10-YEAR SURVIVAL AND QUALITY OF LIFE IN PATIENTS WITH HIGH-RISK \( pN_0 \) PROSTATE CANCER FOLLOWING DEFINITIVE RADIOTHERAPY

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Purpose: To evaluate long-term overall survival (OS), cancer-specific survival (CSS), clinical progression–free survival (cPFS), and health-related quality of life (HRQoL) following definitive radiotherapy (RT) given to \( T_{1-4}pN_0M_0 \) prostate cancer patients provided by a single institution between 1989 and 1996.

Methods and Materials: We assessed outcome among 203 patients who had completed three-dimensional conformal RT (66 Gy) without hormone treatment and in whom staging by lymphadenectomy had been performed. OS was compared with an age-matched control group from the general population. A cross-sectional, self-report survey of HRQoL was performed among surviving patients.

Results: Median observation time was 10 years (range, 1–16 years). Eighty-one percent had high-risk tumors defined as \( T_{3-4} \) or Gleason score (GS) \( \geq 7B \) (4+3). Among these, 10-year OS, CSS, and cPFS rates were 52%, 66%, and 39%, respectively. The corresponding fractions in low-risk patients (\( T_{1-2} \) and GS \( \leq 7A \) [3+4]) were 79%, 95%, and 73%, respectively. Both CSS and cPFS were predicted by GS and T-classification; OS was associated with GS only. High-risk, but not low-risk, patients had reduced OS compared with the general population (\( p < 0.0005 \)). When pelvis-related side effects were included in multivariate analyses together with physical function and pain, sexual, urinary, and bowel function were not independently associated with self-reported global quality of life.

Conclusions: Despite surgically proven \( pN_0 \) RT with dosage <70 Gy as monotherapy does not give satisfactory CSS rates after 10 years in patients with \( T_{3-4} \) or GS \( \geq 7B \).

Adverse effects, Lymphadenectomy, Prostate cancer, Quality of life, Radiotherapy.
a self-report survey on HRQoL among patients who were still alive at the end of the observation period.

METHODS AND MATERIALS

Patients

The cohort contains all patients who were treated by definitive RT between 1989 and February 1996 at the Norwegian Radium Hospital (now called the Rikshospitalet-Radiumhospitalet Medical Center). Clinical staging included digital rectal examination, bone scan, and bilateral pelvic lymphadenectomy with resection of the obturator lymph nodes, the latter preferably done at local hospitals before referral to our center.

All prostate tumor biopsies except four were centrally revised according to Gleason’s recommendations (Gleason score [GS]) and further dichotomized into GS ≤7A (3+4) vs. ≥7B (4+3) (5). The four biopsies that were not available were originally graded according to the World Health Organization system (6). Those that were described as well or poorly differentiated were lumped to GS 4–6 or 8–10, respectively. One biopsy was described as moderately differentiated and categorized as GS ≤7A for the purpose of this study. The patients were allocated to a low-risk group (T1–2 and GS ≤7A) or a high-risk group (T3–4 or GS ≥7B) on the basis of the first report in which initial PSA (iPSA) did not show any prognostic impact.

Control group

To compare 10-year overall survival (OS) in PC patients with that of men from the general population, Statistics Norway constructed a control cohort: three age-matched men for each nonemigrating patient were randomly identified. Eligible control subjects had to be alive the year RT was started in the corresponding case. The years of birth and death for each anonymous control subject was made available to the first author.

Radiotherapy

The primary treatment has been previously described in detail (4, 7). Briefly, RT was applied with a four-field box technique (opposing anterior–posterior fields and two opposing lateral fields). During the first years, multiple customized shielding was used. In August 1994, a modification was introduced by using a multileaf collimator. The gross target volume (GTV) was defined by a three-dimensional CT planning system (Helax, Uppsala, Sweden) and covered the prostate and the seminal vesicles. For tumors that did not involve the seminal vesicles, GTV encompassed the prostate only after 50 Gy. All patients received megavolt photon energy, 15 MV, with daily fractions of 2 Gy, 5 days per week. The target dose was 66 Gy in 196 patients, 64 Gy in 3, 68 Gy in 1, and 70 Gy in three patients.

