

Uitwendige radiotherapie

Key question

Is er een voordeel in overleving - van pN+M0 patiënten met prostaatkanker - bij behandeling door EBRT met hormonale therapie in vergelijking met hormonale therapie alleen?

P: prostate cancer, N+M0, primary treatment

I: EBRT (External Beam Radiation Therapy), +/- hormonal therapy

C: hormonal therapy

O: primary: survival (all types); secondary: toxicity, quality of life

Search strategy

Searches were run on May 25 for systematic reviews (SRs), randomised controlled trials (RCTs) and observational studies. Pubmed Medline, OVID Embase and the Cochrane Database of Systematic Reviews (CDSR) were searched. Detailed search strings are given below. Studies published in Dutch or English, and including 500 lymph node + patients or more were included.

4. Search results

Systematic reviews and meta-analyses

The Medline search yielded 22 hits, while the Embase search yielded 46 hits. The search in the CDSR yielded 5 Cochrane reviews.

Full-text evaluation

After merging the 3 search files into 1 file and removal of the duplicates, 56 records were screened on title and abstract. Of these 44 were excluded. The most important reasons for exclusion were that studies were on other interventions or populations. Of the remaining 12 studies, the full-text was retrieved, mainly for the purpose of reference tracking (all studies were used for reference tracking). Table 8 provides an overview of the evaluation of these studies.

Table 8. Overview of reviews evaluated full-text

	Reference	In-/Excluded	Reason(s)
1	Akduman, B. and E. D. Crawford (2003). "The management of high risk prostate cancer." <i>J Urol</i> 169 (6): 1993-1998.	Ex	Narrative review
	Antonarakis, E. S., A. L. Blackford, et al. (2007). "Survival in men with nonmetastatic prostate cancer treated with hormone therapy: a quantitative systematic review." <i>J Clin Oncol</i> 25 (31): 4998-5008.	Ex	Other populations and/or comparisons
	Bastian, P. J., S. A. Boorjian, et al. (2012). "High- risk prostate cancer: From definition to contemporary management." <i>European Urology</i> 61 (6): 1096-1106.	Ex	Narrative review based on a systematic search
	Hamstra, D. A., K. Bae, et al. (2011). "Older age predicts decreased metastasis and prostate cancer-specific death for men treated with radiation therapy: meta- analysis of radiation therapy oncology group trials." <i>Int J Radiat Oncol Biol Phys</i> 81 (5): 1293-1301.	Ex	Other comparisons
5	Horwich, A. (2004). "Prostate cancer management." <i>Annals of Oncology</i> 15 (SUPPL. 4): iv307- iv312.	Ex	Narrative review
	Karazanashvili, G. and S. Muller (2007). "Is radical prostatectomy an option in high-risk prostate cancer patients?" <i>Georgian Med News</i> (143): 21-26.	Ex	Narrative review
	Kumar, S., M. Shelley, et al. (2006). "Neo- adjuvant and adjuvant hormone therapy for localised and locally advanced prostate cancer." <i>Cochrane Database Syst Rev</i> (4): CD006019.	Ex	Other comparisons
	Mottet, N., J. Bellmunt, et al. (2011). "EAU guidelines on prostate cancer. Part II: Treatment of advanced, relapsing, and castration- resistant prostate cancer."	Ex	Summary of a guideline

	Reference	In-/Excluded	Reason(s)
	European Urology 59 (4): 572-583.		
	Nilsson, S., B. J. Norlen, et al. (2004). "A systematic overview of radiation therapy effects in prostate cancer." Acta Oncologica 43 (4): 316-381.	Ex	Other patients or no control group
10	Schroder, F. H. (2007). "Early versus delayed endocrine therapy for prostate cancer." Endocrine-Related Cancer 14 (1): 1-11.	Ex	Narrative review
	Shelley, M. D., S. Kumar, et al. (2009). "A systematic review and meta-analysis of randomised trials of neo-adjuvant hormone therapy for localised and locally advanced prostate carcinoma." Cancer Treat Rev 35 (1): 9-17.	Ex	Other patient groups
12	Verhagen, P. C., F. H. Schroder, et al. (2010). "Does local treatment of the prostate in advanced and/or lymph node metastatic disease improve efficacy of androgen deprivation therapy? A systematic review." Eur Urol 58 (2): 261-269.	Ex	Other population or comparisons

Randomized controlled trials

The Medline search yielded 688 hits, while the Embase search yielded 488 hits.

