Retrospective Study

Association between the Risk of Relapse and the Type of Surgical Procedure for Herpes Zoster-related Pain

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Background: Pulsed radiofrequency (PRF) on the dorsal root ganglion (DRG) is a common minimally invasive surgery for herpes zoster (HZ)-related pain, including acute zoster pain and postherpetic neuralgia (PHN); however, some patients still have no obvious pain relief, a high recurrence rate, and short-term recurrence. Radiofrequency thermocoagulation (RF-TC) has a higher temperature; however, it is still unknown whether the degree of complete damage will affect the recurrence rate and if there is any difference compared with the effect of PRF.

Objectives: This study mainly aimed to explore whether there was a difference in the recurrence rate following CT-guided PRF and RF-TC for HZ-related pain. This is also a preliminary exploration of RF-TC for treatment of HZ-related pain.

Study Design: A retrospective cohort study.

Setting: The study was carried out in the Affiliated Hospital of Jiaxing University in Jiaxing, China.

Methods: We included a total of 134 patients who underwent CT-guided PRF or RF-TC for HZ-related pain in the pain department. Medical records related to relapse, numerical rating scale scores (NRSs), Pittsburgh sleep quality index (PSQI), adverse events, and satisfaction were reviewed. The Kaplan-Meier analysis was used to estimate the cumulative survival rates of the surgical procedures. After controlling for related confounders, the relationship of surgical procedure and recurrence rate was analyzed by interval-censored multivariable Cox regression. A time-independent receiver operating characteristic (ROC) curve analysis confirmed the signature's predictive capacity. A nomogram was used to predict postoperative recurrence. Multiple imputations was used to deal with the randomly missing data. Repeated-measures analysis of variance (ANOVA) was applied to analyze NRSs and PSQI at each time interval, and multiple comparisons were made.

Results: In 134 patients with HZ-related pain, the ratio of patients receiving PRF to those receiving RF-TC was 1:1. Interval-censored multivariable Cox regression analysis demonstrated that lesion space (1-2% / ref: adjusted hazard ratio (HR), 2.075; 95% confidence intervals (CI), 1.002-4.210; > 2% / ref: adjusted HR, 3.406; 95% CI, 1.670 - 6.950), pain grade (adjusted HR, 2.249; 95% CI, 1.221 - 4.143) and surgical procedure (adjusted HR, 2.392; 95% CI, 1.308 - 4.375) were significantly associated with a higher risk of the primary outcome. There were 20 cases of recurrence in RF-TC group, while there were 30 cases in PRF group. The short-term (within 3 months) postoperative recurrence rate was 14.93% in the RF-TC group and 37.31% in the PRF group. The differences in PSQI and NRSs between 2 groups were also statistically significant.

Limitations: The study uses a small sample size from a single center. The model built is not validated internally or externally. The conclusions of randomized controlled trials will be more convincing. Subgroup analysis of the disease course was not performed.

Conclusion: In the treatment of HZ-related pain, the use of PRF is significantly associated with a high short-term recurrence rate. However, compared with RF-TC, PRF results in milder numbness and less intraoperative pain. RF-TC may be a feasible procedure if patients can accept pain relief at the cost of long periods of numbness, whether RF-TC has the value of clinical promotion still needs to be further explored.

Key words: Herpes zoster, postherpetic neuralgia, pulsed radiofrequency, thermocoagulation

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Herpes zoster (HZ) is a common skin disease in humans and at least 15% of people worldwide will have HZ at least once in their lifetime (1). It is therefore concerning that the incidence of HZ may still be on the rise, with a cohort study showing that the incidence of HZ has increased more than fourfold in the past 60 years (2). The immune system weakens with age, so HZ is more common in older people and those with immunosuppression (3). Postherpetic neuralgia (PHN) is one of the most common complications of HZ (4). A study has shown that the risk of PHN increases with age, with nearly 30% of HZ patients ≥ 65 years old are diagnosed with PHN (5). The high incidence and severe symptoms of PHN require physicians to begin treatment measures as soon as possible. Drugs are an important means of early treatment. The European Federation of Neurological Societies has proposed tricyclic antidepressants, pregabalin, and gabapentin as first-line clinical drugs. In recent years, some scholars have also proposed that mirogabalin and Botox injections can also be effectively used in the treatment of PHN (6,7).

