Interventional Nerve Blocks in Cancer Pain

Meghan McAlice, DO; Faten Ragaban, MD
VCU Hospice and Palliative Medicine Fellowship

Palliative Care Project ECHO | November 16, 2020

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The following Planning Committee and Presenting Faculty Members report having **no relevant financial relationships**:
Danielle Noreika, MD; Egidio Del Fabbro, MD; Diane Kane, LCSW; Tamara Orr, PhD, LCP, PMHNP-BC; Brian Cassel, PhD; Felicia Barner, RN; Candace Blades, JD, RN; Jason Callahan, M.Div.

No commercial or in-kind support was provided for this activity

Faten Ragaban, MD; Meghan McAlice, DO – nothing to disclose

Introductions

Our ECHO Team: Planning Committee

Clinical Leadership	Egidio Del Fabbro, MD VCU Palliative Care Chair and Program Director Danielle Noreika, MD, FACP, FAAHPM Medical Director/Fellowship Director VCU Palliative Care
Clinical Experts	Candace Blades, JD, RN – Advance Care Planning Coordinator Brian Cassel, PhD – Palliative Care Outcomes Research Jason Callahan, MDiv – Palliative Care Specialty Certified Felicia Hope Coley, RN – Nurse Navigator Diane Kane, LCSW – Palliative Care Specialty Certified Tamara Orr, PhD, LCP – Clinical Psychologist
Support Staff	Teri Dulong-Rae & Bhakti Dave, MPH – Program Managers David Collins, MHA – Telemedicine Practice Administrator Frank Green – IT Support

Case Presentation

Initial Presentation November 2018

- 58yo male presented to the emergency department after he was found on the ground in a trailer, soiled, malnourished
- Poor PO intake for a week prior to arrival due to limited access to food and water
- Generalized pain and weakness, nausea/vomiting, urinary incontinence
- Has been having foot pain related to diabetic neuropathy that caused him to stop working in 2016

Medical History

- PMH – depression, diabetes, HCV
- Surgical history – none
- Home medications – none
- Allergies – NKDA
- Family history – not reported

Social History

- + tobacco use when he can afford it, + EtOH last drink one week ago and history of withdrawals, + cocaine use in the last 3 months
- Polysubstance/alcohol started 2004
- He had been in and out of treatment facilities and had no contact with his daughter for over a year, left last treatment facility after 6-7 months because he was unable to keep up with the program
- No source of income, no insurance, no phone, no SNAP benefits, intermittently homeless for 2 years, has used shelters
- Hospitalized summer 2017 for 1 month and discharged to rehab, family indicated they could not allow him to live with them due to concern for substance abuse history

Physical Examination

- General: Alert and oriented, **cachectic, unkempt**.
- Eye: Pupils are equal, round and reactive to light, Extraocular movements are intact, Normal conjunctiva.
- HENT: Normocephalic, **poor dentition, mucous membranes dry**.
- Neck: Supple, No carotid bruit, No jugular venous distention.
- Respiratory: Lungs are clear to auscultation, Respirations are non-labored, Breath sounds are equal, moderately decreased breath sounds throughout.
- Cardiovascular: **Tachycardic**, No murmur, no edema, **thready pulses**
- Gastrointestinal: Soft, Non-distended, **endorses mild diffuse tenderness**, no rebound or guarding.
- Genitourinary: No lesions.
- Musculoskeletal: unable to fully perform due to patient's resistance to physical exam.
- Feet: Sensation intact.
- Integumentary: Warm, **Dry, flaking skin on chest and lower extremities; stool visualized on scrotum and penis**.
- Neurologic: Alert, Oriented to person and place**, disoriented to date and year**, patient unwilling to fully comply with neuro exam.
- Psychiatric: **flat affect; delayed verbal responses**.

Supportive Care Initial Visit 1/21/2019

- Reports feeling depressed, isolated
  - Taking escitalopram 10mg daily, mirtazapine 15mg qHS, Tylenol and oxycodone 5mg q6hr PRN, helping with pain, weight continues to decline
- Started developing chemotherapy-induced peripheral neuropathy predominantly in feet, switched to duloxetine 20mg daily
- Difficulty with SNF not administering opioids
- Referred to palliative radiation 3/29/2019

- ESAS
  - Pain 6/10
  - Fatigue 8/10
  - Nausea 5/10
  - Depression 2/10
  - Anxiety 2/10
  - Drowsiness 8/10
  - Appetite 9/10
  - Wellbeing 7/10
  - Shortness of Breath 0/10
  - Sleep 5/10

Supportive Care 2/28/2020

- Had not been seen in SCC since April 2019
- Has lost resources including ostomy supplies, food, money
- Has worsening wounds on his feet

- ESAS:
  - Pain 9/10
  - Fatigue 7/10
  - Nausea 4/10
  - Depression 10/10
  - Anxiety 10/10
  - Drowsiness 4/10
  - Shortness of Breath 4/10
  - Appetite 4/10
  - Well-being 4/10
  - Sleep 10/10
  - Financial distress 10/10
  - Spiritual distress 7/10
  - Sexual health 0/10

Disease course

- Multiple no-show appointments in oncology and supportive care in April and May 2020
- In June threatened with eviction from independent living due to concerns of going into people's rooms, drug use on premises
- Back in oncology clinic in July, had to take care of his family, was living on the streets, had lost his phone, wallet, and ID and had difficulty finding resources as a result, ran out of medications
- Moved to healing place in August, but had to move out as they would not allow controlled substances

Supportive Care Clinic 8/26/2020

- 10/10 diffuse abdominal pain, had partial improvement when he was taking oxycodone but reports difficulty taking it as most places would not allow controlled substances
- Concern being without stable housing and having opioids, declined opioid prescription

- ESAS:
  - Pain 10/10
  - Fatigue 7/10
  - Nausea 5/10
  - Depression 7/10
  - Anxiety 5/10
  - Drowsiness 7/10
  - Shortness of breath 6/10
  - Appetite 5/10
  - Well-being 5/10
  - Sleep 3/10
  - Financial distress 7/10
  - Spiritual distress 5/10
  - Sexual health 5/10

Let's Pause

- What questions do you have about the case thus far?
- Thoughts about what to offer for symptom management?
- Any ideas on psychosocial challenges and barriers?

