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Hospital Authority Head Office
Professional Services & Medical Development Division

Clinical Effectiveness Unit
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How could clinically localised prostate cancer be best managed?

From the Review Panel .....

Current evidence does not allow definite recommendations to be made on the relative merits of the major treatment options available for clinically localized prostate cancer in terms of overall survival, cancer-specific outcomes (mortality and morbidity), treatment-related complications, and quality of life issues.

In the absence of good evidence, treatment varies according to prevailing believes of doctors and patients. The following considerations, adapted from the American Urological Association's recommendation[a], constitute a reasonable and practical approach in managing patients presenting with clinically localized prostate cancer:

i) Radical prostatectomy, radiation therapy (external beam / interstitial) and surveillance are acceptable alternative treatment options for localised prostate cancer. Current best evidence available is insufficient to indicate superiority of any one of them.

ii) Patient's life expectancy (rather than age), overall health status, and tumour characteristics (histological grade and stage) are important determinants to guide treatment decision.

iii) Patient should be informed of the commonly accepted initial interventions, including radical prostatectomy, radiation therapy and surveillance, and have their benefits and harms discussed. It is important to note that treatment-related outcomes could have serious implication on patient's quality of life.

[a] *Middleton RG, Thompson IM, Austenfeld MS, Cooner WH, Correa RJ, Gibbons RP, et al. Prostate cancer clinical guidelines panel summary report on the management of clinically localized prostate cancer. J Urol 1995 Dec;154(6):2144-8.*

Does conservative management has a role in managing clinically localised low-grade prostate cancer?

There is insufficient evidence to conclude whether early intervention improves survival, reduces disease-specific death or morbidity, or improve patient's quality of life compared with conservative management. Few trials[1,2] compared expectant management with immediate treatment but they were of poor scientific quality. A number of observational studies[3,4,5,6] reported reasonably long survival in conservatively managed patients with clinically localised low-grade prostate cancer.

A. Trials comparing expectant management with alternative treatments:

<table>
<tr><th>Ref.</th><th>Study features</th><th>Potential bias</th><th>Main findings</th></tr>
<tr><td>1.</td><td>Randomised controlled trial: radical prostatectomy vs expectant management for clinically localised (VACURG stage I and II) prostate cancer. 142 patients with VACURG stage I & II prostate cancer (corresponds to T0-1NxM0, & T2NxM0, respectively) were recruited and randomised</td><td>Small sample size (with limited statistical power).
As patients were recruited from 15 hospitals over 8 years, it was unlikely that they received uniform care.
There were more elderly patients in the placebo arm.
Cause of death could not be ascertained.
Not intention-to-treat analysis (31 patients excluded)</td><td>Outcome of 111 patients, 50 managed conservatively (age 50-84, mean 66.0) and 61 with radical prostatectomy (age 44-82, mean 62.7), after following up for 19-27 years (median 23) were compared.
The overall survival was significantly correlated ($p < 0.001$) to tumor grade (Gleason score ≤4, 5-6, & 7-10) but not to treatment strategy. Median survival for expectant management and radical prostatectomy were 8 years and 10.6 years, respectively (not statistical significant).</td></tr>
<tr><td>2.</td><td>Prospective cohort study: Of 642 patients (mean age at diagnosis 72 years) with prostate cancer (of any stage) consecutively diagnosed between 1977 and 1984, 300 cases were clinically localized. These patients received initial or deferred treatment & were prospectively followed-up for a mean of 168 months (range 126 to 210).
[Level III evidence]</td><td>Small sample size.
Non-random assignment to treatment: patients with moderately and poorly differentiated palpable tumours were apparently more likely to receive initial treatment.
84% of cases relied on fine-needle aspiration for diagnosis. This suggested many cancers were of low-grade</td><td>300 patients presented (not detected by screening) with clinically localized prostate cancer (T0-T2 and M0). 77 of them received initial treatment.
Patients were assessed every 2-12 monthly, and a bone scan performed every 6-12 monthly. The 15-year survival rate was similar between the 2 groups:
<table>
<tr><th rowspan="2"></th><th colspan="2">% disease-specific survival (95% CI)</th></tr>
<tr><th>10-year</th><th>15-year</th></tr>
<tr><td>Deferred treatment</td><td>85.6 (79.8 – 91.4)</td><td>80.9 (72.4 - 89.4)</td></tr>
<tr><td>Initial treatment</td><td>84.7 (72.6 – 96.8)</td><td>80.7 (66.8 – 94.6)</td></tr>
</table>
</td></tr>
</table>

