Interventional Pain Medicine 1 (2022) 100147

Contents lists available at ScienceDirect

Interventional Pain Medicine

journal homepage: www.journals.elsevier.com/interventional-pain-medicine

Cost-effectiveness of radiofrequency neurotomy to treat zygapophysial joint pain compared with pain rehabilitation programs

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ARTICLE INFO

Keywords:
Zygapophysial joint pain
Chronic pain
Pain rehabilitation
Radiofrequency neurotomy
Cost-effectiveness
Health-related quality of life

ABSTRACT

Background: Chronic pain is a widespread condition that causes much suffering and significant cost to society. Pain rehabilitation programs (REH) have dominated the treatment of chronic pain in Sweden in recent decades. Although radiofrequency neurotomy (RFN) was cost-effective in recent studies, the long-term health and economic effects of REH have not been comprehensively evaluated.

Design: Observational study with propensity score weighting to compare RFN and REH.

Methods: Patients assessed and treated between 2010 and 2016 were eligible; 15,357 underwent REH and 254 underwent RFN. Patient data were combined with linked data from national registers. We used propensity score weighting to mimic a randomized controlled trial using baseline gender, age, and baseline health-related quality of life as covariates.

Results: Health-related quality of life improved significantly in both groups, by 0.164 and 0.352 quality-adjusted life years (QALYs) at 1 and 2 years after REH, and by 0.186 and 0.448 QALYs after RFN. The assessment and diagnostic procedures were slightly more expensive for RFN, but the treatment costs were greater for REH. Sick leave decreased after treatment in both groups, particularly after RFN. The cost per QALY gained 1 year after REH was ~121,633 USD, which is considered "very expensive" according to the Swedish National Board of Health and Welfare. By comparison, the cost of RFN was ~13,715 USD, in the "moderate" range. After 2 years the cost per QALY gained was in the "moderate" range for REH and "low" for RFN.

Conclusions: RFN and REH improved health-related quality of life, with significantly greater improvement with RFN. The treatments were comparable based on propensity score weighting, and RFN was cost-effective in the moderate to low range, whereas REH was considered very expensive to moderate. Expanding RFN from 2% currently to 25% of the treatments given in Sweden could save ~21.2 million USD annually in healthcare expenditure.

1. Introduction

Chronic pain is a widespread condition [1–3] that causes much suffering to the affected individuals and imposes a large cost on society [4,5]. Low back pain has remained a leading cause of disability since 1990 based on the World Health Organization Global Burden of Disease studies [6,7]. Pain is one of the most common reasons for individuals to seek primary healthcare [8]. In Sweden, with a population of about 10 million people, about 7% of the population (~700,000) seek medical help for pain every year [9].

Interventional pain management strategies, especially radiofrequency neurotomy (RFN) to treat zygapophysial joint pain (ZJP), have shown promising effects in patients with chronic spinal pain [10–16]. After ruling out obvious causes of pain (e.g., rheumatoid disease, malignancies, fractures), ZJP is diagnosed in 30%–50% of patients with chronic pain [17–20]. The diagnosis of ZJP is established if at least two diagnostic nerve medial branch blocks (MBB) on separate occasions reduce pain by ≥ 80% during the duration of local anesthesia [21,22]. There are no diagnostic imaging tools (radiology or magnetic resonance imaging) that can diagnose or rule out the presence of ZJP [23,24]. Once

Abbreviations: RFN, Radiofrequency neurotomy; REH, Pain rehabilitation program; SEK, Swedish krona; ZJP, Zygapophysial joint pain; QALY, Quality adjusted life years; DDD, Defined daily doses; EQ-5D, EuroQOL 5-dimensional index; EQ-VAS, EuroQOL visual analog score of health; HAD, Hospital anxiety depression scale; MBB, Medial branch blocks.

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https://doi.org/10.1016/j.inpm.2022.100147
Received 1 July 2022; Received in revised form 28 July 2022; Accepted 7 September 2022

ZJP has been diagnosed in the cervical, thoracic, or lumbar region, RFN of the nerves in the zygapophysial joints where the pain is localized can offer long-term pain relief without major side effects [10,12,16,21].

In Sweden, multi-professional interdisciplinary team assessments and treatments have dominated the healthcare of patients with chronic pain, and pain rehabilitation programs (REHs) have been promoted by the National Board of Health and Welfare [5,25]. The assessments and treatments focus on pain as a disease and aim to reduce its effects by targeting behavioral and psychological factors [26–29]. The official Swedish guidelines state that patients with chronic pain should be referred to specialist pain rehabilitation units if the general practitioner needs help with the assessment and treatment [30]. Although the guidelines are not consistently adhered to nationwide, and there is some randomness in terms of which patients are referred and to where they are referred, REHs remain the dominant treatment strategy. However, REHs are resource-intensive, expensive, and often time consuming [31–34]. To date, however, the long-term health and economic effects of REHs have not been comprehensively evaluated, despite the importance of such evaluations for decision makers [35]. A cost-effectiveness study of RFN to treat ZJP, was recently published in which the patients served as their own controls [36].

The aims of the present study were as follows: (i) to compare the characteristics of patients assessed for ZJP and treated with RFN as a type of interventional pain management at a specialist pain clinic with those who underwent a multi-professional REH at specialist clinics in Sweden; (ii) to compare the effects of RFN and REH on health-related quality of life; and (iii) to evaluate the cost-effectiveness of RFN and REH.

