



Platinum Priority – Prostate Cancer

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Oncologic Outcome after Laparoscopic Radical Prostatectomy: 10 Years of Experience

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Abstract

Background: While the published short-term oncologic outcomes after laparoscopic radical prostatectomy (LRP) are encouraging, intermediate and long-term data are lacking.

Objective: We analyzed the oncologic outcome after LRP based on 10 yr of experience.

Design, setting, and participants: This retrospective analysis of data prospectively collected from 1998 to 2007 studies 1564 consecutive patients with clinically localized prostate cancer (cT1c–cT3a) who underwent LRP.

Intervention: LRP was performed by two surgeons at either L’Institut Mutualiste Montsouris (IMM) in Paris, France, or Memorial Sloan-Kettering Cancer Center (MSKCC) in New York City, USA.

Measurements: Progression of disease was defined as a prostate-specific antigen (PSA) of ≥ 0.1 ng/ml with confirmatory rise or initiation of secondary therapy. Patients were stratified as low, intermediate, or high risk based on the pretreatment prostate cancer nomogram progression-free probability of $>90\%$, $89\text{--}71\%$, and $<70\%$, respectively.

Results and limitations: The overall 5-yr and 8-yr probability of freedom from progression (PFP) was 78% (95% confidence interval [CI], 74–82%) and 71% (95% CI, 63–78%), respectively. For low-, intermediate-, and high-risk cancer, the 5-yr PFP was 91% (95% CI, 85–95%), 77% (95% CI, 71–82%), and 53% (95% CI, 40–65%), respectively. Surgical margins (SMs) were positive in 13% of the cases. Nodal metastases were detected in 3% of the patients after limited pelvic lymph node dissection (PLND) and in 10% after a standard PLND ($p < 0.001$). The 3-yr PFP for node-positive patients was 49%. There were 22 overall deaths and 2 deaths from prostate cancer.

Conclusions: LRP provided 5- and 8-yr cancer control in 78% and 71% of patients, respectively, with clinically localized prostate cancer and in 53% of those with high-risk cancer at 5 yr. A PLND limited to the external iliac nodal group is inadequate for detecting nodal metastases.

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1. Introduction

Over the last century, urology has seen major contributions in the surgical treatment of prostate diseases. In 1905, Young reported his technique and results of perineal prostatectomy for prostate cancer [1]. In 1945, Millin popularized the retro-pubic approach, which allowed the possibility of pelvic lymph node dissection (PLND) and better knowledge of the intricate pelvic anatomy via a wider surgical field [2]. In 1982, Walsh and Donker introduced the anatomic technique of nerve-sparing radical prostatectomy, offering for the first time the possibility of sexual function preservation for men with prostate cancer and thus opening a new era in the surgical treatment of prostate cancer [3]. A number of technical modifications ensued that rendered open retro-pubic radical prostatectomy the standard treatment that provides men with clinically localized prostate cancer the best chances for optimal outcome [4].

In 1998, a standardized and reproducible technique of minimally invasive laparoscopic radical prostatectomy (LRP) was published [5], which has shown promising short-term oncologic outcome over the last decade [6–8]. This approach achieved comparable positive surgical margin rates and quality of pelvic lymphadenectomy when prospectively compared with the open approach [9] and has since gained worldwide acceptance.

Long-term oncologic outcomes, however, have been lacking. In this paper, we report a detailed analysis of oncologic outcomes based on 10 yr of consecutive experience of LRP.

2. Methods

2.1. Study population

From January 1998 to July 2007, 1564 consecutive patients (median age: 61 yr; interquartile range: 56–66) with clinically localized prostate cancer (cT1c–cT3a) were treated with LRP at L'Institut Mutualiste Montsouris (IMM) in Paris, France, or at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York City, USA, by one of two surgeons (BG or KT). Although the dataset includes patients treated from 1998 to 2007, the majority were treated after 2003. This is a result of increased volume in laparoscopic procedures performed in recent years as well as the addition of a surgeon in 2004.

2.2. Study design

This is an institutional review board–approved retrospective analysis of prospectively collected data.

2.3. Preoperative treatment planning

Both surgeons used a uniform preoperative evaluation and risk assessment. Preoperative clinical parameters, including the patient's age, 2002 TNM clinical stage, preoperative prostate-specific antigen (PSA), and Gleason sum on prostate biopsies, were prospectively recorded. Results from clinical staging, PSA level, Gleason sum, biopsy data, endorectal coil magnetic resonance imaging (MRI) findings, and the patient's preoperative potency status along with Kattan's nomogram-predicted disease risk have been taken into consideration in surgical planning since November 2002 [10].

