Responses after spinal interventions in a clinical pain practice – a pragmatic observational study

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Abstract

Introduction:

There is a limited evidence for effect of interventional treatment, and pragmatic studies are needed to assess these interventions within a clinical setting. The aim of the study was to describe patients referred to an interventional pain clinic and investigate responses after spinal intervention in general and for radiofrequency ablation (RFA) and transforaminal epidural corticosteroid administration (TECA), specifically.

Methods: This is a prospective, non-controlled study of patients with chronic spinal pain. The procedures were performed in accordance with the Spine Intervention Society recommendations. Outcome data after a median of 4,5 months are presented, and for those treated with RFA also after 6 and 12 months.

Results: Among 815 patients, 190 patients underwent diagnostic blocks only and 625 interventional treatment. Of these 94 received RFA and 246 TECA. In the sample who received interventional treatment, 70% reported pain reduction, for 49% it was ≥50%, while 9% were pain free (p<0,001). Highest pain intensity decreased from 7,1 to 5,4 (95% Confidence Interval of the Difference (95%-CI):1,4-1,9) (p<0,001), while EQ-VAS improved from 48 to 58 (95%-CI: 7,6-11,9) (p<0,001), and EQ-5D-5L Index from 0,489 to 0,628 (95%-CI: 0,123-0,157) (p<0,001). The proportions, not taking analgesics, increased from 16% to 30%, and proportion taking strong opioids decreased from 14% to 9% (p<0,001). We found no significant change in proportion receiving physiotherapy or other treatment nor occupational status. No complications were reported.

Among patients treated with RFA, 77% reported pain reduction, for 56% it was ≥50%, while 9% were pain free (p<0,001). Highest pain intensity decreased from 6,9 to 4,6 (95%-CI: 1,6-3,0) (p<0,001), while EQ-VAS improved from 47 to 57 (95%-CI: 4,8-13,6 (p<0,001), and EQ-5D-5L Index from 0,489 to 0,643 (95%-CI: 0,117-0,191) (p<0,001). The proportion not taking analgesics, increased from 7% to 23% and proportion taking strong opioids decreased from 16% to 10%. Among patients who responded at 6- and 12-month follow up, the proportions reporting pain reduction, EQ-VAS, and EQ-5D-5L Index remained significantly improved from baseline, and the change in proportions taking analgesic and opioids achieved statistical significance. We found no significant change in proportion receiving physiotherapy or other treatment nor occupational status.

Among patients treated with TECA, 58% reported pain reduction, for 36% it was ≥50%, while 5% were pain free (p<0,001). Highest pain intensity decreased from 7,2 to 6,2 (95%-CI 0,5-1,4) (p<0,001), while EQ-VAS improved from 46 to 52 (95%-CI: 2,0-3,6) (p<0,001), and

EQ-5D-5L Index from 0,456 to 0,571 (95%-CI: 0,077-0,138) (p<0,001). The proportions, not taking analgesics, increased from 17% to 27% and proportion taking strong opioids decreased from 15% to 10%, but the changes did not reach statistical significance. We found no significant changes in the proportion who recieved physiotherapy or other treatment nor occupational status.

Conclusion: The study demonstrates substantial responses at a median of 4,5 months after spinal intervention and long-lasting improvement for a subsample of the RFA treated patients, after 6 months for at least 50% and after 12 months for at least 25%.

Implementation: Quality assessment should be implemented in interventional pain clinics to improve treatment quality.

Introduction

Chronic neck and low back pain represents a substantial health problem [1] with prevalence rates above 20% [2, 3]. The mechanisms of chronic spinal pain are multifactorial [4, 5], but for neck pain there seems to be a causal relation to biomechanical factors [2]. Researchers have demonstrated a disturbed interplay between lumbar multifid muscles and the zygapophysial (facet) joints in animal [6, 7] and clinical models [8] and in a group of patients with a history of whiplash, the prevalence of facet joint related pain was found to be as high as 60% [9]. For lumbar back pain the rate is considerably lower and therefore difficult to define even with diagnostic test blocks [10].

How patients with spinal pain should be treated is controversial. According to a growing number of systematic reviews and metaanalyses, non-opioids [11, 12] and opioid analgesics [13] do not have any effect, while the effect sizes of physical training [14] and psychological programs are limited [15-17]. This raises the question whether a subsample of spinal pain patients can benefit from invasive treatment modalities or more specifically; can these techniques provide substantial long-lasting pain relief and improved functioning?

Radiofrequency nerve ablation (RFA) and epidural corticosteroid injectons are widely used, but clinical evidence is limited [18, 19]. In a randomized, double-blinded trial including patients subjected to an automobile accident, Lord et al researchers [20] found that RFA of cervical medial branches of the ramus dorsalis provides significantly longer pain relief compared with sham treatment, and a systematic review, published in 2015, rated the clinical evidence of radiofrequency neurotomy to be level II [21]. However, for lumbar neurotomy this evidence has recently been challenged by a large randomized study from the Netherlands including patients with lumbar pain [22].

