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Dorsal Root Ganglion Stimulation Outcomes

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AAPM 2022
38TH ANNUAL MEETING

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Disclosures

- Consultant: Texas Medical Board; various legal firms

- Speaker: American Society of Regional Anesthesia & Pain Medicine (ASRA), American Academy of Pain Medicine (AAPM), Spine Intervention Society (SIS), Texas Pain Society (TPS), American Academy of Physical Medicine & Rehabilitation (AAPM&R)

- Committee Membership:
  - SIS Guidelines Committee (Chair), Standards Division (Vice Chair), Annual Meeting Program Planning Committee, Online Learning Committee, Ultrasound Committee
  - AAPM&R Self Assessment Committee (Chair), Pain Management & Opioid Task Force, AMA Opioid Task Force Physician Delegate
  - TPS Education Committee
  - ASRA Annual Program Planning Committee

- Medical Directorship: Dannemiller, Inc.

- Question Writer & Oral Board Examiner: American Board of Physical Medicine & Rehabilitation

- There **IS** discussion of off-label products or drugs in this content.

INDICATION FOR USE

The Proclaim™ DRG Neurostimulation System is indicated for spinal column stimulation via epidural and intra-spinal lead access to the dorsal root ganglion as an aid in the management of moderate to severe chronic intractable* pain of the lower limbs in adult patients with Complex Regional Pain Syndrome (CRPS) types I and II.[1]**

KEY UPDATES

- Causalgia (CRPS II) further defined as **TRAUMATIC OR SURGICAL NERVE INJURY**
- Budapest criteria **NOT A DIAGNOSTIC REQUIREMENT** for CRPS II

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Objectives

- Interpret outcome data associated with DRG stimulation, will rely on recent systematic review
- Describe indications for DRG stimulation based upon strength of evidence
- Focus on mainly pain
- Disclosure: I am the lead author of the systematic review
- Will not spend much time on complications

The Effectiveness of Dorsal Root Ganglion Neurostimulation for the Treatment of Chronic Pelvic Pain and Chronic Neuropathic Pain of the Lower Extremity: A Comprehensive Review of the Published Data

Pain Medicine, 22(1), 2021, 49–59

Ameet Nagpal, MD, MS, MEd,* Nathan Clements, MD,† Belinda Duszynski,‡ and Brian Boies, MD*

- What we know:
  - Spinal cord stimulation (SCS) is an effective treatment for certain chronic pain conditions
  - SCS traditionally does not perform as well with focal pain

What Else We Know

- The DRG as a target for neuromodulation has good face validity
- DRG stimulation (DRGS) should provide coverage for focal pain conditions better than traditional SCS
- CRPS specifically is thought to have a part of its mechanism based upon increased excitability at the DRG

Pre-Existing Data

- NACC 2018: *Strong evidence* for DRGS in patients with CRPS I & II according to USPSTF and *Pain Physician* grading criteria

- Deer et al 2020 (just one month prior to our study): *Moderate Level II evidence* for DRGS chronic focal neuropathic pain and CRPS according to USPSTF criteria

- This systematic review was NOT designed to be a clinical guideline, but rather an assessment of the existing literature