Follow-up after radiotherapy

All patients were seen at the Norwegian Radium Hospital outpatient department 3 months after RT. Thereafter, they were followed up at their urologist’s discretion. Many patients were referred to the hospital during the observation time for reevaluation or because of disease progression. Each patient’s survival status on the cutoff date of the study (December 31, 2005) was retrieved from the Central Population Registry based on the national 11-digit personal identification number. The cause of death was retrospectively determined by reviewing the hospital records and contact with the responsible local clinicians. These sources also provided information on eventual date and type of progression.

Clinical endpoints

Death of any cause was evaluated for OS. The endpoint of cancer-specific survival (CSS) was death due to PC, to complications from PC treatment, from unknown causes in patients who had been proven to suffer from progressive PC, excluding unexpected deaths suggestive of cardiovascular events in patients with stable PC. The critical event for clinical progression-free survival (cPFS) was the first proof of clinical progression: locoregional progression was defined as symptomatic and clinically detectable growth of the prostate tumor or regional lymph nodes. Distant progression was defined as radiographic evidence of metastases. PSA progression alone was not considered to be an endpoint, because serum PSA was not routinely determined during follow-up of PC early in the 1990s in Norway.

Long-term health-related quality of life

Patients who were still alive on December 31, 2005, were included in a self-report survey. By mail, they received the Brief Male Sexual Function Inventory (BSFI) (8), questions regarding urinary and bowel function/bother from the University of California at Los Angeles Prostate Cancer Index (PCI) (9) and the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Instrument, version 3.0 (QLQ-C30) (10, 11). Two ad hoc questions regarding fecal control and the use of pads were added to cover this potentially important side effect from RT.

The results were compared with published, age-adjusted normative data from population studies (12–15). Furthermore, some important single items regarding pelvis-related morbidity were considered. In the QLQ-C30, self-rating of global health status and quality of life is assessed by two separate items scored by 7-point Likert scales ranging from very poor to excellent. The scores are combined in a global health status/quality of life domain (GlobQL). We have studied the impact of other, more specific cancer-related domains and pelvic morbidities on this general domain.

Statistics

All analyses were performed by the Statistical Package for Social Science (SPSS for Windows 12.0, SPSS, Chicago, IL) using descriptive parametric or nonparametric tests, as appropriate. The Kaplan–Meier method was used to evaluate OS, CSS, and cPFS. The observation time started at the first day of RT and ended at the date of the specific endpoint, death, emigration, or cutoff date, whichever occurred first. When OS was compared with the control group from the general population, the time-interval started the year RT was commenced in the patients and ended at the year of death or in 2005 for living men. The predictive impact of pretreatment variables was assessed by log-rank tests for univariate comparisons and by backward conditional Cox regression for multivariate analyzes.

The questionnaires were scored according to published recommendations (9, 10, 15). Missing values were substituted by the respective items’ mean value if the patient had responded to at least 50% of the single items in a domain. Otherwise the individual domain was excluded from further analysis. Domains constructed of more than one item were analyzed for correlation with GlobQL by Spearman’s rho. Scores from important single-item domains were dichotomized, and differences of GlobQL between groups were tested by the Mann–Whitney test. Domains that had statistically significant impact on GlobQL in univariate comparisons were included in a logistical regression backward conditional analysis with GlobQL-score split by 75 on the 0 to 100 scale being the dependent
variable. Domains with strong intercorrelation (Spearman’s rho >0.7) were represented by the domain that correlated most strongly with GlobQL in the univariate analysis.

Tests were two-sided, and a p value <0.05 was considered to be statistically significant.

Because of low sample-size in our cohort, statistical comparisons between scores from the questionnaire with normative data were not considered reliable and therefore not performed. A difference of at least 10 points on a 0 to 100 scale in the QLQ-C30 was, however, regarded as clinically relevant (16).

