Laparoscopic uterine nerve ablation versus vaginal uterosacral ligament resection in postmenopausal women with intractable midline chronic pelvic pain: a randomized 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.

Health technology
The study compared two methods for the surgical treatment of postmenopausal women with severe and intractable chronic pelvic pain (CPP). The method compared were laparoscopic uterine nerve ablation (LUNA) and vaginal uterosacral ligament resection (VUSR). These are characterised as minimally invasive pelvic denervations.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised postmenopausal women suffering from severe midline pelvic pain for more than 6 months and who did not respond to common medical treatment (e.g. paracetamol, non-steroidal anti-inflammatory drugs). Postmenopausal state was assessed by measuring serum follicle stimulating hormone (FSH) and 17-beta-estradiol levels. Severity of pain was assessed using a visual analogue scale (VAS) and women with a minimum value of 80 were included. Women with major medical diseases, psychological or psychiatric disorders, neurological alterations of lumbar-sacral tract, or previous pelvic surgery were excluded from the study. Also excluded were women with a history of severe abdominal or pelvic infections, a history of infertility, the presence of other gynaecological pathologies, and women who had been or were currently undergoing hormone replacement therapy. Women who were unable to complete the daily diary and those who had a history of alcohol or drugs abuse, psychological syndromes, psychiatric disorders, or a history of physical or sexual abuse were also excluded from the study.

Setting
The setting was secondary care (i.e. university departments of gynaecology). The economic study was carried out in Italy.

Dates to which data relate
Participants were enrolled between October 2001 and January 2003, and all patients were followed for up to 12 months. Dates relating to the cost data and resource use were not reported. The price year was also not reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
Although not explicitly stated, the costing appears to have been carried out prospectively on the same sample of patients.
as that used in the effectiveness study.

Study sample
Power calculations showed that a sample of at least 40 participants per group was required to find a statistically significant difference of 30% in mean procedural costs between the two groups. The expected mean procedural costs were estimated beforehand, and the estimated sample size was adequate to detect the estimated difference of around EUR 150 (95% confidence interval, CI: 61 to 239) with a statistical power of 90% at a 5% significance level (alpha 0.05). Power calculations were demonstrated using SamplePower software version 2.0. Consecutive patients with severe midline pelvic pain for more than 6 months were selected for the study. Initially, 236 patients were selected. Of the 156 (66.1%) patients that were excluded, 42 (17.79%) did not meet the inclusion criteria, 86 (36.4%) met the exclusion criteria, while 28 (11.86%) refused to participate in the study. Overall, 80 patients were randomised to the two groups (40 to LUNA and 40 to VUSR).

Study design
The analysis was based on a randomised trial conducted in multiple centres (four university gynaecology departments). Blocked-randomisation was achieved using computer-generated random allocation sequence in single blocks. The patients were initially followed up at 2, 12 and 24 hours after surgery, at hospital discharge, and at 6 and 12 months after surgery. At 12 months, 4 (10%) women from the LUNA group and 2 (5%) women from the VUSR group were lost to follow-up and were therefore excluded from the analysis. However, the reasons for withdrawal were not reported. Researchers blinded to the intervention assessed patients at 6 and 12 months' follow-up. The assessment was conducted using clinical examinations and VAS questionnaires.

Analysis of effectiveness
It was reported that the analysis was conducted on an intention to treat basis. The patient groups were reported to have been comparable in terms of their demographic and baseline clinical characteristics (e.g. age, time since menopause, parity, body mass index, duration of pelvic pain, lateral component of the CPP, incidence of deep dyspareunia), and in haematological characteristics (e.g. red blood cell count, haemoglobin, haematocrit, serum iron).

The primary health outcomes used in the analysis were the cure rate, severity of CPP and deep dyspareunia, defined as pelvic pain during or within 24 hours after sexual intercourse. Post-surgery pain was estimated by measuring the number of vials of analgesic (e.g. 100 mg tramadol) used during hospitalisation and by employing the VAS on a score range of 0 to 10. The severity of CPP and deep dyspareunia were assessed using a 100-mm VAS extending from "least possible pain" to "worst possible pain" with complete numerical values. In order to estimate the cure rates, a patient without CPP or with CPP not necessitating medical treatment at 6 and 12 months' follow-up was assumed to be cured. The secondary outcomes assessed were all intra- and postoperative complications and the time required to return to full activity and/or work.

Normally distributed data were analysed using the Kolmogorov-Smirnov test. Continuous variables that were not normally distributed (e.g. parity, global operative time, blood loss, vials drugs used, hospital stay and time to return to full activity and/or work) were analysed using the Mann-Whitney U-test. The General Linear Model repeated measures with Bonferroni's test for multiple comparisons was used to evaluate differences within groups in severity of CPP and deep dyspareunia, with group as the between-subjects factor and centre as a covariate.

Effectiveness results
No complications during surgery were observed in either group.

At 24 hours after surgery, there was no statistically significant difference between the two groups in terms of the VAS score. However, at hospital discharge, the VAS score was higher in the LUNA group than in the VUSR group (3.3 +/- 1.1 versus 2.4 +/- 1.0; p<0.001). No long-term complications were observed in either group.

