中山醫學大學附設醫院

攝護腺癌診療指引

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泌尿道癌小組經驗作編修
泌尿道癌醫療小組

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2010/05/28 Version 2.0
2009/12/16 Version 1.0

癌症委員會主任委員	癌症委員會執行長	癌症防治中心主任	團隊負責人

修訂內容

頁數	原文	修訂/新增
第 1 頁	依據行政院國民健康署 2010 年公佈，攝護腺(前列腺)惡性腫瘤發生個案數占全部惡性腫瘤發生個案數的 4.5%，發生率的排名於男性為第 5 位	據行政院衛生署的統計，前列腺癌的發生率與死亡率近年來均呈逐年增加之現象
第 7 頁	臨床局限性腫瘤－非常高/高度復發風險 T3a 期或 Gleason score 8-10 分或 PSA＞20 ng/ml- 放射線治療 ±2-3 年前置/伴隨/輔助性荷爾蒙治療 或根除性攝護腺切除手術+骨盆腔淋巴結(切除)擴清術(選擇性患者)	臨床局限性腫瘤-非常高/高度復發風險 T3a 期或 Gleason score 8-10 分或 PSA＞20 ng/ml- 放射線治療 ± 2-3 年前置/伴隨/輔助性荷爾蒙治療 或根除性攝護腺切除手術+骨盆腔淋巴結(切除)擴清術(選擇性患者) 新增-或荷爾蒙治療
第 8 頁	PSA 偵測不到 (＜**0.04**) PSA 仍可偵測 (≧**0.04**)	修改成 PSA (<10ng/ml) PSA (>10 ng/ml)
第 10 頁	放射治療後血清 PSA 升高(最低值後上昇≧2.0)	修改成-放射治療後核醫 PSA 升高(最低值後上昇≧2.0)
第 10 頁	切片陽性-追蹤觀察(暫不治療)或根除性攝護腺切除手術冷凍治療或視部位組織插種近接治療	刪除(暫不治療)修改成-切片陽性-追蹤觀察或根除性攝護腺切除手術冷凍治療或視部位組織插種近接治療
第 11 頁	轉移性病灶及血清 PSA 升高-復發-停止服用抗男性荷爾蒙藥物(使用 CAB 者)或第二線荷爾蒙藥物治療：(抗男性荷爾蒙藥物或 ketoconazole 或女性荷爾蒙藥物等)或全身性化學治療 Docetaxel 或支持性療法(Palliative R/T，BISPHOSPHONATE 類藥物)或臨床試驗用藥	修改成-停止服用抗男性荷爾蒙藥物(使用 CAB 者)或第二線以上荷爾蒙藥物治療：(抗男性荷爾蒙藥物或 ketoconazole 或女性荷爾蒙藥物等)或全身性化學治療 Docetaxel 或支持性療法(Palliative R/T，BISPHOSPHONATE 類藥物)或臨床試驗用藥
第 11 頁	Cisplatin / etoposide 或 Carboplatin / etoposide 或 Docetaxel 為主的化學治療或臨床試驗用藥	~~Cisplatin / etoposide~~ 或 ~~Carboplatin / etoposide~~ 或 ~~Docetaxel~~ 修改成化學治療為主的化學治療或臨床試驗用藥

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。

據行政院衛生署的統計，前列腺癌的發生率與死亡率近年來均呈逐年增加之現象；2012 年死亡排名佔男性癌症的第 7 位。本院登錄攝護腺惡性腫瘤 5 年個案數近為 240 例，發病年齡在 65 歲以上明顯增加，在 80 歲以上的組距佔最大族群。隨著老年化人口的來臨，攝護腺惡性腫瘤的篩檢顯得的格外重要。

隨著篩檢工具（攝護腺特定抗原 PSA 檢測）的準確率提高，病患健康意識的提昇，將來攝護腺癌的發生率必將持續增加，也因此本院積極整合泌尿外科、病理科、腫瘤內科、醫學影像部與放射腫瘤科以堅強的團隊，提供攝護腺癌有效的預防與全方位的治療。本院治療攝護腺(前列腺)惡性腫瘤具有相當優異成果，於民國 90 年成為中部第一所完成攝護腺組織插種近接治療單位，日前更引進先進且精準的光子刀/亞瑟刀放射定位治療儀器；在微創(局部)治療部分，也陸續引進海福刀(HIFU)及冷凍療法(Cryotherapy)。本團隊目的是整合現有人力、資源、研究計劃、臨床試驗、空間設備針對攝護腺癌做完善的的診斷及治療。