However, based on the uncertainty of the efficacy and individual differences, it may not be appropriate for most patients to rely on drug therapy alone. Temporary spinal cord stimulation (tSCS) may be effective (8), but the financial situation of the patient needs to be taken into account. Pulsed radiofrequency (PRF) is a neuromodulation technique that generates a pulsed current to form a high-voltage environment around the target nerve, thus affecting the activity of ion channels and inhibiting the excitatory afferent of C fibers to interfere with pain transmission. KooHyun Kim et al (9), pointed out that the pain scores of all patients decreased significantly after PRF. In fact, the scope of clinical application of PRF is gradually expanding and it has a broad application prospect in the field of pain (10,11). When the nerve fiber and myelin sheath are destroyed, conduction of the action potential of the nerve fiber is blocked, which significantly reduces the afferent pain and achieves analgesia (12). At present, radiofrequency thermocoagulation (RF-TC) has been proven to be effective in the treatment of neuralgia (13,14) Selective nerve root destruction based on RF-TC for the treatment of intractable neuralgia has been recognized (15).

Based on previous observations, the short-term recurrence rate after PRF is high, and patients often require additional treatments. RF-TC destroys the dorsal root ganglion (DRG) more thoroughly, but there is still a lack of sufficient evidence for its therapeutic effect in HZ-related pain. In addition, no research has pointed out the impact of different surgical procedures on the recurrence rate. In this study, patients who underwent RF-TC on the DRG were included in the treatment of HZ-related pain for the first time. The main purpose of this study was to explore the effects of surgical procedures on the recurrence rate using a Cox proportional hazards model. In addition, we systematically analyzed secondary endpoints, such as numeric rating scores (NRS), Pittsburgh sleep quality index (PSQI), adverse events, and satisfaction.

Methods

Patients

This study was reviewed by the Medical Ethics Committee of the Affiliated Hospital of Jiaxing University. A total of 162 patients who underwent CT-guided PRF or RF-TC on the DRG for HZ-related pain in the Affiliated Hospital of Jiaxing University from June 2017 to May 2020 were included.

Inclusion and Exclusion

The inclusion criteria were as follows: 1) clinically diagnosed with acute zoster pain or PHN; 2) disease course of at least a month; 3) lesion located in the innervated area of the spinal nerve; 4) full understanding of the risks of surgeries and agreement to undergo CT-guided PRF or RF-TC; 5) effect of conservative treatments, such as drugs were not good, which significantly affected daily work and sleep; and 6) NRS ≥ 4 before the operation.

The exclusion criteria were as follows: 1) trigeminal nerve (TN) radiofrequency for craniofacial HZ; 2) limb HZ pain; 3) history of multiple radiofrequencies on the DRG; and 4) refusal to provide treatment information and clinical data for scientific research.

The flowchart for patients' inclusion and exclusion is shown in Fig. 1.

Surgical Procedure

PRF: The patients were placed in a prone position with soft pillows under their chest (or abdomen). Each patient inhaled oxygen through a nasal duct and vital signs, such as, blood pressure, heart rate, and oxygen saturation were continuously monitored. The body surface locations of the target nerve and puncture points were located according to their lesions and involved nerve segments. Then, taking the puncture point as the

center, the skin was disinfected with iodophor, and local infiltration anesthesia was carried out with 1% lidocaine. Under the guidance of CT, the 22G puncture needle was inserted into the upper 1/3 of the corresponding intervertebral foramen (Fig. 2). Then, the needle core was pulled out, and the matching electrode was inserted along the cannula. The tip position was adjusted repeatedly until the resistance of the surrounding tissue at the tip of the test electrode was between 250 - 550 Ω. After confirming that there was no blood or gas, sensory and exercise tests were performed. The parameters of the sensory test were set at a voltage of 0.5 V and a frequency of 100 Hz; if any discomfort, such as, soreness, numbness, or tingling, was induced, the sensory test was considered positive. Low-frequency current was used in the exercise test and the parameters were set at a voltage of 0.5 V and a frequency of 2 Hz. If fibrillation and pulsation of the trunk muscle fibers in the corresponding segments appeared, the exercise test was considered positive. When it was confirmed that the needle was near the target nerve, about 1 mL of 2% of lidocaine was used for local anesthesia and then the radiofrequency procedure was performed. The temperature, time, pulse width, and frequency were set at 42°C, 300 seconds, 20 msec and 2 Hz, respectively (10), and the voltage was set up at 45V. After the end of the PRF and removal of the needle, an aseptic patch was applied. All patients were observed in the treatment room for 20 minutes to ensure that vital signs were stable and then sent back to the ward when no obvious discomfort was present. If the postoperative NRSs was < 4, then the operation was considered to be successful.

RF-TC: The process of puncture and sensorimotor testing were basically the same as that of PRF, but after the puncture needle entered the target, the operator set the temperature to 95 °C. Thermocoagulation lasted for 120 seconds, and 2 cycles of procedure were performed.