Randomized, controlled trials are in general characterized by strict patient selection and external validity (generalizability) may be limited. Pragmatic studies, assessing responses to these interventions within the frame of standard clinical care, are therefore needed. This is essential to establish effective and safe treatment programs for patients who do not respond to the non-invasive treatment programs. In this paper we present outcome measures for a large sample treated in an interventional pain clinic in Sweden.

The aim of the study

The aim of the study was to describe 1) patients in an interventional pain clinic, and 2) responses among patients treated with a spinal intervention and radiofrequency nerve ablation (RFA) or transforaminal epidural corticosteroid administration (TECA), specifically.

Material and methods

Design

This is a prospective, non-controlled, observational study. All patients had a 4 to 5-month follow up, and for those treated with RFA, a 6- and 12-month follow up was added.

Setting

The study includes patients examined and treated in a Swedish private, interventional pain clinic ran by a pain physician (LM) and specially trained nurse specialized in critical care medicine (LT). The clinic had approval to accept referrals from the Swedish public health system. The pain physician was a well-trained interventionist and authorized instructor at the Spine Intervention Society (SIS) courses. The clinic was equipped with real-time fluoroscope (Fluorostar 2 Compact Model number 7900, GE Healthcare) operating with cine-fluorography and digital subtraction radiography.

Ethics

The study was performed in accordance with the Declaration of Helsinki's statement of ethical principles for medical research involving human subjects and was approved by the head of the Surgical Unit at Central Hospital Karlstad responsible for scientific and research projects. All patients received detailed information about potential side effects and complications before a written informed consent was obtained. As this was considered a quality-assurance study, approval by the local ethical committee was not required.

Patient recruitment

Between March 2012 and August 2014, we recruited patients suffered from long standing neck or low back pain. They were in general referred from spine surgeons at the Orthopedic clinic and pain doctors at the Central Hospital Karlstad, who had permission to refer patients to the clinic.

The patients were thoroughly examined by the pain physician (LM) and discussed at regular meetings with spine surgeons at Central Hospital Karlstad and qualified physiotherapists. Medial branch blocks were performed in order to diagnose facet joint related pain. All procedures were performed by the pain physician (LM) in accordance with recommendations from the Spine Intervention Society (SIS) [23]. Those with serious psychiatric disorder, suspected or manifest bacterial infection, and those with a history of hypersensitivity to local anesthetic, were pregnant or had a bleeding diathesis were not offered these X-ray guided

injections. Anticoagulants and drugs affecting platelet function were omitted before treatment in agreement with the prescribing doctor.

Under aseptic conditions, with the patient placed in a lateral or prone position (depending on level of intervention), and with intermittent X-ray guidance, 23/25-gauge needles were inserted close to the target nerve(s). Small doses of bupivacaine 5 mg/ml (0,3-0,5 ml) were injected while for cervical third occipital nerve (TON) blocks (facet joint C2-3), bupivacaine was injected at three different sites to compensate for anatomical variations. The reported response to medial branch blocks during the first 4 hours was assessed by the physician (LM), and only patients who reported a substantial pain reduction after at least two repeated test blocks were offered RFA.

Main procedures

RFA is a nerve destructive technique where high-frequent, alternating electrical current (500.000 Hz) is applied to heat the target nerve and stop transmission of nociceptive signals [23]. Prior to the ablation skin, paravertebral muscles and the nerve(s) were anesthetized with 2-4 ml of bupivacaine 5 mg/ml. With intermittent fluoroscopic guidance, we inserted an 18-gauge, curved introducer needle with a 10 mm active tip along a posterolateral plane until the needle tip was placed close and tangentially to the target nerve(s) (medial branches of the ramus dorsalis). With an RF generator (Neurotherm® NT 2000, Abbott) the nerves were heated by 2-5 parallel paths (less than one electrode-width in between) to 80 ˚C for 60 seconds.

Patients with serious lumbar or cervical pathology (acute disc herniation, radiculopathy, or myelopathy) were not offered RFA. Other precautions are listed in the paragraph about diagnostic test blocks. For safety reasons, patients treated at the clinic were not given sedatives nor intravenous opioids during the procedure. Being awake they were still able to respond if a nerve root was exposed to thermal or mechanical stimulation. For post-procedural pain oral administration of ibuprofen 1200 mg was recommended.

Transforaminal epidural corticosteroid administration is widely used and has shown to be effective for patients suffering from radiculopathy after disc herniation [24]. The evidence on radiculopathy and spinal stenosis is, however, not well established [25, 26]. To ensure adequate needle placement 1 ml radiopaque contrast (Joheksol 300 mg) was injected and digital subtraction radiography performed before 1 ml lidoocaine 20 mg and subsequently a non-particulate corticosteroid solution; dexamethasone 10 mg/ml was injected [23].

Data collection

To describe the sample at baseline and to assess treatment responses we applied a variety of measures in accordance with the IMMPACT recommendations [27]. A self-reporting questionnaire provided information about a) pain reduction, b) pain intensity, c) health-related quality of life, d) level of analgesics and use of gabapentinoids/amitriptyline, e) occupational status, and f) physiotherapy or other treatment. The baseline questionnaire included also demographic data (gender, age, height and weight and smoking habits) and a body map to locate the pain with the categories neck, thoracic and lumbar pain. The questionnaire was sent to the patients prior to the screening consultation (S1), at a 4- 5 month follow up (T2), and for those who were treated with RFA, also after 6 (T3), and 12 months (T4). No reminder was sent if patients did not return the questionnaires.