The cure rate did not differ significantly between the two groups at the 6 and 12-month follow-ups. At 6 months, the
The cure rate was 82.5% in the LUNA versus 87.5% in the VURS group, (p=0.530; RR 0.94, 95% CI: 0.78 to 1.13). At 12 months, the cure rate was 75% in the LUNA group and 73.7% in the VUSR group, (p=0.901; RR 0.9, 95% CI: 0.78 to 1.33).

The severity of CPP, although significantly lower from baseline (p<0.001), did not differ between the two groups at 6 months, (p=0.067) or 12 months, (p=0.063). The same trend applied for deep dyspareunia, where the difference between the two groups was not statistically significant, (p=0.25 at 6 months and p=0.99 at 12 months).

There was no statistically significant difference in median time to return to full activity and/or work between the two groups.

**Clinical conclusions**
The analysis demonstrated that the two treatment options were equally effective in terms of the cure rates, decrease in severity of CPP, and deep dyspareunia at 6 and 12 months after surgery.

**Measure of benefits used in the economic analysis**
The authors did not use a summary measure of benefit in the economic analysis. As the effectiveness analysis demonstrated equal effectiveness for the two treatment options, the economic analysis was characterised as a cost-minimisation analysis.

**Direct costs**
The health service costs included in the analysis were fees for hospital stay, surgical room, surgical team (including surgeon anaesthetist and assistant), disposables and instrumentation. Data on resource use were taken from the effectiveness study, while costs were taken from official regional sources (personnel costs) and from the centres included in the study (disposables and instrumentation). The costs and the quantities were not reported separately, and only summary costs were reported for certain cost categories (e.g. hospital stay, surgical room, surgical team, disposables and instrumentation). The dates relating to the resource use and cost data were not reported, and nor was the price year. Discounting was not relevant as the costs were incurred during less than 2 years.

**Statistical analysis of costs**
The costs were expressed as mean costs with standard deviations. The cost-differences between groups were analysed using an unpaired Student’s t-test. Continuous variables for resource use, namely parity, global operative time, vials of pain drug used (amount of analgesic used) and hospital stay, were analysed using the Mann-Whitney U-test.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
Euros (EUR).

**Sensitivity analysis**
No sensitivity analysis was carried out.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.
Cost results
The mean total costs per patient were reported.

The mean (+/- standard deviation) total cost was EUR 2,078 (+/- 637) for LUNA and EUR 1,497 (+/- 297) for VUSR. The cost-difference between the two groups was statistically significant, (p<0.001).

However, it was reported that when only the mean costs of LUNA conducted using poly-use instrumentation alone were accounted for, the cost-difference between the two groups was not statistically significant (EUR 1,632 +/- 282 for LUNA and EUR 1,497 +/- 297 for VUSR; p=0.088).

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors’ conclusions
Although the analysis demonstrated that both surgical treatment options were equally effective in postmenopausal women, vaginal uterosacral ligament resection (VUSR incurred significantly less costs than laparoscopic uterine nerve ablation (LUNA).

CRD COMMENTARY - Selection of comparators
The technologies compared were chosen as they comprised pelvic denervation procedures that are less invasive in comparison with other surgical procedures (e.g. hysterectomy). In addition, laparoscopic procedures were used for diagnosis as well as the surgical treatment of pelvic pain. However, if other treatment methods exist, which is likely, this means that the study was only a partial analysis. You should decide if these comparators are valid technologies in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a multi-centre randomised trial, which was appropriate given the study question. The study sample was representative of the study population and the patient groups were comparable at baseline in terms of their clinical and demographic characteristics. However, the characteristics of patients who refused to participate in the study were not discussed, which might have introduced bias into the results. The methods of randomisation, duration of follow-up, losses to follow-up and blinding were all reported, which suggests that the internal validity of the study should be high. Power calculations were reported and an adequate sample size was used.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of benefit in economic analysis. As equal effectiveness was demonstrated, the study was characterised as a cost-minimisation analysis.

Validity of estimate of costs
Although the perspective adopted was not explicitly reported, it was not societal as no indirect costs were included in the analysis. The unit costs and the quantities of resources used were not reported separately, which will hinder reworking the analysis in other settings. In addition, as only summary costs were reported, it is difficult to be certain whether all the cost categories were included in the analysis. For example, it appears that medication costs were not accounted for. The dates of the cost data and the price year were not reported, which will prevent future reflation exercise and make it difficult to establish whether adjustments for inflation were necessary. The sources of the cost data were not explicitly reported and it was unclear whether the authors used charges (especially for consumables) to proxy costs. A sensitivity analysis was not carried out to assess the robustness of the estimates used, which may introduce uncertainty into the results and limit their interpretation.
Other issues
The authors extensively reported the results of other studies, but direct comparisons were not possible as the effectiveness of the health technologies in postmenopausal women had not been evaluated. The authors do not appear to have presented their results selectively, but the issue of the generalisability of the results to other settings was not addressed. The study enrolled postmenopausal women with intractable midline CPP and this was reflected in the authors' conclusions. The authors acknowledged, as a limitation to their study, the absence of a control group that would allow the placebo effect of the treatment to be evaluated. However, the duration of the follow-up period (12 months) was assumed to be long enough to minimise bias due to any placebo effect.

Implications of the study
The authors did not make explicit recommendations for changes in policy or practice. However, the analysis and the discussion highlighted areas where more research-based information is needed if more robust conclusions are to be derived.

Source of funding
None stated.

Bibliographic details

Other publications of related interest
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