Original Article

Running Title: RFA & alcohol vs alcohol alone for celiac ganglion block

Received: November 13, 2024; Accepted: February 15, 2025

Comparing the Effect of RF Ablation and Alcohol Injection vs Alcohol Injection Alone on Celiac Ganglion Block in Patients with Primary and Metastatic Malignancy Involving the Celiac Ganglion: A Randomized Clinical Trial

Mohammad Reza Babaei[*], MD, Mohammad Amin Akbarnezhad[**], MD, Vahid Kaveh[***], MD Mohammad-Ali Mohammadi-Vajari[*♦], MD, Atefe Shafiee[****], MD, Ghazale Tefagh[*****], MD

[*]*Department of interventional radiology, Firouzgar hospital, Iran university of medical sciences, Tehran, Iran*
[**]*Department of radiology, Imam Reza hospital, Army University of medical science*
[***]*Medical Oncology and Hematology, Iran University of Medical Sciences, Tehran, Iran*
[****]*Rajaie Cardiovascular Medical and Research center, School of Medicine, Iran University of Medical Sciences*
[*****]*Department of Radiology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran*

♦ **Correspondence:**
Mohammad-Ali Mohammadi-Vajari, MD, Radiologist,
Department of interventional radiology, Firouzgar hospital, Iran university of medical sciences, Tehran, Iran.
Fax Number: 02164351021
Email: malimv71@yahoo.com

Abstract

Background: Pain is one of the most common symptoms in cancer patients, and celiac block has been introduced as an alternative for patients who are not satisfied with narcotic treatment. The present study aimed to compare the effects of Radiofrequency ablation (RFA) and alcohol injection against alcohol injection alone on celiac ganglion block in patients with primary and metastatic malignancy involving the celiac ganglion.

Methods: In this randomized, single-blind clinical trial, primary and metastatic malignancy patients with unresponsive pain were investigated. Group A only received 90% alcohol bilaterally. Group B received RFA, and alcohol injection. Both methods were performed under Computed Tomography (CT) guidance. Then, patients were followed up for 6 months. All

analyses were done with SPSS version 24 software. Spearman's nonparametric rank, Chi-square, and multivariate analysis were simultaneously used to analyze correlations, compare categorical variables, and analyze variables, respectively. A *P*-value <0.05 was considered to be statistically significant.

Results: The study participants were 42 patients with a mean age of 64.1 +/- 4.87. Comparing alcohol injection with and without RFA on celiac ganglion block in patients with primary and metastatic malignancy involving the celiac ganglion showed that there is not any significant difference between these two methods (P-value>0.05). Finally, 90.48% of patients in both groups showed at least partial response.

Conclusions: We showed that alcohol injection alone can be an appropriate technique for celiac ganglion block in patients with primary and metastatic malignancy involving celiac ganglion, with no significant difference between alcohol injection alone vs RFA & alcohol injection.

Keywords: Nerve block, Radiofrequency ablation, Palliative Care, Chemoablation

Introduction

Pain is one of the major and most important stressors in cancer patients. Despite the great advances of pharmacology in the field of Analgesics, the prevalence of pain in affected patients is reported to be 39% after completion of the treatment, 55% while receiving anticancer drugs, and 66% in metastatic stages and end stage[1]. Currently, opioid narcotics and alkaloid analgesics are used in Iran. But all over the world, celiac plexus block is the standard method in patients who are not satisfied with opioid narcotics[2, 3, 4].

Celiac ganglion ablation can be performed in several ways: Chemoablation, which uses particular chemicals and aims at neurolysis of nerve cells of celiac ganglion. 70-90% alcohol and phenol are among the chemicals used in this technique. Thermoablation, which uses heat produced by a variety of methods for cell proteolysis which leads to the destruction of the nerve cells of the celiac ganglion. Thermoablation includes Macrowave Ablation, Radiofrequency Ablation (RFA), Laser Ablation, Cryoablation and Electro vaporization methods[5, 6].

RFA and alcohol injection to celiac chain both are minimally invasive methods with slight side effects and are more effective in pain relief and palliative therapy than opioids or placebo for patients with malignant involvement. The effectiveness of either treatment alone or in combination has been proven in earlier studies[7,8].

The combination of these two treatments has been suggested to be more effective than each treatment alone. Accordingly, the purpose of our study was to investigate the effectiveness of combination treatment and to compare it with alcohol injection alone quantitatively and qualitatively[9].