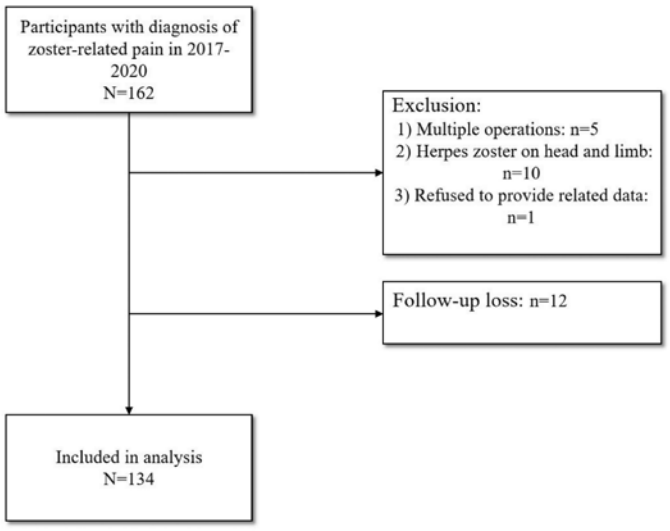

Fig 1. *Flowchart depicting the patients' inclusion and exclusion.*

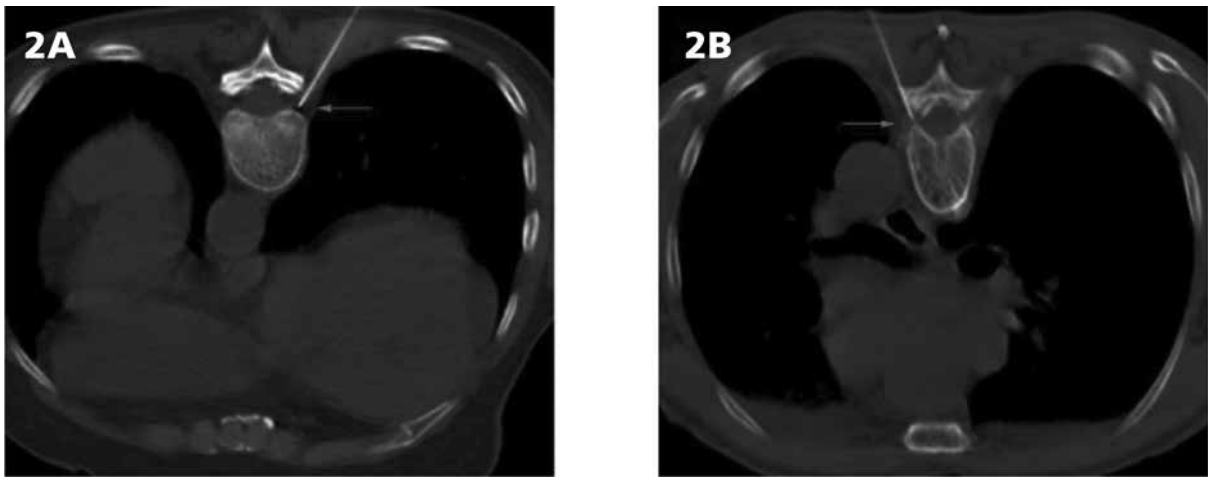

Fig 2. *Needle was punctured to the upper 1/3 of the intervertebral foramen in two sides. Arrow indicates that the tip has reached the target.*

Surgical Instruments

The surgical instruments used in this study included the following: 1) CT machine, Siemens Somatom Emotion system (Siemens HealthCare Malvern, PA, USA); 2) puncture needle (Inomed Health Ltd. Hopwood Lane; Halifax, Germany); 3) vital signs monitor (Radical-7; Masimo Medical Company Inc. Irvine, California, USA); and 4) radiofrequency machine (Baylis Medical Company Inc. Toronto, ON, Canada).

One-year follow-up

In this study, all patients were followed up for 1 year (follow-ups were conducted every 3 months). The primary outcome was the recurrence rate. Postoperative NRSs ≥ preoperative values indicated relapse. The secondary outcomes were NRS, PSQI, adverse events, and satisfaction at each time interval during the follow-up year. Sensation after the operation was evaluated by Barrow Neurological Institute (BNI) numbness grade (I–IV) as follows: I, no numbness; II, mild numbness, causing no impact; III, moderate numbness, somewhat bothersome; and IV, severe numbness, very bothersome (16).

Statistical Analysis

SPSS 26.0 (IBM, Chicago, USA) was used to analyze all the data. The Shapiro–Wilk test was used to determine whether the measurement data had a normal distribution. Normally distributed data are expressed as the mean ± standard deviation, while the nonnormally distributed data are expressed as the median (interquartile). The proportionality of hazards was assessed for each variable and Schoenfeld residual analysis showed that none were significant based on a *P*- value threshold of 0.05. (17).

