TAIPEI VETERANS GENERAL HOSPITAL PRACTICES GUIDELINES FOR

Bladder Cancer

2021年9月28日修訂

壹、前言

一、適用範圍

For urothelial carcinoma of urinary bladder in all age groups

二、目的Purpose

To establish the consensus of the clinicians regarding their views of currently accepted approaches to treatment of urothelial carcinoma of urinary bladder

三、指引使用者The target users of the guideline

Medical team focusing on bladder cancer treatment in TPEVGH， including urologist， medical oncologist， radiation oncologist.

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貳、重要臨床準則

一、評估Assessment

History:

should include known risk factors including smoking history, occupation exposure(including aromatic amines, polycyclic aromatic hydrocarbons and chlorinated hydrocarbons)

Physical examination

Complete blood count

Urinalysis

Cytology of urine

Chest X-ray

CT urography or IVP

CT urography or Sonography of urinary bladder

Whole body bone scan (optional for non muscle invasive bladder cancer)

二、診斷依據Diagnosis criteria

Urine cytology

CT urography or IVP

Sonography of urinary bladder

Cystoscopy with biopsy

CT scan of staging

TURBT (transurethral resection of bladder tumors)

三、鑑別診斷Differential Diagnosis

- **Inverted papilloma**

- **Metastasis or direct tumor invasion from colon, uterine, or cervix**

- **Direct tumor invasion from prostate Ca**

- **Cystitis glandularis**

四、疾病（病理）分期Disease and Pathology stage

2016 TNM classification of bladder cancer

Histologic Grade：

- **2016 WHO/ISUP grading system**

  Urothelial Histologies

  - **Low-grade urothelial carcinoma**
  - **High-grade urothelia carcinoma**

- **Squamous cell carcinoma and Adenocarcinoma**
  - **Gx:grade cannot be assessed**
  - **G1: well differentiated**
  - **G2: moderate differentiated**
  - **G3: poorly differentiated**

TNM Staging System for Bladder cancer (AJCC 2016)

Definition of Primary Tumor (T)

Tx Primary tumor cannot be assessed
T0 No evidence of primary tumor
Ta Non-invasive papillary carcinoma
Tis Urothelial carcinoma in situ " flat tumor"
T1 Tumor invades lamina propria (subepithelial connective tissue)
T2 Tumor invades muscularis propria
pT2a Tumor invades superficial muscularis propria (inner half)
pT2b Tumor invades deep muscularis propria (outer half)
T3 Tumor invades perivesical tissue
pT3a Microscopically
pT3b Macroscopically (extravesical mass)
T4 Extravesical tumor directly invades any of the following: prostatic stroma, seminal vesicles,uterus, vagina, pelvic wall, abdominal wall
T4a Extravesical tumor invades directly into prostatic stroma，uterus, vagina
T4b Extravesical tumor invades pelvic wall, abdominal wall

Definition of Regional Lymph Node (N)

Nx lymph nodes cannot be asscessed
N0 No lymph node metastasis
N1 Single regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node)
N2 Multiple regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node metastasis)
N3 Lymph node metastasis to the common iliac lymph nodes

Definition of Distant Metastasis(M)

M0 No distant metastasis
M1 Distant metastasis
M1a Distant metastasis limited to lymph nodes beyoun the common iliacs
M1b Non-lymph-node distant metastasis

AJCC PROGNOSTIC STAGE GROUPS

Stage 0a	Ta	N0	M0
Stage 0is	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2a	N0	M0
	T2b	N0	M0
Stage IIIA	T3a	N0	M0
	T3b	N0	M0
	T4a	N0	M0
	T1-T4a	N1	M0
Stage IIIB	T1-T4a	N2-3	M0
Stage IVA	T4b	N0	M0
	AnyT	AnyN	M1a
Stage IVB	AnyT	AnyN	M1b

Classification – Histologic Type

- **Noninvasive carcinoma**
  - **--Low grade papillary urothelial carcinoma**
  - **--High grade papillary urothelial carcinoma**
  - **--Urothelial carcinoma in situ**
- **Invasive carcinoma**
  - **--Conventional urothelial(transitional cell)carcinoma**
  - **--Urothelial carcinoma variants**
    - **Urothelial carcinoma with divergent differentiation (squamous,glandular,and/or trophoblastic)**
    - **Nested urothelial carcinoma (including large nested carcinoma)**
    - **Microcystic urothelial carcinoma**

- **Micropapillary urothelial carcinoma**
- **Lymphoepithelioma-like urothelial carcinoma**
- **Plasmacytoid urothelial carcinoma**
- **Giant cell urothelial carcinoma**
- **Lipid-rich urothelial carcinoma**
- **Clear cell(glycogen-rich) urothelial carcinoma**
- **Sarcomatoid urothelial carcinoma**
- **Poorly differentiated urothelial carcinoma (including those with osteoclast-like giant cells)**

-- Squmous cell

--Adenocarcinomacarcinoma

--Small cell carcinoma

五、臨床症狀signs and symptoms

Hematuria Frequency, urgency of urination, Dysuria, urine retention , Anemia

六、發生率與盛行率Incidence and prevalence

- **Bladder cancer: 90% of cancers of the urinary collecting system (renal pelvis, ureters, bladder, urethra). Incidence is lowest in Asia. Incidence of bladder cancer increases with age[5]. The disease is more prevalent in blackfoot disease area in Taiwan and may have unfavorable outcomes[6].**
- **民國102年，膀胱惡性腫瘤發生個案數占全部惡性腫瘤發生個案數的2.07%，當年因此惡性腫瘤死亡人數占全部惡性腫瘤死亡人數的1.86%。發生率的排名於男性為第9位、女性為第16位；死亡率的排行於男性為第12位、女性為第13位。**

民國102年癌症登記年報. (n.d.). Retrieved September 5, 2016, from http://www.hpa.gov.tw/BHPNet/Web/Stat/StatisticsShow.aspx?No=201604210001

七、檢驗與其他檢查

Laboratory and other examination

Urine routine

Urine cytology

Biochemistry including renal function and basic liver function for anesthesia

IVP

Sonography

CT scan

Bone scan

Chest x-ray

Diagnosis of invasive bladder cancer

- **Cystoscopy and biopsy**

  Imaging only if staging will make a difference to the selection of treatment options

- **Adequate TURBT including muscularis propria**

- **Local staging for patients considered suitable for radical treatment**
  - Multidetector-row CT with contrast enhancement
  - Magnetic resonance imaging with fast dynamic contrast enhancement

For patients with confirmed muscle-invasive bladder cancer

- **Chest X-Rays, and chest multidetoctor-row CT when indicated, abdomen and pelvis, including multidetector-row CT urography for complete examination of the upper urinary tracts**
- **Whole body bone scan is indicated**

八、住院及出院條件

Admission and Discharge criteria

Admission criteria

For diagnosis of urothelial carcinoma of urinary bladder

For treatment of urothelial carcinoma of urinary bladder

Discharge criteria

Stable condition after treatment

A second TUR at 2-6 weeks after the initial resection when it was incomplete[8-10] or fulfilled either one of the following criteria: all HG tumors, all T1 tumors.