2.4. Surgical technique

This series includes the very first patients treated by LRP and therefore includes a period of trials and tribulations with the surgical technique and the established Montsouris technique as described by Guillonnet and Vallancien [11]. After June 2003, modifications of the previously described Montsouris technique were introduced. One modification involved apical dissection, with transection of the urethra at the end of the prostatectomy after the neurovascular bundles have been dissected off the apex and completely freed to better delineate the prostate apical anatomy. The other modification involved a systematic intraoperative gross examination of the specimen before completion of the urethrovesical anastomoses [12].

2.5. Indications and anatomic limits of pelvic lymph node dissection

Between January 1998 and January 2005, the nomogram-predicted probability of pelvic lymph node invasion was used to decide on the indication for PLND [13]. In general, patients with a predicted lymph node invasion of <1% did not undergo a node dissection, whereas those with a probability >1% underwent a PLND limited to the external iliac nodal group. This strategy was changed on February 1, 2005, whereby all patients, regardless of their risk stratification, underwent a standard PLND that included the external iliac, internal iliac, and obturator fossa nodal groups [14,15].

2.6. Pathologic examination

The radical prostatectomy specimen was coated with india ink to delineate the surgical margins and then fixed in 10% formalin. Prostate and seminal vesicles were step-sectioned transversely at 3–4-mm intervals. The prostate's most apical tissue was sectioned in the sagittal plane. Specimens were examined for the following variables: Gleason sum, pathologic stage, seminal vesicle invasion, bladder neck invasion, and extraprostatic extension. A positive surgical margin (PSM) was defined as the presence of cancer at the inked margin of resection in the radical prostatectomy specimen, regardless of whether or not additional tissue was resected.

2.7. Postoperative follow-up

Postoperatively, the planned PSA monitoring schedule consisted of a measurement at 6 wk, then every 6 mo for 4 yr, and

Table 1 – Clinical and pathologic characteristics

	Median (interquartile range) or frequency (%)
Age at RP (yr) (n = 1419)	61 (56–66)
Preoperative PSA (ng/ml) (n = 1415)	6.08 (4.28–8.75)
Preoperative nomogram probability of recurrence at 5 yr (%) (n = 1231)	13 (9–20)
Low risk (0–10%)	443 (36%)
Intermediate risk (10–30%)	642 (52%)
High risk (30–100%)	146 (12%)
Clinical stage (n = 1392)	
T1	967 (69%)
T2a	150 (11%)
>T2a	275 (20%)
Biopsy Gleason grade (n = 1363)	
<7	886 (65%)
7	405 (30%)
>7	72 (5%)
Pathologic Gleason grade (n = 1383)	
<7	501 (36%)
7	794 (57%)
>7	88 (6%)
Extracapsular extension (n = 1331)	357 (27%)
Seminal vesicle invasion (n = 1384)	75 (5%)
Non-organ-confined disease (n = 1314) ^a	378 (29%)
Positive surgical margins (n = 1384)	173 (13%)
RP = radical prostatectomy; PSA = prostate-specific antigen.	
^a Presence of extracapsular extension, seminal vesical invasion, or lymph node invasion.	

then yearly afterwards. Progression of disease was defined as a PSA of ≥ 0.1 ng/ml with confirmatory rise or initiation of secondary therapy; this information was available for 1422 patients (91%).

Patients were stratified as low, intermediate, or high risk based on the pretreatment prostate cancer nomogram progression-free probability of >90%, 89–71%, and <70%, respectively.

2.8. Statistical analysis

The probability of freedom from recurrence following radical prostatectomy was estimated using the Kaplan-Meier method. The Fisher exact test was used to compare rates of lymph node involvement among patients with a standard or limited PLND. Only patients with a predicted probability of lymph node involvement of >1% were compared because this was the requirement for lymph node dissection before February 2005. All statistical analyses were conducted using Stata 10.0 (StataCorp, College Station, TX, USA).

3. Results

3.1. Clinical and pathologic characteristics

The clinical and pathologic features in this series fit the characteristics of prostate cancer treated in the

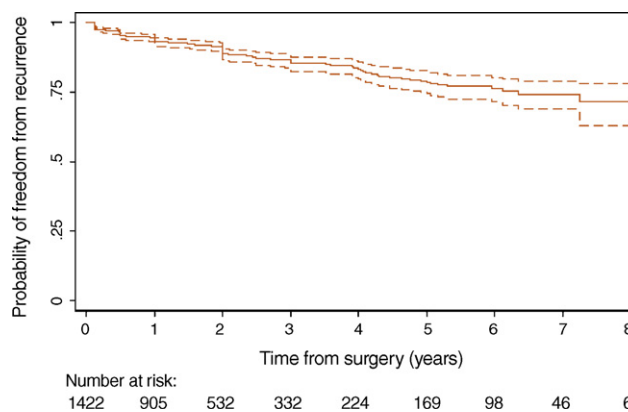


Fig. 1 – Kaplan-Meier probability of freedom from progression, with 95% confidence intervals.

modern post-PSA era. The intermediate- and high-risk groups, as defined in this study, represented 52% and 12% of the patient population, respectively (Table 1). The overall positive surgical margin rate was 13%.