This study is based on the principle of 10 events per variable (10EPV) to screen independent variables. According to the previous studies (4) and research experience, the authors included independent variables such as age, gender, disease course, position, history of conservative treatments, lesion space, pain grade, surgical procedure, and so on. The disease course was set to 3 classification variables (3 and 6 months as the boundary). The lesion space was calculated based on the body surface area (approximately 1% of the body surface area of a single palm). Less than 1% of the body area is defined as a small area, 1% to 2% of the area is defined as a medium area, and a large range refers to an involved area of more than 2%. The degree of pain was reassessed according to the preoperative NRSs (0 - 10). An NRSs of 4 - 6 was considered moderate pain, and a score ≥ 7 was considered severe pain. Except for age as a continuous variable, all the variables were adjusted to binary variables.

The positive outcome was recurrence and no recurrence or censoring was regarded as a negative outcome. The time to recurrence of all patients with recurrence was also observed. The cumulative survival rates of the surgical procedures were estimated by the Kaplan-Meier analysis and compared with the log-rank test. To further explore the independent influence of surgical procedures on postoperative recurrence, the correlation between baseline characteristics and outcome was analyzed by univariate Cox regression. To prevent the independent variables of important significance from being included in the regression model as much as possible, the adjusted significance level was set to 0.20. The independent variables with significant differences after screening were included in the interval-censored multivariable Cox regression, excluding the collinearity between independent variables, then the model was controlled for all the confounding factors.

The importance of the variables to be included in the multifactor analysis was evaluated using categorical regression (CATREG). The corresponding variables were classified, virtual variables were set, and the reference was adjusted according to the variable change correlation. For the HR and its 95% CI, $P < 0.05$ was considered to indicate statistical significance. Finally, a prognostic nomogram including the lesion space, pain grade, and surgical procedure was constructed. A time-independent ROC curve was used to evaluate the overall differentiation of the model. The NRS and PSQI of each time interval were tested by repeated measures analysis of variance. Multiple comparisons were conducted with the Bonferroni test and the significance level was adjusted.

Assuming that the missing data in this study was random, multiple imputation was used to deal with the missing data and parallel data sets were generated.

The R software version 4.0.2 (2020-06-22) was mainly used to perform the data manipulation. Descriptions of cumulative hazards, survival probability, and ROC curves were based on the packages survminer_0.4.8, survival_3.2-7 and survival ROC_1.0.3. Nomograms and box plots were generated by the addition of VRPM_1.2, rms_6.0-1, and ggpubr 0.4.0.

Results

Baseline Characteristics

Based on the inclusion and exclusion criteria, 146 patients diagnosed with HZ-related pain in 2017–2020,

without a history of radiofrequency on the DRG were included. A total of 12 patients were lost to follow-up and 134 patients were involved in the statistical analysis. The baseline characteristics of all included patients are shown in Table 1. There was no significant difference ($P > 0.05$) in demographic data between the 2 groups.

Risk for Recurrence Rate

In the 134 patients included, the mean ± standard deviation follow-up period was 8.45 ± 4.01 months. During the follow-up period, 50 patients (37.3%) developed the primary outcome (20 cases after RF-TC and 30 cases after PRF). According to the cumulative incidence curves (Fig. 3), those treated with RF-TC had a significantly lower risk for the primary outcome than those treated with PRF ($P < 0.05$, log-rank test). We performed univariate and multivariate Cox proportional hazard regression analyses to identify the independent risk factors for recurrence rate following zoster-related pain (Table 2). Univariate analysis was performed on age, gender, position, disease course, conservative treatment history, side, lesion space, surgical procedure, and pain grade. After univariate analysis, there was a significant correlation between lesion space, pain grade, and surgical procedures and the primary outcome. Lesion space was still an important factor affecting the primary outcome (1-2% / ref: crude HR[95% CI], 2.437[1.252-4.745]; adjusted HR[95% CI], 2.075[1.002 - 4.210]; > 2% / ref: crude HR[95% CI], 3.744 [1.881 - 7.449]; adjusted HR[95% CI], 3.406[1.670 - 6.950]). Pain grade and surgical procedure were also positively correlated with the primary outcome (pain grade: crude HR[95% CI], 2.329[1.333 - 4.069]; adjusted HR[95% CI], 2.249[1.221 - 4.143]; surgical procedure: crude HR[95% CI], 2.121[1.201 - 3.747]; adjusted HR[95% CI], 2.392[1.308 - 4.375]). The areas under the curve (AUCs) at 3, 6, 9, and 12 months were 0.816, 0.748, 0.738, and 0.758, respectively (Fig. 4). A nomogram was used to predict the recurrence rate of HZ-related pain after radiofrequency (Fig. 5).

