Contemporary Results of Anatomic Radical Prostatectomy

William J. Catalona, MD, Christian G. Ramos, MD, Gustavo F. Carvalhal, MD

Abstract
With current clinical practice, most newly diagnosed cases of prostate cancer are potentially life-threatening yet still curable. The anatomical (nerve-sparing) radical prostatectomy has dramatically improved the results of surgical treatment. Other new management options, including conformal (three-dimensional) external beam radiation therapy, radioactive seed implantation (brachytherapy), cryoablation, and hormonal therapy, may be useful in some patients, but they are all probably less effective than radical prostatectomy.

Suitability for radical prostatectomy generally requires a clinically localized, potentially life-threatening tumor [as defined by Gleason grade, tumor stage, and serum prostate-specific antigen (PSA) level], a life expectancy of 10 years, and no serious co-morbid medical conditions.

With contemporary radical prostatectomy, about 70% of men with clinically localized disease will be cured, depending on tumor grade, tumor stage, and the serum PSA level.

Urinary continence and sexual potency can be preserved in most patients, but substantially better results have been reported from centers of excellence than from community-based series. Other complications occur in about 10% of patients and with greater frequency in older patients. The operative mortality rate is less than 0.5%.

Neoadjuvant hormonal therapy does not appear to affect treatment failure rates in patients undergoing radical prostatectomy. Prostatectomy may be beneficial in patients with microscopic lymph node metastases. Postoperative adjuvant radiotherapy may also be beneficial for patients with adverse pathologic findings.

Salvage radical prostatectomy after radiation failure is associated with a 10-fold higher risk of complications and limited prospects for cure.

Prospective, randomized clinical trials are underway to compare the results of radical prostatectomy with other treatments. Currently, radical prostatectomy is considered the preferred treatment for men with localized disease and a 10-year life expectancy. (CA Cancer J Clin 1999;49:282-296.)

Introduction
It is estimated that in 1999, 179,300 new cases of prostate cancer will be diagnosed in the United States.¹ The majority of these will be moderately- or poorly-differentiated and localized to the prostate gland. Thus, most will be both potential-
ly life-threatening and curable with radical prostatectomy.

Radical prostatectomy was described by Young in 1905 for the treatment of localized prostate cancer. Because of the anatomic inaccessibility of the prostate gland, radical prostatectomy is a difficult operation to perform with the potential for significant adverse side effects. Therefore, over the years, simpler means of treating patients with prostate cancer have been sought. Alternatives to surgery have provided options for some patients, but because of questions concerning the relative efficacy of alternative treatments, they have not supplanted radical prostatectomy.

Surgical Techniques

Radical prostatectomy was not adopted widely until recently for two reasons. First, until the development of modern surgical techniques, the morbidity and mortality rates associated with radical prostatectomy were major deterrents to surgical therapy. In 1982, Walsh introduced a refined technique for performing radical retropubic prostatectomy. This operation, called the anatomic or nerve-sparing radical prostatectomy, involves removing the prostate with controlled hemostasis and clearer visualization of the external urethral sphincter mechanism and of the neurovascular bundles that innervate the corpora cavernosa of the penis. These neurovascular bundles are responsible for erections. With this operation, urinary continence and erections can be preserved in the majority of patients, and the reported operative mortality rate is 0 to 0.4%. Subsequent refinements allow radical prostatectomy to be safely and effectively performed via either a perineal or retropubic approach.

In addition, radical prostatectomy was usually not effective in eradicating cancer entirely until the development of prostate specific antigen (PSA) testing for early cancer detection, which made it possible to identify prostate cancer at a curable stage. With the advent of PSA testing, there was an initial rapid increase in the use of radical prostatectomy that peaked in 1992 and has been followed by a sharp decrease in utilization, corresponding to the declining number of new cases diagnosed.

Other Management Options

For a man with a potentially life-threatening, clinically localized prostate cancer, radical prostatectomy is the only treatment that reliably ablates the prostate gland. Thus, if the cancer is truly confined to the prostate gland, cure is assured. The same cannot be said for the other management options.