At the screening or treatment visit, diagnosis, pain location, type of spinal intervention, levels of the injections/ablations, and adverse effects were recorded.

The *primary* outcome measure was pain reduction assessed by a 5-pointed categorical scale: pain free, ≥50% pain reduction, <50% percent pain reduction, unchanged and worse.

The *secondary* outcome measures included changes in: a) highest and lowest pain intensity rated by a 10 cm visual analogue scale (VAS), "highest" was defined as maximal and "lowest" as minimal experienced pain during the last 24 hours, b) health-related quality of life assessed by the EuroQol-5D-5L [28, 29] which includes EQ-VAS, a 101-graded scale to describe how total life situation is experienced (Swedish population norm has a mean of 83,3, and declines with age [30]), and five descriptive domains rated by a 5-level scale. In this study the domain scores were converted according to a Danish specific value set into an EQ-5D-5L Index where minimum health status is -0,624 and maximum 1 (Swedish population norm based on EQ-5D-3L has a mean of 0.866, and declines with age [30]), c) number of patients at each of the analgesic levels; no analgesics, non-opioids, light opioids, or opioids, and use of gabapentinoids/amitriptyline (dichotomic variable: "yes" or "no"), d) number of patients using physiotherapy or other treatment (dichotomic variable: "yes" or "no"), and e) number of patients within each of the five occupational categories; employed, unemployed, sick leave, retired or others.

Statistics

For the statistical analyses we used the SPSS statistical package, version 25 and Excel (Microsoft Office 2016) and performed in accordance with a statistician at the Oslo University Hospital.

For continuous, Normally distributed variables Paired-Samples T-tests were used to assess 4-5-month responses. For RFA patients with one-year follow up, General Linear Model Repeated Measures was applied as Q-Q plots indicated Normal distribution of residuals. For categorical variables we performed One-Sample Chi-Square test for "Pain reduction" using comparison of observed to hypothesized data and considering an equal probability of the five categories. For paired comparisons of other categorical variables, we used McNemar Test for binomial distribution and McNemar-Bowker Test when more than two categories.
The null-hypothesis (suggesting no change) was rejected, and differences considered statistically significant if the p-value was less than 5%. The data analyses of the secondary outcome variables were considered exploratory, and multiple tests were carried out without multiplicity correction [31].
A sample size calculation to demonstrate significant pain reduction was not carried out as we expected that a sample of more than 600 patients would be sufficient to test clinically important, within-group differences when we compared to previous randomized, controlled trials on interventional treatment [21, 25, 26].

Results:

Characteristics of patients subjected to spinal interventions

Out of 863 patients referred to the clinic, 815 suffered from spinal pain. Almost three out of four (72%) reported lumbar pain and one out of four (26%) pain in the neck. A thorough examination by spine surgeons and diagnostic test blocks for a large number of subjecs indicated; 28% with spinal stenosis, 11% with discogenic pain, 10% with disc herniation and 29% with facet joint related pain. Among those who underwent spinal interventions, 190 patients received spinal diagnostic blocks only, while 625 patients were treated with a spinal intervention, and of these 246 with TECA, and 94 with RFA. Baseline characteristics of those who were received treatment are shown in Table 1. Average number of treatments for the whole sample was 2,6 (SD 1,1), but data for this follow up study is only limited to the first treatment.

Spinal interventions applied

One third of all interventions were medial branch blocks, 11 % intraarticular facet joint corticosteroid injection, and 12% RFA of medial branches of ramus dorsalis (Table 2). Patients with radicular pain or signs of painful radiculopathy received epidural steroid

injections, 30% transforaminally vs. 8% interlaminary or caudally. Most of the spinal injections (64%) targeted the lower lumbar levels L4-S1, 8% C2-3 and 16% C3 and C7 (Table 2). Pulsed radiofrequency stimulation of medial branches or the dorsal root ganglion, SI-joint corticosteroid injection, and discography were rarely performed.

The responses among the whole sample treated with spinal interventions

Of the 625 patients undergoing a therapeutic intervention, 483 returned the questionnaire for the T2 follow up at a median of 4,5 (interquartile interval: 3,3-5,6) months after treatment. A total of 70% of the patients experienced pain reduction, for 49% it was ≥50% and of these 9% were pain free (p<0,001), while 5% experienced worse pain, but no complications were reported (Figure 2). Highest VAS pain intensity decreased from 7,1 to 5,4 (mean difference: 1,6, 95% Confidence Interval of the difference (95%-CI): 1,4-1,9) (p<0,001). EQ-VAS increased from 48 to 58 (mean difference: 9,8, 95%- CI: 7,6-11,9) (p<0,001) and EQ-5D-5L Index from 0,489 to 0,628 (mean difference 0,140, 95%- CI: 0,123-0,157) (p<0,001) (Table 3a). We additionally found statistically significant improvement (p<0,001) for each of the EQ-5D-5L five dimensions (Figure 4).