Repeated Measures ANOVA for the NRS and PSQI

The results of Mauchly's test of sphericity suggested that $P < 0.05$ and Geenhouse-Geisser was used to correct the significance. The results suggested that there was an interaction between time and grouping ($P < 0.05$). The Emmeans function was used to analyze the multiple comparisons of intergroup and intragroup

Table 1. *Baseline characteristics of patients with 2 procedures.*

Variables	RF-TC (n = 67)	PRF (n = 67)	*P*-value
Age, Median (IQR), year	72 (63-77)	68 (61-73)	> 0.05
Gender, n (%)			
Men	39 (58.2)	35 (52.2)	> 0.05
Women	28 (41.8)	32 (47.8)	
BMI, Mean ± SD, kg/m²	23.24± 2.76	23.13 ± 2.50	> 0.05
Position, n (%)			
Chest	51 (76.1)	51 (76.1)	> 0.05
Waist and abdomen	16 (23.9)	16 (23.9)	
Course of disease, Median (IQR), months	2 (1-3)	1.5 (1-4)	> 0.05
Conservative treatment history, n (%)			
Yes	49 (73.1)	48 (71.6)	> 0.05
No	18 (26.9)	19 (28.4)	
Side, n (%)			
Left	29 (43.3)	34 (50.7)	> 0.05
Right	38 (56.7)	33 (49.3)	
Lesion space, n (%)			
< 1%	40 (28.8)	37 (26.6)	> 0.05
1-2%	17 (12.2)	19 (13.7)	
> 2%	10 (7.2)	11 (7.9)	
Pre-NRS, Median (IQR)	6 (6-7)	6 (5-7)	> 0.05
Pre-PSQI, Median (IQR)	15 (13-16)	13 (13-15)	> 0.05

BMI: body mass index; Lesion space: every 1% of the body surface area corresponds to the size of a palm; Pre-NRS or Pre-PSQI: Numerical rating scale or Pittsburgh sleep quality index before operation.

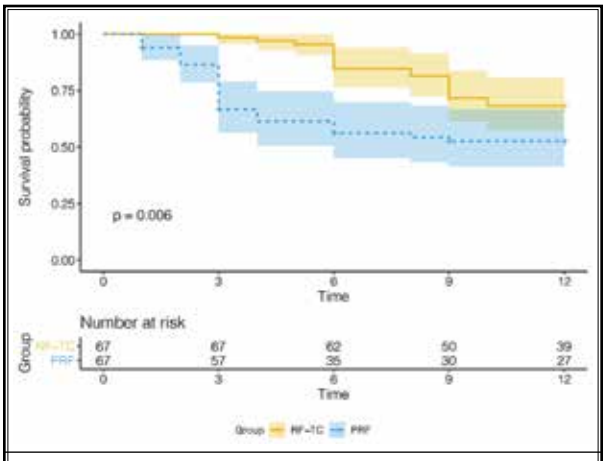

Fig 3. *Kaplan-Meier analysis calculates the cumulative survival rates of surgical procedures and compared with log-rank test.*

Table 2. *Factors Associated with Relapse after Herpes Zoster.*

Independent variables	Crude HR [95% CI]	Adjusted HR [95% CI]
Age, Year	1.007 [0.978-1.037]	1.018 [0.986-1.050]
Gender		
Women	0.765 [0.439-1.332]	0.633 [0.345-1.160]
Men		
Position		
Chest	1.066 [0.557-2.041]	1.068 [0.543-2.100]
Waist and Abdomen		
Course of disease		
1-3 months	Ref	Ref
3-6 months	0.810 [0.428-1.533]	0.805 [0.410-1.580]
> 6 months	1.747 [0.417-7.314]	1.091 [0.244-4.878]
Treatment History		
None	0.999 [0.539-1.853]	0.985 [0.517-1.877]
Yes		
Side		
Left	0.980 [0.562-1.710]	1.212 [0.671-2.189]
Right		
Pain Grade		
Moderate	2.329 [1.333-4.069]	2.249 [1.221-4.143]
Severe		
Lesion space		
< 1% Body surface area	Ref	Ref
1-2% Body surface area	2.437 [1.252-4.745]	2.075 [1.002-4.210]
> 2% Body surface area	3.744 [1.881-7.449]	3.406 [1.670-6.950]
Surgical Procedure		
RF-TC	2.121 [1.201-3.747]	2.392 [1.308-4.375]
PRF		

Moderate: NRSs 4-6; Severe: NRSs≥7; Lesion space: the size of a palm is equal to about 1% of the body surface area; RF-TC: radiofrequency thermocoagulation; PRF: pulsed radiofrequency

factors. The NRS and PSQI of the 2 procedures at each time interval were compared. The results showed a significant difference between the 2 groups at T2 and T3 ($P < 0.05$). In addition, there were significant differences in the pairwise comparison results of all time intervals in the RF-TC group. In contrast, in the PRF group, there were no significant differences in the results of T2 versus T3, T2 versus T4 or T3 versus T4 ($P > 0.05$). The comparison of the PSQI at each time

