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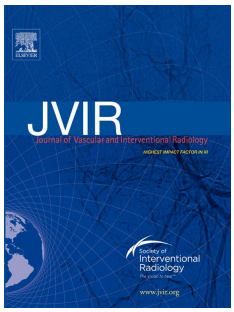

Response To Celiac Plexus Block Confirms Neurogenic Etiology of Median Arcuate Ligament Syndrome

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PII: S1051-0443(21)01016-2

DOI: https://doi.org/10.1016/j.jvir.2021.04.003

Reference: JVIR 5993

To appear in: *Journal of Vascular and Interventional Radiology*

Received Date: 15 October 2020

Revised Date: 31 March 2021

Accepted Date: 4 April 2021

Please cite this article as: Barbon DA, Hsu R, Noga J, Lazzara B, Miller T, Stainken BF, Response To Celiac Plexus Block Confirms Neurogenic Etiology of Median Arcuate Ligament Syndrome, *Journal of Vascular and Interventional Radiology* (2021), doi: https://doi.org/10.1016/j.jvir.2021.04.003.

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Acknowledgements:

The Office of Research at Stamford Hospital for their contribution to this study.

Author contribution:

All authors have contributed towards the conception and design of the article, acquisition of data, analysis and interpretation of data, drafting the article and revising it critically for important intellectual content. The final approval of the article being submitted has been given by all the authors and the institution.

Funding:

No funding was provided for this study

Conflict of interest:

Dr. Stainken serves on the medical advisory board of Hatch Medical, which is outside the submitted work.

There are no other conflicts of interest to disclose.

SIR Annual Scientific Meeting:

This study was presented as a poster presentation at the SIR Annual Scientific Meeting 2021

ABSTRACT

Purpose

To evaluate the response of Median Arcuate Ligament Syndrome (MALS) symptoms, including postprandial pain, nausea, and vomiting to celiac plexus block (CPB) and to correlate response with arterial anatomy.

Materials and Methods

In a single-institution, retrospective cohort of clinically diagnosed MALS patients, 96 patients (75 female, 21 male, mean age 27 years) underwent 103 CT-guided percutaneous CPB procedures. Imaging, procedural, and clinical reports were reviewed. Primary outcomes evaluated were technical success, change in self-reported pain score, and change in nausea and vomiting.

Results

Preprocedural computed tomography (CT) imaging was available in 81/96 patients, demonstrating findings of celiac artery compression in 22/81 (27%) patients. Technical success was achieved in 102/103 cases. No major adverse events and one moderate adverse event were reported. Postprandial pain score decreased in 86 patients (84%), and mean score decreased from 6.3 to 0.9 points ($p < .001$). Prevalence of postprandial nausea decreased from 37.9% to 11.6% ($p < .001$), and vomiting decreased from 15.5% to 4.9% ($p = .019$). There were no differences in post-CPB pain relief between patients with and without celiac artery compression ($p = .745$).

Conclusions

In patients with a clinical diagnosis of MALS, a large majority reported pain relief and decreased gastrointestinal symptoms after CPB. Pain relief did not correlate with presence of celiac arterial

abnormalities. This supports neuropathy as the primary etiology of MALS, and suggests that absence of celiac stenosis should not be used as an exclusion criterion.

INTRODUCTION

Median Arcuate Ligament Syndrome (MALS) is defined by a complex of clinical symptoms: chronic postprandial abdominal pain, nausea, vomiting, and unintentional weight loss[1,2]. These symptoms have been attributed to foregut demand ischemia secondary to extrinsic celiac artery compression, and therapeutic approaches have focused primarily on restoring celiac arterial flow[3].

An alternative theory proposed by Weber et al in 2016 suggested that the symptoms are not the result of a vascular stenosis but are neuropathic, the result of median arcuate ligament impingement upon nerve fibers of the celiac plexus rather than the artery[4]. The authors proposed that the resulting compressive neuropathy causes an "autonomic imbalance" or failed post prandial vasodilatory response with resulting hypoperfusion and pain transmission via visceral nociceptive fibers[2,5].