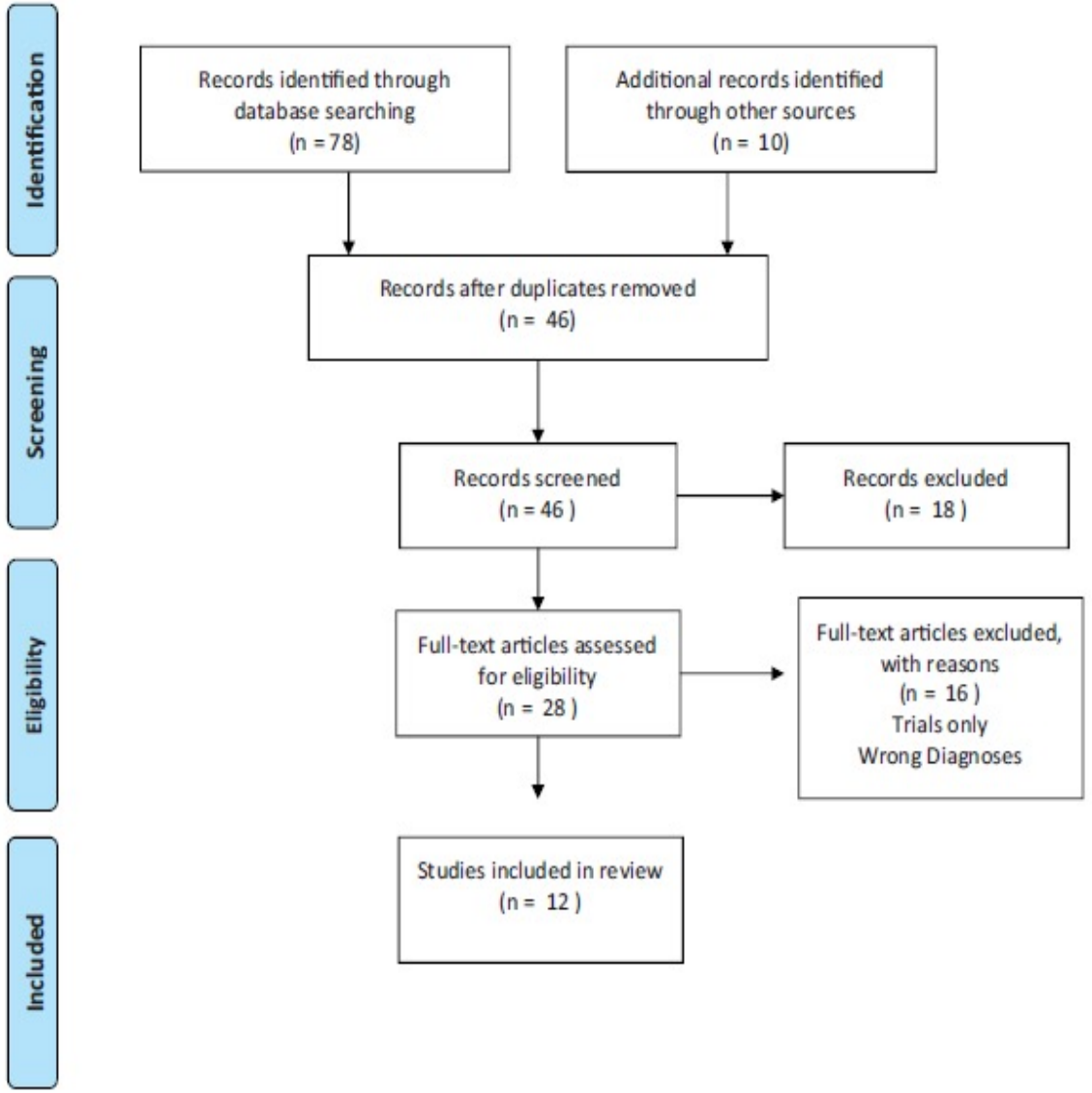
Our Study

- Population: Pelvic and/or lower extremity neuropathic pain
- Intervention: DRGS implant
- Comparison: Anything!
- Outcome: Reduction in pain by VAS or NRS with the usual secondary outcomes
- Studies: Anything! (*this is atypical)*

Included Articles

- Chapman & Kallewaard LTTE: Not a replicable search

- Response to LTTE:
- "Our original search was performed in Medline and EMBASE for the search terms "dorsal root ganglion AND (stimulation OR neurostimulation OR neuromodulation)", with a time period of the years 2000-2018, yielding 6,157 results. Duplicates were removed and additional filters were applied including the addition of human subjects, English language, and adults 19+ to address our inclusion criteria, which brought the results to 78 studies. During our review of the 78 studies, an additional 10 studies were identified for potential inclusion. This accounts for the 88 search results included on the first line of the PRISMA flow chart in Figure 1 of our manuscript."
    - Another search performed on 10/30/19 did not add any results



Methodology

- True intention-to-treat analysis was performed when possible, including "worst case analysis"

- Used GRADE criteria to evaluate the available data
  - https://bestpractice.bmj.com/info/us/toolkit/learn-ebm/what-is-grade/

Letter To the Editor

- "Our second, and most serious, concern is with the authors' apparent 're-analysis' of the ACCURATE RCT's data as what the authors term a "true ITT (intent to treat)" analysis....