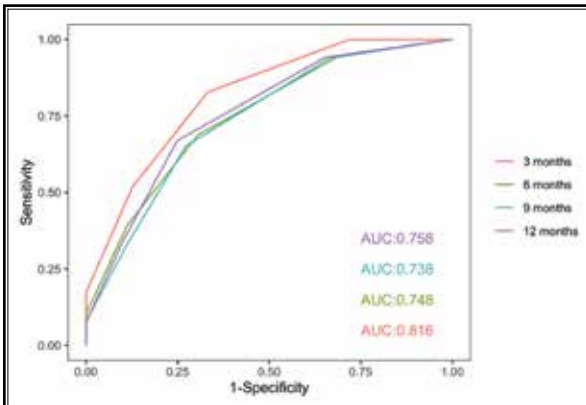

Fig 4. *Time-independent receiver operating characteristic (ROC) curve.*

interval showed that only at T4 was there a significant difference between the 2 groups ($P < 0.05$). In the RF-TC group, the differences among all time intervals were statistically significant ($P < 0.05$). In the PRF group, only the comparison of T3 versus T4 showed no significant difference ($P > 0.05$). Figure 6 shows the distribution of NRSs and PSQIs for each time interval.

Adverse Events and Satisfaction

Regardless of whether patients underwent RF-TC or PRF, there were different degrees of innervation region numbness after the operation. There were 29 cases of postoperative numbness lasting more than half a year in the RF-TC group, but only 10 cases in the PRF group. The proportion of numbness ≥ grade 3 in the RF-TC group was 55.2%, compared with only 20% in the PRF group. The intraoperative NRS was 7 (5 -7) in the RF-TC group and 3 (2 - 4) in the PRF group. The difference was statistically significant ($P < 0.05$). The satisfaction score ranged from 0 - 10, with 0 for very dissatisfied and 10 for very satisfied. The results showed that the overall satisfaction of patients in the RF-TC group was 5.83 and 6.11 and the difference was not statistically significant ($P > 0.05$). Table 3 shows the adverse events and satisfaction.

Discussion

HZ is caused by the reactivation of varicella zoster virus infection (18). Age is an important factor affecting the incidence of HZ. Adults over 50 years old have a significantly increased risk of HZ, which may be related to a decrease in immune function (19). The typical clinical manifestation of HZ is a zoster on one side of the skin, which usually does not cross the midline (3). It is not very difficult to diagnose HZ with typical clinical

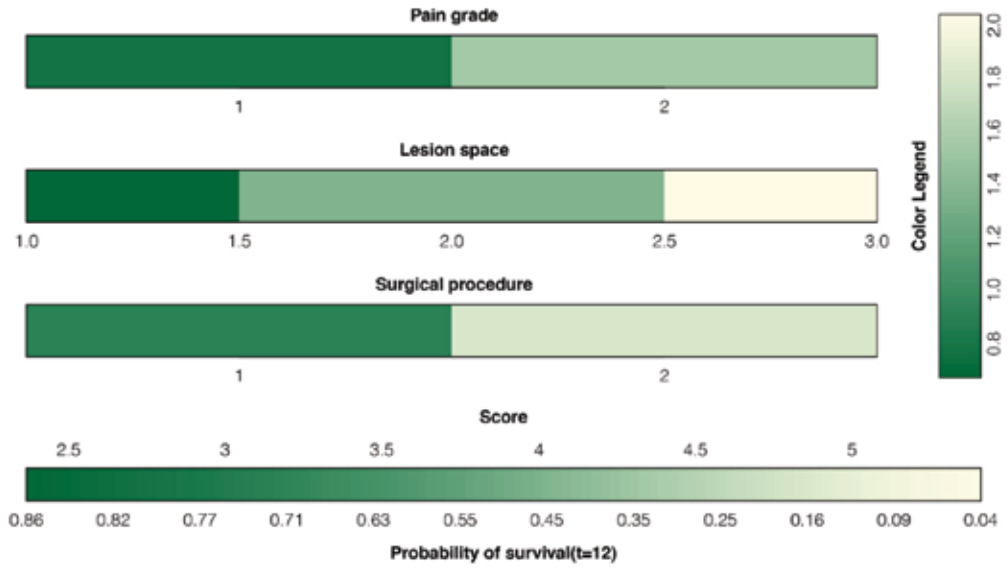

Fig 5. *Nomogram for predicting the recurrence rate of HZ-related pain after radiofrequency.*
The score obtained by the addition of every risk factor corresponds to the predicted recurrence rate.

