

## Surgical Treatment of Carcinoma of the Prostate

a report by

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Despite the development of alternative techniques and improvements in the delivery of radiation, surgical removal of the prostate maintains a cardinal role in the management of localized carcinoma of the prostate. Early detection programs have allowed identification of more men who are candidates for surgery. Furthermore, refinements in surgical technique have significantly reduced some of the side effects of surgery.

The term 'radical prostatectomy' implies removal of the entire prostate as well as the seminal vesicles. Typically, pelvic lymph nodes are also removed. There are several different surgical approaches by which radical prostatectomy can be performed. Each approach has its strong proponents and some identifiable pros and cons. Furthermore, there is a rapidly developing interest in laparoscopic and robotic-assisted approaches.

### Patient Selection

Patients selected for radical prostatectomy typically have a tumor that is clinically confined within the capsular margin of the prostate. In most contemporary series, almost 80% of cancers are diagnosed on a biopsy prompted by an abnormality in serum prostate-specific antigen (PSA) levels. Approximately 20% of patients have a palpable abnormality of the prostate but a PSA that would be considered within normal limits.

There are a number of variables that can be used to predict the likelihood of an organ-confined tumor. Different nomograms have been established to combine these variables into predictive models. Most incorporate serum PSA as one of the variables. In general, a PSA level of less than 10ng/ml is considered favorable, but there is wide variability. PSA values are also strongly influenced by the volume of benign tissue.

Digital rectal examination (DRE) is an important staging maneuver. Most cancers detected because of PSA elevation are non-palpable (T1c). As tumors become locally advanced, they are typically palpable and there can be evidence of palpable tumor extension to the seminal vesicle or outside the capsular margin. Despite the relative lack of both sensitivity and specificity for DRE, no imaging modality has been

shown to provide superior results. Prostate cancers can be imaged by transrectal ultrasonography and magnetic resonance imaging (MRI), but, again, neither study has been shown to provide greater accuracy than DRE.

An additional variable commonly employed in most predictive nomograms is the tumor grade. The Gleason scoring system is used most commonly. With this, two numbers are assigned. The first describes the dominant histologic pattern while the second is assigned for any secondary pattern. The scoring system potentially ranges from two to 10 but very low grade lesions, i.e., Gleason 2, 3, and 4 are rarely seen. Gleason 5 and 6 cancers are most common. High grade tumors, Gleason 8, 9, or 10, often have extracapsular or distant metastatic spread at the time of diagnosis. Nonetheless, patients with high grade cancers who otherwise have no evidence of disease outside the prostate are candidates for radical prostatectomy.

In addition to tumor-related factors, characteristics of the individual are also important in patient selection for surgery. In general, since prostate cancer is usually a relatively slowly progressive disease, a patient should otherwise have a life expectancy of 10 years or greater in order to benefit from surgery. Both chronologic and physiologic age are important. Most life-year analyses indicate that a man in his mid-seventies has a median 10-year life expectancy, assuming there is no overriding co-morbidity.

### Staging of Prostate Cancer

The methods for staging the local extent of cancer have been previously mentioned. In addition, distant metastatic spread must be considered. Pelvic lymph nodes and bone are the most common sites of metastatic spread. The best test for detecting bone metastasis is a radionuclide bone scan. Bone scans are not clinically useful in most patients with apparently localized cancers as the risk of finding a positive scan is extremely low. Routine bone scans as a staging maneuver, therefore, are usually restricted to individuals with high grade tumors or a markedly elevated serum PSA. Similarly, pelvic computed tomography (CT) scanning to determine lymphadenopathy, is rarely useful.



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The value of pelvic lymph node dissection as a staging maneuver is still a matter of debate. Few patients benefit from an independent staging pelvic lymph node dissection but lymphadenectomy at the time of radical prostatectomy is commonly performed; most current series report histologically positive nodes in only 1% to 2% of patients. This has led to the argument that pelvic lymph node dissection could be omitted. Others promote the concept of a more extended pelvic lymph node dissection, claiming both improved staging and possible therapeutic benefits.

The morbidity of pelvic lymph node dissection is low. Although the overwhelming majority of patients have histologically negative lymph nodes, there can be important prognostic information learned from nodal status. The key lymph nodes to be removed lie along the hypogastric artery and proximal obturator nerve, and at the bifurcation of the common iliac artery.

### **Surgical Approaches for Radical Prostatectomy**

The goal of radical prostatectomy, i.e., complete removal of the prostate and seminal vesicles, can be achieved through several different surgical approaches. On-going comparative studies are attempting to show the benefits of one approach over the other. In addition, hospital and physician marketing can strongly influence patient perceptions of differences in outcome and patient-driven choices and expectations.