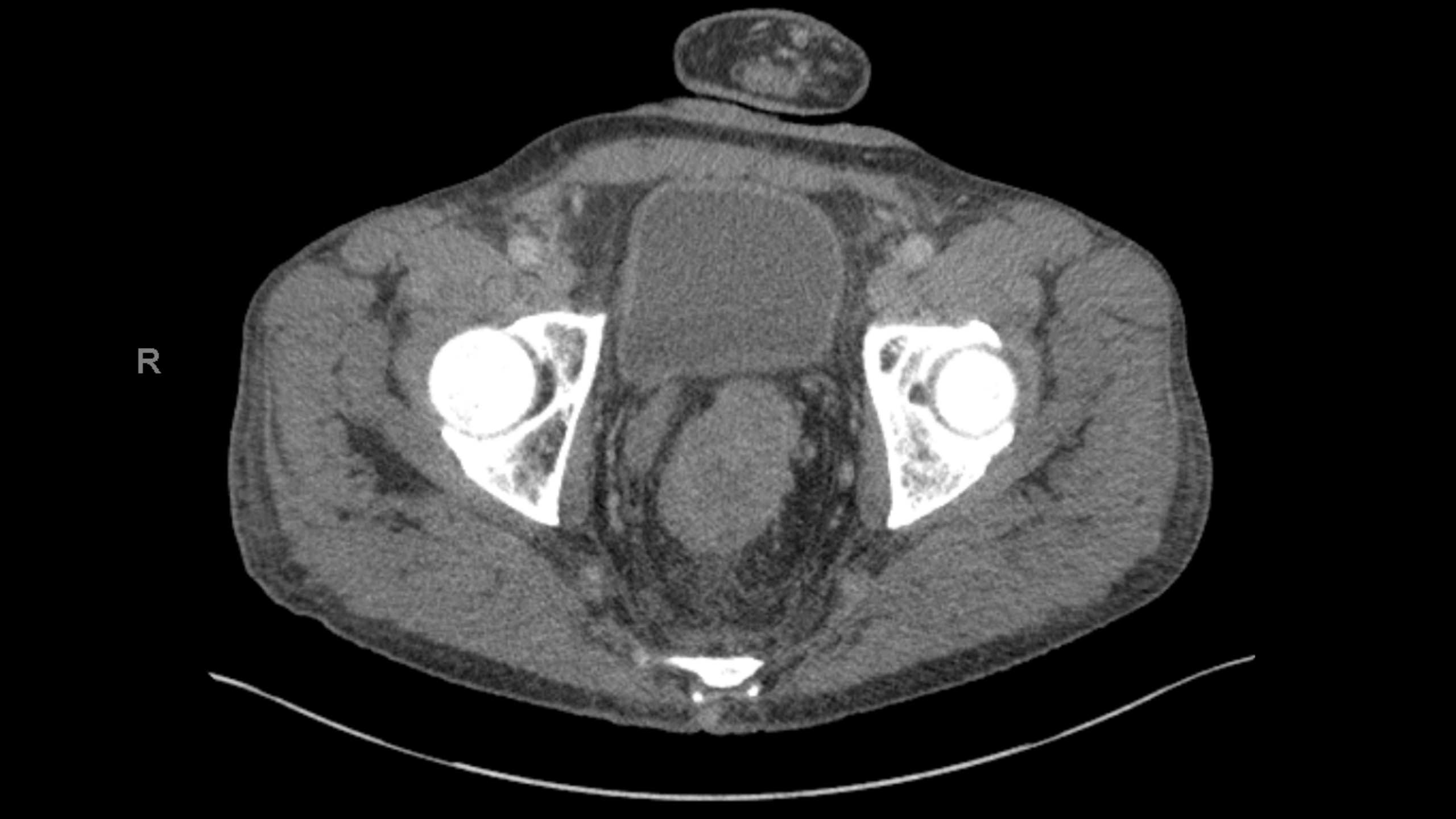
Supportive Care Clinic 10/7/2010

- 10/7 – supportive care clinic, having 10/10 pain, has missed chemotherapy since March, having fevers, cough/congestion – was not able to follow up with interventional radiology and was not taking duloxetine or pain medications until ER visit
- Admitted to palliative care unit directly from clinic, decided he did not want resuscitation, code status changed to DNAR/DNI, DDNR signed

- ESAS:
  - Pain 10/10
  - Fatigue 10/10
  - Nausea 0/10
  - Depression 7/10
  - Anxiety 0/10
  - Drowsiness 10/10
  - Shortness of breath 8/10
  - Appetite 9/10
  - Sleep 10/10
  - Financial distress 10/10
  - Spiritual distress 0/10
  - Sexual health 5/10

