Clinical basics

# Prostate cancer: 6. Surgical treatment of localized disease

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**The case**

A 65-year-old man undergoes a routine checkup before retiring. His wife has urged him to have his prostate examined, because she has read about testing for prostate cancer and a friend has just died of this disease. During the rectal examination, the man's physician discovers some firmness in the right lobe of the prostate gland. The patient has had no urinary symptoms and is in excellent general health. Sexual function is normal. There is no history of prostate cancer; his father died of a stroke at age 86 years. Testing shows that the patient's prostate-specific antigen level is 9.3 ng/mL, and he is referred to a urologist. Transrectal ultrasound-guided needle biopsy reveals adenocarcinoma with a Gleason score of 7 (intermediate grade). At a follow-up meeting with his physician, the patient says, "I have been doing some research, and it appears that I should have treatment. However, what is less clear to me is what form of therapy is best — surgery or radiation treatment. Please tell me what you can about the state of the art with respect to surgery."

The patient described in this case is an appropriate candidate for radical prostatectomy (total removal of the prostate and surrounding tissues). At age 65, in good general health and with a family history of longevity, he has excellent life expectancy. He has clinical stage T2a adenocarcinoma (i.e., it is detectable during digital rectal examination [DRE] but is confined to one lobe of the prostate) with a Gleason score of 7 and a baseline prostate-specific antigen level of 9.3 ng/mL.[1]

Conservative management, such as watchful waiting, is not a good option for this patient because of the tumour grade and the elevated PSA. A meta-analysis[2] has indicated that only 26% of men with untreated high-grade prostate cancer survive for 10 years without metastasis. In contrast, if radical prostatectomy is performed at this stage, there is a 33% probability that the disease will be confined to the prostate, a 52% chance of capsular penetration, a 10% likelihood of seminal vesical involvement and only a 4% probability of lymph node involvement.[3] Overall, this patient has a reasonable chance of cure with surgery.

## Candidates for radical prostatectomy

In the appropriate patient, radical prostatectomy may be curative, and the procedure is both logically and emotionally appealing. However, it is not for everyone. Suitability for radical prostatectomy is based on several criteria.

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*Education*

*Éducation*

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- The tumour must appear to be confined to the prostate, that is, stage T1 or T2. If the disease is more advanced, radical prostatectomy is unlikely to be curative, and the risks and side effects of the operation cannot be justified.
- The PSA level should generally be below 20 ng/mL.
- The patient must be medically fit to withstand anesthesia and major surgery.
- Older age is not an automatic disqualification for surgery, but unless the patient has a life expectancy of at least 10 years, surgery is not likely to improve overall survival. Therefore, prostatectomy is usually performed only in patients under the age of 70 who are otherwise in good health.

When a man discusses the option of prostate removal with his urologist, he needs to be aware of both the benefits and the risks. The potential benefits are clear: the cancer could be completely eradicated, and the man cured of the disease. The risks, however, may be considerable. These include the risks of perioperative and postoperative complications, as well as the risks of long-term complications.

## Procedures

Once prostate cancer has been confirmed by biopsy, staging involves all of the information gathered from the digital rectal examination, the PSA test and nuclear bone scanning. Bone scanning may be omitted if the PSA level is below 10 ng/mL and the Gleason score is less than 7, because the chance of skeletal metastasis in this setting is less than 1%.[4]

For more locally advanced but still clinically confined cancers, some urologists recommend a course of neoadjuvant hormone therapy for a limited time before surgery.[5] Such therapy will cause the prostate, and the cancer within it, to shrink. Studies have confirmed that a 3-month course of treatment significantly improves the odds of achieving negative margins[5] (i.e., "getting it all out"). Current trials are evaluating longer-duration therapy (8 months), and continuing follow-up in all studies is necessary to determine whether this double-barrelled approach will lead to longer survival times.[6] However, it is not routinely recommended at present outside the clinical trial setting.

Of the 2 techniques used in radical prostatectomy, the most common is radical retropubic prostatectomy. The other option, radical perineal prostatectomy (in which the prostate is approached through an incision in the perineum), has several advantages. These include minimal loss of blood, easier reconstruction of the bladder–urethra connection once the prostate has been removed and a shorter stay in hospital. The disadvantages are a higher rate of impotence and the inability to assess the state of the lymph nodes near the prostate without a second operation. At present, only a few urologists perform this procedure.