Inferring from sample sizes, it appears that the authors included all randomized subjects in their analysis…

To make a simple analogy, this would be competing in the 40 yard dash, except starting 10 yards behind the others; anyone can see that's not fair play."

Table 1. GRADE certainty ratings

Certainty	What it means
Very low	The true effect is probably markedly different from the estimated effect
Low	The true effect might be markedly different from the estimated effect
Moderate	The authors believe that the true effect is probably close to the estimated effect
High	The authors have a lot of confidence that the true effect is similar to the estimated effect

Table 1. Included studies

	DRGN	Design	Inclusion Criteria	Follow- Up Interval	Outcome Measures
Falowski (2019) [16]	8	Case series	Diagnosis of peripheral neuropathy; primarily lower-extremity pain; pain intractable to conventional treatment; successful DRG trial with >50% relief	6 weeks postop	VAS, opioid consumption
Gravius (2019) [17]	12	Prospective cohort study	Chronic neuropathic pain	3 months	NRS, BDI, PSQI
Hunter (2019) [18]	4	Case series	Severe chronic pelvic pain; successful DRGS trial with L1 and S2 DRGs	Variable	VAS, function, opioid consumption, satisfaction
Huygen (2019) [19]	56	Prospective observational cohort	Adults; psychologically appropriate for implantation; lower body pain; chronic pain of 6 months' duration; intractable pain; VAS >60 mm	1 week and 1, 3, 6, and 12 months	VAS, quality of life, EQ-5D, mood disturbance
Morgalla (2019) [20]	12	Prospective cohort study	Age >18 years; chronic NP unilaterally affecting groin or lower limb; probably NP pain based on NP grading scale; refractory pain control with conservative measures	1 and 6 months	NRS, SF-36 (function)
Skaribas (2019) [21]	5	Case series	Age >18 years; chronic foot pain	1, 3, and 6 months	NRS, opioid consumption
Eldabe (2018) [22]	7	Case series	Implantation of DRG neurostimulator for phantom limb or residual limb pain	6 and 12 months	VAS
Deer (2017) [23]	76	Prospective RCT	Chronic intractable neuropathic pain with diagnosis of CRPS or causalgia; naïve to neurostimulation; tried and failed two pharmacological measures; free from psychological contraindications	3 and 12 months	VAS, BPI, satisfaction, POMS, total mood disturbance
Morgalla (2017) [24]	30	Case series	Age > 18 years; chronic neuropathic pain of the groin as a result of nerve injury; failure of conservative treatment; no indication for further surgical intervention	3 months and 1, 2, and 3 years	VAS, PDI, BPI, opioid usage, PCS
Van Buyten (2017) [25]	8	Case series	Age > 18 years; met Budapest Criteria for the diagnosis of CRPS	1 week, 1 month, 5 weeks, and 2, 3, and 6 months	VAS, BPI, EQ-5D3L, POMS
Zuidema (2014) [26]	3	Case series	Refractory groin pain patient who underwent DRG stimulatory placement	3 months	VAS
Liem (2013) [27]	32	Case series	Age >18 years; chronic intractable pain in the trunk, limbs, or sacral region for ≥6 months; baseline VAS of >60 mm; stable pain medication dosage	1 week and 1, 2, 3, and 6 months	VAS

Table 2. Studies presenting continuous data on pain relief

	DRGN	Follow-Up Interval	% Mean Improvement in Remaining Subjects at Each Time Point
Falowski (2019) [16]	8	6 weeks	80%
Gravius (2019) [17]	12	3 months	61%
Huygen (2019) [19]	56	3 months	62%
		6 months	52%
		12 months	49%
Morgalla (2019) [20]	12	6 months	69%
Eldabe (2018) [22]	7	6 months	66%
		12 months	64%
Deer (2017) [23]	76	3 months	81%
		6 months	75%
		9 months	77%
		12 months	69%
Morgalla (2017) [24]	30	3 months	63%
		1 year	56%
		2 years	50%
		3 years	44%
Van Buyten (2017) [25]	8	3 months	68%
		6 months	63%
		12 months	62%
Liem (2013) [26]	32	2 months	51%
		3 months	51%
		6 months	56%