### **Radical Retropubic Prostatectomy**

Almost 80% of radical prostatectomies are currently performed via the retropubic route. An incision is made from below the umbilicus to the pubis. Extraperitoneal development of the prevesical space allows exposure of the anterior portion of the prostate. Simultaneous pelvic lymph can be performed readily through this surgical approach.

Most techniques for radical retropubic prostatectomy involve initial dissection of the prostatic apex. This requires division of the dorsal vein complex, which has the potential for significant bleeding. The urethra is divided at the prostatic apex. The prostate is then dissected in a retrograde fashion up to the level of the bladder neck. The prostatic pedicles are controlled and the seminal vesicles dissected free to the tip. The bladder neck is divided and the surgical specimen is removed. Vesicourethral anastomosis is then performed with interrupted sutures tied over an indwelling Foley catheter.

An advantage of radical retropubic prostatectomy is the widespread familiarity with this surgical approach. Furthermore, the technique for preservation of the

neurovascular bundle is well described. Bleeding from the dorsal vein complex can be more significant with the retropubic route compared with alternative techniques.

### **Radical Perineal Prostatectomy**

The earliest descriptions of radical prostatectomy were via the perineal route. With this surgical approach, an incision is made between the scrotum and anus. Dissection is performed along the anterior rectal wall to obtain exposure of the prostate. The entire seminal vesicles can be dissected free as with a retropubic prostatectomy and the pedicles are ligated. The prostatic apex is usually well visualized and the urethra divided. The dorsal vein complex is less disturbed by this method since the approach is posterior and does not require division of the complex prior to control of the urethra.

Post-operative pain is usually minimal with the perineal route. Proponents place this as one of the primary advantages although comparative studies show no substantial difference in post-operative pain. The risk of rectal injury with a perineal prostatectomy is higher and pelvic lymph node dissection cannot be performed through the same incision.

### **Laparoscopic Prostatectomy**

Laparoscopic radical prostatectomy was described almost 20 years ago but was found to be extremely technically demanding and gained little acceptance until recently. Improvement in laparoscopic equipment and surgeon technical skills have allowed development of a number of series of radical prostatectomy using pure laparoscopy. Performance of the anastomosis has characteristically been the most difficult technical aspect of laparoscopic radical prostatectomy. Some surgeons have sufficiently advanced laparoscopic skills that a running anastomosis can be accomplished with a high degree of accuracy and within a reasonable time. Either an intraperitoneal or extraperitoneal approach can be used. No substantial difference in outcome between these two has been identified.

### **Robotic-assisted Laparoscopic Prostatectomy**

Currently, there is great enthusiasm and interest for robotic-assisted laparoscopic prostatectomy (RALP). The only device commercially available is the DaVinci surgical robot (Intuitive Surgical, Sunnyvale, California). This is a master/slave device wherein the surgeon is seated at a console adjacent to the operating table. The robotic arms are inserted through laparoscopic ports. The surgeon can manipulate the

surgical arms using hand and wrist movements that mimic open surgical maneuvers; however, there is added flexibility and freedom. Furthermore, there is superb three-dimensional (3-D) magnified vision. The console surgeon manipulates the camera with a foot pedal and hand movements. A table-side surgeon assists with passing and cutting of suture, retraction, and suction.

For the overwhelming majority of surgeons, robotic assistance greatly facilitates laparoscopic prostatectomy. The technical skills are easier to learn than those required for pure laparoscopy. The primary drawback is the expense of the robotic equipment. The DaVinci robot costs in excess of US\$1 million and there are additional hundreds of thousands of dollars in expenses for equipment and maintenance contracts.

### Outcomes After Radical Prostatectomy

As the goal of radical prostatectomy is to remove all prostatic tissue, whether benign or malignant, the operation should be curative for patients whose tumor is confined within the prostate. PSA becomes an extremely sensitive and specific marker to follow patients after radical prostatectomy. PSA should fall below a minimum level of detectability. Any measurable PSA is a likely indication of residual prostatic cancer cells. Although a detectable post-operative PSA is not specific as to the location of any malignant cells, the time-point at which PSA becomes detectable and increases can be suggestive. PSA levels that decline to the undetectable range but rise slowly more than a year after surgery are indicative of local recurrence of cancer. PSA levels that never reach undetectable or rise quickly are more often associated with metastatic disease.

Most series show that 70% to 80% of patients can expect PSA-free recurrence survival at 10 years after radical prostatectomy. Moreover, many with PSA recurrence remain asymptomatic for an extended period of time. Radical prostatectomy, then, remains a proven and effective long-term method for cure or control of carcinoma of the prostate.

