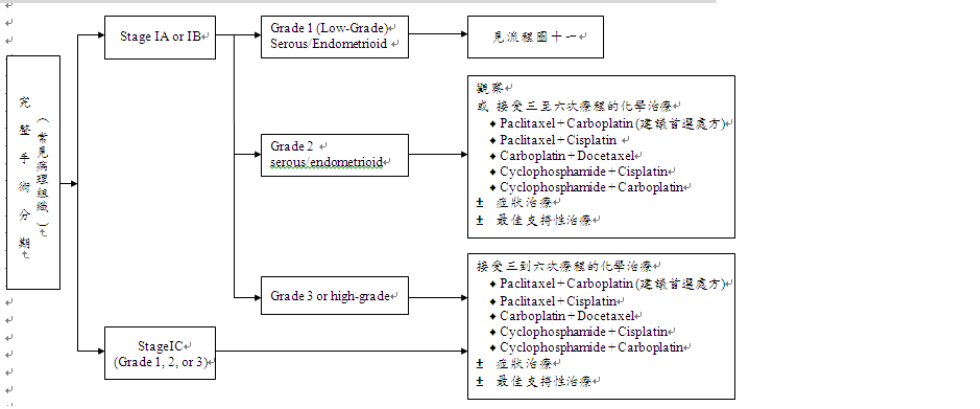
六、 卵巢上皮癌第一期之處置(一)



六、 卵巢上皮癌之處置-Stage IA、IB、IC：修訂為



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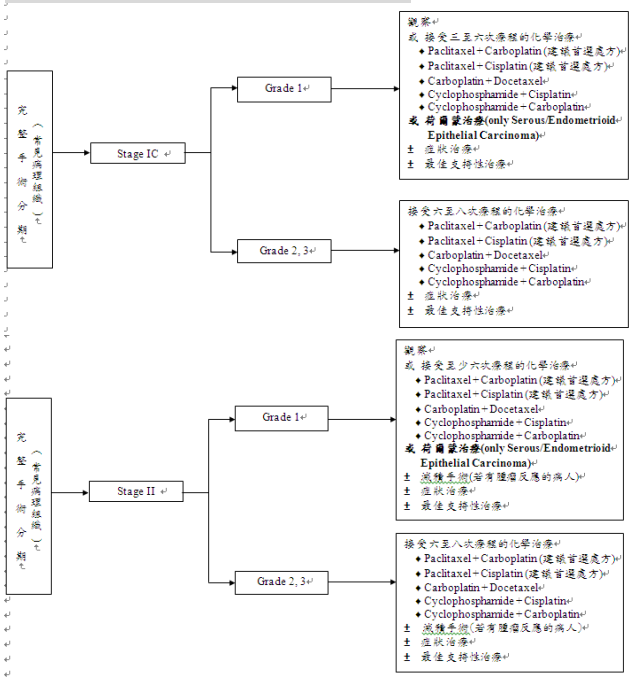
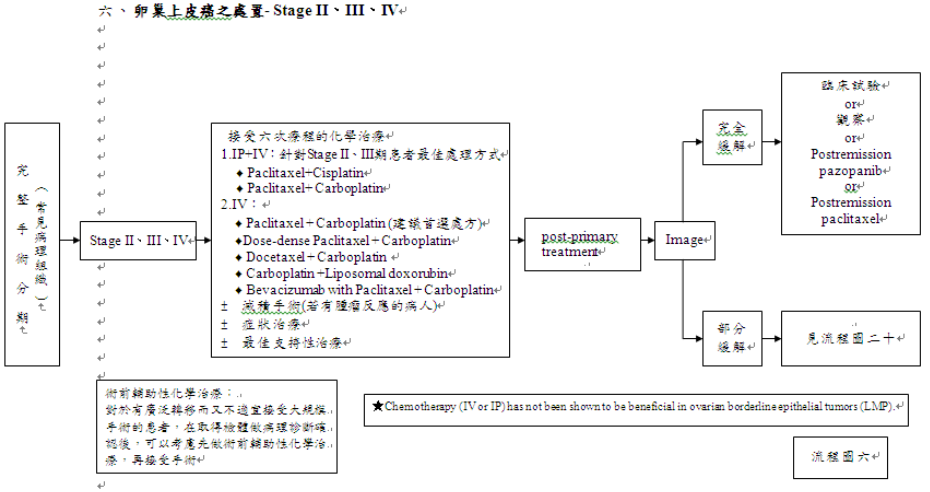
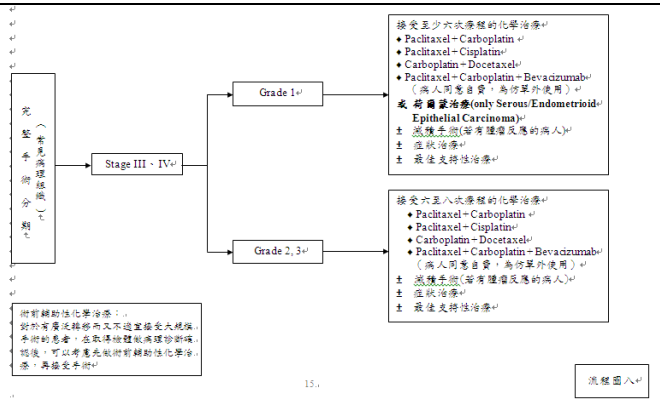
卵巢上皮癌第一期之處置(二)



六、卵巢上皮癌之處置- Stage II、III、IV：修訂為





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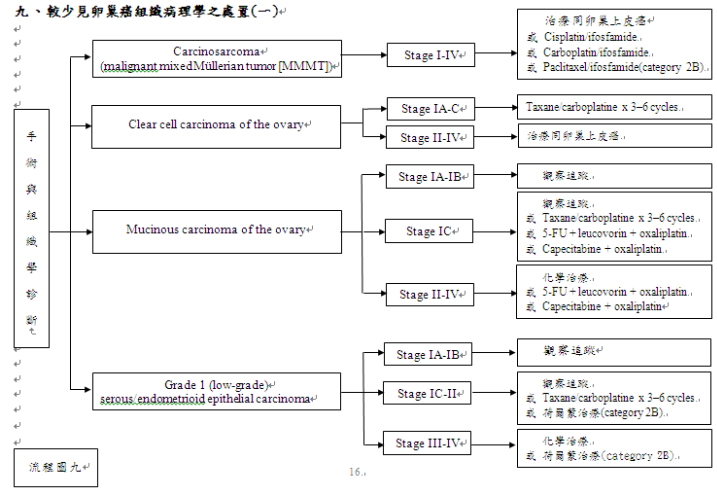
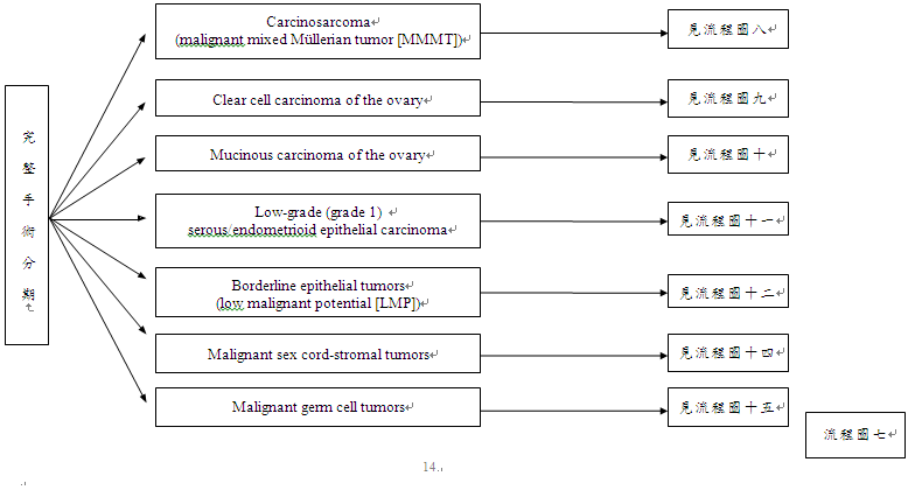
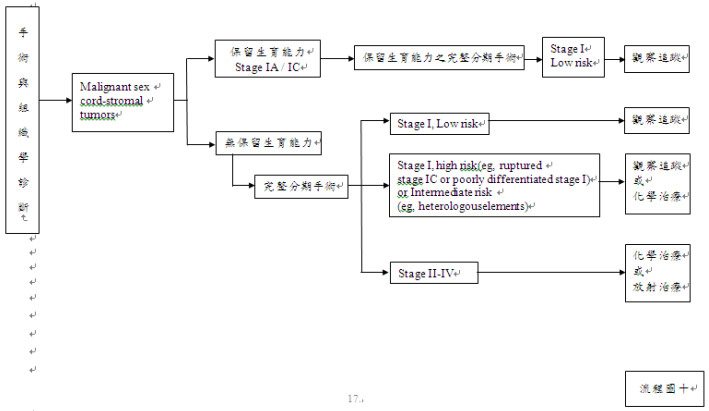
九、較少見卵巢癌組織病理學之處置(一)



七、較少見卵巢癌組織病理學之處置：修訂為



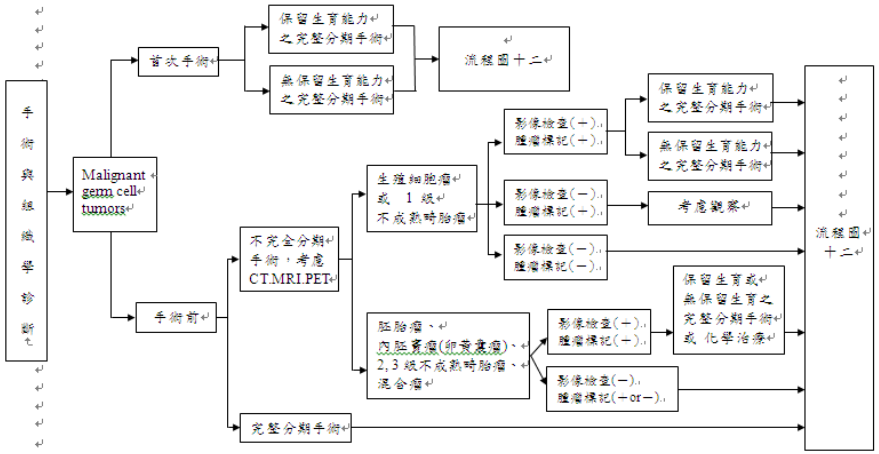
較少見卵巢癌組織病理學之處置(二)



17.

流程圖十

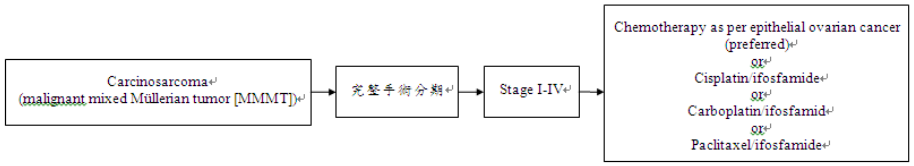
較少見卵巢癌組織病理學之處置(三)



18.

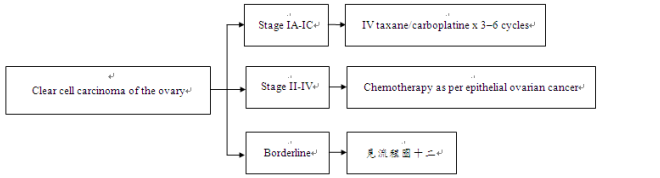
流程圖十一

七、較少見卵巢癌組織病理學之處置– Carcinosarcoma(malignant mixed Müllerian tumor [MMMT])



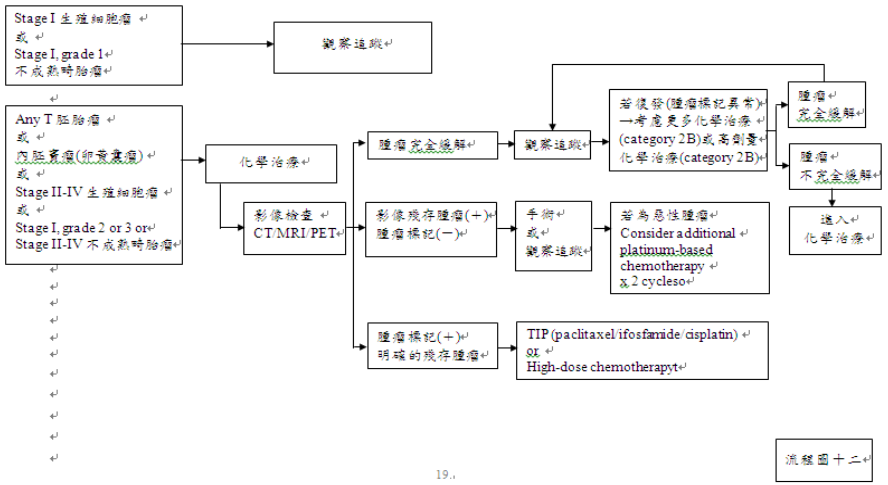
流程圖八

七、較少見卵巢癌組織病理學之處置– Clear cell carcinoma of the ovary



流程圖九

Malignant Germ Cell Tumors (生殖細胞癌)



19.

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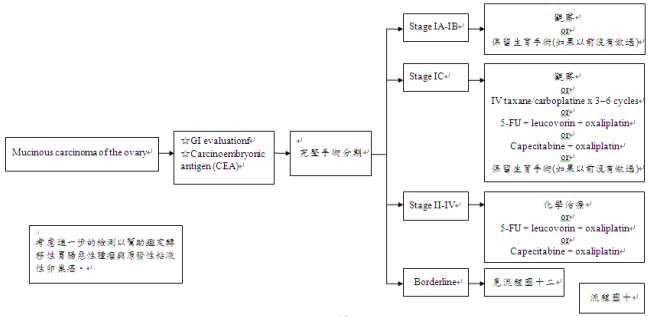
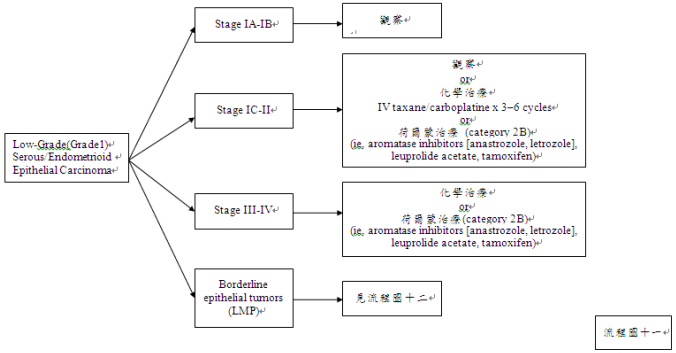


17.

七、較少見卵巢癌組織病理學之處置- Low-grade (grade 1) serous/endometrioid epithelial carcinoma



18.

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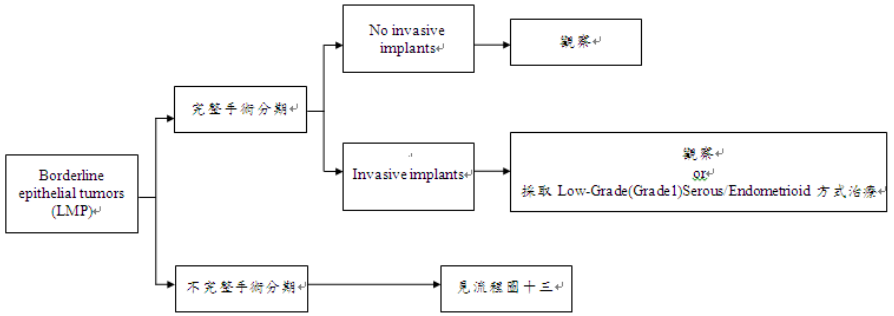
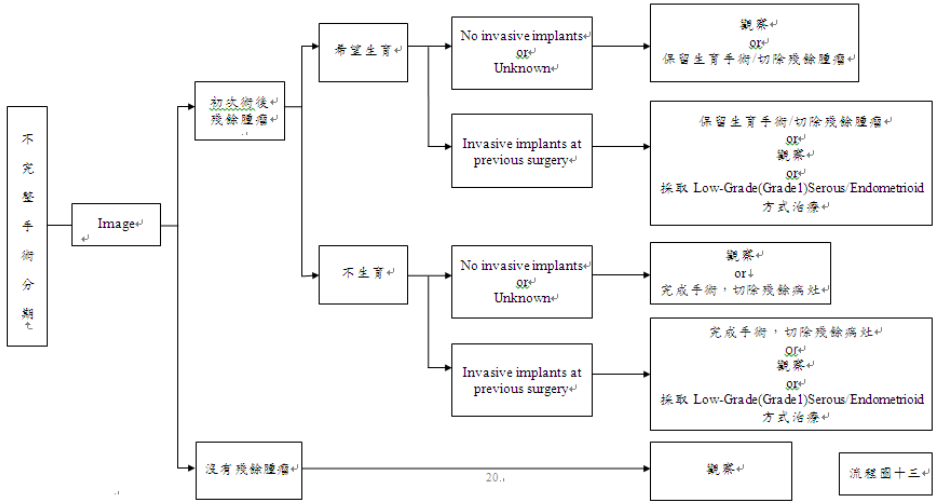
七、較少見卵巢癌組織病理學之處置- Borderline epithelial tumors(low malignant potential [LMP])