RESULTS

Survival outcomes

Demographics and clinical outcome. A total of 165 men (81%) had high-risk tumors before treatment (Table 1). Minimum observation time was 10 years for surviving patients, except for two men who were lost to follow-up after 1 and 5 years because of emigration. Clinical progression was reported in 109 patients (54%). Of these, the first appearance was local growth of the prostate gland in 40 patients (37% of those who progressed), growth of regional lymph nodes in 2 (2%), distant metastases in 59 (54%), and combined locoregional and distant progression in 8 patients (7%). Overall, locoregional progression was reported in 53 patients (26% of all patients) and distant metastases in 82 (40%). The 10-year cumulative probabilities of OS, CSS, and cPFS were 79%, 57%, 72%, and 45% respectively (Fig. 1A). The overall death rate remained relatively constant for 15 years after therapy, whereas the risk of clinical progression tended to decline after 10 years. For low-risk patients, the 10-year cumulative probabilities of OS, CSS, and cPFS were 95%, 90%, and 73%, respectively, the comparable fractions in high-risk patients being 52%, 66%, and 39% (Fig. 2). The number of resected lymph nodes also had no impact on any of the endpoints, either when dichotomized by the median (data not shown). The number of resected lymph nodes was local growth of the prostate gland in 40 patients (37% of those who progressed), growth of regional lymph nodes in 2 (2%), distant metastases in 59 (54%), and combined locoregional and distant progression in 8 patients (7%). Over-all, locoregional progression was reported in 53 patients (26% of all patients) and distant metastases in 82 (40%).

Predictive impact of pretreatment factors. GS $\geq$7B compared with GS $\leq$7A was significantly associated with reduced OS (p = 0.02), CSS (p = 0.002), and cPFS (p < 0.0001) in univariate analyses (Fig. 1B). Compared with T1-2, T3-4 was associated with reduced CSS (p = 0.002) and cPFS (p = 0.0002) (Fig. 1C). No association was observed between iPSA and any of the endpoints (Fig. 1D). Neither did treatment delay nor age at treatment start have a significant impact on outcome when dichotomized by the median (data not shown). The number of resected lymph nodes also had no impact on any of the endpoints, either when dichotomized by the median (8) or when using a cutoff number of 15.

In multivariate analyses, including all factors from Table 1, GS and T-classification remained independently associated with cPFS and CSS (Table 2). Only GS had independent influence on OS.

Self-report survey on health-related quality of life

Demographics. Of 90 patients who were alive on December 31, 2005, 64 (71%) returned the questionnaire. Nonre-
among American men >70 years as reported by O’Leary et al (15). Despite this, only 39% of the patients and 32% of the general population considered their inability to get and keep erections as a medium or big problem. Furthermore, 63% of the patients reported that they had felt no sexual drive the last 4 weeks, in contrast to 26% in O’Leary’s study.

**Urinary and bowel function.** According to the PCI, patients scored lower on urinary function, urinary bother, and bowel bother compared with age-adjusted men from the general population in the United States (Fig. 4B). The mean score on bowel function was similar, however. Compared with patients who had no clinical progression or HT, patients who

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**Fig. 1.** Clinical outcome among 203 T1-4pN0M0 prostate cancer patients following definitive radiotherapy (RT). (A) All patients. (B–D) Patients categorized by Gleason score, T-classification, and prostate specific antigen.
had progressed or used HT had slightly lower mean score on urinary function but scored similar in urinary bother, bowel function, and bowel bother (Fig. 4B). Some degree of urinary leakage was reported by 46% of the patients (Table 3). In addition, two patients who did not answer the questions regarding urinary function stated that they had a permanent urethral catheter. Among elderly American men without PC, 30% reported some degree of fecal leakage (17, 18).

**EORTC QLQ-C30.** In the 15 domains within the QLQ-C30, patient scores were similar to Norwegian normative data, except that patients overall reported more diarrhea and that those who had progressed clinically, used HT, or both reported some degree of urinary leakage on the same questionnaire (13). In our study, 44% reported some degree of fecal leakage (Table 3), in contrast to 1% to 11% reported in general-population-based studies applying different definitions of fecal leakage (17, 18).

From both surveys could be compared with each other in a longitudinal fashion. In the second survey, the mean outcomes were worse for most domains (Fig. 5A). Furthermore, the differences between mean scores tended to be larger among patients who had progressed clinically, were on HT, or both at the time of the second survey. These findings corresponded to larger reduction in GlobQL and function domains and more aggravation of symptoms compared with patients who remained free of progression (Fig. 5B).

**Interdomain correlations—prediction of Global Health Status/Quality of Life.** In univariate analyzes, GlobQL correlated statistically significantly with physical function, role function, emotion function, cognitive function, social function, fatigue, pain, erection, ejaculation, urinary function, and bowel function (Spearman’s rho). The difference in GlobQL were not statistically significant according to the Mann–Whitney test in patients when they were dichotomized by bowel bother \((p = 0.07)\), urinary bother \((p = 0.49)\), sexual satisfaction \((p = 0.74)\), or clinical progression status (no progression vs. clinical progression and/or HT, \(p = 0.82)\). In a multivariate analysis of GlobQL, physical function was included at expense of role function and fatigue because of strong intercorrelation (Spearman’s rho >0.7). For the same reason, erection was included at the expense of ejaculation. Thus, physical function, emotional function, cognitive function, social function, pain, erection, urinary function, and bowel function were included for logistical regression analyzes. Physical function \((RR = 1.09 \ [CI: 1.03–1.15])\), pain \((RR = 0.94 \ [CI: 0.87–1.00])\), and pain \((RR = 0.94 \ [CI: 0.87–1.00])\) remained in the final model independently associated with GlobQL.