The complications of celiac ganglion block are rare[8, 9, 10]. Common complications include diarrhea, postural hypotension, and transient back pain; however, pneumothorax is an exceedingly rare complication. Adverse side effects such as gastrointestinal side effects are said to be

less common with celiac plexus cryoablation compared with ethanol[11].

Numerous studies have been conducted around the world exploring the efficacy of different methods of celiac block in pain management. However, according to our knowledge, similar study has not been conducted in Iran.

We designed this study to compare the effects of RF (Radiofrequency) ablation in combination with alcohol injection with alcohol injection alone on the celiac ganglion block in patients with primary and metastatic malignancy involving the celiac ganglion.

Material and Methods

This was a randomized single-blind clinical trial study among patients with primary and metastatic malignancy involving celiac ganglion. The study population included patients with primary and metastatic malignancy involving celiac ganglion who had unresponsive or minimally responsive pain.

The inclusion criteria were: patients over 18 years of age with typical abdominal and epigastric pain spreading to the back and concurrent unresectable advanced malignant or metastatic cancer, who chose this intervention after consultation and consent and whose pain was not controlled by analgesics and narcotics. All of the study participants had severe pain prior to treatment.

The exclusion criteria were: patients who did not consent with the procedure, patients under 18 years of age, patients satisfied with opioid treatment who have accepted its side effects, patients with coagulopathy with platelet count below 50000 and/or INR (International Normalized Ratio) >1.6, pregnant patients with low O2 saturation and patients on anticoagulants.

The sample size was calculated using G*power software and based on previous articles, with alpha error=0.05, beta error=0.95, effect size (d)=0.7, and n=42. Each group consisted of twenty-one patients.

The study proposal was approved by the Ethics Committee with the ethics code number (IR.IUMS.FMD.REC.1402.162). Data confidentiality was maintained. The study adhered to the principles of the declaration of Helsinki.

The census sampling method was used and sampling was continued until predetermined sample size reached. All required information had been given to patients and patients were enrolled into the study only if they were willing to sign the consent form.

The patients were divided into two groups using the random number table. In group A, ganglion block was done with alcohol injection only. In group B, ganglion block was done with alcohol injection with RF ablation. The researcher conducting the clinical trial and the analyst were aware of the groups, while the patients were not. The consort diagram of patient allocation to the two groups is shown in figure 1.

Both alcohol ablation and RF ablation can be performed through transcrural and retrocrural approaches, depending on the availability of ganglion, patient's weight, and patient's anatomical condition, and the procedure was performed under CT scan guidance. In the transcrural approach, celiac nerve ganglions directly underwent neurolysis, but in the retrocrural approach splanchnic network neurons (more peripheral bundles forming the celiac ganglion) underwent neurolysis.

In the alcohol injection method, we used 70-90% alcohol for neurolysis. The doses were 0.5 to 1 cc per kilogram (maximum dose 40 cc and 25-30 cc in patients with lower body weight) divided in 5cc syringes, and the injection was done slowly over 10 minutes. A total of 25 or 15 cc alcohol was injected bilaterally through transcrural or retrocrural approaches, respectively.

In the RF method, an electrode with a total length of 10-15 cm was used, and the active part of the electrode (active tip with different lengths (0.5, 1, 1.5, 2, 5 cm)) was inserted into the celiac ganglion of splanchnic nerve network and neurolysis of

nerve cells occurs as a result of the heating effect.

Before RF ablation, all patients had IV access established and vital signs were monitored throughout the procedure, including oxygen saturation, blood pressure, and heart rate. Sedation was achieved using ketamine and propofol. The patients were placed in the prone position on the CT scan table. T12 vertebral body was identified and marked as a landmark using CT Scan guide, and a G-14 stylet with was inserted with an approximate angle of 35 to 45 degrees via preferred technique and location (transcrural or retrocrural) (Figure 2). Then, the stylet was removed, and a 150 mm 20-G electrode was inserted into the nerve ganglion through puncture site. Before RF neurolysis, a motor test was performed using 2 Hz (up to 2V), and a sensory test was performed using 50-100 Hz (up to 1V) to ensure the correct placement of the electrode. In the sensory stimulation, an unpleasant feeling in the epigastrium will be the correct response. Motor stimulation is performed to ensure that the intercostal muscles do not contract. If both of these responses were satisfactory, then neurolysis was performed with 300000 MHz (applying a temperature of 80°C for 60 seconds to neural networks). The patients were closely monitored for 4-6 hours after surgery.

