

Review

## Prostate Cancer in the Elderly

KONSTANTINOS N. SYRIGOS<sup>1,2</sup>, ELENI KARAPANAGIOTOU<sup>1</sup> and KEVIN J. HARRINGTON<sup>2</sup>

<sup>1</sup>Oncology Unit, Third Department of Medicine, Athens Medical School, Sotiria General Hospital, Athens, Greece;

<sup>2</sup>Cancer Research Centre for Cell and Molecular Biology, Chester Beatty Laboratories, Institute of Cancer Research, Royal Marsden NHS Trust Hospitals, Fulham Road, London, U.K.

**Abstract.** *With the significant increase of the average lifespan in the industrial world, the number of elderly people, as a proportion of the total population, has risen dramatically. It has been estimated that this trend will accelerate and that, by the year 2020, the number of people aged >80 years will soar by 135%. With age being the greatest risk factor for prostate cancer, this disease has understandably become one of the greatest public health concerns. Recently, considerable attention has been focused on prostate cancer management in the elderly, with specific emphasis on the question of whether, or not, it should differ from that of younger patients. We thoroughly reviewed the existing evidence on screening, diagnosis and treatment of prostate cancer in the elderly and concluded that age alone should not constitute an obstruction for optimal treatment administration. Physicians treating aged prostate cancer patients should be trained in an individualized approach, based on clinical performance status and comorbidities.*

The last half century has been marked by a significant shift in the age distribution of the general population. An enormous increase in the number of elderly people as a proportion of the total population is the most obvious feature of this demographic change. It has been estimated that this trend will accelerate and that, by the year 2020, the number of people aged >80 years will soar by 135%. It is also important to consider that these older individuals can anticipate a longer life, with the concomitant risk of cancer

increasing (1, 2). Although the average life expectancy for men is 70-75 years, those who attain the mean can look forward to living an additional 14 years, those reaching 80-85 years can expect a further 8 years of life and those alive at 85 years can anticipate to live for another 6 years (3). The risk of developing cancer increases with advancing age up to the age of 80-85 years and then declines. It has been estimated that, in the near future, 70% of cancers will arise in the over 65-year age group (4, 5). Normal aging refers to a common complex of diseases that characterize many of the elderly. However, not all individuals age in the same manner. Some acquire diseases and impairments, while others experience "successful" aging, which is not accompanied by debilitating disease and disability. The percentage of the latter is augmenting.

Age is the greatest risk factor for prostate cancer. In autopsy studies, the prevalence of the disease is about 30% in men aged over 50 years, while foci of adenocarcinoma occur in virtually all men aged over 90 years. As a result of increased life expectancy, there are now many more elderly men with prostate cancer (6, 7). Recently, considerable attention has been focused on prostate cancer management in the aged, with specific emphasis on the question of whether, or not, it should differ from that of younger patients.

### Elderly Patients and Co-existing Diseases

Ageing is a complex biological process. In addition to previously discussed increases in the incidence of malignant diseases, a variety of non-malignant diseases also become more common. The most common co-existing diseases in elderly patients with cancer are arthritis, hypertension, digestive tract ailments, cardiac and respiratory disorders (8). These co-existing conditions vary and many patients experience a number of fundamental tissue and organ function disturbances.

Of vital importance is the patient's underlying mental state. Mental function disturbances and depressive disorders

*Correspondence to:* Konstantinos N. Syrigos, MD, Ph.D., Asst. Prof. of Oncology in Medicine, Athens University School of Medicine, Head, Oncology Unit, 3rd Department of Medicine, Building Z, Sotiria General Hospital, 152, Mesogion Avenue, 115 27 Athens, Greece. Tel: +30 210 7475 034, Fax: +30 210 7781 035, e-mail: knsyrigos@usa.net / ksyrigos@med.uoa.gr

*Key Words:* Prostate cancer, aged, prevention, detection, review.

frequently complicate elderly patient care, impairing their ability to fully understand the disease and its management, thereby restricting optimal therapy. Furthermore, the existence of co-morbid conditions can have a significant impact on the diagnostic process and subsequent therapeutic interventions, by reducing the ability of elderly patients to tolerate these procedures.