### Morbidity and Side Effects of Surgery

Undoubtedly, the morbidity of radical prostatectomy has changed greatly over the past decade. This is partly due to increased surgeon experience but also to refinements in surgical technique. There is the promise that new surgical approaches, such as robotic-assisted laparoscopy, can decrease the impact of surgery even further.

### Hospitalization

Hospital stay after radical prostatectomy is usually limited to only one or two days. Even when the operation is performed with a surgical incision, most contemporary clinical pathways target post-operative day two, or perhaps three, for discharge. With laparoscopic approaches, and in many perineal series, post-operative day one is the expected date of discharge. Patients are often allowed to drive a car and return to most activities within a couple of weeks of surgery. Resumption of strenuous activity is usually limited for a month or so to avoid incisional hernias, even with laparoscopic approaches.

### Intra-operative Blood Loss

Historically, radical prostatectomy had been considered to be an operation associated with considerable blood loss. While that potential still exists, some contemporary series have shown transfusion requirements as low as 1% to 2%, even with the retropubic route. With laparoscopic approaches, bleeding is usually a negligible consideration. A requirement for transfusion is exceedingly rare. The pneumoperitoneum effectively tamponades the venous bleeding commonly associated with radical prostatectomy. There is a statistically significant decrease in blood loss with laparoscopic compared with open surgical approaches. This may be of clinical relevance since bleeding can obscure the operative field and, in particular, make dissection of the neurovascular bundle and prostatic apex more difficult.

### Duration of Catheterization

Due to the fact that radical prostatectomy requires a primary anastomosis between the bladder neck and the urethra, a Foley catheter is left indwelling for a period of time post-operatively. The duration for which catheterization is required varies and is largely a matter of surgeon preference. Historically, catheters have been left indwelling for two to three weeks, but this clearly is unnecessary in most patients. Since the anastomosis is performed with a running, and often watertight, suture with laparoscopic approaches, there has been some thought that earlier catheter removal can be accomplished with laparoscopy; however, others have shown that catheter removal as early as three to four days can be performed even with interrupted sutures. If catheter removal after a few days is to be attempted, a cystogram should be obtained as some patients will still have evidence of extravasation and require longer catheterization. Some 10% to 15% of patients will also be unable to void initially with early catheter removal, presumably because of edema at the anastomotic site. It has therefore been decided to leave the catheter indwelling for approximately one week post-operatively, regardless of whether an open or robotic-assisted procedure is performed. With this, a routine

cystogram is not required and urinary retention is quite unusual.

### Post-operative Pain

Pain is not typically a prominent feature for patients recovering from radical prostatectomy. With radical retropubic prostatectomy, a limited infraumbilical incision is required. There is minimal pain with a perineal incision and laparoscopic approaches require only small incisions. In fact, using a peri-operative care pathway that routinely employs the use of Ketoralac post-operatively, no difference in peri-operative narcotic requirement or patient reported pain after radical prostatectomy has been reported, regardless of whether a retropubic or robotic-assisted laparoscopic approach has been used.

### Surgical Margins

A key outcome measure in comparing the various surgical approaches for radical prostatectomy is margin status. If the operation is performed in the proper anatomic plane, stage T2 tumors (those pathologically confined within the prostatic capsule), should have negative surgical margins. On the other hand, good surgical technique can allow negative margins even in some patients with established extracapsular extension. The prostatic apex is the most common site of positive surgical margins. Several factors contribute to this finding. Firstly, identification of the proper plane of dissection at the prostatic apex can be difficult, particularly when there is bleeding from the dorsal vein complex. Secondly, the apical region is a common location for carcinoma. Finally, there can be some artifact in the histologic interpretation of positive apical margins, partially because of retraction of the prostatic urethra but also because the surgical capsule of the prostate is less defined at the apex.

Comparison of margin status from one series to another is difficult. The method and detail of pathologic analysis can be highly influential in assessing margins and may not be uniform between institutions. Patient selection is also highly influential. Existing data, as best as it can be assessed, show no substantial difference between various surgical approaches in margin positivity. This would validate the impression of most experienced surgeons. The operation can be performed anatomically via any of the described routes. Likewise, poor surgical technique can lead to positive margins in patients with T2 tumors, whether the operation is performed with an open approach or laparoscopically. The key is an anatomic dissection that does not violate the prostatic capsule and that allows clear vision of the prostatic apex.

### Continence

One of the greatest concerns for men undergoing radical prostatectomy is the risk of post-operative incontinence. Despite the long history of radical prostatectomy and the frequency with which the procedure is performed, the reason for some male incontinence after surgery is still poorly understood. The periurethral sphincter and the genitourinary diaphragm provide passive continence. The voluntary external sphincter typically remains intact after radical prostatectomy, even in men who have significant problems with incontinence. The method for bladder neck dissection or closure probably contributes little to post-operative continence. This statement is validated by parallel experience in patients undergoing orthotopic bladder reconstruction after radical cystectomy. Typically, excellent daytime continence is achieved with orthotopic neobladders even though there is no functional bladder neck.

