Chapter 01 / Capítulo 01

Advanced Prostate Adenocarcinoma and Androgen Deprivation Therapy. Clinical Outcomes, Risk Stratification, and Therapeutic Results
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Clinical Context and Problem Statement

Cancer has become a major health problem due to its high incidence and mortality rates, which have been increasing in recent years for various reasons, including increased life expectancy.

Prostate cancer affects older men more frequently than younger men do. Consequently, it is a greater health problem in developed countries, as they have a greater proportion of this age group, which affects mainly men over the age of 50.[1]

Since 1985, there has been a slight increase in the number of deaths from prostate cancer in most countries, even in countries or regions where it is not common, increasing the probability of developing this disease by 15 %, a risk that increases progressively with age, and the risk of dying from it by 3 %.[2]

In Europe, prostate cancer is the most common cancer, with an incidence of 214 cases per 1,000 men, surpassing that of lung and colorectal cancers.[3]

The highest incidence rates are found in Austria and North America (111,6 and 97,2 cases per 100 000 men, respectively). The lowest rates are reported in Asian countries (4,5—10,5 cases per 100 000 men).[4]

In South Africa and the Caribbean, mortality rates are highest in populations of African descent (19 to 24 deaths per 100 000 men).

In the United States in 2015, 220 800 new cases were diagnosed, and 27 540 people died from this cause in the same period, making it the second leading cause of death. It is estimated that 75 % of new cases are detected in people over 65 years of age, with an estimated 31 620 deaths from this disease this year.[5]

However, the death rate declined by more than half from the mid-1990s to the mid-2000s. From 2014–2018, the death rate remained stable. The survival of a particular person depends on the type of prostate cancer and the stage of the disease. There are more than 3,1 million prostate cancer survivors in the United States today.[6]

In Latin America, according to the World Health Organization's International Agency for Research on Cancer, it has an annual incidence of 54,2 %. Prostate cancer is the leading cause of death in Mexico, accounting for 21,4 % of all cancers, with an incidence of 27,3 per 100 000 men, causing 6 367 deaths in 2012, with a rate of 11,3 per 100 000 men.[7,8]

In Cuba, cancer is the second leading cause of death after cardiovascular disease in people over 50, and in men, malignant tumors of the airways are the leading cause of death. In 2017, prostate cancer was the leading cause of cancer death in men in Cuba, with a mortality rate of 55.7 per 100,000 inhabitants.[9]

Cuba's annual health statistics report that the mortality rate per 100 000 inhabitants in urban areas is 30,1 and that in rural areas is 25,2. One in ten patients may develop prostate cancer, and three in 100 may die from it. Symptoms may appear when the cancer is already very

advanced, requiring increasingly aggressive procedures that affect the patient's quality of life and life expectancy.[10]

When the disease presents, it is necessary to identify the hereditary risk factor, as this risk factor is 2–3 times greater in first-degree relatives. The most common type of prostate tumor is adenocarcinoma, and the role of mutations and changes observed in the function of various genes in its development has recently been revitalized. Most cases are located preferentially in the peripheral zone of the prostate gland (55 %-70 %) or in the transitional zone (25 %-50 %); this circumstance facilitates its eventual detection by digital rectal examination, since growth in the central zones of the gland is rare (<10 %).[11]

In patients with advanced prostate cancer, the available treatment options are very varied, and criteria such as quality of life and treatment tolerance, assuming therapeutic efficacy, have become increasingly important, as the average survival rate is approximately three years.

The therapeutic focus in these progressive forms of prostate disease is androgen deprivation, the basis for which was historically established by Huggings and Hodges in 1941 when they observed the androgen dependence of prostate cancer. Its palliative, although not curative, nature over the last 50 years allows us to emphasize its acceptance and therapeutic efficacy in this disease and its common complications, such as bone pain and obstructive uropathy.[12]

Problem and purpose of the study

Advanced prostate adenocarcinoma represents a sustained clinical challenge in contemporary urological practice. Its evolution, marked by considerable biological heterogeneity and variable clinical trajectories, requires therapeutic decisions that transcend strictly curative logic. In advanced stages, the approach is geared toward disease control, prolonging survival, and preserving quality of life.