The pathological report should specify the grade, the depth of tumour invasion and whether the lamina propria and muscle are present in the specimen

九、主要治療處置

Primary treatment and management

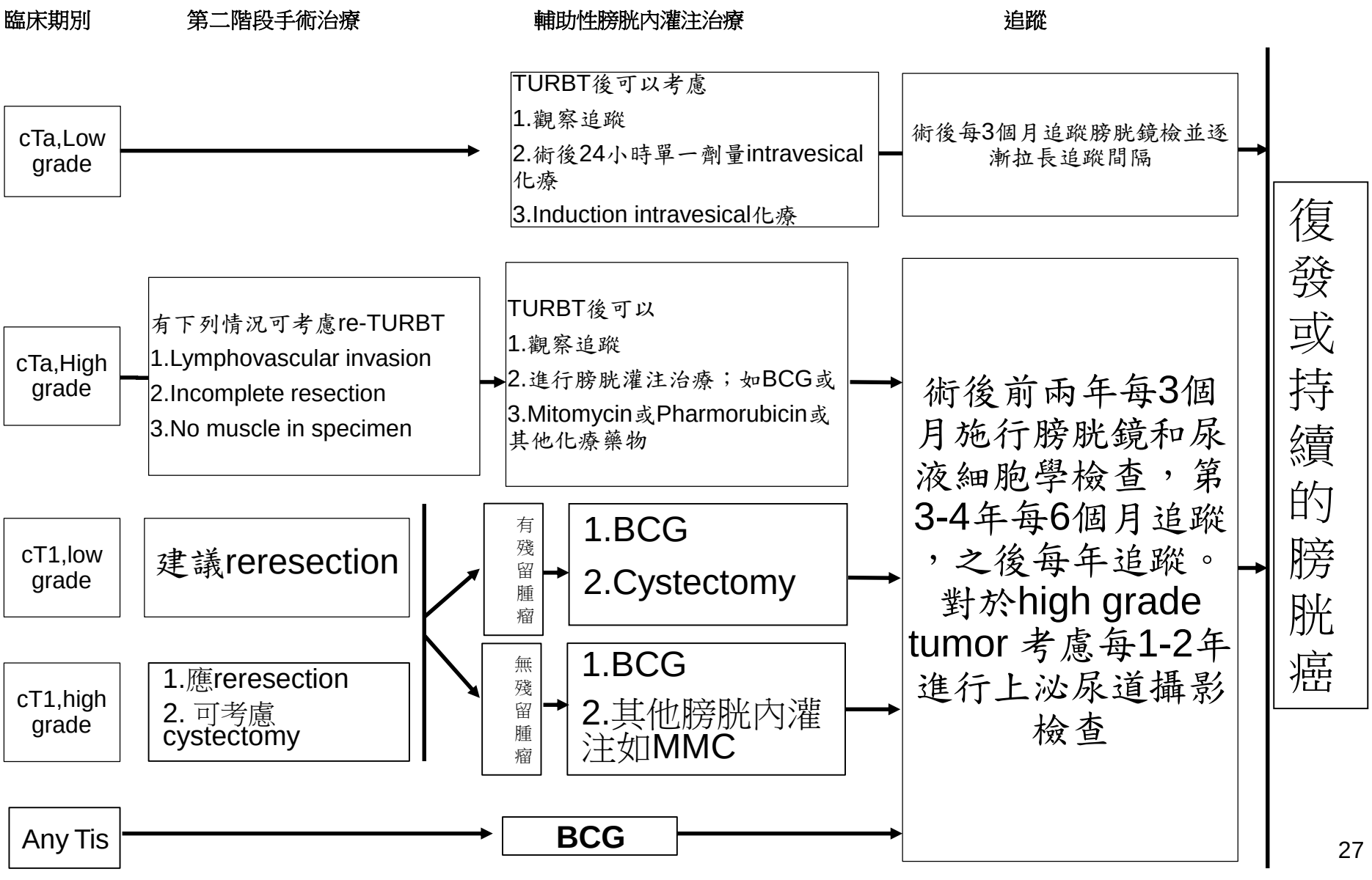
非肌肉侵犯型膀胱癌，起始評估/手術

1.當臨床分期預期為非侵犯性(non-invasion)的膀胱癌時，可選擇加做上泌尿道攝影(超音波、或靜脈尿路攝影、或電腦斷層尿路攝影、或核磁共振尿路攝影)。

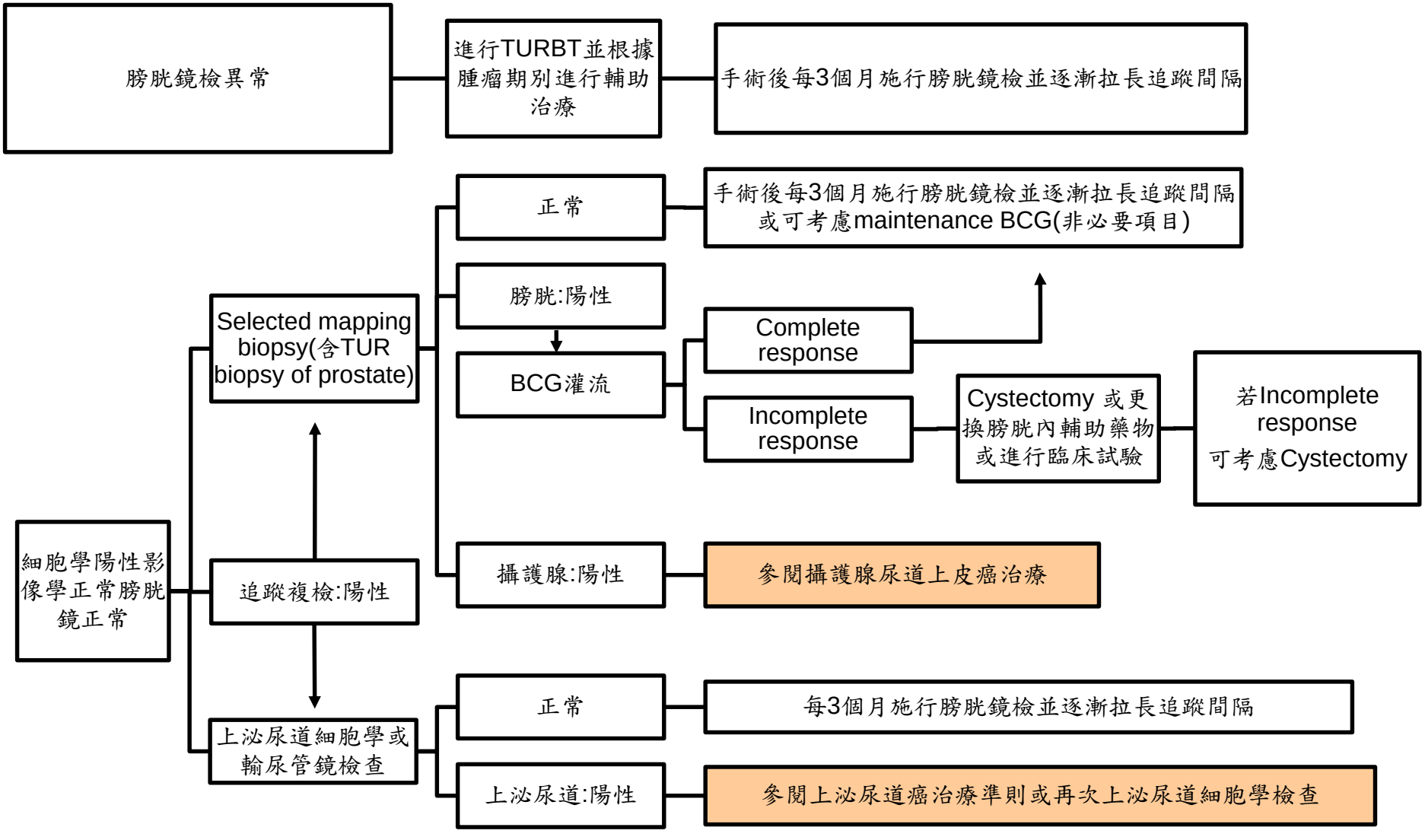
2.當腫瘤型態為sessile或high grade時，可以選擇在進行TURBT之前進行腹部或骨盆腔電腦斷層檢查。