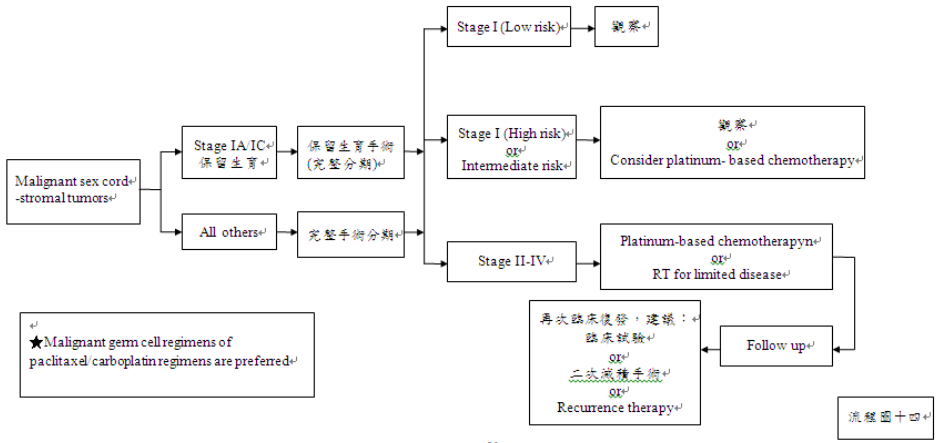
流程圖十二

七、較少見卵巢癌組織病理學之處置- Borderline epithelial tumors(low malignant potential [LMP])

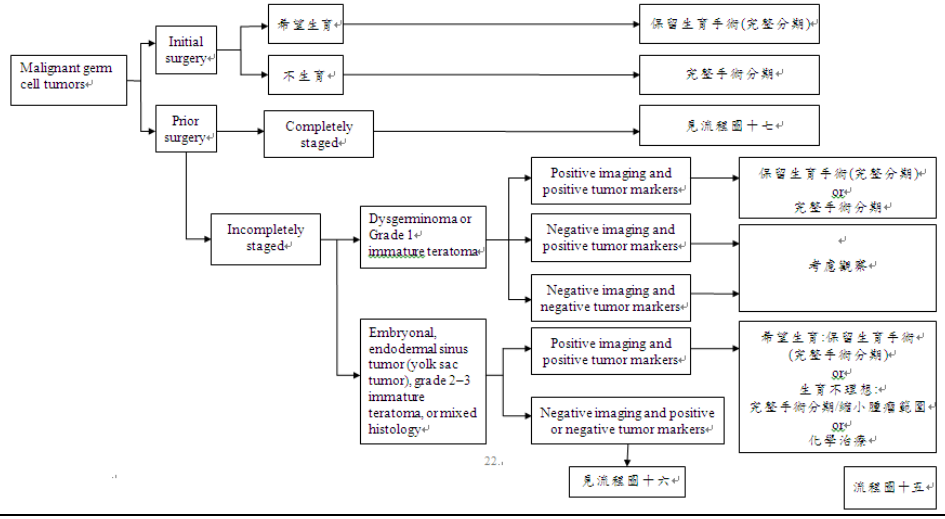


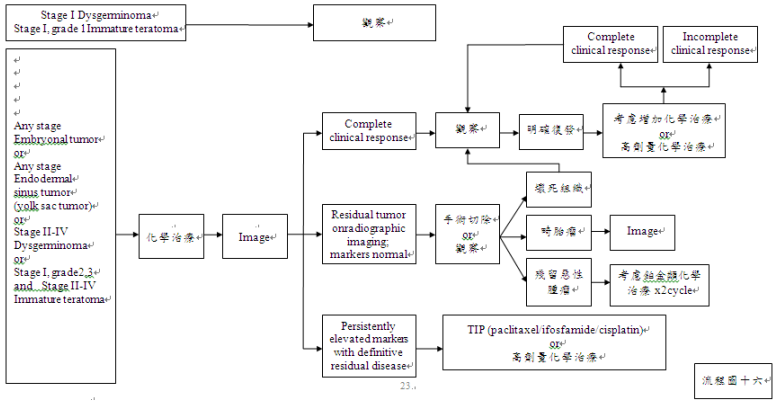
無

七、較少見卵巢癌組織病理學之處置- Malignant sex cord-stromal tumors



七、較少見卵巢癌組織病理學之處置- Malignant germ cell tumors

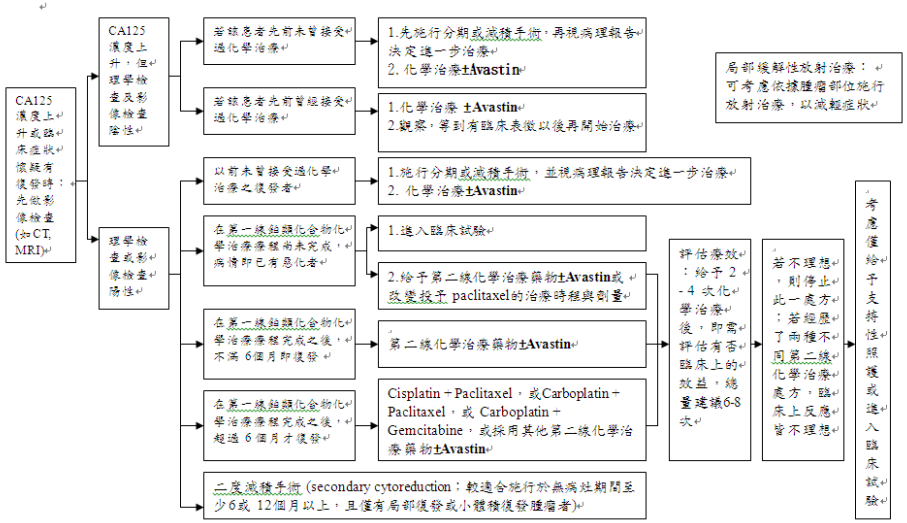
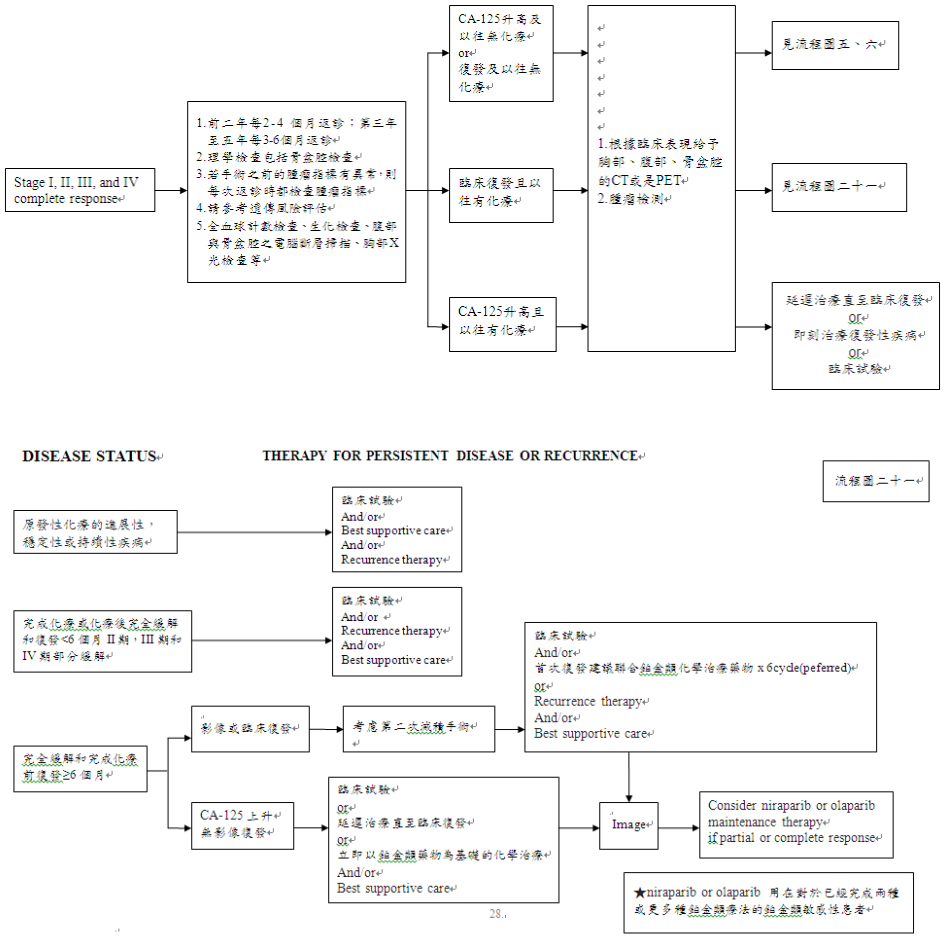


		七、較少見卵巢癌組織病理學之處置- Malignant germ cell tumors  流程圖十六
第 25 頁	無	新增-八、 化學治療期間之監測 -對惡性生殖細胞和性病性角質腫瘤的監測 八、 化學治療期間之監測 –對惡性生殖細胞和性病性角質腫瘤的監測

	Germ cell tumors					Sex cord-stromal tumors				
追診	<1 年	1-2 年	2-3 年	3-5 年	>5 年	<1 年	1-2 年	2-3 年	3-5 年	>5 年
理學檢查	每 2-4 個月		每年			每 2-4 個月		每 6 個月		
腫瘤指標	每 2-4 個月		NA			每 2-4 個月		每 6 個月		
影像學檢查	如臨床表現 (除非一開始檢驗為正常)		如臨床表現			數據不足以支持日常使用				
懷疑復發	CT scan and tumor markers									

★Chest x-ray, chest/abdominal/pelvic CT, MRI, PET/CT, or PET; with contrast unless contraindicated，臨床復發可依影像為判斷依據

流程圖十八

<table>
<tr><td>第 26 頁</td><td>十一、 療程完成之後的追蹤處置</td><td>九、 療程完成之後的追蹤處置 –新增
遺傳學檢查：若以往未做過，建議檢察</td></tr>
<tr><td>第 27 頁</td><td>十二、 卵巢癌的復發
 
</td><td>十、卵巢癌的復發處置：修訂為
 
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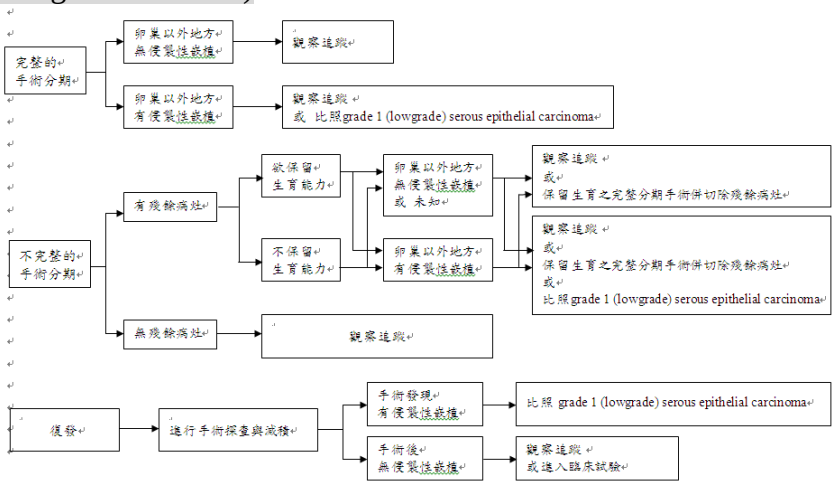
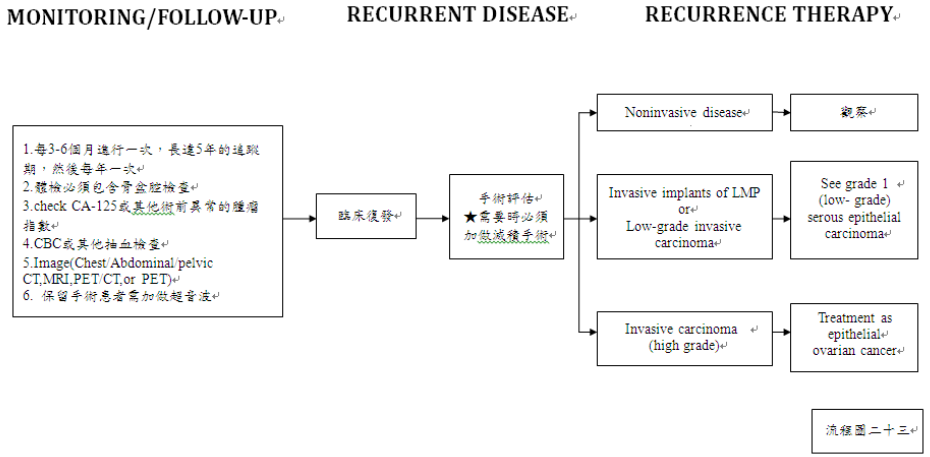
<tr>
<td>第 30 頁</td>
<td>十三、 低惡性度卵巢癌 Borderline Epithelial Tumors (Low Malignant Potential)
 
</td>
<td>十二、Borderline epithelial tumors(low malignant potential [LMP]) 的追蹤處置：修訂為
 
</td>
</tr>
<tr>
<td>第 31 頁</td>
<td>十五、化學治療</td>
<td>十三、化學治療 - Primary Systemic Therapy Regimens：新增
PRINCIPLES OF SYSTEMIC THERAPY
★在聯合使用 IP 和 IV 方案之前，與單獨使用 IV 化療相比，患者必須被告知聯合方案的毒性增加（增加骨髓抑制，腎毒性，腹痛，神經病變，胃腸道毒性，代謝毒性，和肝毒性）。
★輔助治療：癌症手術後的藥物，放療或其他形式的補充治療，旨在降低疾病復發的風險，或主要治療手術細胞減滅術後殘留疾病，無論是粗大還是微觀。
★新輔助治療：在癌症手術前給予藥物，放射線或其他形式的治療，以減少手術準備時的腫瘤負擔。
★老年患者和合併症患者可能對這些 NCCN 指南中推薦的聯合化療方案不耐受。單劑鉑劑可能適用於選定的患者。
★復發治療：用於治療復發性癌症，控制症狀，或在初始治療後復發性癌症的臨床，生化或放射學證據時增加生命長度和/或生活質量的藥物，放射或其他形式的治療。</td>
</tr>
</table>

十三、化學治療 - Primary Systemic Therapy Regimens

Stage II-IV

1. IP/IV Regimen (for optimally debulked stage II-III disease)：

Paclitaxel 135 mg/m² IV continuous infusion over 3 or 24 h Day 1;
cisplatin 75–100 mg/m² IP Day 2 after IV paclitaxel;
paclitaxel 60 mg/m² IP Day 8.
Repeat every 3 weeks x 6 cycles.

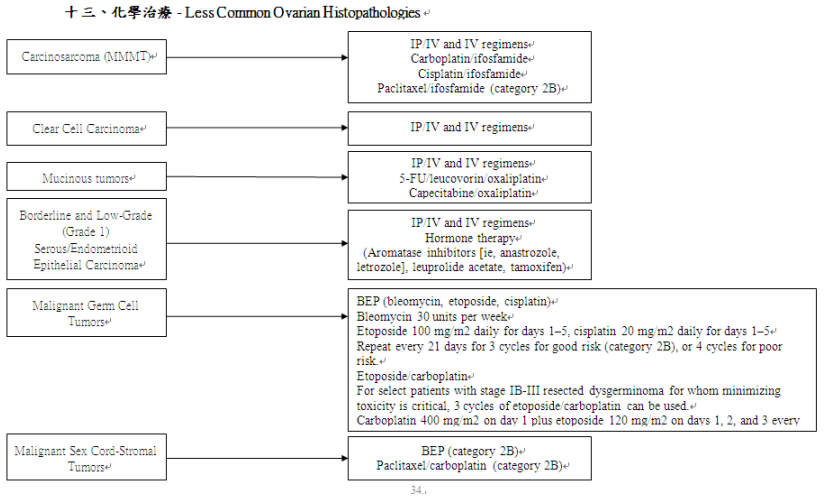
2. IV Regimens：

- Paclitaxel 175 mg/m² IV over 3 hours followed by carboplatin AUC 5–6 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles.
- Dose-dense paclitaxel 80 mg/m² IV over 1 hour Days 1, 8, and 15 followed by carboplatin AUC 5–6 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles.
- Paclitaxel 60 mg/m² IV over 1 hour followed by carboplatin AUC 2 IV over 30 minutes. Weekly for 18 weeks.
- Docetaxel 60–75 mg/m² IV over 1 hour followed by carboplatin[c] AUC 5–6 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles.
- Carboplatin AUC 5 + pegylated liposomal doxorubicin 30 mg/m² every 4 weeks for 6 cycles.
- Bevacizumab-containing regimens per ICON-7 and GOG-218:
  Paclitaxel 175 mg/m² IV over 3 hours followed by carboplatin AUC 5–6 IV over 1 hour, and bevacizumab 7.5 mg/kg IV over 30–90 minutes Day 1. Repeat every 3 weeks x 5–6 cycles. Continue bevacizumab for up to 12 additional cycles.
  or
  Paclitaxel 175 mg/m² IV over 3 hours followed by carboplatin AUC 6 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles. Starting Day 1 of cycle 2, give bevacizumab 15 mg/kg IV over 30–90 minutes every 3 weeks for up to 22 cycles.

