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ONCOLOGY

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# Prostate Cancer

## Why We Need to Focus on Early Detection and Treatment

### Should we perform annual digital rectal examination and prostate-specific antigen testing on all male patients over 40 years old?

Adenocarcinoma of the prostate is presently the most commonly diagnosed visceral malignancy in men in the United States and the second only to lung cancer as a cause of cancer death in both the United States and New Zealand. In New Zealand, it is the second most commonly diagnosed male cancer and the third most common cause of death in males. About 1 in 10 men will be diagnosed with prostate cancer and of those, one quarter will die from this disease. This emphasises the importance of early diagnosis and treatment.

This article puts forward the case for annual digital rectal examination and prostate-specific antigen testing in all males 40 to 45 years old. Table I summarises the main points of the article.

### Does Radical Prostatectomy Affect Mortality?

The long-term results of 441 patients (mean and median age of 65 years) who underwent radical prostatectomy for early stage (T1-2) prostatic adenocarcinoma have been reported.[1-2] Patients were followed up for 13.5 years after radical prostatectomy. The following results were obtained:

1. Cancer-specific death rate following radical prostatectomy in patients with organ confined and specimen confined disease was *10%* at 13.5 years. (Organ confined = diseases into but not through the capsule; specimen confined = cancer does not contact the surgical margin of the radical prostatectomy specimen.)

2. Cancer-specific death rate in patients with margin-positive disease was *40%* at 13.5 years.

In both groups the noncancer death rate was 20%. Therefore patients with organ-confined and specimen-confined disease experienced a 30% possibility of any death at 13.5 years as opposed to a 60% possibility of death for patients with margin-positive disease.

In 105 of the 441 patients, cancer was diagnosed by trans-urethral resection of the prostate (TURP) without a palpable abnormality. Although this was done in the pre-PSA era, it still confirms the importance of surgical removal of clinically benign enlarged prostates in symptomatic patients as 10 to 15% contain cancer on histology. Initial TURP did

**TABLE I. Importance of early detection and treatment of prostate cancer**

- Prostate cancer is second only to lung cancer as a cause of cancer death in men
- Cancer-specific death rate in patients with completely removed tumours was **10%** at 13.5 years[1,2]
- Cancer-specific death rate with tumours extending to surgical margins was **40%** at 13.5 years[1,2]
- PSA-detected disease is in a more favourable disease category than palpable tumours
- The best curable tumours are those with a PSA level of 10 ng/ml and below
- A low grade tumour at biopsy is most often not an innocent, slow progressing tumour
- PSA is increased by 2.2 ng/ml for each gram of malignant tissue present
- PSA testing is not likely to detect indolent malignancies which are smaller than 0.5ml
- 91% of tumours detected in PSA screening programmes are likely to be clinically important
- Significant tumours may be present even with a PSA of < 4 ng/ml
- Annual DRE and PSA (± TRUS) on all male patients above 40 years of age is suggested

*Abbreviations:* PSA = prostate specific antigen; DRE = digital rectal examination; TRUS = transrectal ultrasound.

not change the prognosis after radical prostatectomy.[1]

In my personal experience with radical prostatectomies over the last 8 years since the PSA test became available, approximately 20% of the radical prostatectomies were performed on patients with a PSA of less than 4 ng/ml. In these patients the diagnosis was made by palpation of a small tumour (i.e. digital rectal examination (DRE) or on histology following TURP. None of these patients had margin-positive disease.

## Significance of Routine Prostate-Specific Antigen Testing

Disease detected by prostate-specific antigen (PSA) rather than DRE appears to be of smaller volume and to have a higher possibility of negative margins. Thus, PSA-detected patients will be in a more favourable disease category at surgical intervention than those with prostate cancer detected by DRE. For example, margin-positive disease exists in around 14% of those whose disease is detected only by PSA, compared to 31% with a palpable nodule on DRE.[2] The margin-positive rate decreases to 9% and 4% if a PSA level of 20 ng/ml or 10 ng/ml, respectively, is used as the upper limit. The best curable tumours are those with a PSA of 10 ng/ml and below.

In patients with elevated PSA and normal DRE, as well as in patients with palapable nodules, only 24% had the same histological grade of tumour at prostate biopsy and final radical prostatectomy specimen. In the remainder (76%), the final specimen contained a histologically-defined more aggressive tumour. A low grade tumour at biopsy is therefore most often *not an innocent, slow progressing tumour with low biological risk.*[2]

In a Mayo Clinic study,[3] there were 257 patients who were treated with radical prostatectomy for impalpable tumours detected by elevated PSA. Of these patients, 91% had clinically significant tumours. (Note however, that PSA is increased by 2.2 ng/ml for each gram of malignant tissue present and therefore PSA testing is not likely to detect indolent malignancies because such tumours are not large enough to cause elevations in serum PSA.[3])

The pathological features of carcinomas have been assessed in 100 consecutive, completely-embedded radical prostatectomy specimens from men whose cancer was detected in a PSA-based screening programme.[4] Of the 100 carcinomas, 68% were larger than 0.5ml in volume. The mean amount of carcinoma in the surgical specimen was 10.3%. Of the 100 tumours, 94% had a Gleason score of 5 to 8 (moderate to poorly differentiated) and only 6% were well differentiated. The conclusion was that the pathological features of most prostatic carcinomas detected via PSA-based screening do not resemble that of autopsy cancers and that most prostatic cancers detected in screening programmes are likely to be clinically important. [Autopsy cancers, clinically undetected during the life of the patient, are often small (less that 0.5ml), well differentiated and organ confined.]

## Conclusions

Patients usually do very well after radical prostatectomies with minimal major complications. Incontinence is normally not a major problem if a meticulous surgical technique is used. Impotence is a complication but patients respond very well to alprostadil injections. Most complications can be prevented with proper bowel preparation, prophylactic antibiotics and anticoagulants.

Keeping in mind that the median overall survival in patients with stage D2 metastatic disease, even on total androgen blockade, is less than 36 months[5] there is no doubt in my mind that early diagnosis of prostate cancer with DRE and PSA (and transrectal ultrasound where necessary) and early radical prostatectomy is the treatment of choice for prostate cancer. We all have to aim for a 90%, 13.5 year cancer-specific survival rate and currently the best way to do this is to do an *annual DRE and PSA* on all our patients above 40 to 45 years of age.

## References


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### About the Author:


Dr *Dirk Drent* is a urologist in private practice in Hamilton and in Auckland. His special interests are prostate cancer surgery and female incontinence. He has done research in bladder augmentation surgery comparing cecocystoplasty, ileocystoplasty and sigmoidcystoplasty. He was involved in clinical trials for Upjohn to evaluate the safety of Caverject injection over a 3-year period. He has also done research on the antibacterial properties of cervical mucus compared to patients who had hysterectomies and were more susceptible to recurrent urinary tract infections.

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