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METHOD

Chronic Abdominal Discomfort Syndrome (CADS): Defining and Discussing a Novel Diagnosis

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Abstract: In this article, we propose a new diagnostic paradigm known as Chronic Abdominal Discomfort Syndrome (CADS). Patient's presentation centers around chronic abdominal pain not explained by acute pathology with or without accompanying dyspepsia, bloating, nausea and vomiting among other symptoms. The pathophysiology is noted to be neurogenic, possibly stemming from visceral sympathetic nerves or abdominal wall afferent nerves. Diagnosis is supported by signs or symptoms traversing clinical, diagnostic and functional criteria. Included is a tool which can assist clinicians in diagnosing patients with CADS per those domains. We hope to facilitate primary care physicians' and gastroenterologists' utilization of our criteria to provide guidance for selecting which patients may benefit from further interventions or evaluation by a pain physician. The pain physician may then offer interventions to provide the patient with relief.

Keywords: CADS, chronic abdominal pain, neurogenic abdominal pain, chronic abdominal discomfort

Introduction

Chronic Abdominal Pain (CAP) is a condition that affects millions of patients annually. Generally, it is a challenging diagnosis to manage with a range of heterogeneous etiologies. Current diagnostic criteria define CAP as constant or recurrent pain that lasts for at least 3 months.[1] It is estimated that approximately 1–2% of the adult population is affected by CAP, with greater frequency of occurrence in females compared to males.[2] The etiology of CAP is elusive, with high concordance with previous abdominal surgery, namely herniorrhaphy, adhesiolysis and cholecystectomy.[3] Other identifiable components of CAP include visceral pain (chronic pancreatitis, mesenteric angina, etc), somatic pain, psychogenic pain and functional pain. Also associated can be symptoms of nausea, anorexia, bloating and early satiety. Treatment typically centers around pharmacotherapy with nonsteroidal anti-inflammatory drugs (NSAIDS), opioids, proton pump inhibitors and tricyclic antidepressants most commonly used.[4] In some cases, medications can potentiate exacerbation of symptoms, as in the development of peptic ulcer disease secondary to NSAID overuse or constipation secondary to opioid use. The pathophysiology of CAP can be multifactorial thus requiring a broad spectrum of treatment modalities.

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Within the umbrella of CAP, we propose a diagnostic subclassification that we describe as "Chronic Abdominal Discomfort Syndrome" (CADS). Our goal is to establish a consensus CADS definition encompassing clinical symptomatology and pathophysiology with suspected neuronal etiology.

The patient may report a history of previous abdominal surgery with/without potential neuronal injury such as entrapment, adhesions, and neuroma formation. Patients may also carry a diagnosis of chronic pancreatitis. Inflammatory bowel diseases such as Ulcerative Colitis and Crohn's disease would be excluded. Associated symptoms can include abdominal bloating, nausea, vomiting or dyspepsia. These diseases may result in a reduced quality of life and inability to complete activities of daily living, objective surveys can be administered to quantify extent of impairment.

On examination, signs may include generalized tenderness to palpation of the abdomen with poor localization. Patient's positioning should not change the character of pain. There should be no signs of acute abdomen such as rigidity, guarding or hemodynamic instability. The abdomen should show no discoloration or signs of external trauma. Patients demonstrating hyperalgesia or allodynia of the abdomen should also be considered if acute abdomen is ruled out. Specifically, if abdominal pain is more localized (i.e can be pointed out with one finger), consideration should be given to Chronic Abdominal Wall Pain (CAWP) – also known as Abdominal Cutaneous Nerve Entrapment Syndrome (ACNES).[5] An effective tool to diagnose these patients is Carnett's Sign: worsening of abdominal pain with increased tension placed on the abdominal wall.[6] These patients would qualify for a diagnosis of CADS as they would fulfill criteria as outlined below.

Diagnostically, lab values for lipase, amylase, liver enzymes and bilirubin should be stable and within normal range. Imaging may show prior interventions but no acute pathology such as increased stool burden, dilation or edema of the bowel or tumors and other obstructions should be visualized.

If no other diagnosis explains signs and symptoms, consider Chronic Abdominal Discomfort Syndrome. It is possible that a diagnostic nerve block of the abdomen (eg Transverse Abdominal Pain) can solidify the diagnosis, particularly if accompanied by decrease in quantity of oral pain medications consumed. What follows is a set of diagnostic criteria establishing the condition, with further research slated to address patient treatment and long-term management.