十三、化學治療 - Neoadjuvant Therapy

新輔助療法

★任何上述 IV 方案都可以在 IDS 之前用作新輔助療法。
★由於潛在干擾術後癒合，應在使用 Bevacizumab-containing 的方案之前謹慎使用 IDS。
★新輔助治療和 IDS 後，上述任一方案（IV 或 IP / IV）均可視為輔助治療選擇。
★新輔助治療和 IDS 後使用 IP 化療方案的數據有限。
以下是 IDS 後的額外 IP 選項：
IV paclitaxel 135 mg/m2 over 3 hours on Day 1, IP carboplatinAUC 6 IP Day 1, paclitaxel 60 mg/m2 IP Day 8.
★建議至少 6 個週期的治療，包括 IDS 後至少 3 個週期的輔助治療。

		
第 25 頁	十五、化學治療 Acceptable Recurrence Therapies for Epithelial Ovarian/Fallopian Tube/Primary Peritoneal Cancer	十三、化學治療Acceptable Recurrence Therapies for Epithelial Ovarian/Fallopian Tube/Primary Peritoneal Cancer –新增 ☆**Preferred Agents** **Cytotoxic Therapy**： **Additional options for mucinous carcinoma only:** 1.5-FU/leucovorin/oxaliplatin ± bevacizumab (category 2B for bevacizumab) 2.Capecitabine + oxaliplatin **Targeted Therapy**：Rucaparib (platinum-resistant disease) ☆**Other Potentially Active Agents** **Cytotoxic Therapy**： CombinationsCarboplatin/paclitaxel/bevacizumab(platinum-sensitive disease) **Targeted Therapy**： 1.Rucaparib(platinum- sensitive disease) 2.Pembrolizumab(for microsatellite instability- high [MSI-H] or mismatch repair deficient [dMMR]solid tumors)

目 錄

一、前言

本共識手冊內所提之各種診治意見，為原則性之建議，希望能為癌症患者及其家屬提供一個正確的指引；但對臨床醫師之醫療行為無絕對之法律性約束力！由於醫藥科技持續在進步，每位患者的病情亦不盡相同；醫師應就病人之病情做個別的考量，病人和家屬亦應與醫師溝通討論，以決定最適當之診治方式。

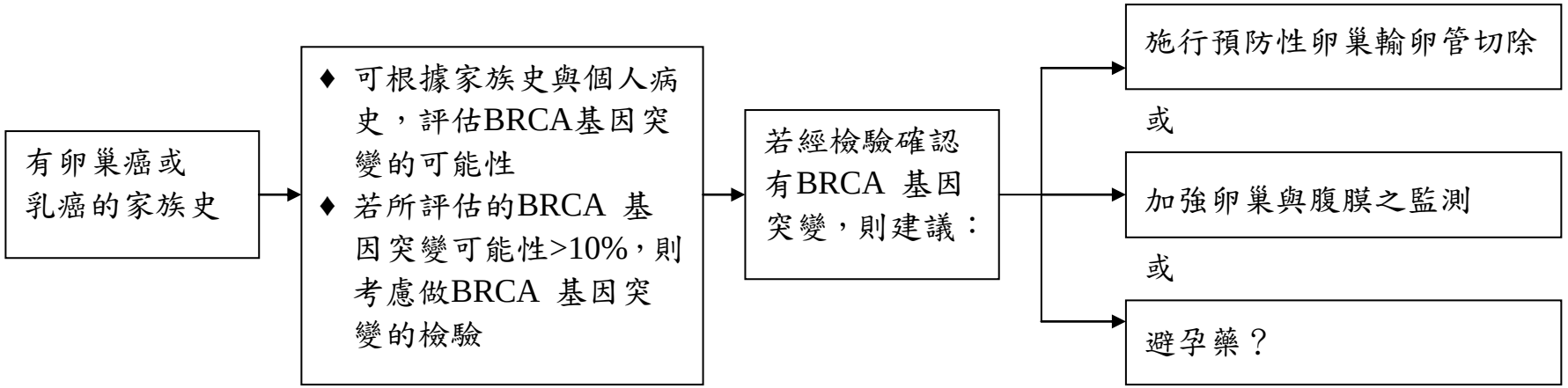
早期的卵巢癌往往沒有症狀，因而一旦發現，75%的患者已達到第III /IV期；症狀多半為腹部腫大、脹氣等腹部不適症狀。上皮性卵巢癌通常經由局部的瀉落 (local shedding) 在腹膜腔裡擴散；淋巴結轉移之機會，在肉眼認為是第一期的患者中有24%，肉眼認為第二期中有50%，肉眼認為第三期中有74%；轉移到骨盆淋巴結 (pelvic lymph node) 與主動脈旁淋巴結 (para-aortic lymph node)的機會類似]；也有經由橫膈膜而侵襲肋膜腔的情況發生。

卵巢癌患者若有下列條件則預後較佳；反之則預後較差。這些較佳預後因素(favorable prognostic factors)有：年紀較輕、良好的身體狀況(good performance status)、細胞組織型態不是黏液性 (mucinous) 細胞或亮細胞(clear cell)型、較低的分期期別(lower stage)、細胞分化良好(well differentiated)、較少的腫瘤體積、無腹水(ascites)、以及減積手術(cytoreductive surgery) 之後僅剩下較小的殘留腫瘤 (smaller residual tumor)。

本卵巢癌診斷及治療指引的建立，除了依據已發表的實證醫學證據及專家意見外，並參考國家衛生研究院卵巢癌臨床指引、美國 National Comprehensive Cancer Network (NCCN) 的 Practice Guide-lines in Ovarin Cancer 2017,V5版、FIGO Staging Classifications and Clinical Practice Guidelines in the Management of Gynecologic Cancer、及中山醫學大學附設醫院卵巢癌治療經驗進行編修。

二、風險因子、篩檢與預防

在25歲之前懷孕，對嬰兒哺育母乳可減少發生卵巢癌的風險。發生卵巢癌的風險因子 (risk factors) 有：未曾生產 (nulliparity)、第一胎生產時已逾35歲、家族史(主要是家族內有兩個或以上的親戚包括母、女及姐妹罹患卵巢癌者) 等。不孕症本身也是風險因子，連續使用排卵藥 (如clomiphene) 超過一年，有增加卵巢癌的風險。



三、疑似惡性卵巢腫瘤治療前的評估

- ♦ 身體理學檢查
- ♦ 個人病史探詢
- ♦ 家族史評估
- ♦ 超音波檢查
- ♦ 胸部X 光檢查
- ♦ 建議進行遺傳學檢查(如果以往都沒做過，建議檢查)
- ♦ 腫瘤指標 (tumor marker)包含：CA125、CEA*。
- ♦ 若年齡小於35歲(含)治療前應評估的腫瘤指標：CA125、AFP、β-hCG、CEA 、LDH*。
- ♦ 全血球計數、血清生化檢查
- ♦ 可安排電腦斷層掃描或核磁共振掃描來協助擬定適當的手術計畫
- ♦ 若臨床上懷疑有腸道之壓迫或阻塞、或疑似轉移性卵巢癌，則可安排上消化道內視鏡、大腸鏡或鋇劑顯影等胃腸道檢查
- ♦ 對於固體性 (solid) 或複雜性 (complex) 卵巢腫瘤，一般都避免用細針抽吸 (fine-needle aspiration) 的方式來做細胞學檢查
- ♦ 腹腔鏡不宜使用於懷疑是卵巢惡性腫瘤的患者

*: option

四、治療之主軸

(A) 完整徹底的分期手術 (staging operation)，或
(B) 盡可能手術切除所有卵巢腫瘤與卵巢外的癌組織，即最大程度的減積手術 (maximal cytoreduction)

↓

使用以鉑類化合物為基礎的輔助性化學治療 (platinum-based adjuvant chemotherapy)

五、 分期、分期手術、減積手術及保留生育手術

FIGO 分期		TNM Categories
N/A	Primary tumor cannot be assessed 原發腫瘤無法評估	TX
N/A	No evidence of primary tumor 沒有原發腫瘤的證據	T0
I	Tumor limited to ovaries (one or both) or fallopian tube(s) 腫瘤限於卵巢（一個或兩個）或輸卵管（S）	T1
IA	Tumor limited to one ovary (capsule intact) or fallopian tube, no tumor on ovarian or fallopian tube surface; no malignant cells in ascites or peritoneal washings 腫瘤限於一個卵巢（表面完整）或輸卵管，卵巢或輸卵管表面無腫瘤;腹水或腹腔沖洗液中無惡性細胞	T1a
IB	Tumor limited to both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in ascites or peritoneal washings 腫瘤局限於兩個卵巢（表面完整）或輸卵管;卵巢或輸卵管表面無腫瘤;腹水或腹腔沖洗液中無惡性細胞	T1b
IC	Tumor limited to one or both ovaries or fallopian tubes, with any of the following: 腫瘤限於一個或兩個卵巢或輸卵管，具有以下任何一種：	T1c
IC1	Surgical spill (手術破裂)	T1c
IC2	Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface 手術前囊膜或卵巢或輸卵管表面腫瘤破裂	T1c
IC3	Malignant cells in the ascites or peritoneal washings (腹水或腹腔沖洗有惡性細胞)	T1c
II	Tumor involves one or both ovaries or fallopian tubes with pelvic extension below pelvic brim or primary peritoneal cancer	T2

	腫瘤包括一個或兩個卵巢或輸卵管，在盆骨邊緣或原發性腹膜癌	
IIA	Extension and/or implants on the uterus and/or fallopian tube(s) and/or ovaries 擴散只限於子宮或輸卵管或卵巢	T2a
IIB	Extension to and/or implants on other pelvic tissues 擴散至骨盆腔內的其他組織	T2b
III	Tumor involves one or both ovaries or fallopian tubes, or primary peritoneal cancer, with microscopically confirmed peritoneal metastasis outside the pelvis and/or metastasis to the retroperitoneal (pelvic and/or para-aortic) lymph nodes 腫瘤包括卵巢或輸卵管或原發性腹膜癌中的一種或兩種，顯微鏡確認盆腔外的腹膜轉移和/或向腹膜後（盆腔和/或主動脈旁）淋巴結轉移	T3
IIIA1	Positive retroperitoneal lymph nodes only (histologically confirmed) 僅有腹膜後淋巴結陽性（組織學證實） *IIIA1(i)* metastasis≦10㎜(轉移≦10 毫米） *IIIA1(ii)* metastasis＞10㎜(轉移＞10 毫米）	T1/T2 N1-M0
IIIA2	Microscopic extrapelvic (above the pelvic brim) peritonealinvolvement with or without positive retroperitoneal lymph nodes 顯微鏡下外膜（盆骨邊緣以上）腹膜穿刺有或無腹膜後淋巴結陽性	T3a NX, N0, N1-M0
IIIB	Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension with or without metastasis to the retroperitoneallymph nodes 肉眼可見的腹膜轉移超過骨盆 2 厘米或以下的最大維度有或無腹膜後淋巴結轉移	T3b NX, N0, N1-M0
IIIC	Macroscopic peritoneal metastasis beyond the pelvis more than2 cm in greatest dimension with or without metastasis to the retroperitoneal lymph nodes (includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ) 最大尺寸超過 2 厘米的肉眼可見的腹膜轉移，有或沒有轉移到腹膜後淋巴結（包括腫瘤向肝和脾的囊腫延伸而沒有任何器官的實質累及）	T3c NX, N0, N1-M0
IV	Distant metastasis, including pleural effusion with positive cytology; liver or splenic parenchymal metastasis; metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity); and transmural involvement of intestine	T4Any T Any N-M1

	遠處轉移，包括伴有細胞學陽性的胸腔積液;肝或脾實質轉移;轉移到腹外器官（包括腹股溝淋巴結和腹腔外淋巴結）;和腸壁的透壁受累	
IVA	Pleural effusion with positive cytology 胸腔積液細胞學陽性	Any T, Any N,M1a
IVB	Liver or splenic parenchymal metastases; metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity); transmural involvement of intestine 肝或脾實質轉移;轉移到腹外器官（包括腹股溝淋巴結和腹腔外的淋巴結）;透壁涉及腸道	Any T, Any N,M1b

五、 分期、分期手術、減積手術及保留生育手術- 完整的分期手術

- ♦ 術前做腸道準備 (bowel preparation)
- ♦ 宜用中央垂直開腹切口，評估新診斷或複發性卵巢癌患者是否可以達到最大化減瘤效果時，微創手術方法可能有用。如果臨床判斷表明最大減量不能達到，應考慮新輔助化療，故建議婦科腫瘤醫師進行適當的手術
- ♦ 進入腹腔即抽取腹水或經由腹腔灌洗 (peritoneal lavage) 取得腹膜腔細胞學檢查的標本
- ♦ 應盡可能採取BSO和子宮切除術，以在移除過程中保持腫瘤完整性
- ♦ 檢體常規性送冷凍切片 (frozen section)
- ♦ 全子宮及兩側卵巢輸卵管切除手術
- ♦ 儘量完整切除輸卵管漏斗部骨盆韌帶 (infundibulopelvic ligaments)
- ♦ 所有粘黏處需切片送檢
- ♦ 評估所有的腸道表面
- ♦ 若無明顯的卵巢外擴散病灶，則自子宮直腸陷窩 (cul-de-sac)、骨盆腔側壁、膀胱漿膜 (serosa)、兩側大腸側窩 (para-colic gutters)、橫膈膜下表面 (subdiaphragmatic surfaces) 等處隨機腹膜取樣
- ♦ 橫結腸下網膜切除手術 (infra-colic omentectomy)
- ♦ 取主動脈旁淋巴結 (para-aortic lymph nodes) 與骨盆淋巴結 (pelvic nodes) 送病理檢查。主動脈旁的淋巴結，至少需取樣至IMA之高度(建議儘量能拿到renal vein 之高度)。主動脈旁淋巴結清掃應通過將腔靜脈和主動脈的淋巴結組織雙側剝離到至少腸系膜下動脈水平，最好達到腎血管水平
- ♦ 若是黏液性 (mucinous) 卵巢癌，則應施行闌尾切除手術
- ♦ 若在卵巢癌的診斷過程中，曾使用腹腔鏡者，考慮切除腹腔鏡埠管路徑 (trocar tracks)
- ♦ 若首次紀錄需詳細記載

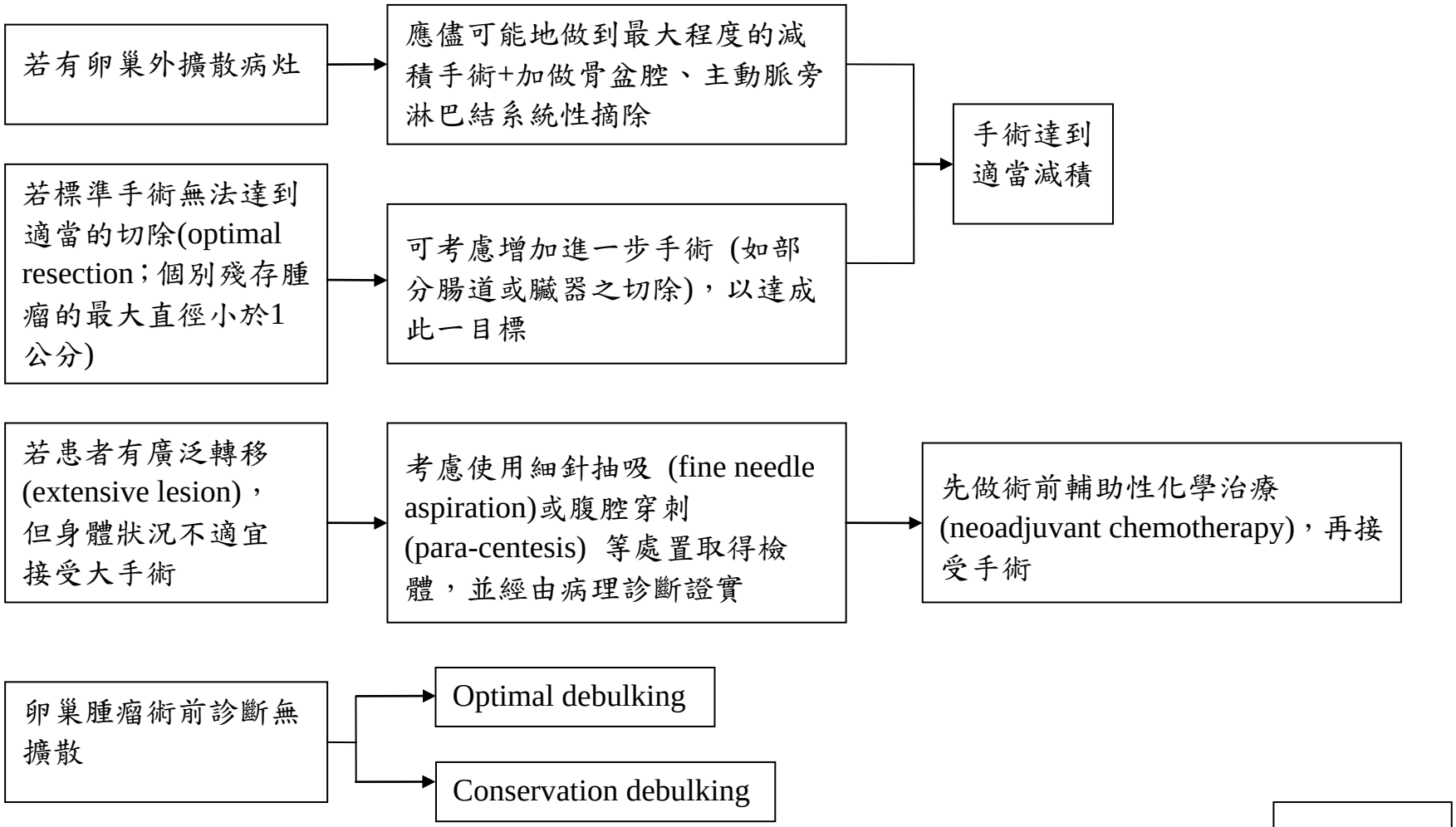
  1.傷口長度範圍、

  2.腫瘤完整切除或不完整切除

  3.殘存腫瘤(residual lesion)狀態、及大小的比率。

流程圖一

五、 分期、分期手術、減積手術及保留生育手術- 減積手術



流程圖二

五、 分期、分期手術、減積手術及保留生育手術 – 保留生育之完整分期手術 (仍強烈想要懷孕的患者)

♦對於有明顯早期疾病和/或低風險腫瘤（早期浸潤性上皮性腫瘤，LMP病變）的患者，可考慮採用USO（保留子宮和對側卵巢）或BSO（保留子宮）的保留生育的手術

♦如是惡性生殖細胞腫瘤，粘液性或惡性性索間質腫瘤，仍希望保持生育能力者，則應進行全面的手術分期以排除隱匿性高級別疾病，但可根據小兒外科手術文獻在兒童/青少年臨床明顯的早期惡性生殖細胞腫瘤患者中省略

