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CLINICAL INVESTIGATION **Prostate**

COMPARATIVE STUDY OF INGUINAL HERNIA REPAIR RATES AFTER RADICAL PROSTATECTOMY OR EXTERNAL BEAM RADIOTHERAPY

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Purpose: We tested the hypothesis that patients treated for localized prostate cancer with radical prostatectomy (RP) have a higher risk of requiring an inguinal hernia (IH) repair than their counterparts treated with external beam radiotherapy (EBRT).

Methods and Materials: Within the Quebec Health Plan database, we identified 6,422 men treated with RP and 4,685 men treated with EBRT for localized prostate cancer between 1990 and 2000, in addition to 6,933 control patients who underwent a prostate biopsy. From among that population, we identified patients who underwent a unilateral or bilateral hernia repair after either RP or EBRT. Kaplan-Meier plots showed IH repair-free survival rates. Univariable and multivariable Cox regression models tested the predictors of IH repair after RP or EBRT. Covariates consisted of age, year of surgery, and Charlson Comorbidity Index.

Results: IH repair-free survival rates at 1, 2, 5, and 10 years were 96.8, 94.3, 90.5, and 86.2% vs. 98.9, 98.0, 95.4, and 92.2%, respectively, in RP vs. EBRT patients (log-rank test, $p < 0.001$). IH repair-free survival rates in the biopsy population were 98.3, 97.1, 94.9, and 90.2% at the same four time points. In multivariable Cox regression models, RP predisposed to a 2.3-fold higher risk of IH repair than EBRT ($p < 0.001$). Besides therapy type, patient age ($p < 0.001$) represented the only other independent predictor of IH repair.

Conclusions: RP predisposes to a higher rate of IH repair relative to EBRT. This observation should be considered at informed consent. **Crown Copyright © 2010 Published by Elsevier Inc.**

Inguinal hernia, Inguinal hernia repair, Radical prostatectomy, External beam radiotherapy.

INTRODUCTION

Inguinal hernia (IH) represents a complication of radical prostatectomy (RP). In previous studies, the incidence of post-RP IH diagnosis ranged from 7 to 21%, with most cases occurring within 24 months after RP (1–10). The etiology of post-RP IH is unclear. Ischemia caused by self-retaining retractors may play a role (1–3). The disruption of transversalis fascia caused by the surgical incision may also contribute (11, 12).

Advanced patient age (2, 7, 9), low body mass index (3, 9, 10), postoperative urethral stricture (2, 7), and postoperative wound-related problems (6) have also been implicated as potential risk factors. To date, none of those factors have been unequivocally involved in the pathogenesis of post-RP IH.

Several surgical variables may contribute to the development of IH (1–10). Conversely, patients treated with radiotherapy may be relatively free of the risk of developing an IH. This discrepancy may represent an important advantage for external beam radiotherapy (EBRT) relative to RP, at least in the eyes of some patients who do not wish to be at an increased risk of having to undergo an IH repair after definitive therapy for localized prostate cancer (PCa). To date, only one study ($n = 171$ subjects) compared the rate of IH diagnosis after RP vs. EBRT (9). In that report, the 2-year IH diagnosis rate after EBRT was less than 5% vs. 13% incidence after RP (9). Multivariable analyses showed

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that open or laparoscopic RP predisposed to a 14-fold increase in IH diagnosis rate relative to EBRT. These findings confirmed that IH may represent a potential disadvantage of RP relative to EBRT. However, the reported IH diagnosis rates may be biased due to a higher rate of physical examination in surgically treated patients. Under such a premise, clinically asymptomatic IHs could spuriously inflate the overall IH rate associated with RP relative to that of EBRT. To circumvent the problem of diagnostic bias in surgically treated patients, we examined the rates of IH repair after RP or EBRT within a large population-based cohort of men treated for clinically localized PCa with either RP or EBRT between 1990 and 2000. Additionally, we examined the IH repair rates in a control population of patients who underwent a prostate biopsy between 1990 and 2000.

METHODS AND MATERIALS

Study cohort

The Quebec Health Plan (Regie de l'Assurance Maladie du Quebec [RAMQ]) represents the exclusive insurer in the province of Quebec. Its database allows ascertainment of all health services covered by the plan that is provided in the province of Quebec. These services include all treatment modalities for PCa, including definitive EBRT and RP. Moreover, the Quebec Health Plan relies on International Classification of Disease, 9th Revision (ICD-9) (9) codes, which allow defining the baseline Charlson Comorbidity Index (CCI) scores prior to either RP or EBRT.