Pathophysiology of Nerve Related Abdominal Discomfort

The pathophysiology of abdominal pain is important to consider as this can allude to therapeutic targets. Spinal nerves are the key conduction entity in the circuitry that informs the abdominal wall and its contents. Input from the posterior body wall is communicated via the posterior ramus, input from the anterior lateral regions of the body wall is communicated by the anterior ramus of the spinal nerve. The posterior and anterior ramus come together to form the spinal nerve which feeds into the sensory (spinal) ganglion, making its way to the posterior root and into the posterior horn of gray matter within the spinal cord. The signals are then transmitted to the brain.[7]

Within the abdominal body wall lie important structures such as smooth muscle and glands, which require sympathetic innervation to function. The sympathetic system operates in a distinct pathway; their cell bodies reside in the lateral great horn of the spinal cord. These fibers exit the spinal cord via the anterior root, converge into the spinal nerve and course into the paravertebral sympathetic ganglia – A collection of sympathetic fibers arranged in a chain on either side of the vertebral column.[8] Within the ganglion, sympathetic fibers can pass along – unmyelinated – back to the spinal nerve where they are then distributed to the anterior and posterior rami residing with somatic motor and sensory fibers. It is important to note that sympathetic innervation is limited to spinal cord levels T1-L2 therefore, some fibers within the ganglion run up-and-down the sympathetic trunk to spinal cord level beyond T1-L2.

Innervation inside of the abdominal cavity is primary to the viscera. Pain arising from the viscera is generally triggered by distention, ischemia and inflammation. It is relatively insensitive to stimuli such as cutting or burning.[9] Often the pain is described as a diffuse, dull ache accompanied by occasional nausea, vomiting and transient changes in vital signs.[10]

Sympathetic fibers coming off the spinal cord can also enter another collection of nerves known as the prevertebral ganglia. The course of those fibers is as follows: exit the spinal cord, pass through the paravertebral ganglion at the same level (without synapsing) and into the splanchnic nerves (sympathetic). The splanchnics then synapse in the prevertebral ganglia found along the anterior surface of the abdominal aorta. The three prevertebral ganglia are: the celiac ganglion, superior mesenteric ganglion and inferior mesenteric ganglion.

Specifically, visceral pain is thought to be conveyed by splanchnic nerve roots arising from T5-T12. These nerve roots form the greater, lesser and least splanchnic nerves converging upon the Celiac plexus.[11]

Generally, the spinal sympathetic outflow is strongly regulated by the brain therefore spinal cord stimulators have proved to be an effective treatment modality.[12,13]

Running along with the sympathetic fibers are visceral afferent fibers which project back into the posterior root, to the dorsal root ganglion and finally synapse in the posterior horn of gray matter within the spinal cord.[14] Here, the phenomenon of referred pain occurs - the visceral and somatic fibers are in close proximity making it challenging for the brain to discern where exactly pain signals are coming from. Hence, pain from internal organs is referred to sites of the body wall. This phenomenon is described as a "viscerotome".[15] The somatic fibers far outnumber the splanchnic afferents (80% vs 20% respectively) therefore the pain is characterized as dull, vague and poorly localized.[16] With this phenomenon in mind, it is posited that terminology such as 'abdominal discomfort syndrome' better encapsulates symptoms.

Diagnostic Criteria

The proposed diagnostic criteria for Complex Abdominal Discomfort Syndrome are:

At least 6 months of symptoms of primarily generalized abdominal discomfort with no change in patient's baseline bowel or bladder program. If a patient has a major psychiatric history (anxiety, depression, bipolar, schizophrenia, etc.), it needs to be well managed with an assessment from a psychiatrist or psychologist noting that this condition is not a causal factor resulting in the below symptoms of CADS. Diagnosis can be recognized per the table described in "Figure 1: Chronic Abdominal

<table>
<tr><th>Clinical Criteria</th><th>Diagnostic Criteria</th><th>Functional Criteria</th></tr>
<tr><td>Constant diffuse or focal abdominal pain which is disproportionate to any inciting event</td><td>No findings of acute pathology on imaging (ERCP, MRCP, Gastric emptying, CT scan, MRI) – no increased stool burden, dilation or edema of the bowel, tumors or other obstructions</td><td>Decrease in daily function secondary to abdominal discomfort[a] (SF 36)</td></tr>
<tr><td>Hyperalgesia and/or allodynia of the abdomen</td><td>Response to Diagnostic local anesthetic blocks[b]</td><td></td></tr>
<tr><td>History of Irritable Bowel Syndrome</td><td colspan="2" rowspan="10">Clinical criteria for diagnosis of CADS:
1. > 50% of Clinical Criteria (6/12) should be positive
2. 100% of Diagnostic and Functional Criteria should be positive</td></tr>
<tr><td>History of visceral organ manipulation or pathology (e.g. Whipple, pancreatitis, appendectomy, cholecystectomy, hernia repair surgeries)</td></tr>
<tr><td>No peritoneal signs present</td></tr>
<tr><td>Abdominal bloating</td></tr>
<tr><td>Nausea</td></tr>
<tr><td>Vomiting</td></tr>
<tr><td>Generalized tenderness to palpation of the abdomen or Carnett's Sign positive</td></tr>
<tr><td>No notable skin discoloration or abdominal trauma</td></tr>
<tr><td>No firm abdominal distension, rebound or guarding</td></tr>
<tr><td>No hematochezia, melena or hematemesis</td></tr>
</table>