Table 3. Studies presenting categorical data on pain relief

	DRGN	Follow-Up Interval	>50% Improvement (95% CI)	>75% Improvement (95% CI)	100% Improvement (95% CI)
Falowski (2019) [16]	8	6 weeks	88% (65–100%)	50% (15–85%)	25% (0–55%)
Gravius (2019) [17]	12	3 months	58% (30–86%)		
Hunter (2019) [18]	4	>3 months	100%	75% (33–100%)	25% (0–67%)
Huygen (2019) [19]	56	12 months	43% (30–56%)		
Skaribas (2019) [21]	5	6 months	100%	60% (17–100%)	0%
Eldabe (2018) [22]	7	3 months	43% (6–80%)	29% (0–62%)	14% (0–40%)
		6 months	43% (6–80%)	29% (0–62%)	14% (0–40%)
		12 months	29% (0–62%)	29% (0–62%)	14% (0–40%)
Deer (2017) [23]	76	3 months	81% (72–90%)		
		12 months	74% (64–84%)		
Morgalla (2017) [24]	30	3 months	83% (70–97%)		
		3 years	27% (11–42%)		
Van Buyten (2017) [25]	8	12 months	63% (29–96%)		
Zuidema (2014) [26]	3	2 months	100%	100%	33% (0–87%)
Liem (2013) [27]	32	2 months	41% (24–58%)		
		3 months	47% (30–64%)		
		6 months	41% (24–58%)		

Table 4. AEs and complications

	AEs/Complications
Falowski (2019) [16]	None reported.
Gravius (2019) [17]	Mild IPG pocket irritation (1), percutaneous placement restriction in a trial patient (1).
Hunter (2019) [18]	None reported.
Huygen (2019) [19]	7 SAEs related to procedure: implant site infection (1), implanted neurostimulator pocket infection (4), transient motor deficit (1), dural puncture (1).
Morgalla (2019) [20]	None reported.
Skaribas (2019) [21]	None reported.
Eldabe (2018) [22]	2 AEs related to procedure: failure to capture primary pain area and dural puncture.
Deer (2017) [23]	8 SAEs related to procedure; 2 infections required device explantation. Most frequent AEs reported were pain at incision site (7.9%), IPG pocket pain (13.2%), and overstimulation (3.9%).
Morgalla (2017) [24]	5 AEs related to procedure: lead breakage (2), infection (1), lead generator relocation (1), additional electrode (1).
Van Buyten (2017) [25]	3 AEs related to procedure: discomfort from stimulation, pain over IPG implant, intermittent calf cramping.
Zuidema (2014) [26]	None reported.
Liem (2013) [27]	70 events in 24 subjects included infection, cerebrospinal fluid hygroma, loss of paresthesia coverage, prolonged hospital stay, inflammation, temporary cessation of stimulation, and ataxia.

GRADE

- With an RCT [23], the GRADE rating of the evidence quality starts as "high," but it is downgraded to "moderate" because of the potential for the risk of bias due to author conflicts of interest and lack of blinding of physicians and subjects. It is further downgraded to **"low"** because of imprecision of results due to a lack of a clinically meaningful difference at the lower end of the confidence interval for the difference between proportions of the two arms of the ACCURATE trial.

- This holds true for both the 3-month and 12-month data in the ACCURATE trial, despite nonsignificant results when the data were analyzed from an ITT perspective and a modified ITT perspective with worst-case assumptions for comparing groups.

Response to Letter to the Editor

- "the recommendation can be made for DRGS to be classified as a first-line neuromodulatory therapeutic treatment option for CRPS or the diagnosis that the ACCURATE authors define a "lower limb pain associated with a diagnosis of CRPS or causalgia" for the first 3 months. The data demonstrate results comparable to traditional SCS—and therefore first-line neuromodulation therapy—at 12 months, as well."

- "It is worth noting that if even just one more RCT was published with similar findings to the ACCURATE study, the GRADE criteria score for the use of DRGS in the treatment of CRPS and/or causalgia would be elevated to 'high' on the basis of the reproducibility of the findings."

GRADE Criteria

- On the basis of the GRADE criteria, the rating for the use of DRGS for the treatment of pain related to chronic pelvic pain, chronic neuropathic groin pain, phantom limb pain, chronic neuropathic pain of the trunk and/or limbs, or diabetic neuropathy is **very low.** This in large part is due to the fact that these diagnoses have been studied only in retrospective or prospective case series and cohort studies. There are no reasons to upgrade or downgrade these ratings of evidence quality.