本攝護腺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攝護腺癌臨床指引、美國 National Comprehensive Cancer Network (NCCN) 的 Practice Guide-lines in Prostate Cancer V4. 2013版、及中山醫學大學附設醫院攝護腺癌治療經驗進行編修。

二、症狀、診斷和檢查

攝護腺癌在初期很少有症狀，多半都是在腫瘤較大且壓迫到膀胱或尿道時，才會出現像頻尿，解尿困難，排尿時有疼痛及燒灼的感覺，甚至解血尿。不過由於良性的攝護腺肥大也會有類似的症狀產生，所以有時也很難以這些症狀來判斷是否罹患攝護腺癌。攝護腺癌發生遠端轉移的時候，最常轉移到骨骼，此時多半會引起骨頭疼痛，或壓迫神經引起神經痛的症狀，嚴重的話，還會有病理性骨折的情形。要診斷攝護腺癌，首先要詳細的詢問病史，並要進行完整的身體檢查及評估，這些檢查包括：

（1）肛門指檢：直腸就在攝護腺的後側，所以醫師可以用食指經肛門放入病人的直腸，來觸診攝護腺，這樣的檢查就稱為「肛門指檢」。正常的攝護腺應該是柔軟有彈性的，如同握拳時大姆指旁虎口的肌肉，而攝護腺癌觸摸起來卻是如結節般的硬塊，甚至硬如石頭。但如果遇到攝護腺肥大、攝護腺發炎、攝護腺結石、或做過經尿道攝護腺切除手術及切片的病人，則肛門指檢就不易判讀。

（2）攝護腺特異抗原**(prostate specific antigen**，簡稱**PSA)**：這是一種攝護腺產生的蛋白質，其生理功能是使射精後的精液液化，可能有助於精子游走和授孕。攝護腺的上皮細胞與癌細胞都會分泌PSA，但癌細胞會分泌數倍以上的量。血中PSA的正常值是小於4.0 ng/ml，若抽血檢驗PSA大於正常值，就要懷疑有攝護腺癌的可能。但由於攝護腺肥大、攝護腺發炎、肛門指檢、導尿管的置放、膀胱鏡的檢查、經直腸超音波檢查及攝護腺的切片，都會使PSA有不同程度的升高，所以一旦發現病人有PSA升高的情形，必頇先排除其他非攝護腺癌所引起的PSA升高因素，才能下診斷。

（3）經直腸攝護腺超音波檢查：由於攝護腺是深埋在人體的一個小器官，一般的X光只能看到外形的影子，而肛門指診有時又會有人為因素的誤差，因此就發展出經直腸超音波檢查，可由距離攝護腺最近的位置直接掃描，觀察攝護腺的變化。當發現病灶時，還可藉由超音波的引導，將病變切片送檢查，但切片正常，並不一定代表就沒有癌症，有可能是因為切片採樣時沒有取到病變細胞。

（4）電腦斷層及核磁共振攝影：為了確實了解病灶與鄰近器官的關係，可以做電腦斷層及核磁共振攝影，較清楚的評估骨盆腔內的淋巴結，及其他器官是否有被癌細胞侵犯。

（5）其他：倘若懷疑有骨頭的轉移，還要做骨骼掃描，或是胸部X光檢查，以觀察是否有肺部轉移。

三、組織病理分類與分化

攝護腺癌的分類還可根據癌細胞分化程度來區隔，稱為分級系統。
而此一分級系統又可再分為一般分級系統及格里森分級系統二種。

(1)一般分級系統、依據病理組織切片進行細胞分化程度的分類：

Gx: 分級無法評估
G1: 分化良好(well differentiated)
G2: 中度分化(moderately differentiated)
G3-4: 分化不良或不分化(poor differentiated)

(2)格里森分級系統 (Gleason grading system)：

此為攝護腺癌分級中最常使用的分級系統，此系統是將腫瘤標本置於顯微鏡下，依據細胞分化的成熟度將其分成 1~5 級，分化最成熟的為 1 級，分化最不成熟的則為 5 級；而考慮攝護腺癌的多發性以及客觀評估預後，此系統從攝護腺癌組織切片中，取前二大面積者的級數相加而成格里森分數(2~10) (Gleason score)。格里森分數在 7 以上的病人預後明顯比格里森分數在 6 以下的病人來得差。