Group A only received 90% alcohol bilaterally (70% alcohol is enough for neurolysis) with a dose of 0.5 cc per kilogram (maximum dose of 40 cc). Group B received alcohol injection in combination with RF ablation at 90°C for 3 min each area.

After the procedure, the patients were hospitalized and monitored for 12 hours. Then, a pain level related-satisfaction checklist was completed for each patient. We asked each patient to rank their satisfaction level from 0 to 10. The patients were followed up at one week, four weeks, and six months. In this study, relevant information was recorded in pre-designed checklists (Table 1).

Finally, all data were entered into the SPSS 24 software and analyzed with appropriate statistical tests. For qualitative variables, frequencies and frequency percentages were calculated. For quantitative variables, the mean and standard deviations were calculated. Spearman's nonparametric rank was used to analysis the correlations. Chi-square test was used to compare categorical variables. Multivariate analysis was also used to analysis the variables simultaneously. A *P*-value<0.05 was considered to be statistically significance.

Results

Aa total number of 16 men (42%) and 26 women (64%) participated in this study. Each group consisted of 8 men (28.09) and 13 women (61.9). The mean age of the patients was 64.1 ± 4.87. The mean age of the participants in the combination therapy and alcohol injection group were 62.8±13.7 and 65.7±12.1, respectively. Since only patients with severe pain were enrolled in the study, we used post-treatment pain scores to compare the efficacy of the two treatment methods.

Given the patients' level of satisfaction measured by pain score in the combination therapy group, four patients (19.04%) reported score 0 (no pain and complete response), one patient (4.7%) reported score 1-3(mild pain), 14 patients (66.6%) reported scores 4-6 (moderate pin) and 2 patients (9.5%) had scores 7-10 which indicated very low or no response to treatment and severe pain. The other group of patients treated only by alcohol injection, five (23.8%), two (9.5%), 12(57.1%) and two (9.5%) reported scores 0, 1-3, 4-6 and 7-10, respectively. The statistical analyses showed no significant difference between these two methods in reducing patients' level of pain (*P*-value>0.05) (Table 2).

None of the patients who reported mild pain in either group needed re-treatment. However, among the 26 patients in both groups who reported moderate pain after treatment, 8 patients (30.77%) needed retreatment and repeat ablation due to

partial response to their first course of treatment.

All of the patients with scores between 4 to 6, received opioid doses lower than their previous therapeutic dose, indicative of partial response (Table 3).

Regarding complications most patients in both groups (36 out of 42), reported transient post-intervention back pain. No major complication was reported by any of the patients.

Discussion

In this study, we showed similar efficacy of both RF ablation in combination with alcohol injection on the celiac ganglion block and alcohol injection alone in patients with primary and metastatic malignancy involving celiac ganglion, in reducing patients' pain. We also showed that even patients with persistent pain after treatment, needed lower dose of opioid which indicates partial response.

We showed similar efficacy of the two treatment methods, with 90.48% of patients showing at least partial response in both groups. Ji Young Bang et al., (2018) conducted a study to determine the effects of Endoscopic Ultrasound-guided Celiac Plexus Neurolysis (EUS-CPN) and EUS-RFA methods, and despite better results in RFA group, high recovery rates were achieved in both group[7]. However, a review study has proposed more longevity of effects of RFA on pain control in comparison with chemical neurolysis[12]. One of the reasons for similar efficacy of alcohol ablation alone in comparison with combination therapy in this study could be our methods of chemical neurolysis. We injected alcohol bilaterally which may have better results in comparison with central injection method since bilateral injection has been proposed to be slightly more prone to complications[13].

In a similar study, Gao et al. evaluated the efficacy of celiac block using bupivacaine and ethanol injection in patients with pancreatic cancer. Their results showed significant pain reduction and improvement of quality of life in the celiac neurolysis

group compared with control group[14]. Celiac plexus neurolysis with alcohol injection alone has also been reported to be effective in reducing patients' pain in both primary and metastatic cancers involving celiac ganglion[15]. In our study, although 26 patients showed partial response and therefore needed continuation of opioid treatment, their opioid dose post neurolysis was lower than their baseline therapeutic dose in both alcohol injection and combination therapy groups.

Therefore, the results of our study show that any of the aforementioned methods (alcohol injection or RFA) or a combination of both can reduce pain. Also, depending on the conditions and availability of these techniques, we could consider either of them for our patients.

