

## Evaluation of Safety and Efficacy of Radiofrequency Lesioning of Thoracic Dorsal Root Ganglion in Chest Cancer Pain Patients Daily Activities and their Quality of Life

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### ABSTRACT

**Background:** in controlling cancer pain it is commonly inadequately managed for these patients leading to suffer in the form of physical disabilities, psychological disturbance, avoiding treatment. Therefore pain that is caused by cancer may directly affect the patient's quality of life; by having an effect on his/her daily activity, physical state and also psychological and emotional status. Thus, making pain relief and control the patient's right; right for a new life "pain free" or at least tolerable non-disabling pain.

**Aim of the work:** this study aimed to test both the efficacy and safety of thermo-coagulative ablation of the thoracic dorsal root ganglia for pain control in cancer patients that have refractory chest pain And the impact on quality of life for patients.

**Patients and Methods:** our prospective study was done on sixty-five patients selected from pain clinics of both the National Institute of Cancer, Cairo University and Aswan University with refractory chronic chest cancer pain according to the inclusion and exclusion criteria. The complete duration of the follow up lasted 3 months post-interventional; with assessments after 1 week, 1 month and 3 months. At each follow up each patient was re-assessed with the following assessments; VAS, ECOG performance status, QOLS, drug consumption, side-effects (complications) and patient satisfaction. **Results:** we found that with effective pain relief there was a significant reduction in the mean VAS values which means that there was functional improvement, in all the post-interventional follow ups. Also, there was an improvement in the functional state of the patients throughout the follow-up post-intervention with regards to the ECOG performance status from the results. In addition to the ECOG improvement there was also a significant improvement in the QOL (Quality of Life) results, which was due to the pain relief. Regarding drug consumption, it was recorded that all three drugs; pregabalin, oxycodone and amitriptyline, should maximum reduction after 1 month following the intervention, with a slight increase 3 months post-interventional, which matched the degree of pain reduction based on the pain scaling scores. Only 11% of our patients were found with numbness and neuritis, which were the only two complications reported. With regards to our patients, 30.6% certainly would repeat the procedure, 54.8% probably would, and 12.9 % probably would not while, only 1.6% certainly would not repeat it. With 25.8% certainly would recommend the same procedure, 56.5% probably would, 14.5% probably would not and only 3.2% certainly would not recommend it.

**Conclusion:** we concluded that thermal radiofrequency ablation is considered an alternative for treating refractory chronic chest cancer pain of several types and causes. This is because of its efficacy, safety and ease of use, patient's quality of life of was largely affected.

**Keywords:** QOL, Radiofrequency, Chest cancer.

### INTRODUCTION

It has been postulated that 3-3.5% of the visitors of pain clinics are thoracic pain sufferers <sup>(1)</sup>. Pain of the thoracic region may arise from a variety of structures. Firstly, the thoracic spine (discs, spinal dura, nerve roots, facet, costovertebral joints and myofascial structures) is a considerable source of chronic chest pain. Secondly, pain may be referred to chest and upper abdomen from internal organs<sup>(2)</sup>; this referred pain may be due to inflammation, cancer or metastatic disease e.g. of the thoracic vertebrae. Third quarter, thoracic neuropathic pain syndromes include primary intercostal neuralgia, postherpetic neuralgia, complex regional pain syndrome (CRPS). Finally iatrogenic chronic chest pain may follow thoracic surgical procedures such as postmastectomy and postthoracotomy pain syndromes <sup>(3)</sup>. Chronic post-

thoracotomy pain syndrome is one of the most challenging and refractory pain entities confronting pain physicians. Its prevalence rate ranges from 22%-67% <sup>(4)</sup>. Even, the definition of being chronic pain is still a controversy; the delineation between acute and chronic post-surgical pain ranges from 2 months, 3 months and up to one year <sup>(5)</sup>. IASP defines it "pain that persists beyond the normal time of healing". The reported incidence of post breast surgery pain varies greatly from less than 10% to up to 60% in some women <sup>(6)</sup>. Regarding malignant chest pain, lung cancer is the most common cancer in the world as 1.61 million of new cases are discovered annually<sup>(7)</sup>. Pain was found to be the presenting symptom among 20% of these patients. Patients with lung cancer experience more distressing symptoms than other