2. Material and methods

2.1. Study setting and population

Patients with chronic pain in Sweden can either be referred to any of the many pain rehabilitation clinics or to one of the few RFN clinics. The assessments performed at pain rehabilitation clinics are designed to evaluate whether the patient would benefit from a REH. The assessments for RFN involve diagnostic blocks to localize the pain foci (mainly ZJP) that can be treated. If ZJP is identified, the treatment involves RFN of the nerves that supply the identified zygapophysial joints.

All patients who underwent assessment of chronic pain in Sweden between 2010 and 2016 were eligible for this study. A total of 36,712 patients were assessed at pain rehabilitation clinics, of which 18,471 (50.3%) were selected for pain rehabilitation. Patients who had been assessed or treated with both REH and RFN ($n = 71$), those who underwent multiple assessments for REH ($n = 2230$), and patients without EuroQOL Five-Dimension (EQ-5D) scores at the assessment or follow-up ($n = 884$) were excluded. Therefore, the REH group comprised 15,357 patients (Table 3).

Of 873 patients assessed at a specialist RFN clinic during the study period, 402 (46.0%) were diagnosed with ZJP and treated. Patients that had been assessed at a REH clinic ($n = 71$) and patients without EQ-5D scores at the assessment or follow-up ($n = 77$) were excluded. Thus, 254 patients were included in the RFN group (Table 3). Of these, 159, 52, and 43 patients were diagnosed with lumbar, thoracic, and cervical ZJP, respectively. Because prior studies reported similar outcomes of RFN for ZJP regardless of the affected level, all RFN patients were combined in a single group [16,36].

The sociodemographic and clinical variables of eligible patients in the REH and RFN groups were compared with all patients assessed for REH and RFN to confirm whether the eligible patients were representative of the overall populations (Table 1).

2.2. Description of the interventions

2.2.1. RFN

After pain analysis by semi-structured interviews, diagnostic MBBs were performed at the suspected locations. The patients completed a form hourly for 7 h to report any reductions in pain. If two MBBs performed at the same level on two different occasions reduced the pain by $\geq 80\%$, the patient was diagnosed with ZJP and offered RFN. The MBB and RFN in the cervical and lumbar region were performed according to the Spine Intervention Society guidelines [21], and those in the thoracic region were performed using a previously described method in which several parallel lesions at 80 °C were made using an 18G needle covering the area where the nerve is usually located on the actual vertebrae [16,36].

2.2.2. REH

The team-based assessments were conducted over 1 day. The team members conducted their examinations individually and completed their assessments at a joint meeting where they discussed the findings and recommendations for each patient.

REH was a group-based program involving 8–10 patients per group. The program started with patients attending two meetings during which they received information about the program, goal-setting practices, and other relevant information. Ten weeks later (on average), the patients underwent a 5-week outpatient program with sessions on 4 days per week. This goal-oriented, interdisciplinary pain program was based on cognitive behavioral therapy principles. Discharge meetings were held with each patient in the fifth week, to which the patients could invite additional guests. A 2-day follow-up was scheduled 9 weeks after discharge. At 1 year after discharge, questionnaires covering self-reported outcomes were posted to all patients [37].

Table 1
Patient characteristics.

	Pain rehabilitation program			Radiofrequency neurotomy group		
	Assessed	Patients selected for rehabilitation		Assessed	Patients treated with radiofrequency neurotomy	
	2010–2016	2010–2016	Included in study	2010–2016	2010–2016	Included in study
n	36,712	18,471	15,357	873	402	254
Selected for treatment (%)		50.3%			46.0%	
Age, years, mean (SD) [range]	44.3 (12.3) [13–95]	43.3 (11.0) [14–92]	43.4 (11.0) [14–92]	52.2 (15.7) [16–94]	51.0 (15.6) [17–89]	52.2 (15.9) [17–89]
Women, *n* (%)	26,312 (71.7%)	13,855 (75.0%)	11,533 (75.1%)	553 (63.3%)	260 (64.8%)	158 (62.2%)
Men, *n* (%)	10,400 (28.3)	4616 (25.0%)	3824 (24.9%)	320 (36.7%)	142 (35.2%)	96 (37.8%)
Pain duration, months, mean (SD) [range]	103 (110) [0–1346]	100 (108) [0–1152]	99 (108) [0–1152]	110 (113) [1–768]	120 (120) [2–744]	116 (118) [2–744]
HAD-anxiety, mean (SD)	9.7 (6.0)	9.6 (5.5)	9.6 (5.6)	7.2 (4.5)	6.9 (4.3)	7.0 (4.4)
HAD-depression, mean (SD)	9.1 (5.7)	9.0 (5.2)	8.9 (5.2)	7.7 (4.4)	7.9 (4.5)	7.9 (4.6)
EQ-5D index, mean (SD)	0.254 (0.317)	0.267 (0.312)	0.276 (0.314)	0.262 (0.318)	0.216 (0.281)	0.221 (0.285)
EQ-5D VAS, mean (SD)	41 (20)	42 (19)	42 (19)	44 (20)	42 (18)	42 (19)

SD standard deviation, *HAD* Hospital Anxiety Depression scale, *EQ-5D* EuroQOL five-dimension scale of health, *EQ-5D VAS* EuroQOL visual analog scale of health.

2.3. Data collection

Data were prospectively collected and entered into clinical databases before and during assessment and treatment.