[Source:

1. *Iversen P, Madsen PO, Corle DK. Radical prostatectomy versus expectant treatment for early carcinoma of the prostate: twenty-three year follow-up of a prospective randomized study. Scand J Urol Nephrol Suppl 1995;172:65-72.*

2. *Johansson JE, Holmberg L, Johansson S, Bergstrom R, Adami HO. Fifteen-year survival in prostate cancer: a prospective, population-based study in Sweden. JAMA 1997 Feb 12;277(6):467-71.]*

B. Non-comparative observational studies on conservative management:

<table>
<tr><th>Ref.</th><th>Study features</th><th>Potential bias</th><th>Main findings</th></tr>
<tr><td>3.</td><td>Systematic review: 6 non-randomised studies (MEDLINE; 1985-1992) on treatment of clinically localised prostate cancers by observation & delayed hormone therapy.
Individual patient data were assessed for suitability of combined analysis: 828 cases were included.
[Level III evidence]</td><td>Unknown selection bias: studies were neither randomised nor population based. Data were further selected for pooled analysis.
Small sample size.
155 patients (19%) had very early stage (A1, focal, T0a, or T01) cancer.
3 studies used delayed local therapy with external-beam radiation (18 patients), interstitial radiation (46 patients), & radical prostatectomy (6 patients)</td><td>Rate of progression to metastasis differed significantly among the 3 tumor grades (Gleason score 2-4; 5-7 & 8-10). 10-yr disease-specific survival was significantly inferior in grade 3 cancers (Gleason score 8-10).
<table>
<tr><th>Survival at 10 years \ Grade (Gleason score)</th><th>1 (2-4) (n=492)</th><th>2 (5-7) (n=265)</th><th>3 (8-10) (n=62)</th></tr>
<tr><td>Disease-specific survival *</td><td colspan="2">87%</td><td>34%</td></tr>
<tr><td>Metastasis-free survival *</td><td>81%</td><td>58%</td><td>26%</td></tr>
</table>
* Excluding men who died from causes other than prostate cancer
The authors concluded, “The strategy of initial conservative management and delayed hormone therapy is a reasonable choice for some men with grade 1 or 2 clinically localized prostate cancer, particularly for those who have an average life expectancy of 10 years or less. New treatment strategies are needed for men with grade 3 prostate cancer.”</td></tr>
<tr><td>4.</td><td>Cohort study: compared survival of patients with clinically localized prostate cancer treated conservatively with the general population.
Disease cohort: 451 men, cancer diagnosed in 1971 to 1976, age 65-75 years at diagnosis (mean 70.9), tumour stage: A (51%), B (49%).
[Level III evidence]</td><td>Retrospective review of cancer registry data.
Brief description of treatment strategy: “untreated or treated with immediate or delayed hormonal therapy”.
55% of tumours with Gleason score of 2-4 were detected incidental to transuretheral resection for benign prostatic hyperplasia</td><td>Among 451 patients, 202 received immediate hormonal treatment. After a mean follow-up of 15.5 years, 40 men (9%) were alive, 154 (34%) had died of prostate cancer, 221 (49%) had died of other causes, and 36 (8%) had died but cause of death unknown.
Study revealed cancer histology and comorbidity as powerful independent predictors of survival.
<table>
<tr><th>Gleason score</th><th>Maximum estimated loss of life expectancy with reference to the general population (years)</th></tr>
<tr><td>2-4</td><td>No significant difference</td></tr>
<tr><td>5-7</td><td>4-5</td></tr>
<tr><td>8-10</td><td>6-8</td></tr>
</table></td></tr>
<tr><td>5.</td><td>Prospective observational study: 122 men (mean age at diagnosis 68 years) with palpable, clinically localised (T1-2, Nx, M0), low-grade (77 well differentiated, 45 moderately differentiated) prostate cancer diagnosed between 1971-1984 were managed conservatively (surveillance and treat upon symptomatic progression of disease) and followed up to 1994.
[Level III evidence]</td><td>Small sample size.
Outcomes after 10 years are speculative as data are not definitive beyond such duration of follow-up.
Deferred treatment was hormonal therapy in 45 patients, external beam radiation therapy in 12, radical prostatectomy in 4, and brachytherapy with ^{125}I in 3.</td><td>121 patients had been observed for ≥10 years and 48 for 15 years. 48% of patients did not required anti-tumour therapy before death or at follow-up. The chance of being untreated 5 and 10 years after diagnosis, if still alive, was 71% and 43%.
87 (71%) patients died, 25 from prostate cancer. The actual overall and disease-specific survival rate at 10 years was 52% (95%CI 43% to 61%) and 90% (95%CI 85% to 95%). Of the patients with a possible observation period of 15 years of more, 25% died of prostate cancer. Using a survival plot, the projected overall and disease-specific survival rate at 15 years was 24% (95%CI 15% to 33%) and 62% (95%CI 49% to 76%). The actual metastasis-free survival rate at 10 years was 82% (95%CI 75% to 89%). The projected metastasis-free survival rate at 15 years was 48% (95%CI 32% to 64%). There was no difference in disease-specific survival between patients with well and moderately differentiated tumours.</td></tr>
<tr><td>6.</td><td>Observational study: data of 767 men (age 55-74 yrs) with localized prostate cancer diagnosed between 1971-1984 were retrospectively reviewed.
Primary outcome: Probability of dying from prostate cancer or other competing causes stratified by age (at</td><td>Retrospective review.
Small sample size.
Accurate staging information was lacking for many patients.
42% of patients received hormonal therapy within 6 months of diagnosis.</td><td>At 1 March 1997, 610 patients were dead; the remaining (alive or lost to FU) had been follow-up for mean of 15.4 years. The probability of dying from prostate cancer (first column) or other diseases (second column) stratified by age and Gleason score (at diagnosis) were:
<table>
<tr><th rowspan="2">Gleason score</th><th colspan="8">Age at diagnosis</th></tr>
<tr><th colspan="2">55-59</th><th colspan="2">60-64</th><th colspan="2">65-69</th><th colspan="2">70-74</th></tr>
<tr><td>2-4</td><td>4%</td><td>27%</td><td>5%</td><td>40%</td><td>6%</td><td>56%</td><td>7%</td><td>73%</td></tr>
<tr><td>5</td><td>6%</td><td>27%</td><td>8%</td><td>39%</td><td>10%</td><td>55%</td><td>11%</td><td>71%</td></tr>
<tr><td>6</td><td>18%</td><td>25%</td><td>23%</td><td>36%</td><td>27%</td><td>48%</td><td>30%</td><td>59%</td></tr>
<tr><td>7</td><td>70%</td><td>15%</td><td>62%</td><td>24%</td><td>53%</td><td>36%</td><td>42%</td><td>51%</td></tr>
<tr><td>8-10</td><td>87%</td><td>10%</td><td>81%</td><td>16%</td><td>72%</td><td>25%</td><td>60%</td><td>38%</td></tr>
</table></td></tr>
</table>