types of cancer and pain is the most distressing together with dyspnea<sup>(8)</sup>. Thoracic pain of chronic nature may be relieved by pharmacotherapy, palliative radiotherapy, physiotherapy, occupational therapy or interventional blocks. These interventions range from intercostal nerve blockade up to percutaneous cervical cordotomy (PCC) and include rhizotomy<sup>(8)</sup>. Rhizotomy means selective segmental or multisegmental destruction of the dorsal sensory roots either neurosurgically, using chemical neurolytics or percutaneous radio frequency ablation<sup>(9)</sup>. Untreated cancer pain is associated with both physical and psychological problems; which causes suffering and a reduction in the quality of life. Patients with uncontrolled pain have physical symptoms such as: anorexia, insomnia, prolonged fatigue, reduced cognition and an overall reduction in their vital capacity. Cancer patients with unrelieved pain tend to withdraw themselves from both social and family interactions, which lead to isolation and psychological distress<sup>(10)</sup>. Cancer pain may directly have an effect on the quality of life of the patient, by affecting his/her daily activity, physical state and also both psychological and emotional status<sup>(11)</sup>. In this prospective study, the effect of thermal radiofrequency lesioning of selective thoracic dorsal root ganglia on cancer patients had chronic chest pain due to different etiologies was assessed.

**Aim of the Study:**

This study was designed to test both the efficacy and safety of thermo-coagulative ablation of the thoracic dorsal root ganglia for pain control in cancer patients that have refractory chest pain And the impact on quality of life for patients.

**Patients and Methods:**

#### **Design of the study**

This prospective randomized study was conducted in the National Cancer Institute, Cairo University and Aswan University after board approval from October 2016 to March 2018. Sixty-five patients with refractory chronic chest cancer pain were selected randomly and prospectively from the pain clinic of both the National Cancer Institute of Cairo University and Aswan University, after taken an informed written consent from the patient. These patients were selected according to the following criteria:

#### **Inclusion criteria**

1. Patient Age >18 years with refractory chronic chest pain
2. VAS (Visual Analogue Score) > or 5
3. Distribution of pain between dermatomes T2 - T8
4. Refractory chronic pain in the thoracic region > or of 3 months, and not responding to analgesics and adjuvants.

Multiple evidence-based biomedical therapies used in a clinically appropriate and

acceptable fashion have failed to reach treatment goals that may include adequate pain reduction and/or improvement in daily functioning or have resulted in intolerable adverse effects.

#### **Exclusion criteria:**

1. Refusal of the patient
2. Uncooperative patient or patient unable to lie prone
3. Psycho-mental disorders
4. Pregnancy
5. Allergy to medication (local anesthetic, contrast material, glucocorticoids)
6. Intraspinal -intramedullary tumor (especially in mesothelioma after excision of intramedullary extension by MRI or Ct contrast)
7. Evidence of neurological deficit
8. Severe cardio-respiratory compromise
9. Local or systemic infection
10. Coagulopathy (uncorrectable)

#### **Technique**

#### **PRE-PROCEDURAL PREPARATIONS and EQUIPMENTS:**

- Reassuring the patient and explaining the procedure and possible complications in a simple easily understood manner.
- Scales used to assess the patient were explained to the patient before the procedure, and they were trained on how to use them.
- Check pre-operative investigations such as; CBC (complete blood count), and coagulation profile.
- Detailed history should be taken
- Clinical examination to exclude any sensory or motor deficits
- Localization of the affected dermatomes (T2-T8); by checking local rib tenderness.
- Prepared equipment for the procedure which included:
  - C-arm real time fluoroscopy
  - Radiofrequency generator• Neurotherm®.NTI 100 (Generator which is manufactured by Neuro-Therm INC-Ma, 1949, USA, supplied by Morgan IAT LTD, GU 323 QA, U.K)
  - Radiofrequency needle (NeuroTherm model)• 20G, 100mm, 10 mm active T.P
  - Omnipaque dye (non-ionic contrast dye)• in 3 cc syringe
  - Sterile skin preparations used for draping before the procedure.
- Intra-venous (18G) peripheral cannula should be inserted
- Apply ASA standard monitoring, such as• ECG, Pulse oximetry, NIBP, should be applied just before

and during the procedure in the intervention room.