### *What the patient should know before surgery*

At most hospitals, patients attend a preadmission assessment clinic well in advance of their surgery. During this clinic, a variety of admission procedures and laboratory assessments, including a blood crossmatch, are carried out. The patient is then admitted to hospital on the day of surgery.

Because the rectal wall may (rarely) be lacerated during the procedure, the bowel must be cleansed of feces beforehand. Patients are also given antibiotics to minimize the chances of infection. Some surgeons prescribe oral tablets to be started a day or two before surgery; others request intravenous administration of antibiotics to be started just before the operation and to continue for a few days afterward.

### *What happens during surgery*

The first step in the surgical procedure is to examine the regional lymph nodes. If the nodes are obviously abnormal and metastatic tumour is confirmed on quick section, the disease is almost certainly metastatic elsewhere and therefore incurable, so proceeding with the surgery would be inappropriate. However, if the cancer is at an early stage (T1a, T1b or T2a) and is of low grade (Gleason score below 7) and the PSA level is below 10 ng/mL,

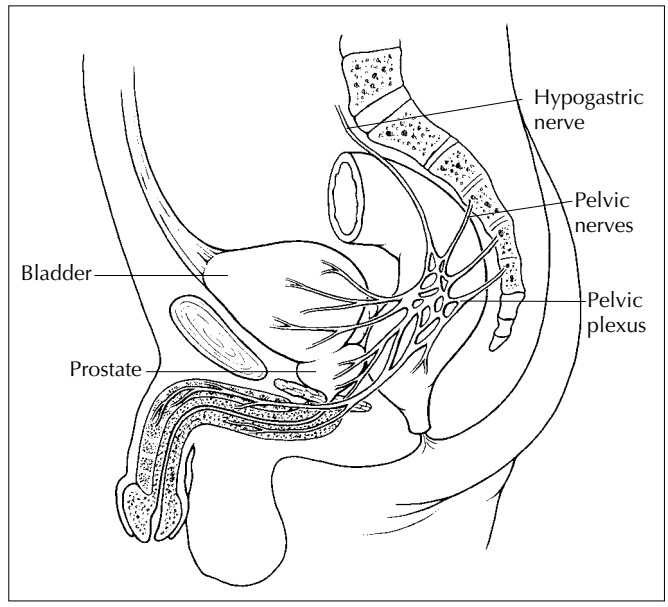


**Fig. 1: Side view showing sagittal section of the male pelvis, detailing the normal anatomic features of the prostate region.**

the probability of metastasis to the lymph nodes is low (less than 5%).[3] In this situation, the surgeon may elect to forego lymph node dissection, thus reducing the operating time and associated intraoperative and postoperative complications. Before the operation begins, it should be clear to both the patient and the surgeon what will be done in any of the situations that might be encountered.

Before the 1980s the traditional procedure involved wide resection of the prostate gland and, as a result, 80% to 90% of patients lost their ability to attain an erection. In 1983, the nerve-sparing or anatomic prostatectomy was introduced to minimize the problem of postoperative impotence (Figs. 1–3). In theory, if the nerves are spared on both sides of the prostate, the patient should remain potent, and this hypothesis has been borne out particularly among younger patients, in whom some degree of erectile capacity may be preserved in 60% to 70% of cases. However, if the patient is older or has a history of erectile dysfunction, the likelihood of maintaining postoperative potency drops dramatically, to approximately 15%.

Nerve-sparing or anatomic prostatectomy should be used only when the cancer does not extend to the edge or the apex of the gland. If there is doubt as to whether the entire cancer can be taken out, a wider margin of tissue must be removed. Ultimately, the preservation of potency depends on the patient's age, his current sexual ability, the extent of the cancer, the use of unilateral or bilateral nerve-sparing surgery, and the skill and experience of the surgeon.

During the prostatectomy, special care is also given to the apical dissection. Minimizing the amount of surgical trauma around the external sphincter, the puboprostatic ligaments and the membranous urethra increases the likelihood that the patient will regain full continence at an early stage. It is common for the patient to dribble some urine involuntarily after the catheter is removed, but in most cases this clears up within a few months or even weeks.