- TaN0M0
- T1N0M0
- TisN0M0

第二階段手術治療，輔助性膀胱內灌注治療，追蹤



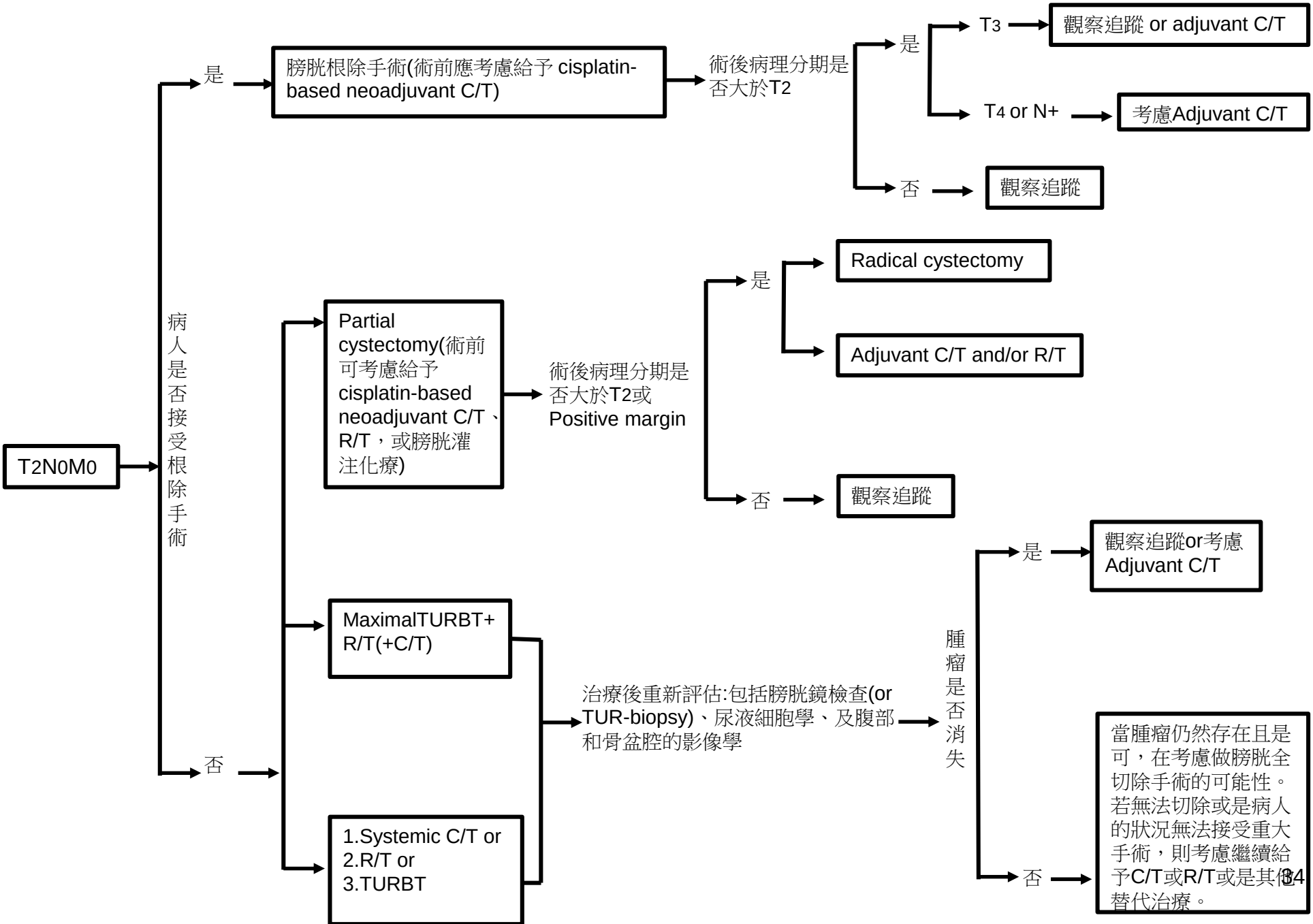
非肌肉侵犯型膀胱癌術後追蹤-復發或持續的膀胱癌

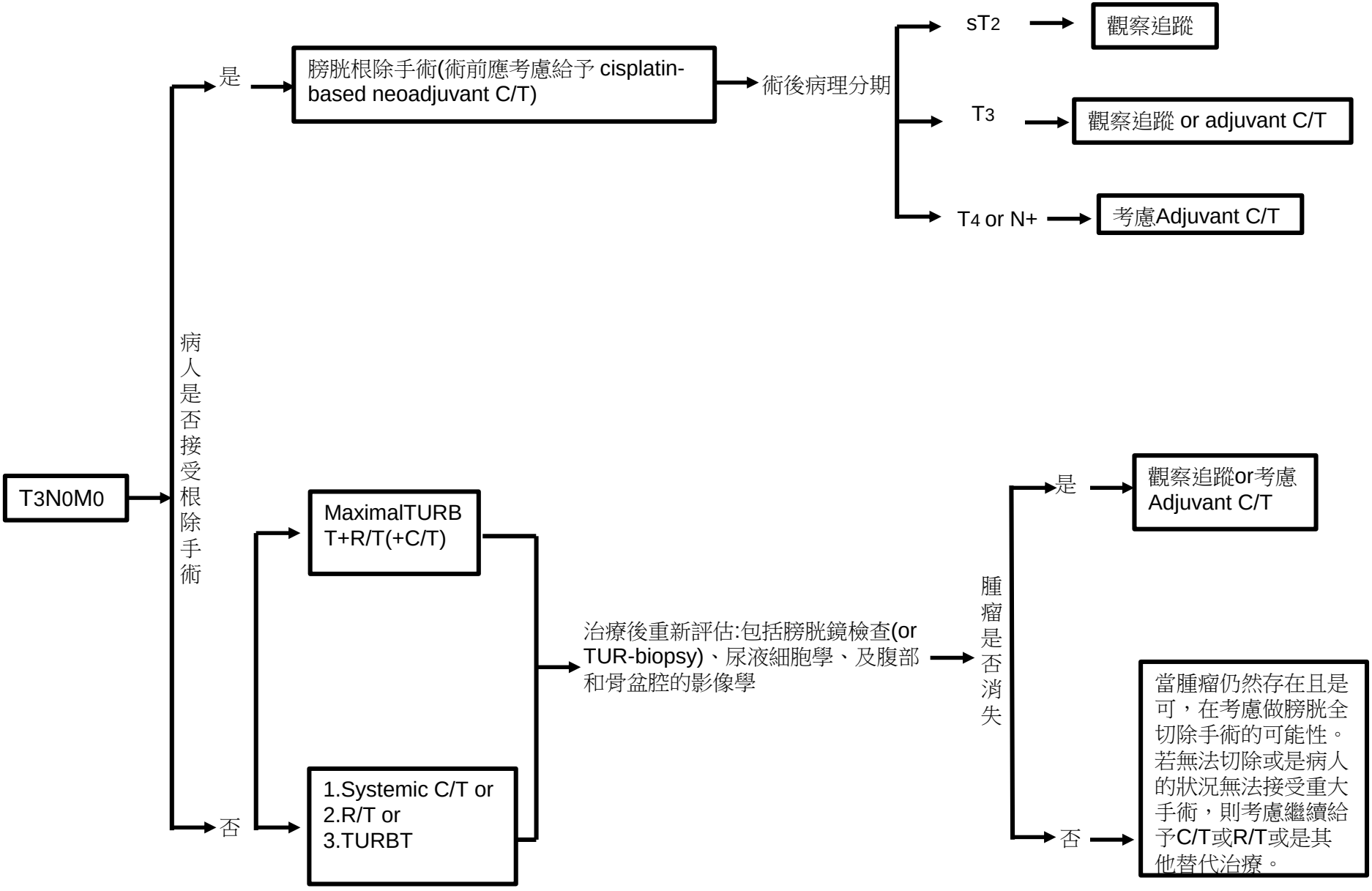


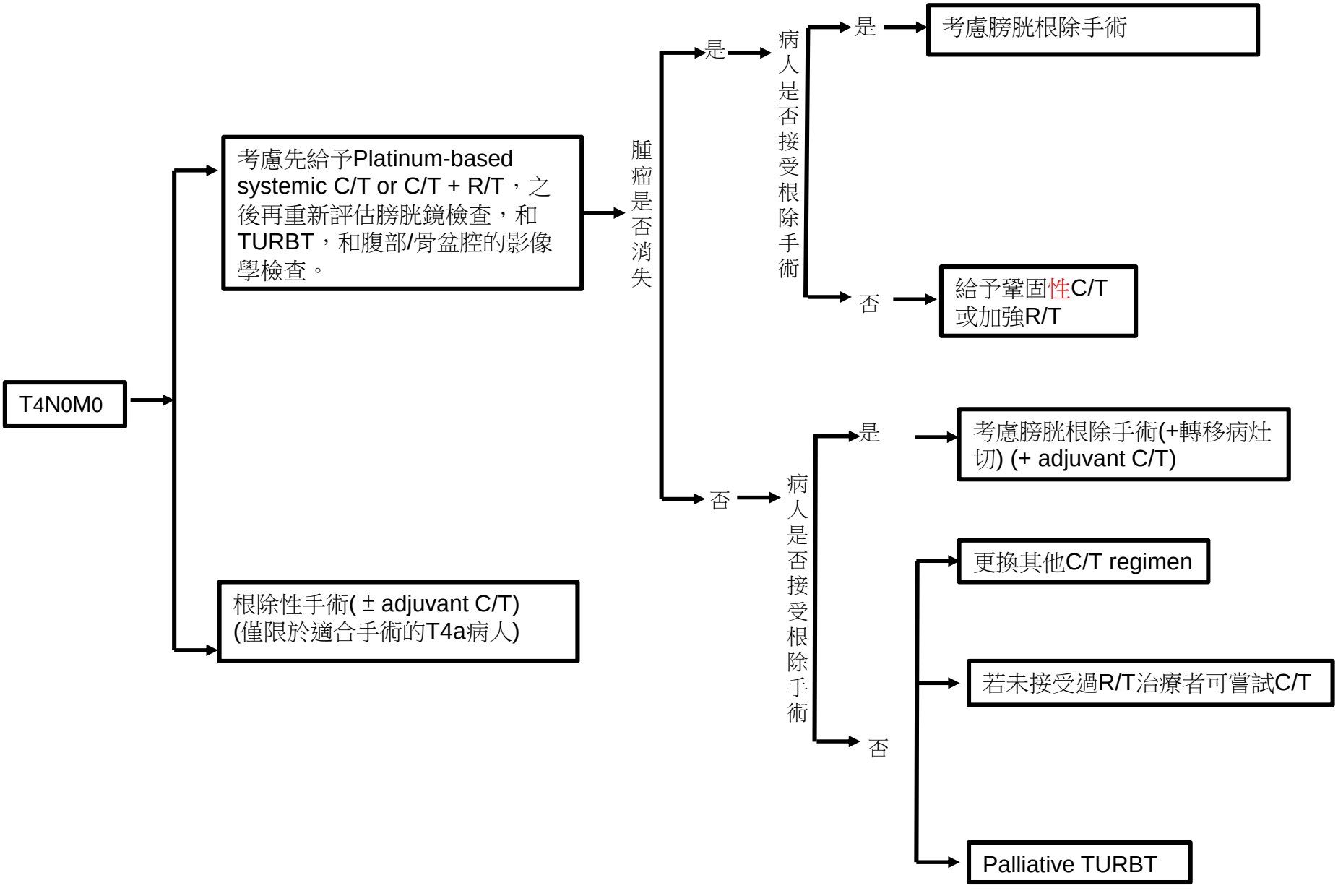
肌肉侵犯型膀胱癌-初始評估及治療

當臨床分期預期為肌肉侵犯(muscle invasive)的膀胱癌時，考慮做一般血液常規檢驗、生化檢驗、上泌尿道攝影(靜脈連路攝影、電腦斷層尿路攝影、腎臟超音波、逆行尿路攝影或核磁共振尿路攝影)、腹部/骨盆腔電腦斷層或核磁共振檢查、胸部X光(X光有懷疑轉移病灶建議加做胸部電腦斷層；若是ALP上升或有骨頭疼痛症狀建議加做骨骼掃描)。

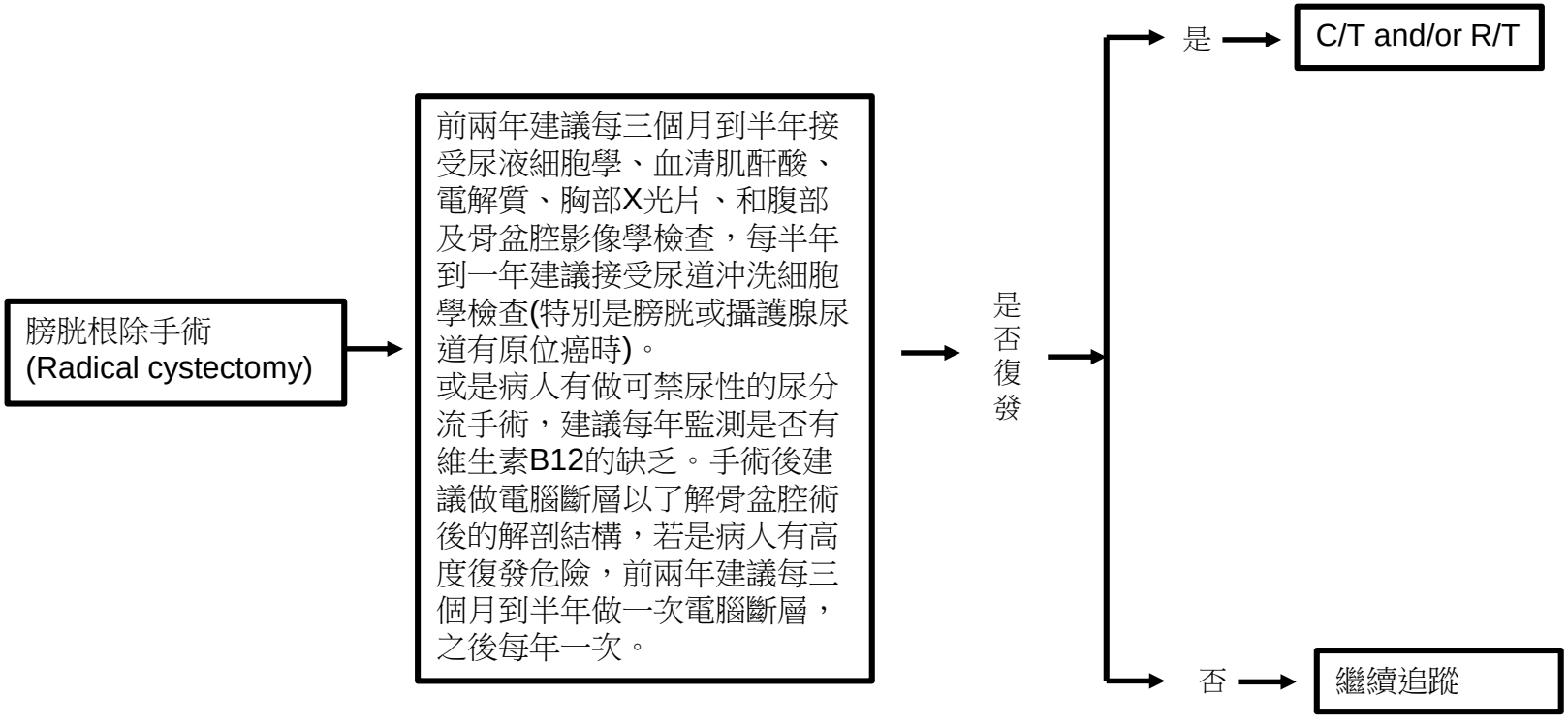
- $T_2N_0M_0$
- $T_3N_0M_0$
- $T_4N_0M_0$
- Any T,N+ or M+


T2N0M0
病人是否接受根除手術
是
膀胱根除手術(術前應考慮給予 cisplatin-based neoadjuvant C/T)
術後病理分期是否大於T2
是
T3
觀察追蹤 or adjuvant C/T
T4 or N+
考慮Adjuvant C/T
否
觀察追蹤
否
Partial cystectomy(術前可考慮給予 cisplatin-based neoadjuvant C/T、R/T，或膀胱灌注化療)
術後病理分期是否大於T2或Positive margin
是
Radical cystectomy
Adjuvant C/T and/or R/T
否
觀察追蹤
MaximalTURBT+ R/T(+C/T)
1.Systemic C/T or
2.R/T or
3.TURBT
治療後重新評估:包括膀胱鏡檢查(or TUR-biopsy)、尿液細胞學、及腹部和骨盆腔的影像學
腫瘤是否消失
是
觀察追蹤or考慮Adjuvant C/T
否
當腫瘤仍然存在且是可，在考慮做膀胱全切除手術的可能性。若無法切除或是病人的狀況無法接受重大手術，則考慮繼續給予C/T或R/T或是其他替代治療。