With external beam radiation therapy, for example, a significant proportion of tumors contain some cancer cells that are resistant to therapeutic doses of radiation, as judged by rates of tumor recurrence or persistence within the fields of treatment. Radiotherapy administered by implantation of radioactive seeds (brachytherapy) is also unreliable. Moreover, with brachytherapy, the success of the procedure depends more on the skill of the treating physician than it does with external beam radiotherapy. Even in the best of hands, at least 15% of cases treated with brachytherapy are subject to an uneven distribution of the radiation dose due to an imperfect distribution of the radioactive seeds.

Cryoablation is similarly limited by non-uniform freezing of the prostate gland, leading to a high rate of local treatment failure. Primary hormonal thera-
therapy does not eradicate all cancer cells, as evidenced by the inevitable emergence of androgen-independent cancer cells over time in most patients, although hormonal therapy may suppress the tumor for the life of the patient, in some instances. And finally, watchful waiting risks allowing the cancer to progress to a stage where treatment options are more limited.17,18 Nevertheless, radical prostatectomy has its drawbacks, too. If the cancer has spread beyond the prostate, the operation becomes merely the first step in multimodality therapy (e.g., postoperative radiotherapy, hormonal therapy, chemotherapy, etc.), potentially adding its side effects to those of subsequent treatments. Despite this risk, the reported results of radical prostatectomy are unsurpassed by any other treatment for clinically localized prostate cancer,5,6,19 such that radical prostatectomy is considered the “gold standard” for treatment of early-stage disease in otherwise healthy men with localized disease.

Patient Selection

If a patient with clinically detectable prostate cancer is not effectively treated, signs or symptoms of disease progression requiring treatment will usually emerge within seven to 10 years of diagnosis.17 Thus, in current practice, suitability for radical prostatectomy requires a clinically localized, potentially life-threatening tumor (judged by tumor stage and grade, and, recently, PSA levels), a life expectancy of 10 years, and no serious co-morbid medical conditions that would preclude a major operation.

In recent years, life expectancy estimates for men in the United States have increased. An otherwise healthy 75-year-old man now has a life expectancy of more than 10 years.20 The generally accepted upper-age limit for performing radical prostatectomy has been 70 to 75 years of age because this age range defined a 10-year life expectancy. However, an increasing proportion of men in their mid to late 70s now technically meet the criteria for radical prostatectomy. This is especially true in men with high-grade tumors that can be rapidly lethal.

Careful consideration of the risks and benefits of each of the management options should be evaluated on an individual basis. It is important to recognize that postoperative complications occur more frequently in older patients.4 In addition, patients whose life expectancy is limited will derive fewer benefits from the more aggressive potentially curative treatments compared with palliative treatment alone.

Clinically Significant Versus Possibly Harmless Prostate Cancer

At the lower limits of tumor aggressiveness, it is impossible to accurately distinguish harmless prostate cancers from potentially life-threatening ones based upon tumor size and grade alone.

In attempting to define the tumor volume criterion for harmless prostate cancer, Epstein et al 21 found that 13% of tumors as small as 0.2 to 0.5 cc had spread beyond the prostate at the time of treatment. In general, patients whose tumor volumes are larger than 0.2 cc and whose tumor Gleason grades are greater than 5 are considered at risk for illness or death from prostate cancer.17 Studying a group of men with clinically localized prostate cancer that was managed conservatively, Albertsen et al 17 calculated the relationship between Gleason grade and death from prostate cancer after 15 years of follow-up. Death occurred in 4% to 7% of patients with Gleason grades 2 to 4; in 6% to 11% of those with Gleason grade 5 or less; in 18% to 30% with Gleason grade 6; in 42% to 70% of those with Gleason grade 7; and in 60% to 87% with Gleason grades 8 to 10.