In circumstances where treatment options are not limited by the presence of severe co-existing diseases, the elderly should not be offered management strategies that differ from those used for younger patients (9-11). Although the age of 70 years is frequently used as a cut-off point between different management strategies, a life expectancy of 10 years is probably more important than chronological age *per se*.

### Diagnosis and Screening of Prostate Cancer in the Elderly

With the development of prostate specific antigen (PSA) testing, transrectal ultrasound (TRUS) and TRUS-guided biopsy, screening for prostate cancer is now a realistic goal (12, 13). Until recently, routine PSA screening for prostate cancer was controversial and opinion on its utility was divided. Now, the American Cancer Society, the American Urological Association and the U.S. Preventive Services Task Force on Periodic Health Examination favor routine screening. While the use of PSA to diagnose subclinical prostatic carcinoma is controversial in younger men, it is easier to be categorical in older men (14, 15). Most authorities agree that there is no indication for routine screening in men aged 75 years and older or those with a medical status that renders them unlikely to live long enough for prostate cancer to become symptomatic. There is a consensus that PSA should only be measured in the elderly if there is clinical evidence of prostate cancer (16, 17). Most urinary symptoms in the elderly are not due to cancer and a marginally raised PSA level frequently causes confusion. The mean size of the prostate gland increases with age due to the development of benign prostate hyperplasia and this can account for low-level elevated PSA values. The concept of age-related PSA is useful. Age-specific reference ranges have been proposed, since PSA values and prostatic volume normally increase with age. In fact, the level of PSA above which investigation is appropriate increases with age and an 80-year-old man can be reassured that, for him, a PSA of 6.0 is normal (18). Use of such adjusted reference ranges would increase the test's sensitivity in younger men and its specificity in older men. As a result, there would be a reduction in the number of biopsies performed, but it is likely that large numbers of organ-confined tumors would be diagnosed, with questionable benefit for elderly, asymptomatic, patients.

PSA has proved most helpful in elderly men with possible prostate cancer symptoms (*e.g.* back or other bone pain)

because serum PSA is a good marker of tumor volume; the higher the level, the greater the likelihood of extraprostatic disease. Although the patient could still have localized early disease that is unlikely to cause significant problems, a PSA of less than 10 ng/ml excludes advanced prostate cancer. However, a PSA of less than 10 ng/ml could be associated with advanced high-grade prostate cancer, in androgen-deficient elderly patients. If the PSA is >100 ng/ml, it is diagnostic of prostate cancer and usually is associated with metastatic disease (19). PSA tests merely identify those for whom a biopsy should be considered.

Transrectal ultrasound may demonstrate lesions in the prostate gland that are not palpable on rectal examination. However, its main use is in guiding needle biopsy. TRUS-guided biopsy is an uncomfortable procedure and its value in older men is limited. It is recommended for patients in whom the initial biopsy is negative, although there is strong indication that they may have the disease (20). The false-negative rate is about 25%. Considering both the morbidity and discomfort of the approach, histological confirmation is somewhat academic, since a negative biopsy does not rule out the presence of prostate cancer (21-24).

### Staging of Prostate Cancer in the Elderly

Staging of prostate cancer includes a bone scan, CT scan and, in the past, an acid phosphatase measurement. With the increasing use of PSA measurement, most urologists are dropping these tests since the results are rarely positive when PSA levels are less than 10 ng/ml. For patients with PSA values higher than 20 ng/ml, imaging studies must be performed (25, 26). PSA is a good marker for tumor volume and an important survival predictor. Men older than 60 years with cancers smaller than 0.5 ml in volume are unlikely to live long enough for the tumor to grow and metastasize (27). However, volume is difficult to estimate accurately before surgery. As a surrogate marker, it has been suggested that a tumor-containing core length of 3 mm or more on one of six biopsy cores indicates a tumor volume of more than 0.5 ml.