- Apply O2 nasal cannula at 3L/min
- Conscious sedation was done by using midazolam 0.04 mg/kg + fentanyl 0.5 mc/kg, and for the period during TRF application: propofol shots 20:30mg given.
- The RF needle was introduced to the targeted dermatome (between T2-T8) using a tunnel vision technique under C-arm fluoroscopic machine guidance. Then, 0.2 to 0.4 ml of the non-ionized contrast dye (omnipaque TM) is injected to delineate the dorsal selected nerve root, intercostals nerve path and the epidural spread. This is confirmed at A-P and lateral views. Before TRF lesioning 2 ml prepared of lidocaine 2% + 2mg of betamethasone sodium phosphate and 5 mg betamethasone dipropionate, in a 10 cc syringe is prepared at each level. After confirming the needles positions by both sensory and motor stimulation, two lesions are done each at 80° for 90 seconds, both supero-medial and infero-medial directions to ensure thermal destruction of the DRG.

**Evaluation parameters**

Each patient's pain was evaluated by the following assessments:

**1. Visual Analogue Scale:**

Patients are asked to choose a number that relates to their pain intensity: 0 at the left = no pain and 10 at the right end = the worst possible pain, (1-3) = mild, (4-7) = moderate, (8-10) = severe. Patients point the number on the scale which represents their pain level.

**2. Visual Analogue Scale (VAS) Reduction**

*VAS reduction, measures functional improvement, were:*

1. VAS score improvement > 75% was considered a successful block with excellent response.
2. VAS score improvement 50-75% was considered a successful block with good response.
3. VAS score improvement 25-50% was considered an unsuccessful block with fair response.
4. VAS score improvement < 25% was considered an unsuccessful block with poor response.

**3. Quality of Life Scale**

Quality of life scale (QOLS), a measure of function for people with pain. The scale ranges from 0 (stay in bed all day and feel hopeless and helpless about life) to 10 (normal daily activities each day). For simplicity the QOLS is classified into four groups, as poor QOLS = 0-2, fair QOLS =3-4, good QOLS = 5-7, excellent QOLS =8-10.

**4. ECOG Performance Status**

To conduct clinical trials for treatment of cancer in a consistent manner, many participating hospitals, cancer centers, and clinics require the use

of standard criteria for measuring how the disease impacts a patient's daily living abilities (known to physicians and researchers as a patient's performance status). The ECOG scale of Performance Status is one such measurement. It describes a patients level of function in terms of ability to care for themselves, daily activity, and physical ability (walking, working ,etc.) <sup>(12)</sup>.

ECOG	Description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
5	Dead

**6. Patient Satisfaction**

Every patient was asked two questions, post-interventional (after 1 week, 1 month, and after 3 months).The two questions were "If you could go back in time, would you like to repeat the procedure?" and "Would you recommend the same procedure to a family member or friend?" Answers were classified as: certainly would repeat/recommend, probably would repeat/recommend, probably would not repeat/recommend, and certainly would not repeat/recommend <sup>(13)</sup>.