Hospital Course

- 10/10 dull, aching, constant pain located in his right upper quadrant, previously a golf-ball sized area now the size of his palm, non-radiating, worse with movement. Also pain on right side of ribs especially when lying on that side.
- Burning pain in his feet, did improve with duloxetine
- Any suggestions?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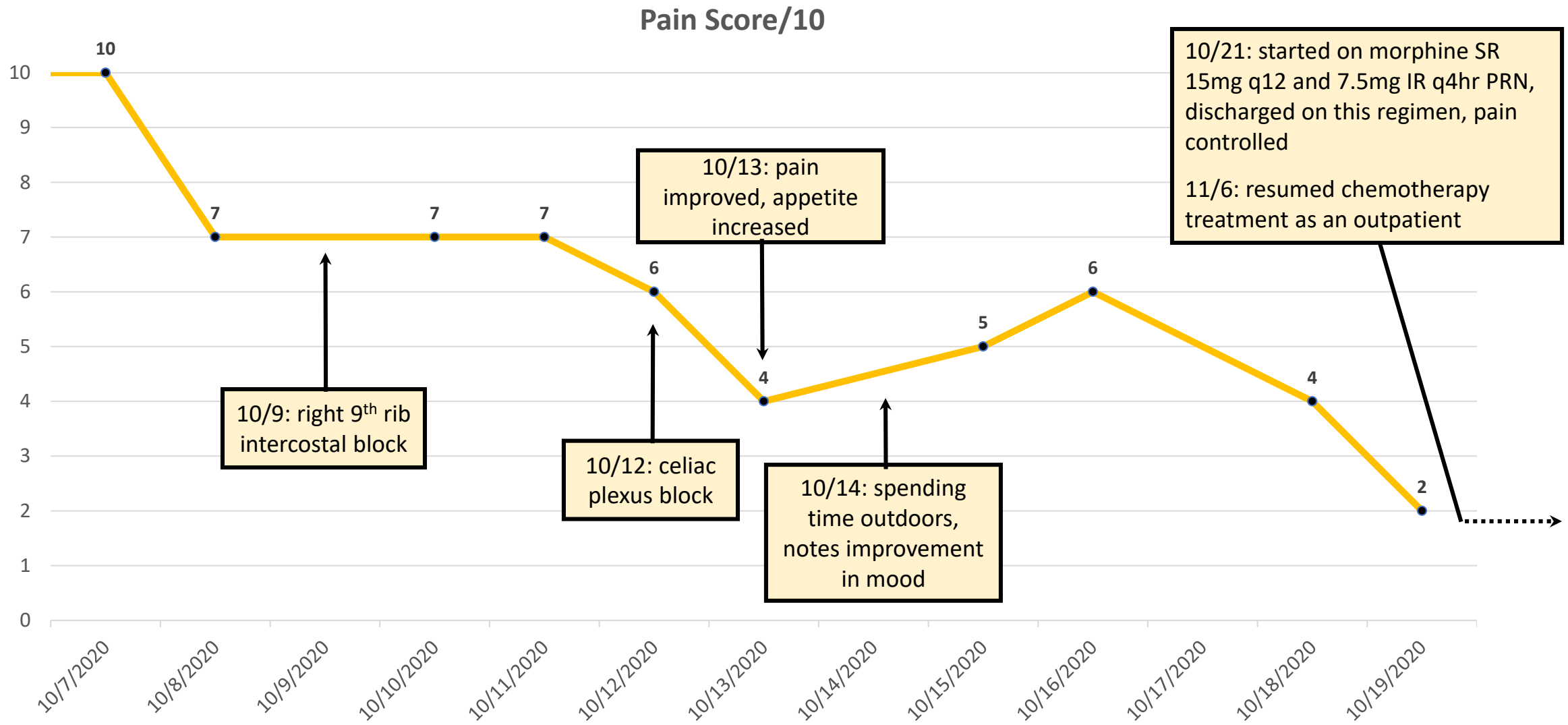
Change in Pain Score over Time



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Learning Objectives

- Discuss history and procedure of Intercostal and Celiac Plexus nerve blocks
- Review appropriate patient populations, success rates, complications for each procedure
- Discuss management of pain medications over existing nerve blocks and expectations for change over time

Interventional Pain Management History

- In 1899, Tuffer described the first nerve block (spinal cocaine) in sarcoma
- In the 1930s, doctors started experimenting with procaine for diagnostic
- Not until 1996, that “interventional pain management” coined and became a subspecialty
- Done by Interventional Radiologists & Anesthesiologists

Definition of Neurolytic Block:

- Deliberate injury of a nerve by application of chemicals→ degeneration of the nerve's fibers→ *temporary* interference of pain signal transmission
- Neurolytic chemical is usually alcohol/ethanol 50–100%; phenol >5%

Manchikanti, et al. The Evolution of Interventional Pain Management. Pain Physician. 2003:6:485-494

Interventional Nerve Blocks

National Comprehensive Cancer Network (NCCN) 2019 Adult Cancer Pain, Clinical Practice Guidelines in Oncology:

Major indications for referral for interventional therapies include:

1. Patient suffering from pain that is likely to be relieved with nerve block
2. Patients unable to achieve adequate analgesia
3. Presence of intolerable side effects with pain medications

European Society for Medical Oncology (ESMO) 2018 Management of Cancer Pain in Adult Patients :

1. Similar indications for referral as NCCN
2. "Neurolytic blocks should be limited to those patients with *short life expectancy* because they usually produce a block lasting 3–6 months"
3. "The use of *neurolytic agents on peripheral nerves can lead to neuritis*; therefore, for patients with good prognosis, this can result in symptoms more difficult to control than the original pain"

Intercostal Nerve Block

Intercostal Nerve Block Technique

-Peripheral Nerve block
-Done either by feel of anatomic landmarks or US-guided
-Anesthetic delivered between two intercostal muscles where the VAN neurovascular bundle runs

