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HIGH-FREQUENCY SPINAL CORD STIMULATION AS RESCUE THERAPY FOR CHRONIC PAIN PATIENTS WITH FAILURE OF CONVENTIONAL SPINAL CORD STIMULATION

Running head: 10-kHz high-frequency spinal cord stimulation after failure of conventional stimulation

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Significance:

This study shows that high-frequency stimulation may be useful in patients with failure of conventional tonic stimulation for chronic pain, both in the trial phase and in previously implanted subjects. The novelty of this study lies in the use of implanted epidural electrodes, which avoids the need for further surgery. The results in terms of pain control and functional recovery are satisfactory. In addition, variables such as male gender and high body mass index could be predictors of therapy failure.

ABSTRACT

BACKGROUND

This study aims to evaluate the efficacy of 10-kHz high-frequency (HF10) devices as a rescue treatment in patients with failure of conventional spinal cord stimulation (SCS) therapy for chronic pain without the need to change the spinal hardware.

METHODS

In this real-world prospective study, patients with neuropathic pain treated with conventional tonic SCS in whom the therapy had failed, either during the trial phase or after a period of optimal

functioning, were recruited throughout 2 years for HF10-SCS therapy. Data on analgesia, functionality, analgesics use and treatment safety were collected 12 months after treatment.

RESULTS

Eleven of the 18 (61%) patients included in the study were successfully rescued with HF10-SCS. Of them, 5 out of 12 (45%) were in the trial phase and 6 out of 6 (100%) had previously functioning implants. A significant improvement in low-back and limb pain was obtained ($p = .003$ and $p = .0001$, respectively). Treatment success was significantly associated with gender ($p = .037$), weight ($p = .014$), body mass index (BMI) ($p = .007$) and time of rescue ($p = .015$). A linear regression test confirmed a significant association between treatment failure and BMI and gender ($p = .004$).

CONCLUSIONS

Our results suggest that analgesic rescue with HF10-SCS is an effective therapeutic option for non-responders to conventional SCS**,** although obesity might be a limiting factor for treatment success. Nevertheless, more comprehensive studies are needed to corroborate our findings.

SIGNIFICANCE

This study shows that high-frequency stimulation may be useful in patients with failure of conventional tonic stimulation for chronic pain, both in the trial phase and in previously implanted subjects. The novelty of this study lies in the use of the implanted epidural electrodes, which avoids the need for further surgery. The results in terms of pain control and recovery of functionality are satisfactory. In addition, variables such as male gender and high body mass index could be predictors of therapy failure.

Key words:

Spinal cord stimulation, high frequency stimulation, HF10, neuromodulation, failed back surgery syndrome, complex regional pain syndrome, neuropathic pain.

BACKGROUND

The management of chronic pain remains one of the main challenges for physicians in their regular clinical practice. Lumbar spinal pain represents one of the most common chronic pain syndromes, affecting more than 500 million people worldwide, and is the leading cause of years lived with disability (GBD, 2016). A significant number of patients suffer from persistent low-back/radicular pain secondary to the so-called Failed Back Surgery Syndrome (FBSS). Another less prevalent but still challenging cause of persistent chronic pain is Complex Regional Pain Syndrome (CRPS). In both entities, spinal cord stimulation (SCS) is a therapeutic option when other pain management strategies have failed, traditionally at low frequency with associated paraesthesia. In general, it is accepted that the success rate of SCS follows a 50/50 rule, i.e. 50% pain relief is achieved in approximately 50% of patients (Kapural et al., 2017).

In recent years, new SCS therapies without paraesthesia have been developed and are increasingly used worldwide because they seem to increase success rates according to published studies. One of these novel modalities is 10-kHz high-frequency (HF10) SCS, which achieved success rates between 73% and 83% (Kapural et al., 2015; Russo et al., 2016). In addition, other studies showed a similar safety profile and adverse effects compared to conventional SCS (cSCS) (Al-Kaisy et al., 2014). The mechanism of action of this new therapy remains unknown. Proposed mechanisms include depolarization blockade, desynchronization of neuronal signals, membrane integration, and glial-neuronal interaction. However, recent preclinical models which mimic this therapy suggest that its analgesic effect might differ substantially from that of cSCS due to the fact that, in HF10-SCS, a lack of robust activation in the dorsal columns, weak inhibition of wide dynamic range (WDR) neurons in the deep dorsal horn and slow onset of pain inhibition have been observed (Chakravarthy et al, 2018).

