

2éme Forum des cancers urologiques Alger juin 2022

Symposium IPSEN

DE PROSTATE LOCALISÉ À HAUT RISQUE
RADIOTHÉRAPIE VS PROSTATECTOMIE

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Introduction

Le cancer de prostate localisé à haut risque représente 15 à 20 % des cancers localisés

C'est une entité grave et nécessite un traitement adapté car risque de récurrence et progression

C'est un groupe très hétérogène

Le traitement de référence demeure la hormono-radiothérapie selon les guidelines

La prostatectomie a une place importante dans une approche thérapeutique multimodale

La prostatectomie seule permet le contrôle de la maladie et une survie spécifique à 10 ans dans 95 % des cas pour des malades HR sélectionnés ,

Il n'existe pas d'étude randomisée qui compare les deux attitudes de traitement mais les résultats des études rétrospectives et par méta analyses sont comparables voire un léger avantage à la PR ,

Intérêt majeur accordé pour les RCP afin de personnaliser le traitement de chaque patient selon les caractéristiques de la maladie et du malade

Recommandations de EAU HR CaP localisé

Recommendations	Strength rating
Radical prostatectomy (RP)	
Offer RP to selected patients with high-risk localised PCa as part of potential multi-modal therapy.	Strong
Extended pelvic lymph node dissection (ePLND)	
Perform an ePLND in high-risk PCa.	Strong
Do not perform a frozen section of nodes during RP to decide whether to proceed with, or abandon, the procedure (see Section 6.2.4.1).	Strong
Radiotherapeutic treatment	
In patients with high-risk localised disease, use intensity-modulated radiation therapy (IMRT) /volumetric modulated arc therapy (VMAT) plus image-guided radiation therapy (IGRT) with 76–78 Gy in combination with long-term androgen deprivation therapy (ADT) (2 to 3 years).	Strong
In patients with high-risk localised disease and good urinary function, use IMRT/VMAT plus IGRT with brachytherapy boost (either high-dose rate or low-dose rate), in combination with long-term ADT (2 to 3 years).	Weak
Therapeutic options outside surgery or radiotherapy	
Do not offer either whole gland or focal therapy to patients with high-risk localised disease.	Strong
Only offer ADT monotherapy to those patients unwilling or unable to receive any form of local treatment if they have a prostate-specific antigen (PSA)-doubling time < 12 months, and either a PSA > 50 ng/mL or a poorly-differentiated tumour.	Strong

Guidelines AUA 2022;HR prostate localized cancer

For patients with unfavorable intermediate- or high-risk clinically localized prostate cancer, definitive local therapy is advised. The optimal treatment for these patients remains a topic of active study, and prior published metaanalyses have reported relatively disparate findings as to comparative survival following each of these treatment approaches. The Panel supports **offering patients with unfavorable intermediate- and high-risk disease either radical prostatectomy or radiation with ADT** (see Principles of Surgery and Principles of Radiation). For patients with sufficiently high-risk disease (clinically node positive, or with 2 of 3 of the following criteria: clinical stage T3 or T4, PSA \geq 40 ng/mL, or \geq Gleason 8), treatment with radiation and ADT can include two years of concurrent abiraterone acetate plus prednisone as well.

Classification d'Amico

CLASSIFICATION DE D'AMICO

Afin de mieux guider la prise en charge, D'Amico a proposé de **classer les cancers de prostate localisés** en trois groupes **en fonction de leur risque de progression** :

	Faible risque	risque intermediaire	haut risque
Stade clinique	≤T2a	T2b	T2c-T3a
Score de Gleason	≤6	7	>7
PSA sérique(ng/ml)	<10	>10 et <20	>20

Stratification of high-risk prostate cancer into prognostic categories: a European multi-institutional study

Steven Joniau 1, Alberto Briganti 2, Paolo Gontero 3, Giorgio Gandaglia 2, Lorenzo Tosco 4, Steffen Fieuws

Background: High-risk prostate cancer (PCa) is an extremely heterogeneous disease. A clear definition of prognostic subgroups is mandatory.

Objective: To develop a pretreatment prognostic model for PCa-specific survival (PCSS) in high-risk PCa based on combinations of unfavorable risk factors.