Contemporary Results of Radical Prostatectomy

There are only a few large contemporary
published series of patients treated with radical prostatectomy that have had prospective, continuous follow-up from one to 15 years.\textsuperscript{5,6,8,19,22-24} Even in these series, relatively few patients were followed for 10 years or more. Moreover, all series that span a 15-year interval begin to lose relevance as the nature of the prostate cancers detected changes with modern methods of detection.\textsuperscript{25} In most of these series, for instance, the great majority (80\% to 90\%) of patients had intermediate or high-grade cancers.

In general, statistics from these published contemporary series have been remarkably similar, suggesting that about 70\% of men with clinically localized disease are cured with radical prostatectomy. Our own series of 2,275 consecutive radical prostatectomies performed by one author (WJC) at Washington University during the 16-year interval from 1983 to 1999 has yielded cancer-control results that are fairly representative of those reported by other high-volume academic centers. A recent analysis of 1,778 consecutive patients\textsuperscript{19} is summarized briefly here.

**Tumor Recurrence, Overall Survival, Cancer-Specific Survival**

In a patient who has undergone radical prostatectomy, a rising serum PSA level is virtually always the first sign of cancer recurrence, with clinical evidence of cancer progression usually following, albeit at varying rates. In our series, 64\% of patients had pathologically confirmed organ-confined disease (this percentage has increased in recent years with PSA screening); 4\% had extraprostatic tumor extension with negative (tumor-free) surgical margins; 21\% had extraprostatic tumor extension with positive (cancerous) margins; 9\% had seminal vesicle invasion; and 2\% had lymph node metastases.

To date, with follow-up ranging between one and 15 years, 19\% of these men have had biochemical, clinical, or radiographic evidence of cancer recurrence. Most of recurrences occurred within two to three years of surgery, although some occurred as late as 11 years or more after surgery.

The seven-year all-cause survival rate was 90\% and the cancer-specific survival rate was 97\% (i.e., only 3\% of patients died of prostate cancer within seven years of surgery). This cancer-specific survival rate is consistent with the results reported from other contemporary radical prostatectomy series\textsuperscript{5,6,22} but is higher than that reported from earlier radical prostatectomy series,\textsuperscript{8,23,26,27} (rates ranged from 75\% to 97\% cancer-specific survival, depending on tumor grade and stage). It is also higher than the cancer-specific survival rates reported with conservative management\textsuperscript{17,18} and external beam radiation therapy.\textsuperscript{28}

**Cancer Control Results**

**Clinical and Pathological Stage**

In our series,\textsuperscript{19} patients with nonpalpable prostate cancer (i.e., clinical stage T1, detected solely through PSA testing without a palpable abnormality in the prostate gland) had a seven-year PSA progression-free survival rate of 79\% versus 66\% for men with palpable tumors (stage T2) (Fig. 1). Seven-year progression-free survival was 81\% in patients whose cancer was pathologically confined to the prostate; 76\% in those with extraprostatic tumor extension and negative surgical margins; 57\% with extension of cancer beyond the capsule of the prostate with positive surgical margins; 26\% with seminal vesicle invasion; and 19\% with lymph node metastases (Fig. 2).

**Tumor Grade**

Seven-year progression-free survival was 84\% in patients with Gleason grade 2 to 4 tumors, 68\% with Gleason grade 5 to 7 tumors, and 48\% with Gleason grade 8 to 10 tumors (Fig. 3).
PSA Level

Seven-year progression-free survival was 93% for patients with preoperative serum PSA levels less than 2.5 ng/ml; 80% with levels of 2.5 to 4.0 ng/ml; 76% with levels of 4.1 to 10 ng/ml; and 40% with levels greater than 10 ng/ml (Fig. 4).

Results at other large centers have been similar. At Johns Hopkins University, Walsh et al5,24 reported an overall 68% 10-year PSA progression-free survival rate and a 93% cancer-specific survival rate. The 10-year likelihood of progression-free survival by clinical stage in that series was 100% for stage T1a; 89% for T1b; 86% for T1c; 68% for T2a; 57% for T2b; 53% for T2c; and 52% for T3a (eight years).

The 10-year progression-free survival was 94% for those with tumors of Gleason grade 2 to 4; 91% for Gleason grade 5; 78% for Gleason grade 6; 46% for Gleason grade 7; and 23% for Gleason grade 8 to 10.

