Retrospective Study

Effect of Radiofrequency Thermocoagulation of Thoracic Nerve Roots in Patients with Cancer and Intractable Chest Wall Pain

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Background: Interventional pain management is essential for patients with cancer who experience medically uncontrollable chest wall pain to help control their symptoms and improve their quality of life. However, there is a lack of data on this topic, so there is an urgent need for further research.

Objectives: To identify the effects of radiofrequency ablation (RFA) of the thoracic nerve roots on pain outcomes in patients with cancer and intractable chest wall pain.

Study Design: Retrospective, observational cohort study.

Setting: National Cancer Center in Korea.

Methods: The medical records of patients with cancer who were referred to the pain clinic at our National Cancer Center for intractable chest wall pain and who underwent thoracic nerve root RFA between Jan. 1, 2011 and Dec. 31, 2015 were analyzed. The primary outcome was the change in Numeric Rating Scale (NRS) scores between pre-procedure and one week, one month, and 6 months post-procedure. The secondary outcomes were the change in morphine equivalent daily dose (MEDD) between pre-procedure and one week, one month, and 6 months post-procedure, and whether the primary cancer type (lung vs. non-lung) or radiotherapy to the chest within one month affected the outcomes of RFA. The Wilcoxon signed-rank test was used to compare RFA data between pre and post-procedure and P values less than 0.05 were considered statistically significant.

Results: One hundred patients were included in the final analysis. The median NRS score in patients who underwent RFA decreased from 7 (range 3–10) pre-procedure to 4 (0–9) at one week and one-month post-procedure (both $P < 0.001$) and 4 (1–8) at 6 months post-procedure ($P < 0.001$). The median MEDD value decreased from 200 (range 30–1800) mg pre-procedure to 180 (10–1600) mg at one week post-procedure ($P < 0.001$), but there was no statistically significant change at one month ($P = 0.699$) or 6 months ($P = 0.151$) post-procedure. There was no difference in RFA outcome according to type of primary cancer or radiotherapy to the chest within one month.

Limitations: Retrospective design.

Conclusion: Radiofrequency thermocoagulation of the thoracic nerve roots achieved effective short-term pain control in patients with cancer and intractable chest wall pain.

Key words: Radiofrequency ablation, thermocoagulation, thoracic nerve root, cancer, chest wall pain, radiotherapy, pain relief

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Primary or metastatic cancer, including lung, breast, and colon cancer, may involve the chest wall, ribs, and pleura, and induce pain (1). Most tumors that invade the chest wall are in the advanced stages, which directs the focus of treatment to pain control and improving quality of life (QoL) (2). In general, opioid analgesics are used to control pain in patients with cancer, but opioids alone fail to achieve acceptable pain relief in about 10%–15% of cases (3). Further, given that opioid therapy has multiple side effects and is associated with tolerance, additional interventional pain management is now considered of importance in these patients (1,4).

Interventional procedures that are currently used to control intractable chest wall pain include intercostal/paravertebral nerve blocks and neurolysis, along with radiofrequency ablation (RFA) of the thoracic nerve roots (5-8). According to the paradigm suggested by Gulati et al (9), traditional RFA, where thermocoagulation is performed at a high temperature (> 90 degrees), is appropriate for posterior chest wall pain or a paravertebral tumor only when pulsed RFA is ineffective. However, most patients with cancer who develop intractable chest wall pain have advanced or terminal disease and a short life expectancy, so more aggressive treatment options that can provide effective pain relief in the short term are needed. Despite the importance of such treatment, none of the studies reported to date have investigated the effectiveness of traditional RFA of the thoracic nerve roots in controlling chest wall pain.

The aim of this study was to investigate the effectiveness of traditional RFA of the thoracic nerve roots in controlling intractable chest wall pain in patients with cancer. We hypothesized that traditional RFA would decrease the pain scores and the use of opioid analgesics in these patients.

Methods

This retrospective cohort study was undertaken with approval from the Institutional Research Board at the National Cancer Center in Korea (NCC2016-0242). We analyzed the electronic medical records of patients with cancer who were referred to the pain clinic at the National Cancer Center with a chief complaint of medically intractable chest wall pain and underwent RFA between Jan. 1, 2011 and Dec. 31, 2015. The exclusion criteria were: treatment with other pain relief procedures within 8 months of RFA; RFA performed on 2 or more occasions; RFA performed for chest wall pain not related to cancer; death within one week of RFA; and incomplete medical records. Data were obtained from medical records by a medical records technician with no conflict of interest in this study, and all authors were blinded to the data until the results of the statistical analysis were available.