Design, setting, and participants: We conducted a retrospective multicenter cohort study including 1360 consecutive patients with high-risk PCa treated at eight European high-volume centers.

Intervention: Retropubic radical prostatectomy with pelvic lymphadenectomy.

Outcome measurements and statistical analysis: Two Cox multivariable regression models were constructed to predict PCSS as a function of dichotomization of clinical stage (< cT3 vs cT3-4), Gleason score (GS) (2-7 vs 8-10), and prostate-specific antigen (PSA; ≤ 20 ng/ml vs > 20 ng/ml). The first "extended" model includes all seven possible combinations; the second "simplified" model includes three subgroups: a good prognosis subgroup (one single high-risk factor); an intermediate prognosis subgroup (PSA > 20 ng/ml and stage cT3-4); and a poor prognosis subgroup (GS 8-10 in combination with at least one other high-risk factor). The predictive accuracy of the models was summarized and compared. Survival estimates and clinical and pathologic outcomes were compared between the three subgroups.

Results and limitations: The simplified model yielded an R^2 of 33% with a 5-yr area under the curve (AUC) of 0.70 with no significant loss of predictive accuracy compared with the extended model (R^2 : 34%; AUC: 0.71). The 5- and 10-yr PCSS rates were 98.7% and 95.4%, 96.5% and 88.3%, 88.8% and 79.7%, for the good, intermediate, and poor prognosis subgroups, respectively ($p = 0.0003$). Overall survival, clinical progression-free survival, and histopathologic outcomes significantly worsened in a stepwise fashion from the good to the poor prognosis subgroups. Limitations of the study are the retrospective design and the long study period.

Conclusions: This study presents an intuitive and easy-to-use stratification of high-risk PCa into three prognostic subgroups. The model is useful for counseling and decision making in the pretreatment setting.

Résultats de cette étude de la stratification du haut risque

Cette étude multicentriques (8 centres européens menée de 1987 à 2009

Nombre de malades de 1632 de CaP de HR qui ont subi une PR ,

Groupe de bon pronostic survie spécifique à 10 ans = 95,44%

et chirurgie seule a suffit groupe de mauvais pronostic ;traitement multimodal RT =30,5%
ADT +74,2 %

survie spécifique à 10 ans =79,7 %

Classification du HR CaP localisé

Le haut risque est un groupe très hétérogène

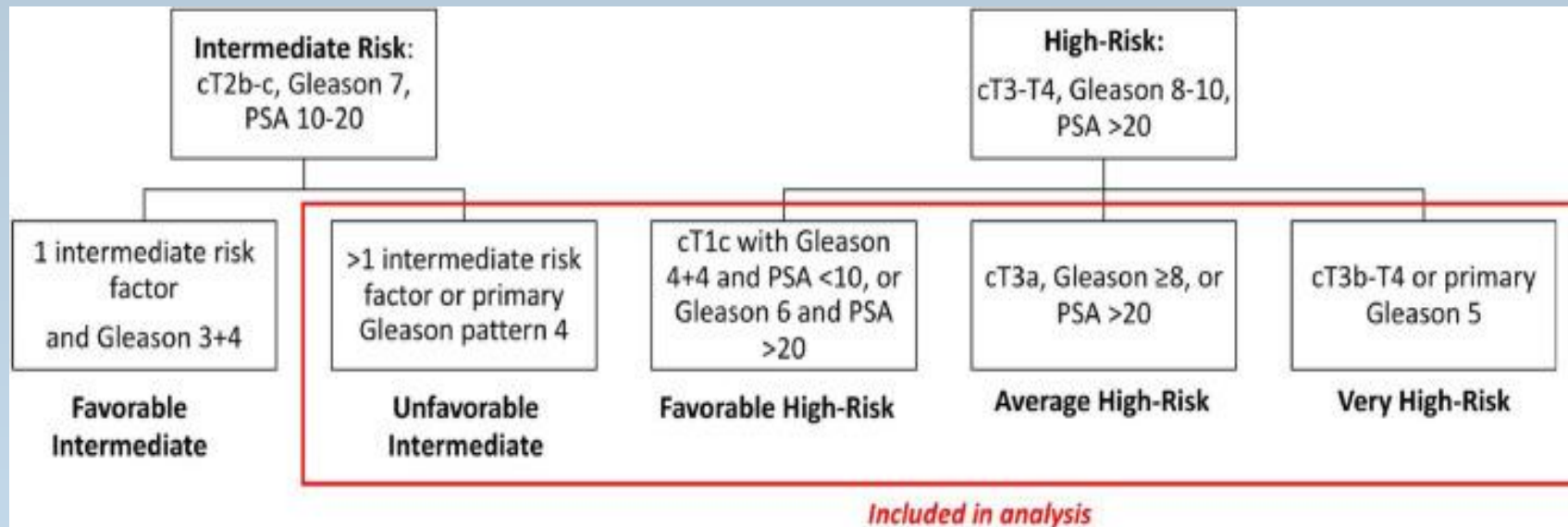
La survie spécifique varie de 50 à 80 % selon la définition du haut risque ,d'où la classification amélioré de D'Amico