The 10-year progression-free survival for men with preoperative serum PSA levels of 0 to 4 ng/ml was 87%; for levels between 4.1 and 10 ng/ml, 75%; for levels from 10.1 to 20 ng/ml, 30%; and for levels greater than 20 ng/ml, 28%.

In the large contemporary series from the Baylor College of Medicine, Eastham and Scardino6 reported five-year PSA progression-free survival results of 95% for
organ-confined disease, 81% for extraprostatic tumor extension, 40% for seminal vesicle invasion, and 35% with lymph node metastases. In a recent update of the Baylor series, the overall 10-year progression-free survival was 71% and the cancer-specific survival was 98%. At the University of California, Los Angeles, Stein et al reported less favorable survival results. In the Mayo Clinic series, 10-year PSA progression-free survival rates were 70% for stage T1 disease, 56% for stage T2a, and 47% for T2b/c (not all patients underwent PSA testing). The cancer-specific survival rate was 92% at 10 years and 80% at 15 years of follow-up.

**Postoperative Complications**
Outcomes of prostate cancer treatment have generally improved over the past two decades. Nevertheless, it has been suggested that, because of patient selection, results from high-volume centers may not be generalizable to other patient populations; in addition, there is a tendency for studies from large centers with better outcomes to be over-represented in the literature.

**Urinary Incontinence**
Preservation of urinary continence requires meticulous dissection at the apex of the prostate.

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**Figure 2**
Probability of Non-Progression Following Radical Prostatectomy According to Pathologic Stage

Seven-year probability (and 95% confidence intervals) of non-progression following radical prostatectomy stratified by pathologic stage: 81% (77% to 84%) with pT1 or pT2 disease; 76% (59% to 92%) with pathologic pT3a/pT3b disease with negative margins; 57% (49% to 65%) with pathologic stage pT3a/pT3b disease, with positive margins; 26% (15% to 36%) with pathologic stage pT3c disease; and 19% (0 to 34%) with stage N1 disease. Adapted with permission from Catalona and Smith.
the prostate to avoid injury to the external urinary sphincter mechanism. Due to individual anatomic variability, however, even in the most experienced hands, at least 8% of patients are affected to some degree with postoperative urinary incontinence. Stress incontinence is mild in the great majority of incontinent patients, but incontinence severe enough to require surgical treatment, such as collagen injection, bladder neck suspension, or implantation of an artificial urinary sphincter, occurs in 1% to 2% of patients. Although most patients adapt reasonably well to incontinence and impotence, patients usually consider urinary incontinence a more bothersome side effect than impotence.

In our series, patients were considered incontinent if they had urinary leakage that required any type of protection (e.g., pads, tissue, etc.) to keep their clothing dry. Using this definition, 96% of men younger than 70 years of age and 87% older than 70 years recovered urinary continence within 18 months of radical prostatectomy. In more recent years, approximately half of patients have had recovery of urinary control immediately after catheter removal, and most of the remaining patients recovered continence within weeks to a few months of catheter removal. Some patients, however, expe-
rienced slower recovery of urinary control, which can take 12 to 18 months after surgery. Similar results have been reported from Baylor, Johns Hopkins, and the Mayo Clinic.

At Johns Hopkins, Walsh et al reported complete urinary control in 92% of patients, stress incontinence in 8%, 6% wore one or fewer pads per day, and 0.3% required an artificial urinary sphincter for severe incontinence. At Baylor, Eastham reported that 91% regained continence, including 95% of those treated after 1990. The median time to return of continence was 1.5 months in the patients treated after 1990.