Data on patient demographics, psychological distress, and health-related quality of life were collected using questionnaires completed by the patients. Linked data on medications, sick leave, and healthcare consumption were obtained from national registers (Swedish National Board of Health and Welfare and the National Social Insurance System).

The patients completed the questionnaires at the time of assessments in both groups. In the REH group, the questionnaires were to be completed immediately after REH and at 1 year after REH. For RFN, the questionnaires were to be completed at the time of RFN, and at 3, 6, and 12 months after RFN. A short telephone interview was also performed 1 month after RFN to ask how long the patient's pain persisted after treatment.

2.4. Questionnaires

Psychological distress was measured using a Swedish version of the Hospital Anxiety and Depression Scale (HAD) [38]. Health-related quality of life was measured using Swedish versions of the EQ-5D index and the EuroQOL visual analog scale (EQ-VAS) under license from EuroQOL. We used the time trade-off-derived UK values set to calculate the EQ-5D index.

2.5. Intervention costs

2.5.1. REH

For REH, the costs associated with assessment and treatment were calculated by multiplying the number of treatment days by the unit cost per day. The unit cost per day had been negotiated with the purchasing neighboring regions to generate a 'price-list' for each combination of diagnosis and possible treatment. In this study, we used 2016 as the price year and the price list from the Region Skåne.

The unit cost for a 'team with a physician' (10,632 Swedish krona [SEK]) was used for the assessment of patients eligible for REH. The unit cost for 'daycare without a physician' (4637 SEK per day) was used to calculate the cost of the REH sessions. The assessment period was 1 day and the period of REH was 24 days.

2.5.2. RFN

For RFN, the mean number of visits to the clinic and the mean number of procedures performed were determined for all patients assessed (n = 873). On average, 3.2 visits and 4.3 procedures were needed to diagnose or rule out ZJP in the assessed patients, with a unit cost of 12,635 SEK for each assessed patient, and 8.3 visits and 33,324 SEK per patient diagnosed with ZJP. The costs per procedure were obtained from the reimbursement price list for Swedish public procurement 2010–2016 (Supplement S1). Among the assessed patients who were not diagnosed with ZJP, some were tested several times with medial branch blocks, some received nerve root blocks or sympathetic blocks while trying to figure out where their pain focus was located. Only those diagnosed with ZJP and treated with RFN were included in the "benefit" calculations while all patients were included in the "cost" calculation. This was carried out to capture the whole pathway cost for RFN.

2.6. Medications

Data on prescribed and dispensed drugs were collected for all treated patients (n = 15,611). In Sweden, people are limited to purchasing prescribed drugs for a 3-month period, and the purchase is registered in a central register administered by the Swedish National Board of Health and Welfare. Thus, each patient prescribed chronic medications must purchase their drugs at least four times per year, but more frequent purchases may be required when purchasing smaller amounts. All purchases are registered with the total amount of drugs (defined daily doses; DDD, i.e. the assumed average maintenance dose per day for a drug used for its main indication in adults) and the total cost paid to the manufacturer. Data were obtained for the 3-month period before RFN/REH and for the 3-month period at 1 year after treatment. Drugs associated with the treatment of chronic pain were identified using the Anatomical Therapeutic Chemical Classification codes (Supplement S2).

2.7. Healthcare consumption

The patients' use of all types of specialized healthcare was obtained from the Swedish National Board of Health and Welfare registers for the same period as for prescribed medications, and analyzed similarly. Only healthcare associated with chronic pain (i.e., with relevant diagnoses according to the International Classification of Diseases 10th Revision codes) were included in the cost calculations because diseases not associated with chronic pain (e.g., cardiovascular diseases, respiratory diseases, contagious diseases, or cancer) are considered not to be affected by pain management (Supplement S3).

To calculate the unit cost per visit, we used data from the Swedish Association of Local Authorities and Regions [39]. The average cost was calculated as 3792 SEK for specialist outpatient visits and 11,423 SEK per day for inpatient care (Table 2). Daycare visits, defined as inpatient care of <24 h, were handled similarly to the outpatient visits, with an estimated average cost of 3792 SEK.

2.8. Patient's time and travel costs

The patients' time spent at the clinics and their travel costs were estimated for all visits. The time and travel costs associated with the assessment (REH) and for the diagnostic procedures (RFN) were classified as diagnostic costs, whereas the time and travel costs during REH and those associated with RFN were classified as treatment costs. The assessment at the REH clinics took 1 day (i.e., 6 h) and the total treatment time was 24 days (6 h per day). Each visit for assessment and treatment at the RFN clinic was assumed to be 1 h. We used the Swedish average wage in 2016 as the unit cost for time (217 SEK per hour including 32.46% payroll tax) [40]. We assumed travel time as 2 h and a cost of 180 SEK (100 km/62 miles, 1.8 SEK per km) per visit.

2.9. Productivity loss and sick leave

Linked data on the number of sick leave days were obtained from the Swedish Social Insurance System. In Sweden, four levels of sick leave are used: 25%, 50%, 75%, or 100%. Data were collected for the same periods as for medications and health consumption to calculate the changes in sick leave after treatment. Data were also collected for the month before and after RFN because many patients are temporarily unable to work for

Table 2
Cost per outpatient visit in specialized care and inpatient care days, in 2016, according to the Swedish Association of Local Authorities and Regions.