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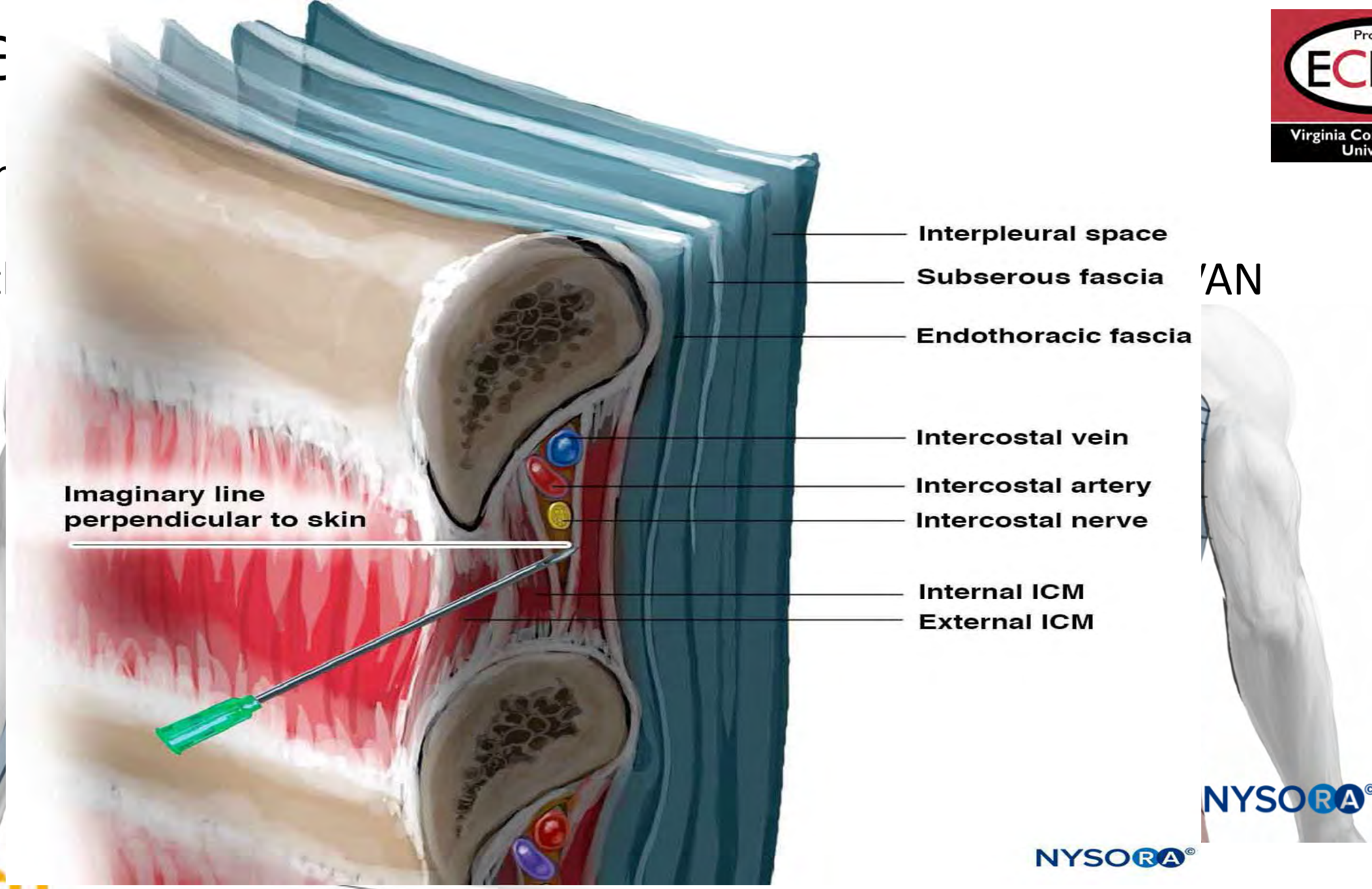

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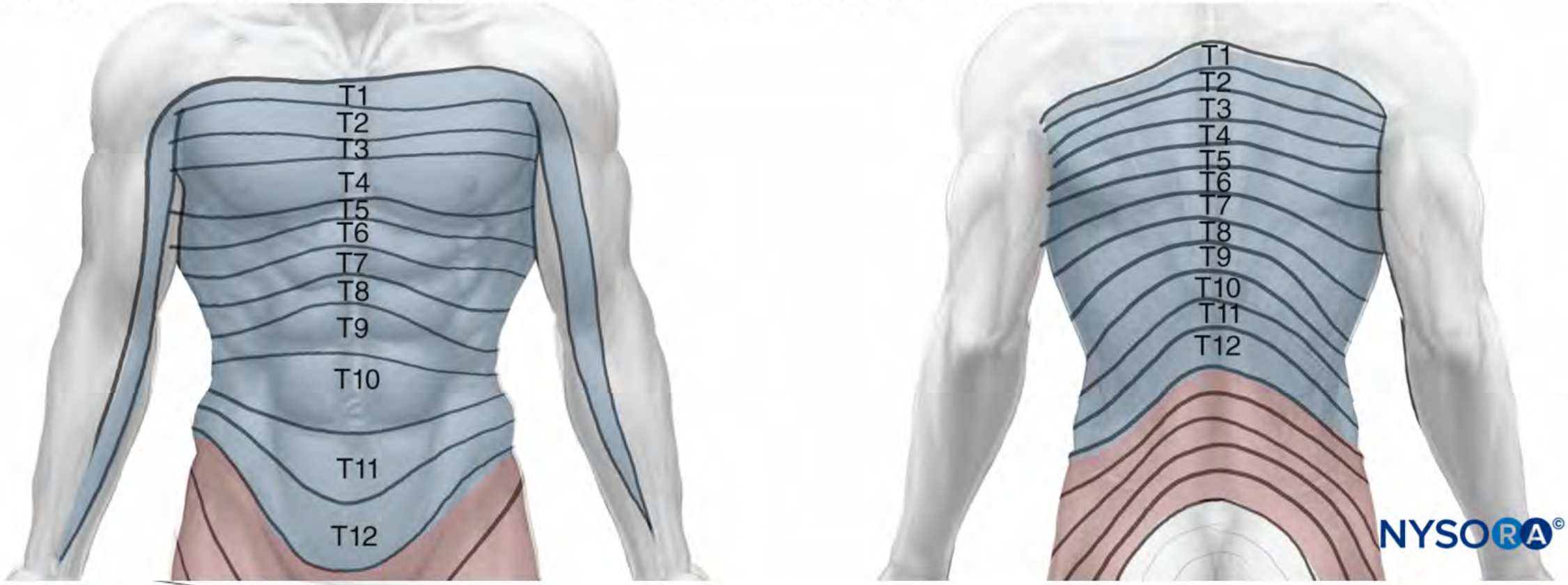
Intercostal Nerve Block Technique

-Peripheral Nerve block
-Done either by feel of anatomic landmarks or US-guided
-Anesthetic delivered between two intercostal muscles where the VAN neurovascular bundle runs

-Diagnostic (ropivicaine/bupivicaine) block then neurolytic block (steroid, phenol, alcohol)
-Aim is to provide relief to unilateral dermatome at that level

Intercostal Nerve Block Technique

-Peripheral Nerve block
-Done either by feel of anatomic landmarks or US-guided
-Anesthetic delivered between two intercostal muscles where the VAN



