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Differences in prostatic biopsy results in patients with prompt and delayed assistance after indication

ABSTRACT

At prostate cancer screening by serum prostate-specific antigen (PSA) and digital rectal examination (DRE) the interval between the first suspicion of malignancy and the diagnostic procedure may impact on disease treatment and progression. Assistential difficulties of Health Care Providers can postpone prostatic biopsy beyond the 60 days limit recommended by ANS (National Health Agency). Here we compare biopsy results from patients with prompt and delayed assistance. We included165 consecutive patients seen on Public Health Care (May -Oct/2010) of which 76 were biopsied after 6 months from indication (Delayed) and 89 within 3 months (Control). Disease extension was analyzed as to the total and the percentage of cores with cancer (Tcore and Pcore), the total and percentage of mm of cancer (Tmm and Pmm), and the maximum extent of cancer in a single core (ExtMax). Mean total PSA and age at the time of indication and percentage of malignant diagnosis were similar between the two cohorts (65.8 vs. 67.7 years; 10.4 vs. 9.4ng/dl; 46% vs. 42%) as well as disease extension and Gleason score. However, in the population with unilateral disease (n = 40), the Delayed group had higher Tmm, Pmm, Tcore, and Pcore (12.5 vs. 7.5mm; 9.4 vs. 5.7%; 2.62 vs. 2.0 cores; 22 vs. 16%; P >0.05). Five of 24 (21%) patients of the Delayed group had Pmm > 25%, 1:3 had > 25% of Pcore losing criteria for potential T2a; and 1:4 had ExtMax > 50% losing criteria for minimum volume disease (controls: 1/16, 6%; 1:8 and 1:12, respectively). In conclusion, the interval between biopsy indication and procedure seems to impact on disease extension particularly in patients with unilateral disease yielding an agile assistance as a fundamental strategic resource for early diagnosis. Studies on larger cohorts with follow up are needed to confirm these results.

INTRODUCTION

Prostate cancer ranks as the second cause of death by cancer in Brazilian men and third in São Paulo State, with more than 60,000 new cases estimated for the current year nationwide [1]. Early diagnosis is crucial for patient outcome. Prostate cancer screening involves prostatic biopsy. The major indications are elevated serum PSA dosage and altered digital rectal examination. Although the Brazilian National Health Agency (ANS) recommends immediate biopsy procedure to be performed ideally within 2 months after indication [2], difficulties in the health care system may delay the procedure. Not infrequently the patient subscribes on a waiting list which progresses with no criteria other than the order of inclusion and availability of the network. Since most prostate cancers behave indolently we sought to investigate if postponing the biopsy procedure impacts on biopsy results and ultimately disease extension.

MATERIAL AND METHODS

Criteria for biopsy indication included: elevated total serum prostate-specific antigen (PSA, > 2.5ng/ml for patients < 55 years and > 4.0 ng/ml for patients > 55 years), increase in annual PSA velocity (> 0.75ng/ml), and abnormal digital rectal examination. We included 165 consecutive patients seen on public health care between May and October 2010, by the same medical group (Urology, Radiology and Pathology), assisting different hospitals in the same geographic area (São Paulo State, 2nd Region). Depending on the availability of the health unit, patients were offered prompt or delayed biopsy schedule. Seventy-six patients were biopsied after 6 months from indication (Delayed group) while 89 were biopsied within the first 3 months (Control group).

Disease extension in each sextant biopsy specimen was quantified as the total number of cores with cancer (Tcore), the percentage of cores with cancer (Pcore), the sum of millimeters of cancer in all positive fragments (Tmm), the percentage of millimeters of cancer relative to the total millimeters of prostatic tissue

sampled (Pmm), and the maximum extent of cancer in a single core (ExtMax).

The different methods of quantification of prostate cancer were compared between Delayed and Control groups using the 1-way ANOVA test. On unilateral disease (only left or right side with positive cores) cut-offs were applied to simulate clinical significance: Pmm and Pcore < 25% as potentially pT2a at prostatectomy, and ExtMax > 50% as potentially losing Epstein criteria for clinical insignificant disease.

RESULTS

The mean number of cores per biopsy was 13.11 (range 9 to 23). PSA information was available for 118/165 (71%) patients and estimated gland weight by ultrasound in 40/165 (25%). Mean tPSA and age at the time of indication were similar between Delayed and Control groups (65.8 years vs. 67.7 years, and 10.4 ng/dL vs. 9.4 ng/dl). Percentage of malignant diagnosis was 46% in the Delayed group and 42% in the Control group. Gleason score also showed similar distribution but with inverted profiles for Gleason 6 and 7 with predominant Gleason 7 in the Control group (Table 1).