	diagnosis) and histology (Gleason score). [Level III evidence]		Apparently, men with well-differentiated disease (Gleason scores 2-4) face a minimal risk of death from prostate cancer within 15 years of diagnoses. Men with poorly differentiated disease (Gleason scores 7-10) face a high risk of death from prostate cancer when treated conservatively even when diagnosed as late as age of 74 years. Men with moderately differentiated disease (Gleason scores 5-6) face a modest risk of death from prostate cancer that increases slowly over at least 15 years of follow-up.

[Source:

3. *Chodak GW, Thisted RA, Gerber GS, Johansson JE, Adolfsson J, Jones GW, et al. Results of conservative management of clinically localized prostate cancer. N Engl J Med 1994 Jan 27;330(4):242-8.*
4. *Albertsen PC, Fryback DG, Storer BE, Kolon TF, Fine J. Long-term survival among men with conservatively treated localized prostate cancer. JAMA 1995 Aug 23-30;274(8):626-31.*
5. *Adolfsson J, Steineck G, Hedlund PO. Deferred treatment of clinically localized low-grade prostate cancer: actual 10-year and projected 15-year follow-up of the Karolinska series. Urology, 1997 Nov;50(5):722-6.*
6. *Albertsen PC, Hanley JA, Gleason DF, Barry MJ. Competing risk analysis of men aged 55 to 74 years at diagnosis managed conservatively for clinically localized prostate cancer. JAMA 1998 Sep 16;280(11):975-80.]*

[***Editorial note:***

i) Only limited evidence of poor quality is available. Findings reported were inconclusive.

ii) In appraising studies reporting the natural history or treatment outcome of early prostate cancer, it is important to consider lead-time bias for tumours detected by PSA screening compared to other modes of presentation.

iii) To defer treatment of clinically localised prostate cancer until symptomatic progression avoids (or delays) treatment-associated hazards, many of which have serious impact on quality of life. However, it gives up the opportunity to cure the cancer at a stage when it is potentially possible. Prostate cancer, once metastasised, will progress relentlessly and fatality is relatively rapid.]