Which patient does this work for? Intercostal Nerve Block

-thoracic wall malignancies: lung, breast, metastases

-post-op after esophagectomy, mastectomy, thoracic surgery

-Rib fractures

-post-herpetic neuralgia

-ideally, does not have pain on more than one dermatomal level

Success of Intercostal Nerve Block

Retrospective Review of 25 patients at a Hong Kong Hospital

-Tried to differentiate which group of patients may benefit

Group 1: 4 who didn't tolerate low dose morphine

Group 2: 10 who had pain despite high dose opioids (>180 MEDD)

Group 3: 11 who had been referred for early intervention to avoid needing higher opioid doses in future

Results

-80% of all patients noted optimal local pain control and 56% experienced reduction in analgesic use

Group 1: 50% achieved optimal pain control
Group 2: 90% obtained optimal local pain control (P=0.23) and significant reduction in analgesic use (P=0.019)
Group 3: 33% had reduction in use of analgesics

Pain returned after median 12-120 days; Median survival of these pts 66-300 days

Wong, et al. Intercostal nerve blockade for cancer pain: effectiveness and selection of patients. Hong Kong Med J 2007: 13: 266-70

Success of Intercostal Nerve Block

Retrospective Review of 146 patients

-Examined effectiveness of various interventional procedures for the treatment of thoracic chest wall pain in the oncologic population

Procedure	# of Patients	# of Patients with VAS improved>1	Other results
Diagnostic intercostal N. block	146	116 (79%)	33 pts had prolonged relief (avg 21.5 days)
Intercostal Neurolysis	37	23 (62%)	14 pts with NO improvement
Intrathecal pump	7	7 (100%)	

Gulati, et al. A retrospective review and treatment paradigm of interventional therapies for patients suffering from intractable thoracic chest wall pain in the oncologic population.Pain Med. 2015:16(4):802-10

Evidence of Decreased Opioid Use?

NO!

Case series of 4 pts but only one of the cases was intercostal nerve block

MEDD decreased from 225mg to 30mg

How long does it last? Intercostal Nerve block

-Diagnostic block: 6-24hrs

-Neurolytic block: lasts weeks to months?

Complications of Intercostal Nerve Block

-Pneumothorax

-Infection at injection site

-Bleeding

-Neuritis

Celiac Plexus Block

Celiac Plexus Nerve Block Technique

-Autonomic nerve block

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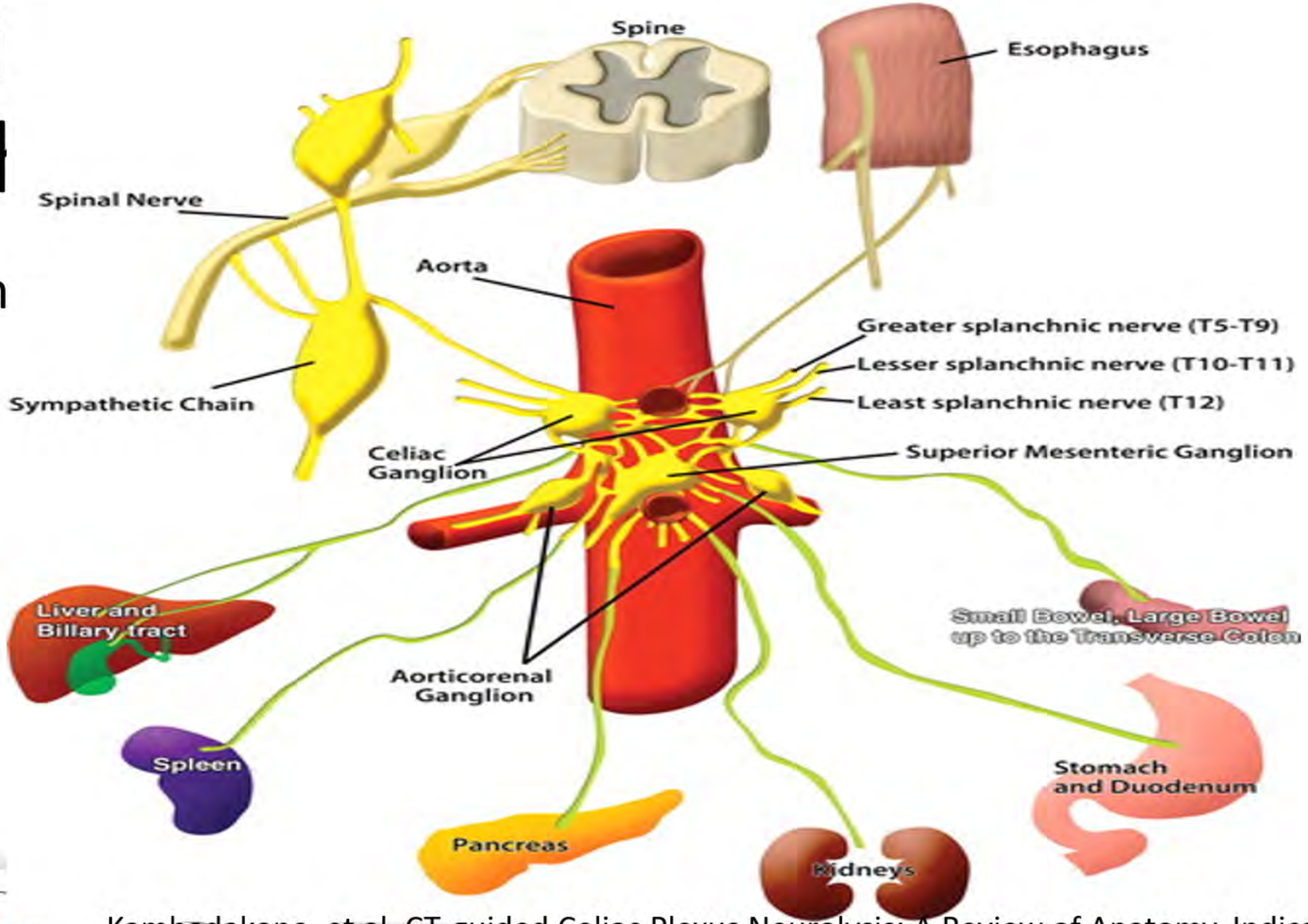