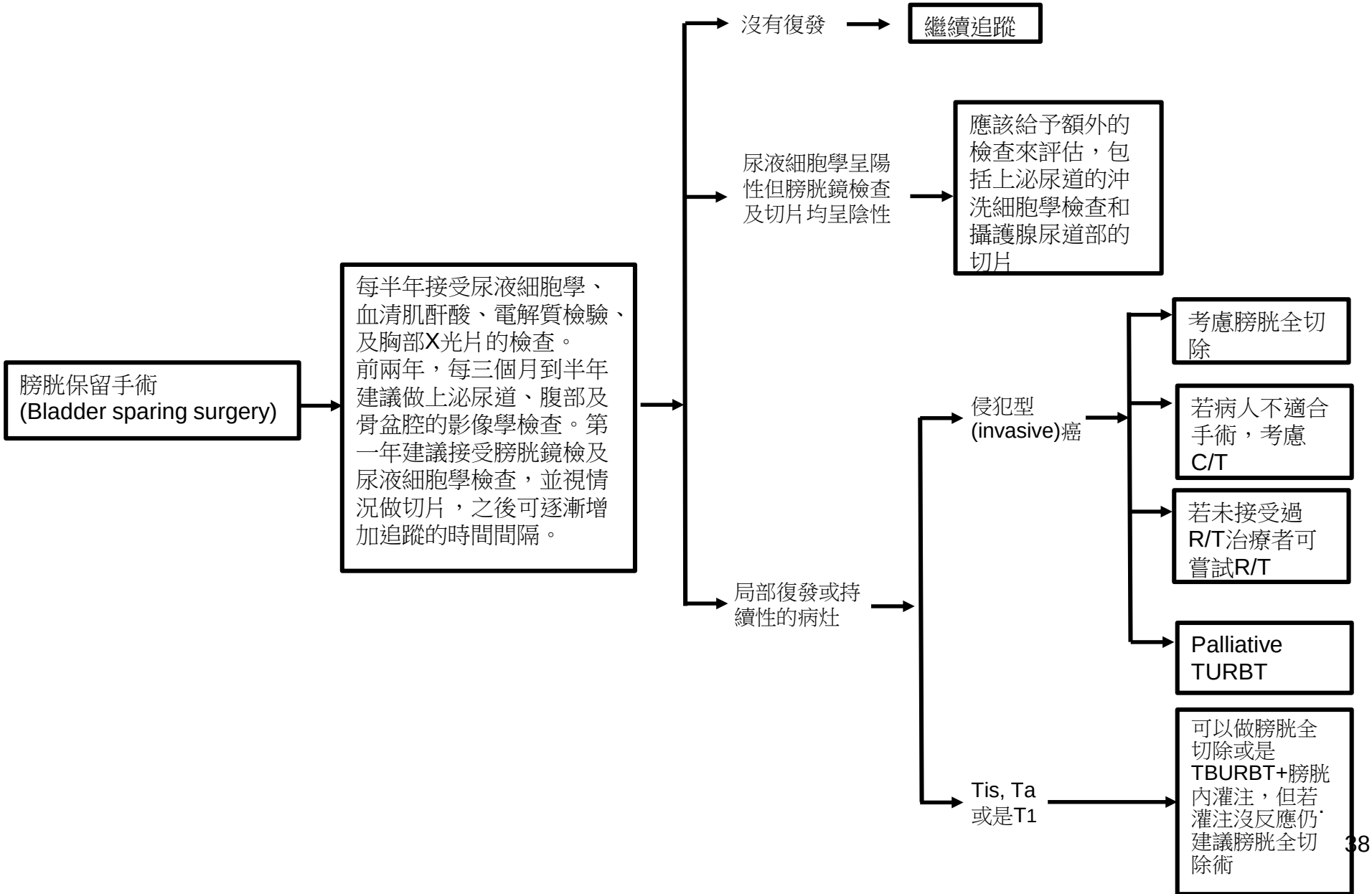

T3N0M0
病人是否接受根除手術
是
膀胱根除手術(術前應考慮給予 cisplatin-based neoadjuvant C/T)
術後病理分期
sT2
觀察追蹤
T3
觀察追蹤 or adjuvant C/T
T4 or N+
考慮Adjuvant C/T
否
MaximalTURBT+R/T(+C/T)
1.Systemic C/T or
2.R/T or
3.TURBT
治療後重新評估:包括膀胱鏡檢查(or TUR-biopsy)、尿液細胞學、及腹部和骨盆腔的影像學
腫瘤是否消失
是
觀察追蹤or考慮Adjuvant C/T
否
當腫瘤仍然存在且是可，在考慮做膀胱全切除手術的可能性。若無法切除或是病人的狀況無法接受重大手術，則考慮繼續給予C/T或R/T或是其他替代治療。


T4N0M0
考慮先給予Platinum-based systemic C/T or C/T + R/T，之後再重新評估膀胱鏡檢查，和TURBT，和腹部/骨盆腔的影像學檢查。
根除性手術(± adjuvant C/T)
(僅限於適合手術的T4a病人)
腫瘤是否消失
是
病人是否接受根除手術
是
考慮膀胱根除手術
否
給予鞏固性C/T
或加強R/T
否
病人是否接受根除手術
是
考慮膀胱根除手術(+轉移病灶切) (+ adjuvant C/T)
否
更換其他C/T regimen
若未接受過R/T治療者可嘗試C/T
Palliative TURBT