3.2. Oncologic outcome

3.2.1. Survival and progression

Only 2 patients died of prostate cancer during the study period, and 20 died of other causes. There was 1 local recurrence documented by biopsy and 10 cases of metastasis following surgery. Among the 1422 patients in our cohort, 153 experienced biochemical recurrence following surgery. The median follow-up for patients without recurrence was 1.5 yr; 167 patients (12%) were recurrence-free at 5 yr and were followed for >5 yr. The actuarial probability of remaining free of progression at 5 and 8 yr postoperatively was 78% (95% CI, 74–82%) and 71% (95% CI, 63–78%), respectively (Fig. 1). The 5-yr progression-free probability for men with low-, intermediate-, and high-risk prostate cancers was 91% (95% CI, 85–95%), 77% (95% CI, 71–82%), and 53% (95% CI, 40–65%), respectively (Fig. 2). When stratified by pathologic stage, 5-yr freedom from progression of disease after LRP was 83% (95% CI, 66–91%) and 69% (95% CI, 52–80%) for organ-confined (pT2, node-negative) and non-organ-confined cancers (pT3, node-negative), respectively (Fig. 3).

3.2.2. Pelvic lymph node dissection

Among patients with a nomogram-predicted probability of lymph node involvement >1% and who had a lymph node dissection performed, the number of lymph nodes retrieved and positivity rate detected were higher among those treated by a standard PLND (internal iliac, external iliac, and

Table 2 – Summary of lymph node dissection and lymph node involvement

	Overall (n = 1422)	Before February 1, 2005 (n = 849)	After February 1, 2005 (n = 573)
Lymph node dissection performed	828 (58%)	262 (31%)	566 (99%)
Number with predicted probability of lymph node involvement >1%	962	596	366
Lymph node dissection performed	603 (63%)	239 (40%)	364 (99%)
Lymph node involvement	45 (7%)	7 (3%)	38 (10%)
Median number of nodes removed (range)	12 (1–48)	9 (1–27)	13 (2–48)

obturator fossa groups) than among those treated by a limited PLND (external iliac group only) (10% vs 3%, $p < 0.001$) (Table 2). While no patient with positive lymph nodes was followed without recurrence to 5 yr, the 3-yr probability of freedom from recurrence for these patients was 49% (95% CI, 32–64%) (Fig. 3).

4. Discussion

The introduction of the laparoscopic approach to performing radical prostatectomy was carried by the hope that better visualization and access to the tight confines of the male human pelvis would eventually translate into better oncological, functional, and morbidity outcomes, and while hypothetically it all made sense, the available scientific evidence has not been able to confirm any major advantages. In fact, the gold standard of evidence-based medicine (ie, randomized study) has not been possible to accomplish in order to test the above hypothesis. Prospective comparative analysis of open and LRP, however, demonstrated equivalency of oncologic results with regard to positive surgical margin rate, quality of PLND, and short-term progression-free probability [9]. One important clarification is that the end point of the present report is not a comparison of oncologic efficacy of LRP versus other approaches or treatment modalities but rather a description of oncologic results of 10 yr of experience with LRP across all risk groups. The reported data in the literature are discussed in this manuscript to provide perspective and should by no means be used for a comparative analysis, since the methodology, time frame of the study, and end point definitions vary greatly from one study to another.

Large, single-institution experiences from both Europe and the United States have reported favorable short-term oncologic outcomes, providing another level of evidence that cancer control after LRP would compare favorably to other large series of open radical prostatectomy, but long-term data are awaited [6–8]. After a decade of LRP, midterm cancer control data are now available and show that LRP effectively controlled the disease in 78% (95% CI, 74–82%) of men with prostate cancer at 5 yr after surgery. Comparable results were reported by our MSKCC group using the open surgical approach, with 82% freedom from progression at 5 yr after surgery [16]. We expect the overall midterm oncologic results obtained in this laparoscopic

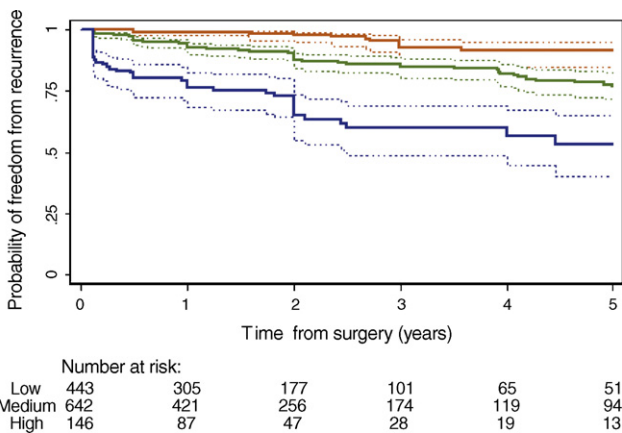


Fig. 2 – Kaplan-Meier probability of freedom from progression by preoperative risk, with 95% confidence intervals.