Kambadakone, et al. CT-guided Celiac Plexus Neurolysis: A Review of Anatomy, Indications, Technique, and Tips for Successful Treatment. RadioGraphics 2011

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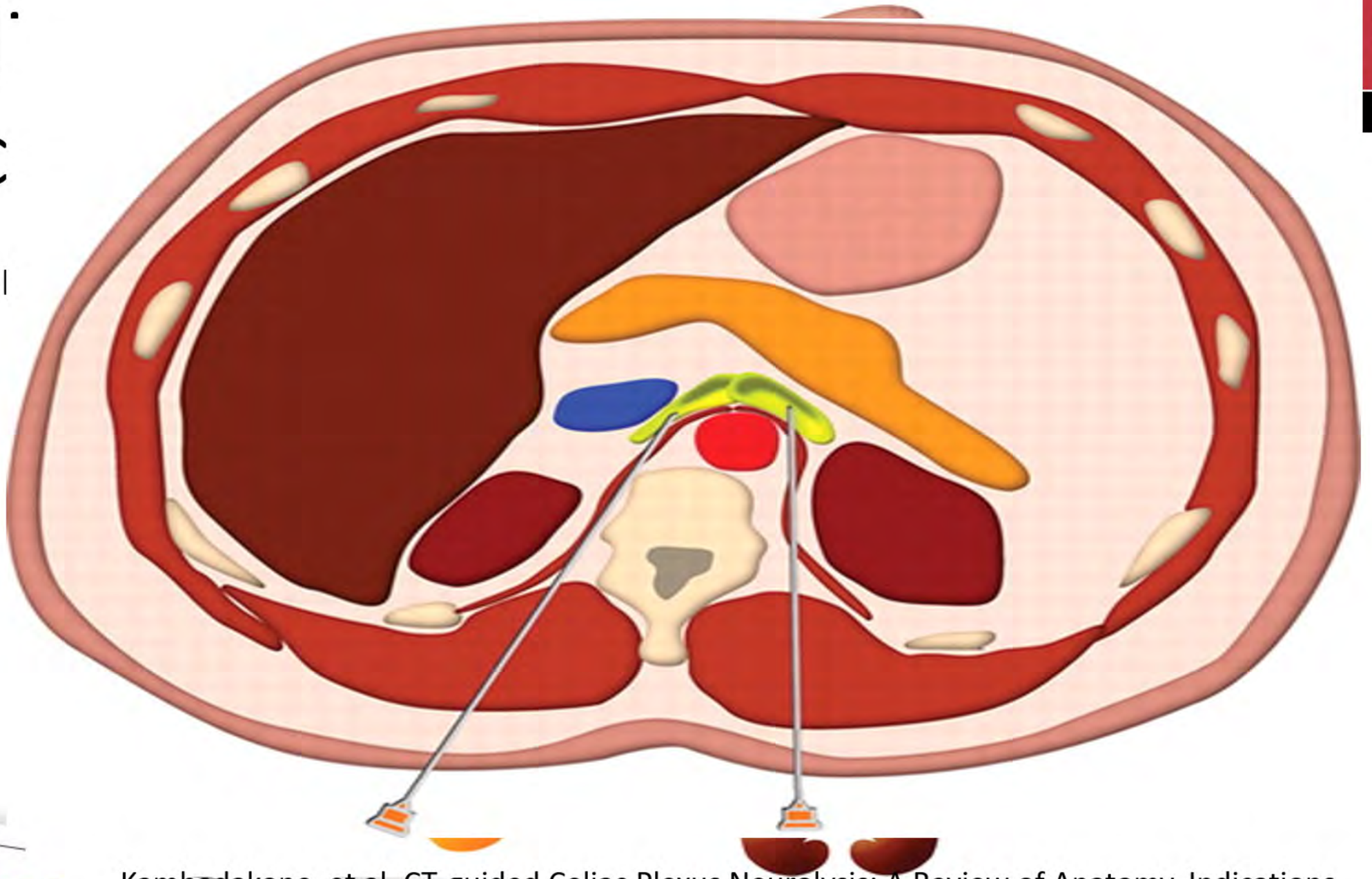