Few trials directly compared treatment alternatives for clinically localised prostate cancer

As it is difficult to draw conclusion about the relative effectiveness of a particular intervention from observational studies without a control group, we have not included individual reports of such evidence in the following discussion. There are few trials that directly compared treatment alternatives for clinically localised prostate cancer.

C. Apart from one RCT[1] described above, we found another RCT comparing radical prostatectomy with external beam irradiation in men with clinically localized prostate cancer (stage A2-B/T1-2N0M0; and staging pelvic lymphadenectomy negative). 106 patients were randomised but data of 97 patients analysed. Study reported metastasis in 4 prostatectomy patients and 17 radiation patients. Analysis of the time to failure curves revealed surgery had disease control advantage over radiation therapy ($p = 0.037$).

[Source: Paulson DF, Lin GH, Hinshaw W, Stephani S. Radical surgery versus radiotherapy for adenocarcinoma of the prostate. J Urol 1982 Sep;128(3):502-4.]

[***Editorial note:***

i) The study used 'first evidence of treatment failure' rather than 'survival data' as endpoint of treatment efficacy.

ii) Small sample size with insufficient power to confidently rule out a clinically important difference between treatment arms.

iii) An intention-to-treat analysis was not used.]

D. A retrospective cohort study of 1872 men with clinically localised prostate cancer compared PSA outcome after radical prostatectomy (n = 888), external beam radiation (n = 766), or interstitial radiation therapy with (n = 152) or without (n = 66) neoadjuvant androgen deprivation. It found that low-risk patients had similar estimates of 5-year PSA outcome for all treatment strategies, whereas intermediate- and high-risk patients treated with radical prostatectomy or external beam radiation had lower risk of PSA failure than those treated by interstitial radiation.

Relative risk (RR) of PSA failure compared with radical prostatectomy:

Treatment	Low risk (Stage T1c-T2a and PSA ≤10ng/mL and Gleason score ≤6)			Intermediate risk			High risk (Stage T2c or PSA >20ng/mL or Gleason score ≥8)		
	RR	95%CI	p	RR	95%CI	P	RR	95%CI	P
External beam radiation	1.1	0.5-2.7	0.79	0.8	0.5-1.2	0.26	0.9	0.7-1.1	0.26
Interstitial radiation	1.1	0.3-3.6	0.91	3.1	1.5-6.1	0.006	3.0	1.8-5.0	0.0002
Interstitial radiation plus androgen deprivation	0.5	0.1-1.9	0.21	1.6	0.8-3.3	0.22	2.2	1.2-4.0	0.02

[Source: D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Blank K, Broderick GA, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA 1998 Sep 16;280(11):969-74.]

[***Editorial note:*** Study used a surrogate marker as primary outcome measure.]

Indirect comparison of radical prostatectomy, radiotherapy and conservative management outcomes are difficult, if not impossible

E. A systematic review of evidence on localized prostate cancer (search Medline from 1966 to 1993) managed by radical prostatectomy, external beam radiotherapy, brachytherapy, or surveillance identified poor evidence base (165 reports, mostly observational studies). The authors noted significant difference in patient age, tumour grade and pelvic lymph node status among studies to the extent precluding meta-analysis and valid comparison of outcomes. **Qualitative analysis** of outcomes found:

a) Survival:

- All measures of 5-year survival were excellent for all 4 treatments.
- There are significantly fewer reports with 10 and 15-year survivals. The difference observed in overall 10 and 15-year survivals between treatments could be explained by patient selection (confounding) factors. Evidence on 10 and 15-year progression-free and disease-specific survival was too few or too variable to permit reasonable conclusion to be made on the relative effectiveness of different treatments.

b) Disease progression: Inconsistent definitions used in individual studies invalidated comparison of progression outcome data.

c) Adverse outcomes:

- Treatment related death was uncommon.
- Published rates of urinary obstruction and incontinence were higher following surgery, whereas cystitis and bowel/rectal injury were more frequent with radiotherapy.
- Few reports compared pre- and post-treatment potency carefully. Impotence seemed more frequent after prostatectomy but could be biased by patient selection factors.

