Spanish Researchers at the Forefront of Clinical Investigation: the case of quality of life in prostate cancer

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As most readers are undoubtedly aware, the appropriate management of localised prostate cancer is a topic of intense debate among physicians, especially considering the lack of comparative randomised clinical trials. A recent systematic review [1] identified 18 randomised trials and 473 observational studies carried out to evaluate the effectiveness of treatments for this disease. However, most of these studies compared variations of a single treatment modality, and among the clinical trials only the Scandinavian prostate cancer group study [2, 3] compared radical prostatectomy with the more conservative option of “active surveillance”. The Scandinavian study showed that prostatectomy significantly reduced prostate-specific mortality [2] at 6- years follow-up (4.6% vs. 8.9%, $p=0.02$), but overall mortality was not statistically significant [3] until 10 years of follow-up (27% vs. 32%, $p=0.04$). The authors of the systematic review [1] concluded that little high-quality evidence is available and that the relative benefits and side effects of treatments are not well-characterised, facts that underline the need for new high-quality studies to facilitate clinical recommendations.

However, conducting randomised clinical trials in prostate cancer patients has presented considerable difficulties. Recruitment for the aforementioned Scandinavian clinical trial [2, 3] took more than 10 years (1989–1999). The 2003 Surgical Prostatectomy vs. Interstitial Radiation Interven-

tion Trial (SPIRIT), with an intended sample size of 2000 patients in the USA and Canada, had to be closed due to insufficient enrollment. At the moment, there are two clinical trials ongoing: the ‘Prostate Cancer Intervention Versus Observation Trial (PIVOT)’ study, designed [4] by the Department of Veterans Affairs and National Cancer Institute (EEUU) with a sample size of 1000 patients under age 75; and the Prostate Testing for Cancer and Treatment Study (ProtecT) [5], performed in the UK, which has attempted to improve recruitment by embedding this trial within qualitative research to make it more acceptable to patients and clinicians. It will be some years before the results of these clinical trials are available and in the meantime doctors face the problem of briefing patients on the many therapeutic options, as recently published in the *New York Times* (26 February 2008: “A review of prostate cancer leaves men in a muddle”).

Even though evidence from randomised clinical trials comparing treatments is not yet available, the Agencies for the Evaluation of Medical Technology of Quebec and Catalonia [6, 7] conducted a systematic review of studies that compared different treatments and included determination of pre- and post-treatment PSA. Two of the studies [8, 9] in that review evaluated the three main treatment options (radical prostatectomy, prostate brachytherapy and external radiotherapy) and found overall biochemical progression-free survival rates at five years of 70% [8] and 85% [9], respectively. More importantly, for low-risk patients, neither study found a statistically significant difference between the 3 treatment groups. These results weaken the established criterion of radical prostatectomy as the first option of treatment for localised prostate cancer and lend support to the greater use of brachytherapy and external beam radiotherapy.

The upshot of all this uncertainty is that other aspects of treatment –in particular, health-related quality of life (HRQL)– have become increasingly important, especially if we bear in mind that locally-confined prostate cancer can be asymptomatic whereas treatment can have serious side effects. Studying the side effects and HRQL may help men and clinicians to decide between treatment options. In this context, interest in understanding how treatments will affect HRQL has grown enormously, and the first longitudinal studies including the main treatment options

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with pre-treatment evaluation and mid-term follow-up have been published recently. Two of these were conducted in the USA [10, 11] and one in Spain, the ‘Spanish Multicentric Study on Prostate Cancer’ [12], with similar results to those from the USA: sexual dysfunction and urinary incontinence were greatest in the prostatectomy group, impairment of bowel function was highest in the external beam radiotherapy group and urinary irritation symptoms were greatest in the brachytherapy group.

Indeed, the present issue of *Clinical and Translational Oncology* includes the study of 304 patients treated at the Institut Català d’Oncologia (ICO)/Bellvitge University Hospital with the three main treatment modalities. These results are a subset analysis of the ‘Spanish Multicentric Study on Prostate Cancer’ [12] carried out by a research group coordinated through the Health Services Research Group (IMIM, Barcelona) and composed of radiation oncologists and urologists from 10 hospitals from all over Spain (Institut Català d’Oncologia, Barcelona; Hospital Universitari de Bellvitge, Barcelona; Instituto Oncológico de Guipúzcoa, San Sebastián; Cípro Hospital General de Catalunya, Barcelona; Centro Oncológico de Galicia, La Coruña; Hospital Ramón y Cajal, Madrid; Hospital Re-

gional Carlos Haya, Málaga; Hospital Virgen del Rocío, Sevilla; Fundación Puigvert, Barcelona and Hospital de la Santa Creu i Sant Pau, Barcelona).

The Spanish Multicentric group has been very active since it was created several years ago. The group recently published preliminary results of the 3-year follow-up [13] for HRQL in prostate cancer and also developed the Spanish-language version of the Expanded Prostate Cancer Index Composite (EPIC) [14], a questionnaire designed to evaluate the impact of prostate cancer treatment on patient quality of life. We are now working on the 5-year follow-up (grant PI08/90090 ISCIII – FEDER) to assess long-term effects of these treatments.

To conclude, the aim of this editorial is to highlight the relevant research of this group in order to illustrate what can be accomplished when Spanish researchers apply their knowledge, skills, and resources in a focused way. There is no reason why we should not be at the forefront of research and publication in our respective areas of expertise. The opportunity to provide leadership on the wider world stage is available, but it is up to us to seize the initiative, to expand our horizons, and above all, to act—with energy, passion, and conviction.

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