None of the patient reported any major complication following the treatment in either groups. This could be due to the fact that all of the interventions were performed by one experienced intervention radiologist. Retrospective studies comparing efficacy and complication rates among different interventionalist can be more helpful to evaluate complication rates more thoroughly.

One of the main limitations of these study is that the burden of biopsychosocial factors has not been fully evaluated. Future studies should use larger sample sizes to better determine the diagnostic value of these findings. Also, paying attention to a wider range of symptoms, including social support and interpersonal communications, is important to assess the correlation between pain relief and mood improvements with improvement in psychosocial experiences.

Conclusion

We showed that alcohol injection alone can be an appropriate technique for celiac ganglion block and pain relief in patients with primary and metastatic malignancy involving celiac ganglion, with no significant difference between alcohol injection alone vs RFA & alcohol injection.

Authors' Contributions:

MR.B: Study design and conception, data analysis and interpretation, critical reviewing
MA.A: Drafting and reviewing the manuscript, data gathering and analysis
V.K: Study design, drafting and reviewing the manuscript
MA.MV: Drafting and reviewing the manuscript, data analysis and interpretation
A.SH: Data gathering, drafting, data analysis and interpretation
GH.T: Drafting and reviewing the manuscript, data analysis and interpretation
All authors read and approved the final manuscript version and agree with all parts of the work in ensuring that any queries about the accuracy or integrity of any component of the work are appropriately investigated and handled.

Funding: None.

Conflict of interests: The authors declare no conflict of interests.

Refrences

1. Snijders RAH, Brom L, Theunissen M, van den Beuken-van Everdingen MHJ. Update on Prevalence of Pain in Patients with Cancer 2022: A Systematic Literature Review and Meta-Analysis. Cancers (Basel). 2023 Jan 18;15(3):591. doi: 10.3390/cancers15030591. PMID: 36765547; PMCID: PMC9913127.

2. Al-Jumah R, Urits I, Viswanath O, Kaye AD, Hasoon J. Radiofrequency Ablation and Alcohol Neurolysis of the Splanchnic Nerves for a Patient With Abdominal Pain From Pancreatic Cancer. Cureus. 2020 Oct 1;12(10):e10758. doi: 10.7759/cureus.10758. PMID: 33150109; PMCID: PMC7603893.

3. Abdel-Ghaffar ME, Ismail SA, Ismail RA, Abdelrahman MM, Abuelnaga ME. Comparison between two volumes of 70% alcohol in single injection ultrasound-guided celiac plexus neurolysis: A randomized controlled trial. Pain Physician. 2022 May;25(3):293-303 PMID: 35652769.

4. Vahedian J, Babaei MR, Mehrjardi AZ, Almasi A, Ahmadi SAY, Hadizadeh O. Long-term survival of a patient with locally advanced hilar cholangiocarcinoma (Klatskin tumor): a case report and review on high level evidence. Archive of Oncology. 2019 June 25(2):25-7. doi: 10.2298/aoo190220004v .

5. Prologo JD, Patel I, Buethe J, Bohnert N. Ablation zones and weight-bearing bones: points of caution for the palliative interventionalist. Journal of Vascular and Interventional Radiology. 2014 May;25(5):769-775.e2. doi: 10.1016/j.jvir.2014.01.033. PMID: 24745905

6. Chary A, Edalat F, editors. Celiac Plexus Cryoneurolysis. Seminars in Interventional Radiology; 2022: Thieme

Medical Publishers, Inc 2022 Jun 30;39(2):138-141. doi: 10.1055/s-0042-1745762. PMID: 35781989. PMCID: PMC9246493

7. Bang JY, Sutton B, Hawes RH, Varadarajulu SJGE. EUS-guided celiac ganglion radiofrequency ablation versus celiac plexus neurolysis for palliation of pain in pancreatic cancer: a randomized controlled trial (with videos). 2019 Jan;89(1):58-66.e3. DOI: 10.1016/j.gie.2018.08.005. PMID: 30120957

8. Cornman-Homonoff J, Holzwanger DJ, Lee KS, Madoff DC, Li D, editors. Celiac plexus block and neurolysis in the management of chronic upper abdominal pain. Seminars in interventional radiology; 2017 Dec;34(4):376-386. doi: 10.1055/s-0037-1608861. PMID: 29249862 PMCID: PMC5730442