The challenge remains for those patients without significant pain improvement despite treatment with cSCS. In fact, half of the patients treated with this therapy do not achieve satisfactory pain control, and long-term studies suggest that treatment effectiveness decreases over the years in patients who initially respond well (Provenzano et al., 2017). Moreover, the paraesthesia required in low-frequency SCS is uncomfortable for some patients, especially if they experience overstimulation during postural

changes (Levy, 2014). Because the mechanism of action of cSCS seems to differ from HF10-SCS, the latter could be an adequate option in these cases.

The aim of this study is to evaluate HF10-SCS as a rescue analgesic therapy for patients unsuccessfully treated with cSCS –i.e., those who did not experience significant improvements in the trial phase and initial responders who reported loss of treatment effectiveness over time-, without changing the spinal implant. The study was conducted in a hospital-based referral centre for neuromodulation therapy.

METHODS

We conducted a real-world prospective study between October 2016 and October 2018. Following our institution's protocol and with the approval of the Multidisciplinary Committee on Implants, we recruited a group of patients who were candidates for traditional tonic SCS and in whom this therapy had been unsuccessful, either due to failure during the trial phase or to decreased effectiveness following a period of optimal functioning. These patients were offered a "rescue" therapy with an HF10-SCS system without changing the previously implanted spinal electrodes. After a trial phase, the new generator was implanted. Of note, the cSCS had already been discontinued at the time of the HF10-SCS trial.

Procedure and patient selection

In our institution, spinal neuromodulation is mainly used to treat patients suffering from CRPS or FBSS in whom other pharmacological and invasive treatments (e.g., nerve blocks, neuroaxial blocks) administered according to current clinical evidence have failed. Accordingly, following the failure of all conservative pain measures, eligibility of patients for cSCS therapy was discussed in the Multidisciplinary Committee on Implants, formed by Neurosurgeons, Anaesthesiologists, Rehabilitators and Neurologists. Consultation with a psychologist to evaluate the patient's mental health prior to implantation was mandatory.

The technique used for neuromodulation in these patients consisted of percutaneous implantation of 2 epidural electrodes (Medtronic®) under local anesthesia. Intraoperative mapping of the pain area was performed until it was covered in the most satisfactory way possible. After implantation, the device was connected to electrodes and set up with a minimum of 3 different programs which were gradually changed over a trial period of at least 2 weeks, including conventional and high-density tonic stimulation (1,000 Hz frequency, 90-120 μs pulse width). After the trial phase of SCS, patients who

did not achieve at least 50% improvement relative to their previous condition (combination of analgesic improvement and quality of life) were considered to have experienced failure of tonic SCS therapy. The patients who successfully passed the trial phase underwent implantation of the generator, and follow-up was carried out through consultations with specialists.

The patients were recruited from two different sources, namely candidates for tonic SCS considered as "failure" during the trial phase, and patients already carrying a system with conventional low-frequency SCS which ceased to be effective during follow-up. In the former group, a "rescue" was offered to all patients who were implanted during the time of study and did not meet the implantation criteria after the trial phase. The latter group was recruited from a cohort of patients who had already undergone implantation with two epidural electrodes, carried the tonic low-frequency SCS system for at least two years with optimal functioning (improvement of previous condition by 50% or more) and referred at least one of the following issues during follow-up: loss of analgesic efficacy below 50%, development of very uncomfortable paraesthesia, or changes in the coverage of paraesthesia that could not be remedied by reprogramming. The only exclusion criterion was that the system carried by the patient was so outdated that it did not allow for connection to the adapter.

Patients selected for HF10-SCS treatment were invited to join the study after providing informed consent. Once they accepted, an external high-frequency generator (SENZA, Nevro®) was connected to the lead extensions, applied to epidural leads, using an adapter provided by the manufacturer. At least 3 different programs were again tested over a period of at least 2 weeks. Following the recommendations of the manufacturer, a first program was set with a cathode in the electrode closest to the anatomical target (T9-T10), and the other two programs slightly above and below that location. If improvement of the previous condition by 50% or more was achieved, we proceeded to implant the definitive generator in the operating room, without removing or modifying the epidural leads. To do so, an adapter was connected in the pocket where the generator was implanted. If there was no significant improvement, the entire system was removed.