Once the prostate has been removed, the bladder neck is anastomosed to the urethra. The catheter must be left in the bladder for 10 to 15 days to allow the newly formed urethral connection to heal. A small drain is inserted to remove any blood or urine that might otherwise collect in the retropubic space in the first days after surgery.

**Teaching points**

- Radical prostatectomy is a good option for patients who are otherwise in good health and have a life expectancy of at least 10 years, provided the tumour is confined to the prostate and the level of prostate-specific antigen is below 20 ng/mL.
- Radical prostatectomy is a relatively safe procedure; the associated mortality rate is low, and early complications are rare.

### *What the patient should expect after surgery*

Most patients can tolerate fluids by mouth within a day

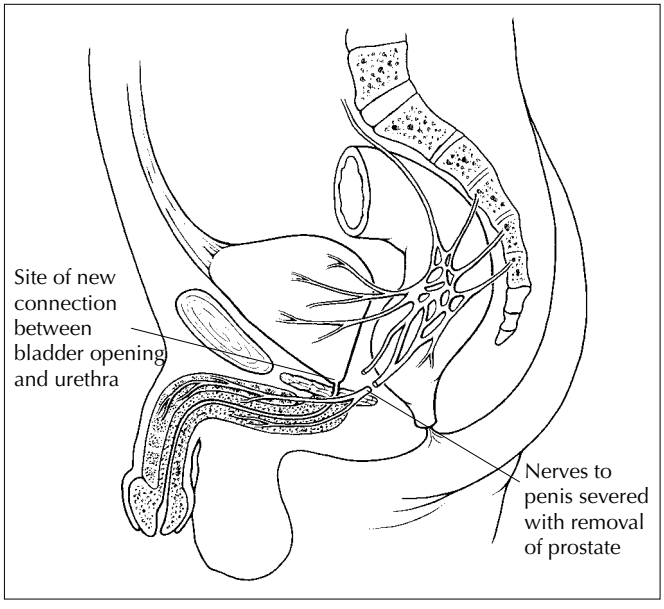


**Fig. 2: Side view showing the nerves that are severed during classical radical prostatectomy.**

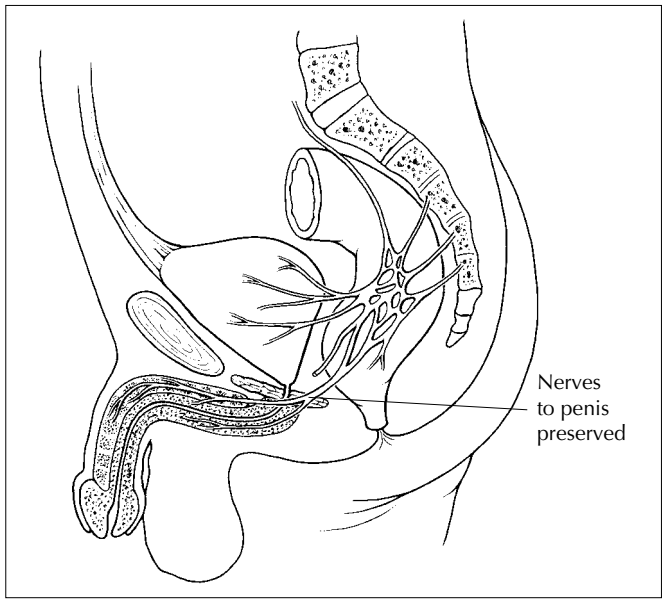


**Fig. 3: Side view showing the result of the nerve-sparing procedure.**

after surgery, and a regular diet can usually be resumed by the second or third postoperative day — sooner after radical perineal surgery.

Pain after surgery can usually be controlled with narcotic analgesics. Some hospitals offer patient-controlled analgesia, such that the patient can dispense his own medication when he begins to feel pain. A push button activates a pump that delivers a small, preset amount of morphine into the intravenous set, which gives immediate pain relief. In this way, the level of analgesic in the blood is kept relatively constant. Patients using this system actually use less narcotic overall during the postoperative period than those who must rely on other sources. Another option offered by some hospitals is an epidural catheter, which affords excellent analgesia to the pelvis and perineum. Non-narcotic pain medication, which has a lower risk of constipation or paralytic ileus, may be prescribed.