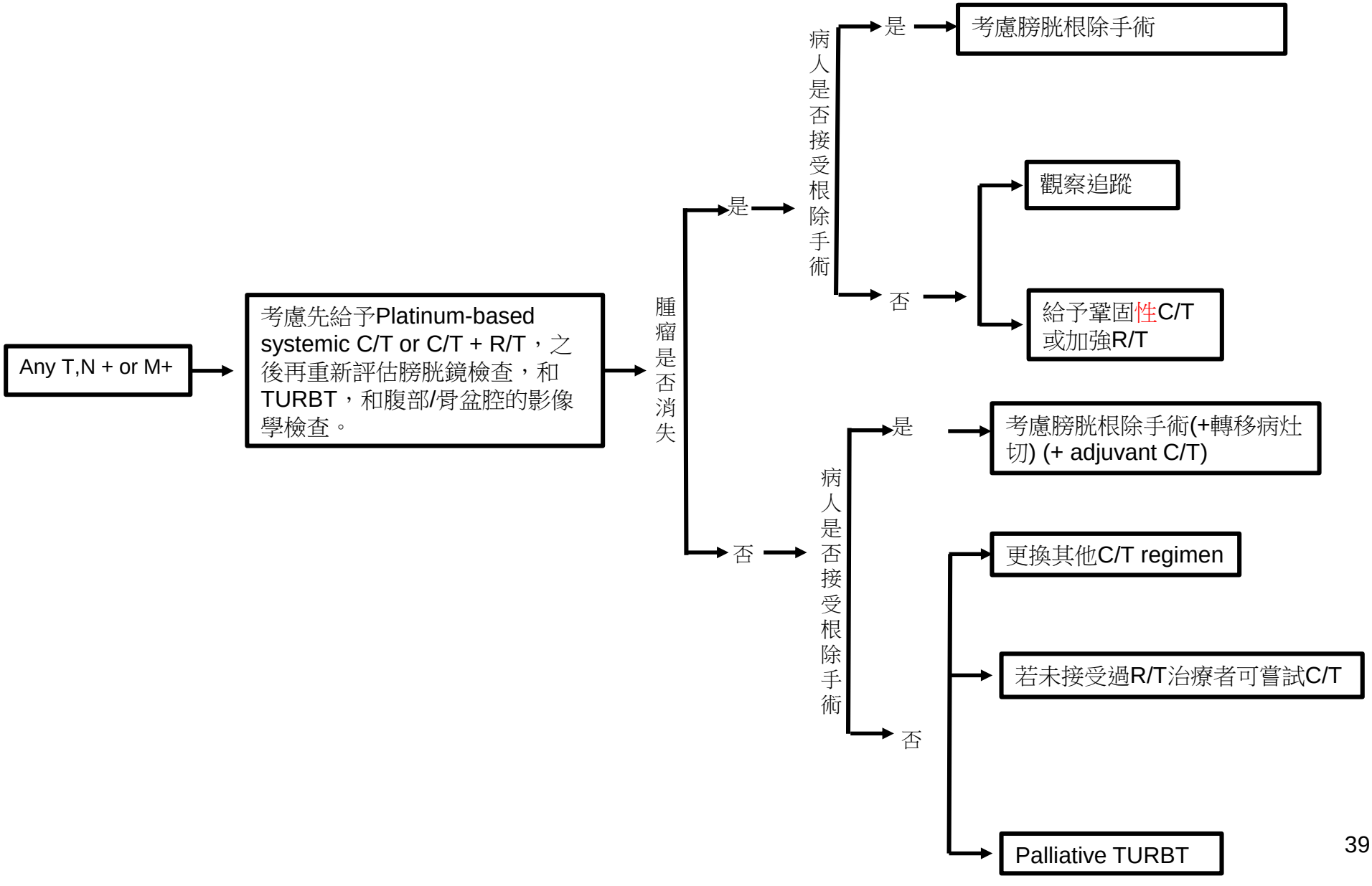
肌肉侵犯型膀胱癌-術後追蹤

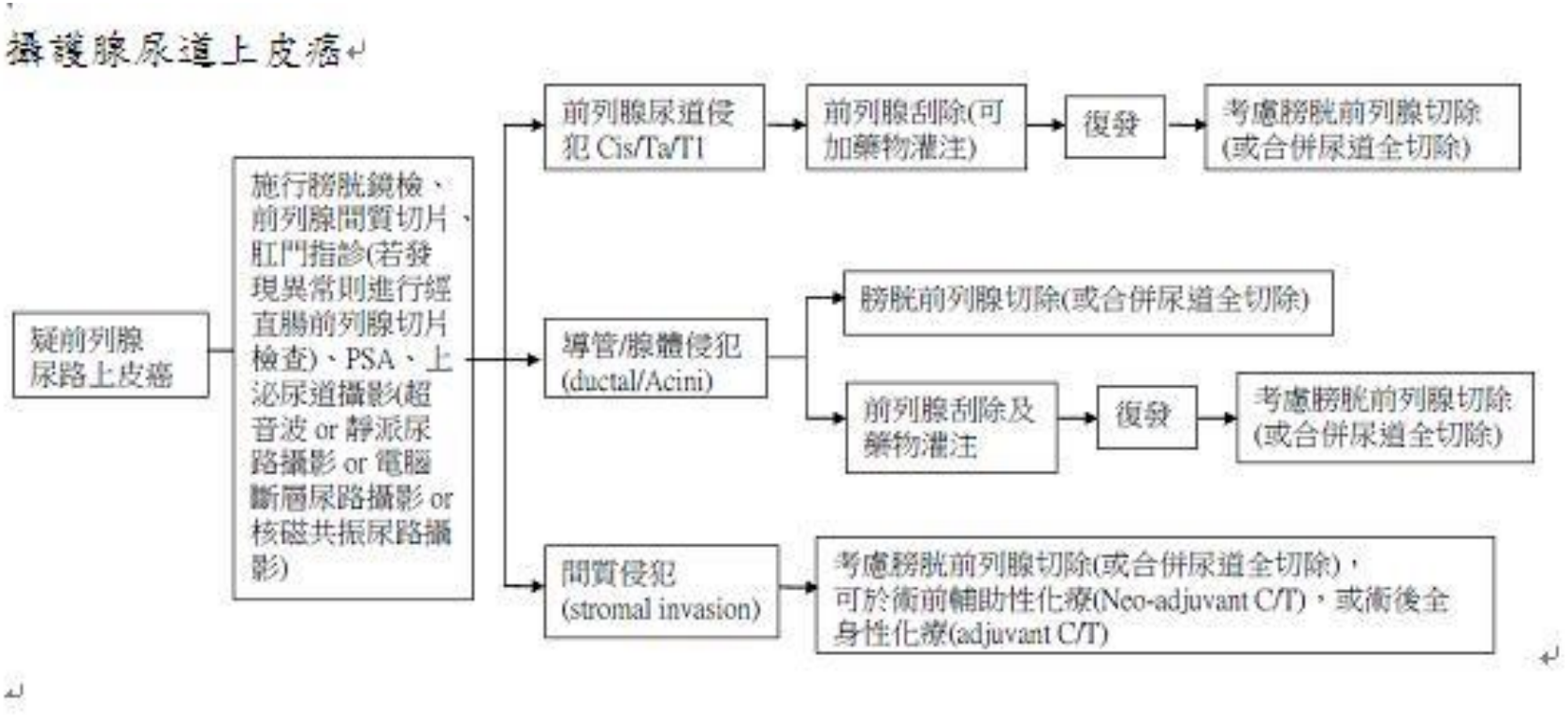


肌肉侵犯型膀胱癌-術後追蹤



轉移型膀胱癌


Any T,N + or M+
考慮先給予Platinum-based systemic C/T or C/T + R/T，之後再重新評估膀胱鏡檢查，和TURBT，和腹部/骨盆腔的影像學檢查。
腫瘤是否消失
是
病人是否接受根除手術
是
考慮膀胱根除手術
否
觀察追蹤
給予鞏固性C/T或加強R/T
否
病人是否接受根除手術
是
考慮膀胱根除手術(+轉移病灶切) (+ adjuvant C/T)
否
更換其他C/T regimen
若未接受過R/T治療者可嘗試C/T
Palliative TURBT


攝護腺尿道上皮癌
疑前列腺尿路上皮癌
施行膀胱鏡檢、前列腺間質切片、肛門指診(若發現異常則進行經直腸前列腺切片檢查)、PSA、上泌尿道攝影(超音波 or 靜派尿路攝影 or 電腦斷層尿路攝影 or 核磁共振尿路攝影)
前列腺尿道侵犯 Cis/Ta/T1
前列腺刮除(可加藥物灌注)
復發
考慮膀胱前列腺切除(或合併尿道全切除)
導管/腺體侵犯(ductal/Acini)
膀胱前列腺切除(或合併尿道全切除)
前列腺刮除及藥物灌注
復發
考慮膀胱前列腺切除(或合併尿道全切除)
間質侵犯(stromal invasion)
考慮膀胱前列腺切除(或合併尿道全切除)，可於術前輔助性化療(Neo-adjuvant C/T)，或術後全身性化療(adjuvant C/T)

十、輔助或替代治療Adjuvant /Substitute treatment

In contrast to TURBT or cystectomy

1.Bladder instillation(mitomycin C, or BCG) for non- muscle invasive carncer

2.Partial cystectomy

3.Palliative cystectomy for muscle-invasive bladder cancer

4.External beam radiotherapy

5.Chemotherapy for advanced diseases

6.Supportive treatment for terminal diseases

Recommendations for adjuvant therapy

•In patients at low risk of tumour recurrence and progression, one immediate instillation of chemotherapy is strongly recommended as the complete adjuvant treatment. But should consider the operative finding of bladder perforation of post OP bleeding.

•In patients at an intermediate or high risk of recurrence and an intermediate risk of progression, one immediate instillation of chemotherapy should be followed by further instillations of chemotherapy or a minimum of 1 year of BCG.

•Immediate radical cystectomy may be offered to patients at highest risk of tumour progression. In patients with BCG failure, cystectomy is recommended.

•The absolute risks of recurrence and of progression do not always indicate the risk at which a certain therapy is optimal. The choice of therapy may be considered differently according to what risk is acceptable for the individual patient and the urologist.

十一、無法切除的腫瘤

(A).Usually cT4a, cT4b, or Any T N1, N2, N3

a.Regional node (-) : biospy proven or no suspicious LN

Chemotherapy 3-4 cycles followed by 1.or 2.or 3.

1.Cystectomy followed by 2-3 cycles of chemotherapy

2.Chemotherapy + R/T (curative intent)

3.Further chemotherapy ± palliative R/T

b. LN (+), biopsy proven or highly suspected(> 2cm or by roentgenologist): Chemotherapy ± R/T, 3-6 cycles

1.No tumor:Boost with R/T, cystectomy,

2.Tumor persists:

Invasive:i.cystectomy,

ii.chemotherapy or radiotherapy alone

iii.chemotherapy ± R/T

(B). M1

a.Node only : Chemotherapy ± R/T, 3-6 cycles

1.No tumor : Boost with R/T, cystectomy, or observation.