There was also a significant reduction in the number who used analgesics (including opioids) and gabapentinoids/amitriptyline (p≤0,001). The proportion, not taking analgesics, increased from 16% to 30%, and for those taking strong opioids it decreased from 14% to 9% (Figure 3). We found no significant change in the proportions who received physiotherapy or other treatment nor in occupational status, although the proportion on sick leave decreased from 13% to 10%.

Characteristics of RFA treated patients

The 94 patients, treated with RFA, did not differ significantly from the whole sample in terms of age, gender, BMI or smoking, but the proportion reporting neck pain (48%) was higher and equaled the proportion reporting lumbar pain (47%). A total of 95% suffered from facet joint related pain, and as much as 45% of the RFAs were carried out between L4-S1, 34% at C2-3 and 16% between C3-C7.

The responses among RFA treated patients

Of those subjected to RFA 77% reported pain reduction after 4,5 months, for 56% it was ≥50% and of these 9% were pain free (p<0,001), and only 1% reported worse pain. Highest pain intensity decreased from 7,0 to 4,8 (mean difference: 2,3, 95%-CI: 1,6 -3,0) (p≤0,001).

EQ-VAS improved from 48 to 57 (mean difference: 9,2, 95%-CI: 4,8-13,6) (p=0,001), and EQ-5D-5L Index increased from 0,489 to 0,643 (mean difference: 0,154, 95%-CI: 0,117-0,191(p<0,001) (Figure 3b, Table 4). The proportions, not taking analgesics, increased from 7% to 23% and for those taking strong opioids it deceased from 15% to 10% (p<0,001). Among the patients who returend the questionnaire at 6- and 12-month follow up, the reduction in pain intensity, improvements in EQ-VAS, EQ-5D-5L Index, and proportion not taking analgesics and opioids remained at the same levels (Table 3b). After 6 months 69% reported pain reduction, for 51% it was ≥50% and 9% were pain free (p= 0,001). After 12 months the corresponding percentages were 70%, 59% and 11%, respectively (p= 0,017), and no patients reported worse pain (Figure 2 and Table 3b). We found no change in the proportions who received physiotherapy or other treatment nor in occupational status.

Characteristics of patients treated with TECA

The 246 patients, treated with TECA, did not differ significantly from the whole sample in terms of age, gender, BMI or smoking. A total of 47% had spinal stenosis, 27% disc herniation, but only 9% reported pain in the neck vs. 91 % had lumbar pain. Consequently, as much as 83% of the injections were carried out between L4-S1, and only 7% between C3-C7. See Table 2.

Responses among TECA treated patients

The responses among those undergoing TECA were generally less pronounced. A total of 58% experienced pain reduction after median 4,5 months, for 36% it was ≥50% and of these 5% were pain free (p<0,001) (Figure 2 and Table 3c) while 7% reported worse pain, but no complications were reported.

Highest pain intensity decreased from 7,1 to 6,2 (mean difference: 0,9, 95%-CI: 0,5- 1,4 (p:<0,001) while EQ-VAS improved from 45 to 52 mean difference: 7,5, 95%-CI: 3,6-11,36 (p:<0,001) and EQ-5D-5L Index from 0,456 to 0,571 (mean difference: 0,107, 95%-CI: 0,077-0,13) (p<0,001) (Table 3c). The proportion not taking analgesics, increased from 17% to 27% and for those taking strong opioids it decreased from 15% to 10%, but the changes did not reach statistical significance (Figure 3, Table 3c). We found no significant changes in the proportion who received physiotherapy or other treatment nor in occupational status.

Discussion

Interventional pain treatment is still controversial and outcome data from private pain units have been requested. In this context the physician at this pain clinic took the initiative to this outcome study. Existing evidence-base needs to be suplemented with reports from clinical practice. To our knowledge this is the first, European follow up study from a private pain clinic outside a hospital setting with such a large number of patients.

The patient sample

Those who were subjected to treatment, reported high pain intensity before treatment, the majority used analgesics (one third opioids) and experienced substantially reduced health related quality of life. The gender distribution, employment status, pain intensity, and health related quality of life correspond to samples from multidisciplinary pain clinics in both Sweden [32] and in Norway [33] which indicate that our sample is representative for patients referred to larger, multidisciplinary pain clinics. The large number of patients with spinal pain (94%) reflects the selective refferals from spine surgeon and specific competence at this pain clinic. The proportion with facet joint related pain (29%) may reflect that medial branch blocks were carried on a large proportion (34%) of the patients. More than 40% of the medial branch blocks targeted either lower lumbar or cervical facet joints, respectively. The high number of cervical blocks (11%) targeting TON (C2-3) are supported by findings in a prevalence study from Australia [20].

