

Case for resurgence of radical perineal prostatectomy in Indian subcontinent

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ABSTRACT

Introduction: Radical perineal prostatectomy was the first surgery described for prostatic carcinoma (Young, 1904) but it lost its eminent status after Walsh's description in 1982 of anatomic radical retropubic prostatectomy followed by the enthusiasm in laparoscopy and now robotics. It made resurgence after it was realized in early 1990s that the pelvic lymph node dissection is needed only in selected cases. Last decade witnessed over 80 publications addressing the results and advances in the perineal approach. Strangely, centres from the subcontinent have chosen to ignore this resurgence. We describe our early experience with the technique in 35 patients and present the case for its more widespread usage.

Patients and Methods: Thirty five patients of clinically localized carcinoma prostate were operated by perineal route in our institution from December 2006 onwards. All patients had serum prostate specific antigen levels less than 10 ng/ml.

Results: Operating time was 2 to 3.5 hours (mean 2.5 hours). Rectal injury occurred in three patients but was closed primarily in all and none required a colostomy. Mean duration of hospital stay was four days. The disease was organ confined in 25(71%). Positive margins were seen in 5(14%) patients. Biochemical recurrence occurred in 17% patients at one year. Seventy six percent patients had achieved continence at one year.

Conclusions: As the world is taking note of radical perineal prostatectomy again, with a very small learning curve, minimal invasion and good oncological control urologists from Indian subcontinent should also embrace this procedure in view of the relative limited resources available.

Key words: Carcinoma prostate, perineal, radical prostatectomy

INTRODUCTION

Radical perineal prostatectomy (RPP) was the first surgery described for Carcinoma of Prostate (CaP) by Young in 1904. After the understanding of concept of regional lymphadenectomy and description of anatomic nerve sparing radical retropubic prostatectomy (RRP) by Walsh and Donker in 1982,^[1] RRP has achieved the status of Gold standard for surgical management of CaP and is the benchmark against which others are

compared but it continued to remain highly morbid and invasive surgery. The zest for laparoscopy amongst urologists helped to decrease the invasiveness and to maintain same oncological outcome of RPP but the learning curve and the costs involved were substantial. In the background during this era RPP virtually died its own death until Weldon and Tavel in 1988 applied the same anatomic principles of nerve sparing to RPP demonstrating potency preservation in 5 of 9 patients.^[2] Urologists' ability to perform laparoscopic pelvic lymphadenectomy brought RPP again into being.^[3-5] After it was realized that pelvic lymph node dissection can be omitted for a select group of patients with serum prostate specific antigen (PSA) less than 10 ng/ml,^[6] the literature world over has again shown interest in RPP. In the decade of 1991 to 2000, there have been 44 publications indexed in Pubmed keeping RPP alive. In the last decade i.e. 2001- 2011 the number rose to above 80 and reports from every part of the world are showing equivalent oncological control with minimal invasiveness at a significantly low cost. These developments have brought a resurgence of this forgotten surgery adding a lot of modifications in the contemporary technique. But strangely, in India there has been no interest shown by the urologists in reviving RPP.

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We at our institute realized the potential benefits of RPP especially with regards to Indian conditions and present our initial experience of 35 cases with a review of literature and scope for improvement.

PATIENTS AND METHODS

Thirty five patients of clinically localized carcinoma prostate were operated by perineal route in our institution from December 2006 onwards. The patients were selected on digital rectal examination findings, prostatic biopsy Gleason's sum, serum PSA, Computerized Tomography or Magnetic Resonance Imaging of the Pelvis and bone scan. Baseline lower urinary tract symptoms (LUTS) and erectile function were assessed for all patients. Pre-operative erectile function was assessed in all patients by self-assessment questionnaire (international index of Erectile Function-IIEF-5).

All patients who had PSA levels >10 ng/ml, presumed life expectancy <10 years, higher Gleason's sum and those having disseminated disease were excluded from the purview of this study. Prostates more than 100 grams and patients with history of perianal surgery were also excluded.