Exemple un HR avec un seul facteur de risque a une survie qui dépasse 90% et une PR seul suffit et c'est un HR de bon pronostic,

D'où la classification du HR de d'Amico amélioré

Bon pronostic	Un facteur de risque
Pronostic intermédiaire	T3 –T4 +SG 8-10
Mauvais pronostic	03 facteurs de risques

Classification pronostic de D'Amico amélioré



Etudes comparatives et méta-analyses

Comparative effectiveness of radical prostatectomy and radiotherapy in prostate cancer: observational study of mortality outcomes

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Setting Sweden, 1996-2010.

Participants 34 515 men primarily treated for prostate cancer with surgery (n=21 533) or radiotherapy (n=12 982). Patients were categorized by risk group (low, intermediate, high, and metastatic), age, and Charlson comorbidity score.

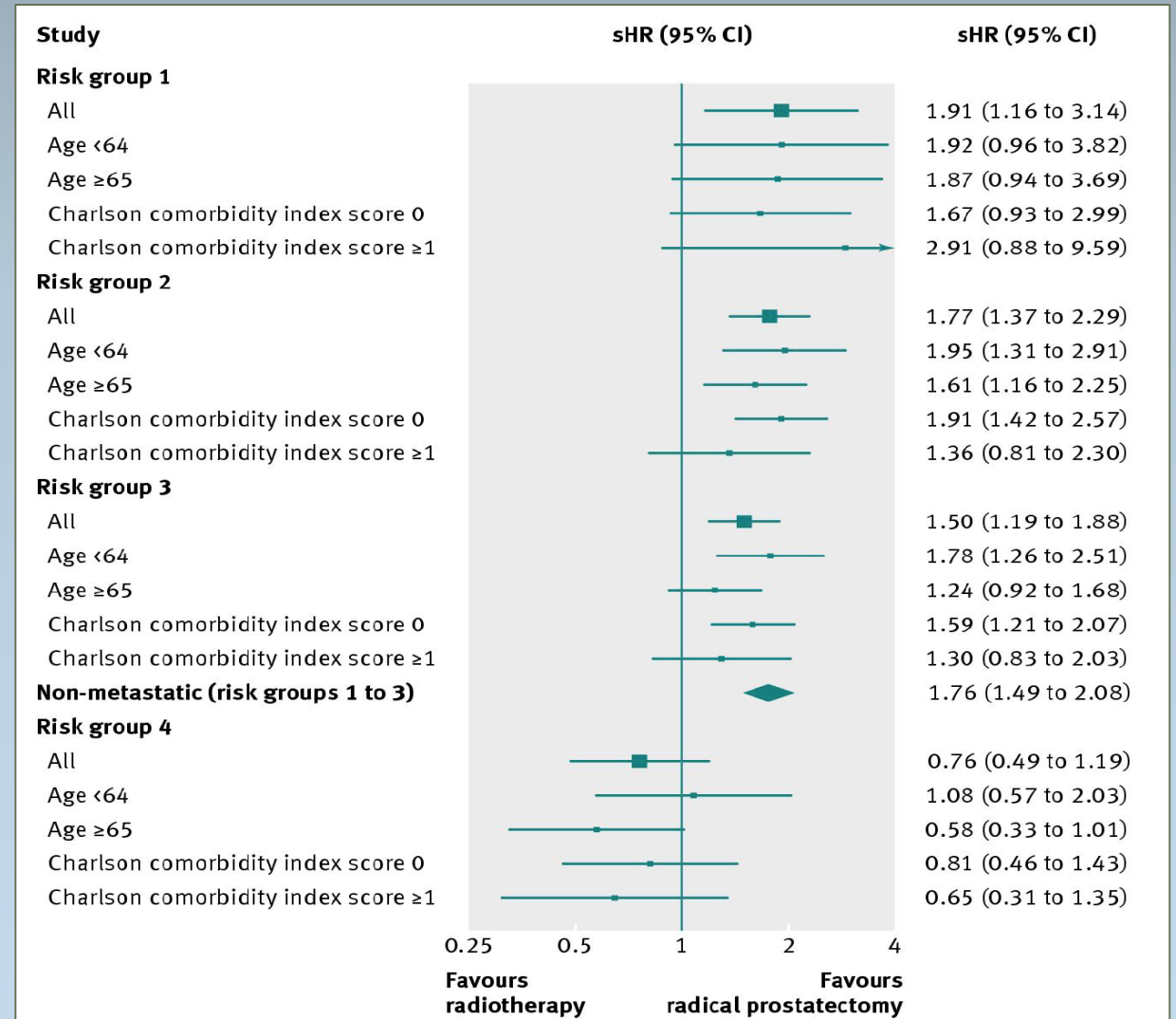
Main outcome measures Cumulative incidence of mortality from prostate cancer and other causes. Competing risks regression hazard ratios for radiotherapy versus surgery were computed without adjustment and after propensity score and traditional (multivariable) adjustments, as well as after propensity score matching. Several sensitivity analyses were performed.