**DISCUSSION**

This study represents one of the largest published RT series with pN0 category in hormone-naive patients with PC, the overwhelming majority being in a high-risk group. We found a steady decline in OS, CSS, and cPFS the first 10 years after definitive RT. CSS and cPFS were associated with GS and T-classification, whereas OS only was predicted...
by GS. Initial PSA did not predict outcome. Overall survival was significantly lower among high-risk patients than in a control group from the general population. Ten years after RT, surviving patients had increased risk of pelvis-related morbidity compared with normative data, however, with similar scores on GlobQL.

Despite negative CT scan, 13% to 52% of T2-3M0 PC-patients are expected to have regional lymph node metastases (19), which are associated with poor prognosis and by many considered to be a sign of systemic disease (20). Magnetic resonance imaging after administration of lymphotropic superparamagnetic nanoparticles might be a noninvasive alternative to surgical staging in the future (21). Presently, however, pelvic lymphadenectomy is the gold standard for locoregional staging and may have several therapeutic benefits: patients with pN0 can, for example, avoid RT of pelvic lymph nodes and possibly adjuvant HT. Furthermore, patients with pN+ may be considered for specific treatment of lymph-node metastases or less mutilating palliative therapy if the chance of cure seems small.

The evaluation of various staging and treatment strategies in nonmetastatic PC is hampered by lack of large prospective, randomized trials. Outcomes from our study are compared with other pN0-series and selected series of non-lymphadenec tomized patients in Table 5, although the validity of such comparison is limited by differences in patient characteristics, treatment strategies, stratification according to prognostic factors, and endpoint definitions. Taking these reservations into account, our results compare well with published 10-year OS (22), CSS (23), and cPFS (24, 25) rates in pNx patients. Clinical and anatomic studies have shown that

### Table 2. Pretreatment factors with independently predictive impact on survival endpoints in patients with pN0M0 prostate cancer treated by definitive radiotherapy (Cox backward conditional regression)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Overall survival</th>
<th>Cancer-specific survival</th>
<th>Progression-free survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR CI p</td>
<td>RR CI p</td>
<td>RR CI p</td>
</tr>
<tr>
<td>Gleason score*</td>
<td>1.6 1.1-2.3 0.02</td>
<td>1.9 1.2-3.3 0.02</td>
<td>2.3 1.5-3.5 &lt;0.0005</td>
</tr>
<tr>
<td>T-classification†</td>
<td>2.3 1.2-4.7 0.02</td>
<td></td>
<td>2.0 1.2-3.2 0.004</td>
</tr>
</tbody>
</table>

Abbreviations: RR, relative risk; CI, confidence interval (95%).

* Gleason score 3+4 vs. 4+3.
† T1,2 vs. T3,4.
‡ T-classification was excluded from the final model of factors with independent impact on overall survival.

![Fig. 4.](image-url) (A) Mean scores from the Brief Male Sexual Function Inventory 10 to 16 years after definitive radiotherapy (RT) for prostate cancer compared to age-adjusted men from the Norwegian general population (15). The domains are constructed of 1 to 4 items scored by Likert scales ranging from 0 to 4. Higher score reflects better function, fewer problems, and higher degree of satisfaction. (B) Mean scores from the University of California at Los Angeles Prostate Cancer Index in patients 10 to 16 years after definitive radiotherapy and in American age-adjusted men without prostate cancer (13). Scores are linearly transformed to 0 to 100 based on raw scores from 3- to 6-point Likert scales. The function domains are constructed of 4 to 5 items and the bother domains of one item. Higher score reflects better function and less bother.
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Table 3. Urinary and fecal leakage at least 10 years after definitive radiotherapy for prostate cancer