Celiac plexus block (CPB) performed with computed tomography (CT) guidance can be used as a diagnostic test for patients presenting with the MALS clinical symptom complex. A symptomatic response to CPB, regardless of the patency of the celiac artery, is considered by some to be a prerequisite to resection of the median arcuate ligament and celiac plexus. The primary objectives of this study were to assess technical success, pre-CPB and post-CPB pain scores and the presence of nausea or vomiting in a cohort of patients diagnosed with MALS based on clinical symptoms, and to correlate response with celiac arterial anatomy.

METHODS

Study Design

A single-institution cohort of 96 patients carrying a clinical diagnosis of MALS was studied from data available from the electronic medical record. Patients underwent a total of 103 CT-guided percutaneous CPBs between January 1, 2017 and April 3, 2020. This retrospective study was approved by the hospital's institutional review board on April 7, 2020. Waiver of consent was obtained.

Indications

Indications for CPB included a history of chronic post-prandial epigastric pain, nausea and vomiting, and unintentional weight loss without an identifiable source. Patients with chronic abdominal pain with identifiable etiologies (e.g. chronic mesenteric ischemia, gastric outlet obstruction, or gastroparesis) were excluded from referral for CPB. Past medical and surgical history are displayed in Table 1. Ehlers-Danlos syndrome was noted in 12.5% of patients and postural orthostatic tachycardia syndrome (POTS) in 28.1%.

CPB Procedure

Technical and clinical outcomes were assessed by the proceduralist. Percutaneous CPB were performed by one of four board-certified interventional radiologists. All pediatric patients and any adult patients who expressed preference underwent general anesthesia or anesthesiology-monitored sedation. Procedure duration, type of sedation, and the use of intravenous contrast medium to resolve retroperitoneal structures was recorded. The needle target was bilateral, juxtaceliac, antecrural spaces, and correct placement was confirmed by injection of contrast medium and documentation of dispersal in the anterior paraaortic space. Alternative approaches and planned transgression of intervening structures were recorded. Based on patient weight, a mixture of 0-5mL 1% lidocaine, 15-30mL 0.25% bupivacaine, and 12-24mg betamethasone was

injected for CPB. Celiac plexus neurolysis with ethanol or phenol was not offered due to lack of safety data for this patient population.

After recovery from sedation, patients were instructed to ingest foods that were known to elicit their symptoms. After eating, patients self-reported pain using the numeric rating scale (NRS-11), a linear scale ranging from 0 to 10. The presence of subjective nausea and objective vomiting were recorded after CPB. Results were recorded in procedure reports. After CPB, all patients were referred to, and 91/96 (95%) consulted with a vascular surgeon to discuss elective MALS surgery.

Data Collection

Patients were identified by a search and procedural information was collected from the institutional Radiology Information System using mPower™ Clinical Analytics (Nuance Communications, Burlington, Massachusetts). A CPB database was created using Microsoft Excel (Microsoft Corporation, Redmond, WA). Preprocedural and postprocedural imaging were reviewed for each patient, including inspiratory and expiratory abdominal CT angiography when available. Technical outcomes were extracted from procedural reports. Clinical outcomes were extracted from electronic medical records on MEDITECH (Medical Information Technology, Inc., Westwood, MA) and outpatient office charts.

Outcomes

From the imaging review, differences in post-CPB pain relief between patients with normal anatomy findings and MALS anatomy (focal eccentric celiac artery stenosis, celiac trunk arterial stenosis, inferiorly displaced celiac trunk, celiac trunk hook-shape configuration, celiac vessel collateralization, or celiac stenosis with respiratory variability) were compared. Contrast and anesthetic dispersal patterns (into all four quadrants, upper quadrants, or lower quadrants

relative to the celiac axis) were correlated with mean pain score change. The primary clinical outcomes assessed were changes in postprandial pain, nausea and vomiting. Since all patients were offered elective MALS surgery after their CPB, differences between CPB outcomes in patients that elected surgery and those who did not were assessed.