2.Tumor persists: Invasive

i.cystectomy,

ii.chemotherapy or radiotherapy alone

iii.chemotherapy ± R/T

b.Disseminated:

1.Chemtherapy

2.Chemotherapy + palliative R/T

(C). T2, T3, T4 with comorbid disease or poor performance status, not suitable for cystectomy

a.TURBT alone

b.RT alone

c.chemotherapy ± R/T

十二、手術前化療及手術後化療

手術前化療:

(A). T3 N0, strongly suggested:

a.Chemotherapy 3-4 cycles, followed by

1.cystectomy, radical

2.selective bladder sparing following maximum TURBT with concurrent C/T + R/T (only for without hydronephrosis)

(B). T2 N0, optional:

a.chemotherapy, followed by :

1.radical cystectomy

2.segmental cystectomy (highly selected)

3.selective bladder sparing following maximum TURBT with concurrent C/T + R/T (only for without hydronephrosis)

手術後化療

(A). T2N0, optional : chemotherapy was suggested for

a.segmental cystectomy (± R/T)

b.bladder sparing, (± R/T)

c.radical cystectomy with lymphovascular involvement

d.microscopic residual tumor

(B). T2 N1-3, T3 any N

a. Regional node (-) : biospy proven or no suspicious LN

Chemotherapy 3-4 cycles followed by 1. or 2. or 3.

1. Cystectomy followed by 2-3 cycles of chemotherapy

2. Chemotherapy + R/T (curative intent)

3. Further chemotherapy ± palliative R/T

十三、轉移性疾病

a. Node only : Chemotherapy ± R/T, 3-6 cycles

1. No tumor : Boost with R/T, cystectomy, or observation.

2. Tumor persists: Invasive

i. cystectomy,

ii. chemotherapy or radiotherapy alone

iii. chemotherapy ± R/T

b. Disseminated:

1. Chemtherapy

2. Chemotherapy + palliative R/T

Chemotherapy Regimen for Neoadjuvant Therapy

	Chemotherapy regimen	Schedules
MVAC/ddMVAC	vinblastine 3mg per BSA in D5W 100ml IV for 15mins ST D1 methotrexate 30mg per BSA in D5W 100ml IV for 30mins ST D1 doxorubicin 30mg per BSA in D5W 100ml IV for 45mins QD D1 Cisplatin 70mg per BSA (adjusted by CCr) in NS 500ml IV for 3.5hrs ST D1 Leucovorin (15 mg) 1tab PO QID D2-3	Q4W for 3-6 cycles (ddMVAC: Q2W with GCSF support)
GC-G(GC)	Gemcitabine 1000mg per BSA in NS 100 ml IV for 30mins ST D1 cisplatin 70mg per BSA (adjusted by Ccr) in NS 500ml IV for 4hrs ST D1	Q3W or Q4W for 4 cycles
GCarbo*-G	gemcitabine 1000mg per BSA in NS 250ml IV for 30mins ST D1 carboplatin 4mg AUC in D5W 250ml IV for 1hrs ST D1 *Carboplatin should be given only if cisplatin infeasible	Q3W or Q4W for 4 cycles
CMV	methotrexate 40mg per BSA in D5W 100ml IV for 30mins ST D1 vinblastine 4mg per BSA in D5W 100ml IV for 20mins ST D1 cisplatin 70 mg per BSA (adjusted by CCr) in NS 500ml IV for 3.5hrs ST D1 Leucovorin 1tab PO QID D2-3	Q3W for 3 cycles

Chemotherapy Regimen for Adjuvant Therapy

	Chemotherapy regimen	schedules
MVAC/ddMVAC	vinblastine 3mg per BSA in D5W 100ml IV for 15mins ST D1 methotrexate 30mg per BSA in D5W 100ml IV for 30mins ST D1 doxorubicin 30mg per BSA in D5W 100ml IV for 45mins QD D1 Cisplatin 70mg per BSA (adjusted by CCr) in NS 500ml IV for 3.5hrs ST D1 Leucovorin (15 mg) 1tab PO QID D2-3	Q4W for 3-6 cycles (ddMVAC: Q2W with GCSF support)
GC-G(GC)	Gemcitabine 1000mg per BSA in NS 100 ml IV for 30mins ST D1 cisplatin 70mg per BSA (adjusted by Ccr) in NS 500ml IV for 4hrs ST D1	Q3W or Q4W for 4-6 cycles
GCarbo*-G	Gemcitabine 1000mg per BSA in NS 100ml IV for 30mins ST D1 carboplatin 4mg AUC in D5W 250ml IV for 1hrs ST D1 *Carboplatin should be given only if cisplatin infeasible	Q3W or Q4W for 4-6 cycles
CMV	methotrexate 40mg per BSA in D5W 100ml IV for 30mins ST D1 vinblastine 4mg per BSA in D5W 100ml IV for 20mins ST D1 cisplatin 70 mg per BSA (adjusted by CCr) in NS 500ml IV for 3.5hrs ST D1 Leucovorin 1tab PO QID D2-3	Q3W for 4-6 cycles

Chemotherapy Regimen for CCRT

	Chemotherapy regimen
GC-G(GC)	Gemcitabine 1000mg per BSA in NS 100 ml IV for 30mins ST D1 cisplatin 70mg per BSA (adjusted by Ccr) in NS 500ml IV for 4hrs ST D1
GCarbo*-G	gemcitabine 1000mg per BSA in NS 250ml IV for 30mins ST D1 Carboplatin 4mg AUC in D5W 250ml IV for 1hrs ST D1 *Carboplatin should be given only if cisplatin infeasible
CMV	methotrexate 40mg per BSA in D5W 100ml IV for 30mins ST D1 vinblastine 4mg per BSA in D5W 100ml IV for 20mins ST D1 cisplatin 70 mg per BSA (adjusted by CCr) in NS 500ml IV for 3.5hrs ST D1 Leucovorin 1tab PO QID D2-3
Weekly cisplatin	weekly cisplatin 30 mg per BSA× 6 doses

*concurrent 5-FU and mitomycin C or gemcitabine could also be considered for CCRT regimen in patients with impaired renal function or unfit for platinum

Chemotherapy Regimen for Metastatic

	Chemotherapy regimen	schedules
MVAC	vinblastine 3mg per BSA in D5W 100ml IV for 15mins ST D1 methotrexate 30mg per BSA in D5W 100ml IV for 30mins ST D1 doxorubicin 30mg per BSA in D5W 100ml IV for 45mins QD D1 Cisplatin 70mg per BSA (adjusted by CCr) in NS 500ml IV for 3.5hrs ST D1 Leucovorin (15 mg) 1tab PO QID D2-3	Q4W for Till PD or maximal 8 cycles
GC-G(GC)	Gemcitabine 1000mg per BSA in NS 100 ml IV for 30mins ST D1 cisplatin 70mg per BSA (adjusted by Ccr) in NS 500ml IV for 4hrs ST D1	Q3W or Q4W till PD or maximal 8 cycles
Gemzar + Paclitaxel*	gemcitabine 1000mg per BSA in NS 100ml IV for 30mins ST D1, D8; paclitaxel 175mg per BSA in D5W 500ml IV for 3hrs ST D1;	Q3W for Till PD or maximal 8 cycles
GCarbo-G	gemcitabine 1000mg per BSA in NS 250ml IV for 30mins ST D1 carboplatin 4mg AUC in D5W 250ml IV for 1hrs ST D1	Q3W or Q4W till PD or maximal 8 cycles
CMV	methotrexate 40mg per BSA in D5W 100ml IV for 30mins ST D1 vinblastine 4mg per BSA in D5W 100ml IV for 20mins ST D1 cisplatin 70 mg per BSA (adjusted by CCr) in NS 500ml IV for 3.5hrs ST D1 Leucovorin 1tab PO QID D2-3	Q3W for till PD or maximal 8 cycles
Nivolumab†	3mg/kg IVA 30mins ST D1	Q2W till PD
Pembrolizumab†	2-3mg/kg (maximal 200mg/time) IVA 30mins ST D1	Q3W till PD
Atezolizumab	1200mg fixed dose IVA 30 mins ST D1	Q3W till PD
Avelumab	10 mg per kilogram of body weight, administered intravenously every 2 weeks	Q2W till PD

*Other taxane based regimen could be also considered for platinum-refractory diseases
†Both Nivolumab and pembrolizumab are suggested for platinum-refractory diseases