四、臨床分期與病理分期

臨床T期可依肛門指診及影像學檢查來評估腫瘤是否於攝護腺包膜內 (T1, T2) 或包膜外 (T3,T4)

分期目標：(1) 評估預後、(2) 引導治療方向、(3) 不同治療方式的比較基準。

TNM staging system 為採用 AJCC 2010 出版的第七版。

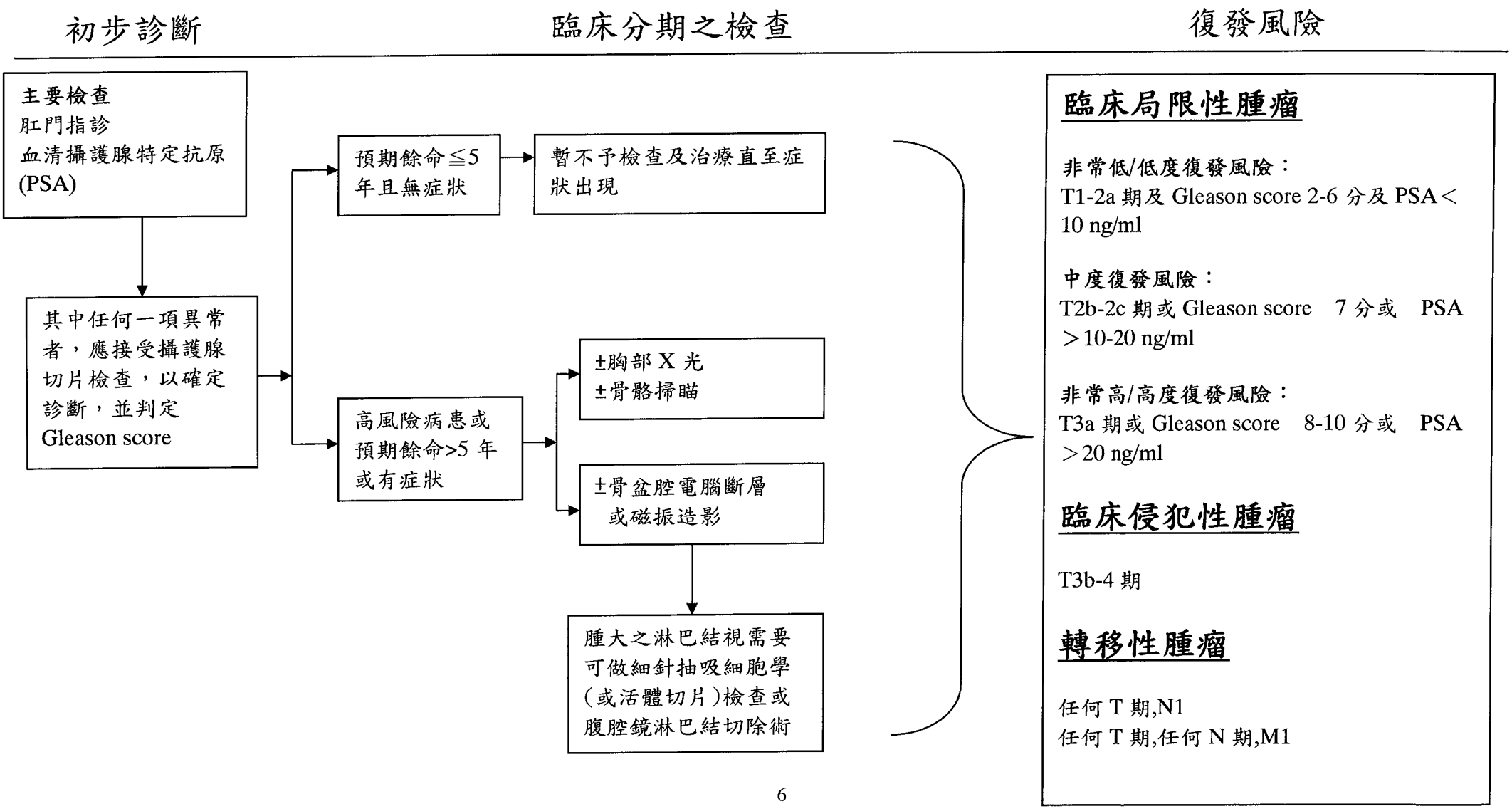
	PRIMARY TUMOR (T)		
TX	Primary tumor cannot be assessed		
T0	No evidence of primary tumor		
T1	Clinically inapparent tumor neither palpable nor visible by imaging		
T1a	Tumor incidental histologic finding in 5% or less of tissue resected		
T1b	Tumor incidental histologic finding in more than 5% of tissue resected		
T1c	Tumor identified by needle biopsy (e.g., because of elevated PSA)		
T2	Tumor confined within prostate*	**pT2**	Organ confined
T2a	Tumor involves one-half of one lobe or less	**pT2a**	Unilateral, one-half of one side or less
T2b	Tumor involves more than one-half of one lobe but not both lobes	**pT2b**	Unilateral, involving more than one-half of side but not both sides
T2c	Tumor involves both lobes	**pT2c**	Bilateral disease
T3	Tumor extends through the prostate capsule**	**pT3**	Extraprostatic extension
T3a	Extracapsular extension (unilateral or bilateral)	**pT3a**	Extraprostatic extension or microscopic invasion of bladder neck***
T3b	Tumor invades seminal vesicle(s)	**pT3b**	Seminal vesicle invasion
T4	Tumor is fixed or invades adjacent structures other than seminal vesicles: such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall	**pT4**	Invasion of rectum, levator muscles and/or pelvic wall