Most patients are ready for discharge on the fourth or fifth day; the catheter, which must remain in place for several more days, is attached to a leg drainage bag.

## Early complications

A wide variety of early complications may occur, some specific to this procedure and others that represent the general complications of surgery (Table 1).[7–11]

### *Blood loss*

The prostate is surrounded by an extensive plexus of veins, and blood loss associated with radical prostatectomy has been a major problem. Improvements in surgical techniques related to control of the dorsal venous complex have led to a decline in blood loss. In 1987 Igel and colleagues[8] reported a mean blood loss of 1018 (range 50–7000) mL in a series of 692 patients; in 1992 Leandri and associates[9] reported a mean blood loss of only 300 (range 100–1500) mL in 220 procedures. A review of the 878 radical prostatectomies carried out in Manitoba between 1985 and 1995 indicated that the mean blood loss decreased from 2500–3000 to 1000–1500 mL during that period.[7]

Autologous blood donation before surgery was popular for some years, but because few patients require transfusion these days, the use of this expensive option has declined.[12] A technique gaining increasing acceptance is intraoperative normovolemic hemodilution. After induction of anesthesia, 2–3 units of blood are removed, the circulating volume is re-established by means of intravenous solutions, and the units are retransfused once blood loss has been controlled.[13]

This technique has also been combined with the preoperative administration of erythropoietin. Erythropoietin (which can be manufactured in large quantities by recombinant DNA technology) helps to return the blood level to normal after surgical bleeding. However, this product should not be used if there is a history of heart or cerebrovascular disease or uncontrolled hypertension.

### *Thromboembolic complications*

Deep venous thrombosis and pulmonary embolism are serious and potentially fatal complications of radical prostatectomy (Table 2).[7–10,14]

### *Rectal injury*

Because of its proximity to the prostate, the rectum can be injured during mobilization of the gland. Fortunately, this occurs only rarely.[7–9,11,15]

Although rectal injury is a serious complication, most cases can be treated by primary repair without temporary colostomy. Some surgeons routinely perform preoperative mechanical and antibiotic bowel prep; others use only a fleet enema on the evening before surgery.

### *Death*

Current surgical and anesthetic techniques and perioperative care are such that radical prostatectomy is a safe

**Table 1: Early complications of radical retropubic prostatectomy[7–11]**

| Complication | Prevalence, % |
|---|---|
| Pulmonary embolism | 0.7–2.7 |
| Deep venous thrombosis | 0.9–2.3 |
| Wound infection, seroma, dehiscence | 0.4–1.7 |
| Lymphocele | 0.4–1.4 |
| Rectal injury | 0.1–1.3 |
| Prolonged ileus | 0.1–1.0 |
| Cardiac arrhythmia | 0.3–0.6 |
| Myocardial infarction | 0.4 |
| Ureteral injury | 0.1–0.3 |

**Table 2: Reported annual incidence of deep venous thrombosis (DVT) and pulmonary embolism (PE) after radical prostatectomy**

| | Complication; incidence, % | |
|---|---|---|
| Reference | DVT | PE |
| Igel et al[8] | 1.2 | 2.7 |
| Leandri et al[9] | 2.3 | 0.8 |
| Litwiller et al[14] *(n = 428)* | 0.9 | 0.7 |
| Ramsey et al[7] *(n = 878)* | 1.3 | 1.7 |
| Walsh[10] *(n = 900)* | 1.0* | 1.0* |

*Total incidence for either condition was 1%.

procedure, and death related to the surgery is rare. Keetch and collaborators[11] reported no deaths in a series of 810 patients, and Igel and colleagues[8] reported a mortality rate of 0.6%. Reviews of Medicare patients over 65 years of age in the United States have reported 30-day mortality rates ranging from 0.5% to between 1% and 2%,[16,17] and a review of 1059 patients younger than 65 years reported a 30-day mortality rate of 0.28%.[18] Careful selection of patients for this procedure is important and, for those with serious coexisting conditions, the alternatives of radiation therapy or watchful waiting should be considered.