Figure 1 Chronic Abdominal Discomfort Syndrome (CADS) diagnostic criteria. [a]Based on Short Form 36 (SF36) instrument by Rand Corporation to measure quality-of-life. [b]Favorable Diagnostic Block (eg thoracoabdominal block, subcostal block, or iliohypogastric block) defined as providing > 50% relief in pain based on patient report.[17–19]

Discomfort Syndrome (CADS) diagnostic criteria". Quality-of-life measurement is based on administration of the Short Form 36 (SF36) instrument by Rand Corporation further described below. A favorable Diagnostic Block (eg thoracoabdominal block, subcostal block, or iliohypogastric block) defined as providing >50% relief in pain based on patient report.[17–19]

SF36 Instrument for Measurement of Quality-of-Life

The SF36 was chosen based on its established validity for clinical practice and research.[20,21] Its potential for extrapolation and capture of overall health status and its effects on perceived quality of life have been strongly established.[22] The instrument is composed of 36 items that are assessed on 8 domains as listed:

1. Limitations in physical activities because of health problems
2. Limitations in social activities because of physical or emotional problems
3. Limitations in usual role activities because of physical health problems
4. Bodily pain
5. General mental health (psychological distress and well-being)
6. Limitations in usual role activities because of emotional problems
7. Vitality (energy and fatigue)
8. General health perception

The survey has been validated for self-administration in age groups greater than 14 years.[23]

A higher score defines a more favorable health state (0–100) in step 1 of scoring

In step 2 of scoring, specific items are averaged together such that they are divided amongst the above 8 listed domains.

An identified objective of future studies will be to validate a threshold score on the SF36 which can be used as a corollary to graded benefits of PNS implantation for CADS (ie expected mild, moderate or significant improvement expected based on intake scores).

Conclusion

Currently, a diagnostic subclassification of Complex Abdominal Discomfort Syndrome (CADS) does not exist. Given the wide prevalence of chronic abdominal pain, a consensus to define CADS and to establish diagnostic criteria for the diagnosis is imperative. We propose a set of diagnostic criteria that includes a range of symptoms, imaging results, and response to diagnostic blocks. Where we believe the pathophysiology will be neuronally modulated. Additionally, we hope to facilitate primary care physicians' and gastroenterologists' utilization of our criteria to provide guidance for selecting which patients may benefit from further interventions or evaluation by a pain physician. For pain physicians, we hope that the disease definition and the set of diagnostic criteria will allow proper categorization of patients with CADS and use of available interventions to provide pain relief.

Disclosure

Mayank Gupta and Anand S Patil are co-first authors for this study. Dr Michael Schatman is a research consultant for Modoscript and advisory committee for Syneos Health, outside the submitted work. Dr Timothy Deer reports personal fees for consultant and/or research from Abbott, Vertos, SpineThera, Saluda Medical, Cornerloc, SPR Therapeutic, Boston Scientific, PainTeq, Spinal Simplicity, Biotronik, and MainStay, outside the submitted work; In addition, Dr Timothy Deer has a patent pending to Abbott. Dr Dawood Sayed reports personal fees from and/or stock options for Painteq, Abbott, Neuralace, MainStay, Vertos, Saluda, SPR, and Surgentec, outside the submitted work. Dr Amol Soin reports ownership of Soin Neuroscience, JanOne, Neuros Medical, Soin Bioscience, and Avanos, during the conduct of the study. Dr Ganesan Baranidharan reports grants, personal fees from and advisory board for Abbott; grants and/or personal fees from Nevro Corp, MainStay Medical, Boston Scientific, Stryker, Saluda Medical, and Artha Medical, outside the submitted work. Dr Peter Staats reports personal fees from electroCore, outside the submitted work; in addition, Dr Peter Staats has a patent abdominal pain and vagus licensed to electroCore. Dr Paul Verrills reports consultant to Saluda, Presidio. The authors report no other conflicts of interest in this work.

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