Relation between prostate gland volume and some histological markers of malignancy

C. González-Enguita\textsuperscript{a}, M.J. Fernández-Aceñero\textsuperscript{b,\ast}, J.V. García-Cardoso\textsuperscript{a}, L. López-Pérez\textsuperscript{a}, F. Manzarbeitia\textsuperscript{b}, R. Vela-Navarrete\textsuperscript{a}

\textsuperscript{a} Servicio de Urología, Fundación Jiménez Díaz, Universidad Autónoma, Madrid, Spain
\textsuperscript{b} Servicio de Anatomía Patológica, Fundación Jiménez Díaz, Universidad Autónoma, Madrid, Spain

Received 23 August 2011; accepted 14 October 2011
Available online 14 May 2012

Abstract

Objectives: The relation between the total volume of the prostate gland or its weight after radical prostatectomy and the histological markers of malignancy in cases of prostate cancer is a controversial subject. We have analyzed 100 consecutive radical prostatectomy specimens in order to determine the relation between volume or weight of the prostate gland and the biological aggressiveness of the tumor process by different histological markers.

Material and methods: One hundred consecutive radical prostatectomy specimens in patients who had not received pre-operative hormone treatment were retrospectively reviewed. These surgical samples were processed according to a standardized protocol. In a subsequent evaluation, the following were studied with greater detail: Gleason grade, tumor volume, multimodality, neural or vascular invasion, put stage, and presence of PIN foci. The histological findings were compared with the prostate gland weight using Windows SPAS, 13.0 statistical package with a significance value of \( p < 0.05 \). According to the prostate gland weight, three groups were established: <40 g (33%), 40–90 g (61%), and >90 g (6%).

Results: A statistically significant association (\( p = 0.001 \)) was found between the prostate gland weight and tumor volume since 15 of the 33 glands with weight under 40 g accounted for more than 50% of the glands affected by tumor compared to none of the 6 patients with total weight over 90 g. A significant relation was also found between the multimodality and weight (\( p = 0.03 \)), so that 24 of the 33 glands under 40 g had bilateral multimodality compared to only 1 out of the 6 glands over 90 g. The neural invasion, number of PIN foci and the highest combined Gleason grade were frequent in low volume prostates, but the difference did not reach statistical significance.

\textsuperscript{\ast} Please cite this article as: González-Enguita C, et al. Relación entre volumen de la glándula prostática y algunos marcadores histológicos de malignidad. Actas Urol Esp. 2012;36:86–90.

\textsuperscript{\ast\ast} Corresponding author.

E-mail address: mgg10167@gmail.com (M.J. Fernández-Aceñero).

2173-5786/$ - see front matter © 2011 AEU. Published by Elsevier España, S.L. All rights reserved.
Prostate Gland Volume and Histological Markers of Malignancy

Introduction

The total volume of the prostate gland (TVPG) determined by transabdominal ultrasound or, more precisely, by transrectal ultrasound (TRUS), or the weight of the gland after radical prostatectomy has been associated for years with different variables of malignancy, but rarely incorporated to prognostic nomograms. Simultaneously, the TVPG has been considered an argument in diagnostic procedures (PSA level, PSA density), for instructions and number of biopsies (sextant, saturation), repeat biopsies, as well as markers of malignancy such as Gleason score, tumor volume, and multifocality. Similarly, the total volume or weight of the prostate gland has been used to compare the Gleason score obtained with the biopsy to the corresponding one measured in the surgical piece, or to the incidence of recurrence after radical prostatectomies. Finally, the greater malignancy of the cancer process in low-volume prostates has been the argument used to question therapeutic strategies such as watchful waiting or focalized treatment projects. The aim of this study is to assess whether there is any relation between prostate volume and some histological criteria of malignancy.

Material and methods

We reviewed the radical prostatectomy specimens of 100 consecutive patients who received no preoperative hormonal treatment, operated at the Urology Department of the Fundación Jiménez Díaz in Madrid. These surgical samples were processed in the Pathological Anatomy laboratory following a common protocol. The information on the Gleason score, tumor volume, multifocality, vascular or neural invasion, pT stage, and presence of PIN foci was retrospectively collected. We performed a statistical analysis with the Chi-square technique to assess the possible association between the size of the gland (estimated from the weight and classified into three groups: <40 g (33%), >40 and <90 g (61%) and >90 g (6%), and various variables suggestive of poor tumor prognosis (grade, multifocality, stage, vascular invasions, etc.). For this analysis, the statistical package SPSS...
13.0 for Windows has been used, setting a $p < 0.05$ value for significance.

**Results**

We found a statistically significant association ($p=0.001$) between the weight of the gland and the tumor volume, as 15 out of 33 glands weighing less than 40 g showed tumor involvement of more than 50% of the gland, which contrasts with 0 out of 6 patients with total weight exceeding 90 g. We also found a significant association between multifocality and weight ($p=0.03$), since 24 out of 33 glands under 40 g had bilateral multifocality compared with just 1 out of 6 glands weighing more than 90 g. Neural invasion and a greater number of PIN foci were more frequent in small prostates, but the difference did not reach statistical significance. The combined Gleason grade was higher in small glands.

**Discussion**

Despite the small sample size, which limits the statistical power, our results seem to confirm previous observations and remind us of the convenience of using the TVPG as a reference for the indication of diagnostic procedures, especially prostate biopsy, and support of therapeutic strategies.