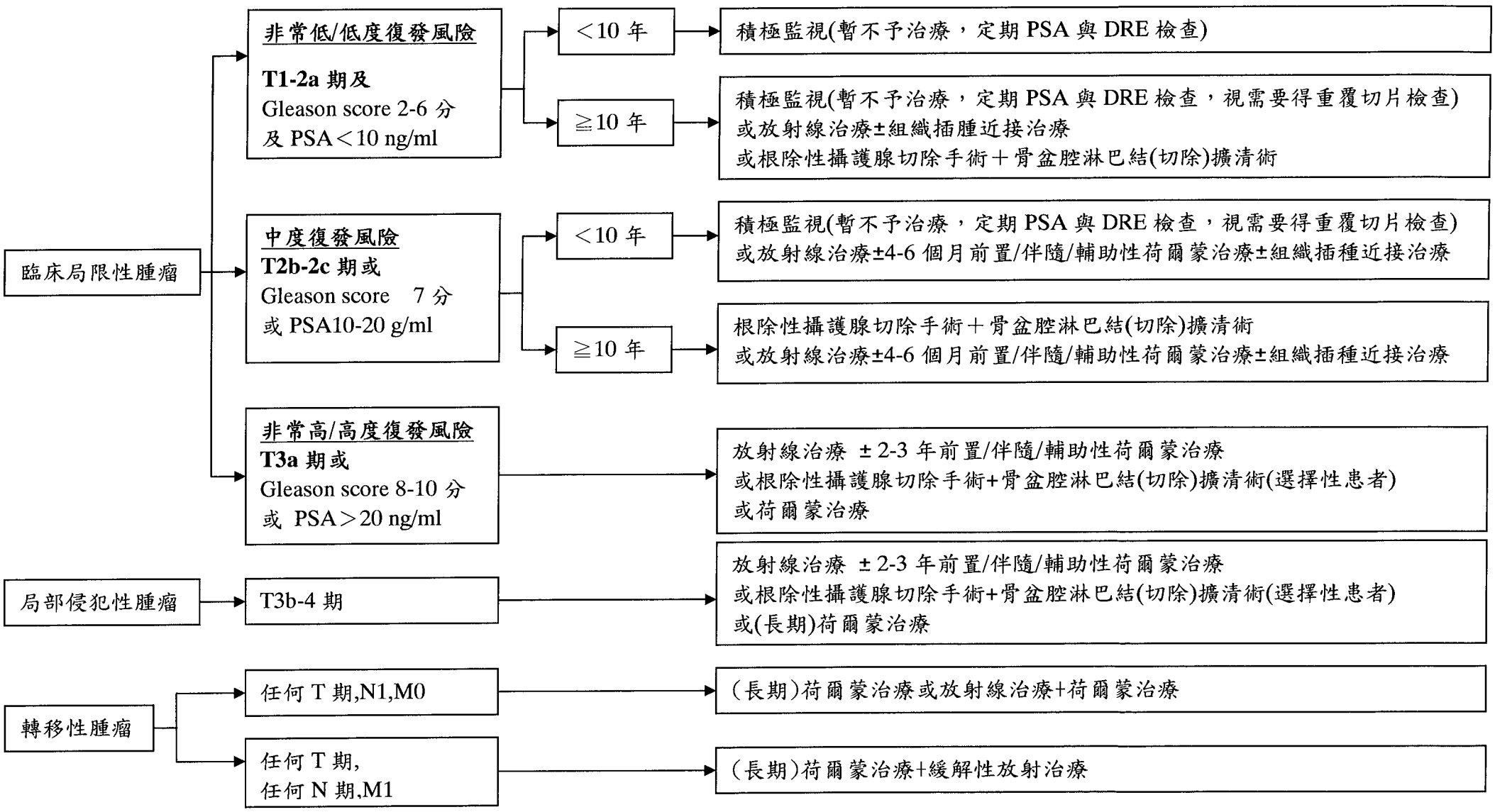
REGIONAL LYMPH NODES (N)			
NX	Regional lymph nodes were not assessed	**pNX**	Regional nodes not sampled
N0	No regional lymph node metastasis	**pN0**	No positive regional nodes
N1	Metastasis in regional lymph node(s)	**pN1**	Metastases in regional node(s)

