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Prostate Cancer, Treatment Modalities and Complications: An Evaluation of the Scientific Literature

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ABSTRACT

Prostate (PR) cancer (CA) is one of the most common malignant neoplasms in men all over the world. In general, if prostate cancer (PC) is detected early, treatment usually involves either surgical removal of the prostate or radiotherapy (RT). Hormone Therapy (HT) or chemotherapy (CH) is the preferred treatment for more advanced cases of PC or if CA spreads beyond the PT. A number of complications, such as urinary incontinence (IU) or erectile dysfunction (ED), can be associated with some modalities of treatment of the PC. The aim of this work is to evaluate, in PubMed, the number of publications related with prostate cancer and the main modalities of treatment, as well as some clinical complications. The searches were performed in PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi) in the period 1950 to 2008 using the words: (i) CA, (ii) CA and PR or penis or testis, (iii) CA and PR and RT, CA and PR and surgery (SU), CA and PR and CH and, CA and PR and HT and (iv) CA and PR and RT and IU or ED, CA and PR and SU and IU or ED, CA and PR and CH and IU or ED and, CA and PR and HT and CH and IU or ED, and (V) PC and the same modalities of treatment. The data was obtained on July 20th, 2008. PC, as expected has been cited extensively and surgery has been identified as the most widely referenced modality of treatment. Furthermore, urinary incontinence and erectile dysfunction are important complications that have attracted significant scientific interest. In conclusion, these findings have shown the relevance of the PubMed to analyze quantitatively the publications in cancer and this information could be worthwhile in aiding the comprehension of some clinical aspects related with PC, as well as the development of preventative actions. The analysis of the scientific interest, considering the number of publications in the PubMed, reveals research trends in the field and demonstrates the importance of the surgical procedures in the treatment of the prostate cancer. Moreover, this finding is relevant due to the fact that surgery is the treatment of choice when early detection of PC is achieved. However, it is important to consider clinical complications related to such procedures, such as urinary incontinence and erectile dysfunctions that can reduce the quality of life of the patient.

Key words: Prostate cancer, radiotherapy, PubMed, scientific interest

INTRODUCTION

Prostate (PR) cancer (CA) is one of the most common malignant neoplasm in men all over the world (Antilla et al., 2005), as well as in Brazil (http://www.inca.gov.br/estimativa/2008/finalversao.pdf) in particular and is the third most common cancer worldwide and the most common cancer in
Prostate cancer metastasizes to regional lymph nodes and bone. The incidence of metastasis has been reduced over the last years, mainly due to early detection based on the determination of prostate-specific-antigen (PSA) (Garin, 2006), as well as the digital rectal examination, transrectal ultrasonography (TRUS) and TRUS-guided biopsies (Futterer et al., 2008).
MATERIAL AND METHODS

The searches were performed in PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi) for the period 1950 to 2008 using the words: (i) cancer (CA), (ii) CA and PR, (iii) CA and testis and (iv) CA and penis.

A search using the words CA and PR were associated with the modalities of treatment, RT or surgery (SG) or CT or HT. Moreover, another search using the words “prostate cancer” (PC), also associated with the modalities of treatment, was performed to evaluate consistency.

Statistical analysis involved Chi-Squared Test, with a significance level of $P<0.05$, was performed comparing the searches using “CA and PR and modalities of treatment” and “PC and modalities of treatment”. InStat Graphpad software was used to perform statistical analysis (GraphPad InStat version 3.01 for Windows 95/NT, GraphPad Software, San Diego Ca, USA).

Another search was performed using (a) CA and PR and RT and urinary incontinence (UI) or erectile dysfunction (ED), (b) CA and PR and SG and UI or ED, (c) CA and PR and CT and UI or ED or anal incontinence (AI) and (d) CA and PR and HT and CT and UI or ED or AI.