The treatment responses

We observed substantial responses in the sample treated with spinal intervention, and about half of the sample reported >50% pain reduction. There was also substantial reduction in pain intensity (24%), change in the proportions taking analgesics and opioids, and a noteworthy improvement in health related quality of life (21%). The pain reduction after RFA, interestingly, corresponds with results from comparable, randomized controlled trials [34, 35]. In a double blind, randomized sham-controlled study by van Kleef et al 60% reported >50% pain relief 3 months after RFA, vs. 47% after 6 and 12 months [34], and in a more recent double blind, randomized, controlled trial where Cohen et al compared efficacy after no, single or double test blocks, 64% of those who underwent double test blocks, reported >50% pain relief three months after RFA [35]. The success rate in our study indicates that the

procedures were performed in accordance to the international recommendations with a rather strict selection of patients for RFA.

The success rate after TECA (36% reported >50% pain reduction after 4,5 months) was inferior to the results from a recent, randomised, controlled trial. In this study by Manchikanti et al [24], including patient with chronic lumbar disc herniation, 57 % reported >50% pain relief two years after the treatment. In our study only 27% of those who received TECA had disc herniation and 47% spinal stenosis. In a systematic review and metaanalysis Chou et al found less effect in patients with radiculopathy and spinal stenosis [25], and this may explain the lower success rate in our study.

We did not observe any serious complication, but a minor proportion reported worse pain after a median of 4,5 months; 5% of the whole sample, and 1% among the RFA treated patients, but none after 1 year. This illustrates that any kind of intervention has a potential to increase pain, although some of the reports may also reflect spontaneous variation of the chronic pain condition.

We also observed a slight reduction in the proportion of patients on sick leave, but this change did not reach statistical significance. This may reflect that a large number of the patients were retired and high social benefits in Sweden compared with other countries. Thus, a more active work rehabilation is probably needed to get patients back to work [36, 37].

Strength and limitation

The large sample of patients of this study (N: 625) makes our findings interesting, and the categorical primary outome measure, pain reduction, provides a transparent description of the response variation. To assess treatment responses is indeed difficult due to the complexity of pain and hetrogeneity of the patients, and we therefore applied a large battery of outcome variables in accordance with the IMMPACT recommendations [27].

On the other hand, our study did not include a randomized, and sham-controlled design, and we can thus not define the efficacy of the interventions. A single-centre design with only one operator also limits the external validity of our findings, and the study suffers from a large drop-out rate which increases the risk of selection bias. However, high drop-out rates represent a problem in many clinical studies, even those based on registries at university pain clinics [33] (the drop-out rates of follow up data from the referred registry are not yet published).

Conclusion and implications

To conclude, this pragmatic, follow up study demonstrates that spinal interventions, performed by a well-trained clinical team in accordance with SIS international recommendations [23], can provide intermediate- to long-term improvement for a substantial number of chronic pain patients, even when applied in a clinic outside a hospital setting. These findings are also relevant if interventional treatments are to be integrated as part of a bio-psycho-sosial approach to improve the effect size. A dilemma is the limited effect duration of these procedures which over time may lead to a request for repeated interventions. Adequate information before the procedure, about duration and a preset limit of repetetions, are therefore mandatory to provide realistic expectations. Spinal intereventions always carry the risk of serious complications and a thorough montioring should therefore be implemented in interventional pain clinics.

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Informed consent: Informed consent was obtained from all participants individuals included in the study and have been scanned into the electronic medical record.

Ethical approval: The study was performed in accordance with the Declaration of Helsinki's statement of ethical principles for medical research involving human subjects and approved by the head of the Surgical Unit at Central Hospital Karlstad responsible for scientific and research projects. As this was considered as a quality-assurance study, approval by the local ethical committee was not required.

