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Original article

Results of a cohort of 200 hormone-naïve consecutive patients with prostate cancer treated with iodine 125 permanent interstitial brachytherapy by the same multidisciplinary team

Résultats d'une série continue de 200 patients atteints d'un cancer localisé de la prostate traité par curiethérapie à l'iode 125

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ABSTRACT

Purpose. – To report survival and morbidity of a cohort of 200 hormone-naïve consecutive patients with localized prostate cancer, treated by low-dose rate brachytherapy within the frame of multidisciplinary approach.
Patients and methods. – Between 2001 and 2011, 200 patients were treated by the same team with 125 iodine seeds: 167 low-risk and 33 intermediate risk according to the d'Amico classification; eligible patients had clinical stage T1/T2a-b, Gleason score 3+3 or 3+4, baseline prostate-specific antigen level below 15 ng/mL, prostate volume less than 60 cm^3. The median number of random biopsies was 12 (range 6–32) and the breakdown of positive cores was as follows: 1 (29%), 2 (35%), 3 or more (36%). Acute morbidity was assessed according to the Common Terminology Criteria for Adverse Events and late toxicity according to the EORTC/RTOG scale. Data were prospectively collected.
Results. – The median follow-up was 69 months (range 16 to 135). The 5- and 10-year biochemical relapse free survivals were 95.6% (95% confidence interval [CI]: 91–98) and 89.7% (95% CI: 79.4–95.0). The 5-year and 10-year overall survival were respectively 96.4% (95% CI: 92–98.4) and 89.7% (95% CI: 80.8–94.6%) and the 10-year disease specific survival, 99.1% (95% CI: 93.0–99.9). The 5- and 10-year grade 3 acute toxicity cumulative rate were respectively 3.3% (95% CI: 1.4–6.6) and 4% (95% CI: 1.4–6.6) and the 5- and 10-year grades 3 cumulative late toxicity 2.5% (95% CI: 2.0–5.9) and 4% (95% CI: 2.0–5.9).
Conclusion. – Brachytherapy managed within the frame of a multidisciplinary approach – from diagnosis to evaluation – may offer optimized results with a reduced late toxicity rate, while remaining opened to dosimetry and technical improvements.

Mots clés :
Cancer de la prostate localisé
Curiethérapie
Iode 125

RÉSUMÉ

Objectif. – Rapporter la survie à long terme et la toxicité d'une série continue de 200 patients atteints d'un cancer localisé de la prostate après curiethérapie à l'iode 125.
Patients et méthodes. – Entre juillet 2001 et janvier 2011, 200 patients atteints pour 167 d'un cancer localisé de la prostate à faible risque et 33 à risque intermédiaire selon la classification de d'Amico ont eu une curiethérapie par iode 125, répondant aux critères d'inclusion suivant : stade clinique T1/T2a-b, score de Gleason 3+3 ou 3+4, concentration sérique d'antigène spécifique de la prostate inférieure à 15 ng/mL, volume prostatique inférieur à 60 cm^3. Le nombre médian de biopsies randomisées était de 12

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(6–32) et le pourcentage de biopsies positives se répartissait comme suit : 29 % (une biopsie), 35 % (deux biopsies) et 36 % (3 biopsies ou plus). La toxicité aiguë a été évaluée avec l'échelle Common Terminology Criteria for Adverse Events et la toxicité tardive avec l'échelle de l'European Organisation for Research and Treatment of Cancer (EORTC) et du Radiation Therapy Oncology Group (RTOG).
Résultats. – Le suivi médian était de 69 mois (16 à 135). La probabilité de survie sans récidive biochimique à 5 et 10 ans était respectivement de 95,6 % (intervalle de confiance à 95 % [IC 95 %] : 91 à 98) et 89,7 % (IC 95 % : 79,4 à 95,0) et celle survie globale à 5 ans et 10 ans de 96,4 % (IC 95 % : 92 à 98,4) et 89,7 % (IC 95 % : 80,8 à 94,6 %). L'incidence de toxicité aiguë de grade 3 était : dysurie : 1,5 % ; pollakiurie : 1,6 % ; incontinence : 0,5 % ; rétention urinaire : 1,6 % ; 1,5 % des patients ont souffert d'une toxicité urinaire tardive de grade 3 et 1 % une toxicité digestive tardive de grade 3.
Conclusion. – La curiethérapie gérée de façon multidisciplinaire du diagnostic à l'évaluation, offre de bons résultats avec un risque de toxicité réduit, laissant la porte ouverte à une optimisation dosimétrique et technique concertée.