Results Prostate cancer mortality became a larger proportion of overall mortality as risk group increased for both the surgery and the radiotherapy cohorts. Among patients with non-metastatic prostate cancer the adjusted subdistribution hazard ratio for prostate cancer mortality favored surgery (1.76, 95% confidence interval 1.49 to 2.08, for radiotherapy v prostatectomy), whereas there was no discernible difference in treatment effect among men with metastatic disease. Subgroup analyses indicated more clear benefits of surgery among younger and fitter men with intermediate and high risk disease. Sensitivity analyses confirmed the main findings.

Conclusions This large observational study with follow-up to 15 years suggests that for most men with non-metastatic prostate cancer, surgery leads to better survival than does radiotherapy. Younger men and those with less comorbidity who have intermediate or high risk localised prostate cancer might have a greater benefit from surgery.

CHIIRURGIE VERSUS RADIOTHERAPIE

Etude observationnelle sur 30 000 PATIENTS



Long-term survival after radical prostatectomy versus external-beam radiotherapy for patients with high-risk prostate cancer

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Background: The long-term survival of patients with high-risk prostate cancer was compared after radical prostatectomy (RRP) and after external beam radiation therapy (EBRT) with or without adjuvant androgen-deprivation therapy (ADT). **Methods:** In total, 1238 patients underwent RRP, and 609 patients received with EBRT (344 received EBRT plus ADT, and 265 received EBRT alone) between 1988 and 2004 who had a pretreatment prostate-specific antigen (PSA) level ≥ 20 ng/mL, a biopsy Gleason score between 8 and 10, or clinical tumor classification $\geq T3$. The median follow-up was 10.2 years, 6.0 years, and 7.2 years after RRP, EBRT plus ADT, and EBRT alone, respectively. The impact of treatment modality on systemic progression, cancer-specific survival, and overall survival was evaluated using multivariate Cox proportional hazard regression analysis and a competing risk-regression model.

Results: The 10-year cancer-specific survival rate was 92%, 92%, and 88% after RRP, EBRT plus ADT, and EBRT alone, respectively ($P = .06$). After adjustment for case mix, no significant differences in the risks of systemic progression (hazard ratio [HR], 0.78; 95% confidence interval [CI], 0.51-1.18; $P = .23$) or prostate cancer death (HR, 1.14; 95% CI, 0.68-1.91; $P = .61$) were observed between patients who received EBRT plus ADT and patients who underwent RRP. The risk of all-cause mortality, however, was greater after EBRT plus ADT than after RRP (HR, 1.60; 95% CI, 1.25-2.05; $P = .0002$).