Data collection and follow-up

Information on demographic and personal variables (e.g. body mass index, BMI) was collected. Pain intensity in the lumbar area and in the affected limb was measured by the visual analogue scale (VAS). Quality of life was assessed at baseline using the Functional Rating Index (FRI). Preoperative analgesic consumption was also analysed. During the trial phase, follow-up was conducted via telephone interview as well as during the visits for wound healing assessment by the neurosurgical nursery staff, where the VAS was again assessed. The "rescue" therapy was considered successful when two criteria - pain improvement based on low-back VAS, limb VAS, or both, and perceived

improvement in the lower back, the limb, or both (assessed through direct questioning) - were both greater than or equal to 50%.

Once the system was implanted, the patient had periodic follow-up visits in the clinic. At 12 months, the VAS and FRI were again assessed. In addition, variations in analgesic consumption -with particular focus on the use of opioids- and the Patient Global Impression of Improvement (PGI-I) score were recorded. For VAS calculations, data were transformed into numerical pain rating scale (NPRS) values and the degree of improvement was classified into three categories, as shown in Fig. 1. For the PGI-I score, ratings of 1 or 2 points were considered to be successful.

Fig. 1 approximately here

Statistical analysis

After completing 2 years of recruitment and 1 year of follow-up, frequency statistics (mean, median, percentage and standard deviation) for the different variables were analysed. Overall improvement after treatment was evaluated using the Student's t-test. In addition, an ANOVA analysis was performed to determine the effect of other variables on the success of the HF10-SCS therapy, and a multivariate linear regression test was used to confirm the significant relationships found (no correction for multiple comparisons was applied, considering the small sample size and the nature of this study). Values of $p < .05$ were considered statistically significant. The SPSS Statistics 26.0 software was used for statistical analysis.

RESULTS

A total of 18 patients were included in the study, 12 during the trial phase and 6 during follow-up. No patients met the exclusion criteria and none refused therapy. There were no losses to follow-up during the study period.

Subject demographics and baseline characteristics

First, frequency statistics were calculated for the variables of the group. The demographic characteristics of these patients are shown in Table 1.

Of the 6 patients rescued during follow-up, 5 were carrying Medtronic® devices and 1 was carrying an SJM® device. The reasons for requiring rescue therapy included decrease in pain improvement

below 50% (4 patients), development of very uncomfortable paraesthesia (1 patient), and change in the coverage area of pain that could not be remedied by reprogramming (1 patient).

Table 1 approximately here

Treatment effectiveness and pain control

Eleven patients (61% of the total) were rescued with a high-frequency system, 5 during the trial phase (45% of all patients in the trial phase group) and 6 during follow-up (100% of all patients in the follow-up group) (Fig. 2). The results of each patient during the trial phase, according to established criteria, is shown in Table 2.

Fig. 2 approximately here

Table 2 approximately here

The average improvement in terms of the NPRS and PGI-I score at 12 months of follow-up is shown in Fig. 3. For low-back pain, the average NPRS improvement was 1.84 points (CI 95%: 0.71 - 2.96) and, for limb pain, it reached 3.55 points (CI 95%: 2.14 - 4.96), both statistically significant ($p = .003$ and $p = .0001$, respectively). Fig. 4 shows the distribution of the NPRS and PGI-I score improvement categories stratified by anatomical location (i.e., low-back or limb) at 12 months of follow-up. The relative improvement at 12 months was 52% (± 28%) in the low-back area and 56% (± 20%) in the affected limb. With respect to the PGI-I score, "very much improvement" or "much improvement" was reported by 54% of patients for low-back pain and by 72% of patients for limb pain.

Fig. 3 approximately here

Fig. 4 approximately here

Improvement of quality of life

Regarding quality of life, the average improvement in terms of the FRI was 28.4% (95% CI: 21.19 - 35.62), which was statistically significant ($p = .0001$). The distribution of the FRI categories is shown in Fig. 5. The most significant improvement was obtained in Sleeping and Walking, while there were no major differences in other categories such as Personal Care, Work or Recreation. Analysis of opioid use at 12 months after treatment showed significant dose reduction in 5 patients (45%), opioid discontinuation in 4 patients (36%), no significant variations despite improvement in 5 patients (45%), and need to increase the dose of opioids in 1 case (9%). All patients reported a high degree of

satisfaction with the treatment and no complications were recorded preoperatively or at follow-up. Tolerability was also excellent, with no significant adverse effects reported.

