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Handbook of PROSTATE CANCER AND OTHER GENITOURINARY MALIGNANCIES

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To our patients, who have taught us so much; and to our trainees, who have worked so hard to ensure that our patients get the best care possible.

Preface

Genitourinary malignancies represent a wide spectrum of risk and prognosis. The last decade or more has brought an extraordinary evolution in outcomes for patients with these diseases at advanced stages, mainly through development and adoption of new systemic therapies. In addition, greater attention is being paid to comprehensive assessment of the patient before, during, and after treatment. More systematic measurement of influential medical and psychosocial factors has allowed for better treatment selection and symptom management.

This handbook aims to provide a broad overview and current summary of the state of assessment, diagnosis, and treatment of these malignancies. It will be useful for clinicians at multiple stages in medical and surgical specialties: in training, early in a career, and looking for updated information. With the ability to reference quickly for a specific question, or review a larger section all at once, the reader can customize the depth with which he or she uses the handbook.

This remains an exciting time for those dealing with many of these malignancies, with advances and innovations continuing in both the medical and surgical arenas. The dissemination of these developments and collaboration among specialists will continue to bring improved outcomes to our patients living with or surviving these diseases. We are grateful to the patients and providers who work together in clinical trials, which are the foundation of the progress and drive the evolution of the field forward.

We welcome your feedback and suggestions as you use this handbook in practice.

Jennifer Marie Taylor, MD, MPH

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Prostate Cancer

EARLY STAGE PROSTATE CANCER

1 Prostate Cancer Screening

Thiri Khin and Nicholas Mitsiades

INTRODUCTION

Prostate cancer is the most common visceral cancer in the United States and the second leading cause of cancer death after lung cancer. In the United States, approximately one in seven men will be diagnosed with prostate cancer. One in 39 prostate cancer patients will die from the disease. Survival of prostate cancer is related to many factors, including age and stage at diagnosis (1). Although the 5-year survival rate for early localized prostate cancer is 100%, survival is only 29.3% for distant metastatic disease.

With the goal of reducing cancer-related morbidity and mortality by early detection, screening strategies are employed in common and lethal cancers such as prostate cancer. Prostate-specific antigen (PSA) was initially developed as a tumor marker to assess the extent of disease and detect treatment response. Despite a lack of efficacy data from randomized controlled trials (RCTs), PSA was incorporated into prostate cancer screening in the early 1990s, which subsequently lead to a peak increase in the detected incidence of prostate cancer. Most of the cancers detected were early stage disease, which otherwise would have not been discovered and may not have been clinically relevant. However, early detection often led to aggressive treatment. Since then, the benefits of PSA screening have been questioned and have been a major topic of debate among clinicians and guideline organizations.

VARIATIONS OF PSA LEVEL

PSA is a glycoprotein expressed in both normal and neoplastic prostatic epithelial tissue. The PSA level reflects the amount of prostate glandular epithelium in normal healthy men. Prostate size increases with age and in turn increases the PSA level. The PSA increases by 3.2% (0.04 ng/mL) per year for a 60-year old, and reference ranges for different age groups have been proposed.

In addition, multiple factors may influence the PSA level in healthy individuals. African American men have higher PSA levels when compared to White men. Prostatitis, perineal trauma, benign prostatic hypertrophy, prostate biopsy, and ejaculation can elevate the PSA level. Medications such as 5-alpha reductase inhibitors can reduce the PSA level by up to 50%. Nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, statins, and thiazide diuretics can lower the PSA level to varying degrees. Despite these variations, a traditional cutoff of 4 ng/mL or more has been considered abnormal by most clinicians.

PSA TESTING IN MALIGNANCY

PSA levels are raised in malignancy, not only due to increased production by malignant epithelial cells but also due to disruption of vasculature and release of PSA into the bloodstream. Multiple studies have shown that a rise in PSA precedes the development of prostate cancer by 5 to 10 years. Different cancers have varying levels of PSA elevation, and poorly differentiated cancer can have a large tumor burden with minimally elevated PSA.

Using a cutoff value of 4 ng/mL, the estimated sensitivity is 21% for detecting any prostate cancer and 51% for high-grade cancer in pooled analyses. Specificity is estimated to be 91%. Positive predictive value (PPV) is 30%, which means that one in three men with PSA more than 4 ng/mL has prostate cancer. Negative predictive value (NPV) is 85% for a PSA level lower than 4 ng/mL (2). Different strategies have been tested to improve the performance of PSA testing in prostate cancer. Lowering the cutoff level increases the sensitivity level but in turn reduces specificity. Various tests such as PSA velocity, PSA