In the subset with unilateral disease (n = 40), the Delayed group showed higher Tmm, Pmm, Tcore, and Pcore (12.5 vs. 7.5mm; 9.4 vs. 5.7%; 2.62 vs. 2.0 cores; 22 vs. 16%; means, P > 0.05). Five of 24 (21%) patients of the Delayed group had Pmm > 25%, 8/24 (33%) had > 25% of Pcore, and 6/24 (25%) had ExtMax > 50% while the Control group demonstrated 1/16 (6%), 2/16 (12%) and 1/16 (6%), respectively (Table 2).

DISCUSSION

Screening for malignant disease increases early detection of cancer and impacts in Public Health resources. However, preventive outcome is reached through a series of consecutive events with adequate patient follow-up. The availability of exams offered by the Health Care Providers differ between urologic consults, clinical pathology exams and anatomic pathology exams, allowing gaps in patient assistance.

Since most prostate cancers are indolent, biopsy delay has received little attention. Upon an incomplete diagnosis the selection criteria may not be obvious prior to the biopsy results. This study sought to evaluate the differences of biopsy reports from prostate tissues sampled within the first 3 months of indication and after 6 months of waiting. We were able to analyze a relatively large cohort (n = 165) with similar age distribution, PSA values, number of cores sampled per biopsy, and similar cancer detection rates.

We found that postponing biopsy procedure had little - if no impact - in disease extension between the two groups since the differences observed did not reach statistical significance. The Delayed group showed higher sum of positive cores (Tcore) and a higher percentage of cores with cancer (Pcore), with mean of maximum extension above 50% in a single core. However, the sum and the percentage of millimeters with cancer (Tmm and Pmm, respectively) were actually higher in the Control group.

Both groups showed an elevated percentage of malignant diagnosis (46% and 42% in Delayed and Control, respectively). Gleason grade also showed similar distribution with around 20% of high grade disease. Interestingly, the Delayed group showed higher percentage of the well differentiated pattern 3 compared to controls, and a higher percentage of unilateral disease (58% vs. 50% of the malignant cases).

However, when this subset (unilateral disease) was analyzed independently, differences were more evident, although differences still did not reaching statistical significance. While in the Control group one in every 8 patients had > 25% of positive cores, this proportion was one in every 3 patients in the Delayed group. Potentially, this could correspond to migrating from pathological stage pT2a to a pT2b in a prostatectomy specimen [3]. The same logic was also confirmed when looking into the sum of millimeters itself: of the total length of prostatic tissue sampled > 25% corresponded to cancer on one in every 4.8 patients of the Delayed group while only one in every 16 patients from the controls.

Finally, we analyzed the maximum extent of cancer in a single core. Considering that one of the Epstein criteria for clinical insignificant cancer excludes biopsies with > 50% of cancer in a single core [4], we applied a 50% cut-off to ExtMax. The Delayed group had over 4 times more patients falling short of the criterion.

In summary, a better knowledge of prostate cancer progression over a short period of time may be important for establishing criteria for patient selection in the current situation of biopsy delay. The interval between prostate biopsy indication and procedure seems to impact on disease extension particularly in patients with unilateral disease. This subset showed more millimeters of cancer and more biopsy cores with cancer although not reaching statistical significance. Studies on larger cohorts with follow-up are needed to confirm these results and analyze the impact in disease management and outcome.

REFERENCES

1. MP/IBGE (Foundation of the Brazilian Institute of Geography and Statystics). December, 2011; and MS/INCA (National Institute for Cancer). December, 2011.
2. Rocha LCA, Silva EA, Costa RP, Hering FLO. Projeto Diretrizes. Associação Médica Brasileira (Brazilian Medical Association) and Conselho Federal de Medicina (Federal Council of Medicine). July, 2006.
3. van der Kwast TH. International Society of Urological Pathology (ISUP) Consensus Conference on Handling and Staging of Radical Prostatectomy Specimens. Working group 2: T2 substaging and prostate cancer volume. Mod Pathol 2011;24:16-25.
4. Epstein JI, Walsh PC, Carmichael M, Brendler CB. Pathologic and clinical findings to predict tumor extent of non-palpable (stage T1c) prostate cancer. JAMA 1994;271:368-374.