Fig. 5 approximately here

Statistical analysis

An ANOVA analysis was performed to determine whether there were statistically significant differences between the study groups based on treatment success. All measured variables were evaluated, and significant values were observed in four of them: gender ($p = .037$), weight ($p = .014$), BMI ($p = .007$) and time of rescue ($p = .015$), as shown in Table 3. Finally, a stepwise multivariate linear regression analysis was performed to determine the best fitting model, taking into account these significant variables. Two significant models were obtained, one which included BMI ($R^2 = 0.33$, $p = .007$) and another one which included BMI and Gender ($R^2 = 0.45$, $p = .004$). Therefore, weight and time of rescue were excluded from the models. The estimated coefficient for the former model was 7.6% (CI 95%: 2.4% - 12.9%). For the model with BMI and Gender, the estimated coefficients were 6.7% (CI 95%: 1.8% - 11.5%) and -42.7 % (CI 95%: -85% - -0.4%), respectively. These results indicate that increased BMI and male gender have a linear effect on failure of HF10-SCS therapy. Given the low sample size, the normality of the residuals was verified (Fig. 6) and corroborated by the result of the Durbin Watson test (1.77).

Table 3 approximately here

Fig. 6 approximately here

DISCUSSION

We conducted a single-centre study based on real-world clinical practice and with hardly any exclusion criteria. To our knowledge, very few studies to date have assessed the effectiveness of high-frequency stimulation after failure of a cSCS implant without replacing the spinal electrodes. This is very beneficial for patients since complications associated with a new procedure are avoided. The study analysed the effectiveness of HF10-SCS in patients who lack further treatment options. In addition, it was complemented with statistical analyses to determine potential prognostic predictors, which revealed a linear relationship between therapy failure and two of the variables analysed: male gender and increased BMI.

Our study showed a 61% success rate of the HF10-SCS therapy. Our response rate is similar to other published studies that were conducted in conditions of daily clinical practice. For example, an

Australian study by Russo et al. (2016) reported an overall improvement of 73%, but in the subgroup of patients unsuccessfully treated with an SCS system (30% of the sample) the improvement rate was lower (63%). A multicentre study conducted by Stauss et al. (2019) in which 1660 patients treated with HF10-SCS were evaluated, similar results were observed. They also analysed a subgroup of patients with failure of SCS implants (24%) and reported an improvement rate close to 74%. It must be taken into account that our study included both *de novo* patients and carriers of dysfunctional SCS implants. In the latter group, 100% of patients improved after conversion to the 10-kHz system. Conversely, in the trial phase group, the success rate dropped to 45%. We hypothesize that this could be due to the fact that the placement of the electrodes in the spine (both for patients in the trial phase and for those previously implanted) was performed with intraoperative paraesthesia mapping to locate the area of pain (classically with both electrodes in parallel and with their tips between T7 and T8) instead of the recommended anatomical placement without paraesthesia mapping, in which the electrodes are placed at different levels trying to cover from T8 to T11 (Van buyten et al., 2013).

Over the past few years, several studies have been conducted on patients already treated with SCS to assess which type of stimulation they preferred. The recent WHISPER study (North et al., 2020) evaluated the effectiveness of SCS at 1.2 kHz in 140 patients. All of them were carriers of cSCS (i.e., at low frequency and with paraesthesia) and were offered to change to a system without paraesthesia if they were interested. Although no significant differences between the options were found, the authors noted that if the patient could choose between them, the percentage of improvement increased to 74%. Similarly, other studies compared the effectiveness of different sub-paraesthesia SCS therapies versus conventional paraesthesia SCS therapy in previously implanted patients, but using the same system and changing its settings (Courtney et al., 2015). In a recent crossover trial (Duse et al., 2019), the authors compared a multiwave system versus conventional stimulation and found no significant differences between burst SCS with high frequency at 1 kHz and conventional SCS therapy, concluding that patients prefer systems with multiple options.

One of the advantages of our study is that we used a previously implanted epidural electrode system, which had not been useful at low frequency since the moment it was implanted or over time, without the need to replace it with a new device. This is not the case with other published studies. For example, Gill et al. (2019) analysed a subgroup of patients with previous implants in which a high frequency system at 10 kHz was used, obtaining a good response in 71.4% of the cases, but requiring removal and replacement of the device with a new system. In another study (Haider et al., 2018), patients with failure of 10-kHz therapy were converted to a multiwave platform, achieving improvement in 63% of the cases, but several interventions were required as well.