Statistical Analysis

Demographic data were reported per patient, but procedural data were analyzed per procedure to include the 7 repeat CPB procedures in the statistical analysis. The mean ± standard deviation were used to report continuous variables. Percentages were used to report categorical variables. Fisher's exact test was used to compare differences between categorical variables. One-way analysis of variance (ANOVA) test was used to correlate pain score changes with anesthetic dispersal. A two-tailed paired t test was used to compare pain scores before and after CPB, and to compare scores between surgery and no surgery groups. Significance was set at $p = 0.05$. All statistical analysis was performed on Prism 7 (GraphPad Inc., LaJolla, CA, USA).

RESULTS

Imaging Review

Pre-procedural CT imaging was available and independently reviewed in 81/96 (84%) of patients. Dedicated inspiratory and expiratory abdominal CT angiography was available in 9/81 (11%). Imaging revealed focal eccentric celiac artery stenosis in 17/81 (21%) with a mean 68% ± 24% luminal stenosis, inferiorly displaced celiac trunk in 22/81 (27%), celiac trunk hook-shape configuration in 17/81 (21%), vessel collateralization in 19/81 (23%), and respiratory variability in 4/81 (5%). At least one of these CT findings of traditional MALS anatomy was present in 22/81 (27%) of patients. Aforementioned imaging findings traditionally associated with MALS were not present in most patients 59/81 (73%). (Figure 1)

Post-procedural independent imaging review demonstrated needle tip in the supra celiac axial plane in 12/103 (12%), juxta celiac in 51/103 (50%), between celiac and superior mesenteric artery (SMA) region 23/103 (22%), or at or inferior to the SMA 14/103 (14%). (Figure 2) Post-procedural contrast medium dispersal patterns were reviewed and classified based on opacification in the four quadrants surrounding the celiac trunk (as described by Cicco et al)[6]. Contrast medium was present in all four quadrants 66/103 (64.1%), bilateral upper quadrants 75/103 (72.8%), and bilateral lower quadrants 76/103 (73.8%). Contrast medium dispersed into two or more quadrants in all completed CPB. The one-way ANOVA comparing contrast medium dispersal into all four quadrants, upper quadrants, or lower quadrants relative to celiac axis revealed no correlation between dispersal patterns and mean pain score change (p=.999). (Figure 3)

Technical Outcomes

Of CPB procedures attempted, 102/103 (99.0%) were technically successful. One procedure on a patient with a history of POTS and gastroesophageal reflux was discontinued prior to needle insertion at the patient's request due to anxiety. The CPB was subsequently completed four months later with anesthesiology support. The mean procedure length was 36.0 ± 11.6 minutes. Only 5/103 (5%) of patients underwent general anesthesia, and 40/103 (39%) of cases were managed with monitored anesthesia care. The remaining 58/103 (56%) received moderate sedation under an interventional radiologist's supervision.

Intravenous contrast enhancement was required in 43/103 (42%) of patients to resolve vascular structures in the region of the celiac plexus. Planned transgression of intervening structures was required for adequate needle placement in 12/103 (12%) of procedures.

Transgressed structures included: lung or parietal pleura 7/103 (7%), liver 4/103 (4%), kidney 1/103 (1.0%), and pancreas 2/103 (2%).

For most patients, the celiac plexus was approached with bilateral posterior access (61/103 (59%). An anterior approach was used in 3/103 (3%) of cases. Unilateral access was adequate in 41/103 (40%) of procedures. The initial fifty-seven blocks 57/103 (55%) were performed using only local anesthetic with mixtures of 1% lidocaine (3-5cc), 0.25% bupivacaine (15cc) in dilute contrast medium. Steroids (12-24 mg betamethasone or 80mg methylprednisolone) were added in the remainder of procedures.

Technical complications included 3/103 (3%) pneumothoraces: 2 patients were observed and discharged the same day of CPB and 1 patient was admitted for overnight observation: no needle decompression or thoracostomy tube insertion was necessary. One patient (0.9%) reported post-CPB diarrhea. One patient (0.9%) reported self-limited post-CPB left shoulder pain. Utilizing Society of Interventional Radiology Adverse Event Severity Scale, there were 4/103 (4%) minor adverse events and 1/103 (1%) moderate adverse events[7].

