

## Therapeutics

### Radical prostatectomy reduced death from prostate cancer but not all cause mortality

Holmberg L, Bill-Axelsson A, Helgesen F, et al. *A randomized trial comparing radical prostatectomy with watchful waiting in early prostate cancer.* *N Engl J Med* 2002;347:781–9.

Steineck G, Helgesen F, Adolfsson J, et al. *Quality of life after radical prostatectomy or watchful waiting.* *N Engl J Med* 2002;347:790–6.

**QUESTION:** In men with early prostate cancer, is watchful waiting as effective as radical prostatectomy?

#### Design

Randomised (allocation concealed\*), blinded (outcome assessors, data analysts, and monitoring committee)†, controlled trial with median 6.2 years of follow up (Scandinavian Prostatic Cancer Group Study Number 4 [SPCG-4]).

#### Setting

14 centres in Sweden, Finland, and Iceland.

#### Patients

698 men < 75 years of age with newly diagnosed prostate cancer and tumour stage T0d, T1, or T2. Patients with other cancers or signs of metastases were excluded. 695 men (mean age 65 y) had complete follow up.

#### Intervention

Patients were allocated to radical prostatectomy (n=347) or watchful waiting (n=348). Adjuvant treatment was not given. For local progression, prostatectomy group patients received orchidectomy or gonadotropin releasing hormone analogues and some watchful waiting group patients received transurethral resection.

#### Main outcome measures

Death from prostate cancer, distant metastases, local progression, and overall mortality. A subsequent follow up study assessed quality of life outcomes.

#### Main results

Analysis was by intention to treat. During follow up, fewer patients in the radical prostatectomy group than the watchful waiting group died from prostate cancer (relative hazard [RH] 0.50, 95% CI 0.27 to 0.91) (table), developed distant metastases (RH 0.63, CI 0.41 to 0.96), or had local progression (RH 0.31, CI 0.22 to 0.44). The difference between groups for all cause mortality was not statistically significant (RH 0.83, CI 0.57 to 1.2) (table).

Quality of life outcomes were assessed by mailed questionnaire in 326 men (87% of the men enrolled between January 1989 and February 1996): More radical prostatectomy patients than watchful waiting patients reported erectile dysfunction (80% v 45%, relative risk [RR] 1.8, CI 1.5 to 2.2) and urinary leakage (18% v 2%, RR 9.3, CI 2.9 to 29.9); groups did not differ for bowel function, psychological wellbeing, or subjective quality of life values.

#### Conclusions

In men with early prostate cancer, radical prostatectomy reduced deaths from prostate cancer but did not reduce overall mortality more than watchful waiting. Prostatectomy was associated with more erectile dysfunction and urinary leakage but did not adversely affect self assessed quality of life.

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\*See glossary.

†Information provided by author.

Radical prostatectomy v watchful waiting for prostate cancer at median 6.2 year follow up‡

Outcomes	Radical prostatectomy	Watchful waiting	RRR (95% CI)	NNT (CI)
Death from prostate cancer	4.6%	8.9%	48% (8 to 71)	24 (13 to 173)
All cause mortality	15%	18%	14% (-20 to 38)	Not significant

‡Abbreviations defined in glossary; RRR, NNT, and CI calculated from data in article.

#### COMMENTARY

The initial results of SPCG-4 indicate that 24 men with clinically detected early prostate cancer would need to be treated with surgery to prevent 1 additional death attributed to prostate cancer over a 6 year period, without evidence that this would improve length or quality of life. The authors cautiously and correctly concluded that longer follow up was needed to clarify whether the benefit increases or decreases over time and whether a survival advantage would follow. This benefit has to be weighed against the side effects of the operation and the lack of demonstrated difference in overall survival. For these reasons we cannot say that radical prostatectomy is better than watchful waiting for all men with localised prostate cancer.

The SPCG-4 results apply most directly to men similar to most of those enrolled in the trial, (ie, healthy men < 75 years of age with newly diagnosed, clinically detected [as opposed to screen detected] localised prostate cancer that is well or moderately differentiated [Gleason score  $\leq$  7]). The Veterans Administration Cooperative Urological Research Group (VACURG) compared radical prostatectomy with watchful waiting and showed similar overall survival after a median 23 years of follow up, but the study was too small to determine if important survival differences existed between treatments.<sup>1</sup>

Unlike men enrolled in SPCG-4 and VACURG, most men currently diagnosed with prostate cancer are detected by prostate specific antigen (PSA) screening. In such men the risk of death from prostate cancer may be lower than that observed in SPCG-4. Thus, a benefit of surgery (if it exists) would be less. The time before any potential benefit occurs is likely to be even longer.

Rather than showing that prostate cancer screening saves lives or that one treatment approach is superior to another, SPCG-4 reinforces the importance of providing men with balanced information about the relative risks and benefits of screening and early treatment.<sup>2–4</sup> The results of ongoing trials evaluating men with screen detected prostate cancer with all cause mortality as the primary endpoint are needed to determine whether screening is effective and if early treatment options improve length and quality of life in these patients.<sup>5</sup>

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