	Outpatients		Inpatients	
	Specialized care		Specialized care	
	Cost per visit (SEK)	Visits (n)	Cost per day (SEK)	Care days (n)
Physician, somatic care	3428	8,333,000	13,113	5,924,147
Advanced day care	5866	1,079,000	–	–
Physician, psychiatric care	4750	831,000	5126	1,590,007
Average cost	3792 SEK/visit		11,423 SEK/care day	

The average cost of an outpatient visit was calculated according to the number of visits of each type in 2016. For inpatient care, the average of somatic and psychiatric care was calculated.

Table 3
Calculation of costs.

		Pain rehabilitation program			Radiofrequency neurotomy group		
		Specification	Total costs	Cost per patient	Specification	Total costs	Costs per patient
Costs associated with assessments and diagnostic procedures	Patients assessed, *n*	36,712			873		
	Patients treated, *n*	18,471			402		
	Patients in study, *n*	15,357			254		
	Estimated visits, *n*	30,523			1743		
	Visits per patient, *n*	2.0			6.9		
	cost/visit	10,632					
	Calculated total cost		324,518,148	21,132		6,969,267	27,438
	Time/visit, *h*	6			1		
	Travel time/visit, *h*	2			2		
	Travel costs, SEK	180			180		
	Patient time cost, SEK	217			217		
	Total time cost, SEK		19,994,814	1302		378,285	1489
	Travel costs, SEK		9,429,198	614		1,070,355	4213
Treatment costs	Patients treated, *n*	15,357			254		
	Visits, *n*	24			1		
	Time/visit, *h*	6			1		
	Healthcare cost/visit, SEK	4637			5500		
	Healthcare cost, SEK		1,709,049,816	111,288		1,397,000	5500
	Total time cost, SEK		479,875,536	31,248		55,118	217
	Travel costs, SEK		226,300,752	14,736		110,236	434
Cost of pain-related medication	Annual DDD before	460			704		
	Annual DDD after	448			676		
	DDD after/before:						
	Antiemetics	117%			68%		
	Constipation	100%			120%		
	NSAID	69%			57%		
	Muscle relaxants	76%			126%		
	Opioids	85%			95%		
	Antiepileptics	121%			84%		
	Anxiolytics	112%			74%		
	Hypnotics/sedatives	113%			113%		
	Antidepressants	110%			108%		
	Average cost before, SEK	2664			8372		
	Average cost after, SEK	2876			8552		
	Total cost difference	212			180		
Healthcare consumption	Outpatient visits						
	Before, mean *n*	7.6			11.7		
	After, mean *n*	7.2			3.6		
	Cost/visit, total, SEK	3792	−23,293,498	−1516	3792	−7,801,661	−30,715
	Inpatient care days						
	Before, mean *n*	3.2			0.3		
	After, mean *n*	3.2			2.7		
	Cost/day, total, SEK	11,423	0	0	11,423	6,963,461	27,415
Sick-leave	Average annual days						
	Before	154			128		
	After	103			60		
	Days after RFN, SEK				2.07		
	Total cost						
	Before	511,083,918			7,037,172		
	After	343,099,692	−167,984,226	−10,939	3,301,776	−3,735,396	−14,706
	Sick leave after RFN					113,913	448
Total costs			**2,606,948,16**	**169,756**		**5,520,578**	**21,735**
Total QALY-gain	At 1 year		2518.55	0.164		47.24	0.186
	At 2 years		5405.66	0.352		113.792	0.448
Cost/QALY-gained	At 1 year		**1,035,100 (~121,633 USD)**			**116,852 (~13,715 USD)**	
	At 2 years		**481,578 (~56,589 USD)**			**48,461 (~5694 USD)**	

SEK Swedish krona, *USD* US dollars, *DDD* defined daily doses, *NSAID* non-steroid anti-inflammatory drugs, *RFN* radiofrequency neurotomy, *QALY* quality-adjusted life years.

a few weeks after RFN. If there were more days of sick leave during the first month after RFN than before RFN, it was classified as a treatment cost. We converted the number of days of sick leave to productivity by applying the average wage (217 SEK per hour including 32.46% payroll tax, 8 h per day).

2.10. Statistical methods

Propensity score weighting was used in the analyses [41]. A more thorough description and explanation of the use of propensity scores is available in Norström et al. [42].

We used logistic regression with potential confounders (gender, age, pain duration, previous health measured by the EQ-5D index) as covariates to estimate the propensity scores. The propensity score corresponds to the probability of receiving RFN for ZJP instead of being treated with a team-based REH. Thus, comparison between an exposed and unexposed individual with the same propensity measure is similar to analyzing exposure in a randomized controlled trial. Using this propensity score

approach in observational studies represents a quasi-experimental approach.

We used propensity score weighting using an inverse probability weight estimator (*W*), as suggested by Lunceford and Davidian [41],

$$W = Z/ps + (1 - Z) / (1 - ps)$$

where $Z = 1$ for RFN, $Z = 0$ for REH, and ps = propensity score.

The standardized difference (*d*) was calculated, both with and without the weighting, to assess the balance of covariates between the REH and RFN groups for each potential confounder (Table 4) [42–44]. A standardized difference of >10% represents a meaningful imbalance in the given covariate between groups [44].

$$d = 100 * (xRFN - xREH) / sqr((vRFN^2 + vREH^2)/ \quad 2)$$

Here, *xRFN* = mean value for RFN, *xREH* = mean value for REH, sqr = square root, *vRFN* = variance for RFN, and *vREH* = variance for REH. Furthermore, for dichotomous values,

$$d = 100 * (pRFN - pREH) / sqr((pRFN * (1 - pRFN) + pREH * (1 - pREH)) / 2)$$

where *pRFN* = proportion for RFN and *pREH* = proportion for REH.