Radical Perineal Prostatectomy was done using standard Young's suprasphincteric approach. All patients were operated on regular operating tables in exaggerated lithotomy position. The only special instruments used were straight and curved Lowsley tractor [Figures 1a]. The prostate with its covering fascia and seminal vesicles [Figures 1c and 1d] was removed. Wherever nerve sparing was feasible, a midline incision was made over Denonvillier's fascia [Figure 1b] after exposure of prostate and neurovascular bundles were swept away on both or desired side. Care was taken at the apex to dissect out intra prostatic urethra before dividing it. The mean operative time, need for blood transfusion, immediate post-operative complications, mean duration of catheterization and hospital stay was noted. Postoperatively all of the patients were allowed a liquid diet on the evening of surgery and semisolids from next day onwards. Perineal drain was removed on the first post-operative day. Specimen was specifically evaluated for margin status, seminal vesicle invasion and capsular involvement. Patients were followed up monthly for 3

months and 3 monthly thereafter. We defined continence as 'no pad used'. Urinary and fecal incontinence, PSA and new onset urinary symptoms were reported upon. All patients where nerve sparing was performed were started on phosphodiesterase 5 inhibitors before their discharge and their erectile function was assessed at each visit.

RESULTS

Thirty five patients underwent RPP from December 2006 onwards. Age ranged from 54 to 74 years. Thirty two patients presented with LUTS and three were incidentally diagnosed after transurethral resection of prostate (TURP). We waited for four weeks following diagnosis on needle core biopsy and 3 months following TURP. Only seven patients had a palpable nodule. Pre-operative characteristics of the cases are detailed in Table 1.

Bone scan was negative in all patients and cross sectional imaging was done in all patients but no lymphadenopathy or extra capsular extension (ECE) was present in any of them. A sterile urine culture was obtained in all patients prior to surgery and bowel preparation was given to all on the day prior to surgery.

The operations were performed by four faculty staff of the institute. All surgeons had appropriate exposure of RRP. Only one of the surgeons had undergone formal training in RPP and rest three learnt while assisting and observing. Operating time was 2 to 3.5 hours (mean 2.5 hours). Blood transfusion was needed in five patients. One of our initial cases required four units of blood transfusion

Table 1: Pre-operative characteristics of the patients

Preop characteristic (n=35)	No./Range (mean)
Age	54-74 (65.8) years
Prostate size	22-74 (39.75) ml
Se PSA	3.8-10.2 (6.99) ng/ml
Gleason's sum	5-7 (5.8)
Gleason 5=10	
Gleason 6=22	
Gleason 7=3	
ECE, LN or SV involvement on CT/MRI	None
Bone scan	Negative in all

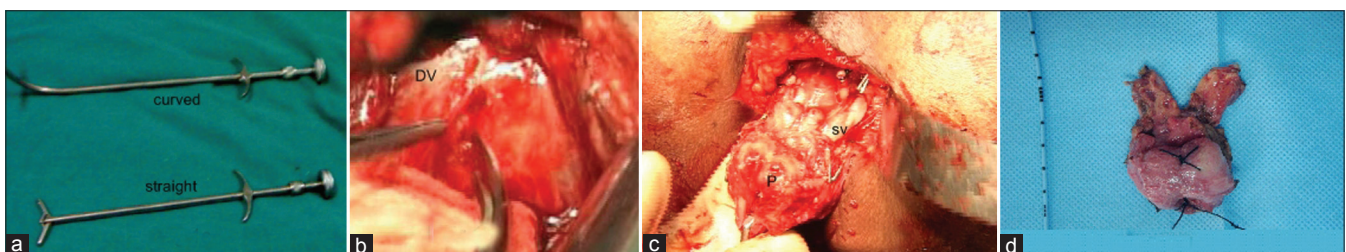


Figure 1: (a) Curved and straight Lowsley tractors. (b) Prostate exposed and Denonvillier's fascia (DV) being incised in midline for nerve sparing. (c) Prostate with seminal vesicles just before specimen was delivered. (d) The specimen (prostate with both seminal vesicles)

due to significant intra operative hemorrhage after a plane between the capsule and the adenoma was inadvertently entered. Rectal injury occurred in three patients but was closed primarily in all and none of the patients required a colostomy. Pelvic lymphadenectomy was not needed even for Gleason's sum 7 patients because all three such patients were 3+4=7 and all had either T1c or T2a disease with probability of having positive nodes <5% according to Partin's tables.

Three patients with rectal injury were kept nil per oral for three days. All the patients were ambulatory from the first post-operative day. All patients were given parenteral opioid analgesics on the first day and needed oral analgesics for next 8-10 days. No case had prolonged urinary leakage. Mean hospital stay was 4 days and the patients were discharged on catheter which was removed between 10 to 14 days without doing a cystogram. Histopathological examination details are shown in Table 2.