Full-text evaluation

After merging the 2 search files into 1 file and removal of the duplicates, 1027 hits were screened on title and abstract. Of these, 1005 were excluded. The most important reasons for exclusion were that studies were on different interventions or comparisons, on different populations or were different study types.

Of the remaining 22 studies, the full-text was retrieved, including studies requested for reference tracking (all studies were used for reference tracking). Table 9 provides an overview of the evaluation of these studies.

Table 9. Overview of full-text evaluated RCTs

	Reference	In-/Excluded	Reason(s)
1	Eble, M. J. and U. Maurer (2002). "Is radiotherapy of pelvic lymph nodes successful in prostate cancer?" Frontiers of radiation therapy and oncology 36 : 43-48.	Ex	Narrative review
	Elliott, S. P., S. L. Jarosek, et al. (2011). "Three-dimensional external beam radiotherapy for prostate cancer increases the risk of hip fracture." Cancer 117 (19): 4557-4565.	Ex	Other population
	Giordano, S. H., Y. F. Kuo, et al. (2008). "Limits of observational data in determining outcomes from cancer therapy." Cancer 112 (11): 2456-2466.	Ex	On methodological issue
	Goldner, G. and R. Potter (2008). Radiotherapy in lymph node positive prostate cancer patients - A potential cure? Single institutional experience regarding outcome and side effects. Controversies in the Treatment of Prostate Cancer: 10th International Symposium on Special Aspects of Radiotherapy . L. Moser, W. Hinkelbein, M. Schostak and K. Miller, S. Karger AG: 68-76.	Ex	No control group
5	Hernes, E., A. Kyrvalen, et al. (2010). "Initial management of prostate cancer: first year experience with the Norwegian National Prostate Cancer Registry." BJU Int 105 (6): 805-811; discussion 811.	Ex	Other outcomes
	Herrador, V. J. and L. Martinez-Pineiro (2011). "Contemporary role of endocrine treatment in patients with localized or locally advanced prostate cancer: A review." Current Cancer Therapy Reviews 7 (3): 201-214.		
	Hobdy, E. M., N. Q. Shafi, et al. (2004). "Prostate cancer metastasis to supraclavicular lymph node." Clin Adv Hematol Oncol 2 (4): 223-224; discussion 224.		
	Iversen, P., J. E. Johansson, et al. (2004). "Bicalutamide (150 mg) versus placebo as immediate therapy alone or as adjuvant to therapy with curative intent for early nonmetastatic prostate cancer: 5.3-year median followup from the Scandinavian Prostate Cancer Group Study Number 6." J Urol 172 (5 Pt 1): 1871-1876.	Ex	Other patients
	Iversen, P., D. G. McLeod, et al. (2010). "Antiandrogen monotherapy in patients with localized or locally advanced prostate cancer: final results from the bicalutamide Early Prostate Cancer programme at a median follow-up of 9.7 years." BJU Int 105 (8): 1074-1081.	Ex	Other comparisons
10	Jani, A. B. (2006). "Management strategies for locally advanced prostate cancer." Drugs Aging 23 (2): 119-129.	Ex	Narrative review
	Lu-Yao, G. L., P. C. Albertsen, et al. (2008). "Survival following primary androgen deprivation therapy among men with localized prostate cancer." JAMA 300 (2): 173-181.	Ex	Other population
	McLeod, D. G., P. Iversen, et al. (2006). "Bicalutamide 150 mg plus standard care vs standard care alone for early prostate cancer." BJU Int 97 (2): 247-254.	Ex	Other comparison