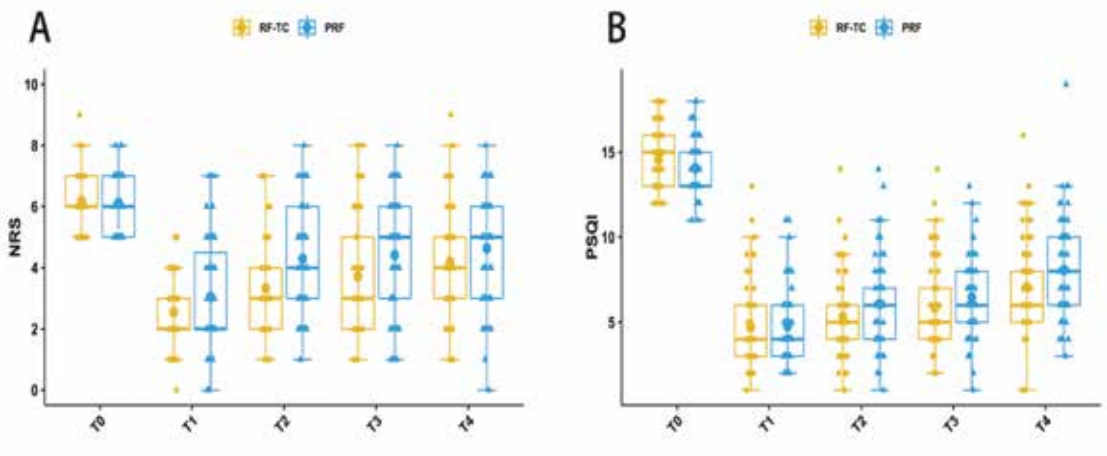

Fig 6. *Distribution of numeric rating scale scores (NRSs) and Pittsburgh sleep quality index (PSQI) for each time interval during one year.*
T0: before operation; T1: 3 months after operation; T2: 6 months after operation; T3: 9 months after operation; T4: one year after operation.

manifestations. The healing of HZ can be accompanied by pigmentation and local sensory abnormalities, but mostly is accompanied by chronic and debilitating pain. It has been reported that approximately 15% to 40% of HZ will eventually develop into PHN (20). PHN is defined as pain that persists for more than 3 months after the onset of the cutaneous lesions of HZ (21). This kind of pain, characterized by hyperalgesia or hyper-

Table 3. *Satisfaction and adverse events between 2 groups.*

Variables	Group		*P*-value
	RF-TC	PRF	
Numbness*, n (%)	29 (43.3)	10 (14.9)	< 0.05
Intraoperative NRS, Median (IQR)	7 (5-7)	3 (2-4)	< 0.05
Satisfaction, Mean ± SD	5.83 ± 1.85	6.11 ± 1.83	> 0.05

Numbness*: Numbness lasting more than half a year.

sensitivity, often significantly affects patients' daily work and life and reduces the quality of their sleep (22). The characteristics of this kind of pain are diverse and often manifest as burning, a pin pricking sensation, and so on. Approximately 30%–50% of patients with PHN have persistent pain for more than 1 year and the intensity of pain varies from patient to patient (23). The mechanism of PHN is not clear, but it has been thought to be related to peripheral sensitization, central sensitization, inflammation, and ectopic discharge of nociceptive receptors (22,24).

At present, there are few ways to effectively control zoster-related pain and severe pain may persist for a long time, which means that drug treatment is also an extremely long process (21). In addition, the therapeutic effect of drugs is often inadequate and unsatisfactory. Taking into account the cost of treatments and patient acceptance, we think that radiofrequency may be a good choice.

The use of PRF for neuromodulation in the treatment of zoster-related pain has been proven to be safe and effective in a number of studies (25-27); however, it could be hindered by an important problem, as relapse easily occurs shortly after the operation. This was confirmed by the follow-up results of 67 patients, the recurrence rate of which the PRF group was 37.31% within 3 months after the operation and total recurrence rate was 44.78%.

Guanglun Xie et al (28), pointed out that the use of RF-TC on the DRG is effective for controlling refractory pain induced by rib metastasis of lung cancer. This may be one of the few clinical applications of RF-TC on the DRG at present. In this study, we included patients with HZ-related pain who underwent RF-TC on the DRG with moderate to severe pain. In the past, we thought that the application of RF-TC in HZ-related pain was debatable, mainly because DRG damage is usually irreversible. Although it may obviously relieve pain, there is still no comprehensive evidence to estimate the complications and severity; however, severe pain seriously affects daily life, some patients even reporting that they want to commit suicide to alleviate the pain. Therefore, many patients are still willing to accept the risk of the operation and undergo RF-TC, hoping to effectively relieve pain and prolong the time of pain relief.

Given the damage to nerve fibers and the myelin sheath with RF-TC, it seems inappropriate to directly destroy the spinal nerve in the early stage, so all patients had a disease course of at least one month. This study preliminarily explores whether there is a difference in the recurrence rate between the 2 surgical procedures and attempts to propose a new way to reduce the short-term recurrence rate of patients with herpes-related pain as much as possible.