On the other hand, the statistical analysis of the data needs to be interpreted with caution because of the limited sample size, which may lead to significant biases. Nevertheless, the analysis revealed that male gender and high BMI were predictors of poor response to therapy in our study. Other authors have also indicated that these variables could be related to poor treatment outcomes, particularly high BMI. In fact, the well-known relationship between pain and obesity has motivated research on the role of BMI in this setting. It should be noted that a large number of patients who end up with an SCS system suffer from FBSS, which is exacerbated by obesity. However, only a few studies have addressed this particular issue (Marola et al. 2017 (Mekhail et al., 2019). Finally, the relationship between male gender and lower success rate of HF10-SCS therapy lacks a clear explanation and should not be overstated considering the potential bias related to the small sample size, although there are some studies with a higher sample size that show similar trends (Bir et al., 2016).

Our study has several significant limitations that should be taken into account. The first and most relevant one is the low sample size, which compromises the statistical analysis as aforementioned. Therefore, despite the prospective nature of the study and the fact that there were no losses to follow-up, our results should be interpreted with caution. Another drawback of this study concerns the heterogeneity of the sample, which limits its reproducibility and conclusions despite being inherent in any real-world study where patients with different pain aetiologies, device manufacturers and rescue times (i.e., during the trial phase or follow-up) are grouped together. However, it should be emphasized that real-world observational studies have several advantages, since they reflect the selection of patients and results in conditions of daily clinical practice. Finally, we believe that the duration of follow-up was another major limitation, despite being similar to other studies published in the literature. In our case, a one-year follow-up might be less than desirable, especially for patients who were already carriers of an SCS system that failed over the years. However, given the aim of the study and the loose inclusion criteria established, we believe that our results provide relevant information on the value of HF10-SCS as a rescue therapy for patients with failure of cSCS.

CONCLUSIONS

The novel sub-paraesthesia SCS systems represent a step further in the treatment of patients with chronic pain and failure of cSCS therapy. Our results showed that 10-kHz high-frequency neuromodulation effectively improved the analgesic effect in a significant number of patients, confirming its utility as a complementary therapy in this population, with the advantage of not requiring replacement of the spinal electrodes. We also found that obesity might limit the success of

this therapy. However, given the limitations of our study, especially regarding its low sample size, more comprehensive studies are needed to corroborate these results.

AUTHOR CONTRIBUTIONS

Doctors Cordero, Sánchez and Gálvez designed and conducted the study. Doctors Ortiz, Jover and Olivares performed most of the surgeries. All authors performed the follow-up visits. Doctors Cordero and Sánchez performed the data analysis and prepared the manuscript. Doctors Cordero and Olivares performed the statistical analysis. All authors reviewed and approved the final version of this manuscript.

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FIGURE LEGENDS

Table 1: Frequencies of demographic and personal variables. m: mean; σ: standard deviation; n: sample number. BMI: body mass index; FBSS: failed-back surgery syndrome; CRPS: complex regional pain syndrome.

Table 2: Results of the trial phase with HF10-SCS in each of the patients according to the established criteria. Those indicators above 50% in both the NPRS and perceived improvement through direct questioning, which defined the success of the trial phase, are highlighted in bold. NPRS: numeric pain rating scale; m: mean.

Table 3: ANOVA test for mean differences between successfully versus unsuccessfully treated groups, considering the demographic variables. HF10-SCS: 10-kHz high-frequency spinal cord stimulation; BMI: body mass index; FBSS: failed-back surgery syndrome; CRPS: complex regional pain syndrome. m: mean; σ: standard deviation; f: absolute frequency. %: within-group frequency.

Figure 1: Assessment of the degree of improvement based on the Numeric Pain Rating Scale (NPRS).

Figure 2: Classification of patients in whom "rescue" with HF10-SCS was attempted, based on whether the therapy succeeded or failed, and whether the "rescue" was performed during a failed trial phase or during the follow-up of a previously implanted device with at least 2 years of adequate functioning that ceased to be effective.

Figure 3: Average values of the Numeric Pain Rating Scale (NPRS) at baseline and at 12-months of follow-up. Average value of the PGI-I in the final interview, one year after implantation.

Figure 4: Number of patients classified according to the improvement categories of the NPRS (left) and PGI-I (right) and stratified by anatomical location, i.e. low-back or limb.

Figure 5: Average values for each category of the Functional Rating Index (FRI) at baseline and 12 months after high-frequency treatment.