<table>
<thead>
<tr>
<th></th>
<th>During the last 4 weeks:</th>
</tr>
</thead>
<tbody>
<tr>
<td>How often have you leaked urine?*</td>
<td>n = 61</td>
</tr>
<tr>
<td>Not at all</td>
<td>33 (54%)</td>
</tr>
<tr>
<td>Less than 1/wk</td>
<td>14 (23%)</td>
</tr>
<tr>
<td>About 1/wk</td>
<td>4 (7%)</td>
</tr>
<tr>
<td>Every day</td>
<td>10 (16%)</td>
</tr>
<tr>
<td>How many pads or adult diapers per day did you usually use to control urinary leakage?*</td>
<td>n = 62</td>
</tr>
<tr>
<td>None</td>
<td>47 (76%)</td>
</tr>
<tr>
<td>1–2</td>
<td>12 (20%)</td>
</tr>
<tr>
<td>3 or more/day</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>How often have you had involuntarily leakage of feces?†</td>
<td>n = 61</td>
</tr>
<tr>
<td>Not at all</td>
<td>34 (55%)</td>
</tr>
<tr>
<td>Less than 1/wk</td>
<td>20 (33%)</td>
</tr>
<tr>
<td>About 1/wk</td>
<td>7 (11%)</td>
</tr>
<tr>
<td>Every day</td>
<td>0</td>
</tr>
<tr>
<td>How many pads or adult diapers per day did you usually use to control leakage of feces?†</td>
<td>n = 63</td>
</tr>
<tr>
<td>None</td>
<td>54 (86%)</td>
</tr>
<tr>
<td>1–2</td>
<td>8 (13%)</td>
</tr>
<tr>
<td>3 or more/day</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

* Single items from the University of California at Los Angeles Prostate Cancer Index.
† Ad hoc questions.

Although we confirm the well-recognized risk of sexual, urinary, and bowel morbidity after RT (32), this might be caused by age-related comorbidities, disease progression, HT, toxicity from RT, or a combination of these. Therefore, randomized trials with baseline data in which RT is compared with conservative treatment are necessary to estimate the proportion of the morbidity that directly is caused by RT. To our knowledge, such studies have currently not been published. Surprisingly, the mean score in the bowel function domain of the PCI was similar to normative data. The lower scores on bowel bother and more diarrhea compared with normative data clearly suggest, however, that a substantial proportion of our patients have bowel side effects from irradiation. The PCI does not cover typical side effects from RT such as proctitis and fecal leakage, and we therefore question the validity of the PCI bowel function domain in evaluating outcome after RT.

General health measures such as physical function and pain were more important predictors of GlobQL than specific pelvis-related morbidities in multivariate analyzes. The patients’ mean score on GlobQL was also similar to Norwegian normative data. The findings might reflect a response shift (33); patients with malignancies adapt well to their organ-specific morbidities and accept them as inevitable side effects from treatment. Others have previously pointed out that the impact of treatment-related side effects on quality of life in PC patients might be overestimated (34, 35), consistent with our findings. However, it can be argued that general questions about subjective health and well-being might be insensitive for changes induced by treatment, possibly limiting their value in evaluating treatment outcome.

In a longitudinal analysis of two surveys applying QLQC30 in the same patients approximately 2 and 10 years after RT, there was a decline in GlobQL and function scores along with increased symptom scores. Some of these changes were expected because of aging (12), but the functional impairment and increase of symptoms were particularly pronounced in patients who had progressed clinically or who were put on HT between the surveys compared with progression-free and hormone-naive patients. We take this in account for that the QLQC30 to a certain degree is sensitive for changes due to disease progression.

There is substantial level 1 evidence that survival outcomes in patients with high-risk PC improve with combined therapy: RT with HT or by RT dose escalation alone (2, 36). We are aware that our low target dose is a shortcoming in this study. With appropriate attendance to volume constrains and neo-adjuvant application of HT (37), higher dosages can likely be applied with modern RT techniques without increase of side effects to the rectum.

In our study, we were not able to assess biochemical progression-free survival (bPFS), which in contemporary studies allows shorter follow-up time compared with studies that apply clinical progression and death as endpoints. The limitations of bPFS as an endpoint lie in uncertainties about clinical relevance and possible overreporting because of...
PSA-bouncing after RT [Hanlon, 2001 (38)]. Although the long-term follow-up in our study allowed more robust clinical endpoints, there are uncertainties related to cPFS and CSS because they were retrospectively assessed. Clinical progression might have been underreported in patients who were put on HT because of PSA elevation, possibly masking symptoms that would have led to search for recurrent disease. OS is, however, extremely reliable because of our updated official death registry and the fact that only two patients were lost to follow-up.