Comparer la survie globale et survie spécifique comparant la PR vs RT sur 10 ans entre 1988 à 2004 incluant 1238 patients

Résultats survie globale à 10 ans : RP 77 % vs RT 62 %

survie spécifique : RP = RT

Characterizing Surgical and Radiotherapy Outcomes in Non-metastatic High-Risk Prostate Cancer: A Systematic Review and Meta-Analysis

Abstract

Background Identifying the optimal management of high-risk non-metastatic prostate cancer (PCa) is an important public health concern, given the large burden of this disease. We performed a meta-analysis of studies comparing PCa-specific mortality (CSM) among men diagnosed with high-risk non-metastatic PCa who were treated with primary radiotherapy (RT) and radical prostatectomy (RP). Methods Medline and Embase were searched for articles between January 1, 2005, and February 11, 2020. After title and abstract screening, two authors independently reviewed full-text articles for inclusion. Data were abstracted, and a modified version of the Newcastle-Ottawa Scale, involving a comprehensive list of confounding variables, was used to assess the risk of bias. Results Fifteen studies involving 131,392 patients were included. No difference in adjusted CSM in RT relative to RP was shown (hazard ratio, 1.02 [95% confidence interval: 0.84, 1.25]). Increased CSM was found in a subgroup analysis comparing external beam radiation therapy (EBRT) with RP (1.35 [1.10, 1.68]), whereas EBRT combined with brachytherapy (BT) versus RP showed lower CSM (0.68 [0.48, 0.95]). All studies demonstrated a high risk of bias as none fully adjusted for all confounding variables. Conclusion We found no difference in CSM between men diagnosed with non-metastatic high-risk PCa and treated with RP or RT; however, this is likely explained by increased CSM in men treated with EBRT and decreased CSM in men treated with EBRT + BT studies relative to RP. High risk of bias in all studies identifies the need for better data collection and confounding control in the PCa research.

Méta analyses qui compare la mortalité spécifique par CaP entre PR vs RT sur 15 ans de 2005 à 2020 sur 131392 patients

Aucune différence significative RP = RT

Metastasis after radical prostatectomy or external beam radiotherapy for patients with clinically localized prostate cancer: a comparison of clinical cohorts adjusted for case mix

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PMID: 20159826 PMCID: PMC3731893 DOI: 10.1200/JCO.2009.22.2265

Purpose: We assessed the effect of radical prostatectomy (RP) and external beam radiotherapy (EBRT) on distant metastases (DM) rates in patients with localized prostate cancer treated with RP or EBRT at a single specialized cancer center.

Patients and methods: Patients with clinical stages T1c-T3b prostate cancer were treated with intensity-modulated EBRT (> or = 81 Gy) or RP. Both cohorts included patients treated with salvage radiotherapy or androgen-deprivation therapy for biochemical failure. Salvage therapy for patients with RP was delivered a median of 13 months after biochemical failure compared with 69 months for EBRT patients. DM was compared controlling for patient age, clinical stage, serum prostate-specific antigen level, biopsy Gleason score, and year of treatment.

Conclusion: Metastatic progression is infrequent in men with low-risk prostate cancer treated with either RP or EBRT. RP patients with higher-risk disease treated had a lower risk of metastatic progression and prostate cancer-specific death than EBRT patients. These results may be confounded by differences in the use and timing of salvage therapy.