Finally, a search using the above parameters was performed for the same date of the years 1968, 1978, 1988, 1998 and 2008 to decipher any trends associated with preferred choices of treatment as new modalities become available. The data were obtained on July 20th, 2008 and the number of citations for each subject was determined.

RESULTS

Table 1 shows the number of publications found in the PubMed on CA as well as CA and various organs of the male reproductive tract. The results show a high number of publications in cancer, of which nearly 3% are associated with PR.

Table 2 shows the number of publications cited in the PubMed on CA and PT and the main modalities of treatment, as well as PC and the same modalities of treatment. Surgery has been shown to be the modality of treatment associated with prostate cancer that is most widely cited when compared with RT, CT and HT, whilst RT and HT are the least cited ones. The comparison between CA and PT and PC was very significant ($P<0.01$) in all modalities of treatment.

Table 3 shows the number of publications cited in the PubMed on some complications associated with modalities of treatment for PC. Urinary incontinence and erectile dysfunction have been mainly associated with surgery. The number of publications involving prostate cancer and the studied modalities of treatment with anal (fecal) incontinence is very poor.

Table 4 shows the number of publications found in PubMed on CA and PR and the main therapeutic modalities in order to demonstrate changes in the trends of research and publications on PC treatments within the last 50 years.

<table>
<thead>
<tr>
<th>Selected subject</th>
<th>Number of publications</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA</td>
<td>2174533</td>
</tr>
<tr>
<td>CA and PR</td>
<td>63560</td>
</tr>
<tr>
<td>CA and testis</td>
<td>12212</td>
</tr>
<tr>
<td>CA and penis</td>
<td>4745</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subject</th>
<th>CA and PT</th>
<th>PC</th>
</tr>
</thead>
<tbody>
<tr>
<td>RT</td>
<td>8585</td>
<td>5467</td>
</tr>
<tr>
<td>SG</td>
<td>18531</td>
<td>11226</td>
</tr>
<tr>
<td>CT</td>
<td>11867</td>
<td>8234</td>
</tr>
<tr>
<td>HT</td>
<td>8202</td>
<td>5936</td>
</tr>
</tbody>
</table>

Table 1 - Number of publications cited in PubMed on CA, as well as, CA and various organs of the male reproductive tract.

Table 2 - Comparison of the number of publications cited in PubMed on CA and PT and the main modalities of treatment, as well as PC and the same modalities of treatment.
DISCUSSION

Although mortality from prostate cancer has been declining over the past decade, metastasis, which is presented in approximately 20% of patients, can substantially shorten survival time and remains a major challenge in maintaining quality of life for survivors (Choueiri et al., 2006; Kabeer et al., 2007). As reported by Schimid et al. (2007), prostate cancer is basically an ideal candidate for exogenous preventive measures, such as dietary and pharmacological prevention. Moreover, Schimid et al. (2007) and Goetzl et al. (2007) have also reported that dietary/nutritional factors may influence the disease development. These scientific considerations are worthwhile in order to develop a prevention strategy against prostate cancer. Our study revealed that a high percentage of publications (about 3%) on cancer, cited in the PubMed, are related with prostate (see Table 1). The analysis of the number of publications found in the PubMed related with the possible types of treatment of prostate cancer has shown that surgery is more studied than the other treatment modalities of this disease. This could be related to the fact that the treatment modality of choice for prostate cancer depend on the stage of the disease, the age of the individual and the presence of other clinical conditions. As a consequence, in general, if prostate cancer is detected early, treatment usually involves radical retropubic prostatectomy (Escudero et al., 2006; Kibel et al., 2007). The improvement of the assays for early detection of prostate cancer has thus favored the use of surgery, as a curative modality to treat prostate cancer. Thus, although other modalities, such as brachytherapy, have come to focus lately with particular applications on prostate cancer, surgery has been and remains the more cited therapeutic approach for prostate cancer (see Tables 2 and 4). Yet, more scientific studies about the use of radiotherapy in the treatment of the prostate could come into focus due to the variety of possible sources of radiation (Marshall, 2007; Fang et al., 2008; Ganswindt et al., 2008) and the potential they offer to reduce the number/intensity of complications associated with surgery. With regards to such trends, it is interesting to note that, although hormone therapy had 5 times more publications than radiotherapy in Jul 1968, it had twice as many in 1978 and 1988 and has the same or slightly less publications in Jul 2008, showing a smaller rate of increase in this field. On the other hand, chemotherapy had the same number of publications with radiotherapy in 1968 but nearly twice as many in 1978 and 1988, a period of peak