### *Other complications*

The first 12 weeks at home are a time of major adjustment — to both the trauma of the surgery and the challenge of reintegrating into family and work life. Transient physical problems include intermittent bouts of abdominal pain, constipation, diarrhea, incontinence, hematuria and fatigue. Constipation and diarrhea may both be treated effectively by fibre supplements such as bran cereal or psyllium hydrophilic mucilloid.

It is important to perform Kegel exercises to strengthen the external urethral sphincter. In addition, the patient should avoid driving a vehicle until the catheter has been removed and should avoid sitting in any one position for too long.

**Teaching points**

- Improvements in surgical techniques have reduced the risks of incontinence and impotence after prostatectomy.
- The risk of excessive blood loss during surgery has also declined.
- Autologous blood donation, which was popular for some time, is expensive and unnecessary for this procedure.
- Normovolemic hemodilution during surgery — the removal of 2–3 units of blood, dilution of the circulating blood to maintain normal volume and the replacement of the units once blood loss is controlled — is of value.
- The administration of erythropoietin before surgery may be appropriate for some men with low hematocrit.

## Late complications

### *Bladder-neck contracture*

Scarring may occur at the site of the vesico-urethral anastomosis, which could lead to stricture and bladder-neck contracture. This has been reported in 1.3% to 22% of patients who have undergone radical prostatectomy.[19] Keetch and collaborators[11] reported that this complication occurred in 5% of a series of 810 patients. Among the first 500 patients, the rate was 7.8%, but among the subsequent 310 patients, it was only 0.6%. Surgical technique is obviously important for this complication. Surya and colleagues[19] found that excessive intraoperative blood loss, extravasation of urine at the anastomotic site and a prior transurethral prostatic operation were significant contributing factors to bladder-neck contracture. Treatment involves dilatation of the stricture or urethrotomy performed transurethrally. Care must be taken when performing urethrotomy to prevent damage to the external urinary sphincter, which could result in incontinence.

### *Urinary incontinence*

This is probably the complication most feared by men undergoing radical prostatectomy. Fortunately, the incidence of severe incontinence after contemporary radical prostatectomy is low and, for those unfortunate enough to experience this problem, effective treatment is available. Complete incontinence rates of 0% to 17% and stress incontinence rates of 0% to 35% have been reported.[20] However, improvements in surgical technique have significantly reduced the occurrence of this problem.

Igel and colleagues[8] reported severe to total incontinence in 5% of the patients in their series and mild stress incontinence in 21%. Leandri and associates[9] reported no patients with complete incontinence and only 5% with mild stress incontinence; 90% of those affected had achieved complete urinary control within 6 months after surgery. Keetch and collaborators[11] reported an overall complete continence rate of 94% by 18 months after the operation.

Of the 543 respondents to a questionnaire mailed to all patients who underwent radical prostatectomy in Manitoba between 1985 and 1995, only 3.9% indicated that dripping urine or wetting their pants had been a significant problem; for 7.1%, this had been a moderate problem, for 12.8% a small problem, for 25.5% a very small problem and for 50.7% no problem.[7] No pads were worn by 76.7%, 1 or 2 pads a day were needed by 17.4%, and 3 or more pads per day were needed by 5.4%.

In a review of 593 men who underwent radical prostatectomy, Steiner and associates[20] found that age, mass of the prostate, prior transurethral resection of the prostate, pathologic stage, and preservation or wide excision of the neurovascular bundles had no significant influence on the preservation of urinary control.

Men should be made aware that they will probably be

incontinent after the catheter is removed but that control will gradually return over the next few months. Before the surgery, patients should be instructed on how to perform Kegel exercises and should continue these exercises in the postoperative period.

### *Potency*

With early detection programs, an increasing number of young men are diagnosed with prostate cancer. For these patients in particular preservation of sexual function is important. Before 1982 it was generally assumed that impotence would occur after radical prostatectomy. However, Walsh and Donker[21] showed that the nerves responsible for penile erection lie within the prostatic fascia on the posterolateral border of the prostate. These nerves can be preserved without necessarily compromising the surgeon's ability to eradicate the cancer.[10] Nerve-sparing radical prostatectomy (Fig. 3) has represented a major advance in surgical technique.