9. Koyyalagunta D, Engle MP, Yu J, Feng L, Novy DMJPP. The effectiveness of alcohol versus phenol based splanchnic nerve neurolysis for the treatment of intra-abdominal cancer pain. 2016 May;19(4):281-92. doi: 10.36076/ppj/2019.19.281 PMID: 27228515

10. Gunduz OH, Kenis-Coskun O. Ganglion blocks as a treatment of pain: current perspectives. Journal of pain research. 2017 Dec 14:10:2815-2826. doi: 10.2147/JPR.S134775 PMID: 29276402 PMCID: PMC5734237

11. Behbahani K, Chary A, Patel S, Mitchell JW, Fleishon H, Prologo JD. Percutaneous CT-guided cryoablation of the celiac plexus: a retrospective cohort comparison with ethanol. Journal of Vascular and Interventional Radiology. 2020 Aug;31(8):1216-1220. doi: 10.1016/j.jvir.2020.04.008 PMID: 32682710

12. Zacharias NA, Karri J, Garcia C, Lachman LK, Abd-Elsayed A. Interventional radiofrequency treatment for the sympathetic nervous system: a review article. Pain and therapy. 2021 Jun;10(1):115-141. doi: 10.1007/s40122-020-00227-8. PMID: 33433856 PMCID: PMC8119558

13. Yasuda I, Wang HP. Endoscopic ultrasound-guided celiac plexus block and neurolysis. Digestive Endoscopy. 2017 May;29(4):455-462. doi: 10.1111/den.12824. PMID: 28160344

14. Gao L, Yang Y-j, Xu H-y, Zhou J, Hong H, Wang Y-l, et al. A randomized clinical trial of nerve block to manage end-stage pancreatic cancerous pain. Tumor Biology. 2014 Mar;35(3):2297-301. doi: 10.1007/s13277-013-1304-z. PMID: 24163058

15. Agarwal A, Gautam A, Rastogi S, Malviya D, Das PK, Harjai M. Effect of celiac plexus neurolysis for pain relief in

patients with upper abdominal malignancy: a retrospective observational study and review of literature. Indian Journal of Palliative Care. 2020 Oct-Dec;26(4):512-517. doi: 10.4103/IJPC.IJPC_37_20. PMID: 33623314 PMCID: PMC7888415

Score	Definition
0	No Pain
1–3	Mild Pain (nagging, annoying, interfering little with ADLs)
4–6	Moderate Pain (interferes significantly with ADLs)
7–10	Severe Pain (disabling; unable to perform ADLs)

ADL: Activities of Daily Life

Table 1. Pain Scale measuring patient's pain intensity in a scale from 0 (no pain) to 10 (maximum pain)

Pain score	Definition	Alcohol and RF		Alcohol		Total		P value
		Number	%	Number	%	Number	%	
0	**No Pain**	4	19.05	5	23.81	9	21.43	
1-3	**Mild Pain (nagging, annoying, interfering little with ADLs)**	1	4.76	2	9.52	3	7.14	
4-6	**Moderate Pain (interferes significantly with ADLs)**	14	66.67	12	57.14	26	61.90	0.76
7-10	**Severe Pain (disabling; unable to perform ADLs)**	2	9.52	2	9.52	4	9.52	

RF: Radiofrequency

Table 2. Comparison of Satisfaction Level and Post treatment Pain Score between Alcohol Injection alone and Combination Therapy with both RF Ablation and Alcohol Injection

Pain Score	Number	Number (percent) needing retreatment
1-3 (mild)	3	0(0%)
4-6 (moderate)	26	8 (30.77%)

Table 3. Need for Re-treatment in patients with mild or moderate pain following the first treatment course