Follow up of more than a year is now available for 29 patients and the long term morbidities were as given in Table 3. Eight patients (23%) were continent soon after the urethral catheter was removed. Seventy percent patients were continent at 3 months. The rate of achieving continence decreased in patients who were incontinent at 6 months. Three patients required injection of bulking agents and one is awaiting sphincteric implant. All the three strictures were at the anastomotic site, two were flimsy adhesions cured by cystoscopy alone while one patient has required optical urethrotomy and dilatation at regular intervals for a tight fibrotic narrowing.

Of the five patients who have developed biochemical recurrence, three had seminal vesicles (SV) involvement on final histopathology. All three SV +ve patients after developing PSA recurrences were straight away started on

androgen deprivation therapy (ADT). Of the other two, one had positive surgical margin (PSM) and the other had no risk factor for recurrence. They were also started on ADT after ruling out local recurrence.

Fourteen patients had IIEF-5 scores more than 20 and were willing to preserve their potency. We did not attempt nerve sparing in our first 10 patients irrespective of their pre-operative erectile status and feasibility. Nerve sparing procedure was performed in 9 suitable cases (unilateral in 3 and bilateral in 6). Five patients (55%) have regained erectile function with phosphodiesterase-5 inhibitors after more than a year of follow up.

DISCUSSION

The world literature regarding RPP has moved from defending it,^[7] to aggressively promoting its benefits. The change is evident by the increasing numbers of articles published on RPP in recent years and modifications in the technique being described. All issues regarding the efficacy of the procedure have been probed in the existing literature. They are as follows:

Oncological control

Iselin, Robertson and Paulson^[8] in 1999 published oncological outcome in 1,242 men undergoing RPP for cT1 to T2N0M0 disease and followed for 20 years. In their study, at 5 years 8, 35 and 65% of patients with Organ Confined (OC), specimen confined and margin positive disease respectively, had biochemical failure and this preceded cancer associated death by 5 to 12 years. Solomon *et al.* in 2002,^[9] published their 12 year experience of different techniques of RP including LRP, RRP and RPP and found three year recurrence free survival rates to be similar between the three techniques. Biochemical recurrence had occurred in 17% of our patients at 18 months follow up which is high probably because of small sample size and learning curve.

A higher risk for surgically induced PSM with RPP as compared to RRP was highlighted by Boccon-Gibod *et al.* (43 vs 29%, *P*<0.05).^[10] Other centres though refuted the above statement. Shalev M *et al.* in their experience from Israel^[11] concluded that the narrow surgical field in RPP does not pose a higher risk for PSM. Korman *et al.*^[12] compared RPP and RRP and found no significant difference in PSMs

Table 2: Histopathological results of the specimen

Histopathology (n=35)	No. (%)
Organ Confined	25 (71)
ECE/perineural infiltration	3 (8)
SV involvement	3 (8)
Positive margins	5(14) (3 at bladder neck and one each at anterior and posterolateral aspects)

Table 3: Follow up results of patients

	1 month (available for all 35 patients)	3 months (available for 33 patients)	6 months (available for 33 patients)	12 months (available for 29 patients)	18 months (available for 26 patients)
Urinary incontinence (%)	27 (77)	10 (30)	8 (24)	7 (24)	2 (7.6)
Urethral stricture (%)	3 (8.5)	1	1	1	1
Fecal Incontinence	None	None	None	None	None
PSA persistence/recurrence (%)	None	2 (6)	2 (6)	5 (17)	5 (19)

between the two approaches. Each surgical approach has propensity for different locations of positive margins^[13] and might signify the most difficult area during the surgery. The apex for RRP, bladder neck for RPP and the posterolateral region for LRP are the most high risk locations for a PSM. Five (14%) of our patients reported a PSM out of which three were at the bladder neck.