With notable exceptions, considerably less favorable results have been reported by most community-based series, mixed academic-community series, and retrospective surveys. For example, 40% of patients from a California HMO reported daily urinary leakage; in a survey of Medicare patients, 31% were incontinent; and 20% of patients in a survey of hospital tumor registries maintained by the American College of Surgeons required pads on a daily basis. A study of patients from a mixed academic-community multidisciplinary
cancer clinic\textsuperscript{38} reported that 14\% to 50\% of patients were wearing pads for urinary leakage. An interesting exception to this pattern is the group of patients treated at Stanford University,\textsuperscript{35} 20\% of whom required pads, whereas 95\% of those who were treated in a California community practice achieved complete continence.\textsuperscript{36}

The reasons for the reported variability in continence rates are unclear. Important factors may be patient selection, surgical expertise, the definition of continence that was used for reporting purposes, and the methods by which the data on continence were collected (i.e., reporter bias). In many of the series from major treatment centers, the data have been largely collected by the operating surgeons. In surveys, the data were collected using validated questionnaires by third-party research assistants. The extent to which each of these factors is responsible for the variability of results is uncertain.

**IMPOTENCY**

With bilateral nerve-sparing prostatectomy, it is possible to preserve erections in most patients who had normal erections preoperatively. Recovery of erections usually takes longer than recovery of continence. In most patients, erections begin to return three to six months after prostatectomy and continue to improve for 18 to 24 months or longer. Presumably, the delay in recovery is due to the time required for the cavernosal neurovascular bundles to recover from the surgical trauma (traction, sutures, etc.) sustained during removal of the prostate.

The early postoperative use of artificial means of inducing erections, such as administration of sildenafil (Viagra), intraduodenal or intracavernosal injections of vasoconstrictors (e.g., alprostadil), or the use of a vacuum erection device is recommended to permit patients to resume normal sexual relations during the period of recovery. It has been suggested that the early use of these agents may hasten the return of natural erections.\textsuperscript{40}

Age is strongly associated with recovery of erections. In our series,\textsuperscript{4} in men with normal preoperative erections, 86\% younger than 50 years of age, 80\% in their 50s, 60\% in their 60s, and 42\% aged 70 or older recovered erections sufficient for penetration and intercourse within 18 months of bilateral nerve-sparing surgery. With unilateral or partial bilateral nerve-sparing surgery, the results were less favorable, with recovery of erections occurring in 42\% to 53\% of various age groups.

There was a strong correlation between the quality of preoperative erections and the likelihood of recovery of erections. For example, only about 20\% of patients with marginal preoperative erections (rated as five on a scale of one to 10) recovered erections as compared with nearly 80\% whose preoperative erections were completely normal (rated 10 on a scale of one to 10). In most patients, postoperative erections were not as rigid as preoperative erections; however, in some patients, erections returned to their preoperative quality.

At Johns Hopkins, Walsh et al\textsuperscript{5} reported on 503 patients who were potent preoperatively and were followed for a minimum of 18 months: 68\% were potent postoperatively. Sexual function was preserved in 91\% of men younger than 50 years old, 75\% of men in their 50s, 58\% of men in their 60s, and 25\% of men aged 70 years or older. Walsh also reported that there was a two-fold increased risk of postoperative impotency if there was extraprostatic tumor extension.

Nerve-sparing surgery can be accomplished with both perineal and retropubic prostatectomy; however, the advantage of the retropubic approach is that it allows the prostate to be lifted off the neurovascular bundles that lie posterolateral to the prostate. With the perineal approach, the prostate lies behind the neurovascular bundles, requiring mobilization and delivery through them, which involves a greater risk of nerve injury from traction.
There are limited reports in small series of nerve-sparing surgery being performed via the perineal approach. Frazier et al\textsuperscript{41} reported a 77% potency rate in 22 patients and Weldon et al\textsuperscript{36} reported a 70% potency rate in 50 patients.

Results of nerve-sparing surgery reported from community series,\textsuperscript{37} mixed academic-community series,\textsuperscript{38} and patient survey series\textsuperscript{30-32} have also been, with exceptions, strikingly less favorable than those reported by high-volume prostate cancer surgery centers. One group of community urologists reported recovery of erections in 46% of patients treated with bilateral nerve-sparing surgery and 28% treated with unilateral nerve-sparing procedures.\textsuperscript{42} In another community series,\textsuperscript{37} only 18% who were potent preoperatively retained potency postoperatively. In a survey of Medicare patients treated between 1988 and 1990, only 11% of patients had erections sufficient for intercourse following surgery.\textsuperscript{31} This series largely comprised older patients with lower rates of preoperative potency.