	Radical Prostatectomy		External beam radiotherapy		Brachytherapy		Surveillance	
	No. of study	Min & Max reported rate	No. of study	Min & Max reported rate	No. of study	Min & Max reported rate	No. of study	Min & Max reported rate
5 yr survival								
– Overall	10	68.9-95.0%	39	51.4-93.0%	8	57.0-93.0%	7	67.0-92.0%
– Progression-free	2	81.9-92.0%	29	32.0-93.0%	14	38.0-90.0%	1	68.0%
– Metastasis-free	0		4	46.0-85.0%	0		0	
– Disease-specific	5	90.0-97.0%	7	63.5-96.0%	3	92.0-100%	3	89.0-99.0%
10 yr survival								
– Overall	7	44.4-88.0%	11	41.4-70.0%	0		5	34.0-70.7%
– Progression-free	1	82.0%	10	40.0-64.0%	7	50.0-90.0%	1	53.0%
– Metastasis-free	0		0		0		0	
– Disease-specific	3	88.5-93.0%	3	66.1-86.0%	0		3	84.0-85.0%
15 yr survival								
– Overall	8	22.2-75.0%	2	31.0-33.0%	0		4	39.0-67.0%
– Progression-free	1	70.0%	0		0		0	
– Metastasis-free	0		0		0		0	
– Disease-specific	5	55.0-93.0%	0		0		0	

[Source: Middleton RG, Thompson IM, Austenfeld MS, Cooner WH, Correa RJ, Gibbons RP, et al. Prostate cancer clinical guidelines panel summary report on the management of clinically localized prostate cancer. J Urol 1995 Dec;154(6):2144-8.]

[***Editorial note:*** It is likely that studies with negative or equivocal results were underrepresented in the evidence base due to publication bias.]

F. In another similar systematic review of slightly restricted search, the authors identified 144 studies (only 1 being RCT) from Medline for the period 1966 to 1993. They were unable to compare treatment effectiveness because (i) only 9 series reporting metastatic rates and 7 series reporting cancer-related mortality stratified outcomes by tumour grade; (ii) in those series reporting metastatic rates, 48% did not account for patients unavailable for follow-up, 92% did not stratified patients by age, and 52% did not stratified patient by the extent of disease at treatment.

[Source: Wasson JH, Cushman CC, Bruskewitz RC, Littenberg B, Mulley AG Jr, Wennberg JE. A structured literature review of treatment for localized prostate cancer. Arch Fam Med 1993 May;2(5):487-93.]

G. Retrospective review of data in the cancer registry "Surveillance, Epidemiology, and End Results (SEER) Program" (involving Connecticut, Hawaii, New Mexico, Iowa, Utah, San Francisco-Oakland, Detroit, Atlanta, and Seattle) identified 59,867 men aged 50-79 who had clinically localised prostate cancer diagnosed between Jan 1, 1983 to Dec 31, 1992. The mean length of follow-up was 44.5 months. Survival outcomes at 10 years by intention-to-treat analysis (avoiding influence of differential staging between treatment options) are:

	Number	10-year disease-specific survival		10-year overall survival		10-year survival relative to age-matched cohort
		%	(95% CI)	Disease cohort (%)	Age-matched cohort (%)	
Gleason score 2-4						
Prostatectomy	3854	94	(91 - 43)	77	65	1.17
Radiotherapy	4065	90	(87 - 92)	63	54	1.17
Conservative	9804	93	(91 - 94)	54	53	1.01
Gleason score 5-7						
Prostatectomy	14287	87	(85 - 89)	71	64	1.11
Radiotherapy	7939	76	(72 - 79)	48	52	0.93
Conservative	6198	77	(74 - 80)	38	49	0.78
Gleason score 8-10						
Prostatectomy	5133	67	(62 - 71)	54	62	0.87
Radiotherapy	2596	53	(47 - 58)	33	52	0.63
Conservative	2236	45	(40 - 51)	17	47	0.36

It is notable that all patients with low-grade disease (Gleason score 2-4) had similar or even better overall survival than the age-matched cohort, whatever the initial treatment.

[Source: Lu-Yao GL, Yao SL. Population-based study of long-term survival in patients with clinically localised prostate cancer. Lancet 1997 Mar 29;349(9056):906-10.]