**Teaching points**

- Incontinence is common in the first few months after surgery, but improvements in surgical techniques have significantly reduced the prevalence of longer-term problems. Incontinence causing significant problems occurs in less than 10% of patients.
- Loss of potency depends on the age of the patient, preoperative erectile function, the stage of the cancer and the surgical technique.
- The frequency of loss of potency is actually higher than reported in select series from major institutions.
- Effective treatment options are available for the management of incontinence and loss of potency.

How successful is this operation? Walsh[10] reported a postoperative potency rate of 68% among 503 patients, with potency being defined as an erection sufficient for vaginal penetration and orgasm. Younger age, clinically and pathologically confined cancer, and preservation of both neurovascular bundles are associated with a higher rate of postoperative potency. Catalona and Basler[22] have reported preservation of potency after bilateral nerve-sparing surgery in 63% of patients overall and in 75% of patients aged 50–59, 60% of those aged 60–69 and 50% of those over 70 years of age. The corresponding results for unilateral nerve-sparing surgery were 41% overall and 25%, 48% and 38% for men aged 50–59 years, 60–69 years and 70 years and over respectively.

Unfortunately, the degree of success reported by these authors has not been generally reproducible. In a series from Stanford University, a major referral centre for prostate cancer, only 51 (11.1%) of 459 men who underwent radical prostatectomy were potent after the procedure.[23] Excluding patients with poor erectile dysfunction before surgery, 15.4% of those who underwent unilateral and 35.1% of those who underwent bilateral nerve-sparing prostatectomy remained potent. In that study the patients were asked about their sexual function by an independent observer. A Medicare series using patient-reported results had a similar low potency rate (only 11% of the patients had engaged in unassisted intercourse during the month before questioning).[24] These latter results may partly reflect the older age of the patients in the study (half were older than 70 years at the time of the operation), as well as the fact that the proportion of patients who underwent a nerve-sparing procedure was unknown.

Of 860 patients who underwent radical prostatectomy in Manitoba between 1985 and 1995, 543 (63%) responded to a quality-of-life questionnaire. Of these, 82% claimed that before surgery they had erections firm enough for intercourse, whereas only 10% reported that degree of erection afterward.[7] Although the reported potency before surgery seems high and may reflect patients' failure to recall their potency status accurately, this value is similar to the 84% reported by Jonler and coworkers.[25]

Geary and colleagues[23] have reported that loss of erectile function after radical prostatectomy does not necessarily mean a loss of erotic sensation or ability to achieve orgasm. However, there will be no significant ejaculation. They reported that, in an informal survey, only 10% of patients (regardless of potency) reported decreased orgasmic sensation, 80% reported postoperative orgasms identical with those achieved preoperatively, and 10% reported better orgasms after radical prostatectomy. However, in the Manitoba series,[7] 60% of respondents reported that their ability to reach orgasm was poor (12%) or very poor (47%).

Patients undergoing radical prostatectomy should not be led to expect a 50% or better chance of recovering potency, and men scheduled to have this procedure should be prepared to accept loss of potency. For many, this is an acceptable trade-off for the possibility of eradicating the cancer. For others, it represents a major loss. Fortunately, effective treatment options are available to allow most of these men to return to relatively normal sexual activity.

## Follow-up

A man who undergoes radical prostate surgery should be seen by his surgeon several months after the operation and intermittently for up to 1 year. After that, follow-up may be carried out by the family physician. Depending on

the final pathologic assessment, closer, more frequent surveillance may be necessary. At each visit, serum PSA will be measured.

After complete removal of the prostate, the PSA level should drop to undetectable levels, which indicates that all of the cancer cells (and the normal prostate cells) were removed or destroyed. If the PSA level remains detectable within the first year, the odds are that the patient has occult metastatic cancer. A later increase may reflect local recurrence or systemic disease. PSA can indicate a relapse or metastasis many months and even years before the patient has any symptoms or signs of recurrence. Because it may take as long as 7 years or more for recurrence to become evident, a man who has undergone surgery must have yearly examinations indefinitely.

If the pathological findings suggest a high risk of recurrence (e.g., a positive surgical margin, spread to the seminal vesicles or a high Gleason score [over 7]), adjuvant treatment such as radiation therapy to the prostate bed or hormonal therapy may be considered. Results of research on adjuvant treatment are not yet available.

In summary, in the hands of an experienced surgeon, radical prostatectomy offers our patient a high probability of cure with a low risk of incontinence.

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