Limitations

- Conflicts of interest
- Length of follow-up is limited
- Many studies had the same authors – might there have been the same cohorts of patients in different studies?
- Lack of RCTs for any diagnosis other than CRPS/"causalgia"
- Unclear reproducibility

Since Then…

Prospective Observational Cohort Study on Dorsal Root Ganglion Stimulation in Chronic Postsurgical Pain: Results of Patient-Reported Outcomes at Two Years

Ahead of Print

Agnes G. C. L. Wensing, MSc[1]; Jennifer S. Breel, MSc[1]; Markus W. Hollmann, MD, PhD[1]; Frank Wille, MD[1,2]

Neuromodulation 2021; ■: 1–8

Table 2. Pain Ratings (Measured With VAS) and Changes Over Time.

Pain area	VAS pain ratings (mm), Mean ± SD			Change (mm), Mean ± SEM (95% CI)		
	Baseline	1 y	2 y	Δ 1 y vs baseline	Δ 2 y vs baseline	Δ 1 y vs 2 y
Primary pain area	76 ± 12	38 ± 25	46 ± 23	−38 ± 7* (−51 to −25)	−29 ± 6* (−42 to −17)	9 ± 7 (−5 to 22)
Overall pain	72 ± 14	47 ± 26	46 ± 19	−25 ± 6† (−37 to −13)	−26 ± 6† (−37 to −14)	−1 ± 6 (−12 to 13)

*Primary area of pain: $p < 0.001$ compared to baseline.
†Overall pain: $p < 0.001$ compared to baseline.

Table 3. Patient-Reported Outcome Measures (PROM) (EQ-5D-3L [index]; BPI [Pain Severity and Pain Interference]) and Change Over Time.

PROM	Mean ± SD			Change over time Mean ± SEM (95% CI)		
	Baseline	1 y	2 y	Δ 1 y vs baseline	Δ 2 y vs baseline	Δ 1 y vs 2 y
EQ-5D-3L	0.48 ± 0.16	0.70 ± 0.20	0.68 ± 0.18	0.22 ± 0.05* (11–33)	0.21 ± 0.05† (10–31)	−0.02 ± 0.06 (−0.12 to 0.10)
Pain severity	6.9 ± 1.3	4.4 ± 2.1	4.5 ± 1.8	−2.5 ± 0.5‡ (−3.5 to −1.5)	−2.3 ± 0.5‡ (−3.3 to −1.3)	0.1 ± 0.5 (−0.8 to 1.2)
Pain interference	4.6 ± 1.6	3.0 ± 1.9	3.5 ± 1.9	−1.6 ± 0.5§ (−2.7 to −0.5)	−1.1 ± 0.5 (−2.2 to 0.1)	0.5 ± 0.6 (−0.6 to 1.6)

*EQ-5D-3L: $p < 0.001$ compared to baseline.
†EQ-5D-3L: $p = 0.001$ compared to baseline.
‡Pain severity: $p < 0.001$ compared to baseline.
§Pain interference: $p = 0.014$ compared to baseline.

Categorical Data

At one year, 53% of patients achieved ≥50% reduction in the primary area of pain and 77% of patients achieved at least 30% reduction. At two years, 37% of patients achieved ≥50% reduction in the primary area of pain, and 58% of patients achieved at least 30% reduction.

Table 4. Patient Satisfaction With Pain Reduction and PGIC Since DRG Stimulation.

Satisfaction and PGIC	1 y (*N* = 22) *n* (%)	2 y (*N* = 21)* *n* (%)
Satisfaction with pain reduction provided by stimulation†		
High satisfaction (8–10)	11 (50)	12 (57)
Medium satisfaction (4–7)	8 (36)	8 (38)
Low satisfaction (0–3)	3 (14)	1 (5)
Satisfaction with therapy in general†		
High satisfaction (8–10)	16 (73)	15 (71)
Medium satisfaction (4–7)	6 (27)	5 (24)
Low satisfaction (0–3)	0	1 (5)
PGIC‡		
Improvement of pain	21 (95)	20 (95)
No change	1 (5)	0
Worsening of pain	0	1 (5)

*Data value for one patient was missing.
†We classified the responses before analysis: 8 to 10 as high satisfaction, 4 to 7 as medium satisfaction, and 0 to 3 as low satisfaction.
‡The marks "much better," "better," and "slightly better" have been classified as improvement of pain; "somewhat worse," "worse," and "much worse" have been classified as worsening of pain.