In multivariate Cox analysis, although older age was significantly associated with PHN (29), there was no significant correlation between age and recurrence rate before or after controlling for confounding factors. In addition, after adjusting disease course to a classification variable, there was no correlation between them, which was contrary to our expectations; however, this may be related to the uneven distribution of data. In either the PRF or RF-TC group, the vast majority of patients with a disease course of 1-3 months and a significant decrease in the number of patients with a course of more than 3 months, which is the reason why we did not perform further subgroup analysis.

The degree of pain was set as a binary variable and was positively correlated with relapse. Compared with moderate pain (NRS 4-6), patients with severe pain (NRS $\geq$ 7) were 1.249 times more likely to experience relapse. This may be because the corresponding nerve involvement was more severe at the peak of virus replication, and even after nerve modulation, the latent virus could continue to invade the nerve and cause persistent pain. In addition, the larger the area of the lesion space, the higher the probability of postoperative recurrence was. When the lesion space exceeds 2% of the body surface area, the risk increases by 2.406 times. Previous studies have proven that the number of lesions is also a risk factor for PHN (30,31). Previous observations found some patients with multisegmental lesions, a rash that was sporadic, and that the extent of the lesions was not large. It may not be accurate to rely solely on the involved segments to judge the extent of the lesions. Therefore, in this study, we quantified the range of skin lesions based on body surface area and present it in the form of dummy variables after classification and reference establishment. The relationship between the surgical procedure and primary outcome was in line with our expectations. The temperature of PRF was lower, the targeted nerve was regulated rather than destroyed, and the risk of recurrence was 1.392 times higher than that with RF-TC. It is worth noting that in the RF-TC group, the recurrence rate within 3 months was only 14.93%, which was a significant result after RF-TC in this study.

The occurrence of adverse events also requires a high degree of vigilance. Numbness in the corresponding innervation area is one of the most common com-

plications after radiofrequency; however, the degree and duration of numbness caused by the different procedures are different. The degree of numbness in the RF-TC group was significantly more severe and lasted longer than that in the PRF group. Although some patients can accept pain relief at the cost of numbness, there are still patients who think that severe and lasting numbness will bring them additional trouble, which is also an important factor affecting patient satisfaction.

In addition, stimulation by high temperature may lead to obvious intraoperative pain. We found that there was an increase in NRSs in patients with HZ-related pain treated by RF-TC. After complete destruction of the targeted nerve and blockage of pain signals, severe pain will soon be relieved; however, this situation was rare in the PRF group. The temperature of the PRF we used was only 42° and few patients felt uncomfortable. Therefore, CT-guided PRF on the DRG is more comfortable in the treatment of HZ-related pain.

Additionally, in patients with waist and abdominal herpes who underwent lower thoracic RF-TC, we observed a local bulge after the operation in 3 cases. Interestingly, this phenomenon was not found in patients with upper thoracic RF-TC, nor was it observed in the PRF group. Generally, DRGs are located in the intervertebral foramen, but there may be individual differences in location and number (32). On the other hand, the temperature of radiofrequency thermocoagulation we used was 95° (33), the time reached 120s and high temperature and long-term radiofrequency may expand the scope of local damage. All of these reasons may lead to injury to the motor nerve during the operation. Because the intercostal muscles are thin and the ribs support the chest, the local bulge is not obvious, but the domination of the abdominal muscles is weakened after motor nerve injury, resulting in muscle relaxation or even atrophy.

Lesion space, pain grade, and surgical procedures are risk factors for postoperative recurrence. Especially for the patients with acute herpes zoster (AHZ), compared with the use of RF-TC, the performance of PRF has a higher risk of short-term recurrence. However, RF-TC could cause more severe intraoperative pain, more severe and longer postoperative numbness, a local abdominal bulge, and other adverse events. If patients are willing to accept pain relief at the cost of significant numbness and the disease course is longer, RF-TC on the DRG may be a feasible method to postpone the process of recurrence; however, the exact indications and the meaning of the clinical promotion of RF-TC in the treatment of HZ-related pain need to be determined by further research.

Limitations

1) Outliers were not excluded. 2) Evidence from randomized controlled trials was needed. 3) NRSs and PSQIs were approximately normalized. 4) Related independent variables were not stratified or analyzed by subgroups. 5) Due to the limited sample size, the data was not further split and validated.

Conclusion

In the treatment of HZ-related pain, CT-guided RF-TC reduced the short-term recurrence rate, but had a higher incidence of adverse events and more severe symptoms. Based on limited research evidence, we do not recommend the use of RF-TC on the DRG in patients with early HZ.

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