Tratamientos del cáncer de próstata localizado: prostatectomía radical robotizada *versus* braquiterapia prostática

Revisión sistemática de la literatura y serie de casos

Treatments for localized prostate cancer: Radical prostatectomy versus brachytherapy. Systematic review of the literature and case series. *Executive summary*

INFORMES DE EVALUACIÓN DE TECNOLOGÍAS SANITARIAS
AETSA

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Autores:
Parte 1: Juliana Ester Martín López, Carmen Beltrán Calvo, Rocío Rodríguez López y Antonio Romero Tabares.

Parte 2: Rafael Antonio Medina López, José Manuel Conde Sánchez, Belén Congregado Ruiz, Juliana Ester Martín López, Carmen Beltrán Calvo y Juan Ramón Lacalle Remigio.

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Avda. de la Innovación, s/n. Edificio ARENA 1. Planta baja.
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España – Spain

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Executive summary

BACKGROUND

Excluding non-melanoma skin cancer, prostate cancer is the most common cancer diagnosed in men in western world. Although radical prostatectomy was traditionally considered the treatment of choice for prostate cancer in men with a life expectancy of 10 years or more, technical advances in the last decade have led to a renewed interest in minimally invasive treatments, for example, brachytherapy or robot-assisted anatomic prostatectomy. The rationale behind the application of a minimally invasive approach is to achieve the same oncological outcomes with better functional results, and less trauma to the patient than for open surgery.

Low–dose rate brachytherapy (LDR-BT) is short-distance radiation therapy that places radiation sources with different durations and rates of dose delivery in or near tumours and inserted into the prostate through a transperineal route guided by transrectal ultrasound. BT is a minimally invasive procedure that can be carried out as an outpatient treatment under spinal or general anesthesia with the patient in the extended lithotomy position. Later, a cystoscopy or imaging test (radiography or computed tomography) are conducted in the prostate for seed implants position verification. This treatment does not require a prolonged treatment time or hospitalization, and this procedure allows to deliver a high radiation dose directly to the tumor while sparing the adjacent normal tissues.

A robotic laparoscopic prostatectomy (RLP) is done through 6 small incisions in the abdomen and the assistance of the da Vinci® robotic system. *Da Vinci* Surgical System is a state-of-the-art surgical platform with 3D, high-definition vision and miniaturized, wristed surgical instruments designed to help doctors take surgery beyond the limits of the human hand. The potential advantages for this procedure are: reduction of surgeon tremor and fatigue, shorter hospital stay, less postoperative pain, less blood loss and faster recovery and return to normal activities.

LDR-BT, as compared to RLP, may have similar survival outcomes but may reduce the incidence of local adverse events and may provide better health-related quality of life (HRQoL). However, randomised controlled trials (RCT) are lacking. In this context, Andalusian Health Technology Assesment has Developed a systematic review and a case series study, joint to Virgen del Rocío Hospital researchers, after a one year of follow-up.

OBJETIVE

The aim of this systematic review was to assess the available comparative evidence on LDR-BT relative to robot-assisted anatomic prostatectomy in terms of quality of life, survival and complications in men with localised prostate cancer.

The aim of this case series was to compare the functional results and quality of life of LDR-BT relative to robot-assisted anatomic prostatectomy in men with localised prostate cancer.

MATERIAL AND METHODS

Systematic Review

The following electronic databases were searched on 5 September 2011 without restrictions on publication year or language: Ovid MEDLINE (from 1950), Ovid EMBASE (from 1980), Cochrane Library, CRD, Emergency Care Research Institute (ECRI) , Web of Knowledge (WOK), Technology Evaluation Center (TEC), Clinical Evidence, Uptodate, Hayes and Drug Effectiveness Review Project (DERP). Terms and syntax used for the search in Medline and Embase via Ovid were tailored to the requirements of the other two databases. Information about trials not registered in these databases was located by searching the reference lists of relevant articles and review articles. Editor letter, case series, grey literature and conference abstracts were excluded. The study population included patients (no age limit) with histological confirmed localized prostate cancer (TNM classification system T1-T2, N0 and M0) in wich test intervention was LDR-BT and/or RLP. The outcomes included were quality of life, urinary function, sexual function and bowel function, survival and complications. An accumulated analysis was conducted for each outcome as event number (incontinence and impotence) regarding to total number of included patients. Quality assessment (Cochrane Manual for intervention study and CASPe for systematic review) and data extraction were performed.

Case Serie

Were included patients with histological confirmed localized prostate cancer. Biopsy-ultrasound guided indication was established regarding to “Proceso Asistencial Integrado Benign Prostatic Hypertrophy” recommendations in patients with anormal digital rectal examination and/or Prostatic Specific Agent (PSA)>10 ng/ml and/or PSA between 3 and 10 ng/ml and free PSA< 20%, with a maximum of three biopsies. The study population included patients with histological confirmed localized prostate cancer with life expectancy greater than 10 years, no comorbility and patient acceptance for the intervention. Patients with metastatic disease were excluded.