<table>
<thead>
<tr>
<th>Domain/item*</th>
<th>Patients with clinical progression and/or HT (n = 33)</th>
<th>Patients without clinical progression or HT (n = 31)</th>
<th>General population &gt;70 years (12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global health status/QoL</td>
<td>68.3</td>
<td>70.2</td>
<td>71.4</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>76.5</td>
<td>79.4</td>
<td>77.7</td>
</tr>
<tr>
<td>Role functioning</td>
<td>73.7</td>
<td>69.4</td>
<td>73.3</td>
</tr>
<tr>
<td>Emotional functioning</td>
<td>87.4</td>
<td>84.0</td>
<td>87.7</td>
</tr>
<tr>
<td>Cognitive functioning</td>
<td>78.5</td>
<td>81.8</td>
<td>77.6</td>
</tr>
<tr>
<td>Social functioning</td>
<td>70.6†</td>
<td>79.6</td>
<td>81.6</td>
</tr>
<tr>
<td>Fatigue</td>
<td>34.4</td>
<td>28.0</td>
<td>28.5</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>5.4</td>
<td>2.1</td>
<td>3.3</td>
</tr>
<tr>
<td>Pain</td>
<td>16.1</td>
<td>19.2</td>
<td>22.5</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>24.4</td>
<td>23.2</td>
<td>26.0</td>
</tr>
<tr>
<td>Insomnia</td>
<td>29.0†</td>
<td>17.2</td>
<td>17.3</td>
</tr>
<tr>
<td>Appetite loss</td>
<td>6.5</td>
<td>4.0</td>
<td>8.6</td>
</tr>
<tr>
<td>Constipation</td>
<td>22.2</td>
<td>25.0</td>
<td>17.7</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>21.5†</td>
<td>24.7†</td>
<td>9.9</td>
</tr>
<tr>
<td>Financial difficulties</td>
<td>5.6</td>
<td>2.1</td>
<td>4.7</td>
</tr>
</tbody>
</table>

Abbreviations: HT, hormone treatment; QoL, quality of life.

* Raw scores from Likert scales were linearly transformed into scales ranging from 0 to 100. Higher scores in global health status/QoL and the functioning domains reflect better function. Higher scores in the symptom domains reflect more symptoms.
† The items in the physical function domain were scored by 2-point scales in the population study (EORTC-QLQ-C30 version 2.0) and 4-point scales in the current study (version 3.0).
‡ Clinically relevantly different from general population (mean score at least 10 points different).

Fig. 5. Longitudinal results from two surveys applying European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Instrument (QLQ-C30) in 54 prostate cancer patients approximately 2 and 10 years after definitive radiotherapy. * The physical function and role function domains were constructed by items scored by 2-point scales in the first survey (version 1.0 of QLQ-C30) and changed to 4-point scales in the second survey (version 3.0). (A) Mean scores of all patients at the first and second survey. † p < 0.05 (Wilcoxon matched pairs signed rank sum test). (B) Differences between means (second minus first survey) in patients stratified by clinical status at the time of the second survey (progression defined as clinical progression and/or hormone treatment). ‡ p < 0.05 (Mann–Whitney test).
Although the translated versions of the QLQ-C30 and BSFI have been validated in large Norwegian surveys, the translated version of the PCI was piloted only in a small group of patients before its application here (not published). Furthermore, the normative data from PCI are retrieved from a U.S. population, which might differ significantly from our Norwegian sample. Finally, lack of baseline data and our small sample size must be taken into consideration when the results from the questionnaire survey are interpreted.

The strengths in our study include follow-up of at least 10 years in survivors, with only two patients lost to follow-up (because of emigration), clinically relevant endpoints, and a control group from the general population. Furthermore, we have presented longitudinal HRQoL measures and their changes.

We conclude that patients with high-risk \( pN_0 \) prostate cancer steadily progress clinically and die due to PC during the first 10 years after insufficient definitive radiotherapy <70 Gy without adjuvant HT. Such therapy might still, however, be regarded as an option in selected elderly patients with T1-2 and GS \( \leq 7A \).

Prospective, randomized studies are necessary to evaluate further the role of pre-RT lymphadenectomy.

**REFERENCES**