The apical dissection is key in avoiding incontinence after radical prostatectomy. Hemostatic sutures or excessive use of electrocautery can damage the periurethral sphincter. Division of the urethra too far distal to the prostatic apex can leave inadequate post-operative urethral length. Dissection of the periurethral sphincter muscle should be very limited. The quality of the anastomosis may also affect continence. Fibrosis due to inadequate mucosal to mucosal approximation or post-operative urinary extravasation may be contributory.

The overwhelming majority of patients regain adequate urinary control after radical prostatectomy. In most reports from centers of excellence, only 2% to 3% of patients have troublesome post-operative incontinence. In population-based studies, reported rates in incontinence are significantly higher. This is likely to underscore the contribution of surgeon experience to post-operative outcomes.

Even in the hands of experienced surgeons, return of urinary control is often not immediate after catheter removal. Rapid improvement typically occurs in the first few months after surgery but can be on-going for up to a year post-operatively. This implies some degree of neuropraxia and subsequent recovery. Kegel exercises are commonly recommended but their contribution to the return of continence is uncertain.

Any relative merits of different surgical approaches in preventing post-operative incontinence are still a matter of debate. Early return of continence is reported in multiple series after RALP. This approach does afford superb visualization of the prostatic apex. Minimal periurethral dissection is required. Placement of

multiple sutures in the dorsal vein complex or in the periurethral tissue is also typically not necessary because of the outstanding hemostasis achieved.

### **Erectile Dysfunction**

Despite the marked advances that have occurred in minimizing peri-operative morbidity and long-term complications after radical prostatectomy, erectile dysfunction remains as a significant issue. The anatomic course of the cavernosal nerves responsible for erection has been described. The nerves lie immediately posterolateral to the prostate and the urethra, making them subject to injury during radical prostatectomy. Nerve-sparing radical prostatectomy can be performed in properly selected patients without a compromise in surgical margins. Post-operative results are directly related to patient age and pre-operative erectile function. Most younger men with no pre-operative problems can anticipate recovery of adequate erectile function post-operatively. PDE-5 inhibitors can facilitate recovery of function.

The concept that nerve injury is the primary insult leading to erectile dysfunction after radical prostatectomy is supported by the prolonged pattern of recovery. Improvement in erectile function is typically an on-going process for several years after surgery. Injection of vasoactive substances directly into the corporal cavernosa is usually effective, further implying that the primary problem is nerve damage rather than vascular compromise. A surgical technical problem is that the anatomic location of the cavernosal nerve varies. Furthermore, rather than being a single, defined nerve trunk, the cavernosal nerves are multiple and intertwined within blood vessels and fibro-fatty tissue. The term 'neurovascular bundle' is therefore typically used to describe the cavernosal nerve complex. The bundle is not readily visible as a distinct anatomic structure. Methods for intra-operative identification of the location of the neurovascular nerve stimulators have, to date, proven to be too imprecise for clinical utility.

The technique for nerve-sparing radical retropubic prostatectomy is well described. One of the primary

potential advantages of robotic-assisted laparoscopic prostatectomy is improved visualization and precise anatomic dissection of the neurovascular bundle. The magnified 3-D imaging and the minimal bleeding allow superb visualization. There is a loss of tactile feedback with robotic surgery but observation of tissue compressibility and tension provides similar information. The robotic approach may also place less traction on the neurovascular bundle.

Again, comparisons between various series and techniques is difficult. Patient selection is a factor but methods of analysis and reporting of post-operative results are highly variable.

### **Summary**

The role of radical prostatectomy in the management of patients with localized carcinoma of the prostate is well-established. No alternative treatment method has been shown to provide superior results. Long-term survival is outstanding after surgery. Post-operative testing, in particular serial PSA measurements, is highly accurate in following patients after radical prostatectomy.

Although the benefit of surgery in treating patients with carcinoma of the prostate has long been accepted, the morbidity of the procedure historically limited its acceptance by some patients. Results of contemporary series show vastly improved outcomes. A hospital length of stay of only one day and a relatively rapid return to all pre-operative activities can be anticipated by most patients. The risk of urinary incontinence is vastly diminished and erectile function can be preserved in most patients having no pre-operative difficulty.

Increased risk of laparoscopic and robotic-assisted approaches provides the promise of even better future results. While there can be a substantial learning curve with these techniques, reports from centers of excellence show outcomes at least comparable with open surgical approaches and, in many circumstances, superior. Greater experience and improved technology are likely to expand further the role of minimally invasive approaches. ■