Brachytherapy versus prostatectomy in localized prostate cancer: results of a French multicenter prospective medico-economic study

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The study evaluated quality of life, treatment related symptoms, and costs of iodine-125 permanent interstitial brachytherapy (IB) compared to radical prostatectomy (RP) in curative prostate cancer treatment. The authors concluded societal costs were similar, quality of life was generally worse with IB, and symptom profiles differed by intervention. The study was generally well reported and conducted. Missing data may affect the results. Survival data and longer follow-up would aid assessment of the comparative cost-effectiveness of the interventions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The study evaluated health related quality of life (HRQoL), treatment related symptoms, and costs of iodine-125 permanent interstitial brachytherapy (IB) to radical prostatectomy (RP) in curative prostate cancer treatment in low-risk patients.

Interventions
The IB intervention implanted all patients with radioactive iodine-125 seeds. IB patient were treated mostly using a real-time ultrasound based planning technique, consisting of real time computer-assisted dosimetry with dynamic seed localization performed in an operating room suite. IB patients at one study centre were treated using an ultrasound based preplanning technique. Based on ultrasound dosimetry, the mean dose to 90% of the outlined prostate volume (D90) was 185.9 Gy and the mean percentage of prostate volume receiving 100% of the prescribed dose (V100) of 145 Gy was 99.4%. Posttreatment computed tomography (CT) dosimetry showed a mean D90 of 172.6 Gy, and a mean V100 of 96.0%, with the mean rectal volume receiving 145 Gy being 1.4cc.

RP patients had either retropubic (86%) or laparoscopic surgery (14%). Iliac node sampling was conducted in 75% of patients with absence of nodal activity confirmed in all these patients.

Location/setting
France/Outpatient and Inpatient

Methods
Analytical approach:
The study was conducted as part of a multi-centre prospective randomised controlled trial. The trial randomised 435 patients to IB (n=308) or RP (n=127) between March 2001 and June 2002. Study follow-up was for two years. The study adopted a societal perspective.

Effectiveness data:
Patients were given questionnaires for baseline, two months, six months, 12 months, 18 months and 24 months follow-up. The primary effectiveness measure was health related quality of life measured by the European Organization for Research and Treatment of Cancer (EORTC) core Quality of Life Questionnaire (QLQ-C30) version 3 and the prostate cancer specific EORTC-PR25 module. Treatment related urinary, bowel, and sexual symptoms were also measured.

Monetary benefit and utility valuations:
Measure of benefit:
Effectiveness outcomes were used as measures of benefit.

Cost data:
Costs included hospital costs, outpatient costs, and costs from productivity losses. Hospital costs were computed using hospital accounting systems for initial treatment with IB, and French Diagnosis Related Groups (DRGs) for initial treatment with RP. Initial treatment for IB included medical and non-medical personnel costs, depreciation, operating theatre time, blood products, iodine-125 seeds, costs for days of hospitalisation, maintenance and logistical costs, and overhead costs. Hospital costs incurred during follow-up were calculated using French DRGs. Outpatient resource use was measured via patient questionnaire and valued using the French National Security fee schedule. Outpatient costs included examinations, visits to general practitioners and specialists, physician and/or nurse home visits, and urogenital retraining visits. Productivity costs were calculated by multiplying patient reported days off work by the French daily national average wage.

All costs were reported as mean costs per patient in 2001 euros (€). No discounting was applied to costs.

Analysis of uncertainty:
Differences within groups and between groups were tested for statistical significance and 95% CI of these differences were reported. Within group differences were tested for significance using t-tests and Bonferonni’s method to adjust for multiple comparisons. Comparisons were made against baseline. Treatment difference were adjusted to account for potential confounding factors such as age, working status, prostate-specific antigen level, Gleason score, hormone therapy status, and pretreatment International Prostate Symptom Score. The level of statistical significance was set at 0.05.