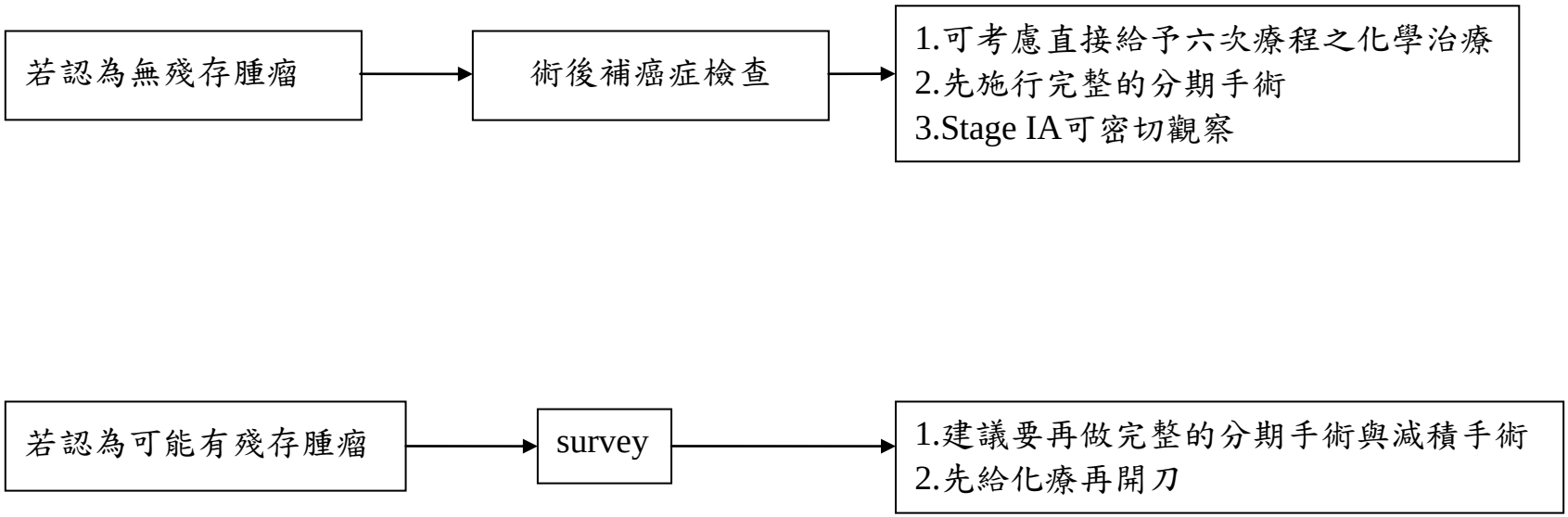
♦粘液瘤：卵巢原發浸潤性黏液性腫瘤罕見。因此，應仔細評估上消化道和下消化道，以排除隱匿性胃腸道原發性卵巢轉移瘤，對疑似或確診為粘液性卵巢腫瘤的患者在初次手術時應進行闌尾切除術。

♦LMP腫瘤：雖然數據顯示淋巴結清掃術的上升，但其他數據顯示淋巴結清掃術並不影響總體生存。然而，腹膜切除術和多次腹膜活檢（腹膜植入物最常見的部位）可能在約30%的病例中升高患者，並可能影響預後。

♦繼發性細胞減滅術：復發性卵巢癌患者可以考慮進行二次細胞減滅手術，這些患者自初始化療完成後復發超過6-12個月，有單獨的重點（或有限的病灶）的疾病可以完全切除，而且不需要有腹水。鼓勵患者參與正在進行的評估二次細胞減滅療效的試驗。

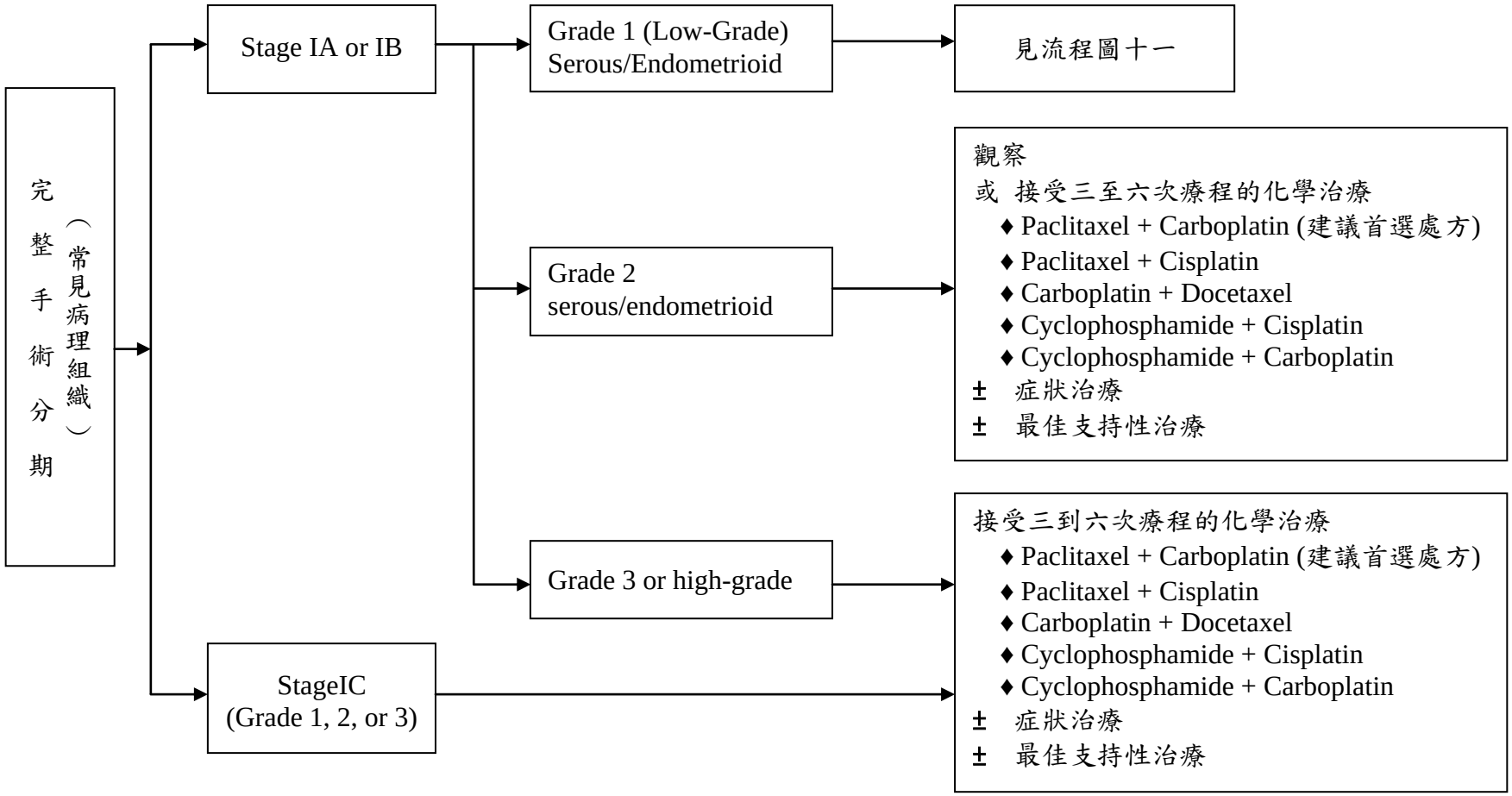
流程圖三

五、 分期、分期手術、減積手術及保留生育手術 – 未接受完整手術的患者



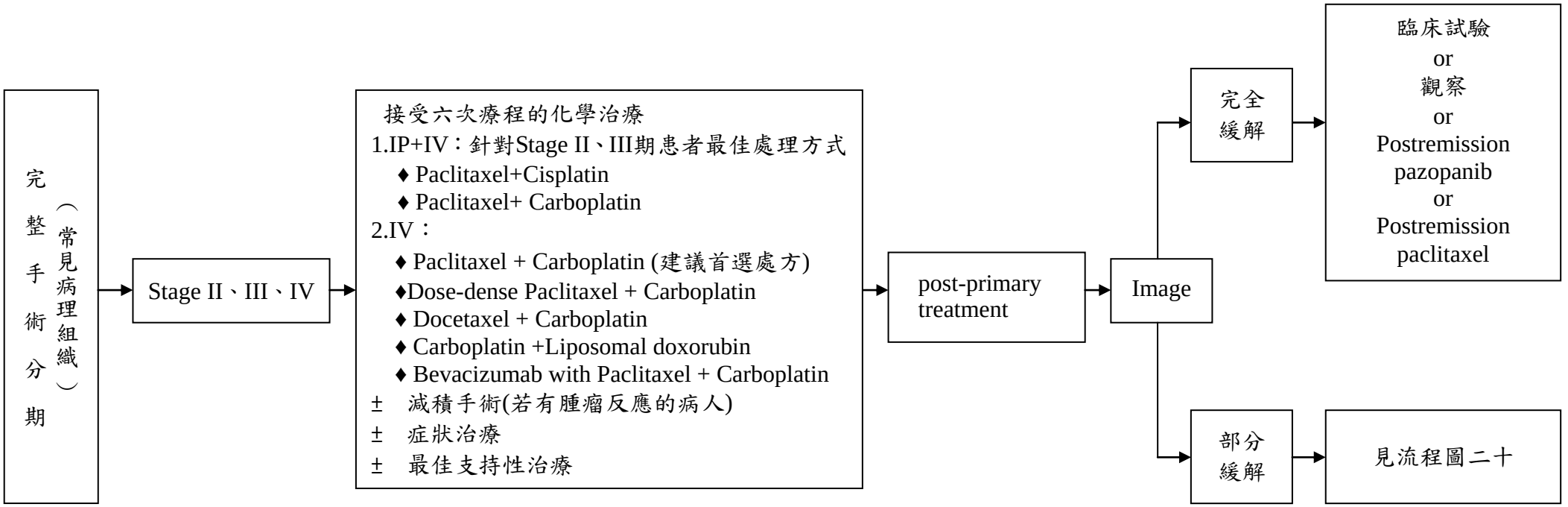
流程圖四

六、 卵巢上皮癌之處置-Stage IA、IB、IC



流程圖五

六、卵巢上皮癌之處置- Stage II、III、IV

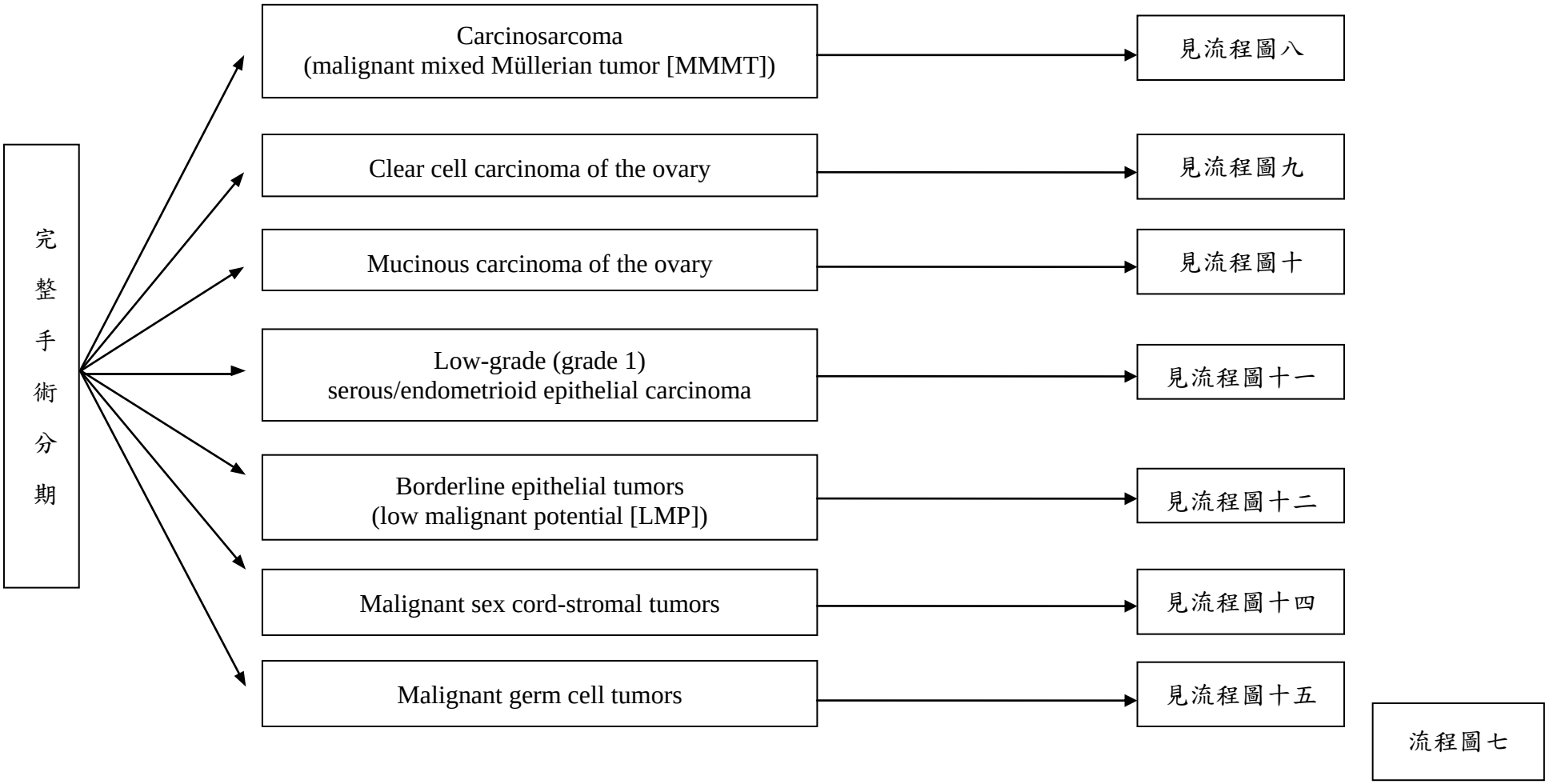


術前輔助性化學治療：
對於有廣泛轉移而又不適宜接受大規模手術的患者，在取得檢體做病理診斷確認後，可以考慮先做術前輔助性化學治療，再接受手術

★Chemotherapy (IV or IP) has not been shown to be beneficial in ovarian borderline epithelial tumors (LMP).

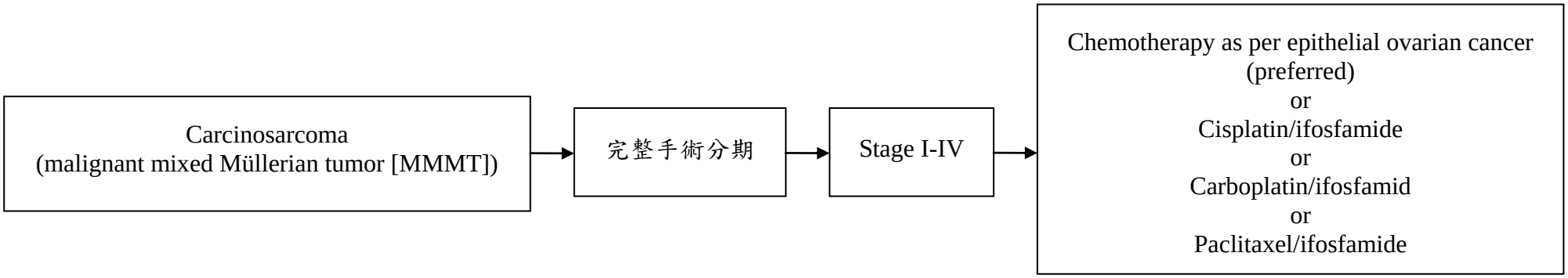
流程圖六

七、較少見卵巢癌組織病理學之處置



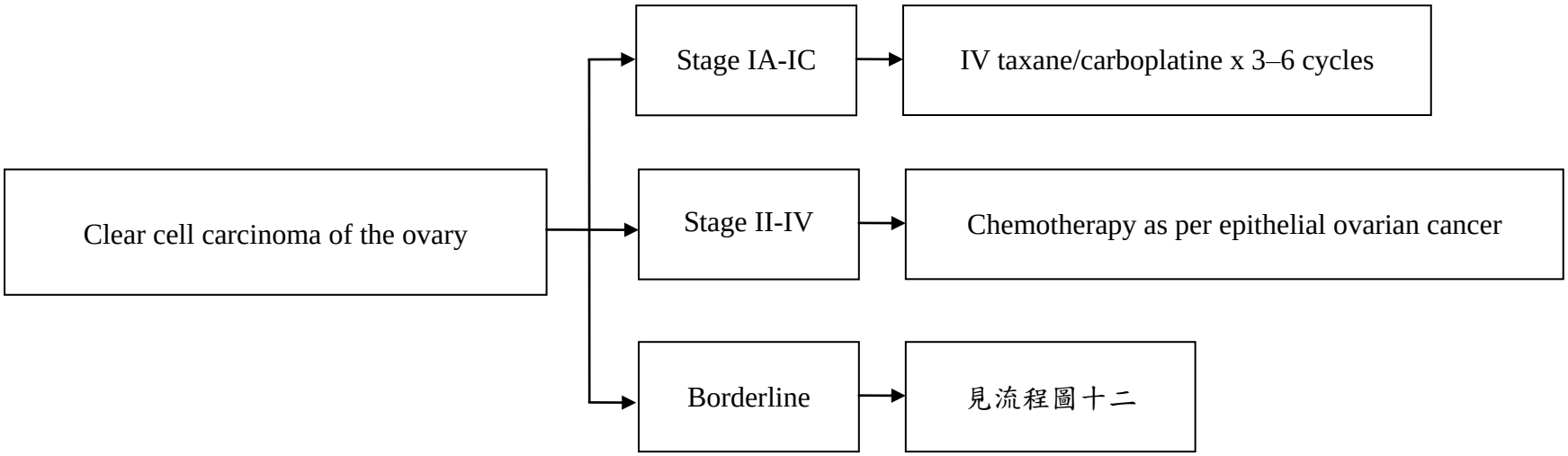
流程圖七

七、較少見卵巢癌組織病理學之處置– Carcinosarcoma(malignant mixed Müllerian tumor [MMMT])