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Figure 1. Flow chart

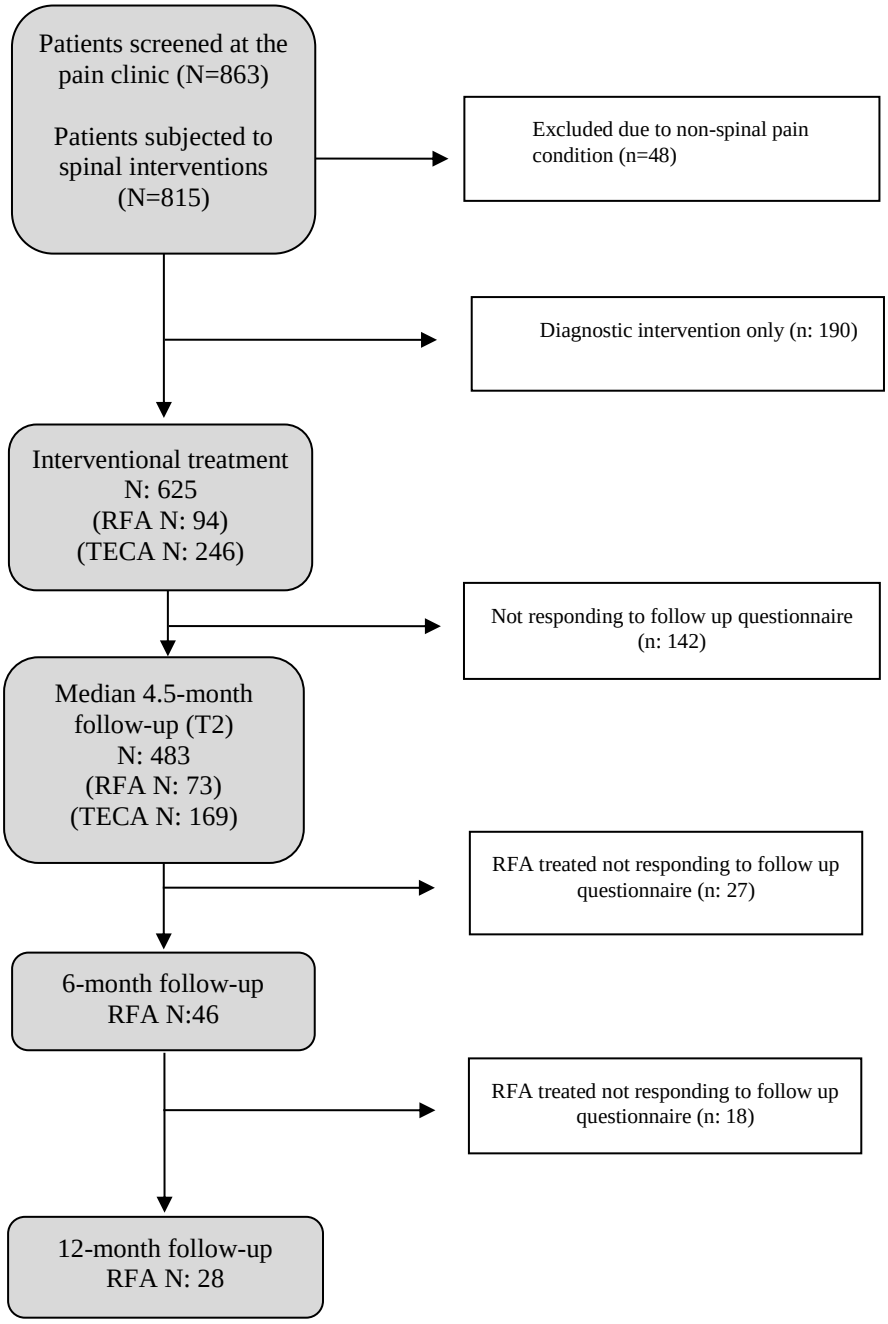