[***Editorial note:*** There was a potential bias in favour of radical prostatectomy as patients were on average 5 years younger in this treatment group.]

There is renewed interest in brachytherapy but evidence is insufficient and inconclusive

H. This followed the publication of several uncontrolled case series in late 90's reporting favourable outcomes with brachytherapy, generally attributed to the development of new technique and improved diagnostic imaging methods. A recent systematic review on the topic revealed poor evidence base due to "absence of controlled trials, incomplete reporting of results, limited comparison with other treatment modalities, inadequate outcome data for these other methods, and differences in patient populations". It is hard to establish the efficacy of brachytherapy, or other treatments, given the long follow-up required for an indolent cancer, and the current variation in patient identification strategy and treatment practice. Main conclusions of the review were: "Biochemical (PSA) outcomes indicate that brachytherapy is a reasonable option for treatment of early prostate cancer in the short-term, or as an adjuvant therapy to external beam irradiation in more advances stages. Biochemical control rates ranged from 95% to as low as 60% with 10 years follow-up, probably reflecting the diversity of study populations and techniques used. Disease recurrence revealed by biopsy ranged from 5-35% (depending on the study protocol and time of follow-up). Disease-specific death ranged from 0-3%. Overall survival ranged from 65% for studies with long follow-up, to no reported deaths". In essence, brachytherapy appears a promising intervention for localized prostate cancer in the short-term but its effect on other outcome measures, particularly long-term morbidity and survival, remains unknown.

[Source: Wills F, Hailey D. Brachytherapy for prostate cancer [online]. Edmonton, Alta.: The Alberta Heritage Foundation for Medical Research, 1999 Dec. HTA 17.
Available from: URL: http://www.ahfmr.ab.ca/hta/hta-publications/reports/HTA17.FINAL.rtf]

[***Editorial note***: Publication bias and patient selection bias (subjecting more promising candidates to brachytherapy) could have favoured brachytherapy.]

Quality of life issues have implications in treatment planning but evidence is scanty

I. A cross-sectional study (by questionnaire) compared health-related quality of life measures in patients with and without prostate cancer. 79% of prostate cancer patients and 46% of control patients responded: patients with clinically localized prostate cancer and radical prostatectomy (n = 98, 23 had nerve sparing procedure), pelvic irradiation (n = 56), or conservative management (n = 60), and age-matched patients without prostate cancer (n = 273). The different patient groups were comparable in terms of age, race, education, income, presence of comorbidity and (for prostate cancer patients) time since diagnosis of cancer. The survey found:

i) General health-related QOL (by RAND 36-Item Health Survey 1.0) did not differ among treatment groups or with comparison patients, except conservatively managed prostate cancer patients reported more role limitation due to emotional problems.

ii) Cancer-targeted scores (by CARES-SF and FACT-G scales) did not differ significantly among the groups, except (i) surgery and radiation patients scored significantly worse on CARES-SF sexual function scale than conservatively managed and comparison

patients, and (ii) comparison patients scored significantly better than surgery and conservatively managed patients on the CARES-SF medical interaction scale. It is notable that patients received nerve-sparing prostatectomy did not differ in cancer-targeted scale scores from those receiving standard prostatectomy, but the power to detect a difference was low.

iii) Disease-targeted scores (measures of sexual, urinary and bowel domains) differed significantly among the patient/treatment groups as depicted below:

	Mean QOL score				P
	Radical prostatectomy	External beam irradiation	Conservative management	Comparison group	
Sexual					
Function scale	19ə	35əϕ	41ϕ	47	< 0.001
Bother item	13ə	29əϕ	37ϕ	48	< 0.001
Urinary					
Function scale	65	82ϕ	86ϕΛ	90Λ	< 0.001
Bother item	68ə	77əϕ	80ϕ	83ϕ	< 0.001
Bowel					
Function scale	82əϕ	81ϕ	84ə	86ə	0.07
Bother item	80ə	77	85ə	85ə	0.07

Means in the same row that share a common symbols (əϕΛ) do not differ significantly from each other by Duncan's multiple range test.

[Source: Litwin MS, Hays RD, Fink A, Ganz PA, Leake B, Leach GE, et al. Quality-of-life outcomes in men treated for localized prostate cancer. JAMA 1995 Jan 11;273(2):129-35.]

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Additional information and comments relative to this issue are welcome, and should be addressed either to EVIDENCE FORUMS, available from <http://ekg> or Dr SP Lim at splim@ha.org.hk.