It is a fact that, in everyday clinical practice, elderly individuals with prostate cancer compatible symptoms receive sub-optimal diagnostic evaluation. A chart review study was performed in 242 prostate cancer patients to determine whether age influenced their physicians' staging strategies. This model indicated that men received less intensive diagnostic evaluations as a function of age, even when the symptoms, co-morbidities and hospitalization were taken into account. The investigators suggested that older prostate cancer patients appear less likely to receive intensive clinical staging and therapy (28).

A number of other molecular staging strategies are currently being evaluated. The reverse transcriptase-

polymerase chain reaction (RT-PCR) assay, targeted against PSA or prostatic-specific membrane antigen (PSMA), can detect occult prostate cancer cells at sites distant from the primary tumor. Another test under investigation is the measurement of telomerase activity, since high levels are frequently found in men with poorly-differentiated prostate tumors. Whether this assay can differentiate between aggressive and more indolent forms of prostate cancer requires further investigation. Currently, such molecular staging techniques are not being used in clinical practice and carry a significant cost implication. However, if proven successful, they have the added benefit of being less invasive and, thus, more acceptable to elderly patients.

### Age and Histological Grade in Prostate Cancer

The relationship of age to histological grade of malignancy has received little attention in the medical literature. Studying the relationship between age and survival in 597 prostate carcinoma patients in England, Smedley *et al.* demonstrated that neither grading based on a modification of the Gleason score, nor survival were related to age at diagnosis (29). The same relationship was studied in 44,300 cases in Sweden; survival was decreased by about 10% in men younger than 45 and older than 75, when compared to those aged between 46 and 74 years at diagnosis, but the effect of histological grade on survival was not examined (30).

Borec *et al.* studied 4,968 cases of prostatic carcinoma, which were stratified into age groups and classified as either well-differentiated (Grades I and II) or poorly-differentiated (Grades III and IV). The cases were distributed by stage as follows: local 3,451 (75%), regional 509 (11%) and distant 636 (14%). The findings indicated that, when all stages of prostatic carcinoma were considered together, there was a direct relationship between tumor grade and patient age. In fact, it was suggested that, in the elderly, clinically apparent prostatic carcinoma is more likely to be high grade. The authors concluded that, in aged patients, there are two varieties of prostatic cancer that differ in their biological behavior: the well-differentiated type may have no ability to spread beyond the prostate while the undifferentiated type is more aggressive (31). An alternative interpretation by the Stanford University group related differentiation directly to tumor volume and evidence of spread beyond the prostate (32). In older patients, increasing tumor volume was accompanied by a rise in the number of poorly-differentiated tumors (33).

The trend towards increased grade with advanced age becomes clear when all stages of the disease are considered together. However, this trend is mainly seen in patients with localized disease and not observed in patients with distant metastases. This apparent discrepancy between

patients with localized disease and patients with regional or distant spread may be due to the biological behavior of prostatic carcinoma.

### Management of Localized Disease in the Elderly

Many aspects of prostate cancer management are controversial. Curative treatment is only considered possible if the tumor is confined to the prostate gland without invasion of the capsule. Options for the management of cancer confined to the prostate gland include watchful observation, radical prostatectomy, external beam radiotherapy, brachytherapy and cryosurgery (34-36). Elderly patients are often excluded from participating in clinical trials on the basis of their age alone, while this could instead be used as one of the inclusion criteria. In fact, more recent studies have suggested that older patients frequently wish to be involved in the decision-making process and opt for treatments comparable to those chosen by younger patients (37).

Confined cancer in this age group is usually managed expectantly. Observation is the preferred approach outside the United States and is fairly common even within the United States for stage A (nonpalpable) cancers. In watchful waiting, as it is alternatively known, the watching is of vital importance. The patient is observed to ensure that if and when an indication for treatment arises, it will lead to prompt consideration of therapeutic intervention. The reason for surveillance is that the majority of cancers will not progress sufficiently rapidly to endanger the life of the patient. With the possible exception of poorly-differentiated tumors, confined disease is only considered a threat to those with a life expectancy of more than 10 years (38). One recent study in Sweden found that the survival of patients with localized disease, who either deferred or received early treatment, was similar (39). Another study reported that men aged 65 to 75 years, with low-grade localized prostate cancer (Gleason score 2 to 4), who were untreated or received only hormone therapy, had the same survival as a control population of men of the same age, *i.e.* they had a 13% risk of dying within 10 years. However, the risk of dying within 10 years was 24% and 46%, respectively, for men with moderate (Gleason score 5 to 7) and high-grade (Gleason score 8 to 10) disease (40).