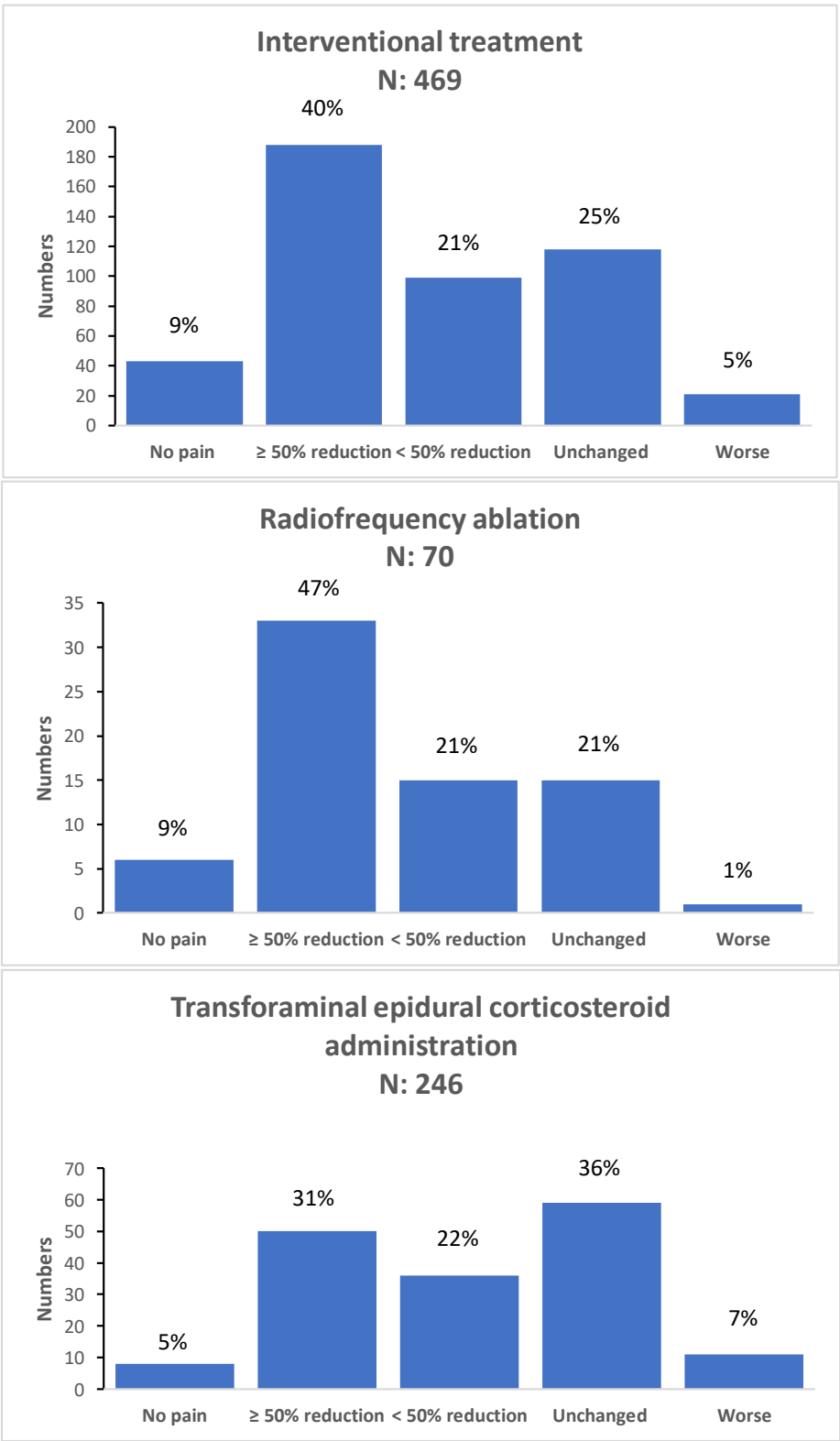
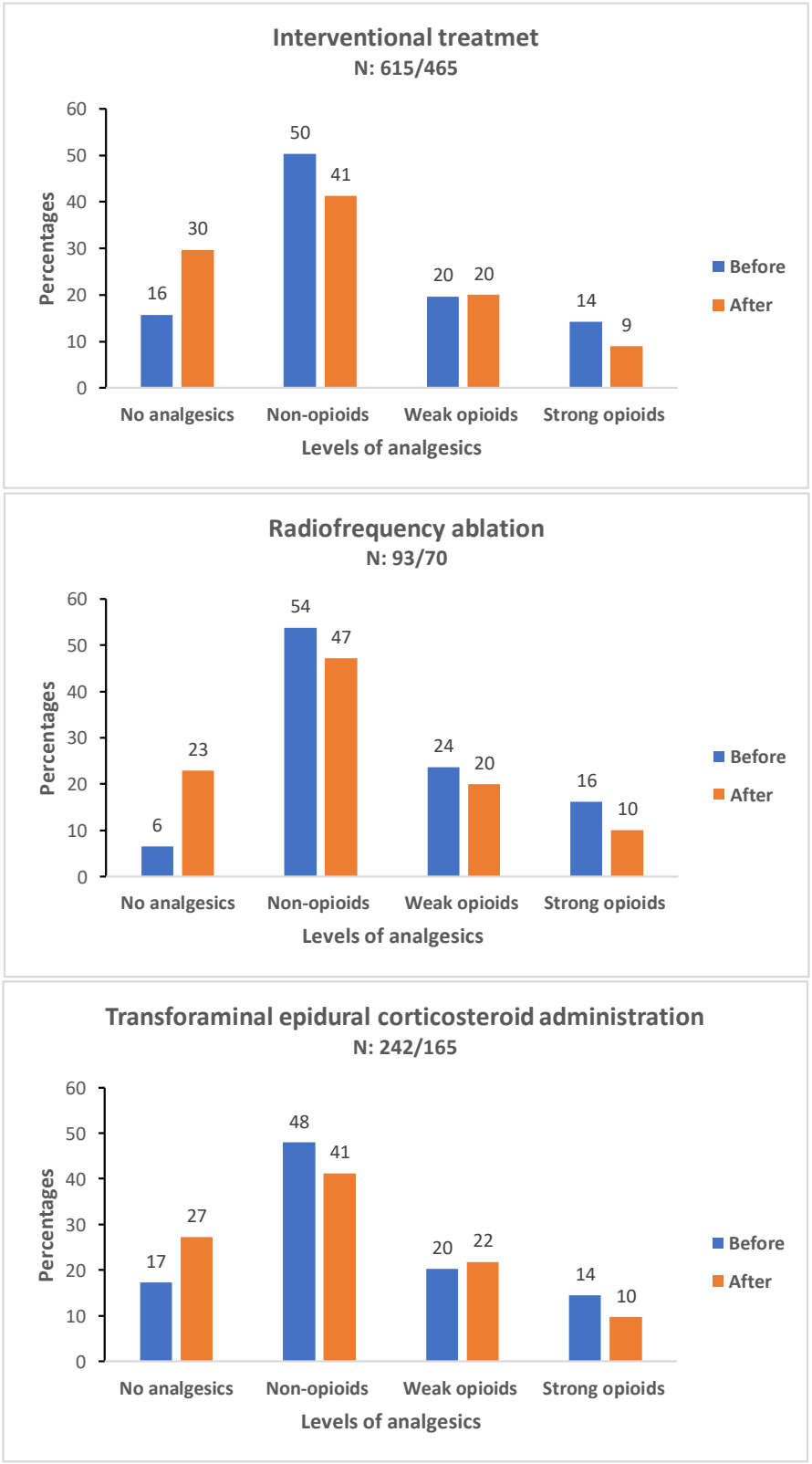