Descriptive statistics were used to present the characteristics of the study groups, and stratified results were derived for each covariate for the outcome variables. Analyses were carried out for the EQ-5D index, EQ-VAS, HAD, medications, healthcare consumption, and sick leave.

Paired *t* tests were used to compare the outcomes at 1 and 2 years after treatment versus those at the time of treatment. Student's *t*-test was used to compare outcomes between the two groups (mean EQ-5D index and proportion of patients with clinical relevant improvement in EQ-5D index).

Patients with missing values were excluded from the analyses. *P* values of <0.05 were considered to indicate statistical significance. JMP 16.1.9 was used for all statistical analyses (SAS Inc., Cary, NC, USA).

2.11. Cost-effectiveness calculations

Quality-adjusted life years (QALYs) were calculated from the propensity score-weighted mean for the EQ-5D index versus time. We assumed that the EQ-5D index changed evenly between measurement points from the time of starting treatment (i.e., 5 weeks before the first follow-up for REH and at the time of RFN for RFN). Data were obtained for 2 years after starting treatment.

Cost-effectiveness was calculated by dividing the total costs with the gain in QALYs (cost/QALY gain) in both groups. The results were compared between the two group and against the limits set by the Swedish National Board of Health and Welfare. All calculations were made in SEK at the 2016 price level. Costs were converted to US dollars (USD) at an exchange rate (USD:SEK) of 1:8.51 in 2016.

The Swedish National Board of Health and Welfare classify cost-effectiveness ratios (cost/QALY gain) into four ranges: low (<100,000 SEK), moderate (100,000–500,000 SEK), high (500,000–1,000,000 SEK) and very high (>1,000,000 SEK) costs, which we used in this study [45,46].

An increase of 0.1 in the EQ-5D index was considered to be clinically relevant [16,47–49].

2.12. Sensitivity analysis

Sensitivity analyses were performed for all variables that were deemed likely to affect the outcome (cost/QALY gain).

We diagnosed ZJP in 46.0% of the patients assessed, but the prevalence of ZJP varied in prior studies between ~30% (lumbar region) and ~50% (cervical region) [17,18,50,51]. Therefore, in sensitivity analyses we assumed that 30% and 50% of the patients underwent RFN. Likewise, 50.3% of those assessed were considered suitable for REH. Therefore, we developed scenarios in which only 30% of those assessed would be treated by REH and if everyone (100%) underwent REH.

We tested the impact of the healthcare cost by performing a sensitivity analysis in which the costs were adjusted by ±25%, and by increasing the travel costs by 25% and 100%. We also tested the impact if we excluded the effects of healthcare consumption. We also tested for differences in the effect on health-related quality of life by changing the mean improvement in EQ-5D index after treatment by ±10%.

When analyzing the data, we found that the 1-year follow-up after treatment was actually performed later than planned, which allowed us to analyze the effects at 2 years after treatment, although in a smaller group. Because the aim of REH is to help the patient cope with the problems and manage their pain, these effects are considered to last for several years. Similarly, the effect of RFN in adequately diagnosed patients was shown to last longer than 1 year [12,13,52]. Therefore, we performed a sensitivity analysis in which we calculated the costs/QALY gained if the effects lasted for up to 6 years.

2.13. Ethics

All patients provided informed consent for inclusion in this study, for the use of their medical records, and for data collection and analysis. The regional ethics board in Umeå, Sweden, approved the study (Dnr

Table 4
Absolute values and standardized difference of baseline demographics and clinical characteristics.

Variable	Radiofrequency neurotomy group	Pain rehabilitation program	Unweighted standardized differences	Weighted standardized differences
Age, mean, years	52.2	43.4	4.42	0.07
Gender (women), %	62.2	75.1	28.1*	7.46
Pain duration, mean, months	116	99	0.13	<0.01
HAD-anxiety, mean	7.0	9.6	10.0*	0.12
HAD-depression, mean	7.9	8.9	4.17	0.10
EQ-VAS, mean	42	42	0.07	0.01
EQ-5D index, mean	0.201	0.276	60.74*	0.25
DDD pain medications, mean	187	115	0.11	<0.01
DDD other drugs, mean	276	138	0.03	<0.01
Outpatient visits pain, mean	0.48	0.65	10.3*	0.03
Outpatient visits other problems, mean	0.45	0.65	11.8*	0.21
Inpatient days pain, mean	0.102	0.208	4.97	1.20
Inpatient days other problems, mean	0.204	0.123	3.87	0.05
Cost of sick leave, mean SEK	32,949	27,410	<0.01	<0.01

HAD Hospital Anxiety Depression scale, *EQ-VAS* EuroQOL visual analog scale for health, *EQ-5D* EuroQOL five-dimension scale for health, *DDD* defined daily dose, SEK Swedish krona.
*Variables with standardized differences of >10%.

2020–04586). The study was registered at ClinicalTrials.gov (NCT04657159) under protocol ID IPM-PRP2020. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

3. Results

3.1. Characteristics of the assessed patients

A total of 36,712 patients were assessed at pain rehabilitation clinics and 18,471 (50.3%) were identified as likely to benefit from a REH, and thus were treated during the study period (2010–2016). During the same period, 873 patients were assessed at RFN clinics. After 2759 visits and 3788 procedures, 402 patients (46.0%) were diagnosed with ZJP and underwent RFN (Table 1). Data were analyzed for 15,357 patients who underwent REH and 254 patients who underwent RFN. There was a statistically significant difference in the gender distribution between the two groups, as well as differences in age and pain duration. After propensity score weighting, the standardized differences showed no significant imbalances between the two groups (Tables 1 and 4).