Baseline demographic and clinical patient data for age, height, weight, gender, primary cancer, type of metastasis, type of RFA, history of radiotherapy, and extent of RFA were collected. Pain scores on the Numeric Rating Scale (NRS) and use (dose) of opioid analgesics calculated as the morphine equivalent daily dose (MEDD) were recorded before and at one week, one month, and 6 months post-RFA. The primary outcome of the study was the change in NRS scores at one week, one month, and 6 months post-RFA when compared with pre-RFA scores. The secondary outcomes were changes in the dose of opioid analgesics at one week, one month, and 6 months post-RFA when compared with pre-RFA doses and the effects of primary cancer type (lung versus non-lung) and radiotherapy within one month of RFA on RFA-induced pain relief.

RFA Procedure

All RFA procedures between Jan. 1, 2011 and Dec. 31, 2015 were fluoroscopy-guided and performed by one anesthesiologist (DHK) with experience performing more than 50 RFA procedures. All patients were taken to the operating room without premedication, and their oxyhemoglobin, blood pressure, and electrocardiogram were monitored. An intact intravenous fluid line was inserted preoperatively. The patients were changed to the prone position for sterile surgical draping with application of povidone-iodine. Prior to the procedure, the vertebral body of the dermatome that induced the chest wall pain, which was preoperatively confirmed by chest computed tomography and physical examination, was identified by fluoroscopy. After intradermal infiltration of 1% lidocaine, a 10 cm blunt RF needle (with a 1 cm active tip) was inserted. The blunt needle was positioned in the vicinity of one thoracic nerve root, and the position was confirmed via fluoroscopic anterior-posterior and lateral views (Fig. 1). Additional blunt needles were inserted by the same method near further thoracic nerve roots involved in the chest wall pain. After confirming the positions of the blunt needles, sensory stimulation was performed (50 Hz, 0.5 V), and the tips of the needles were repositioned to the positions that induced sensory stimulation related to the chest wall pain. Next, 0.8% mepivacaine

with triamcinolone (3 mL) was infused via each needle, and thermocoagulation was performed for more than 90 seconds at 80–90 degrees using an RF generator (Radionics RFG-3C, Burlington, MA, USA). Fentanyl 50–100 mcg was administered intravenously during thermocoagulation for additional pain control if requested by the patient.

Statistical Analysis

The characteristics of 100 patients are presented as the frequency or median (range). The Wilcoxon signed-rank test was performed to compare pre and post-procedural for NRS and MEDD scores. The difference of the 2 groups according to whether radiotherapy to the chest was performed in one month was tested. *P*-values < 0.05 were considered to be statistically significant, and all statistical analyses were performed using SAS version 9.4 software (SAS Institute Inc., Cary, NC, USA).

Results

One hundred and forty-nine patients with chest wall pain were referred to our pain clinic and underwent RFA without complication between Jan. 1, 2011 and Dec. 31, 2015. The following patients were excluded from the primary analysis: 18 who underwent additional procedures (vertebroplasty, medial branch RFA, celiac plexus neurolysis, caudal epidural block) within 6 months of RFA, 12 who received 2 or more RFA procedures, 4 who underwent RFA for non-cancer (chronic thoracotomy) pain, 2 who died within one week of RFA, and 13 who had incomplete medical records. A further 12 patients who died between one week and one month following RFA and 58 patients who died between one month and 6 months following RFA were excluded from the one-week and 6-month analyses, respectively. One patient among those who survived for one month following RFA was excluded from the MEDD analysis for having an incomplete MEDD record (but a complete NRS record).

Table 1 shows the clinical characteristics of the 100 patients whose data were available for analysis. Table 2 compares the pre-RFA and one-week, one-month, and 6-months post-RFA NRS scores and MEDD value for these patients. Compared with the median pre-procedural NRS score (7, range 3–10), median post-procedural NRS scores decreased to 4 (0–9) at one week and one-month post-procedure (both $P < 0.001$) and 4 (1–8) at 6 months post-procedure ($P < 0.001$). The median MEDD value decreased from 200 (range 30–1800) mg pre-procedure to 180 (10–1600) mg at one-week post-procedure ($P < 0.001$), but there was no statistically significant change at one month ($P = 0.699$) or 6 months ($P = 0.151$) post-procedure. The mean and standard deviation pre-RFA and post-RFA NRS scores are shown in Fig. 2; the mean NRS score was 7.1 pre-RFA and 3.93 at one week and 4.05 at