Figure 2. Pain reduction after treatment



Legend to Figure 2: Data are presented as numbers and percentages. At the 4.5 month follow up we found signifcant proportions reporting pain reduction after interventional pain treatment ($p<0.001$), after radiofrequency nerve ablation ($p<0.001$), and after transforaminal epidural corticosteroid administration ($p<0.001$), specifically. Statistical within-group comparisons were performed with One-Sample Chi-Square Test. Post hoc tests were not performed.

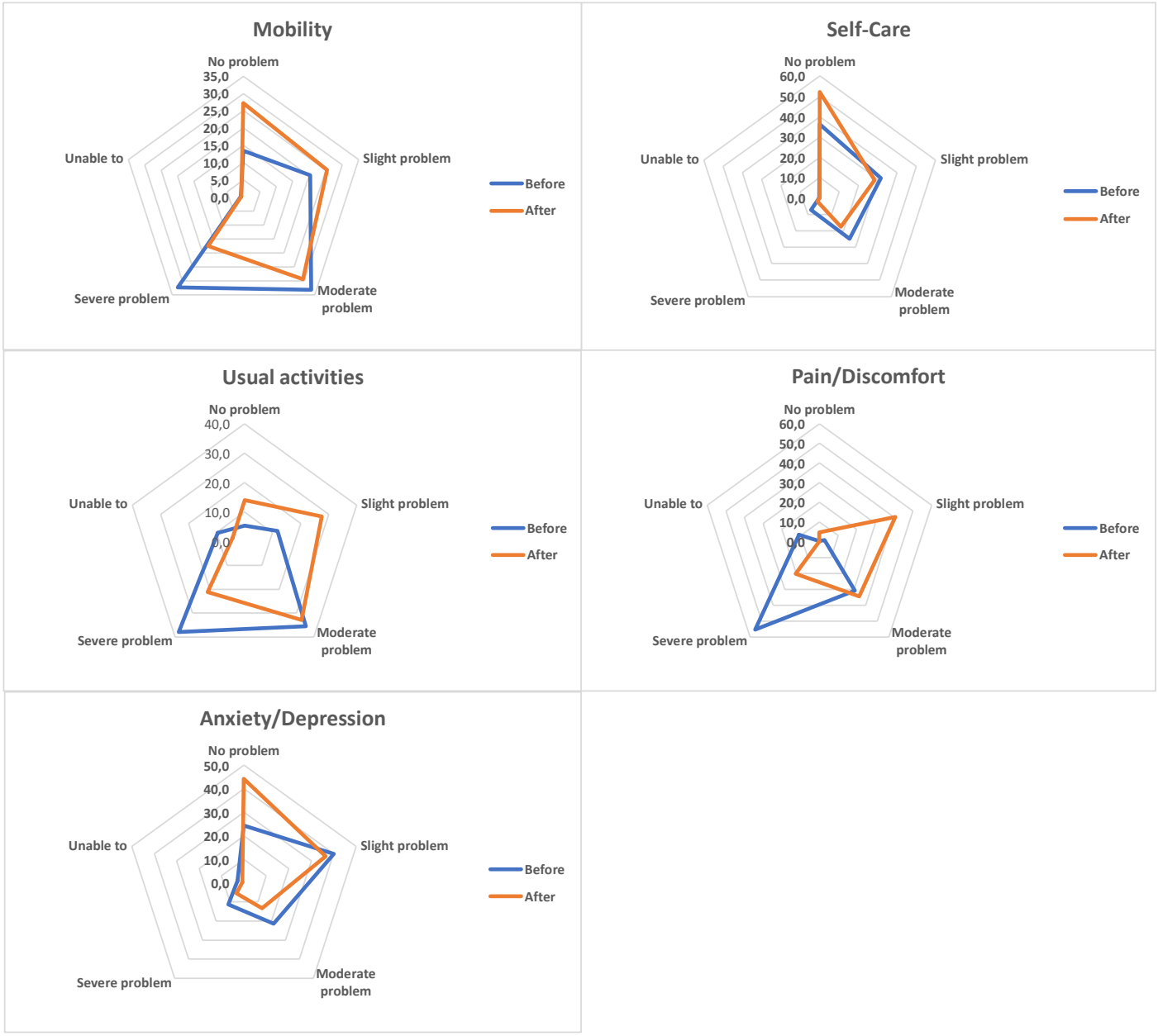
Figure 3
Proportions taking analgesics before and after treatment



Legend to Figure 3: At a median of 4.5-month follow up we found significant reductions in the proportion who used analgesics after interventional pain treatment, radiofrequency nerve ablation ($p<0.001$). After transforaminal corticosteroid administration the reduction did not reach statistical significane. Statistical within-group comparisons were performed with McNemar-Bowker Test. Post hoc tests were not performed.

Figure 4. Health-related quality of life before and after treatment

Five dimensions of EQ-5D-5L



Legend to Figure 4: The five dimensions of EuroQol5D5L are visualized in these spider/radar charts. Statistical within-group comparisons were performed with McNemar-Bowker Test. Post hoc tests were not performed. The numbers on the scale reflect proportions (percentages) of the patients. We observed significant improvement at a median of 4.5 months after treatment ($p<0.001$).