3.2. Health-related quality of life and psychological distress at the initial assessment

The mean EQ-5D index score was 0.221 in the RFN group and 0.276 in the REH group, the EQ-VAS score was 42 in both groups, the HAD-anxiety score was 7.0 in the RFN group and 9.6 in the REH group, and the HAD-depression score was 7.9 in the RFN group and 8.9 in the REH group. There were no statistically significant differences in these factors between the two groups after propensity score weighting (Tables 1 and 4).

3.3. Changes in health-related quality of life at 1 year after treatment

In the REH group, the mean EQ-5D index (from 0.275 to 0.468, $P < 0.0001$), EQ-VAS (from 42 to 54, $P < 0.0001$), HAD-anxiety score (from 9.6 to 7.7, $P < 0.0001$), and HAD-depression score (from 8.9 to 6.9, $P < 0.0001$) improved significantly from the initial assessment to 1 year after treatment.

In the RFN group, the mean EQ-5D index (from 0.288 to 0.537, $P < 0.0001$), EQ-VAS (from 45 to 58, $P < 0.0001$), HAD-anxiety score (from 7.9 to 6.1, $P = 0.0207$), and HAD-depression score (from 8.3 to 7.0, $P = 0.0057$) also improved significantly from the initial assessment to 1 year after treatment.

At 1 year after treatment, there were statistically significant differences between the REH and RFN groups in terms of the EQ-5D index (0.468 vs 0.537, respectively, $P < 0.0001$) and the percentage of patients with a clinically relevant improvement (39% vs 59%, respectively, $P < 0.0001$).

The mean QALY gained calculated from the propensity score-weighted EQ-5D index values was 0.164 and 0.186 in the REH and RFN groups, respectively, at 1 year, and 0.352 and 0.448, respectively, at 2 years after treatment.

There were no major complications in the RFN group. Complications are not handled or registered in the pain rehabilitation register.

3.4. Intervention costs

As described in Section 2.1, 50.3% of the patients assessed at the pain rehabilitation clinics were identified as likely to benefit from a REH, and thus were selected for treatment. Therefore, we assumed that 30,525 patients were assessed, yielding 15,357 patients included in the study. The cost per assessed patient was 10,632 SEK and the total cost of assessment was 21,132 SEK per treated patient (Table 3). Assuming a treatment cost of 4637 SEK per day for 24 days yielded a treatment cost of 111,288 SEK per treated patient in the REH group.

For RFN, 831 patients were assessed and tested at 2759 visits and 3788 procedures, with a total cost of 11,030,100 SEK. Meanwhile, 402 patients (46%) were diagnosed with ZJP and treated. Therefore, the costs for the 254 patients included in the study was estimated based on 254/402 of the total measured costs, corresponding to 27,438 SEK per patient and an average of 6.9 visits per treated patient. RFN was performed during one visit at a cost of 5500 SEK per patient.

3.5. Medications

In the REH group, the total average annual medication consumption was 1016 DDD before treatment and 1044 DDD at 1 year after treatment. The average annual pain-related medication changed from 460 DDD to 448 DDD at 1 year after treatment, whereas the average annual cost of pain-related medications increased from 2664 SEK to 2876 SEK. The total extra cost per patient was therefore 212 SEK per patient.

In the RFN group, the total average annual medication consumption was 1302 DDD before treatment and 1384 DDD at 1 year after treatment. The annual pain-related medication changed from 704 DDD to 676 DDD, but this resulted in an additional cost of 180 SEK per patient. Because there was a reduction in pain-related medications (i.e., reduced DDD), the increased cost was considered not to be a consequence of the treatment but was from external causes and the changes were not included in the cost calculations (Table 3).

3.6. Healthcare consumption

There were changes in healthcare consumption in both groups when comparing propensity score-weighted visits during the 3-month periods before the assessment and 1 year after treatment. The annual average number of pain-related visits decreased from 7.6 to 7.2 in the REH group and from 11.7 to 3.6 in the RFN group. The number of inpatient pain-related-care days remained at 3.2 in the REH group and increased from 0.3 to 2.7 in the RFN group.

In economic terms, this changes in healthcare consumption resulted in a reduced cost for outpatient care of 1516 SEK per patient in the REH group and 30,715 SEK per patient in the RFN group. The cost for inpatient care increased by 27,415 SEK per patient in the RFN group. The numbers of visits and ward days were small and it is uncertain whether the changes were an effect of the treatment. Nevertheless, we decided to include these changes in the cost calculation (Table 3).

3.7. Patient time and travel costs

The costs incurred by patients in the REH group were calculated to be 1302 SEK for the assessments and 614 SEK for travel costs, including time incurred, per patient. The corresponding costs in the RFN group were 1489 SEK and 4213 SEK. For the treatment sessions, the costs incurred by patients were calculated to be 31,248 SEK for treatment and 14,736 SEK for travel in the REH group, and 217 SEK for treatment and 434 for travel in the RFN group (Table 3).