Effect of Patient Characteristics on Clinical Outcomes More Than 12 Months Following Dorsal Root Ganglion Stimulation Implantation: A Retrospective Review

Jonathan M. Hagedorn, MD[1]; Ian McArdle, MD[2]; Ryan S. D'Souza, MD[1]; Abhishek Yadav, MD[3]; Alyson M. Engle, MD[4]; Timothy R. Deer, MD[4]

Neuromodulation 2021; 24: 695–699

Responder status based on 80% pain relief threshold

Variable	Responder (*N* = 8)	Nonresponder (*N* = 49)	β-Coefficient or odds ratio† (95% CI)	*p* value
History of prior opioid use	1 (12.5)	33 (67.3)	OR 0.06 (0.01–0.53)	0.011*

Responder status based on 50% pain relief threshold

	Responder (N = 14)	Nonresponder (N = 43)	β-Coefficient or odds ratio† (95% CI)	*p* value
History of prior opioid use	4 (28.6)	30 (69.8)	OR 0.16 (0.04–0.59)	0.006*

CONCLUSION

This single-center retrospective study found patients prescribed chronic opioids at the time of DRG stimulator implantation had a higher likelihood of less than 50% pain relief and 80% pain relief at one month, three months, and 12 months follow-up visits. There was no correlation with 50% or 80% pain relief response at 12 months and age, gender, BMI, or history of psychiatric disorder, tobacco use, hormone use, neuropathic pain medication use, number of DRG leads placed, OME, or pre-VAS score. This study highlights the importance of chronic opioid weaning and, ideally, discontinuation before DRG stimulator implantation to improve the likelihood of long-term successful outcome. Future directions should include prospective studies, consideration of functional outcomes, and response predictors based on specific DRG stimulation indications.

Dorsal root ganglion stimulation for patients with refractory pain due to anterior cutaneous nerve entrapment syndrome: A case series

Pain Practice. 2022;22:288–294.

Patient	Baseline	Trial	3 months	6 months	9 months	12 months	15 months	18 months	24 months	30 months
1	8.5	5.5	4	4.5	2	5	2	2	7	3.5
2	9	1	1	0	0	unk.	1	8	4	4
3	8.5	3.5	2	1	8	3	unk.	2	unk.	2
4	7	5	3							
5	8	1.5	2							
6	8	2	unk.	2	unk.	2	unk.	4	unk.	2
7	9	6	5							
8	7	5	4	2						
9	8	4	**8.5**							

Note: Underlined numbers show NRS before lead revision. Bold numbers show NRS at the end of treatment. Missing data are marked as unk.

TABLE 3 Medication quantification score (MQS III) from baseline (= before dorsal root ganglion stimulation) until last follow-up ranging from 3 to 30 months

Patient	Baseline	Trial	3 months	6 months	9 months	12 months	15 months	18 months	24 months
1	15.9	11.2	11.2	11.2	11.2	3.8	3.8	3.8	5.7
2	13.6	0	0	1.1	0	0	8.4	6.8	11.1
3	0	0	0	0	0	0	0	0	
4	0	0	0						
5	21.7	12	0						
6	0	0	0	0	0	0	0		
7	39.6	39.6	29.6	15	15	15	15		
8	0	0	0	0					
9	/	/	/						

Neuromodulation for Chronic Pelvic Pain: A Single-Institution Experience With a Collaborative Team