Results
In both IB and RP global quality of life decreased immediately after treatment, remained low at two months follow-up and rebounded by 24 months follow-up. The difference between decreases in global quality of life score indicated that IB was associated with more favourable quality of life (13.5 points, p<0.0001). Between six months and 24 months follow-up global quality of life scores favoured RP, with differences between 7.5 and 8.3 points (p=0.0164 to p=0.0379). While mean differences were larger at 24 months, significance was lower due to patients lost to follow-up. At 24 months there was a mean difference of 8.2 on the global quality of life scale (p=0.0379), but there were no other statistically significant difference in other scales of the EORTC-QLQ30. The authors noted that the difference in quality of life would be considered a minor difference on the scale.

RP patients were more likely to have deterioration in urinary incontinence at 24 months (49% compared to 19.7%). RP patients had less frequent other urinary problems, faecal incontinence, and rectal bleeding than IB. RP patients reported problems between 12.4% and 45.3% less than IB, with most percentages reported around half those of IB, with some less. Erectile dysfunction was more common in RP patients with 88% of sexually active RP patients reporting poorer erectile function compared to 50.8% in IB patients.

Mean initial treatment costs were higher for IB, but mean follow up costs were lower for IB. When initial treatment and follow-up were combined there was no statistically significant difference in hospital costs at any time point. Mean outpatient costs were statistically significantly higher for IB to 6 months, but were not statistically significant afterward. The mean cost of productivity loss was significantly in favour of IB for all time points. Overall societal costs were €7,465 for RP and €7,525 (p=0.8852) for IB at two months follow-up, and €8,715 for RP and €8,019 (p=0.0843) at 24 months follow-up.

Authors’ conclusions
The authors concluded that the two treatments had similar societal costs over two years, but that quality of life was generally worse with IB, with different symptom profiles.

CRD commentary
Interventions:
The interventions were well reported. Some potential comparators were excluded, but justification was provided for exclusion of these treatments relevant to the study setting.

**Effectiveness/benefits:**
Effective and benefit data were comprehensively reported. The measures chosen were appropriate, follow up was frequent and well reported with valid comparisons made and appropriate and well reported methods. Appropriate methods appear to have been taken to account for potential confounding factors.

The study had a long follow up compared to studies listed in the authors’ discussion, but additional information on longer term outcomes could be valuable. As acknowledged by the authors no long term comparative survival outcomes were known at the time of the study, though ten year comparative survival indicated no statistically significant differences between treatments. The time horizon of the study was not long enough to capture the lifetime benefits or costs of the two curative treatments. Additionally, alternative measures of quality of life based on preference based utilities would be useful for further evaluation.

No discounting was applied to benefits. It is not clear what effect discounting would have over the two year study follow-up, but it would likely favour RP in a longer term analysis using this data.

**Costs:**
Costs were extensively reported using appropriate French sources and methods. Productivity costs were calculated using average daily wages for time lost, but no measures of reduced productivity on return to work appear to have been measured. It is not clear what effect reduced productivity would have on results.

No discounting was applied to costs, which is unlikely to cause much difference in the analysis as most costs occurred before one year. In a longer analysis lack of discounting would be inappropriate.

**Analysis and results:**
Reporting was generally excellent with analyses conducted that were relevant to the study objective. Confidence intervals were reported for EORTC-QLQ-C30 measurements and costs and p-values were given for differences. Reporting on uncertainty was sufficient to have a general impression of uncertainty in the data, and consistent with the aim of the study. Not all domains were reported in results tables, but statistical significance of differences was adequately discussed in the text.

There were a significant amount of patients lost to follow-up, with more lost to follow-up in the RP arm. It is not clear why these patients were lost to follow up and what effect their inclusion would have on data. No methods were used to account for missing data.

Outcomes were not long-term, and some costs and benefits of treatment are still unknown. Longer term modelling may be valuable for determining differences between the treatments in outcomes and costs.

The authors conducted a thorough comparison of their study to other work in the area with adequate explanations for similarities and differences between results and appropriate cautions about comparability.

**Concluding remarks:**
The study was well conducted and reported and the results appear valid. Survival data and longer follow-up would aid assessment of the comparative cost-effectiveness of the interventions.

**Bibliographic details**

**PubMedID**
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