In the American College of Surgeons Survey,\textsuperscript{39} only 30% had erections adequate for intercourse. Litwin et al\textsuperscript{32} reported that only 29% of patients treated in a California HMO had erections firm enough for intercourse or foreplay. Talcott et al\textsuperscript{38} reported on a series from a mixed academic-community multidisciplinary cancer clinic; of these, only 18% of men who underwent bilateral nerve-sparing surgery and 3% who underwent unilateral nerve-sparing surgery were potent at 12 months postoperatively.

Again an exception to the pattern was the series from Stanford University\textsuperscript{43} in which only 16% of patients who underwent bilateral nerve-sparing surgery and 5% who had unilateral nerve-sparing surgery had good erections, whereas Weldon et al\textsuperscript{36} in a community series reported that potency was preserved in 70% of patients who were fully potent preoperatively. The extent to which this variability is due to patient selection, surgical expertise, definition of potency, and reporter bias is uncertain.

\textbf{OTHER COMPLICATIONS}

In our series,\textsuperscript{4} other postoperative complications occurred in about 10% of patients. Complications included vesicourethral anastomotic stricture in 4%, thromboembolic complications in 2%, delayed inguinal hernia in 2%, and myocardial infarction, lymphatic complications, infectious complications, neurologic complications, or other miscellaneous complications in fewer than 1% each.

Complications occurred more frequently in older patients (4% in men in their 40s, 9% in those in their 50s, 11% in men in their 60s, and 14% in those in their 70s). Postoperative complication rates were lower with increasing experience of the surgeon. For example, in our series, the postoperative complication rate has decreased from 20% during the mid-1980s to about 6% more recently. Other centers have reported similarly low complication rates,\textsuperscript{6,44} except in previously irradiated patients.\textsuperscript{45}

In our series, there has been no operative mortality. Operative mortality rates reported in other comparable series are less than 0.4%,\textsuperscript{6,23} and in the American College of Surgeons 1993 Survey,\textsuperscript{39} the operative mortality rate was 0.4%.

\textbf{OTHER ISSUES}

Several other important issues with regard to radical prostatectomy include the role of neoadjuvant hormonal therapy; the role of pelvic lymphadenectomy; the management of patients with pathologic evidence of extraprostatic tumor extension, positive surgical margins, seminal vesicle invasion or lymph node metastases; the management of late tumor recurrences; and the role of salvage radical prostatectomy after failure of primary radiation therapy.

\textit{Neoadjuvant Hormonal Therapy}

Several clinical trials\textsuperscript{46,47} have shown that administering neoadjuvant hormonal
therapy for three months before radical prostatectomy will reduce the incidence of positive surgical margins but will not decrease the PSA failure rate. Some researchers have suggested that this may benefit subsets of patients with high-grade tumors and those with higher PSA levels. Moreover, it has been suggested that future studies should evaluate possible benefits of prolonged neoadjuvant hormonal therapy (e.g., six months to one year) before surgery. However, long-term testosterone suppression produces marked testicular atrophy that may take months or years to reverse after cessation of hormonal therapy. Therefore, it is possible that the resultant persistently low androgen secretion in patients who receive prolonged neoadjuvant therapy may significantly delay the development of PSA evidence of cancer recurrence and thus create a misleading impression that neoadjuvant hormonal therapy reduces recurrence rates. The possibility of this misleading effect would be of particular concern in studies with short-term follow-up.

**Pelvic Lymph Node Metastases**

In the post-PSA era, the incidence of pelvic lymph node metastases in patients with clinically localized prostate cancer has decreased from a rate of about 25% to about 2%.

Accordingly, many urologists continue to routinely perform staging pelvic lymphadenectomy with radical prostatectomy. Approximately 80% to 85% of patients with proven pelvic lymph node metastases have biochemical evidence of treatment failure within five to seven years. The question of whether the prostate should be removed if pelvic lymph node metastases are found at operation is controversial, and there are limited published data that shed light on this issue.