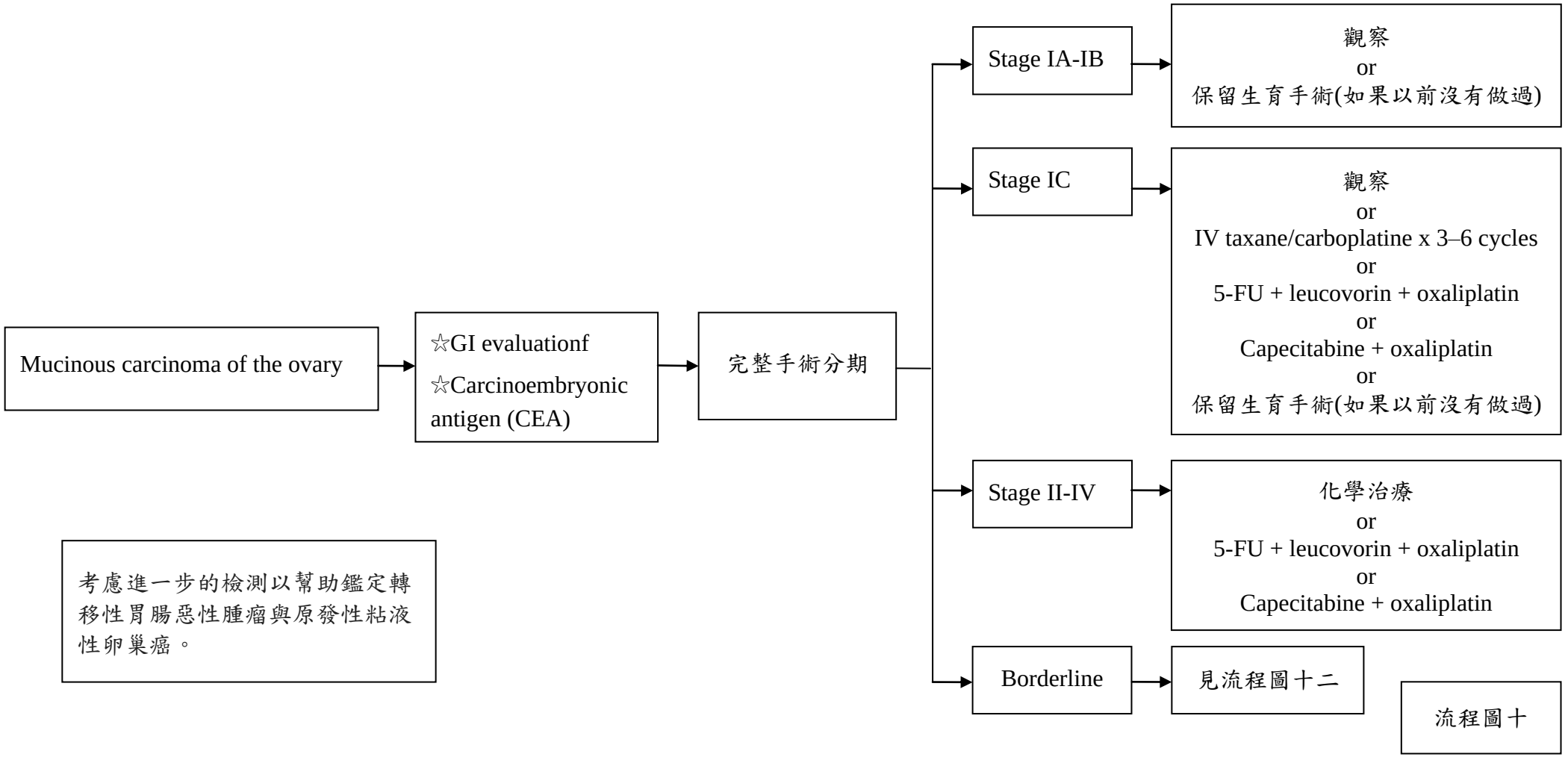
流程圖八

七、較少見卵巢癌組織病理學之處置– Clear cell carcinoma of the ovary

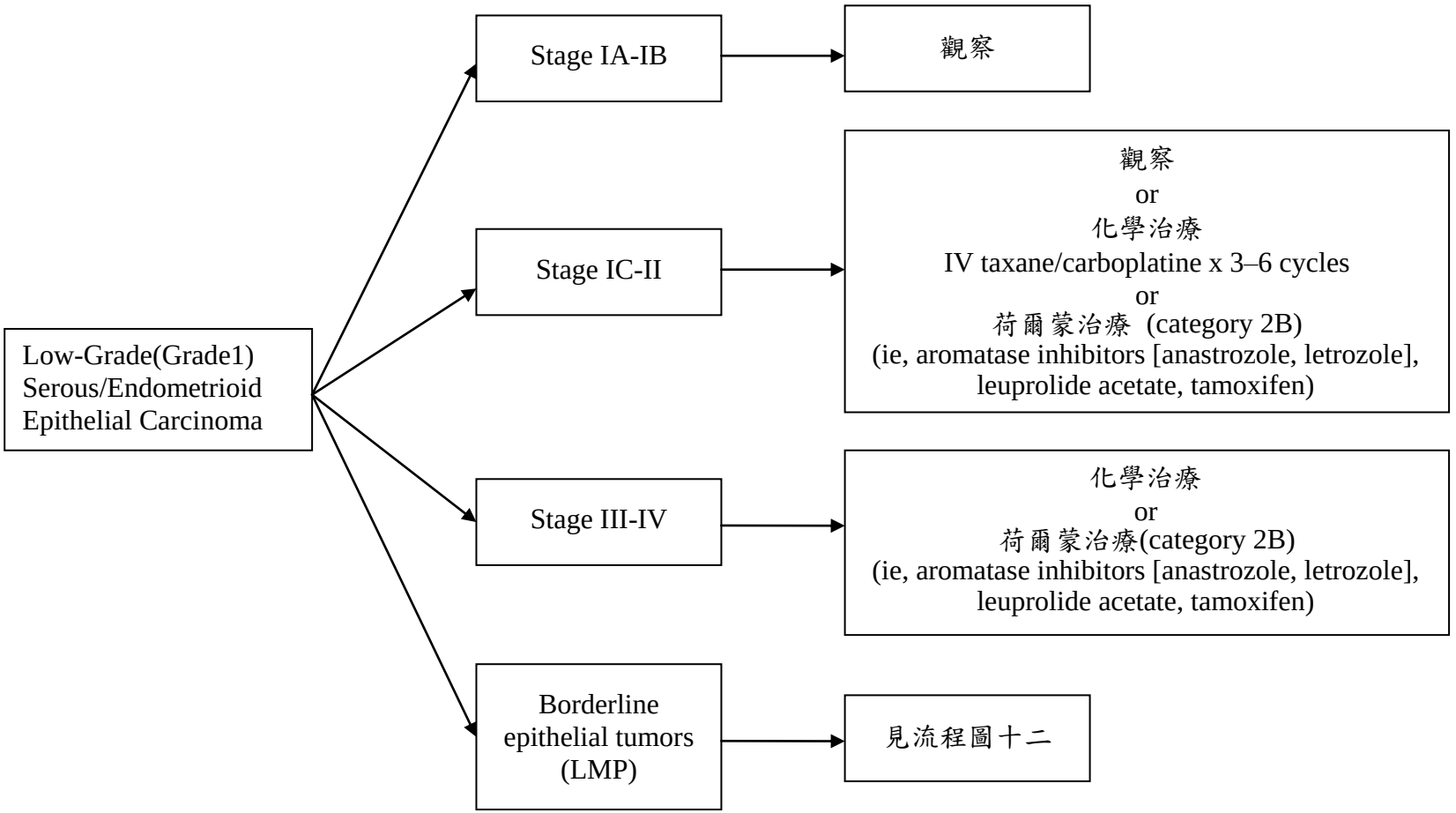


流程圖九

七、較少見卵巢癌組織病理學之處置– Mucinous carcinoma of the ovary

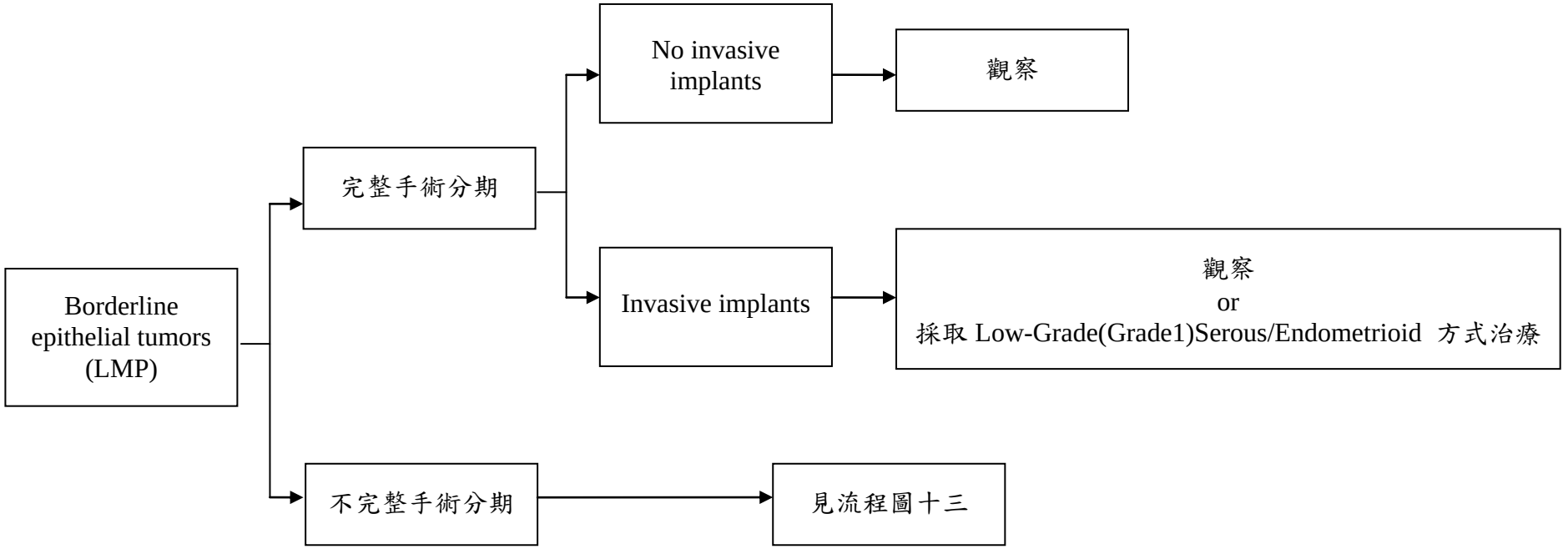


七、較少見卵巢癌組織病理學之處置- Low-grade（grade 1）serous/endometrioid epithelial carcinoma



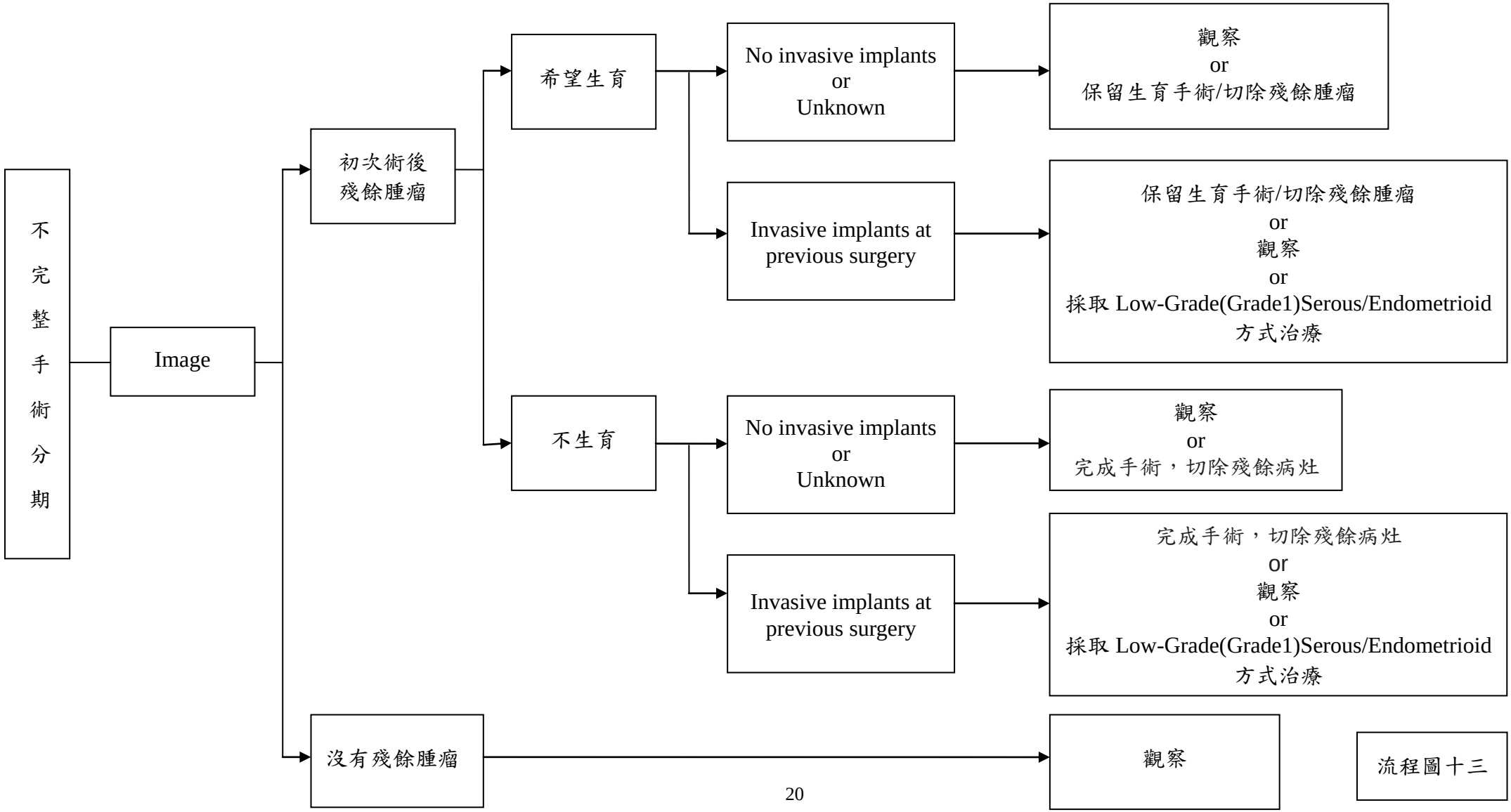
流程圖十一

七、較少見卵巢癌組織病理學之處置- Borderline epithelial tumors(low malignant potential [LMP])



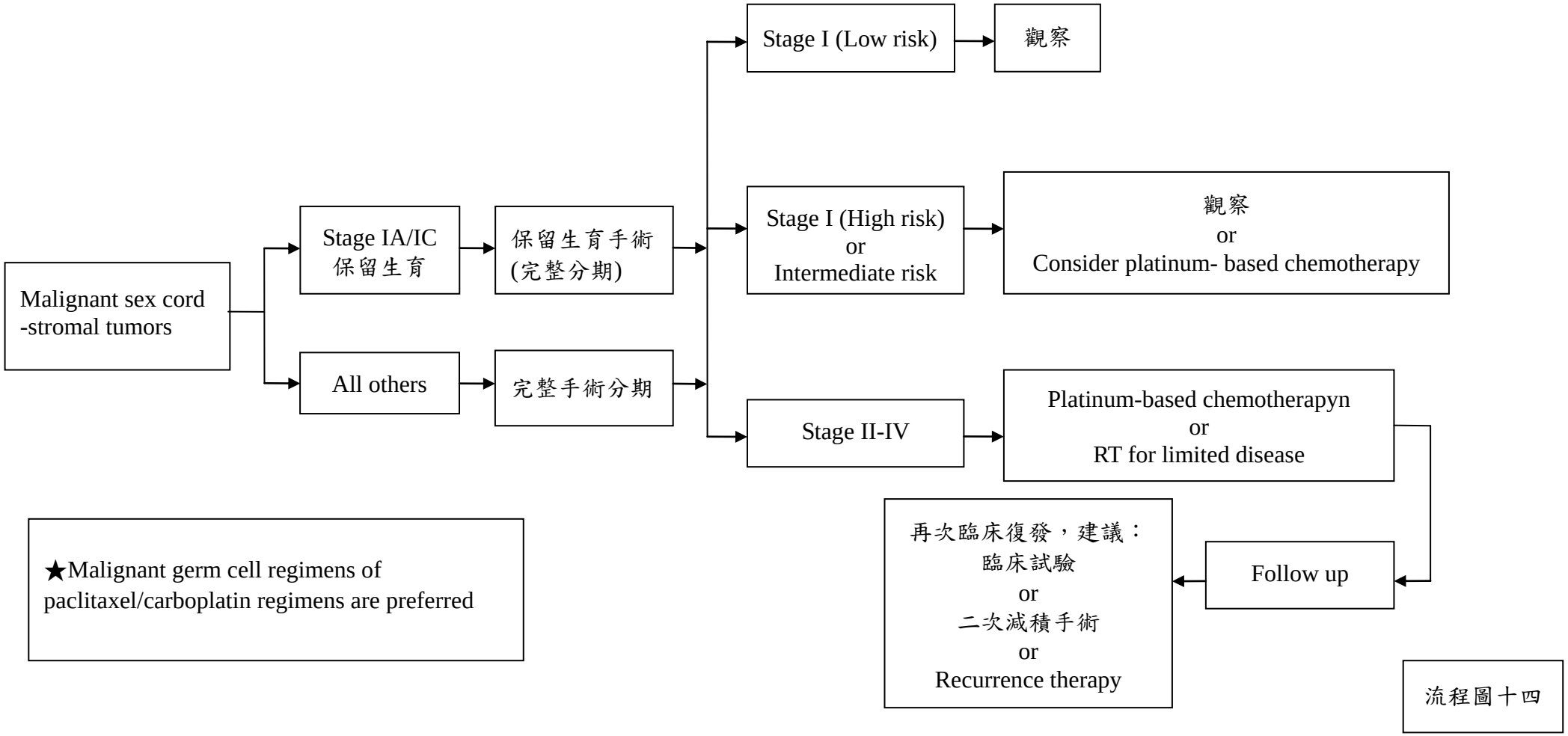
流程圖十二

七、較少見卵巢癌組織病理學之處置- Borderline epithelial tumors(low malignant potential [LMP])



