

| | | |
|-------------------|--|-----------------------------|
| Title: | Cryotherapy for recurrent prostate cancer and renal cancer – September 2009 <i>Part A: Salvage cryotherapy for recurrent or persistent prostate cancer after radiotherapy</i> <i>Part B: Cryotherapy for renal cancer</i> | |
| Agency: | Medical Services Advisory Committee (MSAC) Australian Government Department of Health and Ageing MDP 106, GPO Box 9848 Canberra ACT 2601, Australia http://www.msac.gov.au | |
| Reference: | MSAC Application 1124. First printed December 2009 ISBN (Print) 1-74186-958-7 | ISBN (Online) 1-74186-959-5 |

AIM

To assess the safety, effectiveness and cost-effectiveness of cryotherapy for the treatment of recurrent or persistent prostate cancer after radiotherapy and the treatment of renal cancer.

PART A CONCLUSIONS AND RESULTS

Safety

Eighteen uncontrolled case series and one case study reported on the safety of salvage cryotherapy (\pm neoadjuvant hormone therapy (NHT)) for recurrent or persistent prostate cancer after radiotherapy. No deaths or life-threatening events were reported in the studies identified. Recto-urethral fistula was the most serious complication, although it was not common (0% – 7.1%). A considerable proportion of patients suffered from impotence (60% – 100%) and urinary incontinence (0% – 33.3%) post-procedurally. Other major adverse consequences, including urethral sloughing, bladder neck obstruction, urethral stricture and urethral ulcer, were observed in up to 11 per cent of patients. Minor complications, such as pain in the pelvis and/or perineal and/or rectum, were self-limiting. As an invasive procedure, cryotherapy is unlikely to be as safe as stand-alone hormone therapy and watchful waiting. Due to the lack of direct comparative evidence, the relative safety of salvage cryotherapy (\pm NHT) against radical prostatectomy (\pm NHT), high-intensity focused ultrasound (HIFU) (\pm NHT) or brachytherapy (\pm NHT) is unknown.

Effectiveness

Effectiveness outcomes of salvage cryotherapy (\pm NHT) following radiation failure were reported in 21 uncontrolled case series, of which only one study followed up patients for more than 5 years. Within the short follow-up period, both the overall survival rate and the disease-specific survival rate were above 90 per cent. At least 50 per cent of patients had disease-free survival confirmed by routine or selective biopsy. Two-year prostate-specific antigen (PSA) control was achieved in 38 to 79 per cent of patients across studies, using different PSA threshold values for the definition of biochemical recurrence. Local lymph node involvement and distant metastases were not common (0% – 15.8%) during the follow-up period. In general, patients had a healthy level of functioning and were in a good health state and quality of life (QoL) after salvage cryotherapy, although their sexual and urinary symptoms were exacerbated by the procedure. Overall, salvage cryotherapy (\pm NHT) appears to be effective in the treatment of recurrent or persistent prostate cancer after radiotherapy in the short term. In addition, cryotherapy, as a potential curative treatment, is likely to be more effective than conservative hormone therapy or watchful waiting. As no data compared salvage cryotherapy (\pm NHT) with prostatectomy (\pm NHT), HIFU (\pm NHT) or brachytherapy (\pm NHT), no conclusions can be drawn regarding the relative effectiveness of cryotherapy.

Cost-effectiveness

The cost-effectiveness of salvage cryotherapy (\pm NHT) following radiation failure was not assessed as no comparative studies were identified. A financial incidence analysis indicated that salvage cryotherapy would save the Australian Government between \$688 608 and \$2 739 439 in the first year. However, an additional cost of between \$1 712 230 and \$7 468 032 for cryotherapy would be borne by the Australian healthcare system overall relative to stand-alone hormone therapy and watchful waiting in the first year. The extremely high cost of cryotherapy is mainly due to the expensive disposable Cryokit and gases. The additional cost of cryotherapy in the first year would be offset by the high ongoing expenditure required for androgen deprivation drugs each additional year. If 5-year disease-free survival is

achieved in all patients who receive salvage cryotherapy, the cost implications of cryotherapy to the healthcare system would be a saving of \$454 151 to \$3 316 370.

PART B CONCLUSIONS AND RESULTS

Safety

Data on the safety of cryotherapy for the treatment of presumed renal cancer were reported by three controlled studies, 16 case series and 16 case reports. Limited comparative evidence indicated that laparoscopic cryotherapy was no worse than partial nephrectomy in terms of blood loss, complication rates and pre/post-procedural serum creatinine levels. Cryotherapy (laparoscopic or percutaneous) was likely to be as safe as radiofrequency ablation (RFA) as the major complication rates and blood loss were not significantly different between the two procedures. However, laparoscopic cryotherapy required more anaesthesia time than RFA; whereas percutaneous cryotherapy needed fewer sedatives during the procedure than RFA. One procedure-related death was reported: an elderly woman with multiple cardiovascular and respiratory comorbidities died of a pulmonary embolism on day 20 after renal cryotherapy. Between 0 and 21.4 per cent of patients developed major post-operative adverse events, most of which were heart or pulmonary complications. This might relate to the patient selection criteria, as cryotherapy is usually indicated for elderly patients with comorbidities. Intra-operative complications were not uncommon (0% – 28.6%). Peri-procedural blood loss was minor in all except one patient, who lost 1000 mL of blood during a cryotherapy procedure.

Effectiveness

Twenty-five studies reported on the short-term effectiveness of cryotherapy for presumed renal cancer. Although four comparative studies were identified, there was insufficient evidence to determine the overall effectiveness of cryotherapy relative to partial nephrectomy or RFA. However, there was weak evidence that, during the first year, the local tumour progression rates following laparoscopic cryotherapy were similar to those after laparoscopic partial nephrectomy; and that no significant difference in tumour persistence rates and local tumour progression rates was observed between cryotherapy and RFA within 2 years post-procedure. In general, cryotherapy for the treatment of renal tumours resulted in favourable short-term effectiveness outcomes. The overall survival rates and disease-specific survival rates were 87.5 to 100 per cent and 100 per cent, respectively, during follow-up periods of up to 22 months across studies. Relatively low rates of tumour persistence, local tumour progression, metastases and technical failure were reported.

Cost-effectiveness

As there was not enough evidence indicating the relative effectiveness of cryotherapy against partial nephrectomy, a financial incidence analysis, instead of an economic analysis, was carried out. The use of cryotherapy for the treatment of renal cancer would incur an additional cost of \$729 238 to \$791 664 to the Australian healthcare system overall relative to partial nephrectomy, RFA and currently performed cryotherapy. The cost implications of cryotherapy on the Australian Government is not significant, being an additional \$9568 to \$18 715 per annum.

METHODS

Medline, Embase, The Cochrane Library, and several other biomedical databases, HTA and other internet sites were searched from 1995 until November 2008, as argon-based cryotherapy was first used in clinical practice in the middle of the 1990s. Specific journals were hand searched and reference lists perused. Studies were included in the review using pre-determined PICO selection criteria and reasons for exclusion were documented. Study quality was appraised, data extracted in a standardised manner, and findings synthesised qualitatively.