Table 3 - Number of publications cited in PubMed on some complications associated with modalities of treatment for prostate cancer.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Number of publications</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA and PR and RT and UI</td>
<td>233</td>
</tr>
<tr>
<td>CA and PR and RT and ED</td>
<td>299</td>
</tr>
<tr>
<td>CA and PR and SG and UI</td>
<td>558</td>
</tr>
<tr>
<td>CA and PR and SG and ED</td>
<td>523</td>
</tr>
<tr>
<td>CA and PR and CT and UI</td>
<td>43</td>
</tr>
<tr>
<td>CA and PR and CT and ED</td>
<td>159</td>
</tr>
<tr>
<td>CA and PR and HT and UI</td>
<td>28</td>
</tr>
<tr>
<td>CA and PR and HT and ED</td>
<td>106</td>
</tr>
</tbody>
</table>

Table 4 - Number of publications cited in PubMed on CA and PR and the main modalities of treatment over the past 50 years.

<table>
<thead>
<tr>
<th>Year</th>
<th>CA and PR and RT</th>
<th>CA and PR and CH</th>
<th>CA and PR and SG</th>
<th>CA and PR and HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1968</td>
<td>57</td>
<td>60</td>
<td>359</td>
<td>254</td>
</tr>
<tr>
<td>1978</td>
<td>235</td>
<td>419</td>
<td>1016</td>
<td>573</td>
</tr>
<tr>
<td>1988</td>
<td>797</td>
<td>1427</td>
<td>2540</td>
<td>1446</td>
</tr>
<tr>
<td>1998</td>
<td>2623</td>
<td>3826</td>
<td>7388</td>
<td>3328</td>
</tr>
<tr>
<td>2008</td>
<td>8585</td>
<td>11867</td>
<td>18531</td>
<td>8202</td>
</tr>
</tbody>
</table>
for medicinal chemistry, with the gap slowly decreasing in more recent years. Escudero et al. (2006) and Zagar et al. (2007) have reported that such complications as urinary incontinence or erectile dysfunction can be associated with some treatment modalities of prostate cancer. The anal (fecal) incontinence is also cited as a complication of the treatment of prostate cancer, although its reference in current literature is minimal. Furthermore, the undesirable complications of urinary incontinence and erectile dysfunction have been associated mainly with surgery and radiotherapy treatments. The ratio (erectile dysfunction/urinary incontinence) between these two modalities of treatment was 1.30 to radiotherapy and 0.93 to surgery. However, the ratios are very different if one considers chemotherapy (3.69) and hormone therapy (3.91).

In conclusion, these findings have shown the relevance of PubMed in the quantitative analysis of publications in cancer, although caution should be recommended on the way the searches are performed due to discrepancies in data obtained by using different expressions of the same search terms. This information could be valuable for the comprehension of clinical aspects related to prostate cancer, as well as the development of preventative actions. The analysis of the scientific interest, considering publications in the PubMed, shows the importance of surgical procedures in the treatment of prostate cancer. This finding is relevant due to the fact that surgery is also the indicated treatment for prostate cancer at the early stages (following early detection). However, it is important to consider clinical complications, such as urinary incontinence and erectile dysfunctions, which can reduce the quality of life of the patient.

ACKNOWLEDGMENTS

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