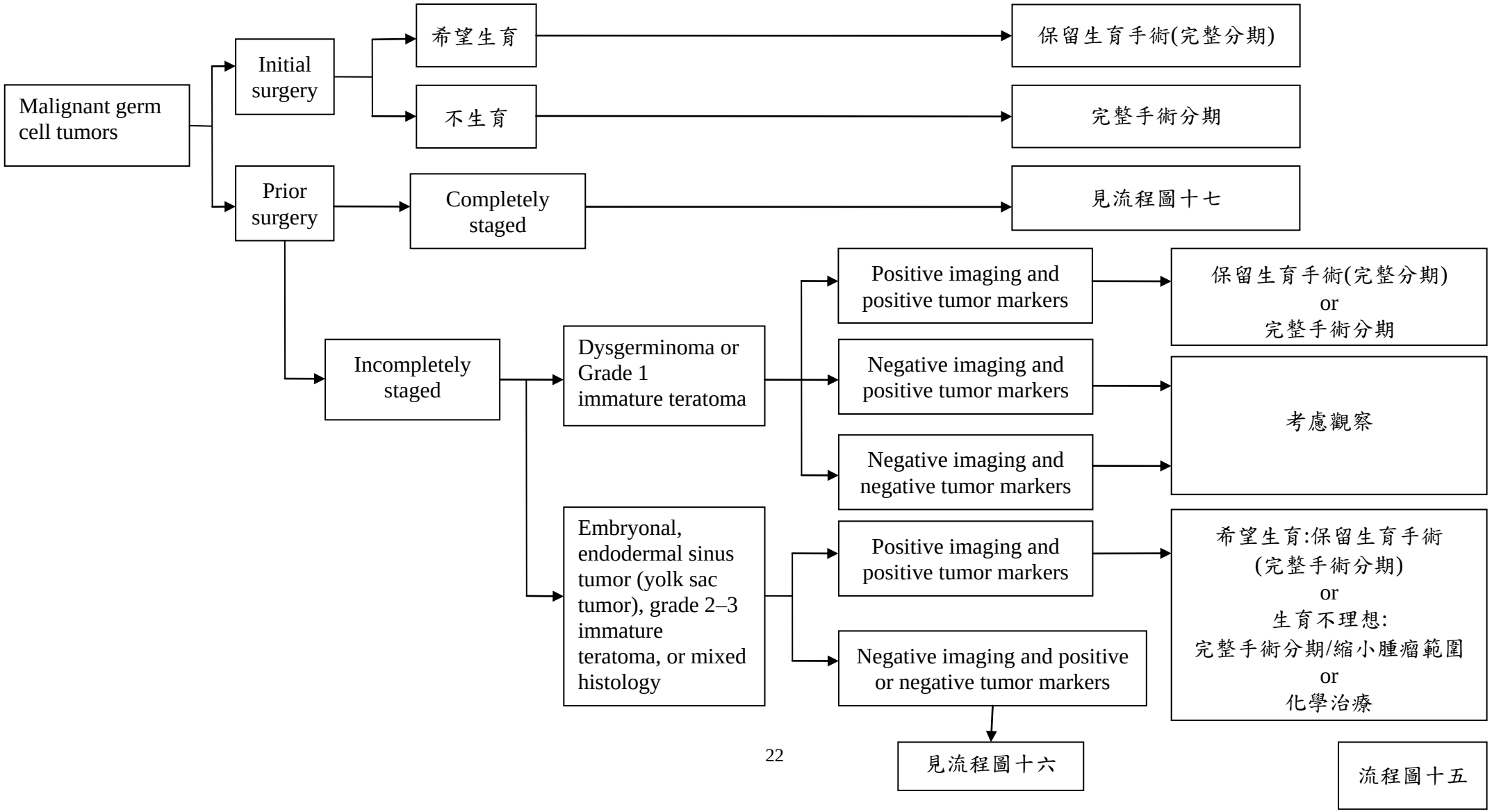
流程圖十三

七、較少見卵巢癌組織病理學之處置- Malignant sex cord-stromal tumors

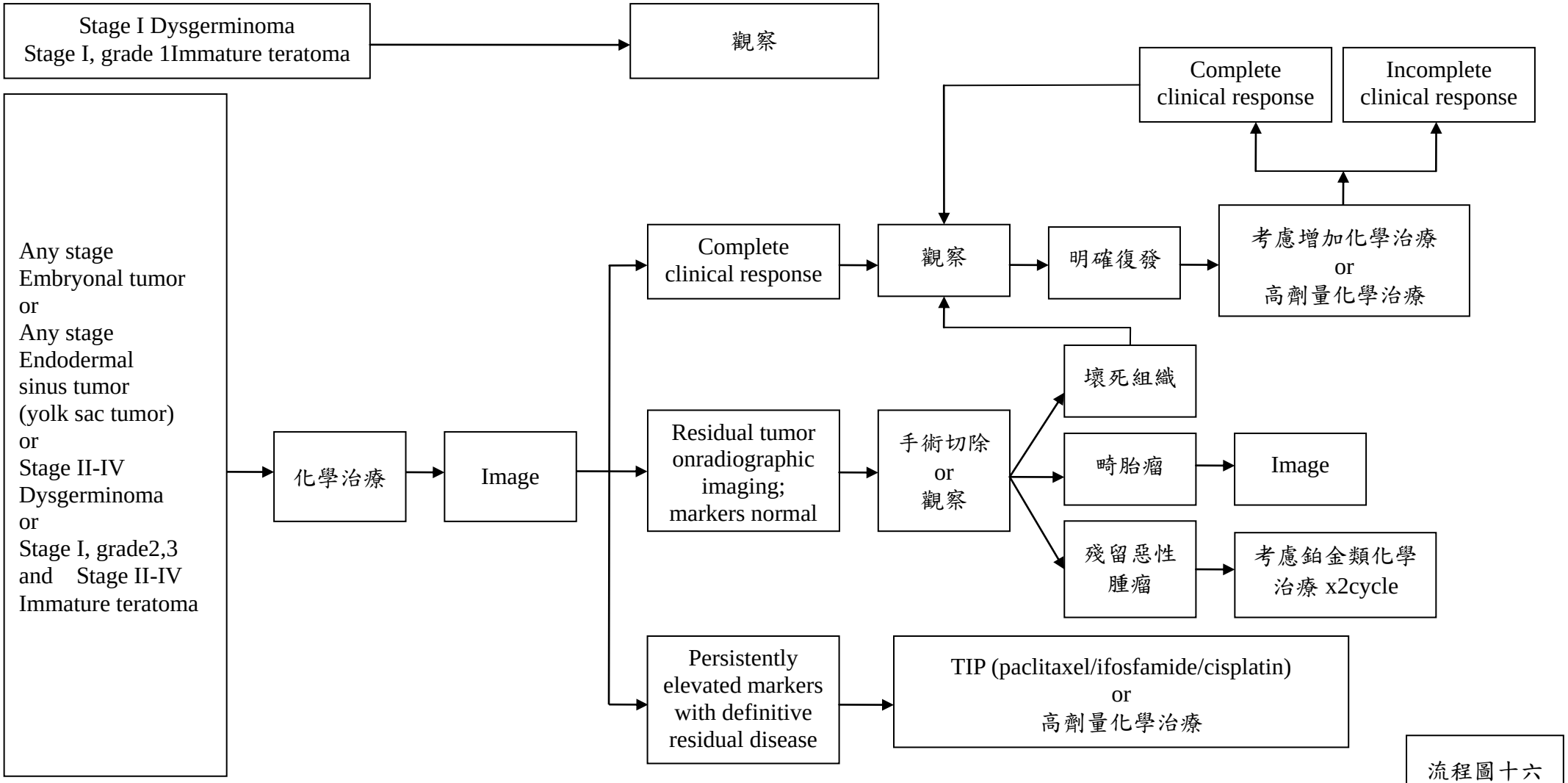


流程圖十四

七、較少見卵巢癌組織病理學之處置- Malignant germ cell tumors

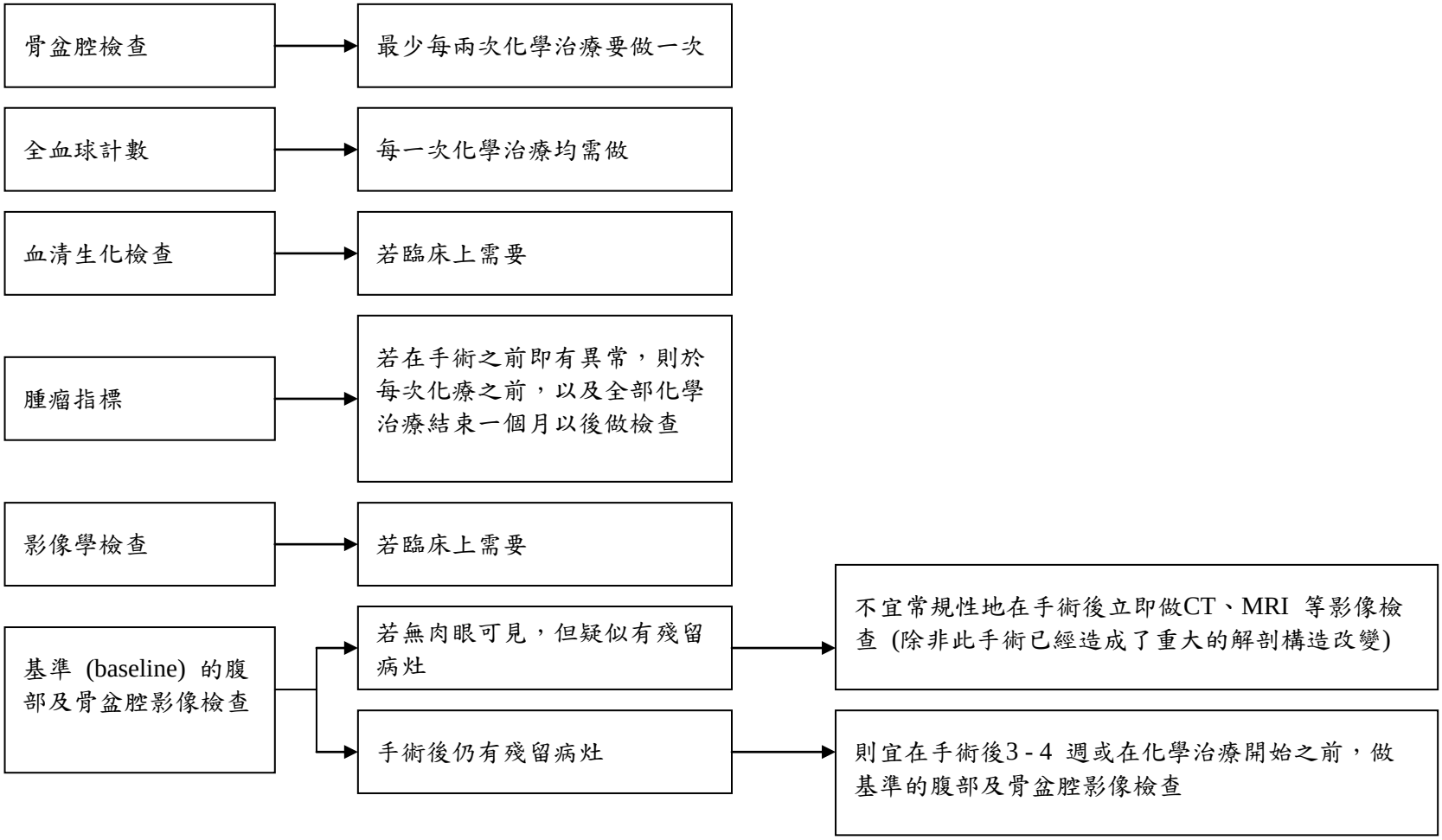


七、較少見卵巢癌組織病理學之處置- Malignant germ cell tumors



流程圖十六

八、 化學治療期間之監測



流程圖十七

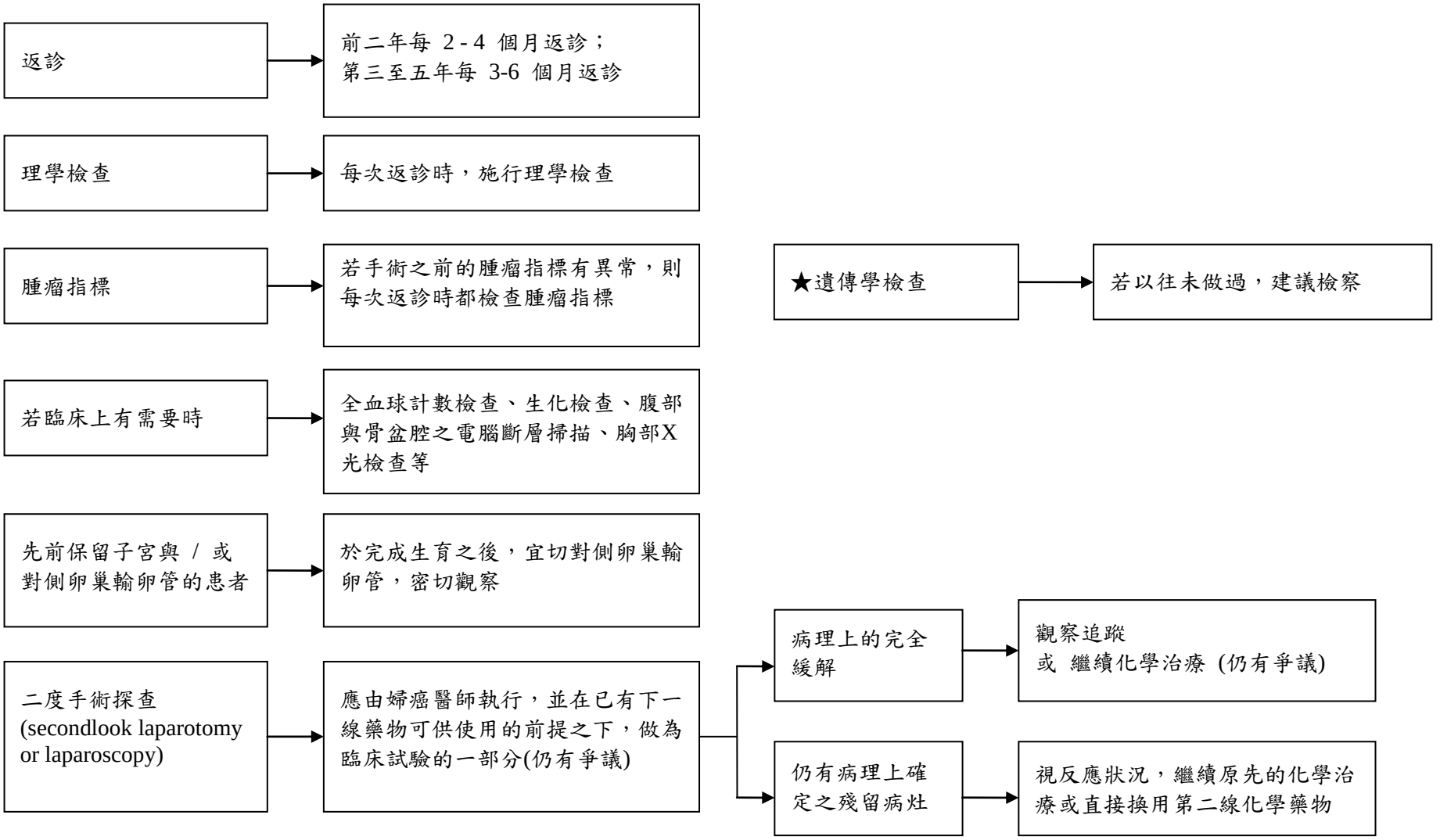
八、 化學治療期間之監測 –對惡性生殖細胞和性病性角質腫瘤的監測

	Germ cell tumors					Sex cord-stromal tumors				
返診	<1 年	1-2 年	2-3 年	3-5 年	>5 年	<1 年	1-2 年	2-3 年	3-5 年	>5 年
理學檢查	每 2-4 個月		每年			每 2-4 個月		每 6 個月		
腫瘤指標	每 2-4 個月		NA			每 2-4 個月		每 6 個月		
影像學檢查	如臨床表現 (除非一開始檢驗為正常)		如臨床表現			數據不足以支持日常使用				
懷疑復發	CT scan and tumor markers									

★Chest x-ray, chest/abdominal/pelvic CT, MRI, PET/CT, or PET; with contrast unless contraindicated，如有復發可依以往影像學檢查作為比較

