Advances and future directions in management of prostate cancer

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Abstract Despite the high cure rates of patients diagnosed and treated with prostate cancer, there is still room for improvement in management of these patients. This includes the identification of patients at highest risk for progression, the usage of focal therapies in low risk disease, and the continued improvement on established modalities. Through these avenues, the morbidity associated with treatment for prostate cancer can be vastly reduced, and thus patient outcomes improved. This article reviews the current treatment modalities and future directions for the treatment of localised prostate cancer.

Keywords Prostate cancer · Future directions · Localised

Introduction

Worldwide, prostate cancer is the most common solid malignancy in men and the incidence is rising. In the past few decades, there has been a significant shift in patients who are diagnosed with prostate cancer. With the advent of widespread PSA testing, most patients are being diagnosed with cancer prior to detection of a palpable nodule. Through transrectal ultrasound (TRUS) guided biopsy, smaller cancers are being detected and undoubtedly some of these are clinically insignificant. Unfortunately, once patients have cancer which has spread outside the prostate, all therapies are palliative. The difficulty in treating prostate cancer resides in the fact that despite an incidence of almost 16%, only 2% of men will actually succumb to their disease [1]. Our ability to identify patients with high-risk disease with likely risk of progression is not reliable enough. Even with extended biopsy techniques, the percentage of patients with more aggressive tumour than that discovered on the biopsy still exceeds 30% [2].

Improved quality-of-life following local therapy for prostate cancer has driven many of the recent advances. Historically, urinary incontinence and sexual dysfunction accompanied treatment for prostate cancer. With the possibility of detecting clinically insignificant cancers, physicians are forced to walk the thin line between over-treatment with exposure to possible adverse quality-of-life, and performing curative therapies in the window of curability. With multiple methods for treating prostate cancer, pairing each patient with the correct treatment is the most difficult decision facing both the physician and the patient. This article is a review of recent advances in the management of prostate cancer, with a focus on surgical therapies, and potential future directions.
Current advances in management options

Nomograms for risk stratification

Improvements in statistical analysis and large datasets of prostate cancer patients have produced several nomograms which can predict likelihood of aggressive prostate cancer. Initially, D’Amico and colleagues discussed the classification of patients into either low, intermediate or high risk groups [3]. The “Partin Tables,” with their most recent update, discuss the likelihood of prostate cancer that being either extraprostatic or metastatic to the lymph nodes [4]. The UCSF-Capra score predicts likelihood of 5 years recurrence, and has been validated in outside cohorts [5, 6]. Perhaps the best known are the Kattan nomograms which discuss likelihood of cancer specific survival taking into account many preoperative values including PSA, digital rectal examination, age, biopsy pathology, early hormone therapy and method of diagnosis [7]. Usage of nomograms has improved the clinician’s ability to identify patients at high risk for prostate cancer progression and death.

Active surveillance

There has been a substantial increase in low-risk patients being placed on active surveillance for the management of their cancer. Previously referred to as “Watchful Waiting,” this option has become structured with regular protocols including repeat prostate biopsy and routine follow-up visits. Clearly this is not the best option for all patients, but recent data suggests that in a highly selected group of patients, active surveillance could provide a safe alternative to radical local therapy [8, 9]. Caveats of this option include psychological distress, poor compliance, and possibly missing the window during which a cancer could be curable. Additionally, there is not a community standard for the appropriate follow-up schedule in these patients, creating many different protocols with potentially differing rates of effectiveness. Currently, data is not mature enough to evaluate this as long-term therapeutic option, however in select motivated patients this is emerging as a very attractive alternative.

Androgen deprivation therapy

Historically, androgen deprivation therapy (ADT) was considered a reasonable option for treatment of localised prostate cancer. Recently evaluation of patient outcomes for men on primary hormonal therapy for prostate cancer has demonstrated that these men are at significantly increased risks for cardiac related deaths. This trend is especially apparent in patients with a previous history of cardiac disease [10]. Overall survival showed no significant improvement with this therapy in several retrospective studies of large cohorts, and this has forced the oncologists to re-evaluate the role of ADT in localised cancer. Therefore, only in select cases ADT is given as primary treatment for localised prostate cancer. In conjunction with external beam radiation therapy, 2 years of androgen deprivation is clearly advantageous [11]. In patients with positive lymph nodes following radical prostatectomy, addition of androgen deprivation improves survival [12]. However, current evidence points to the role of androgen deprivation as a part of multimodal therapy regiment in patients requiring secondary therapies.

Focal therapies

In an effort to decrease the side effects of radical local therapy for prostate cancer, focal therapies have been developed. These therapies are aimed at biopsy sites of prostate cancer. Cryotherapy, which involves freezing specific areas of the prostate with cooling probes, and high-intensity focused ultrasound (HIFU) are the two most widely accepted methods. These are attractive options to many patients due to the precision of the technology, and potential for diminished side-effects of incontinence and erectile dysfunction. Additionally, these can be completed in a single outpatient treatment session which is attractive to physician and patient alike.

In cryotherapy for localised prostate cancer the freezing probes are introduced into the prostate under ultrasound guidance, and the prostate is given either one or two freeze thaw cycles. Physicians can evaluate the efficacy of treatment in real-time mode using ultrasonography, and these images correlate well with cellular destruction. Many technical aspects are difficult; these include the prevention of damage to surrounding tissues due to the enlarging ice ball, achieving the -40C required for tissue necrosis and identifying highly vascular “heat sinks” which may reduce efficacy. There have been early successes in the oncologic utility, as negative biopsy rates following treatment is high. In the United States a consortium of physicians has created a national database evaluating long-term oncologic success, and have demonstrated promising 5 years biochemical recurrence free survival [13].

HIFU uses hyperthermia to cause instantaneous and irreversible coagulative necrosis of the targeted tissue. In vivo and in vitro, HIFU has been demonstrated to effectively destroy prostatic cancers without increasing the risk of metastases. Due to the small focal zone, the surrounding tissues can be avoided and therefore the periprostatic nerves and continence mechanisms are theoretically spared. This can be used in conjunction with real time MRI imaging which may improve the ability to identify the malignant tissue. HIFU often requires prolonged urethral catheterisation following treatment secondary to prostatic “sloughing” which may cause obstruction [14].