Finally, 91 patients were recruited consecutively at the outpatient departments of 1 Spanish hospital, 41 patients underwent RLP and 50 patients underwent LDR-BT from January to December 2011. The outcomes included were personal and familiar history, age, comorbility (diabetes mellitus, hipertensión, chronic obstructive pulmonary disease), digital rectal examination, PSA, Gleason store, risk of anesthesia (ASA), body mass index, pretreatment and postreatment situation (Qol, sexual and urinary function, IPSS, peak flow), employment status and progression criteria. Quality of life was evaluated through interviews that included SF-36, IPSS, IEF and ICIQ).

RESULTS

Systematic Review

The 529 cites recruited, were related to LDR-BT (n=377) results and RLP (n=152) results, while 68 were duplicated. Between the 461 remaining references selected by title or/and abstract, three systematic review were identified. Two of them were related to RLP and the other one was related to LDR-BT (publication years 2009 and 2011, respectively), so the selection process was applied to studies published thenceforth. Of the 103 remaining references, 70 did not related to aim of this review, being excluded. A total of 33 full texts were retrieved and evaluated in detail and 26 met exclusion criteria. Finally, 7 studies were included, four comparative and prospective studies (one direct comparison) and three systematic reviews.

No researcher blinding during data register and interpretation, a short follow-up period of time, no intention-to-treat analysis developed, and patient allocation consecutive were the main methodological aspects deficient in comparative studies. For other hand, no adequate combination of results, irrelevant studies considered or the quality assessment of included studies were the main methodological aspects deficient in systematic reviews. RLP was associated to better scores in physical domain SF-12 ($p<0.01$ in 3º, 4º and 5º week of follow-up) and faster recovery to normal values in comparison to LDR-BT. LDR-BT scores for global quality of life were high (59 points in SF-36 questionnaire and –3,6 points in QLQ-C30), but missing data for global quality of life for RLP limited quantitative analysis between both procedures. However, the quality of life related to urinary function for LDR-BT was significantly higher than RLP during the first three years of follow-up after intervention (78, 92, 94, 90, 90, 90, 90, 88 *vs* 71, 69, 74, 74, 76, 75, 78, $p<0.001$ in 3, 6, 12, 18, 24, 30 and 36 months of follow-up). The analysis of differences in weighted rates in patients with urinary continence for first year of follow-up was favourable for LDR-BT (86,6% *vs* 84,5; 95% confidence interval (CI): 2.568 to 4.432, $p<0.001$).

The score for quality of life related to sexual function were significant better for LDR-BT in comparison to radical prostatectomy (66, 77, 71, 68, 74, 67, 73 *vs* 28, 33, 40, 42, 45, 41, 46; p<0.001). Differences identified about quality of life related bowel function favourable for RLP during first three years of follow-up alter intervention were not significant (p=0.02). Missing data about global survival for patients underwent RLP limited comparative analysis. Complications more frequents were gastrointestinal and urogenital toxicity, urinary incontinence and need of catheterization *vs* others as bleeding or paralytic ileus identified for RLP patients.

Case Serie

In general, the quality of life scores was similar in patients underwent RLP or LDR-BT. Only were identified significant differences for ICIQ questionnaire scores for LDR-BT. The remaining questionnaires the differences were not significant or the analysis was limited by data missing (SF-36). No significant differences were detected for complications between both procedures, although these complications were more severe in group of patients underwent RLP in comparison to LDR-BT. LDR-BT has shown a significant reduction for post intervention pain, measured with EVA scale during follow-up in comparison to RLP.

However, the data proceed from studies with small sample size and incomplete follow-up of included patients until 6-12 months could limit the obtained data interpretation.

Studies with larger sample sizes and with longer follow-up periods are recommended, to adequately explore the long term survival in patients underwent LDR-BT and RLP and the differences about recurrences, quality of life and complications between both procedures.

CONCLUSIONS

Systematic Review

RLP was associated to better scores no significant in physical domain SF-12 and faster recovery to normal values in comparison to LDR-BT. Differences no significant about quality of life related bowel function favourable for RLP during first three years of follow-up alter intervention were shown.

LDR-BT was significantly associated to higher quality of life score related to urinary and sexual function *vs* RLP during the first three years of follow-up after intervention

Included studies showed methodological limitations in relation to lack of randomization or non uniform and short follow-up of all included patients. Missing data about population procedure or patient selection were not clearly described. Indirect comparisons inclusion or questionnaire

employed heterogeneity could limit the data obtained applicability. Studies with high methodological quality are needed, to adequately compare directly the quality of life, survival and complications derived from both procedures.

Case Serie

LDR-BT was significantly associated to higher quality of life score for ICIQ questionnarie *vs* RLP during the first year postintervention of follow-up. LDR-BT has shown a significant reduction for post intervention pain, during follow-up in comparison to RLP

No significant differences were detected for complications between patients underwent LDR-BT or RLP. However, the number of withdrawals during follow up and lack of patients randomization of in the study groups could limit the interpretation of these results.