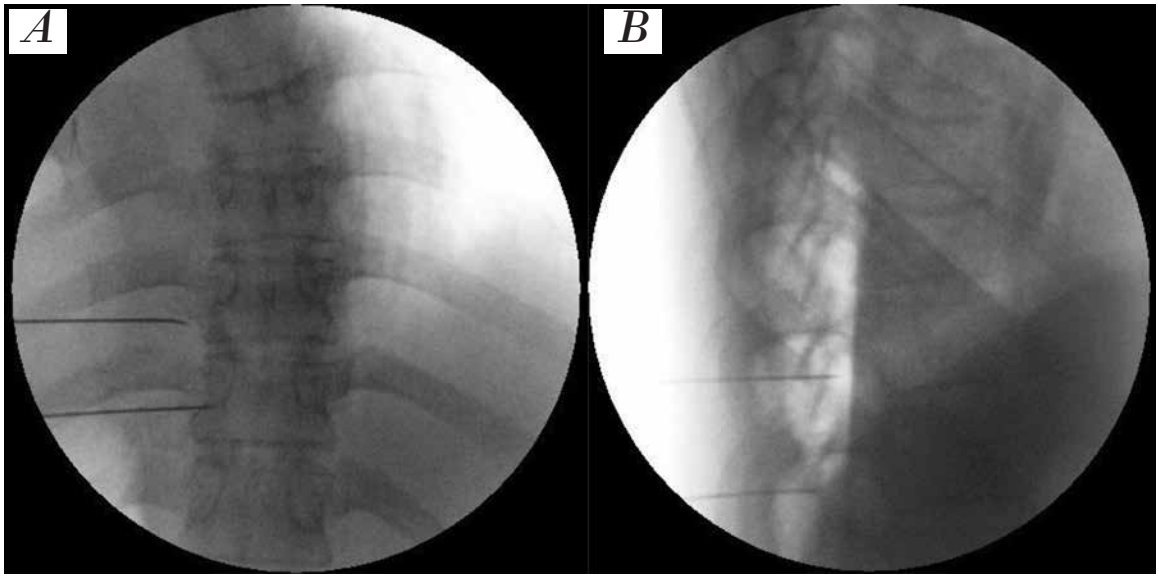

Fig. 1. *Fluoroscopic anterior-posterior view (A) and lateral view (B) during radiofrequency ablation.*

Table 1. *Patient demographic and clinical characteristics.*

		n or median (range)
Age, years		62.5 (34–94)
Height, cm		163.1 (142.3–183)
Weight, kg		56 (36–82)
Gender		
	Male	60
	Female	40
Primary cancer		
	Lung	68
	Non-lung	32
Type of metastasis		
	Chest wall	39
	Rib	51
	Pleural	51
Type of RFA		
	Unilateral	94
	Bilateral	6
Radiotherapy to chest within one month		
	Yes	24
	No	76
RFA level		
	T1	0
	T2	9
	T3	22
	T4	22
	T5	19
	T6	17
	T7	17
	T8	23
	T9	18
	T10	12
	T11	16
	T12	11

Abbreviation: RFA, radiofrequency ablation

Table 2. *Numeric Rating Scale score and morphine equivalent daily dose.*

		n	Median (range)	*P*-value*
NRS score	Pre-procedural	100	7 (3–10)	reference
	One week	100	4 (0–9)	< 0.001
	One month	88	4 (0–9)	< 0.001
	6 months	30	4 (1–8)	< 0.001
MEDD	Pre-procedural	100	200 (30–1800)	reference
	One week	100	180 (10–1600)	< 0.001
	One month	87	180 (0–2220)	0.699
	6 months	30	240 (20–1450)	0.151

The *P*-value* was calculated using Wilcoxon signed-rank test. Abbreviations: NRS, Numeric Rating Scale; MEDD, morphine equivalent daily dose

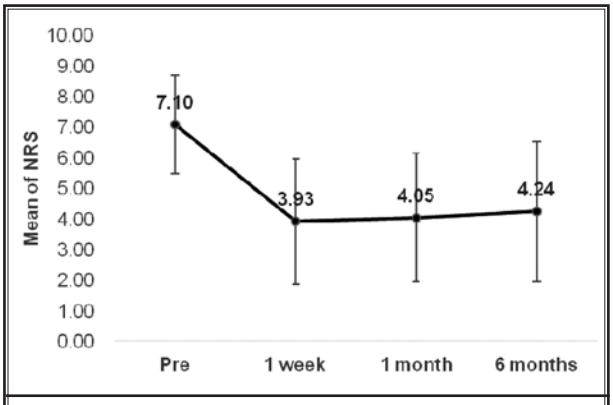

Fig. 2. *Mean (and standard deviation) NRS scores. Abbreviation: Numeric Rating Scale*

one-month post-RFA (both $P < 0.001$) and 4.24 at 6 months post-RFA ($P < 0.001$).