Cadeddu et al. reported on a retrospective, non-randomized 10-year survival analysis of men with proven pelvic lymph node metastases who were treated with or without removal of the prostate. Overall, men who underwent prostatectomy fared better than those in whom the prostate was left in place. Cadeddu et al. also performed a case-control analysis of subsets of comparable patients and found a strong trend for a survival advantage in patients whose prostates were removed. Because the morbidity and mortality rates associated with radical prostatectomy are low, it is not unreasonable to remove the prostate in patients with pelvic lymph node metastases to avoid possible future local problems with the primary tumor, and to provide any possible benefit that may accrue from removing a potential source of future distant metastases.

**Postoperative Adjuvant Radiotherapy**

Another controversial issue is the advisability of adjuvant radiation or hormonal therapy in patients with adverse pathologic findings in the radical prostatectomy specimen. Not all such patients will have tumor recurrence. In general, about 20% to 30% of patients with extraprostatic tumor extension or focally positive surgical margins associated with low or moderate Gleason grade tumors subsequently have rising PSA levels.

Failure rates are higher (50% to 85%) in patients with high-grade tumors, seminal vesical invasion, or lymph node metastases.
The latter patients are more likely to experience failure because of distant metastases than because of local tumor recurrence. Accordingly, patients with minimal adverse pathologic features may opt to receive adjuvant radiotherapy or to simply be followed with close surveillance.

The theoretical advantage of early adjuvant radiotherapy is that it is more likely to be successful when the tumor burden is minimal (i.e., before the PSA begins to rise). The disadvantage is that it may be over-treatment in the majority of patients who are destined not to have tumor recurrence, and it may be inadequate treatment for those who have occult distant metastases.

The risks associated with adjuvant radiation therapy include a 3% to 4% rate of permanent injury to the rectum (causing rectal bleeding, diarrhea, and rectal urgency) or to the bladder (causing hematuria, urinary urgency, and a small capacity, noncompliant bladder), and a 50% risk of radiation-induced damage to the cavernosal neurovascular bundles (causing delayed impotency).

There is increasing evidence suggesting that early adjuvant radiotherapy produces better cancer control results in patients at high-risk for local failure (i.e., those with high Gleason grade tumors, multiple or extensive positive surgical margins, or multiple regions of extraprostatic tumor extension).\(^\text{19,49,50}\) In either case, our preference is to give the adjuvant radiotherapy before the PSA level rises above 1 ng/ml.

Walsh et al\(^\text{5}\) reported that when patients with an isolated elevation of serum PSA underwent delayed radiation therapy to the prostatic bed, PSA decreased to the undetectable range but remained undetectable for at least two years in only 10%. Our results\(^\text{51}\) have been considerably more favorable, with about 68% of patients treated for a delayed PSA elevation having an undetectable PSA after 15 to 47 months of follow-up compared with 33% treated for persistently elevated PSA levels or rising levels within 6 months of surgery, with 8 to 56 months of follow-up.

**Adjuvant Hormonal Therapy**

In patients who are at a high-risk for distant metastases (i.e., those with high-grade cancer, seminal vesical invasion, lymph node metastases, vascular or lymphatic invasion, persistently detectable postoperative PSA levels, or levels that rise soon after the operation, etc.), adjuvant radiation therapy is unlikely to be curative.

Hormonal therapy, which is usually the more appropriate treatment, may be initiated either prophylactically, for a rising PSA, when the bone scan converts from negative to positive, or for symptoms that require treatment. We prefer to initiate hormonal therapy when there is evidence of a rapidly rising PSA level.

In this regard, however, Lerner et al\(^\text{45}\) reported that postoperative hormonal therapy following radical prostatectomy had no effect on cancer-specific survival in patients with aneuploid tumors but did appear to improve progression-free survival in patients with nonaneuploid tumors.