**Duration of Treatment and Follow Up:**

Each patient was assessed pre-interventional and post-interventional; after 1 week, 1 month and after 3 months for comparison (Pre-interventional state versus Post-interventional state) based on the following:

**Data Collection and Interpretation:**

**1. Demographic Data (Pre-Interventional data):**

- a. Age
- b. Gender
- c. Basic character of pain:
  - i. Type of pain:

- Neuropathic burning
- Neuropathic lancinating, tingling
- Neuropathic tingling
- Neuropathic tingling, electric
- Neuropathic tingling, numbness
- Nociceptive dull ache
- ii. Side of pain:
  - Left
  - Right
- iii. Cause of pain:
  - Adenocarcinoma
  - Bronchogenic
  - Mesothelioma
  - Non-small cell carcinoma
  - Post Thoracotomy Adenocarcinoma
  - Post Thoracotomy Mesothelioma
  - Small cell carcinoma
- iv. Number of affected dermatomes
- d. Basic drug consumption:
  - i. Oxycodone
  - ii. Pregabalin
  - iii. Amitriptyline
- e. VAS
- f. ECOG Performance Scale

g. Quality of Life Scale

## **2. Evaluation Data:**

The following data was collected, by a junior pain resident who was blinded to the study.

### **A. Primary Outcome**

- a. Pain assessment using VAS (Visual Analogue Scale)
- b. VAS Reduction (Functional Improvement- Post-interventional)
- c. Dose of opioids and adjuvant medications consumption:
  - i. Oxycodone
  - ii. Pregabalin
  - iii. Amitriptyline

### **B. Secondary Outcome**

- a. Patient Satisfaction
- b. ECOG Performance Status (Functional Activity)
- c. Quality of Life Scale (QOLS)

### **C. Side effects and Complications (Post-Interventional data):**

- a. Numbness
- b. Dorsal back pain
- c. Neuritis
- d. Infection
- e. Pneumothorax
- f. Motor affection
- g. Differentiation pain

**RESULTS**

In this study sixty-five patients were selected from the pain clinics of the National Cancer Institute, Cairo University and Aswan University. But only sixty-two patients completed the follow-up system until the end; which was 3 months post-interventional. Based on the data collected the following results were obtained.

**Table 1- Patient Demographic Characteristics:**

	Mean	Standard Deviation	Median	Minimum	Maximum
<b>Age</b>	54.16	7.45	56.00	40.00	64.00

		Count	%
<b>age groups</b>	<b>&gt;50 years</b>	39	62.9%
	<b>&lt;50 years</b>	23	37.1%
<b>Sex</b>	<b>Male</b>	36	58.1%
	<b>Female</b>	26	41.9%
<b>Type of pain</b>	<b>Neuropathic burning</b>	6	9.7%
	<b>Neuropathic lancinating, tingling</b>	4	6.5%
	<b>Neuropathic tingling</b>	4	6.5%
	<b>Neuropathic tingling, electric</b>	8	12.9%
	<b>Neuropathic tingling, numbness</b>	4	6.5%
	<b>Nociceptive dull aching</b>	36	58.1%
<b>Cause of pain</b>	<b>Adenocarcinoma</b>	9	14.5%
	<b>Bronchogenic</b>	4	6.5%
	<b>Mesotheloma</b>	35	56.5%
	<b>Non-small cell carcinoma</b>	1	1.6%
	<b>Post-Thoracotomy Mesotheloma</b>	1	1.6%
	<b>Post-Thoracotomy Adenocarcinoma</b>	4	6.5%
	<b>Small cell Carcinoma</b>	6	9.7%
<b>Number of affected dermatomes</b>	<b>Breast Cancer</b>	2	3.2%
	<b>1 dermatome</b>	4	6.5%
	<b>2 dermatomes</b>	16	25.8%
	<b>3 dermatomes</b>	24	38.7%
	<b>4 dermatomes</b>	18	29.0%

Based on the data above the greater part of our patients were in the age group above 50 years old, males with 3 or 4 dermatomes affected.