	Reference	In-/Excluded	Reason(s)
	Nguyen, P. L. and A. V. D'Amico (2008). "Targeting pelvic lymph nodes in men with intermediate- and high-risk prostate cancer despite two negative randomized trials." <i>J Clin Oncol</i> 26(12): 2055-2056; author reply 2056-2057.	Ex	Correspondence
	Penson, D. F. (2007). "Survival associated with treatment vs. observation of localized prostate cancer in elderly men. Wong YN, Mitra N, Hudes G, Localio R, Schwartz JS, Wan F, Montagnet C, Armstrong K, Division of Population Science, Fox Chase Cancer Center, Philadelphia, PA." <i>Urologic Oncology: Seminars and Original Investigations</i> 25(5): 440-441.	Ex	Summary of another study
15	Roach, M. (2004). "Neoadjuvant hormonal therapy in men being treated with radiotherapy for localized prostate cancer." <i>Rev Urol</i> 6 Suppl 8: S24-31.	Ex	Narrative review
	Solberg, A., O. A. Haugen, et al. (2011). "Residual prostate cancer in patients treated with endocrine therapy with or without radical radiotherapy: a side study of the SPCG-7 randomized trial." <i>Int J Radiat Oncol Biol Phys</i> 80(1): 55-61.	Ex	Other population
	Wang, D. and C. Lawton (2008). "Pelvic Lymph Node Irradiation for Prostate Cancer: Who, Why, and When?" <i>Seminars in Radiation Oncology</i> 18(1): 35-40.	Ex	Narrative review
	Warde, P., M. Mason, et al. (2011). "Combined androgen deprivation therapy and radiation therapy for locally advanced prostate cancer: a randomised, phase 3 trial." <i>Lancet</i> 378(9809): 2104-2111.	Ex	Other population
	Wirth, M., P. Iversen, et al. (2002). "Immediate therapy in early prostate cancer: Results from the bicalutamide ('Casodex') EPC programme." <i>European Urology, Supplement</i> 1(7): 20-25.	Ex	Other comparisons
20	Wirth, M., C. Tyrrell, et al. (2005). "Bicalutamide ('Casodex') 150 mg in addition to standard care in patients with nonmetastatic prostate cancer: updated results from a randomised double-blind phase III study (median follow-up 5.1 y) in the early prostate cancer programme." <i>Prostate Cancer Prostatic Dis</i> 8(2): 194-200.	Ex	Other comparisons
	Wirth, M. P., W. A. See, et al. (2004). "Bicalutamide 150 mg in addition to standard care in patients with localized or locally advanced prostate cancer: results from the second analysis of the early prostate cancer program at median followup of 5.4 years." <i>J Urol</i> 172(5 Pt 1): 1865-1870.	Ex	Other comparisons
22	Wu, R. Y., G. M. Wang, et al. (2011). "The feasibility and safety of high-intensity focused ultrasound combined with low-dose external beam radiotherapy as supplemental therapy for advanced prostate cancer following hormonal therapy." <i>Asian J Androl</i> 13(3): 499-504.	Ex	Other patients

Observational studies

Full-text evaluation

The Medline search yielded 1099 hits, while the Embase search yielded 1441 hits. After merging the 2 search files into 1 file and removal of the duplicates, 2156 hits were screened on title and abstract. Of these, 2138 were excluded. The most important reasons for exclusion were that studies were on different interventions or comparisons, or on different patients.

Of the remaining 18 studies the full text was retrieved, mainly for the purpose of reference tracking (all studies were used for reference tracking). 18 studies were evaluated full-text (table 10).

NB: 3 studies with <100 patients now excluded

Table 10. Overview of observational studies, evaluated full-text

	Reference	In-/Excluded	Reason(s)
1	Armstrong, A. J. (2011). "Radiotherapy aids survival in clinically staged, node+ prostate Ca: Commentary." <i>Oncology Report</i> (JANUARY): 25.	Ex	Comment
	Briganti, A., F. K. Chun, et al. (2008). "Is Node-Positive Prostate Cancer Always a Systemic Disease?" <i>European Urology</i> 54(2): 243-246.	Ex	Narrative review
	Da Pozzo, L. F., C. Cozzarini, et al. (2009). "Long-term follow-up of patients with prostate cancer and nodal metastases treated by pelvic lymphadenectomy and radical prostatectomy: the positive impact of adjuvant radiotherapy." <i>Eur Urol</i> 55(5): 1003-1011.	Ex	No control group
	Elliott, S. P., M. V. Meng, et al. (2007). "Incidence of urethral stricture after primary treatment for prostate cancer: data From CaPSURE." <i>J Urol</i> 178(2): 529-534; discussion 534.	Ex	Other population
5	Hamstra, D. A., J. M. Michalski, et al. (2010). "Do not count out external-beam	Ex	Comment