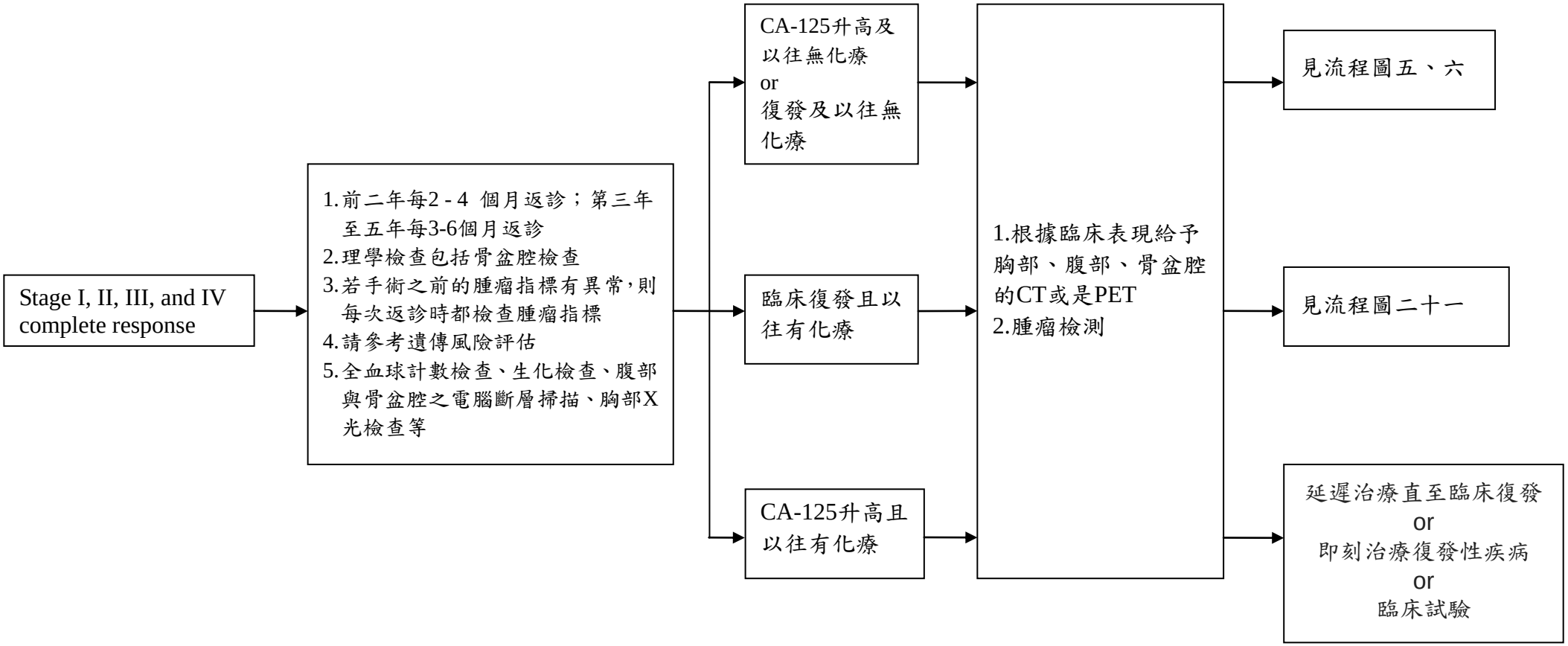
流程圖十八

九、 療程完成之後的追蹤處置



流程圖十九

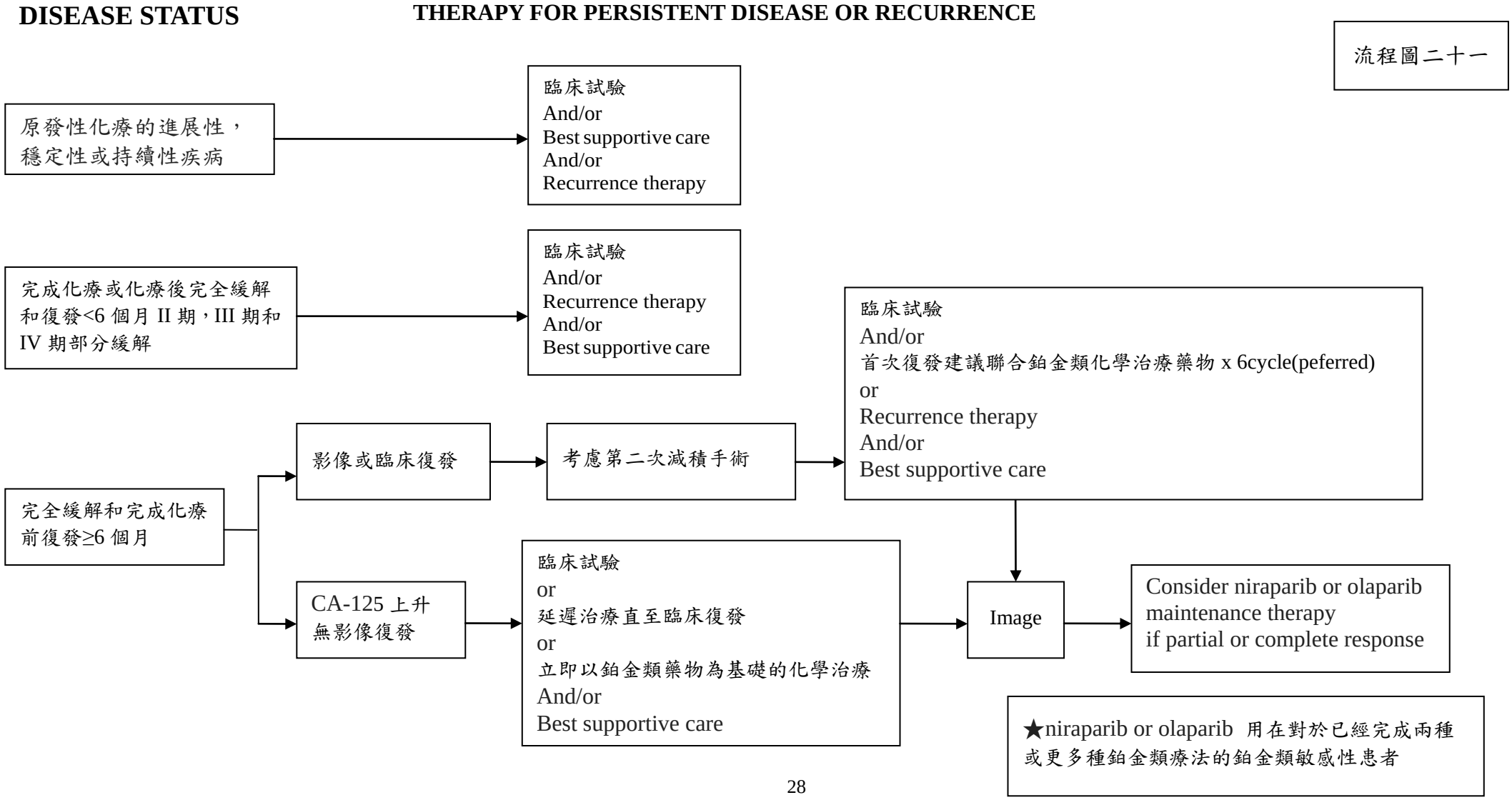
十、卵巢癌的復發處置



流程圖二十

十、卵巢癌的復發處置

流程圖二十一

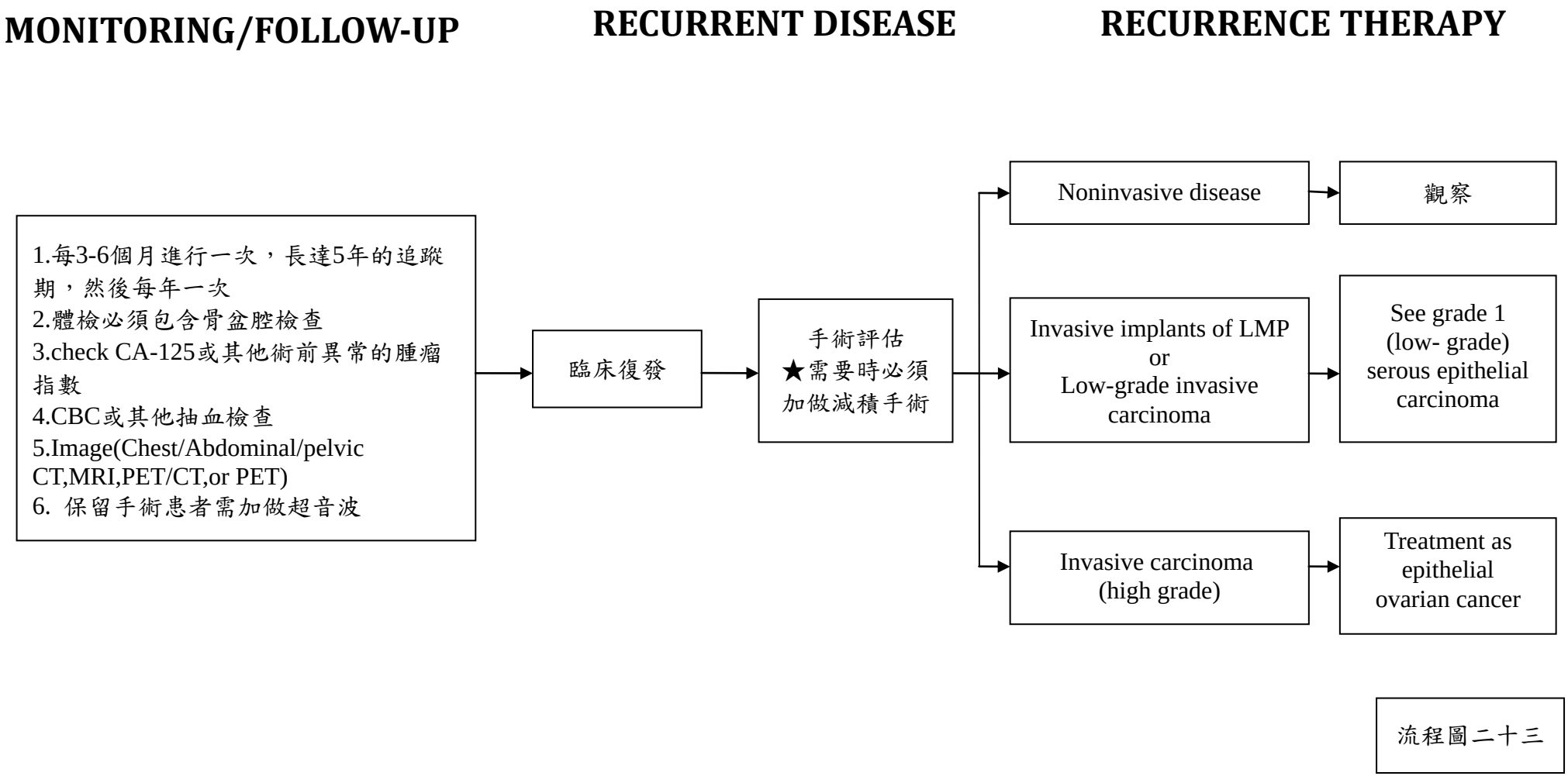


十一、 低惡性度卵巢癌療程完成之後的追蹤處置

返診	前二年每 3個月返診；第三至五年每 3 - 6個月返診；之後可每年追蹤
理學檢查	每次返診時，施行理學檢查
超音波檢查	仍保有卵巢的患者，應定期執行
腫瘤指標	若手術之前的腫瘤指標有異常，則每次返診時都檢查腫瘤指標
若臨床上有需要時	全血球計數檢查、生化檢查、腹部與骨盆腔之電腦斷層掃描、胸部 X 光檢查等
先前保留子宮與 / 或 對側卵巢輸卵管的患者	於完成生育之後，密切追蹤對側卵巢輸卵管

流程圖二十二

十二、Borderline epithelial tumors(low malignant potential [LMP])的追蹤處置



流程圖二十三

十三、化學治療 - Primary Systemic Therapy Regimens

PRINCIPLES OF SYSTEMIC THERAPY

★在聯合使用 IP 和 IV 方案之前，與單獨使用 IV 化療相比，患者必須被告知聯合方案的毒性增加（增加骨髓抑制，腎毒性，腹痛，神經病變，胃腸道毒性，代謝毒性，和肝毒性）

★輔助治療：癌症手術後的藥物，放療或其他形式的補充治療，旨在降低疾病復發的風險，或主要治療手術細胞減滅術後殘留疾病，無論是粗大還是微觀。

★新輔助治療：在癌症手術前給予藥物，放射線或其他形式的治療，以減少手術準備時的腫瘤負擔。

★老年患者和合併症患者可能對這些 NCCN 指南中推薦的聯合化療方案不耐受。單劑鉑劑可能適用於選定的患者。

★復發治療：用於治療復發性癌症，控制症狀，或在初始治療後復發性癌症的臨床，生化或放射學證據時增加生命長度和/或生活質量的藥物，放射或其他形式的治療。

十三、化學治療 - Primary Systemic Therapy Regimens

Stage II-IV

1. IP/IV Regimen (for optimally debulked stage II-III disease)：

Paclitaxel 135 mg/m^2 IV continuous infusion over 3 or 24 h Day 1;
cisplatin 75–100 mg/m^2 IP Day 2 after IV paclitaxel;
paclitaxel 60 mg/m^2 IP Day 8.
Repeat every 3 weeks x 6 cycles.

2. IV Regimens：

- Paclitaxel 175 mg/m^2 IV over 3 hours followed by carboplatin AUC 5–6 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles.
- Dose-dense paclitaxel 80 mg/m^2 IV over 1 hour Days 1, 8, and 15 followed by carboplatin AUC 5–6 IV over 1 hour Day 1. Repeat every 3weeks x 6 cycles.
- Paclitaxel 60 mg/m^2 IV over 1 hour followed by carboplatin AUC 2 IV over 30 minutes. Weekly for 18 weeks.
- Docetaxel 60–75 mg/m^2 IV over 1 hour followed by carboplatin[c] AUC 5–6 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles.
- Carboplatin AUC 5 + pegylated liposomal doxorubicin 30 mg/m^2 every 4 weeks for 6 cycles.
- Bevacizumab-containing regimens per ICON-7 and GOG-218:
  Paclitaxel 175 mg/m^2 IV over 3 hours followed by carboplatin AUC 5–6 IV over 1 hour,
  and bevacizumab 7.5 mg/kg IV over 30–90 minutes Day 1. Repeat every 3 weeks x 5–6 cycles.
  Continue bevacizumab for up to 12 additional cycles.
  or
  Paclitaxel 175 mg/m^2 IV over 3 hours followed by carboplatin AUC 6 IV over 1 hour Day 1.
  Repeat every 3 weeks x 6 cycles. Starting Day 1 of cycle 2,
  give bevacizumab 15 mg/kg IV over 30–90 minutes every 3 weeks for up to 22 cycles.

十三、化學治療 - Neoadjuvant Therapy

新輔助療法

★任何上述 IV 方案都可以在 IDS 之前用作新輔助療法。
★由於潛在干擾術後癒合，應在使用 Bevacizumab-containing 的方案之前謹慎使用 IDS。
★新輔助治療和 IDS 後，上述任一方案（IV 或 IP / IV）均可視為輔助治療選擇。
★新輔助治療和 IDS 後使用 IP 化療方案的數據有限。
以下是 IDS 後的額外 IP 選項：
IV paclitaxel 135 mg/m2 over 3 hours on Day 1, IP carboplatinAUC 6 IP Day 1, paclitaxel 60 mg/m2 IP Day 8.
★建議至少 6 個週期的治療，包括 IDS 後至少 3 個週期的輔助治療。

十三、化學治療 - Less Common Ovarian Histopathologies

Carcinosarcoma (MMMT)	IP/IV and IV regimens Carboplatin/ifosfamide Cisplatin/ifosfamide Paclitaxel/ifosfamide (category 2B)
Clear Cell Carcinoma	IP/IV and IV regimens
Mucinous tumors	IP/IV and IV regimens 5-FU/leucovorin/oxaliplatin Capecitabine/oxaliplatin
Borderline and Low-Grade (Grade 1) Serous/Endometrioid Epithelial Carcinoma	IP/IV and IV regimens Hormone therapy (Aromatase inhibitors [ie, anastrozole, letrozole], leuprolide acetate, tamoxifen)
Malignant Germ Cell Tumors	BEP (bleomycin, etoposide, cisplatin) Bleomycin 30 units per week Etoposide 100 mg/m2 daily for days 1–5, cisplatin 20 mg/m2 daily for days 1–5 Repeat every 21 days for 3 cycles for good risk (category 2B), or 4 cycles for poor risk. Etoposide/carboplatin For select patients with stage IB-III resected dysgerminoma for whom minimizing toxicity is critical, 3 cycles of etoposide/carboplatin can be used. Carboplatin 400 mg/m2 on day 1 plus etoposide 120 mg/m2 on days 1, 2, and 3 every
Malignant Sex Cord-Stromal Tumors	BEP (category 2B) Paclitaxel/carboplatin (category 2B)

Acceptable Recurrence Therapies for Epithelial Ovarian/Fallopian Tube/Primary Peritoneal Cancer

	Cytotoxic Therapy(In alphabetical order)	Hormonal Therapy	Targeted Therapy	Radiation Therapy
Preferred Agents	**Platinum-Sensitive Disease** Carboplatin1 Carboplatin/docetaxel Carboplatin/gemcitabine Carboplatin/gemcitabine/bevacizumab Carboplatin/liposomal doxorubicin (category 1) Carboplatin/paclitaxel, albumin bound (for patients with confirmed taxane hypersensitivity) Carboplatin/paclitaxel (category 1) Carboplatin/paclitaxel (weekly) Cisplatin Cisplatin/gemcitabine **Additional options for mucinous carcinoma only:** 5-FU/leucovorin/oxaliplatin ± bevacizumab (category 2B for bevacizumab) Capecitabine + oxaliplatin		**Single Agents** Bevacizumab Olaparibm **Rucaparib (platinum-resistant disease)**	
	Platinum-Resistant Disease Docetaxel Etoposide, oral Gemcitabine Liposomal doxorubicin Liposomal doxorubicin/bevacizumab Paclitaxel (weekly) ± pazopanib Paclitaxel (weekly)/bevacizumab Topotecan Topotecan/bevacizumab		**Single Agents** Bevacizumab Olaparibm **Rucaparib (platinum-resistant disease)**	

Acceptable Recurrence Therapies for Epithelial Ovarian/Fallopian Tube/Primary Peritoneal Cancer

	Cytotoxic Therapy (In alphabetical order)	Hormonal Therapy	Targeted Therapy	Radiation Therapy
Other Potentially Active Agents	**Single Agentsl** Altretamine Capecitabine Cyclophosphamide Doxorubicin Ifosfamide Irinotecan Melphalan Oxaliplatin Paclitaxel Paclitaxel, albumin bound Pemetrexed Vinorelbine **Combinations** **Carboplatin/paclitaxel/bevacizumab (platinum-sensitive disease)**	Aromatase inhibitors Leuprolide acetate Megestrol acetate Tamoxifen	Pazopanib (category 2B) Rucaparib (platinum- sensitive disease) Pembrolizumab (for microsatellite instability- high [MSI-H] or mismatch repair deficient [dMMR] solid tumors)	Palliative localized radiation therapy

Acceptable Recurrence Therapies For Malignant Germ Cell/Sex Cord-Stromal Tumors

	Cytotoxic Therapy (In alphabetical order)	Hormonal Therapy	Targeted Therapy	Radiation Therapy
Malignant Germ Cell Tumors	**Potentially Curative Therapy:** High-dose chemotherapyn TIP (paclitaxel, ifosfamide, cisplatin) **Palliative Therapy Only:** Cisplatin/etoposide Docetaxel Docetaxel/carboplatin Paclitaxel Paclitaxel/ifosfamide Paclitaxel/carboplatin Paclitaxel/gemcitabine VIP (etoposide, ifosfamide, cisplatin) VeIP (vinblastine, ifosfamide, cisplatin) VAC (vincristine, dactinomycin, cyclophosphamide) TIP Supportive care only			Palliative localized radiation therapy
Malignant Sex Cord-Stromal Tumors	Docetaxel Paclitaxel Paclitaxel/ifosfamide Paclitaxel/carboplatin VAC Supportive care only	Aromatase inhibitors (ie, anastrozole, letrozole) Leuprolide acetate (for granulosa cell tumors) Tamoxifen	Bevacizumab (single agent)	Palliative localized radiation therapy

Neoadjuvant

Cisplatin+Paclitaxel

Cisplatin	(75-100)mg/m^2	iv	d1
Paclitaxel	(135/175)mg/m^2	iv	d1
q 3w			

Ignace Vergote, M.D., Ph.D., Claes G. Tropé, M.D., Ph.D., Frédéric Amant, M.D., Ph.D., et al. Neoadjuvant Chemotherapy or Primary Surgery in Stage IIIC or IV Ovarian Cancer.N Engl J Med 2010; 363:943-953September 2, 2010

Carboplatin+Paclitaxel

Carboplatin	AUC(4-6)	iv	d1
Paclitaxel	(135/175)mg/m^2	iv	d1
q 3w			

Parmar MK, Ledermann JA, Colombo N, et al. Paclitaxel plus platinum-based chemotherapy versus conventional platinum-based chemotherapy in women with relapsed ovarian cancer: the ICON4/AGO-OVAR-2.2 trial. Lancet 2003;361:2099-2106.