Chemotherapy guidelines by treatment line

First line

Cisplatin eligible	Gemcitabine + Cisplatin (category 1)
	MVAC (or ddMVAC with G-CSF support, (category 1))
	May be considered: Atezolizumab + Gemcitabine/Cisplatin *
Cisplatin ineligible	Gemcitabine + Carboplatin
	Atezolizumab (PD-L1 positive required) #
	Pembrolizumab (PD-L1 positive required) ##
	Gemcitabine with or without paclitaxel

* As of 2021/10/25, FDA and TFDA approval are still pending, **therefore use of this regimen is off-label use**

PD-L1 ≥ 5% (IC2/3) by Ventana SP142 IHC staining

##PD-L1 CPS score ≥ 10% by Dako 22C3 staining

Chemotherapy guidelines by treatment line

Second line

Post platinum	**Note: if progression free survival is ≥ 12 months after cisplatin/carboplatin, retreatment with platinum can be considered if patient is still platinum eligible.**
Pembrolizumab (category 1)	
Atezolizumab	
Nivolumab	
Durvalumab	
Docetaxel (or paclitaxel)	
Gemcitabine	
Post checkpoint inhibitor	
Gemcitabine/Cisplatin (or carboplatin if cis-ineligible)	
ddMVAC with growth factor support	
Switch maintenence	Avelumab *no disease progression (i.e., an ongoing complete response, partial response, or stable disease) after the receipt of 4-6 cycles of chemotherapy with gemcitabine plus cisplatin or carboplatin; and a treatment-free interval of 4 -10 weeks since the last dose of chemotherapy

Principles of Radiation Therapy

See Practice Guidelines of Radiation Therapy for general standard operating procedures, tolerance dose of critical normal structures, quality assurance, DVH criteria for plan approval, and etc.

- **Radiation therapy for newly diagnosed bladder cancer**
- **Radiation therapy for postoperative bladder cancer**
- **Radiation Therapy for recurrent or metastatic disease**

General Radiation Information

General Radiation Information

– Treatment recommendations should be made after joint consultation and/or discussion by a multidisciplinary team including surgical, radiation, medical oncologists, radiologists, and pathologists.

– Cystoscopy, urine cytology, pathology, pelvic CT/MR scans, Whole body bone scan reports , when available, should be reviewed by the multidisciplinary team. This will allow an informed determination of treatment volume and field borders prior to simulation.

Simulation

– Immobilization device is strongly recommended for reproducibility of daily set-up

To minimize setup variability, a customized immobilization device for both knee and foot (Alpha Cradle; Smithers Medical Product, Inc., North Canton, OH) was applied to each patient in the supine position.

In the 1st stage of treatment

- Empty bladder and rectum are recommended for every patient.

A treatment planning computed tomography scan was performed using 5-mm slices. The CT scans were obtained from the L2 vertebral body to 5 cm below the ischial tuberosity with an average of 80 images per patient. All patients had a empty bladder and rectum during scanning and simulation. During daily treatment they were instructed to have a empty bladder.

In the 2nd stage of treatment

- Full bladder (300-500 mL water drinking 30 minutes before simulation) and empty rectum are recommended for every patient.

A repeated CT scans were obtained from the L2 vertebral body to 5 cm below the ischial tuberosity with an average of 80 images per patient. All patients had a full bladder and empty rectum during scanning and simulation. During daily treatment they were instructed to have a full bladder in the second phase of treatment.

- Pelvic CT/ MR imagine fusion is recommended
- CT simulation and 3D treatment planning is necessary.

Principle of Target volume delineation

Definitions of target volumes and critical structures

- Following the International Commission on Radiation Units and Measurements ICRU 62 recommendations, a clinical target volume (CTV) was delineated on individual axial computed tomography slices in all patients by our radiation oncologist and reviewed by another.

Gross Target Volume (GTV) delineation

- *Target volume delineation based on CT simulation images. Diagnostic CT/MR reports, and PET/CT scans should be reviewed, when available, for precise delineation of GTV.*
- Pelvic CT/MR imagine fusion is recommended

Clinical Target Volume (CTV) delineation

- *The clinical target volume should include GTV and the areas at risk for microscopic disease*

For definitive radiotherapy:

In the 1st stage of treatment

- CTV_H: whole bladder
- CTV_L: whole bladder+ pelvic LNs# for pelvic radiotherapy

In the 2nd stage of treatment

- CTV_H: Gross bladder tumor

Fort postoperative radiotherapy:

- CTV_H: Surgical bed of bladder and tumor invasion area
- CTV_L: Surgical bed of bladder and tumor invasion area + pelvic LNs# for pelvic radiotherapy

Pelvic LNs:

a. For patients in high risk group of lymph nodes involvement, entirety external iliac, internal iliac and obturator nodal basin should be included.

b. For patients with image or pathology evidence of pelvic LN metastasis, pre-sacral, common iliac should be covered as well

Principle of Target volume delineation

Planning Target Volume (PTV) delineation

- The margins of PTV should consider organ motion and setup errors
- The recommended margins to compensate organ motions are as follows:

PTV_H = CTV_H + 10 mm margin

PTV_L = CTV_L + 10 mm margin

Radiation dose

- For definitive Radiotherapy and postoperative radiotherapy

PTV_H: 61– 66 Gy / 33–36 fractions

PTV_L: 40 – 45 Gy / 22-28 fractions

Radiation technique:

Use multiple fields from high-energy linear accelerator beams.

- 3D-CRT or IMRT
- IGRT

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Other Principles of Radiation Therapy

Other Principles of Radiation Therapy

– Precede radiation therapy alone or concurrent chemotherapy and radiation by maximal TUR of the tumor when safely possible.

– For invasive tumors, consider low-dose preoperative radiation therapy prior to segmental cystectomy. (category 2B)

– Concurrent chemotherapy and radiation therapy or radiation therapy alone is most successful for patients without hydronephrosis and without extensive carcinoma in situ associated with their muscle-invading tumor.

– For patients with stage Ta, T1, or Tis, external beam radiation therapy (EBRT) alone is rarely appropriate.

– For patients with recurrent Ta-T1 disease usually following BCG therapy but without extensive Tis who are not candidates for cystectomy, concurrent chemotherapy and radiation therapy may be considered as a potentially curative alternatives to radical cystectomy, which is the standard treatment by NCCN Guidelines.

–When irradiating the bladder only or bladder tumor boost, consider daily image guidance.

–Concurrent chemotherapy with radiation therapy is encouraged for added tumor cytotoxicity, and can be given without increased toxicity over radiation therapy alone. Concurrent 5 FU and mitomycin C can be used instead of Cisplatin in patient with low or moderate renal function. Such therapy is optimally given by dedicated multidisciplinary teams.

– Concurrent chemotherapy with radiation therapy or radiation therapy alone should be considered as potentially curative for medically in operable patients or for local palliation in patients with metastatic disease.

Principle of Palliative Radiotherapy

When giving palliative radiation for metastatic bladder cancer or for recurrent pelvic tumor, combining radiation with radiosensitizing chemotherapy should be considered.

- Chemotherapy should not be used concurrently with high dose (> 3 Gy) palliative radiation. Version 2016.03.01

Acronym

RT: Radiation Therapy
- **3D-CRT: 3D Conformal Radiation Therapy**
- **IMRT: Intensity Modulated Radiation Therapy**
- **IGRT: imaging guide radiotherapy**
- **GTV: Gross Tumor Volume**
- **CTV: Clinical Target Volume**
- **PTV: Planning Target Volume**
- **MRI: Magnetic Resonance Image**
- **PET: Positron Emission Tomography**

十四、預後Outcome

5-year recurrence-free survival:pT1: 76%, pT2 : 74% , pT3: 52%, pT4 :36%

十五、住院天數Length of stay

5-7 days for non-muscle invasive cancer 14 -21 days for muscle invasive cancer

十六、出院計畫Discharge Plan

Regular outpatient department follow-up

Visiting emergency room if conditions requiring immediate attention

十七、出院衛教Discharge health education

Avoid risk factors

Environmental factors (cigarette smoking)

Chemical exposure:benzene derivatives and arylamines

Antiinflammatory agents (phenacetin)

External beam radiation therapy

Chronic urinary tract infection

Regular follow-up

十八、出院追蹤Discharge Follow up

Every 3 months for the first 2 years, every 6 months for the next 3 years, and yearly thereafter if the patient is free from disease recurrence

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