	Reference	In- /Excluded	Reason(s)
	radiation therapy for high-risk prostate cancer." <i>Journal of Clinical Oncology</i> 28 (28): e518-e519.		
	Hernes, E., A. Kyrдалen, et al. (2010). "Initial management of prostate cancer: First year experience with the Norwegian National Prostate Cancer Registry." <i>BJU International</i> 105 (6): 805-811.	Ex	Other patient group
	Hoffman, R. M., M. J. Barry, et al. (2006). "Health Outcomes in Older Men with Localized Prostate Cancer: Results from the Prostate Cancer Outcomes Study." <i>American Journal of Medicine</i> 119 (5): 418-425.	Ex	Other population
	Huang, G. J., N. Sadetsky, et al. (2010). "Health related quality of life for men treated for localized prostate cancer with long-term followup." <i>J Urol</i> 183 (6): 2206-2212.	Ex	Other population
	Jay, A. P. M., C. Pinnoock, et al. (2012). "Poorly differentiated low PSA prostate cancer: Evaluation of survival and treatment outcomes." <i>BJU International</i> 109 : 14.	Ex	Other population
10	Khurana, K., A. Stephenson, et al. (2011). "Overall survival (OS) and prostate cancer-specific mortality (PCSM) among contemporary men with screen-detected, localized prostate cancer managed by active surveillance (AS) versus definitive local therapy." <i>Journal of Urology</i> 1 : e585.	Ex	Other population
	Mason, M. D., P. R. Warde, et al. (2010). "Intergroup randomized phase 3 study of androgen deprivation therapy (ADT) + radiation therapy (RT) in locally advanced prostate cancer (CAP) (NCIC-CTG, SWOG, MRC-UK, and int: T94-0110; NCT00002633)." <i>International Journal of Radiation Oncology Biology Physics</i> 1 : S2.	Ex	Other population
	Merglen, A., F. Schmidlin, et al. (2007). "Short- and long-term mortality with localized prostate cancer." <i>Arch Intern Med</i> 167 (18): 1944-1950.	Ex	Other population
	Milecki, P. (2011). "Comparison of hormone therapy alone with hormone therapy combined with radiotherapy for high-risk prostate cancer patients." <i>Radiotherapy and Oncology</i> 99 : S379-S380.	Ex	Other population
	Ojha, R. P., L. A. Fischbach, et al. (2010). "Acute myeloid leukemia incidence following radiation therapy for localized or locally advanced prostate adenocarcinoma." <i>Cancer Epidemiol</i> 34 (3): 274-278.	Ex	Other population
15	Penson, D. F. (2006). "Health outcomes in older men with localized prostate cancer: Results from the Prostate Cancer Outcomes Study. Hoffman RM, Barry MJ, Stanford JL, Hamilton AS, Hunt WC, Collins MM, Medicine Service, New Mexico VA Health Care System, Albuquerque, NM." <i>Urologic Oncology: Seminars and Original Investigations</i> 24 (5): 457.	Ex	Other population
	Raldow, A. C., C. J. Presley, et al. (2012). "The relationship between clinical benefit and receipt of curative therapy for prostate cancer." <i>Arch Intern Med</i> 172 (4): 362-363.	Ex	Other population
	Stattin, P., E. Holmberg, et al. (2010). "Outcomes in localized prostate cancer: National Prostate Cancer Register of Sweden follow-up study." <i>J Natl Cancer Inst</i> 102 (13): 950-958.	Ex	Other comparisons
18	Thompson, I. M., C. M. Tangen, et al. (2009). "Is there a standard of care for pathologic stage T3 prostate cancer?" <i>J Clin Oncol</i> 27 (18): 2898-2899.	Ex	Editorial

Included studies

One study, described in two articles, was included for quality appraisal and data extraction (see 2a).