	DISTANT METASTASIS (M)
M0	No distant metastasis
M1	Distant metastasis
M1a	Non-regional lymph node(s)
M1b	Bone(s)
M1c	Other site(s) with or without bone disease

Anatomic Stage · Prognostic Groups					
☐CLINICAL ☐PATHOLOGIC					
Group	**T**	**N**	**M**	**PSA**	**Gleason**
I	T1a-c	N0	M0	PSA < 10	Gleason ≦ 6
	T2a	N0	M0	PSA < 10	Gleason ≦ 6
	T1-2a	N0	M0	PSA X	Gleason X
IIA	T1a-c	N0	M0	PSA < 20	Gleason 7
	T1a-c	N0	M0	PSA ≧ 10 < 20	Gleason ≦ 6
	T2a	N0	M0	PSA < 20	Gleason ≦ 7
	T2b	N0	M0	PSA < 20	Gleason ≦ 7
	T2b	N0	M0	PSA X	Gleason X
IIB	T2c	N0	M0	Any PSA	Any Gleason
	T1-2	N0	M0	PSA ≧ 20	Any Gleason
	T1-2	N0	M0	Any PSA	Gleason ≧ 8
III	T3a-b	N0	M0	Any PSA	Any Gleason
IV	T4	N0	M0	Any PSA	Any Gleason
	Any T	N1	M0	Any PSA	Any Gleason
	Any T	Any N	M1	Any PSA	Any Gleason