The effectiveness of RFA according to primary cancer type (lung or non-lung) is shown in Table 3. The median NRS score in the lung cancer group changed from 7 (range 4–10) pre-RFA to 3.1 (0–9) at one-week post-RFA ($P < 0.001$), 4 (0–9) at one-month post-RFA ($P < 0.001$), and 4 (1–8) at 6 months post-RFA ($P < 0.001$). Similarly, the median NRS score in the non-lung cancer group changed from 8 (range 3–10) pre-RFA to 4.4 (1–8) at one-week post-RFA ($P < 0.001$), 4.5 (1–8) at one-month post-RFA ($P < 0.001$), and 3.5 (2–7) at 6 months post-RFA ($P = 0.031$). The median MEDD value in the lung cancer group decreased from 210 (range 30–1800) mg pre-procedure to 195 (20–1600) mg at one-week post-procedure ($P = 0.003$), but there was no statistically significant change at one month ($P = 0.456$) or 6 months ($P = 0.253$) post-procedure. Similarly, the median MEDD value in the non-lung cancer group decreased from 190 (range 30–1020) mg pre-procedure to 180 (10–1000) mg at one-week post-procedure ($P < 0.001$), but there was no statistically significant change at one month ($P = 0.605$) or 6 months ($P = 0.313$) post-procedure. Table 4 shows that radiotherapy within one month of RFA did not affect the NRS score or MEDD value.

Table 4. *Numeric Rating Scale and morphine equivalent daily dose according to whether radiotherapy to the chest was performed in one month.*

		n	Median (range)		*P*-value*
			Yes	No	
			(n = 24)	(n = 76)	
NRS	Pre-procedural	100	8 (5–10)	7 (3–10)	0.629
	One week	100	4 (0–7)	3.5 (0–9)	0.774
	One month	88	3.75 (1–8)	4 (0–9)	0.801
	6 months	30	3.3 (1–7)	5 (1–8)	0.506
MEDD	Pre-procedural	100	320 (30–1640)	200 (30–1800)	0.239
	One week	100	277.5 (30–1600)	180 (10–1450)	0.167
	One month	87	300 (40–2220)	180 (0–1600)	0.261
	6 months	30	280 (160–900)	160 (20–1450)	0.212

The *P*-value* was calculated using Wilcoxon rank-sum test at each time. Abbreviations: NRS, Numeric Rating Scale; MEDD, morphine equivalent daily dose

Table 3. *Numeric Rating Scale score and morphine equivalent daily dose according to primary cancer.*

		n	Lung (n = 68)		Non-lung (n = 32)	
			Median (range)	*P*-value*	Median (range)	*P*-value*
NRS score	Pre-procedural	100	7 (4–10)	reference	8 (3–10)	reference
	One week	100	3.1 (0–9)	< 0.001	4.4 (1–8)	< 0.001
	One month	88	4 (0–9)	< 0.001	4.5 (1–8)	< 0.001
	6 months	30	4 (1–8)	< 0.001	3.5 (2–7)	0.031
MEDD	Pre-procedural	100	210 (30–1800)	reference	190 (30–1020)	reference
	One week	100	195 (20–1600)	0.003	180 (10–1000)	< 0.001
	One month	87	220 (20–2220)	0.456	160 (0–1200)	0.605
	6 months	30	180 (20–1450)	0.253	325 (90–960)	0.313

The *P*-value* was calculated using Wilcoxon signed-rank test. Abbreviations: NRS, Numeric Rating Scale; MEDD, morphine equivalent daily dose

Discussion

Our findings show that traditional RFA performed in patients with cancer and intractable chest wall pain significantly decreased NRS scores by about 40% (from 7 to 4) and decreased opioid use by about 10% within one week after the procedure. Despite the fact that our results showed significantly lower NRS scores at one month and 6 months after RFA, it is uncertain whether RFA continued to produce significant pain relief after one month and 6 months following the procedure. Many patients died prior to the one-month and 6-month analyses, and it is highly likely that these patients had worse pain and more opioid use as their cancer progressed (10). However, our study results do confirm the short-term effectiveness of traditional RFA. They also show that RFA effectively controlled chest wall pain at 1 week post-procedure in patients with lung cancer and those with metastatic cancer of non-lung origin.