Men in their mid 70's or older, who have low- to moderate-grade localized prostate cancer, are good candidates for observation management. The same applies for men aged 65 or over who have low-grade disease or minimal tumor volume. Men at greater risk of progression may also consider this approach, since currently available treatments have not been shown to control poorly-differentiated disease. In fact, treatment outcomes for localized disease with surgery or radiation therapy are

equally effective in patients with a life expectancy of less than 10 years. Furthermore, the benefit of observation is the avoidance of complications that can occur following aggressive treatment. Another consideration is that, as men live longer, their expectations change. Sexual activity remains important for many elderly men. It is, however, important to inform patients that withholding potentially curative treatment carries the risk of tumor progression and metastasis.

### **Radical Retropubic Prostatectomy in the Elderly**

Elderly patients with surgically resectable prostate cancer require different considerations unique to their age group when this is an option. Even those without significant medical problems may have a prolonged recovery period and be at increased risk of surgical complications. The risk of these complications must be considered in light of the probability of non-cancer-related morbidity and mortality (41).

Surgical resection is considered by many surgeons to be the treatment of choice for healthy men with localized prostate cancer and a life expectancy of more than 10 years. Several investigators have suggested that radical therapy should be withheld from patients with a life expectancy of less than 10 years. The appropriate candidates for surgery are men in reasonably good health, aged 73 years or younger, with a tumor confined to the prostate gland. The morbidity and mortality of pelvic surgery in elderly patients have been examined and it was found that, in well-selected patients, the surgical outcome is positive. In a Mayo Clinic study conducted from 1966-1988, 191 patients who were <55 years old and 51 elderly patients aged >75 years old underwent radical retropubic prostatectomy. Compared with the younger cohort, the elderly patients had a higher stage and two-thirds of them had no perioperative complications. None of the elderly patients died within 5 years of the operation. However, the incidence of respiratory distress and significant urinary incontinence was greater in the elderly patients, while only they experienced delirium or confusion. The major criticism of these studies is that the older patients were well-selected, healthy men.

Unfortunately, in many patients, radical surgery does not appear to improve survival. Lu-Yao and associates found that 24% of men with organ-confined disease at the time of surgery required additional treatment within 5 years of undergoing radical prostatectomy (42). Even when the disease is confined within the prostate gland, radical surgery may be inappropriate for very old patients. All major pelvic surgery carries a high risk of deep venous thrombosis and pulmonary embolism, as well as cardiovascular and infective complications. Elderly patients are more susceptible to such complications. They also accrue less benefit from nerve-

sparing techniques; 80% of patients over 70 years are impotent after radical prostatectomy (43). A chart review study of 216 non-metastatic prostate cancer patients, treated in 10 Southern California hospitals during the years 1980-1982, has been conducted. There were significant variations in treatment intensity as a function of patient age. These data indicated that physicians and patients considered the likelihood of tolerating the therapy when deciding on therapy. The American College of Physicians has concluded that radical prostatectomy potentially adds 3 years of life to men in their 50's, 1.5 years to men in their 60's and 0.4 years to men in their 70's.

### **Radiation Treatment of Elderly Patients with Prostate Cancer**

One of the treatment options presented to patients with localized prostate cancer is radiation therapy. A major concern has been the suggestion that elderly patients are unable to tolerate the conventional radiotherapy treatment schedules. However, this is not necessarily the case and many elderly patients can tolerate radiotherapy treatment as well as younger patients (44, 45).