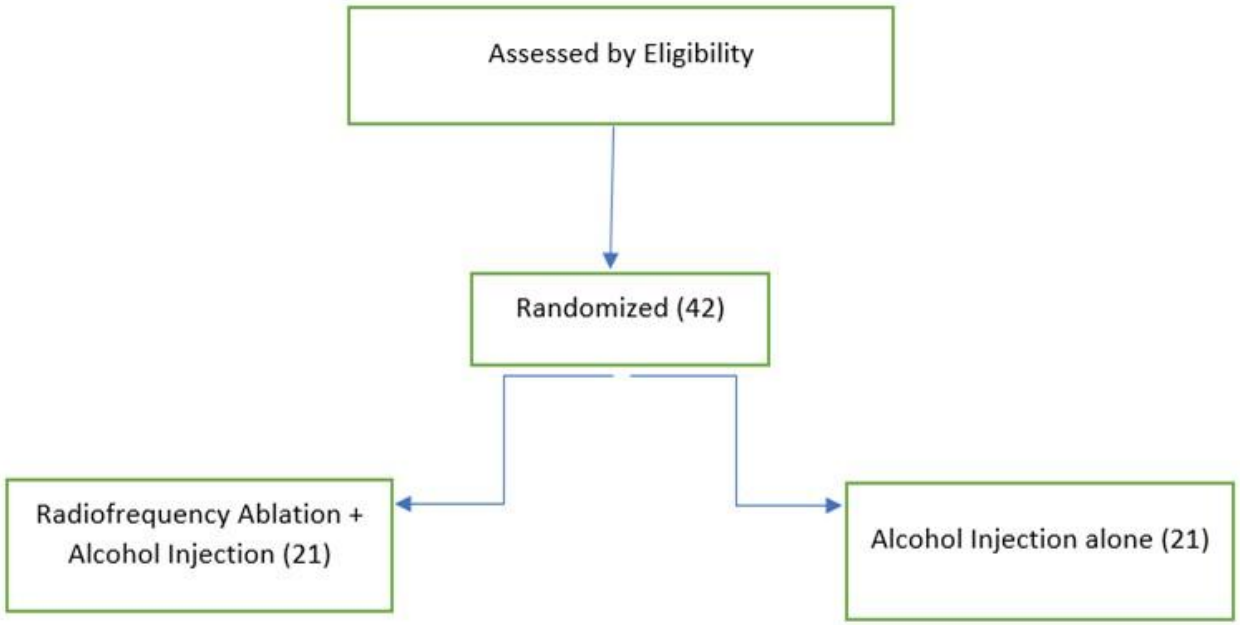

Figure 1. CONSORT diagram representing flow of participants through this randomized clinical trial

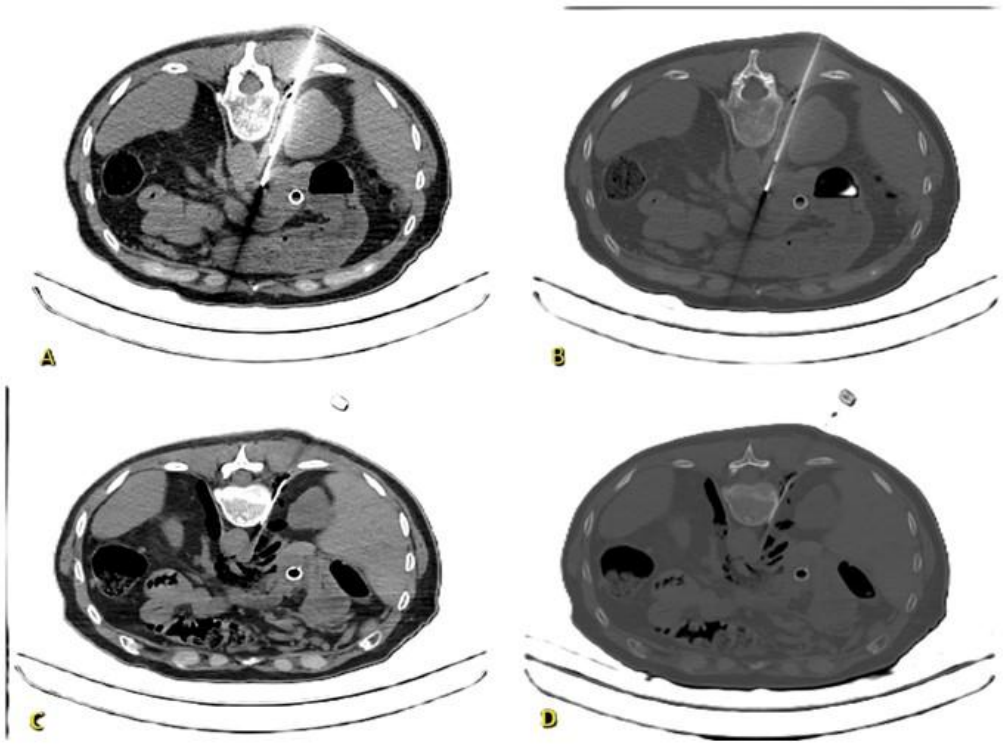

Figure 2. Images show transcrural approach (A; abdomen window and B; bone window) and retrocrural approach (C; abdomen window and D; bone window) for celiac ganglion block.