From the Quebec Health Plan database, we identified all men treated with either RP or EBRT between 1990 and 2000, who were diagnosed with PCa (ICD-9, code 185.9). Each record includes the type of treatment (RP vs. EBRT), the date of RP or of the first EBRT treatment, age at treatment, and the pretreatment CCI score. Surgical codes 545.5 and 545.7 were used to identify patients who, respectively, underwent unilateral or bilateral IH repair after either RP or EBRT. Patients who were diagnosed with and/or surgically treated for IH before RP or EBRT were excluded. Patients who underwent a concomitant IH repair at RP were also excluded. Since androgen deprivation therapy (ADT) may affect tissue healing and may predispose to IH, we also excluded patients who received luteinizing hormone-releasing hormone (LHRH) analogs and antiandrogens or who underwent orchiectomy before RP or EBRT. Since patients who experience PCa recurrence are virtually invariably treated with ADT, we also censored the follow-up of individuals treated with ADT after RP or EBRT from the date of first day of ADT. Finally, since sequential therapy with RP and EBRT does not allow discrimination between the contribution of one or the other treatment modality to the IH repair rates, we also excluded patients treated with salvage RP after EBRT or those in whom salvage or adjuvant EBRT was used after RP. These exclusion criteria resulted in a population of 11,107 patients who underwent RP or EBRT for localized PCa.

Additionally, to examine the effect of ADT on IH repair rates, we repeated the same analyses by using different selection criteria. Instead of censoring patient follow-up at the time of ADT initiation, we included patients who received neoadjuvant or concomitant ADT. Since we had no clear definition of what constitutes concomitant ADT, we restricted our population to those who received ADT within 3 or fewer months after RP or EBRT. This measure resulted in a second study cohort of 12,165 patients. To adjust for different lengths of treatment, the duration of ADT was also quantified and divided into quartiles.

Finally, we examined the rate of IH repair in a control population of 6,933 men subjected to prostate biopsy between 1990 and 2000. The start of follow-up consisted of the prostate biopsy date. IH repair codes were used in the same fashion as in the initial analysis.

Statistical analyses

The chi-square test and Student's *t* test were used for comparisons of means and proportions, respectively, between RP and EBRT patient populations. Kaplan-Meier plots were used to show the IH repair-free survival rates after either RP or EBRT. The log-rank test was used to assess the significance of the observed rate differences. IH repair-free rates at 1, 2, 5, and 10 years after RP, EBRT, or prostate biopsy were estimated using the life table method.

Univariable and multivariable Cox regression models were used to analyze the relative rates of IH repair after either RP or EBRT. Covariates consisted of age categories (<60, 60-64, 65-69, and ≥70 years old), year of treatment tertiles (1990-1993 vs. 1994-1997 vs. 1998-2000), and CCI score categories (0 vs. 1-2 vs. 3-4 vs. ≥5).

The same statistical analyses were repeated for the second population that included patients treated with neoadjuvant or concomitant ADT. In multivariable Cox regression analyses, additional covariates consisted of type and duration of ADT (LHRH analog length-of-treatment quartiles and antiandrogen length-of-treatment quartiles).

All statistical tests were performed using S-PLUS Professional software, version 1 (Mathsoft, Seattle, WA) or Statistical Package for Social Science software, version 15.0 (SPSS, Chicago, IL). Moreover, all tests were two-sided with a significance level set at 0.05.

RESULTS

The first patient population, where patients treated with ADT were censored, consisted of 6,422 (57.8%) RP and 4,685 (42.2%) EBRT patients treated for clinically localized PCa (Table 1). Average age (70.4 vs. 64.4 yrs) was higher in EBRT patients than in RP patients ($p < 0.001$). Similarly, average CCI scores were higher in EBRT (2.7 points) than in RP (1.3 points) patients ($p < 0.001$). Moreover, the rate of RP was higher than EBRT in more contemporary years ($p < 0.001$). The descriptive characteristics of the second patient population ($n = 12,165$ subjects), where the use of neoadjuvant or concomitant ADT was adjusted for, are shown in Table 2. The proportion of patients who were treated with neoadjuvant or concomitant LHRH agonist therapy was 5.4% and 33.6% in, respectively, RP and EBRT patients.

In the first patient population, where patients treated with ADT were censored, IH repair-free rates at 1, 2, 5, and 10 years were 96.8, 94.3, 90.5, and 86.2% vs. 98.9, 98.0, 95.4, and 92.2% after, respectively, RP vs. EBRT (log-rank test, $p < 0.001$) (Fig. 1). The absolute IH repair rate differences were 2.1, 3.7, 4.9 and 6.0% for the same time points. In the second patient population, where the use of ADT was adjusted for, the IH repair-free rates at 1, 2, 5, and 10 years were 96.9, 94.5, 90.8, and 86.8% vs. 99.0, 98.2, 96.1, and 93.4% after, respectively, RP or EBRT. Similarly, the IH repair rate differences between RP and EBRT patients were 2.1, 3.7, 5.3, and 6.6% at, respectively, 1, 2, 5, and 10 years (log-rank test, $p < 0.001$). Since the absolute IH repair-free rates in the second population were virtually the same as in the first population, the Kaplan-Meier plot was omitted.