1. Introduction

Prostate cancer is the most common cancer amongst men in Europe [1]. Thanks to early detection modalities, the diagnosis of localized prostate cancer is more frequent; a large European randomized trial has shown a 20% reduction in prostate cancer mortality by mass screening with a 9-year follow-up [2]. The multidisciplinary approach allows a tailored treatment policy for localized prostate cancer – radical prostatectomy, intensity-modulated radiotherapy (IMRT) or brachytherapy – based on age, comorbidity, prognostic factors, prostate volume, international prostate score symptom (IPSS), WHO performance status, sexual health and quality of life [3–5]. The American Brachytherapy Society, as well as the European Society for Radiotherapy and Oncology (ESTRO), the European Association of Urology (EAU) and the European Organisation for Research and Treatment of Cancer (EORTC) recommend brachytherapy for patients with stage T1–T2a, Gleason score 6 or less, and baseline prostate-specific antigen (PSA) less than 10 ng/mL [6,7]. We report herein the results and the safety of a continuous cohort of 200 patients with low and intermediate risk localized prostate cancer, treated with iodine 125 permanent interstitial real-time brachytherapy by the same multidisciplinary team, with a particular emphasis regarding the results and the potential improvement of the technique.

2. Patients and methods

2.1. Inclusion criteria

From July 2001 to January 2011, 200 consecutive patients with biopsy proven adenocarcinoma of the prostate – 167 low-risk (83.5%) and 33 intermediate risk (16.5%) according to the D'Amico classification [8] – were referred to the Urology and/or Radiotherapy departments of the Grenoble University Hospital, mainly by urologists from private practice or general practitioners. The patients underwent a pretreatment evaluation with medical history, physical examination, uroflowmetry, bone scanning, magnetic resonance imaging (MRI) of the abdomen and pelvis. The eligibility criteria were stage T1c-T2a-b N0 M0 (2002 TNM classification), Gleason score 3+3 or 3+4 assessed on a median of 12 random biopsies (range 6 to 32), baseline PSA below 15 ng/mL, prostate volume less than 60 cm^3, WHO performance status less than 2, no previous transurethral resection of the prostate. No central pathologic review was performed. The patients were examined by the same urologist (JLD) and radiation oncologist (MB) and their medical charts were presented at the multidisciplinary tumour board. Table 1 displays the patient characteristics. The mean age was 66.9 years and the median baseline IPSS score 6 ± 5 (range 0 to 24). The mean prostate volume assessed in the operating room was 40 ± 12 cm^3 (range 14 to 80). The breakdown of positive core was as follows: 1 (29%), 2 (35%), 3 or more (36%). To shrink the prostate volume before the implant three patients received dutasteride (5-alpha-reductase) and three patients a 3-month luteinising hormone releasing hormone (LHRH) agonist implant. One bolus antibiotics was given the morning of the intervention.

Table 1
Characteristics of the patients with prostate cancer treated brachytherapy.
Caractéristiques des patients.

	n (total = 200)	%
T-stage		
T1c	159	79.5
T2a–b	41	20.5
Gleason		
≤ 6	177	88.5
7	23	11.5
Number of positive cores		
1	58	29.0
2	70	35.0
≥ 3	72	36.0
PSA (ng/mL)		
< 4	15	7.5
4–10	168	84.0
> 10	17	8.5
D'Amico risk group		
Low	167	83.5
Intermediate	33	16.5
Prostate volume		
≤ 50 cm^3	161	80.5
> 50 cm^3	39	19.5
Neoadjuvant treatment		
5-α reductase	3	1.5
LHRHa	3	1.5
None	194	97.0

PSA: prostate-specific antigen; LHRHa: luteinising hormone releasing hormone agonist implant.

2.2. Treatment

Brachytherapy was realized under general anaesthesia, except for two patients who underwent a spinal/saddle block because of pulmonary insufficiency. The first 15 patients were implanted under the supervision of Dr Stone (Mount Sinaï Hospital, New York). After calibration of the *BK ultrasound* apparatus by the physician, the urologist realized:

- axial images acquisition at 5 mm intervals from base to apex, downloaded into the brachytherapy treatment planning system;