More accurate methods are needed to identify patients likely to have tumor recurrence and to determine whether the recurrence will be local, distant, or both. Such methods may allow earlier and more appropriate use of adjuvant therapy.\(^\text{52}\)

**Salvage Radical Prostatectomy**

Salvage radical prostatectomy has been recommended in selected patients who have failed primary radiotherapy. The principal drawbacks of salvage radical prostatectomy are the high morbidity rate—which may be 10-fold higher than in patients who have not had radiotherapy—and the relatively low likelihood of achieving complete excision of the cancer.

Approximately 1% to 15% of patients undergoing salvage radical prostatectomy will have rectal injuries, some of which will require colostomy for repair, and between 10% and 64% of the patients will have postoperative urinary in-
continence. Only about 15% to 33% of these patients will develop pathologically confirmed specimen-confined cancer with undetectable postoperative PSA levels. In addition, pelvic node dissection is difficult or impossible to perform following radiotherapy.

Taken together, the proportion of patients that do not have rectal injury, have normal continence, and in whom complete tumor excision is achieved with undetectable postoperative PSA levels is low. These poor prospects for an overall favorable result mitigate against recommending salvage radical prostatectomy in most patients.

Radical Prostatectomy Compared With Other Management Strategies

The outcomes of treatment reported for localized prostate cancer are strongly influenced by the patient mix with regard to tumor grade, tumor stage, serum PSA level, patient age, and co-morbid conditions. Therefore, it is not valid to compare different treatments in non-randomized series. The only published prospective randomized trials comparing prostate cancer treatments were conducted decades ago, were methodologically flawed, and have little relevance to current prostate cancer treatment issues.

A recent population-based study comparing prostate cancer treatments reviewed 59,576 patients in the National Cancer Institute’s Surveillance, Epidemiology, and End Results program. The patients, between 50 and 79 years of age, were treated from 1983 to 1992; the study used as an endpoint the overall 10-year survival rate. The results showed that for men with well-differentiated (Gleason grade 2 to 4) tumors, the 10-year survival rates were 98% for those treated with surgery, 89% for radiotherapy, and 92% for those managed conservatively.

In patients with moderately-differentiated (Gleason grade 5 to 7) tumors, the 10-year survival rates were 91% for those treated with surgery, 74% for radiotherapy, and 76% for conservative management. For patients with poorly-differentiated (Gleason grade 8 to 10) tumors, the 10-year survival rates were 76% for those treated with surgery, 52% for treatment with radiotherapy, and 43% for conservative management.

These results suggest that patients with moderately- or poorly-differentiated tumors fared better with radical prostatectomy than with radiotherapy or conservative management. This study has been criticized because the Gleason grades of patients treated with prostatectomy were determined from the surgical specimens while those of the conservatively treated patients were determined from the biopsy specimens. This criticism does not apply to patients with high-grade tumors whose tumor grade in the surgical specimen is seldom lower than that in the biopsy specimens. Recent studies have also demonstrated that radical prostatectomy is effective in the treatment of high-grade prostate cancers that are organ-confined at the time of diagnosis.

In the past, prostate cancer was usually detected too late for curative treatment. Now, however, through early detection efforts, the proportion of patients diagnosed with organ-confined curable prostate cancer has nearly doubled. Some authors have questioned the value of radical prostatectomy compared with other treatments or with expectant management. Studies to resolve this controversy are currently lacking.

Today, at a time when life expectancies are rising, men are being diagnosed with prostate cancer at younger ages and more frequently are presenting with curable disease. In such patients, prostate cancer treatment outcomes are correspondingly more favorable. These trends will enhance the importance of radical prostatectomy.

As there is no curative therapy for advanced prostate cancer, the use of early detection and effective treatment is the
only practical strategy for reducing prostate cancer morbidity and mortality rates. Prospective, randomized trials are underway to compare the results of radical prostatectomy with other management strategies in patients with clinically localized disease. Until other approaches are proven as effective as radical prostatectomy in a representative patient population, radical prostatectomy should be considered the preferred treatment for men with localized prostate cancer whose life expectancy exceeds 10 years.

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