Figure 6: Stepwise multivariate linear regression test including the variables BMI, gender, weight and rescue time (left). The last two are excluded from the models as they do not reach statistical significance. Analysis of the residual plot (right) confirms the assumption of the normality of the residuals.

Variable	m (σ)	n (%)
Age (years)	49.38 (9.1)	
Gender		
- Male		13 (72.2)
- Female		5 (27.8)
Weight (Kg)	77.44 (13.6)	
Height (cm)	168.83 (7.1)	
BMI	27.07 (4.0)	
- Normal weight (<25)		5 (27.8)
- Overweight (25-29.9)		8 (44.4)
- Obesity (≥30)		5 (27.8)
Occupation		
- With weight lifting		14 (77.8)
- Without weight lifting		4 (22.2)
Diagnosis		
- FBSS		15 (83.3)
- CRPS		3 (16.7)
Preoperative use of opioids		
- Yes		13 (72.2)
- No		5 (27.8)
Preoperative percutaneous techniques		
- Yes		13 (72.2)
- No		5 (27.8)
Duration of pain (y)	5.11 (2.4)	
Time of rescue		
- Trial phase		12 (66.7)
- Follow-up		6 (33.3)

Table 1

	Patient	Low-back NPRS Pre – Post Trial (improvement, %)	Limb NPRS Pre – Post trial (improvement, %)	Perceived improvement in Lower back/Limb (%)
Success of HF10-SCS Trial	1	7-3 (**57.14**)	8-5 (37.5)	**70**/**50**
	2	8-6 (25)	9-3 (**66.66**)	30/**70**
	4	8-4 (**50**)	9-4 (**55.55**)	**80**/30
	7	7-1 (**85.71**)	8-5 (37.5)	**100**/30
	8	8-4 (**50**)	9,5-2 (**78.94**)	**70**/**85**
	10	9-4 (**55.55**)	7-5 (28.57)	**50**/40
	11	8-5 (37.5)	9-3 (**66.66**)	40/**50**
	13	6-3 (**50**)	8-4 (**50**)	**70**/**50**
	14	7-5 (28.57)	9-3 (**66.66**)	40/**60**
	15	6-5 (16.66)	10-2 (**80**)	30/**70**
	18	5-5 (0)	10-2 (**80**)	0/**90**
	m (%)	7.16-4.06 (41.46)	8.77-3.45 (58.91)	52.7/56.8
Failure of HF10-SCS Trial	3	7-6.5 (7.14)	10-9 (10)	10/20
	5	7-5 (28.57)	8-6 (25)	25/25
	6	9-8 (11.11)	10-9 (10)	30/30
	9	8-7 (12.5)	8-8 (0)	20/15
	12	7-7 (0)	9-9 (0)	10/0
	16	0-0 (0)	7-6 (14.28)	0/20
	17	9-9 (0)	9-7 (22.22)	0/25
	m (%)	6.71-6.07 (8.47)	8.71-7.71 (11.64)	13.5/19.2