Etudes MSK : 2380 patients

Critères d'évaluation : la survenue de métastases et récives biochimiques

Diminution de la mortalité spécifique de 68% en faveur PR vs RT

Radical prostatectomy or radiotherapy in high-risk prostate cancer: a systematic review and metaanalysis

Fausto Petrelli

Background: Radical prostatectomy (RP) is one of the treatment options for localized, high-risk prostate cancer (PC), but it has never been compared with external beam radiotherapy (RT), which is an alternative approach, in a large randomized trial. To compare the outcomes of patients treated with surgery versus RT, we performed a metaanalysis of available studies on this topic. **Materials and methods:** We performed a search of MEDLINE, EMBASE, Web of Science, SCOPUS, and The Cochrane Central Register of Controlled Trials (CENTRAL) for randomized or observational studies that investigated overall survival (OS) and PC-specific mortality (PCSM) risks in relation to use of surgery or RT in patients with high-risk PC. Fixed- and random-effect models were fitted to estimate the summary odds ratio (OR). Between-study heterogeneity was tested using χ^2 statistics and measured using the I^2 statistic. Publication bias was evaluated using a funnel plot and Egger regression asymmetry test. **Results:** Seventeen studies were included (1 randomized and 16 retrospective). RP was associated with improved OS (OR, 0.51; 95% confidence interval [CI], 0.38-0.68; $P < .00001$), PCSM (OR, 0.56; 95% CI, 0.37-0.85; $P = .007$), and non-PCSM (OR, 0.53; 95% CI, 0.35-0.8; $P = .002$) compared with RT. Biochemical relapse-free survival rates were similar to those of RT.

Conclusion: Overall and cancer-specific mortality rates appear to be better with RP compared with RT in localized, high-risk PC. Surgery is also associated with a 50% decreased risk of non-PCSM compared with RT.

Métatanalyse de 17 series selectionnées / 1092 dans la literature Bénéfice RP vs RT

Meilleure survie globale et spécifique : RP 95 % vs 85 % RT.

Récidive biochimique était comparable au deux groupes

SPCG-15: a prospective randomized study comparing primary radical prostatectomy and primary radiotherapy plus androgen deprivation therapy for locally advanced prostate cancer

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Objective: To describe study design and procedures for a prospective randomized trial investigating whether radical prostatectomy (RP) ± radiation improves cause-specific survival in comparison with primary radiation treatment (RT) and androgen deprivation treatment (ADT) in patients with locally advanced prostate cancer (LAPC).

Materials and methods: SPCG-15 is a prospective, multi-centre, open randomized phase III trial. Patients are randomized to either standard (RT + ADT) or experimental (RP with extended pelvic lymph-node dissection and with addition of adjuvant or salvage RT and/or ADT if deemed necessary) treatment. Each centre follows guidelines regarding the timing and dosing of postoperative RT and adjuvant treatment such as ADT. The primary endpoint is cause-specific survival. Secondary endpoints include metastasis-free and overall survival, quality-of-life, functional outcomes and health-services requirements. Each subject will be followed up for a minimum of 10 years.

Results: Twenty-three centres in Denmark, Finland, Norway and Sweden, well established in performing RP and RT for prostate cancer participated. Each country's sites were coordinated by national coordinating investigators and sub-investigators for urology and oncology. Almost 400 men have been randomized of the stipulated 1200, with an increasing rate of accrual.

Conclusions: The SPCG-15 trial aims to compare the two curatively intended techniques supplying new knowledge to support future decisions in treatment strategies for patients with LAPC. The Scandinavian healthcare context is well suited for performing multi-centre long-term prospective randomized clinical trials. Similar care protocols and a history of entirely tax-funded healthcare facilitate joint trials.

Seule étude randomisée en cours prospective comparant la RT+ADT à la RP+ PLND sur 10 ans

Que reproche t-on à la PR?

La prostatectomie totale dans le CaP localisé à haut risque ,

03 risques majeurs: risque de marges chirurgicales positives

risques d'incontinence urinaire

risque de N+

PR large sans préservation de bandelettes VN +maitrise technique et exérèse en zones saines

Rigueur technique pour préserver l'appareil sphinctérien avec apport de la coelio-chirurgie et PR robo-assistée

Curage ganglionnaire est extensif

Conclusions

La PR occupe une place prépondérante dans le TRT du HR CaP localisé

Avec un excellent contrôle local, une survie spécifique + de 90 % en 10 ans et qualité de vie correcte,

approche multi modal ,intérêt des RCP ++++

PR seule malades sélectionnés

La chirurgie et la hormono-radiothérapie sont complémentaires ;et l'indication est personnalisée en fonction des caractéristiques de la maladies , les caractéristiques du malade et son désir