3.8. Productivity and sick leave

The annual average number of sick leave days decreased from 154 days to 103 days in the REH group and from 128 days to 60 days in the RFN group. Patients in the REH group and in the RFN group reduced their sick leave after treatment, with a greater reduction in the RFN group. During the period after RFN, 90 patients in the RFN group reduced their sick leave from the month before treatment, 125 patients had no change in sick leave, and 39 patients required an increase in sick leave during the month after RFN. The reduced sick leave was not considered to be caused by the treatment, and thus was not included in the calculations. However, the increased sick leave was considered to be caused by post-RFN pain and was included in the analysis. These values yielded a reduced cost of 10,939 SEK for the REH group and a reduced cost of 14,706 SEK in the

RFN group. The cost increased by 448 SEK per treated patient in patients with increased sick leave during the post-RFN period (Table 3).

3.9. Cost-effectiveness

The total net cost was 169,756 SEK per patient in the REH group and 21,735 SEK per patient in the RFN group. The total QALY gained was 0.164 and 0.186 per patient in the REH and RFN groups, respectively, resulting in a cost/QALY gain of 1,035,100 SEK (~121,633 USD) for REH and 116,852 SEK (~13,715 USD) for RFN. After 2 years, the cost/QALY gain declined to 481,578 SEK (~56,589 USD) and 48,461 SEK (~5694 USD), respectively (Table 3).

3.10. Sensitivity analysis

In all sensitivity analyses scenarios, the cost-effectiveness ratio for RFN remained within the moderate to low range for cost-effectiveness according to the Swedish National Board of Health and Welfare. For REH, calculating an effect duration of >2 years was needed to reach the moderate range for cost-effectiveness (Table 5) [45,46].

A sensitivity analysis was performed to check the effects of the assessment costs. In the REH group, 50% of the patients assessed were expected to benefit from rehabilitation and were treated. Decreasing this proportion to 30% increased the cost/QALY gained by 10%. If all patients assessed were treated, the cost/QALY gained decreased by 7%, resulting in a cost/QALY gained of 959,540 SEK at 1 year and 446,424 at 2 years.

In the RFN group, 46% of the patients assessed were diagnosed with ZJP and treated. Decreasing this value to 30% increased the cost/QALY gain by 37%–212,167 SEK. When the proportion was increased to 50% of those assessed, the cost/QALY gained decreased by 34%.

Changing the costs of healthcare given by −25% and +25% resulted in a change in cost/QALY gained of 20% in the REH group, corresponding to values of 833,240 and 1,236,959 SEK at 1 year. In the RFN, this changed the cost/QALY gained by 34%, corresponding to values of 102,890 and 207,254 SEK at 1 year.

Increasing the travel costs by 25% or 100% resulted in a maximum change of 9% in the REH group and of 19% in the RFN group, with no major changes in the outcomes.

We also performed sensitivity analyses by excluding healthcare consumption. This resulted in a cost/QALY gain of 1,044,348 SEK in the REH group and 134,594 SEK in the RFN group, indicating no major change in outcomes.

When we considered changes in the effectiveness of REH and RFN in terms of improved health-related quality of life, a 10% reduction of the EQ-5D index resulted in a cost/QALY gained of 1,401,965 SEK at 1 year and 850,045 SEK at 2 years in the REH group. Increasing the effect by 10% resulted in cost/QALY gained of 674,883 and 403,939 SEK, respectively. In the RFN group, reducing the effect by 10% resulted in a cost/QALY gained at 1 and 2 years of 153,710 and 62,375 SEK, respectively, and increasing the effect by 10% gave corresponding results of 104,973 and 39,694 SEK, respectively.

Finally, we performed a sensitivity analysis in which the effects of treatment were maintained for >2 years. In this analysis, REH was cost-effective in the moderate range and RFN was cost-effective in the low range (Table 5).

Table 5
Results of the sensitivity analysis.

		Pain rehabilitation program		Radiofrequency neurotomy group	
Assessed patients	*n*	30,523		670	
Treated patients	*n*	15,357		254	
Total assessment costs		382,999,785		10,223,561	
Cost for healthcare	Assessment	243,388,611		8,464,185	
	Treatment	1,281,787,362		1,397,000	
Travel costs	Assessment	18,740,984		1,299,947	
	Treatment	226,300,752		110,236	
Total costs		2,606,948,166		7,326,232	
Rate treated/assessed	Cost/QALY gain	50.3%	1,035,100	46.0%	116,852
		30%	1,138,069	30%	212,167
		100%	959,540	50%	102,770
Cost of healthcare	Cost/QALY gain	−25%	833,240	−25%	72,581
		0%	1,035,100	0%	116,852
		+25%	1,236,959	+25%	161,124
Travel costs	Cost/QALY gain	0%	1,035,100	0%	116,852
		+25%	1,059,423	+25%	123,100
		+100%	1,132,394	+100%	141,842
Health consumption	Cost/QALY gain	As measured	1,035,100	As measured	116,852
		Excluded	1,044,348	Excluded	134,594
Changed effect		1 year	2 years	1 year	2 years
	−10%	1,401,965	850,045	153,710	62,375
	As measured	1,035,100	481,578	116,852	48,461
	+10%	674,883	403,939	104,973	39,694
Duration of effect	Per patient	QALY gain	cost/QALY gain	QALY/gain	cost/QALY gain
	1 year	0.164	1,035,100	0.186	116,852
	2 years	0.352	481,578	0.448	48,461
	3 years	0.534	317,598	0.634	34,255
	4 years	0.716	236,924	0.892	24,380
	5 years	0.898	188,933	1.406	15,464
	6 years	1.080	157,109	1.662	13,073

All costs are given in Swedish krona (SEK).
QALY quality-adjusted life years.