The U.S. national prostate cancer surveys, conducted by the Patterns of Care Study in Radiation Oncology along with the Fox Chase Cancer Center's Department of Radiation Oncology prostate cancer database, have been used to compare processes and outcomes of conventional and conformal three-dimensional (3D) radiation treatment in elderly and younger patients (46). Their data are the result of four national surveys conducted to evaluate 2210 patients treated for prostate cancer in 1973, 1978, 1983 and 1989. The results demonstrated the dramatic shift in the median age of patients treated with radiation therapy in the United States from 65 years in 1973 to 72 years in 1979. From 1973 to 1989, the 70-year or older age group increased from 28% to 63% of the population, the 75-year or older age group increased from 10% to 35%, and patients older than 80 years increased from 3% to 9%. The data suggested no significant differences in late complications of treatment between the two patient age groups (<70 years, >70 years). There was a significant decrease of 1.2 Gy in dose for older patients, but this was not thought to be biologically significant. Conventional radiotherapy techniques were associated with an increase in acute (during treatment) symptoms for patients older than 65. With modern 3D conformal therapy, which uses computer modeling to reconstruct the tumor and shielding to protect surrounding normal tissues, high doses can be delivered to the prostate from outside the body without causing an extensive amount of injury to the skin and adjacent tissues, such as the small bowel, posterior wall of the rectum, anal canal and urethra. When the conformal technique was used, the rate of acute symptoms decreased

by half, with older and younger patients experiencing the same rate of acute symptoms (47, 48).

Cohort studies of patients with clinically localized prostate cancer treated with radiation therapy found that overall survival at 10 years was not different from that for age-matched controls. It has been shown that long-term clinical control is confirmed by a normal PSA in 88% of 10-year survivors of prostate cancer (49-51). Radiation therapy of localized prostate carcinoma is as effective as surgery, while for locally advanced disease, radiotherapy is preferred to surgery, due to fewer associated complications. As for interstitial brachytherapy, there are no studies to suggest that this treatment cannot be used in the elderly.

### Management of Extraprostatic Disease in the Elderly

Metastatic prostate cancer is treated with hormone therapy, aimed at removing the sources of androgen or testosterone in the body. This can be accomplished through bilateral orchiectomy or medical castration. Diethylstilbestrol has also been used, but this non-steroidal estrogen has a higher rate of cardiovascular complications than other approaches (52). Management with luteinizing hormone-releasing analogs (*e.g.* leuporelin or goserelin), that diminish pituitary luteinizing hormone secretion and testicular testosterone production, is now favored by most clinicians (53). Hormone treatment may be more readily accepted in the elderly, being a reasonable alternative to TURP, especially in a man unfit for surgery. Men with prostate cancer presenting with urine retention will often be able to void urine spontaneously after a few weeks of hormone treatment (54, 55). Some clinicians favor total androgen ablation. This is achieved by therapy with anti-androgens (*e.g.* flutamide) whose action is to compete with circulating testosterone for androgen receptors. The adverse effects of hormone therapy include loss of libido and impotence, hot flashes and a small weight gain. Since the introduction of LHRH analogs, the number of elderly men undergoing orchiectomy has decreased. However orchiectomy has some advantages, such as simplicity, which is very important for an elderly immobile man with multiple diseases who may already be taking a wide variety of drugs.

Unfortunately, androgen deprivation therapy is not curative in extensive disease. After a period of time, androgen-resistant cells break through and spread, eventually causing death. Recent studies indicate that a patient whose cancer has become refractory to total androgen ablation may have a temporary remission of disease if anti-androgen therapy is withdrawn, but such responses are usually short-lived. The general consensus is that the majority of patients probably do not benefit from combined androgen ablation. If it has a role, it is probably in the younger patient with low volume disease.

Because hormone therapy primarily relieves metastatic disease symptoms, some clinicians believe that it should be held in reserve until symptoms develop; others favor initiating treatment as soon as metastatic disease is identified. However, early hormone therapy appears to offer no survival advantage over delayed hormone therapy (56, 57). Although advanced prostate cancer is incurable, the intervention of another disease may lead to the elderly man dying before this happens. The right decision in this case is to concentrate on prompt effective symptom palliation (57).