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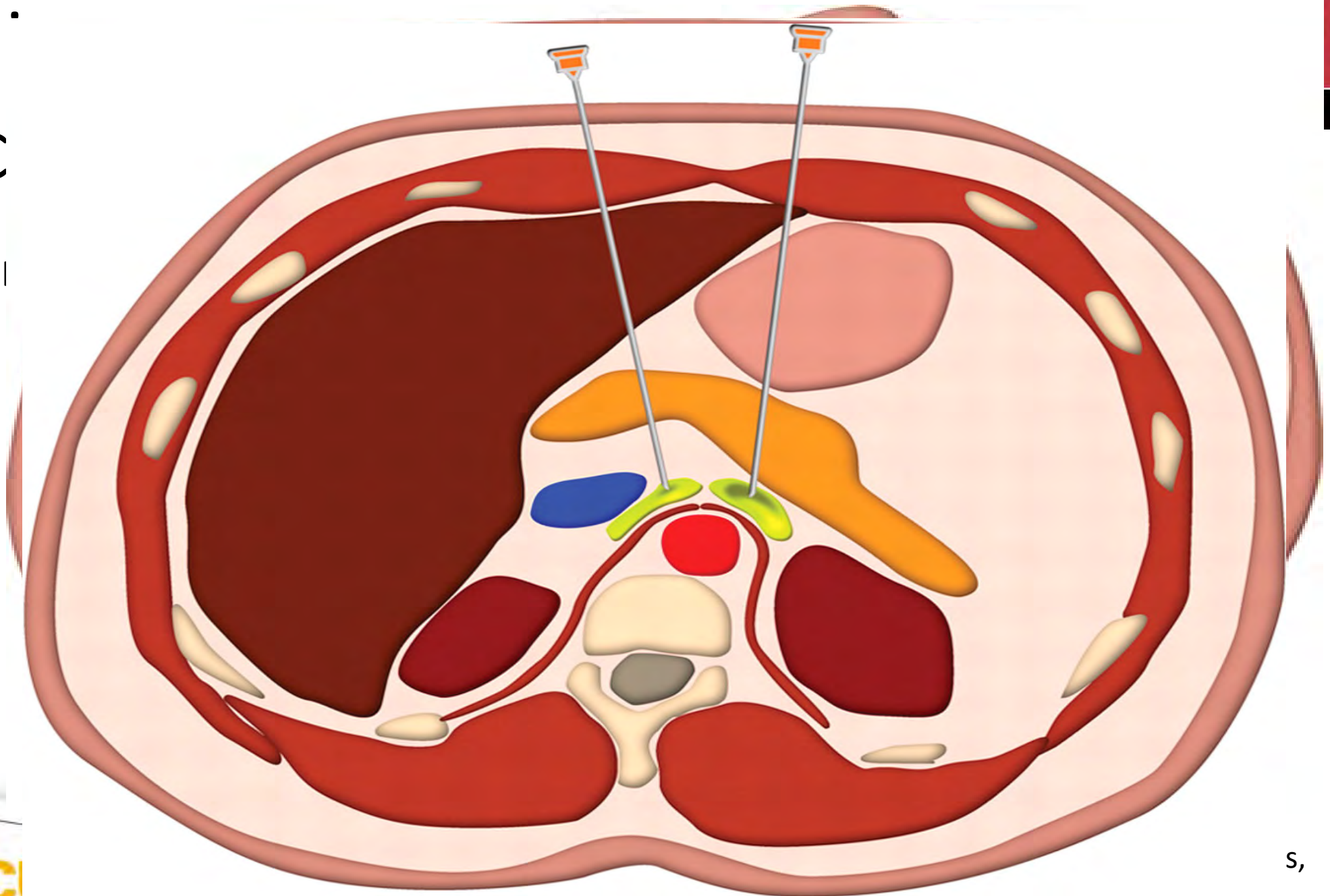

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technique, and tips for successful treatment. RadioGraphics 2011

Which patient does this work for? Celiac Plexus Nerve Block

-Upper abdominal malignancies: pancreatic, gastric, hepatocellular

-Chronic pancreatitis- little evidence for this

Success of Celiac Plexus Nerve Block

Systematic Review and Meta-Analysis

-66 publications were composed of nine randomized and non-RCTs, 32 case series, 24 case reports, and 1 survey.

-Examined effect in abdominal cancer pain

-Most of the studies specified pancreatic cancer and others non-specific “upper abdominal cancers” or inoperable abdominal cancers

Nagels, et al. Celiac plexus neurolysis for abdominal cancer pain: a systematic review. Pain Med. 2013;14(8):1140–1163.

Success of Celiac Plexus Nerve Block

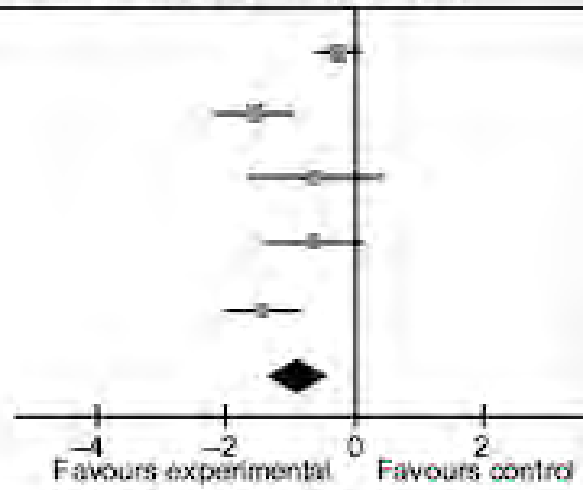
Meta analysis results of the 5 RCTs

CPNB vs Systemic Analgesic at 1-2 weeks post procedure: Pain score decreased by ~0.9 pts

Table 3 Forest plot of CPN (experimental) vs SAT (control) for pain at 1–2 weeks, REM

Study or Subgroup	CPN Mean	CPN SD	CPN Total	SAT Mean	SAT SD	SAT Total	Weight	Mean Difference IV, Random, 95% CI
Jain et al. (2005) [30]	2.26	0.83	45	2.51	0.81	43	24.6%	−0.25 [−0.58, 0.09]
Kawamata et al. (1998) [31]	1.62	0.46	10	3.15	0.92	11	20.9%	−1.53 [−2.14, −0.92]
Mercadante (1993) [27]	2.5	1.42	10	3.09	0.85	10	15.0%	−0.59 [−1.62, 0.44]
Wong et al. (2004) [29]	2.1	1.4	45	2.7	2.1	41	18.7%	−0.60 [−1.36, 0.16]
Zhang et al. (2008) [28]	1.7	1.1	26	3.1	1.1	24	20.9%	−1.40 [−2.01, −0.79]
Total (95% CI)			**136**			**129**	**100.0%**	**−0.87 [−1.47, −0.28]**

Heterogeneity: $Tau^2 = 0.35$; $Chi^2 = 18.81$, $df = 4$ ($P = 0.0009$); $I^2 = 79\%$
Test for overall effect: $Z = 2.86$ ($P = 0.004$)



CPN = celiac plexus neurolysis; REM = random effects model; SAT = systemic analgesic therapy

Nagels, et al. Celiac plexus neurolysis for abdominal cancer pain: a systematic review. Pain Med. 2013;14(8):1140–1163.