五、攝護腺癌臨床指引

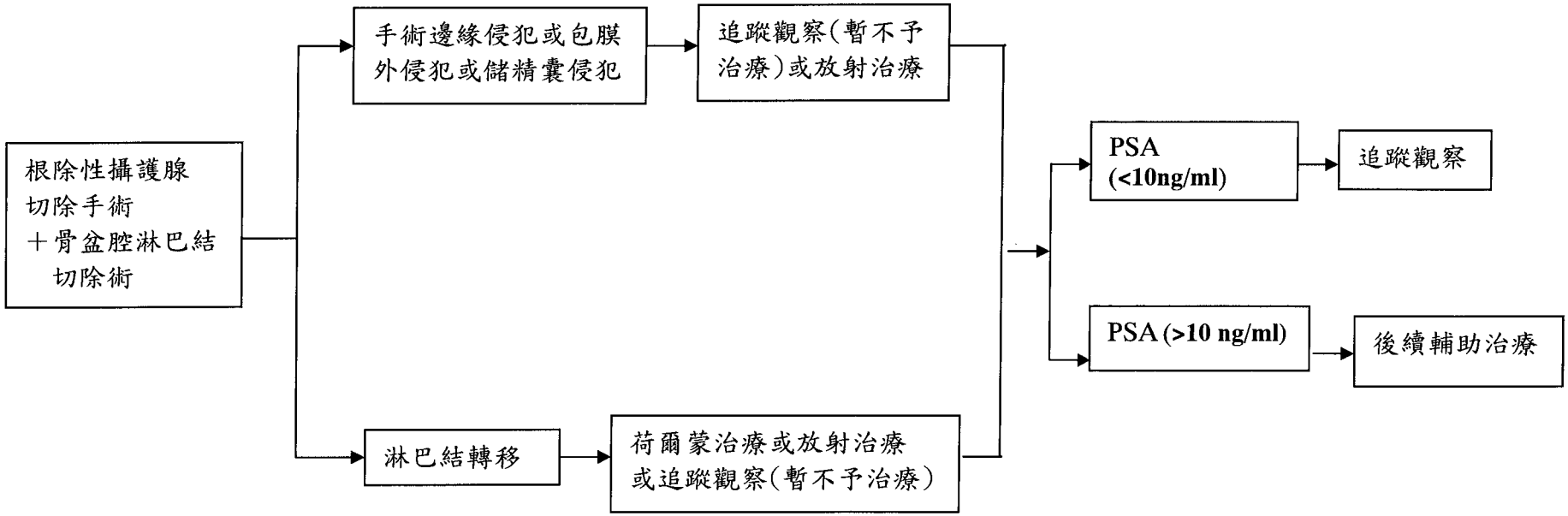

初步診斷
臨床分期之檢查
復發風險
主要檢查
肛門指診
血清攝護腺特定抗原(PSA)
其中任何一項異常者，應接受攝護腺切片檢查，以確定診斷，並判定Gleason score
預期餘命≦5年且無症狀
暫不予檢查及治療直至症狀出現
高風險病患或預期餘命>5年或有症狀
±胸部X光
±骨骼掃瞄
±骨盆腔電腦斷層或磁振造影
腫大之淋巴結視需要可做細針抽吸細胞學(或活體切片)檢查或腹腔鏡淋巴結切除術
臨床局限性腫瘤
非常低/低度復發風險：
T1-2a 期及 Gleason score 2-6 分及 PSA＜10 ng/ml
中度復發風險：
T2b-2c 期或 Gleason score 7 分或 PSA＞10-20 ng/ml
非常高/高度復發風險：
T3a 期或 Gleason score 8-10 分或 PSA＞20 ng/ml
臨床侵犯性腫瘤
T3b-4 期
轉移性腫瘤
任何 T 期,N1
任何 T 期,任何 N 期,M1