Symptom palliation is of paramount importance for elderly patients with metastatic prostate cancer. Analgesia, localized radiotherapy and administration of strontium-89 can usually control metastatic bone pain. The clinician must be alert for complications, notably spinal cord compression, that can often be prevented if radiotherapy is started at the first indication of symptoms and/or signs. Many men suffer from local progression and urinary symptoms or hematuria can often be palliated by a low dose of radiotherapy. Ureteric obstruction in hormone-refractory disease should be considered a terminal event (58). While a remission with nephrostomy drainage or stents might be useful for the younger man, the imposition of these is rarely justified in the elderly.

### Conclusion and Recommendations

Elderly patients with prostate cancer should be carefully evaluated. The choice of therapy for localized prostate cancer should be guided by patient life expectancy considerations and the ability to tolerate treatment. Elderly men are more likely to be left without treatment, since the potential benefits of therapy are small and watchful waiting is a reasonable alternative. Further studies are needed to prospectively investigate patient preferences, quality of life and survival in elderly prostate cancer patients. Meanwhile, physicians need to consider life expectancy and the quality of life in making screening, staging and treatment choices. Decisions based on age alone are likely to result in a reduced cure potential or compromised quality of life in elderly men with this disease. Physicians responsible for the management of prostate cancer patients should always bear in mind that rigid formulae seldom provide solutions and that management strategies should be individualized.

### References

- 1 Coeburg JWW: Significant trends in cancer in the elderly. *Eur J Cancer* 32A: 569-570, 1996.
- 2 Golini A and Lori A: Aging of the population, demographic and social changes. *Aging* 2: 319-336, 1990.
- 3 McKenna RJ: Clinical aspects of cancer in the elderly. *Cancer* 74: 2107-2117, 1994.