Total androgen deprivation has been the fundamental therapeutic approach in this context for decades. Its biological basis, which is based on the hormonal dependence of prostate tumor tissue, has been widely documented. However, the clinical response to this strategy is not uniform. Progression times, the appearance of recurrences, the transition to hormone-resistant states, and variability in biomarker expression raise important questions for both clinical practice and the evaluation of therapeutic outcomes.

Within this framework, there is a need to examine the behavior of advanced prostate adenocarcinoma in specific healthcare contexts. Institutional dynamics, patient profiles, available diagnostic resources, and clinical follow-up regimens can significantly influence the observed evolution. Institutional analysis therefore allows for the identification of clinical patterns, evolutionary timelines, and operational challenges that are not always fully visible in multicenter studies or controlled trials.

The present study was conducted at the Joaquín Albarrán Domínguez Clinical Surgical Teaching Hospital, a leading institution in specialized urological care. This research aimed to characterize the behavior of advanced prostate adenocarcinoma in patients undergoing total androgen deprivation from 2017–2020. This time frame allowed for the examination of clinical evolution within a homogeneous therapeutic framework, considering relevant diagnostic, biochemical, and clinical variables.

The main purpose of the analysis was to understand how the response to total androgen deprivation manifests itself in terms of progression, recurrence, and early detection of tumor activity. Particular attention has been given to the dynamics of biomarkers, especially prostate-specific antigen (PSA), whose interpretation continues to be debated in advanced disease scenarios. The role of testosterone dosing as a complementary tool in identifying hormone resistance was also explored.

The evaluation of disease behavior is not limited to biochemical or tumor progression indicators. The patient's clinical experience, including the impact of treatment on sexual function and overall health, was a particularly relevant analytical dimension. In prolonged hormone therapies, side effects have a substantial effect on adherence, the perception of well-being, and quality of life.

From this perspective, the study integrated clinical, diagnostic, and functional objectives. This study sought to identify the time of recurrence after the start of treatment, analyze the usefulness of PSA in the early detection of signs of tumor activity, examine the sensitivity of testosterone dosing in cases of suspected hormone resistance, and characterize the impact of hormone treatment on the patient's sexual health and overall health.

Rather than offering definitive answers, the analysis aimed to construct a structured clinical interpretation of the phenomenon within the institutional context studied. The complexity of advanced prostate adenocarcinoma requires cautious interpretations, attention to individual variability and the inherent limitations of observational designs.

Justification of the Problem

Androgen deprivation therapy (ADT) is the cornerstone of treatment for advanced prostate cancer and has also been shown to play an important role in the treatment of high-risk localized cancer.

In recent years, in line with the increase in prostate cancer diagnosis owing to PSA testing, there has been a shift toward its increasing use in the early stages of the disease, either as primary treatment or as an adjunct to curative treatments such as radiotherapy.

In the socioeconomic context, it allows for adequate care and treatment of patients with advanced prostate adenocarcinoma, providing them with more personalized follow-up from the moment of diagnosis or with early detection of hormonal escape, in addition to the rational use of healthcare costs by optimizing the resources allocated to androgen deprivation therapy, reducing the use of complementary tests, and improving quality of life. From an educational and research perspective, it is the first point of reference for addressing the problem, in addition to providing updates at the center for specialists and residents in training.

Novelty of the Research

At the hospital, we do not have an evaluation of the results of treatment with total androgen deprivation in advanced prostate cancer patients. This work will allow us to obtain preliminary results related to the survival of these patients according to the risk classification at diagnosis, and the time of onset of signs of progression after treatment has been established.

Contributions

By evaluating the effectiveness of treatment with maximum androgen blockade in advanced

prostate cancer patients, we will contribute valid information to ongoing research that aims to evaluate the quality of adherence to the existing protocol at the center.