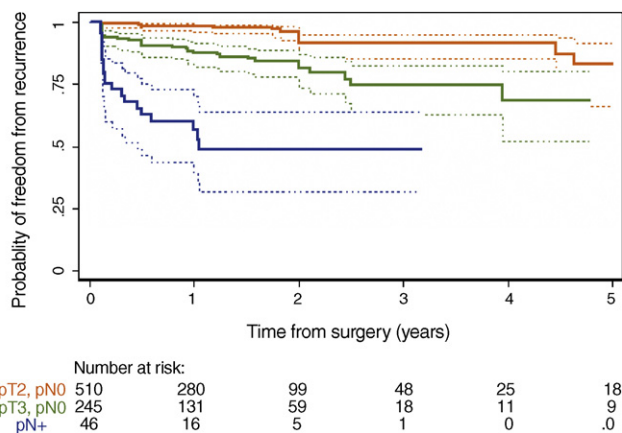


Fig. 3 – Kaplan-Meier probability of freedom from progression by pathologic risk group, with 95% confidence intervals.

experience to continue to compare favorably with long-term results established with the open approach. However, evaluation of the overall results in a disease known for its heterogeneity and width of its prognostic significance spectrum, with cancers ranging from totally indolent to rapidly lethal, is not helpful for a given patient whose cancer carries particular features. Reporting of results based on risk groups can be more informative. When stratified by risk of disease according to Kattan's nomogram-predicted progression-free probability, LRP was effective in controlling cancer at 5 yr postoperatively in 53% (95% CI, 40–65%) of men with high-risk prostate cancer, confirming the fact that high-risk prostate cancer can very well be treated laparoscopically. Hull and colleagues reported 65% 5-yr cancer control in the high-risk group defined according to the D'Amico criteria (ie, presence of clinical stage T2c, or Gleason sum >7, or PSA >20 ng/ml) after excluding patients with clinical T3 cancer [17], while Kupelian et al reported a 37% freedom from progression at 5 yr after open radical prostatectomy [18]. In a risk-stratified comparison of oncologic outcomes after radical prostatectomy, external beam radiotherapy, and brachytherapy with or without hormonal therapy, D'Amico et al [19] reported lower 5-yr freedom from recurrence rates for the high-risk patients than our findings or those of Hull et al [17]. At our institution, the agreed upon definition of biochemical recurrence is 0.1 ng/ml confirmed by a subsequent rising PSA level. According to our data, any detectable postoperative PSA should be interpreted as a recurrence of cancer after radical prostatectomy. Other PSA cut-offs have been shown to correlate better with clinically important end points such as development of metastases [20].

One particularity about our study is that it includes a consecutive experience starting with the very first patients to undergo LRP and, most important, it reflects the evolution of the surgical technique over the last decade as well as the transfer of knowledge from a first- to a second-generation laparoscopic surgeon. One such evolutionary process is the change in indications and anatomic limits of PLND during LRP. By extending the template of PLND to include the external iliac, hypogastric, and obturator fossa nodal groups, detection of nodal metastases significantly increased 3-fold. While this finding is not new and has clearly been demonstrated by Bader and colleagues [21], it does confirm that an extended PLND is feasible laparoscopically, and any lesser anatomic variant is inadequate to properly detect nodal metastasis [22].

5. Conclusions

LRP provided 5- and 8-yr biochemical recurrence-free survival in 78% and 71% of patients, respectively, with clinically localized prostate cancer and 53% biochemical recurrence-free survival at 5 yr in those with high-risk cancers.

A PLND limited to the external iliac nodal group is inadequate for detecting nodal metastases.

These data establish the maturity of the laparoscopic technique and could be used as a proof of principle in designing clinical trials comparing the oncologic efficacy of laparoscopy to other treatment modalities in men with low-, intermediate-, or high-risk prostate cancers.

Author contributions: Karim Touijer had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Guillonneau, Vickers, Touijer.

Acquisition of data: Katz, Secin, Bianco, Vora, Touijer.

Analysis and interpretation of data: Guillonneau, Cronin, Vickers, Touijer.

Drafting of the manuscript: Touijer.

Critical revision of the manuscript for important intellectual content:

Guillonneau, Reuter, Vickers, Cronin, Touijer.

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