The prostate volume and indication for biopsy driven by the increase of the PSA (T1C): the close relation between the PSA level and volume of the prostate gland has been recognized for years. The PSA value along with the digital examination of the prostate gland, which itself provides rough volumetric information, are the first scans performed in the evaluation of patients with potential risk of prostate cancer. Initially, the cut or PSA level of 4.0 ng/ml was considered as a primary reference to raise suspicion of prostate cancer and justify the performance of a prostate biopsy. Although there is still no minimum PSA cut-off point, all comments that follow started from the 4.0 ng/ml reference. However, it soon was recognized that the total volume of the prostate gland, more precisely measured with the progress of transabdominal and transrectal ultrasound, significantly affected the PSA level, and the PSA density concept was applied as a reference to advise or delay the prostate biopsy. The PSA index was proposed for the same purpose. However, the profitability of this new standard has not been considered of sufficient value, therefore, decreasing interest in it. To enhance the certainty of the PSA density, it was proposed to refer it to the volume of the adenoma or transition zone (TZ) with promising results that have not arisen more enthusiasm, although the specificity of the PSA significantly improves in high-volume prostates.

Another alternative to increase the specificity of PSA in patients with total PSA equal to or greater than 4.0 ng/ml was to determine the free PSA (FPSA) and use this figure as a reference, directly or by using the FPSA index. This approach has certainly had greater disclosure and is a common benchmark in clinical practice, considering that when it is greater than 25% it is oriented in the sense of adenoma (BPH), and when it is below 15% toward prostate cancer.

In a recent work, the potential usefulness of PSA density is raised depending on the volume of the transition zone to determine the biopsy in patients with PSA values between 2 and 4 ng/ml, suggesting that it reduces the performance of unnecessary biopsies.

Prostate volume and number of biopsies: assuming similar PSA levels, prostate biopsy yield is reduced in parallel with the volume of the prostate gland. To get a greater profitability of the biopsy in high-volume prostates, we have followed divergent options. On the one hand, we tried to improve the PSA specificity by proposing assessments and indexes, such as those mentioned above (FPSA, FPSA index). On the other hand, we decided simply to increase the number of prostate biopsies which, in general, followed the proposal that the greater the volume, the greater the number of biopsies, categorizing even the number of biopsies that should be performed vs. a specific prostate volume. Thus, we have moved from the traditional sextant biopsy to saturation biopsy, with 21 doses. The number of 11 doses was the most common recommendation for prostate volumes greater than 50 cm³.

In order to try to explain the low yield of the prostate biopsy in patients with PSA greater than 4.0 ng/ml, volumetric reasons have commonly been proposed; in fact, the sextant biopsy obtains a 9 cm (6 times 1.5 cm) sample, representing approximately 10% of a 30 cm³ prostate gland, and only 1% of a 70 cm³ gland. Again, in this case, most multifocality of prostate cancer or high-grade PIN in small volume glands with cancer and the low topography of cancer in high-volume glands have been ignored in the argument.

Prostate volume and Gleason score in biopsies and surgical specimens: the small-volume prostate glands harbor more aggressive cancers and are those that show higher pathologic grades. The existing relation between the volume of the gland and the degree of malignancy expressed by the Gleason score has been the subject of numerous studies. When we analyzed the anatomic distribution and degree of malignancy of prostate tumors of small volume, described as indolent, it was observed that this finding, the genuine small-volume tumor not associated with other features of greater aggressiveness is given precisely in larger prostates.

It is also small volume glands which most frequently show a higher Gleason score in radical prostatectomy pieces compared with the data obtained in the previous biopsy. Turley et al. compared the outcome of the prostate biopsy and radical prostatectomy in 586 patients whose prostate volume was determined by TRUS. The prostate volume was categorized into different groups: 20 cm³ or less, between 20 and 40, between 40 and 60, and more than 60. The Gleason sum was also categorized into three subgroups: between 2 and 6, 3+4, and 4+3, or higher. They found that in 24% of the cases, the piece showed a Gleason score greater than the biopsy, and that most of these cases corresponded to small volume prostates.

Prostate volume and therapeutic alternatives: assuming similar degrees of malignancy, in treatment decisions based only on the outcome of the prostate biopsy (T1C), the prostate volume is another reference to consider. With regard to an extremely interesting topic at the moment, focused treatment of prostate cancer, it seems certain that it is the glands of small volume in which most often is the involvement of both lobes and there is increased tumor spread. This tumor mapping has also shown that it is
precisely very large glands where focal, localized tumors can be found the best candidates for these procedures. These findings can also explain the excellent results obtained with prostate TUR in patients with large prostates and the incidental finding of some tumor focus (A1, in the old terminology).

The prostate volume is also a factor to consider when watchful waiting is chosen in patients who meet the recommended criteria. It has been proposed in these circumstances, so as to be safe and eliminate evolutionary risks, to perform saturation biopsies, and even using the brachytherapy template before making therapeutic decisions. The discussed findings clearly guide in the sense that, in small volume prostates, there should be a more cautious indication of the watchful expectation.

Conclusions

The comparison of the weight of the prostate gland of 100 consecutive samples of radical prostatectomy with histological markers of malignancy has confirmed a close relation between them, so small prostates, especially smaller than or equal to 20 g, harbor tumors of great malignancy, while those of large volume, greater than 90 g, more often harbor unifocal and low grade tumors. We discuss the value of TVPG for diagnostic decisions (biopsies and repeat biopsies) and therapeutic strategies.

Conflict of interest

The authors declare that they have no conflict of interest.

References