**Table 2- ECOG Performance Scale:**

	Mean	Standard Deviation	Median	Minimum	Maximum	P value compared to before
<b>ECOG scale before</b>	3.58	.50	4.00	3.00	4.00	---
<b>ECOG scale after 1 week</b>	1.42	.50	1.00	1.00	2.00	<0.001
<b>ECOG scale after 1 month</b>	1.29	.46	1.00	1.00	2.00	<0.001
<b>ECOG scale after 3 months</b>	1.52	.50	2.00	1.00	2.00	<0.001

	Mean	Standard Deviation	Median	Minimum	Maximum
<b>reduction ECOG after 1 week</b>	59.81	14.67	66.67	33.33	75.00
<b>reduction ECOG after 1 month</b>	63.17	14.44	66.67	33.33	75.00
<b>reduction ECOG after 3 months</b>	57.12	14.85	50.00	33.33	75.00

The ECOG performance status showed that there was an improvement in functional state of the patients throughout the follow up post-interventional.

**Table 3- Quality of Life Scale:**

	Mean	Standard Deviation	Median	Minimum	Maximum	P value compared to before
<b>QOLS before</b>	1.32	1.11	1.00	.00	3.00	---
<b>QOLS after 1 week</b>	7.79	1.03	8.00	6.00	10.00	<0.001
<b>QOLS after 1 month</b>	8.53	1.14	8.50	7.00	10.00	<0.001
<b>QOLS after 3 months</b>	6.98	.88	7.00	6.00	9.00	<0.001

	QOLS before		QOLS after 1 week		QOLS after 1 month		QOLS after 3 months	
	Count	%	Count	%	Count	%	Count	%
<b>Poor</b>	50	80.6%	0	.0%	0	.0%	0	.0%
<b>Fair</b>	12	19.4%	0	.0%	0	.0%	0	.0%
<b>Good</b>	0	.0%	28	45.2%	15	24.2%	47	75.8%
<b>Excellent</b>	0	.0%	34	54.8%	47	75.8%	15	24.2%

According to the above results of the QOLS, showed a most significant improvement was after 1 month, but overall there was an improvement in QOLS post-interventional throughout the follow up.

**Table 4- Patient Satisfaction**

		Count	%
<b>If you could go back in time, would you</b>	<b>certainly would</b>	19	30.6%
	<b>probably would</b>	34	54.8%
	<b>probably would not</b>	8	12.9%
	<b>certainly would not</b>	1	1.6%
<b>Would you recommend the same</b>	<b>certainly would</b>	16	25.8%
	<b>probably would</b>	35	56.5%
	<b>probably would not</b>	9	14.5%
	<b>certainly would not</b>	2	3.2%

Regarding patient satisfaction; with the first question "If you could go back in time, would you like to repeat the procedure?" 30.6% certainly would repeat it, 54.8% probably would, and 12.9 % probably would not while only 1.6% certainly would not repeat this procedure. While with the second question "Would you

recommend the same procedure to a family member or friend?" 25.8% certainly would recommend it, 56.5% probably would, 14.5% probably would not and only 3.2% certainly would not recommend it.

## DISCUSSION

Cancer and pain are clinical entities closely associated. Recent reviews suggest there to be a prevalence of pain in about 51% of cancer patients regardless of type and stage. This prevalence increases with the type of tumor; head and neck, lung, breast cancers are the ones with higher prevalence, and with the staging; advanced, metastatic or terminal reaching a 66% of cases<sup>(14)</sup>. There are 2 modalities of intra-spinal procedures that are available to manage drug resistant pain 2ry to cancer, either continuous spinal drug delivery or spinal neurolytic procedures. Drugs are injected directly into the spinal canal thus achieving more potent analgesic effects with minimal doses. Also, the effect may be restricted to few dermatomes, therefore sparing the possible side-effects to a targeted anatomical area. However, it is associated with uncontrolled intra-spinal spread and high risk for neurological deficits which limit its clinical use<sup>(15)</sup>. In our study we decided to test both the efficacy and safety of thermocoagulative ablation of thoracic dorsal root ganglia for pain control in this category of patients. Chest pain in cancer patients can be multifactorial, visceral, nociceptive, or neuropathic. Our study has shown that thermal radiofrequency lesioning of thoracic dorsal root ganglia was effective in relief of pain since there was a significant reduction of mean VAS values after the procedure in all the follow up measurements. Thermal radiofrequency ablation of the dorsal root ganglia (TRF-DRG) causes thermocoagulative necrosis of the nerve fibers that denature the nerves to interrupt noxious input. It was suggested that even long term central sensitization can be reversed quickly The use of TRF for managing non-malignant pain is becoming of controversy due to its potential hazards such as neuritis, deafferentation pain and motor deficits but it has been postulated that TRF therapeutic effect was attained through partial nerve lesion<sup>(16)</sup>. In the study decided to select thermal and not pulsed radiofrequency (PRF), firstly, as the onset of beneficial effect is delayed in PRF for 3 to 4 weeks<sup>(17)</sup>, which could not be waited for in cancer patients with unbearable pain. Second, PRF has been associated with only short term pain relief<sup>(18)</sup>. With regards to our study, we found that with effective pain relief there was a significant reduction of mean VAS values; which means that there was functional improvement, in all the post-interventional follow ups. Also with regards to the ECOG performance status from the results of our study we found that there was an improvement in the functional state of the patients throughout the follow-up post-intervention. In addition to the ECOG improvement there was also