- 4 Ashkanani F, Heys SD and Eremin O: The management of cancer in the elderly. *J R Coll Surg Edinb* 44: 2-10, 1999.
- 5 Joint NCI-EORTC consensus meeting on neoplasia in the elderly. *Eur J Cancer* 27: 653-667, 1991.
- 6 Coory MD and Baade PD: Urban-rural differences in prostate cancer mortality, radical prostatectomy and prostate-specific antigen testing in Australia. *Med J Aust* 182: 112-115, 2005.
- 7 Sangar VK, Ragavan N, Matanhelia SS, Watson MW and Blades RA: The economic consequences of prostate and bladder cancer in the UK. *BJU Int* 95: 59-63, 2005.
- 8 Repetto L, Granetto C and Venturino A: Comorbidity and cancer in the aged: the oncologists' point of view. *Rays* 22: 17-19, 1997.
- 9 Mor V, Masterson-Allen S, Goldberg RJ *et al*: Relationship between age and diagnosis and treatments received by cancer patients. *J Am Geriatr Soc* 33: 585-589, 1985.
- 10 Wettle VT: Age as a risk factor for inadequate treatment (editorial). *JAMA* 258: 516, 1987.
- 11 Kennedy BJ: Aging and cancer. *J Clin Oncol* 6: 1903-1911, 1988.
- 12 Pepe P and Aragona F: Prostate needle biopsy: 12 vs. 18 cores – is it necessary? *Urol Int* 74: 19-22, 2005.
- 13 Roobol MJ, Roobol DW and Schroder FH: Is additional testing necessary in men with prostate-specific antigen levels of 1.0 ng/mL or less in a population-based screening setting? *Urology* 65: 343-346, 2005.
- 14 Albertsen PC: Screening for prostate cancer is neither appropriate nor cost-effective. *Urol Clin N Am* 23: 521-530, 1996.
- 15 American College of Physicians. Screening for prostate cancer. *Ann Inter Med* 126: 480-487, 1997.
- 16 Barry MJ, Fleming C, Coley CM *et al*: Should Medicare provide reimbursement for prostate-specific antigen testing for early detection of prostate cancer? Part III: Management strategies and outcomes. *Urology* 46: 277-289, 1995.
- 17 Coley CM, Barry MJ, Fleming C *et al*: Early detection of prostate cancer. Part I: Prior probability and effectiveness of tests. *Ann Inter Med* 126: 394-406, 1997.
- 18 Oesterling JE, Cooner WH, Jacobson ST *et al*: Influence of patient age on the serum PSA concentration. An important clinical observation. *Urol Clin N Am* 20: 671-680, 1993.
- 19 Kirk D: Prostate cancer in the elderly. *Eur J Surg Oncol* 24: 379-383, 1998.
- 20 Fleming C, Wasson JH, Albertsen PC *et al*: A decision analysis of alternative treatment strategies for clinically localized prostate cancer. *JAMA* 269: 2650-2658, 1993.
- 21 Reissigl A, Pointner J, Strasser H *et al*: Frequency and clinical significance of transition zone cancer in prostate cancer screening. *Prostate* 30: 130-135, 1997.
- 22 Brewster SF, Rooney N, Kabala J *et al*: Fatal anaerobic infection following transrectal biopsy of a rare prostatic tumour. *Br J Urol* 72: 977-978, 1993.
- 23 Rabrani F, Stroumbakis N, Kaya BR *et al*: Incidence and clinical significance of false-negative sextant prostatic biopsies. *J Urol* 159: 1247-1251, 1998.
- 24 Kanamaru H, Arai Y, Moroi S *et al*: Long-term results of definitive treatment in elderly patients with localized prostate cancer. *Int J Urol* 5: 546-549, 1998.
- 25 Albertsen P: Prostate disease in older men: 2. Cancer. *Hosp Pract* 15: 159-166, 1997.
- 26 Murphy GP, Natarajan N and Pontes JE: The national survey of prostate cancer in the United States by the American College of Surgeons. *J Urol* 127: 928-934, 1982.
- 27 Bosch JL, Bohnen AM and Groeneveld FP: Validity of digital rectal examination and serum prostate specific antigen in the estimation of prostate volume in community-based men aged 50 to 78 years: the Krimpen Study. *Eur Urol* 46: 753-759, 2004.
- 28 Stamey TA: The era of serum prostate specific antigen as a marker for biopsy of the prostate and detecting prostate cancer is now over in the USA. *BJU Int* 94: 963-964, 2004.
- 29 Smedley HM, Sinnott M, Freedman LS *et al*: Age and survival in prostate carcinoma. *Br J Urol* 55: 529-533, 1983.
- 30 Adami HO, Norlen BJ, Malke B *et al*: Long term survival in prostate carcinoma, with special reference to age as a prognostic factor. A nation-wide study. *Scand J Urol Nephrol* 20: 107-112, 1986.
- 31 Borec D, Butcher D, Hassanein K *et al*: Relationship of age to histologic grade in prostate cancer. *Prostate* 16: 305-311, 1990.
- 32 Stamey TA, McNeal JE, Freiha FS *et al*: Morphometric and clinical studies on 68 consecutive radical prostatectomies. *J Urol* 139: 1235-1241, 1998.
- 33 Arredondo SA, Downs TM, Lubeck DP *et al*: Watchful waiting and health related quality of life for patients with localized prostate cancer: data from CaPSURE. *J Urol* 172: 1830-1834, 2004.
- 34 Varkarakis J, Wirtenberger W, Pinggera G *et al*: Evaluation of urinary extravasation and results after continence-preserving radical retropubic prostatectomy. *BJU Int* 94: 991-995, 2004.
- 35 Bott SR, Freeman AA, Stenning S, Cohen J and Parkinson MC: Radical prostatectomy: pathology findings in 1001 cases compared with other major series and over time. *BJU Int* 95: 34-39, 2005.
- 36 Okamoto H, Terai C and Kamatani N: Delayed therapy with curative intent in a contemporary prostate cancer watchful-waiting cohort. *BJU Int* 94: 1401-1402, 2004.
- 37 Samet J, Hunt WC, Key C *et al*: Choice of cancer therapy varies with patient age. *JAMA* 255: 3385-3390, 1986.
- 38 Shah SA, Cima RR, Benoit E, Breen EL and Bleday R: Rectal complications after prostate brachytherapy. *Dis Colon Rectum* 47: 1487-1492, 2004.
- 39 Johansson JE, Holmberg L, Johansson S *et al*: Fifteen-year survival in prostate cancer: a prospective population-based study in Sweden. *JAMA* 277: 467-471, 1997.
- 40 Albertsen PC, Fryback DC, Storer BE *et al*: Long-term survival among men with conservatively treated localized prostate cancer. *JAMA* 274: 626-631, 1995.
- 41 Kerr L and Zincke H: Radical retropubic prostatectomy for prostate cancer in the elderly and the young: complications and prognosis. *Eur Urol* 25: 305-311, 1994.
- 42 Lu-Yao GL, Potosky AL, Albersten PC *et al*: Follow-up prostate cancer treatments after radical prostatectomy: a population based study. *J Natl Cancer Inst* 88: 166-172, 1996.
- 43 Christopher K, Payne I, Joseph W *et al*: Genitourinary problems in the elderly. *Surg Clin N Am* 74: 401-407, 1994.
- 44 Huguenin PU, Bitterli M, Lutolf UM *et al*: Localised prostate cancer in elderly patients. Outcome after radiation therapy compared to matched younger patients. *Strahlenther Onkol* 175: 554-558, 1999.
- 45 Olmi P and Ausili-Cefaro G: Radiotherapy in the elderly: a multicentric prospective study on 2060 patients referred to 37 Italian therapy centers. *Rays* 22(supp): 53-56, 1997.