Clinical Outcomes

A decrease in postprandial pain was reported by 86 /103 (83%) of patients after each CPB. The mean pre-CPB pain score was 6.3 ± 3.0 points. After CPB, the mean pain score decreased to 0.9 ± 2.2 points ($p<.001$). Prevalence of postprandial nausea decreased from 38% pre-CPB to 12% post-CPB ($p<.001$). Prevalence of postprandial vomiting decreased from 16% to 5% after CPB ($p=.019$). Additionally, 89/103 (86%) patients self-reported being able to eat a food item that previously triggered epigastric pain immediately after CPB. (Figure 4, 5) There was no difference in post-CPB pain relief between patients with normal anatomy findings (82% reported relief) versus traditional MALS anatomy (88% reported relief, $p=.745$).

A total of 44 out of 96 unique patients (46%) underwent resection of the median arcuate ligament and celiac plexus during the study period. These 44 patients had statistically higher pre-CPB mean pain scores of 7.0 ± 2.5 points compared to the group that refused surgery, whose pre-CPB mean pain score was 5.6 ± 3.3 (p=.023). After the CPB, the group that elected surgery had a significantly decreased post-CPB pain score of 0.4 ± 1.3 points, compared to the no surgery group post-CPB pain score of 1.3 ± 2.6 points (p=.043).

DISCUSSION

CPB reduced pain in 90% of patients (83% of procedures) and gastrointestinal symptoms in 93% of patients (86% of procedures) with MALS symptoms. There was no difference between the response to the CPB in patients with imaging evidence of celiac arterial displacement or stenosis compared to those with normal arterial anatomy. This suggests that the primary etiology of symptoms is neuropathic, and that arterial impingement is only present in a subset of patients presenting with neuropathy. As such, the absence of a stenosis or celiac displacement on imaging should not be used as an exclusion criterion for the diagnosis of MALS. Conversely, the presence of celiac stenosis does not correlate with postprandial symptoms.

A retrospective multidetector CT angiography review by Gumus et al. demonstrated 21/740 patients with celiac stenosis, yet only 3/21 patient were symptomatic with post prandial pain[8]. Celiac stenosis or median arcuate ligament thickening can be imaged well with CT and CT angiography[8]. However, there are no validated imaging strategies that resolve the relationship between the musculotendinous fibers of the diaphragm and ligament and the nerve fibers of the celiac plexus in MALS patients. Thus, subjective response to CPB, performed in a standardized fashion, may become the gold standard of diagnosis in patients suspected of having MALS.

Cicco et al predicted long-lasting pain relief (30 days) in relation to contrast/neurolytic spread across quadrants around the celiac area in a population with cancer-related pain and using an anterior single needle approach[6]. Additionally, contrast spread across quadrants was hampered by regional anatomic distortions in 92% of their 105 patients[6]. In the current study, contrast dispersal patterns did not result in differences in immediate post- CPB pain scores. Since a single-needle technique for CT-guided neurolytic CPB can be hampered by regional anatomic distortions, Kambadakone et al. found that bilateral injections were more likely to be successful[9]. Our data support the bilateral posterior approach, which was feasible in all patients with minimal risk of transgression of intervening structures in our non-oncologic population, resulting in less than 2% major complications[9].

CPB for MALS symptom relief has previously been reported in two small series of 14 and 36 MALS patients[10,11]. A female predominance was also noted in the current study, albeit the mean age was younger in the current study[10]. Prevalence of rare diseases such as Ehlers-Danlos syndrome (<0.01%) and POTS (<0.01%) in the general population are very low. However, their prevalences in an 11 patient MALS case series were 18.2% and 27.3%, respectively[12]. Similarly, the current study noted Ehlers-Danlos syndrome in 12.5% of patients and POTS in 28.1%. Further work is necessary to uncover causal links between MALS and associated connective tissue or dysautonomia conditions.