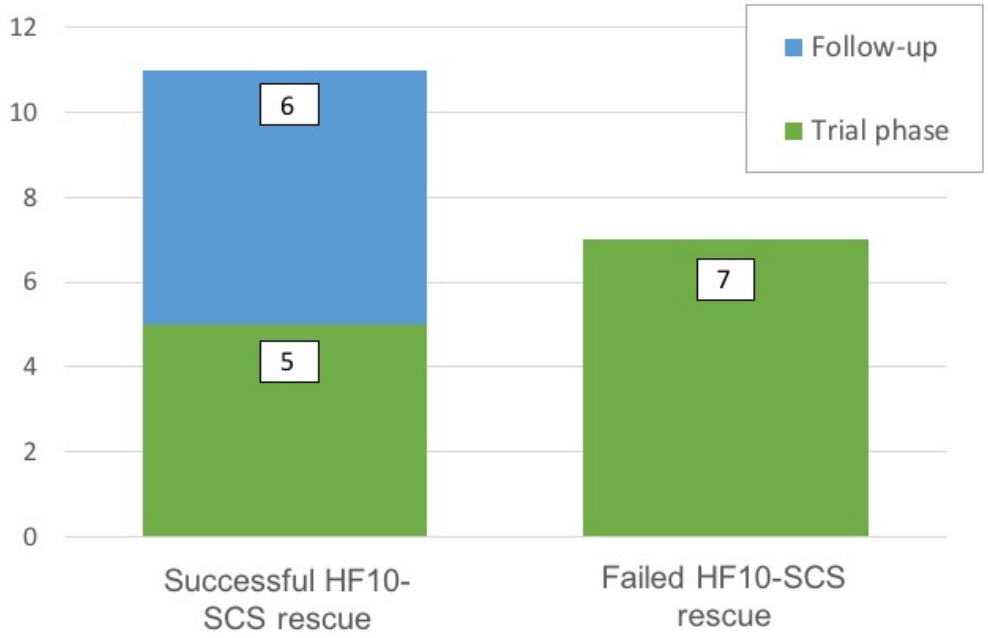
Table 2

Variable	Success of HF10-SCS (n = 11)	Failure of HF10-SCS (n = 7)	p
	m (σ) / f (%)	m (σ) / f (%)	
Age	49.09 (8.23)	49.85 (11.15)	.920
Gender			.037
Male	6 (54.5)	7 (100)	
Female	5 (45.5)	0 (0)	
Weight	71.45 (11.86)	86.85 (11.14)	.014
Height	168.16 (8.89)	169.85 (3.57)	.644
BMI	25.17 (3.33)	30.05 (3.19)	.007
Occupation			.546
Weight-lifting	8 (72.7)	6 (85.7)	
No weight-lifting	3 (27.3)	1 (14.3)	
Diagnosis			.217
FBSS	10 (90.9)	5 (71.4)	
CRPS	1 (9.1)	2 (28.6)	
Preoperative use of opioids			.956
Yes	8 (72.7)	5 (71.4)	
No	3 (27.3)	2 (28.6)	
Preoperative percutaneous techniques			.337
Yes	7 (63.6)	6 (85.7)	
No	4 (36.4)	1 (14.3)	
Duration of pain (y)	5.27 (2.49)	4.85 (2.54)	.737
Preoperative low-back NPRS	8.18 (1.16)	7.80 (1.09)	.547
Preoperative limb NPRS	8.81 (0.98)	8.71 (1.11)	.838
Preoperative FRI	78.18 (9.08)	76.42 (10.29)	.709
Time of rescue	1.54 (0.54)	1 (0)	.015

Table 3

Improvement category	Improvement in NPRS
Great improvement	5 or more points
Moderate improvement	2 to 5 points
No improvement	Less than 2 points

ejp_1776_f1.jpg



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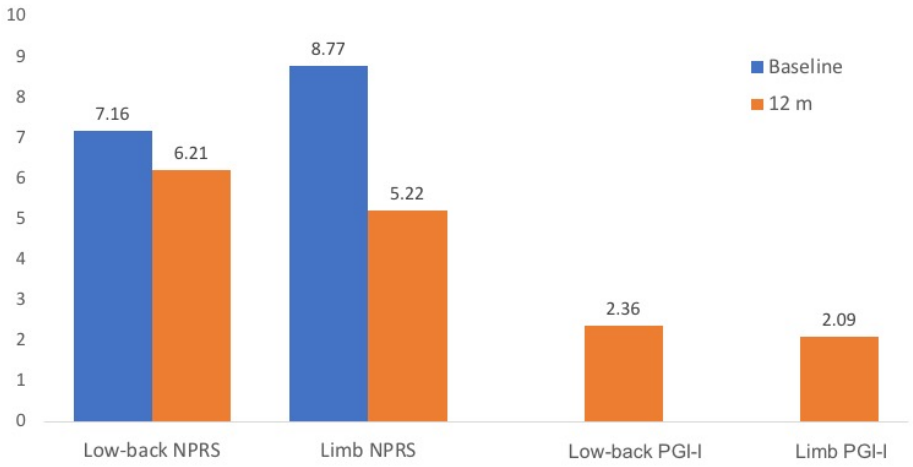