Operative complications

Many centres have compared perioperative outcomes of LRP, RRP and RPP. In a randomized study of 100 patients each of RPP and RRP from Italy,^[14] the differences in hospital stay, duration of catheterization, intra-operative blood loss and transfusion were statistically significant in favor of perineal approach. In two different publications from a single French centre^[9,15] comparing RPP with RRP and LRP, the clinical outcome and complication rates were similar for the three approaches though the operative time was significantly longer for LRP. In a contemporary review of radical prostatectomies between 2003 and 2005 from the United States where data collected from national database were evaluated, the authors noted perineal approach to have favorable outcomes at a significantly lower cost as compared to retro pubic and minimally invasive (MIRP) approaches.^[16] They also expressed concern regarding underutilization of this time tested procedure (only 452 RPPs vs. 1,938 minimally invasive and 6,899 retro pubic radical prostatectomies). Complications specific to or of major concern during RPP are:

Rectal injury

Boeckmann and Jakse^[17] reported a rate of 11% in their series of 109 patients published in 1995, all repaired intra-operatively without further complications. A recent series reported this complication to be in 5.7% cases where 2.3% developed a rectal fistula.^[18] The authors predicted the risk to be high during the learning period. We had rectal injuries in 3 of our first 20 patients which were primarily repaired and none of the patients developed a rectal fistula or needed a colostomy. The risk of recto urethral fistula though has been reported to be 3 fold higher for perineal than for retro pubic approach from Mainz, Germany (7 of 675 patients; 1.04%).^[19]

The risk for fecal incontinence after any form of RP is higher than the baseline for the age but is more for RPP.^[20] Fecal incontinence was not reported in any of our patients.

Incontinence

Performance of the vesico urethral anastomosis under direct vision is the fundamental difference between RPP and RRP. In a radiographic comparison a normal tapering bladder neck to proximal urethra was noticed in 80% of patients after RPP compared to only 2% after RRP^[21] [Figure 2]. This may be the reason for better continence rates noticed after RPP. Weldon and colleagues reported

208 of their 220 patients (95%) to be continent with more than 75% regaining continence in 3 months.^[22] Return to full continence was reported significantly higher in RPP patients than after RRP (70% vs. 53%, $P=0.001$).^[20] In a recently published experience from Turkey, the authors report 36.7% “immediate” continence rates (i.e. continence soon after catheter removal) and 72.5% “early” continence rates (continent at 3 months).^[23] In our experience we had 23% immediate continent patients which rose to 70% at 3 months as early continence. Chances of regaining continence decreased if the patient was severely incontinent by six months. Three of our patients had DefluxTM injections and one patient who is incontinent after 2 years of surgery is planned for artificial urinary sphincter.

Pain and analgesic requirement

In a prospective evaluation of narcotic requirement after RPP, Weizer *et al.* noted mean time to unassisted ambulation to be under 24 hours.^[24] The narcotic requirement was the maximum on day 1 of which close to 90% was met with orally. Pain score decreased in first week and approached baseline by 4 weeks. A review of narcotic prescription data collected from Market scan after MIRP, RRP and RPP revealed RPP to require more narcotic refills than RRP or MIRP.^[25] Most of our patients were ambulatory by first post-operative day. Not having any abdominal incision facilitates early ambulation. Pain scores and analgesic requirement were not recorded.

The procedure however, is still evolving. The renewed interest has contributed to furthering the anatomical understanding of the perineal approach. A group from Vienna, Austria studied five cadavers after preparing the dorsal venous complex (DVC) with colored latex and then studying the anatomy intra-operatively in 60 patients.^[26] They demonstrated how the urethral suspensory ligament and the DVC are preserved during the ventral dissection of prostate in RPP thus helping in preserving the continence.

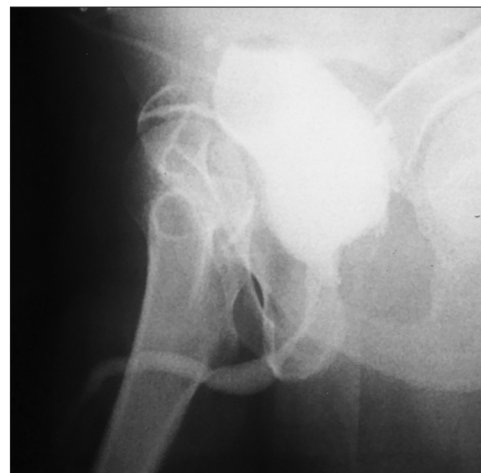


Figure 2: Post-operative voiding cystography demonstrating tapering bladder neck at vesico urethral anastomoses, a contributor to early continence

Apart from better anatomical understanding, recent years have also witnessed a few modifications over the Young's classical method:

Extended RPP (eRPP)