The reduction of nausea and vomiting after CPB demonstrated in the current study has not been reported as a primary outcome in the literature since neurolytic CPB for cancer patients is primarily performed for intractable pain refractory to opiates[5,9]. Singh et al. postulated that the brain perceives noxious stimuli through similar pathways used for chronic pain and chronic nausea[13]. Further research is needed to establish this causal relationship following CPB.

Orthostatic hypotension and diarrhea are common side effects after celiac plexus ablative neurolysis[14], with transient diarrhea reported in up to 44% of patients. The physiologic basis is assumed to be unopposed parasympathetic activity resulting in decreased intestinal transit time and increased peristalsis[9]. In the current series, orthostasis was not directly assessed, but only one patient suffered from diarrhea during post-procedural recovery. It is not clear why the incidence of diarrhea was so low in the MALS population.

In addition to its role in diagnosing MALS, the degree of the response to CPB may serve a prognostic role in determining which patients will elect repair. Patients who experienced greater preprocedural pain and more benefit from CPB were more likely to elect surgery. CPB may transiently mimic celiac plexus resection and may be used to simulate the expected effects of MALS surgery[10,15]. MALS surgical outcomes were not analyzed in the current study; thus, correlation between CPB response and MALS surgery response are still unknown.

Other limitations to this study include the retrospective cohort study design. A portion of cases did not have pre-procedural imaging available for review. Inspiratory and expiratory phase abdominal CT angiography were unavailable in the majority of cases.

In conclusion, relief of pain and relief of nausea and vomiting were reported in 83% and 86% of patients with a clinical diagnosis of MALS after CPB. Pain relief did not correlate with the presence of celiac arterial impingement. This supports the proposal that MALS is primarily neuropathic and that absence of celiac artery involvement should not be used as an exclusion criterion. CPB, performed in a standardized fashion, is a safe and useful tool for the diagnosis of MALS.

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TABLES

Table 1: Patient demographics

FIGURE LEGENDS

Figure 1a: Abdominal CTA, sagittal reformat, arterial phase during inspiratory phase demonstrates <50% stenosis of the celiac trunk.

Figure 1b: Abdominal CTA, sagittal reformat, arterial phase during expiratory phase demonstrates MALS findings: respiratory variability accentuating a focal eccentric celiac artery stenosis attributed to impingement by the median arcuate ligament and celiac trunk hook-shape configuration.

Figure 2a: Prone, planning CT with IV contrast, with axial image demonstrating the proximal celiac trunk.

Figure 2b: Prone, CT without IV contrast, axial image demonstrating co-axial, bilateral, posterior CPB with contrast injection dispersing in bilateral antecrural spaces.

Figure 2c: Prone, CT without IV contrast, axial image demonstrating post-CPB contrast dispersal around the celiac artery (arrows).

Figure 3: Mean Pain Score change versus contrast distribution along quadrants relative to the celiac axis.

Figure 4: Pre-CPB versus Post-CPB pain scores.

Figure 5: Pre-CPB versus Post-CPB nausea and vomiting.

Variables	Count (%)	Mean ± SD
Sex		
Male	21 (21%)	-
Female	75 (78%)	-
Age	-	26.7 ± 16.1 years
Pre-CPB Weight	-	60.8 ± 17.3 kg
Height	-	165 ± 10.2 cm
Pre-CPB BMI	-	22.2 ± 5.85 kg/m^2
Past Medical History		
Asthma	19 (19.8%)	-
Celiac Disease	6 (6.3%)	-
COPD	0 (0%)	-
Ehlers-Danlos	12 (12.5%)	-
Gastritis	10 (10.4%)	-
GERD	10 (10.4%)	-
Gastroparesis	9 (9.4%)	-
Hiatal Hernia	7 (7.3%)	-
Mast Cell Activation Syndrome	9 (9.4%)	-
POTS	27 (28.1%)	-
Past Surgical History		
Prior CPB	12 (12.5%)	-
Central Venous Catheter	6 (6.3%)	-
Cholecystectomy	8 (8.3%)	-
Diagnostic Laparoscopy	3 (3.1%)	-

Table 1: Patient demographics