- 46 Hanks GE, Hanlon A, Owen JB *et al*: Patterns of radiation treatment of elderly patients with prostate cancer. *Cancer 74(supp)*: 2174-2177, 1994.
- 47 Soffen EM, Hanks GE, Hunt M *et al*: Conformal static field radiation therapy treatment of early prostate cancer *versus* non-conformal techniques: a reduction in acute morbidity. *Int J Radiat Oncol Biol Phys 24*: 485-488, 1992.
- 48 Epstein B, Peter R, Martin E *et al*: Low complication rate with conformal radiotherapy for cancer of the prostate. *Radiother Oncol 24 abstract 3*: 94, 1992.
- 49 Hanks GE, Perez CA, Kozar M, Asbell SO, Pilepich MV and Pajak TF: PSA confirmation of cure at 10 years of T1B, T2, N0, M0 prostate cancer patients treated in RTOG protocol 7706 with external beam irradiation. *Int J Radiat Oncol Biol Phys 30(2)*: 289-292, 1994.
- 50 Kim BS, Lashkari A, Vongtama R, Lee SP and Parker RG: Effect of pelvic lymph node irradiation in salvage therapy for patients with prostate cancer with a biochemical relapse following radical prostatectomy. *Clin Prostate Cancer 3*: 93-97, 2004.
- 51 Geinitz H, Zimmermann FB and Molls M: Radiotherapy of the elderly patient. Radiotherapy tolerance and results in older patients. *Strahlenther Onkol 175*: 119-127, 1999.
- 52 Prostate Cancer Trialists Collaborative Group: Maximum androgen blockade in advanced prostate cancer: an overview of 22 randomized trials with 3283 deaths in 5710 patients. *Lancet 346*: 265-269, 1995.
- 53 Huggins C and Hodges CV: Studies in prostate cancer. 1. The effect of castration of oestrogen and of androgen injection on serum phosphatases in metastatic carcinoma of the prostate. *J Urol 168*: 9-12, 2002.
- 54 Okamoto H, Terai C and Kamatani N: Delayed therapy with curative intent in a contemporary prostate cancer watchful-waiting cohort. *BJU Int 94*: 1401-1402, 2004.
- 55 Katz A: Androgen replacement therapy in aging men. *Nurse Pract 29*: 58-64, 2004.
- 56 Templeton H and Coates V: Evaluation of an evidence-based education package for men with prostate cancer on hormonal manipulation therapy. *Patient Educ Couns 55*: 55-61, 2004.
- 57 Siddiqui K, Abbas F, Biyabani SR, Ather MH and Talati J: Role of estrogens in the secondary hormonal manipulation of hormone refractory prostate cancer. *J Pak Med Assoc 54*: 445-447, 2004.
- 58 Paul AB, Love C and Chisholm GD: The management of bilateral ureteric obstruction and renal failure in advanced prostate cancer. *Br J Urol 74*: 642-645, 1994.

*Received May, 2005*  
*Accepted July 26, 2005*