In an effort to decrease the PSMs after RPP, two groups have claimed a modified or extended/expanded RPP. Jakse *et al.* first described expanded RPP in 2000^[27] and presented results of 200 cases in 2001 with initial complete mobilization of posterior aspect of prostate and seminal vesicles before partial suture ligation of DVC.^[28] They claimed significant reduction of PSM and recommended it wherever potency sparing is not indicated. A Japanese group also came up with complete excision of DVC thus bringing the excised specimen closer to that achieved with RRP and thereby decreasing PSM at base and anteriorly.^[29]

Seminal vesicle (SV) sparing RPP

Shafers S *et al.* spared seminal vesicles in 47% of 417 RPPs and claimed oncological outcome to be comparable to standard RPP and RRP at the same time significantly decreasing operation time, better continence rates at 4 weeks and decreasing anastomotic leak rates at day 10.^[30] SV RPP however, did not result in increased PSA relapse rates.

Perineal lymphadenectomy

One of the major reasons why perineal approach went into oblivion was the inability to do a pelvic lymphadenectomy which was being considered essential when Walsh described anatomical RRP. Revival occurred only when it was established that lymphadenectomy is not needed in a certain group of patients. The proponents of perineal approach however, have found out ways to do a pelvic lymphadenectomy with the same incision without need for laparoscopy. Again, Japanese and a German group were the pioneers. Saito and Murakami,^[31] in 2003 published a method wherein a trocar mounted balloon was inserted in the space above levator ani and distended with 200cc air and then with help of several retractors lymphnode dissection could reproducibly be done between the obturator and external iliac vessels. Keller and colleagues^[32] reported technique for extended lymphadenectomy through the perineal incision up to the ureter and the internal iliac artery. They removed a mean of 19 lymph nodes in 90 consecutive patients without altering the outcomes.

Nerve sparing RPP

Applying the anatomical principles of nerve sparing RRP, Weldon and Tavel in 1988^[2] described the technique first in RPP and reported potency preservation in 5 of their 9 patients. We attempted nerve sparing only in the latter part of our initial experience and 44% of those patients are able to perform intercourse after one year of follow up. In a more contemporary report Harris MJ reports more than 80% of nerve spared patients to be able to penetrate during intercourse.^[33] The time to achieve continence was

also significantly decreased in nerve spared patients. Our percentage is attributable to very small number and very early experience with nerve preservation.

Endoscopic assisted RPP

This was first described in a single patient from John Hopkins Medical Institution where a bipolar TUR was used to transect the bladder neck all around and under vision dissection of the seminal vesicles.^[34] Consequently the technique has been advised to be useful in patients with a recent history of transurethral prostate resection.^[35]

Perineal approach has also been described to be advantageous in certain special circumstances like morbidly obese men,^[36] post renal transplant patients^[37] and after mesh repair of inguinal hernia.

That with equivalent oncological control, minimum perioperative complications and excellent continence rates, perineal radical prostatectomy stands the basic requirements as an effective approach for radical removal of prostate is now being realized. Its cost effectiveness is incomparable [The mean and median expenditure for RPP in the first 6 months post-operatively was \$1,500 less than for RRP or MIRP^[16] ($P < 0.001$)]. The technique is as easy as an RRP for trainee residents to learn^[38] and the potential to develop the described modifications especially lymphadenectomy with perineal approach make this procedure a very useful approach to figure in the armamentarium of urologists. Premature abandoning of RPP has been questioned in recent literature (Too soon to abandon perineal approach? - Nature Reviews).^[39] Of all forms of radical prostatectomies, RPP has been chosen as the approach to be taught to surgeons across sub-Saharan Africa to deal with the substantial burden of prostatic adenocarcinoma.^[40]

Shortcomings of this study are; single centre experience, small number of patients and relatively short follow up and thus cannot conclude that RPP is superior to other approaches. Our short term results, inclusive of learning curve, suggest good perioperative outcomes with rapid recovery. All major complications including excessive hemorrhage, rectal injuries and anastomotic strictures occurred in initial 15 patients. The oncological control was comparable to most contemporary series of RRP or RPP. For our initial series we had deliberately selected our cases with PSA < 10 ng/ml and Gleason sum ≤ 7 . With increasing experience more aggressive cases may be taken up with added pelvic lymphadenectomy. Similarly, our experience with nerve sparing is in infancy but once it matures it will surely add up better erectile function to excellent oncological control. Based on our limited experience with RPP and encouraged by the initial results and realizing its greater potential at a very low cost, we propose RPP to be truly minimally invasive procedure and that it should be taken up by more and more centres across the developing nations.

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