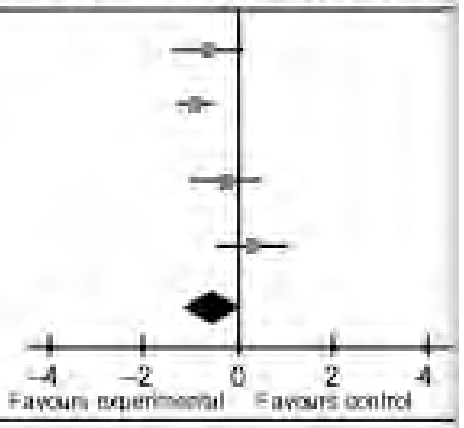
Success of Celiac Plexus Nerve Block

CPNB vs Systemic Analgesic at 8weeks post-procedure: Pain score decreased by 0.3 but lose statistical significance

Table 4 Forest plot of CPN (experimental) vs SAT (control) for pain at 8 weeks, REM

	CPN			SAT				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Kawamata et al. (1996) [31]	2.85	0.54	7	3.31	0.46	7	25.1%	−0.46 [−0.99, 0.07]
Mercadante (1993) [27]	3	0.2	4	3.66	0.17	3	34.3%	−0.66 [−0.93, −0.39]
Wong et al. (2004) [29]	1.6	1.5	36	1.8	1.7	32	17.8%	−0.20 [−0.97, 0.57]
Zhang et al. (2008) [28]	3.4	1	17	3.1	0.8	19	22.7%	0.30 [−0.30, 0.90]
Total (95% CI)			**64**			**61**	**100.0%**	**−0.31 [−0.74, 0.12]**

Heterogeneity: Tau² = 0.12; Chi² = 8.72, df = 3 (P = 0.03); I^2 = 66%
Test for overall effect: Z = 1.40 (P = 0.16)



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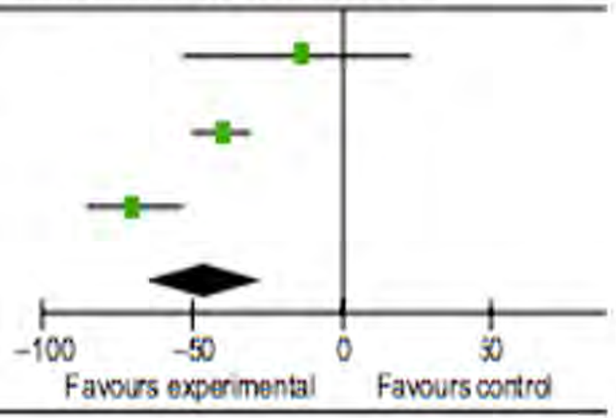
Evidence of Decreased Opioid Use? Celiac Plexus Nerve Block

Opioid Usage at 1-2 weeks

Table 7 Forest plot of CPN (experimental) vs SAT (control) for opioid consumption at 1–2 weeks, REM

	CPN			SAT					
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Kawamata et al. (1996) [31]	30.95	35.71	10	47.62	47.62	11	25.1%	−16.67 [−52.47, 19.13]	
Mercadante (1993) [27]	4	12.65	10	42.25	21.47	10	37.6%	−38.25 [−53.70, −22.80]	
Zhang et al. (2008) [28]	11	23	26	81	34	24	37.2%	−70.00 [−86.22, −53.78]	
Total (95% CI)			**46**			**45**	**100.0%**	**−44.64 [−72.74, −16.54]**	

Heterogeneity: $Tau^2 = 483.77$; $Chi^2 = 11.39$, df = 2 ($P = 0.003$); $I^2 = 82\%$
Test for overall effect: Z = 3.11 ($P = 0.002$)



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Evidence of Decreased Opioid Use? Celiac Plexus Nerve Block

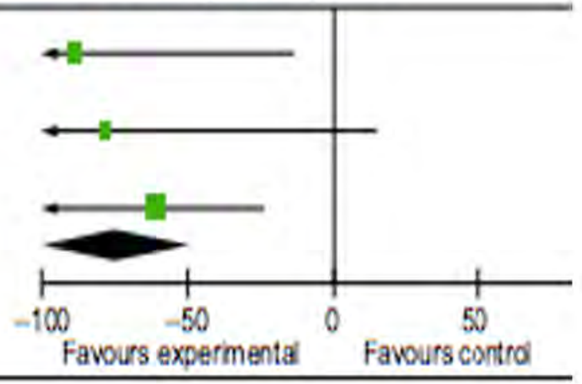
Opioid Usage at 8 weeks

Table 8 Forest plot of CPN (experimental) vs SAT (control) for opioid consumption at 8 weeks, FEM

Study or Subgroup	CPN Mean	CPN SD	CPN Total	SAT Mean	SAT SD	SAT Total	Weight	Mean Difference IV, Random, 95% CI
Kawamata et al. (1996) [31]	66.67	50	7	159	90.48	7	19.7%	-92.33 [-168.91, -15.75]
Mercadante (1993) [27]	40	37.4	4	116.6	73.7	3	14.0%	-76.60 [-167.70, 14.50]
Zhang et al. (2008) [28]	99	59	20	161	73	19	66.3%	-62.00 [-103.79, -20.21]
Total (95% CI)			**31**			**29**	**100.0%**	**-70.02 [-104.05, -36.00]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.49$, $df = 2$ ($P = 0.78$); $I^2 = 0\%$

Test for overall effect: $Z = 4.03$ ($P < 0.0001$)



CPN = celiac plexus neurolysis; FEM = fixed effects model; SAT = systemic analgesic therapy.

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How long does it last? Celiac Plexus Nerve Block

-Diagnostic block: last ~6-24hrs

-Neurolytic block: may take few days to start to work; lasts weeks to months? (literature is varied)

Complications of Celiac Plexus Block

-Diarrhea
-Low blood pressure
-Infection at injection site
-Pain at injection site
-Pneumothorax
-Bleeding

Management of Pain Medications After Nerve Block

-No clear guidelines on how to reduce opioids after nerve block

-Multiple factors involved:

-Did nerve block work

-If nerve block effective, how long does pain relief end up lasting

-Did patient already have intolerance of high opioid dose

Summary

-Interventional nerve blocks can be considered when:

1. Intolerance to opioid therapy
2. Need for multi-modal therapy
3. Pain syndromes meet indications

-Efficacy of INB still needs to be studied with more RCTs

-Need to consider patient's clinical course if choosing to pursue nerve blocks

-No clear guideline on opioid reduction after nerve blocks

THANK YOU!

We hope to see you at our next ECHO