significant improvement in the QOL (Quality of Life) results, which was due to the pain relief. This corresponds to results of **Yinghui et al.**<sup>(19)</sup> who documented that there is a significant improvement in QOL after the reduction of pain. The quality of life is currently considered as a primary end point of the treatment and the clinical trials planning<sup>(20-23)</sup>. Based on such considerations; one could argue that the pain relief could significantly improve the overall quality of life or provide a satisfactory response to the affected daily activities. Similarly, it was noted that the pain had caused a decreased appetite and emotional disturbances in more than 70% of the patients. A study which was done by **Glover et al.**<sup>(21)</sup> on the mood states of oncology patients, showed similar findings as compared to the pain free chest cancer patients, the chest cancer patients with pain had significantly higher levels of anxiety, depression, and anger<sup>(21)</sup>. In addition, more than one \ third of the patients complained that the pain had affected their relationships with other people and that the pain had also affected their visual activities. The difficulty in controlling neuropathic pain with medical treatment even when following the protocol recommendations is a common problem. Therefore the development of other protocols for the use of minimally invasive pain relief interventions becomes a must. These interventions can be considered invasive procedures involving the delivery of drugs into the targeted areas, or ablation of targeted nerves for the control of pain<sup>(22)</sup>. Interventional management of cancer pain does not replace other modalities but can be an alternative to improve pain control and allow for reduction in the number of systemic medication or dose consumption and their side-effects. There were unfavorable side-effects from the use of oral or parenteral opioids<sup>(8)</sup>. Based on our study, drug consumption doses of pregabalin, oxycodone and amitriptyline showed a maximum reduction after 1 month with a slight increase in the following follow up which was 3 months post-interventional. However, this slight increase in dose still remained overall lower than pre-interventional doses. But it is important to note that, regarding the reduction, our results prove that the reduction is considered insignificant since our *P* values turned out to be  $> 0.05$ , therefore insignificant. Regarding the complications post-interventional, our patients were observed and monitored before discharge. And before their discharge the patients were informed of the warning signs, or red flags to look for and report such as: difficulty of breathing for pneumothorax, high fever, severe pain, or motor deficit. Based on our 62 patients the only complications reported and found were numbness and



neuritis in 7 out of the 62. Other complications were not reported or found e.g. pneumothorax, infection, differential pain and dorsal back pain. With regards to our study, patient satisfaction was found to be, with the first question "If you could go back in time, would you like to repeat the procedure?" 30.6% certainly would repeat it, 54.8% probably would, and 12.9% probably would not while only 1.6% certainly would not repeat this procedure. While, with the second question "Would you recommend the same procedure to a family member or friend?" 25.8% certainly would recommend it, 56.5% probably would, 14.5% probably would not and only 3.2% certainly would not recommend it.

## CONCLUSION

We concluded that thermal radiofrequency ablation is considered an alternative for treating refractory chronic chest cancer pain of several types and causes. This is because of its efficacy, safety and ease of use, patient's quality of life of was largely affected.

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