NEUROSURGERY VOLUME 88 | NUMBER 4 | APRIL 2021

- 11 subjects
- 4 had SCS only
- 3 had DRG only
- 2 had SCS + DRG combo

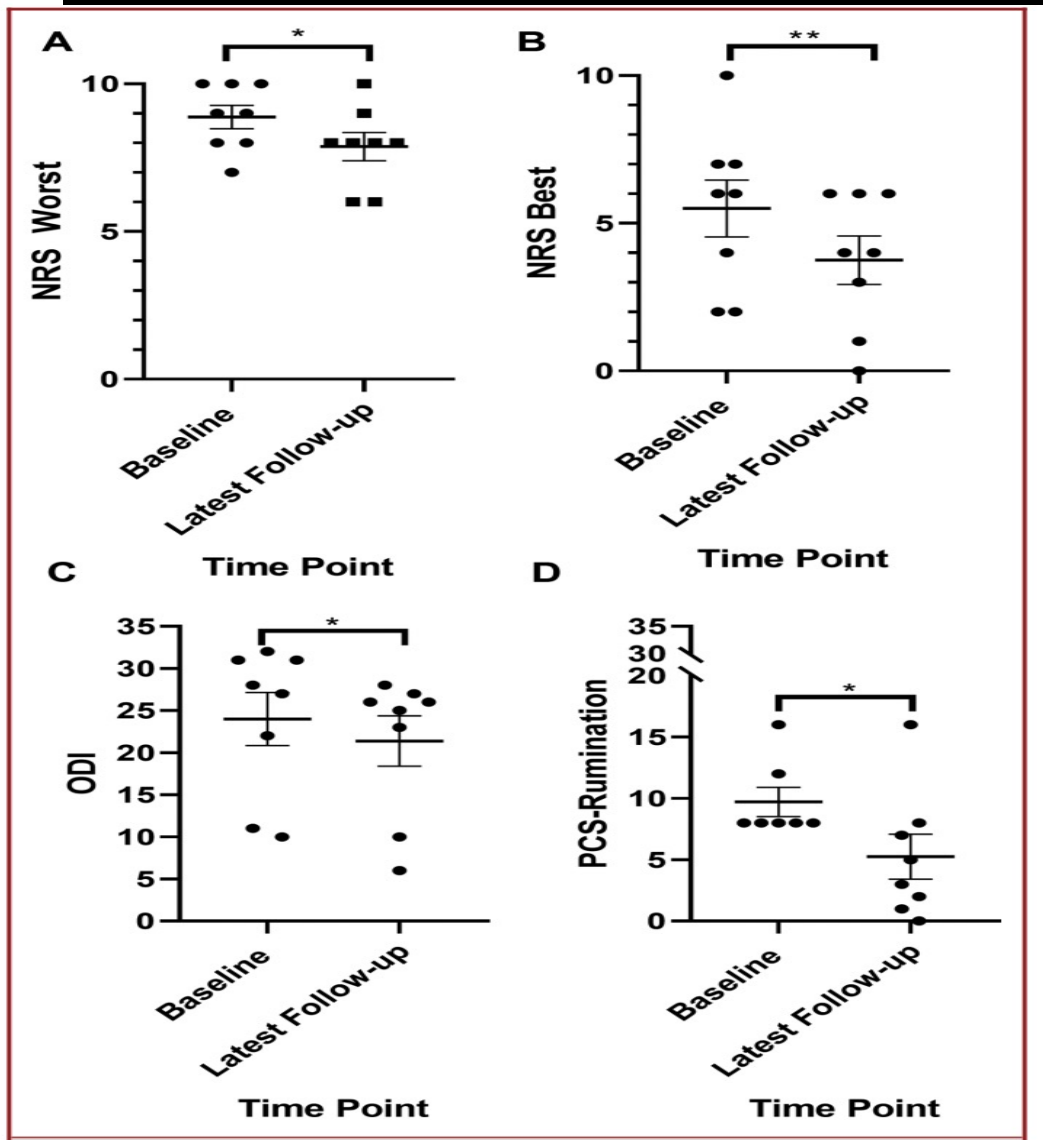


FIGURE 2. A-D, *Pain outcome measure assessment from baseline to latest follow-up.* A, *There was statistically significant improvement in NRS score at patients' worst rated pain (P = .007).* B, *There was statistically significant improvement in NRS score at patients' best during the week (P = .025).* C, *There was significant improvement in ODI (P = .014).* D, *There was significant improvement in PCS-rumination (P = .043). [*P < .05]*

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Final Thoughts

- Lack of evidence isn't evidence of lack

- The plural of anecdote isn't evidence

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Questions?

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