There are pros and cons for all the procedures known to control cancer-related chest wall pain (5-8). In view of these, Gulati et al (9) recommended that the type of pain control be chosen depending on the location of the chest wall pain and extension of the tumor. The suggested paradigm for controlling chest wall pain is to begin with the least invasive procedures and move on to more invasive procedures, e.g., from intercostal nerve block to neurolysis, from paravertebral block to

neurolysis, and from pulsed RFA to RFA or cryoablation, and if those procedures do not work, then eventually an intrathecal pump, spinal cord stimulator, or surgical neurolysis (9). However, most patients with advanced cancer have a short life expectancy, during which their cancer continues to progress (11). Thus, beginning with a minimally invasive procedure, as per the intervention paradigm for pain control, might pose considerable challenges for performing subsequent procedures such as RFA when the chest wall pain has worsened because of progression of cancer, weakening of the patient's general condition, or inability to lie in a prone position. Twelve of the 100 patients included in this study died between one week and one month following RFA, and 70 died within 6 months of the procedure, which demonstrates the need for an aggressive initial intervention procedure for patients with chest wall pain related to advanced cancer. Hence, the patients in this study received traditional RFA as the initial treatment, which resulted in an approximately 40% decrease in NRS pain scores within one week of the procedure.

The fact that thermal neurolysis, not pulsed RFA, was chosen as the initial treatment could be another issue for consideration in this study. Compared with pulsed RFA, continuous RFA is more effective for pain relief but may cause more nerve damage (12,13). Khalid Malik et al (14) reviewed 33 articles on the RF of the dorsal root ganglia, and found a small number of patients newly developed pain and sensory disturbances after continuous RF. These adverse effects were relieved in weeks or months. Therefore, physicians should keep in mind that neuritis can occur due to RF denervation of nerve roots. Also, since traditional RFA (thermal neurolysis) destroys both sensory nerve and motor nerve, patient QoL could become a concern (15). However, thermal neurolysis is unlikely to have had an adverse impact on day-to-day QoL in these patients, because the thoracic nerves (T2–T12) targeted by RFA in our study do not control important motor functions (16). Destruction of up to 3 thoracic nerve roots does not cause significant difficulty in breathing using the intercostal muscles (16). And, none of our patients complained of difficulty in breathing after RFA. However, chest wall pain with an NRS score ≥ 7 would have an adverse effect on QoL, further justifying the choice of neurolysis as the initial treatment. We were unable to assess changes in patients' QoL in this study, but the finding that pain intensity was decreased by 40% without increasing the dose of opioid analgesics suggests that QoL would have improved.

Intrathecal pump and spinal cord stimulation, which are the final interventional procedures for pain control in the paradigm suggested by Gulati et al (9), are effective for controlling chest wall pain and could be considered as treatment options (17,18). However, due to their higher costs, performing them as initial treatment would not be cost-effective for patients with advanced cancer because although many die within 6 months of their diagnosis, even though some do survive in the longer term (19,20). Similarly, surgical neurolysis, such as cordotomy, should be considered as the final treatment option because of the invasiveness of the procedure (9,21). Therefore, it would be best to consider traditional RFA as an initial treatment for controlling intractable chest wall pain in patients with advanced cancer, and consider surgical neurolysis, spinal cord stimulation, or intrathecal drug delivery, as recommended by previous study, for patients in whom RFA fails to achieve effective pain relief (9).

Limitations

This study has some limitations. First, we could not adequately assess patient performance status or QoL due to the retrospective study design. Second, confounding factors were present because the NRS scores represented not only chest wall pain but also pain in other areas of the body. Third, it was difficult to observe changes in each patient's condition accurately because the follow-up intervals for NRS scores and MEDD values were wide (pre-procedure and one week, one month, and 6 months post-procedure). Our findings with regard to the effectiveness of RFA would have been more accurate if NRS scores and MEDD values were measured over consistent and narrower intervals.

Despite these limitations, this is the first study to analyze the effects of traditional RFA, i.e, thoracic nerve root RFA, as the initial intervention procedure for patients with intractable cancer-related chest wall pain. Further, the reliability and clinical significance of our findings are heightened by the fact that the results were obtained by a single physician proficient in interventional pain management in a relatively short period. We also attempted to identify the ability of traditional RFA alone to alleviate pain by analyzing the differences in NRS scores and MEDD values between patients who underwent chest radiotherapy and those who did not. As a result, we were able to verify the short-term effectiveness of RFA in controlling cancer-related chest wall pain.

Conclusion

In conclusion, radiofrequency of thermocoagulation of the thoracic nerve roots was effective for short-term pain control in patients with intractable cancer-related chest wall pain. Our finding that RFA was a suitable initial treatment option for interventional pain management in these patients will need to be confirmed by well-designed prospective studies in the future.

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