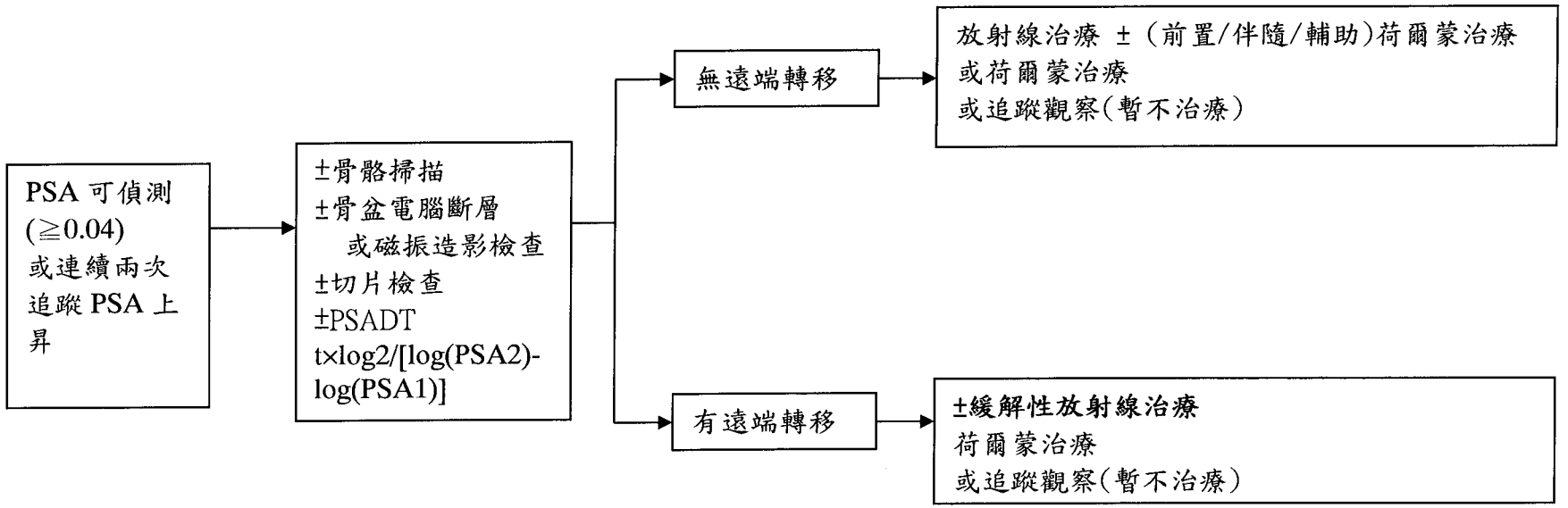
※2012 年預期餘命依據內政部的男性簡易生命表為 76.4 歲

六、根除性攝護腺切除手術治療後之輔助治療

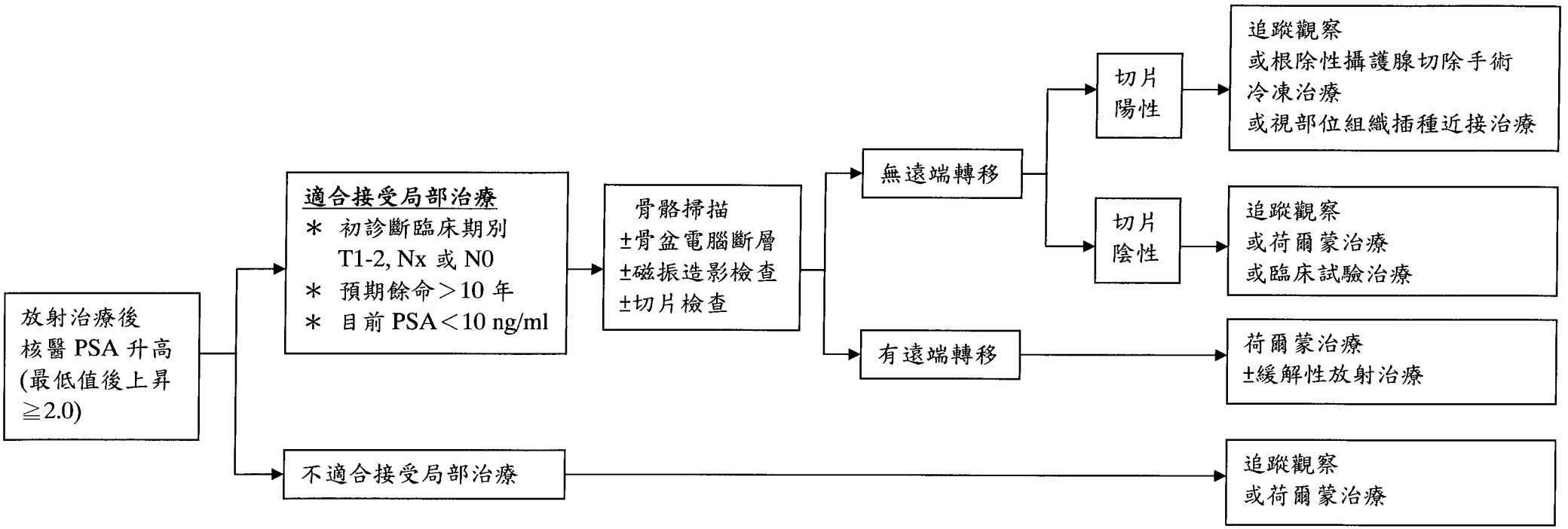
初步治療　　病理狀況　　輔助治療



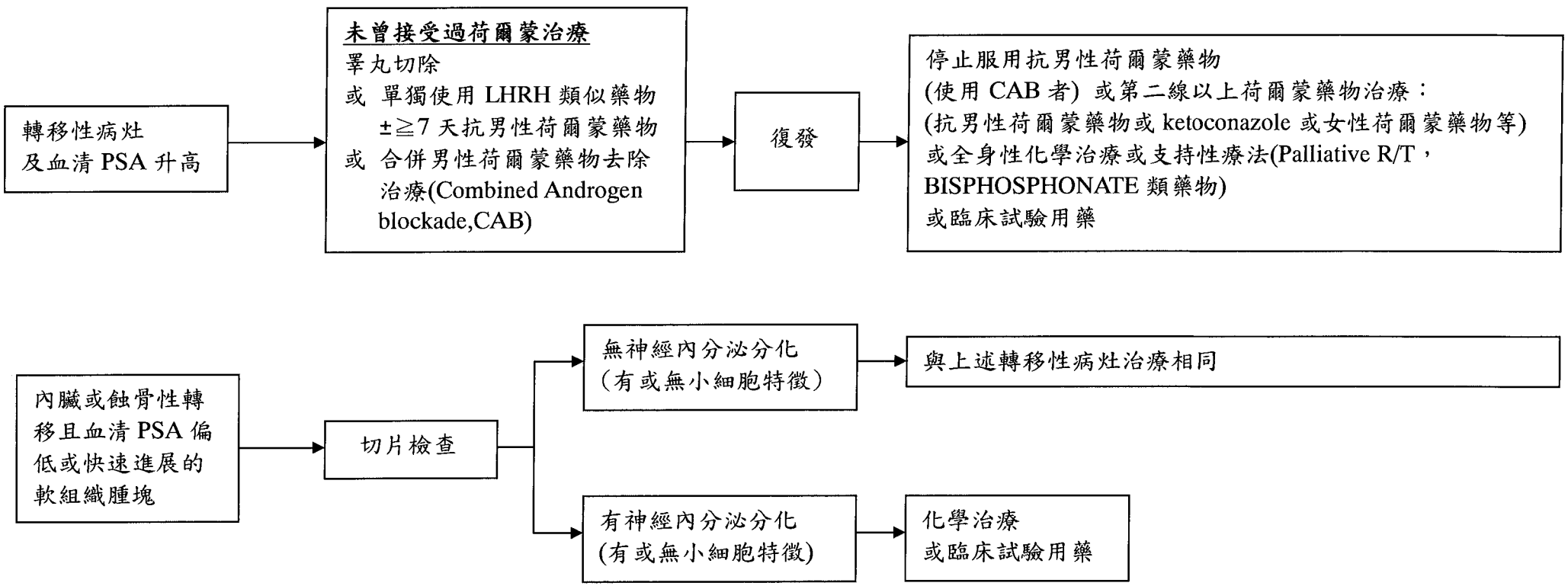
七、根除性攝護腺切除手術治療後復發之救援處置



八、放射治療後復發之救援處置



擴散性疾病 全身性治療 全身性救援治療



九、放射治療及化學治療處置

Principle of Sandwich

Neoadjuvant androgen ablation + radiotherapy*+adjuvant androgen ablation

Principles of radiation

Selective adjuvant radiotherapy * :
If margin positive /residual or LN positive，dose of 50~60Gy depended on the tumor position and the patient condition

Definitive radiotherapy : (1) 70~81 Gy , IMRT/IGRT preferred.
(2) high-dose-rate (HDR) interstitial brachytherapy 15-20 Gy plus 45~55 Gy IMRT/IGRT could be considered for T1a~T2b

Radiotherapy **:
For primary recurrence : 65~76 Gy , IMRT/IGRT preferred.
For distant metastasis : 20~40 Gy.

Radiotherapy# :
palliative radiotherapy:20~40 Gy

Principles of chemotherapy

Docetaxel + Prednisolone

Docetaxel	75 mg/m2	d1
Prednisolone	10mg/day	
Q3w		

Berthold DR et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer: updated survival in the TAX 327 study. J Clin Oncol 2008; 26:242 (link to the article).

Docetaxel + Prednisolone

Docetaxel	3 mg/m2	d1,8,15,22,29
Prednisolone	10mg/day	
Q6w		

Tannock IF et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Eng J Med 2004; 351:1502.

Mitoxantrone + Prednisone

Mitoxantrone	12 mg/m2	d1
Prednisolone	10mg/day	
Q3w		

Tannock IF et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Eng J Med 2004; 351:1502.

十、另類療法

Cryosurgical ablation of the prostate(CSAP) and high-intensity focussed ultrasound(HIFU) have emerged as alternative therapeutic options in patients with clinically localised PCa who are not suitable for RP.
The following factors might be indications: low-or intermediate-risk PCa and prostate size＜40ml at the time of therapy.

十一、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）。

十二、參考文獻

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