4. Discussion

4.1. Main findings

Randomized controlled trials are the gold standard for clinical research and provide the strongest evidence supporting a specific treatment. However, there is discussion regarding a possible paradox in that, if we demand randomized controlled trials of every treatment method used in pain management, the length of time needed and the cost will be incredibly high [53]. Using propensity scores, we can mimic randomized controlled trials and the bias of the estimates depends on how well the propensity scores balance the measured and unmeasured confounders [41,54]. The propensity score represents the conditional probability of being assigned to the exposure group based on baseline covariates (in this case, gender, age, pain duration, and EQ-5D index) [42]. According to Lunceford and Davidian, "stratification via estimated propensity score can lead to biased inference", while "methods based on weighting are consistent and offer approximately unbiased inference for practical sample sizes." [41].

In the present work, the characteristics of the patients treated with RFN did not differ significantly from those treated with REH after applying propensity score weighting. We calculated the standardized differences between the two groups for both unweighted and weighted covariates, and the differences were well below the limit of 10% after propensity score weighting, showing that the groups were well balanced [44].

Both treatments were associated with significant improvements in health-related quality of life, which was significantly greater in the RFN group than in the REH group when expressed as the QALY gains per patient (0.186 vs 0.164). RFN was cost-effective (Table 3), with a cost/QALY gain of 155,072 SEK at 1 year, which is in the moderate range according to the Swedish National Board of Health and Welfare, whereas REH had a cost/QALY gained of 1,035,100 SEK, which is in the very high range [45,46]. Because the treatment benefits are expected to last for >1 year, we also calculated the cost-effectiveness ratios at 2 years, at which time the cost/QALY gained was 481,578 SEK for REH, which was within the moderate range, and the corresponding value was 64,311 SEK for RFN, which was within the low range.

Despite the term "radiofrequency neurotomy", the effects on the nerves will subside and normal nerve function will resurrect. There is no exact time when this will occur, but usually one year is considered as normal. Many patients will experience that the previous pain reappear when the nerve functions resurrect, which means that the average effect on HRQoL in the group will be reduced. Similar effects are described by patients after psychological treatments like REH, when their memories of the treatments fade. However, since we only had data for the first 24 months we decided to ignore those effects when we extrapolated the results in the sensitivity analyses for up to 6 years after treatment, where REH remained within the moderate range (157,109 SEK after 6 years).

The Swedish National Board of Health and Welfare use four criteria (the severity of the condition, the effectiveness of treatment, the cost-effectiveness of the treatment, and the evidence base) to set priorities and make an overall judgement on a medical treatment [45,46]. The severity of the condition and the effectiveness of both treatments are demonstrated in terms of improvements in health-related quality of life. We have demonstrated the cost-effectiveness of RFN, namely ZJP, and REH was found to be cost-effective if the effects were maintained for ≥2 years. Considering all of these criteria, the results suggest a higher ranking for RFN and a lower ranking for REH because of its worse effectiveness and higher costs.

We found that <2% of patients with chronic pain are treated with RFN in Sweden. Our study provides support for expanding RFN. If RFN can be extended to 25% of patients in 10 years, it could save 180 million SEK per year (~21.2 million USD) in healthcare resources.

4.2. Strengths and weaknesses of the present study

The most prominent strength is that we, by using propensity score weighting in an observational study, could compare RFN, especially ZJP, with REH in a manner akin to randomized controlled trials. Furthermore, we used data collected in national registers about medications, healthcare consumption, and sick leave, which avoided the need to collect subjective, retrospective reports from patients. We took a societal perspective and did not focus solely on the healthcare costs. In the cost calculations for RFN we included assessment costs for all patients, regardless of whether they were diagnosed with ZJP or not, which means that the total cost is close to the total "pathway cost" for diagnosing and treating chronic pain patients with RFN. Another strength is that we placed a monetary value on the patient's time, regardless of whether the patients were retired, on permanent sick leave, or working full time. Accordingly, the costs could be extrapolated to other settings involving younger patients. Therefore, the study reflects the results that can be achieved in real life when following strict guidelines for the diagnosis and treatment of ZJP and when performing REH according to the Swedish guidelines for pain rehabilitation.

A weakness of the study is that we only had data from one RFN clinic, because RFN is rarely performed in Sweden. Nevertheless, we had access to data from all active pain rehabilitation clinics in Sweden, providing a robust comparison group.

4.3. Conclusions

We used propensity score weighting to yield two equal groups that were exposed to two different treatments (RFN and REH), resulting in a setting similar to that of randomized controlled trials. We found that the health-related quality of life improved after both treatments, with a greater improvement in the RFN group. At 1 year, only RFN was shown to be moderately cost-effective. However, when the effect was measured at 2 years, REH became cost-effective in the moderate range and RFN became cost-effective in the low range. Our results suggest that expanding RFN to a greater proportion of patients could achieve annual savings in healthcare resources.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Johan Hambraeus reports a relationship with Smartkliniken Eques Indolor that includes: employment and equity or stocks.

Acknowledgements

We would like to thank Elisabeth Persson, PhD, and Marcelo Rivano Fisher, PhD, Lund University, for describing the pain rehabilitation program. We would like to thank the registered nurses Christine Nath, Eva Umaerus and Kjerstin Segerstedt Hambraeus for collecting patient data for the radiofrequency neurotomy group.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.inpm.2022.100147.

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