Paclitaxel+ Doxorubicin liposome

Paclitaxel	(135/175)mg/m^2	iv	d1
Doxorubicin liposome	(35-45)mg/m^2	iv	d1
q 3w			

Eleftherios P. Mamounas, John Bryant, Barry Lembersky, et al. Paclitaxel After Doxorubicin Plus Cyclophosphamide As Adjuvant Chemotherapy for Node-Positive Breast Cancer: Results From NSABP B-28.JCO June 1, 2005 vol. 23 no. 16 3686-3696

Adjuvant

Cisplatin+Cyclophopsamide(For stage I,II)

Cisplatin	(75-100)mg/m^2	iv	d1
Cyclophosphamide	750mg/m^2	iv	d1
q3wx 6cycles			

McGuire WP, Hoskins WJ, Brady MF, et al. Cyclophosphamide and cisplatin compared with paclitaxel and cisplatin in patients with stage III and stage IV ovarian cancer. N Engl J Med 1996;334:1-6.Available at: http://www.ncbi.nlm.nih.gov/pubmed/7494563.

Carboplatin+Cyclophopsamide(For stage I,II)

Carboplatin	AUC (4-6)	iv	d1
Cyclophosphamide	(750-1000)mg/m^2	iv	d1
q3w x 6 cycles			

Swenerton K, Jeffrey J, Stuart G, et al. Cisplatin-cyclophosphamide versus carboplatin-cyclophosphamide in advanced ovarian cancer: a randomized phase III study of the National Cancer Institute of Canada Clinical Trials Group. J Clin Oncol 1992;10:718-726.

Carboplatin+Paclitaxel(For stage <III ,自費)

Carboplatin	AUC (4-6)	iv	d1
Paclitaxel	(135/175)mg/m^2	iv	d1
q 3w x 6 cycles			

1.NCCN Clinical Practice Guidelines in Oncology™. Ovarian Cancer including Fallopian Tube Cancer and Primary Peritoneal Cancer.v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed May 11, 2012.
2.Ozols RF, Bundy BN, Greer BE, et al; Gynecologic Oncology Group. Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study.J Clin Oncol. 2003;21:3194–3200.

Cisplatin+Paclitaxel(For stage <III ,自費)

Cisplatin	(75-100)mg/m^2	iv	d1
Paclitaxel	(135/175)mg/m^2	iv	d1
q 3w x 6 cycles			

Lesnock JL, Darcy KM, Tian C, et al. BRCA1 expression and improved survival in ovarian cancer patients treated with intraperitoneal cisplatin and paclitaxel: a Gynecologic Oncology Group Study. Br J Cancer 2013;108:1231-1237. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23462720.

Adjuvant second line therapy

Cisplatin

Cisplatin	(75-100)mg/m^2 iv	d1
wk x 6 wks		

Aghajanian C, Blank SV, Goff BA, et al. OCEANS: A randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol 2012;30:2039-2045.

Carboplatin

Carboplatin	AUC (4-6) iv	d1
q3w x 6 cycles		

Aghajanian C, Blank SV, Goff BA, et al. OCEANS: A randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol 2012;30:2039-2045.

Paclitaxel

Paclitaxel	(50-80)mg/m^2 iv	d1
q3w x 6 cycles		

Markman M, Blessing J, Rubin SC, et al. Phase II trial of weekly paclitaxel (80 mg/m) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers: a Gynecologic Oncology Group study. Gynecol Oncol 2006;101:436-440.

Cisplatin+Ifosfamide

Cisplatin	(50-100)mg/m^2 iv	d1
Ifosfamide	(3-5)g/m^2 iv	d1
q3w x 6 cycles		

1.Markman M, Hakes T, Reichman B, et al. Ifosfamide and mesna in previously treated advanced epithelial ovarian cancer: activity in platinum-resistant disease. J Clin Oncol 1992;10:243-248. Available at:http://www.ncbi.nlm.nih.gov/pubmed/1732425.
2.Kondagunta GV, Bacik J, Donadio A, et al. Combination of paclitaxel, ifosfamide, and cisplatin is an effective second-line therapy for patients with relapsed testicular germ cell tumors. J Clin Oncol 2005;23:6549-6555. Available at:http://www.ncbi.nlm.nih.gov/pubmed/16170162.

Carboplatin+Ifosfamide

Carboplatin	AUC (4-6) iv	d1
Ifosfamide	(3-5)g/m^2 iv	d1
q3w x 6 cycles		

1.Markman M, Hakes T, Reichman B, et al. Ifosfamide and mesna in previously treated advanced epithelial ovarian cancer: activity in platinum-resistant disease. J Clin Oncol 1992;10:243-248. Available at:http://www.ncbi.nlm.nih.gov/pubmed/1732425.
2.Kondagunta GV, Bacik J, Donadio A, et al. Combination of paclitaxel, ifosfamide, and cisplatin is an effective second-line therapy for patients with relapsed testicular germ cell tumors. J Clin Oncol 2005;23:6549-6555. Available at:http://www.ncbi.nlm.nih.gov/pubmed/16170162.

Doxorubicin liposome

Doxorubicin liposome	(35-45)mg/ m^2 iv	d1
q3w x 6 cycles		

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010;28:3323-3329.

Doxorubicin liposome +Carboplatin

Doxorubicin liposome	(35-45) mg/ m^2 iv	d1
Carboplatin	AUC (4-6) iv	d1
q3w x 6 cycles		

1.Mutch DG, Orlando M, Goss T, et al. Randomized phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in patients with platinumresistant ovarian cancer. J Clin Oncol 2007;25:2811-2818.
2.Ferrandina G, Ludovisi M, Lorusso D, et al. Phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in progressive or recurrent ovarian cancer. J Clin Oncol 2008;26:890-896.

Topotecan(自費)

Topotecan	(0.5-1.25)mg/ m^2 iv	d1
wk x 6 cycles		

1.Sehouli J, Stengel D, Harter P, et al. Topotecan weekly versus conventional 5-day schedule in patients with platinum-resistant ovarian cancer: A randomized multicenter phase II trial of the North-Eastern German Society of Gynecological Oncology Ovarian Cancer Study Group. J Clin Oncol 2011;29:242-248.
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Topotecan(自費)

Topotecan	(0.75-1.25)mg/ m^2 iv	d1
q3w x 6 cycles		

1.Gordon AN, Tonda M, Sun S, Rackoff W. Long-term survival advantage for women treated with pegylated liposomal doxorubicin compared with topotecan in a phase 3 randomized study of recurrent and refractory epithelial ovarian cancer. Gynecol Oncol 2004;95:1-8.
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Paclitaxel+ Doxorubicin liposome

Paclitaxel	80mg/m^2	iv	d1
Doxorubicin liposome	(35-45) mg/m^2	iv	d1
wk x 6 wks			

Elizabeth M. Swisher, M.D., David G. Mutch, M.D., Janet S. Rader, M.D., et al. Topotecan in Platinum- and Paclitaxel-Resistant Ovarian Cancer .Gynecologic Oncology, Volume 66, Issue 3, September 1997, Pages 480–486

Cisplatin+ Topotecan

Cisplatin	100mg/m^2	iv	d1
Topotecan	(2.5-4)mg/m^2	iv	d1
10days x 3 course			

1.M A Bookman, H Malmström, G Bolis, et al. Topotecan for the treatment of advanced epithelial ovarian cancer: an open-label phase II study in patients treated after prior chemotherapy that contained cisplatin or carboplatin and paclitaxel.JCO October 1998 vol. 16 no. 10 3345-3352
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Carboplatin+ Topotecan

Carboplatin	AUC (4-6)	iv	d1
Topotecan	(2.5-4)mg/m^2	iv	d1
10days x 3 course			

1.M A Bookman, H Malmström, G Bolis, et al. Topotecan for the treatment of advanced epithelial ovarian cancer: an open-label phase II study in patients treated after prior chemotherapy that contained cisplatin or carboplatin and paclitaxel.JCO October 1998 vol. 16 no. 10 3345-3352
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Gefitinib +Paclitaxel

Gefitinib(自費)	2pc	d1
Paclitaxel	80mg/m^2 iv	d1

Fortunato Ciardiello2, Rosa Caputo, Roberto Bianco, et al. Antitumor Effect and Potentiation of Cytotoxic Drugs Activity in Human Cancer Cells by ZD-1839 (Iressa), an Epidermal Growth Factor Receptor-selective Tyrosine Kinase Inhibitor1 Clin Cancer Res May 2000 6; 2053

Bevacizumab (自費) **+5FU**

Bevacizumab	5 or 10mg/kg	iv	d1
5FU	600 or 750 or 1000 mg/m^2	iv	d1
q3w x 6 cycles			

Stephen A. Cannistra, Ursula A. Matulonis, Richard T. Penson, et al. Phase II Study of Bevacizumab in Patients With Platinum-Resistant Ovarian Cancer or Peritoneal Serous Cancer.JCO November 20, 2007 vol. 25 no. 33 5180-5186

Etoposide

Etoposide	1pc(oral)1#
QD x 7 day ~ 28 day	

Rose PG, Blessing JA, Mayer AR, Homesley HD. Prolonged oral etoposide as second-line therapy for platinum-resistant and platinum-sensitive ovarian carcinoma: a Gynecologic Oncology Group study. J Clin Oncol 1998;16:405-410.

Cyclophopsamide

Cyclophosphamide	1pc (oral)1#
QD x 7 day ~ 28day	

Swenerton K, Jeffrey J, Stuart G, et al. Cisplatin-cyclophosphamide versus carboplatin-cyclophosphamide in advanced ovarian cancer: a randomized phase III study of the National Cancer Institute of Canada Clinical Trials Group. J Clin Oncol 1992;10:718-726.

Gemcitabine+ Doxorubicin liposome

Gemcitabine	650mg/m^2	iv	d1
Doxorubicin liposome	15mg/m2	iv	d1
weekx3 rest 1 week x 6 cycles			

1.Mutch DG, Orlando M, Goss T, et al. Randomized phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in patients with platinumresistant ovarian cancer. J Clin Oncol 2007;25:2811-2818.
2.Ferrandina G, Ludovisi M, Lorusso D, et al. Phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in progressive or recurrent ovarian cancer. J Clin Oncol 2008;26:890-896.

Bevacizumab (自費)+**Cyclophosphamide**

Bevacizumab	5-10mg/kg q2weeks	iv	d1
Cyclophosphamide	1#(50mg) qd 5days	iv	d1

1.Robert A. Burger, Michael W. Sill, Bradley J. Monk, et al. Phase II Trial of Bevacizumab in Persistent or Recurrent Epithelial Ovarian Cancer or Primary Peritoneal Cancer: A Gynecologic Oncology Group Study.JCO November 20, 2007 vol. 25 no. 33 5165-5171
2.Carol Aghajanian⇓, Stephanie V. Blank, Barbara A. Goff,et al. OCEANS: A Randomized, Double-Blind, Placebo-Controlled Phase III Trial of Chemotherapy With or Without Bevacizumab in Patients With Platinum-Sensitive Recurrent Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancer.JCO June 10, 2012 vol. 30 no. 17 2039-2045

paclitaxel

Paclitaxel	80mg/m^2	iv	d1
wk x 6 wks			

Markman M, Blessing J, Rubin SC, et al. Phase II trial of weekly paclitaxel (80 mg/m) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers: a Gynecologic Oncology Group study. Gynecol Oncol 2006;101:436-440.

Doxorubicin liposome

Doxorubicin liposome	(35-45)mg/m^2	iv	d1
q4w x 6 cycles			

1.Mutch DG, Orlando M, Goss T, et al. Randomized phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in patients with platinumresistant ovarian cancer. J Clin Oncol 2007;25:2811-2818.
2.Ferrandina G, Ludovisi M, Lorusso D, et al. Phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in progressive or recurrent ovarian cancer. J Clin Oncol 2008;26:890-896.

Carboplatin(自費) + **Doxorubicin liposome**

Carboplatin	AUC (4-6) iv	d1
Doxorubicin liposome	(35-45) mg/m^2 iv	d1
q4w x 6 cycles		

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010;28:3323-3329.

Topotecan(自費)

Topotecan	2.5-4mg/m^2 iv	d1
wk x 6 cycles		

1.Gordon AN, Tonda M, Sun S, Rackoff W. Long-term survival advantage for women treated with pegylated liposomal doxorubicin compared with topotecan in a phase 3 randomized study of recurrent and refractory epithelial ovarian cancer. Gynecol Oncol 2004;95:1-8.
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

paclitaxel

Paclitaxel	(50-80)mg/m^2 iv	d1
Monthly		

Markman M, Blessing J, Rubin SC, et al. Phase II trial of weekly paclitaxel (80 mg/m) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers: a Gynecologic Oncology Group study. Gynecol Oncol 2006;101:436-440.

Intraperitoneal for stage III

Paclitaxel+cisplatin

Paclitaxel	135mg/m2	iv	d1
cisplatin	100mg/m2	ip	d2
Q3w x 6 cycles			

David S. Alberts, M.D., P.Y. Liu, Ph.D., Edward V. Hannigan, M.D.,et al. Intraperitoneal Cisplatin plus Intravenous Cyclophosphamide versus Intravenous Cisplatin plus Intravenous Cyclophosphamide for Stage III Ovarian Cancer.N Engl J Med 1996; 335:1950-1955December 26, 1996

Ovary (Dysgerminoma ,Embryonal, endodermal sinus tumor, immature teratoma, or mixed histology)

BEP 3 day regimen		
Etoposide	165mg/m^2	Day1,2,3
Cisplatin	35 mg/m^2	Day1,2,3
± Bleomycin	30 U	Day1,8,15
21 days intervals x 3-4course		

BEP 5 day regimen		
Etoposide	100 mg/m^2	Day1-5
Cisplatin	20 mg/m^2	Day1-5
± Bleomycin	30 units	Per week
21 days intervals x 3-4course		

Patients who do not respond to BEP may benefit from the following as salvage therapy (TIP):		
Cisplatin	35 mg/m^2	Day1,2,3
Ifosfamide	2 gm/m^2	Day2,3,4
Taxol	135 mg/m^2	Day1

Alberta Provincial Gynecologic Oncology Tumour Team. Ovarian germ cell tumours. Edmonton (Alberta): CancerControl Alberta; 2013 Apr. 12 p. (Clinical practice guideline; no. GYNE-001).

十四、放射線治療

Principles of Radiation Therapy for Ovarian cancer

Indication:

- Post-operative Stage ≧ IC Gr.3 and if not a chemotherapy candidate and <2cm residual tumor
  - Whole abdominal irradiation
  - Whole field 30Gy at 1.2-1.5Gy/Fraction , para-aortic boost to 45Gy, pelvic boost to 45-55Gy
- Radiotherapy for palliation of symptomatic tumor deposits

Note: Tomotherapy preferred(Patient have to pay for daily image-guidance.)

十五、安寧緩和照護原則

若預期疾病難以治癒時，病人存活期小於6個月便適合安寧療護(Pomeranz & Brustman, 2005；Waldrop & Rinfrette, 2009) 。若藉由症狀、檢驗數據、及確切的腫瘤診斷，證實臨床上該惡性腫瘤已經廣泛侵犯、或進展快速；功能分數（Palliative Performance Scale）低於70%；拒絕進一步腫瘤治癒性治療，或者在治療之下仍持續惡化者，即可轉介緩和醫療團隊（彭等，2006）

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3. NCI (National Cancer Institute) Ovarian Low Malignant Potential Tumors Treatment Health Professional Version (date last modified: June 19, 2003).
4. FIGO staging classifications and clinical practice guidelines in the management of gynecologic cancers. Int J Gynecol Obstet 2000; 70:209-262.
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十七、卵巢癌Stage IV完治定義

- 卵巢癌接受手術或 C/T 4 次完治。
- 卵巢癌接受『安寧緩和』。