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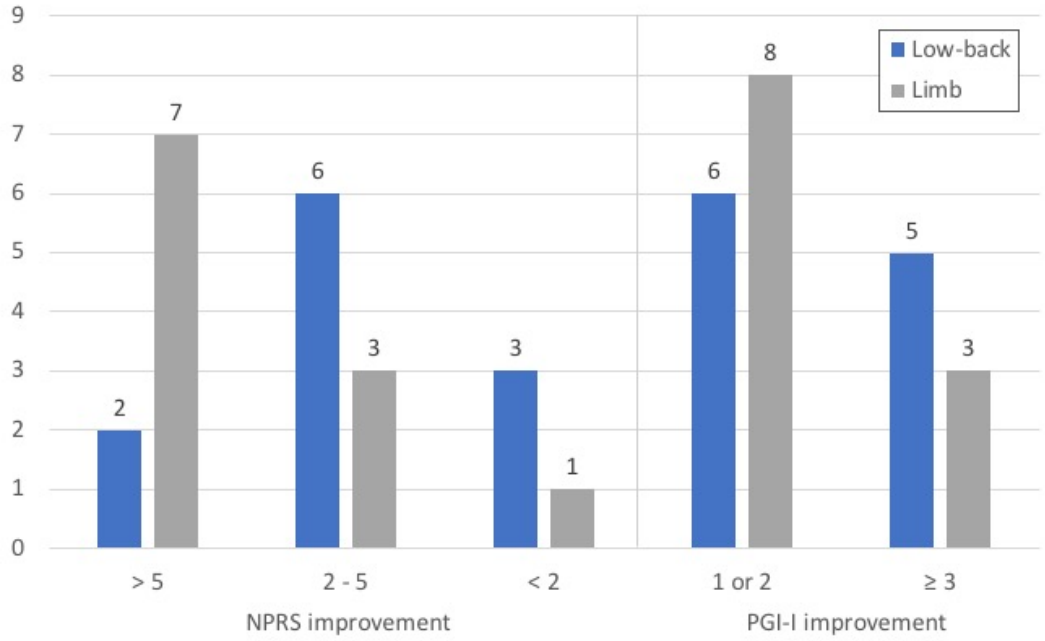

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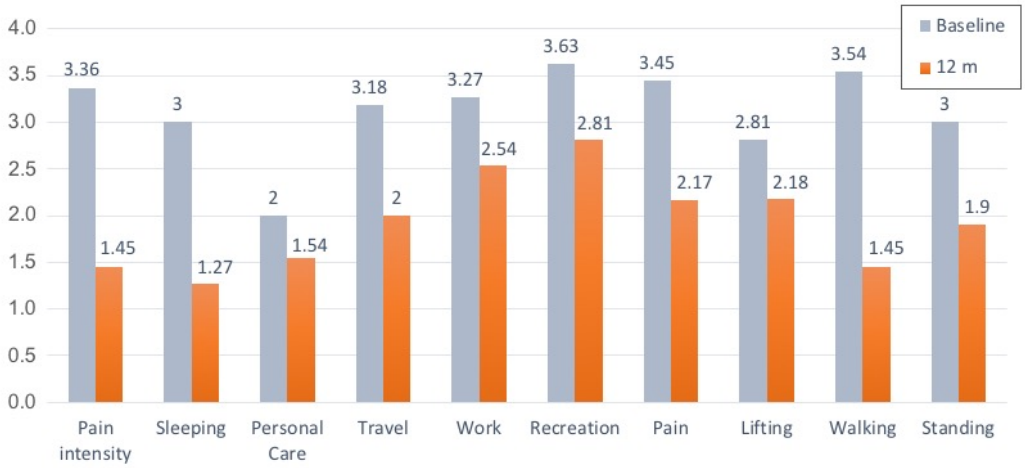

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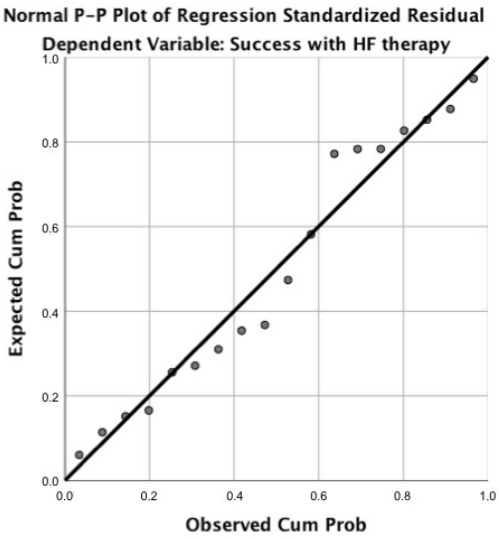
Model	Variable	p
Model 1	BMI	.007
Model 2	BMI	.010
	Gender	.048
Model	Variables excluded	p
Model 1	Gender	.048
	Weight	.827
	Rescue moment	.299
Model 2	Weight	.077
	Rescue moment	.596



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