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CLINICAL IMAGE

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EDITOR'S MESSAGE

What Makes Us Special, Different and Alike?

Paula Gregory, DO, MBA, FACOFP

To better serve you, Osteopathic Family Physician has moved to a quarterly publishing schedule beginning with the Winter 2023 issue. We've retooled to give you more high-quality, focused osteopathic content. Although we all have incredibly busy lives, marking time through the movement of the seasons is something that generally makes sense across the board. The quarterly publication format gives us more time to review original research and to better understand and make informed decisions about the range of content we can offer you, our readers.

Different artists have painted the Mona Lisa and the resulting interpretations of this famous painting are distinctly theirs. Artists like Roy Lichtenstein, Sonia Delaunay, Jean-Michel Basquiat, Miro and others. The results are not copies of the Mona Lisa, but rather a way that another artist visualizes Leonardo da Vinci's famous painting. And that's valid.

As people and physicians, our views are colored by our teachers, our parents and our patients. We come to a unique perspective that helps us script our experiences onto the person in front of us.

We all view certain experiences from our unique perspectives and retell them to attempt to help others understand and grow. At times, meeting with other DOs, they tell me that they have "lost" the art of OMM. It's doubtful that could ever happen, as they are gentle with surgical techniques, spreading the fascia back over, and after the delivery of a child by discussing back pain or making sure things are done symmetrically. Our education runs deep, and our training augments our knowledge. As we work alongside others, sharing what we know and learning from our MDs has been a great adventure. We have sought parity for our students and our educational differences.

We are one voice of healing for our patients. Our one wish is for them to be as healthy as possible given the unique attributes of their health. What makes us distinct from MDs is our gentle touch—either physically through examining our patients or mentally and emotionally through our gentle demeanors. Our training and our relationships with our patients and with the many accomplished physicians and students we work alongside add up to a cumulative body of knowledge that is holistic and gentle.

As we continue to learn from our students' voices, I want to share two letters to help you appreciate the challenges and the grace of our student doctors who are well on their way to becoming exceptional physicians.

LETTERS TO THE EDITOR

Resident as Educator: The Preclinical Years

To the editor:

Although peer education has been a pivotal part of residency education, there has been a recent emphasis on residents acting as educators. This includes near-peer instruction between residents and students; however, residents are also engaged in teaching patients, their families, and even attendings at times. As we progress through our postgraduate years, it is easy to forget where we started in our medical careers and how much we have learned.

I recently had the opportunity to spend one of my elective months at my alma mater, the Arizona College of Osteopathic Medicine. I designed a rotation in faculty development to further my training in the discipline of education. While I am fortunate to be able to teach in our residency clinic, I wanted the opportunity to expand my academic horizons and to instruct medical students who had not yet started their clinical rotations.

During my rotation, with the assistance of our chair of osteopathic, family, and clinical medicine, I was allowed to participate in many distinct aspects of the preclinical curriculum. I was able to debrief second-year students (just beginning their pharmacology and pathology courses) after their standardized patients about what was occurring during their simulation, instruct first year students in normal and pathological heart and lung sounds, and prepare third-year students for their surgical rotations. Interacting with these students reminded me of many things. First and foremost, never forget where you started: the amount of knowledge you have obtained is astronomical. Second, the best way to understand pathology is to understand normal. And, finally, have faith that you will learn it in your own time.

My rotation time was not only a profound learning experience but also humbling. I urge any resident or attending wanting to pursue academia to become engaged with students who have yet to see patients. The learning experiences are reciprocal and will make you appreciate your practice so much more.

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LETTERS TO THE EDITOR

A Heart for Medicine: Palpitations In the Midst of Training

To the editor:

The journey to receiving a medical degree is marked by moments of incredible stress, with few more demanding than the MCAT and USMLE exams. Students spend many caffeine-fueled months preparing for an ominous day of reckoning, whose fateful moments of testing seemingly dictate their future vocation. A poor showing is a devastating prospect.

I began preparing for the MCAT with high hopes of soaring success. Within 2 months of the exam, I experienced my first heart palpitation, and my priorities quickly shifted. A few moments of rapid googling confirmed my suspicions but did little to relieve my anxiety. For the next week, I experienced 20–30 palpitations every day, in a positive feedback loop of stress and palpitations. A visit to the cardiologist and resulting Holter monitor were able to break the compounding cycle.

Anxiety-related heart palpitations are the most common type.¹ They demonstrate the ability of stress not only to affect the mind but also the physical body. As an aspiring medical student who thoroughly admired the fortitude and competence of physicians, palpitations were an unavoidable reminder of my limitations. I was human, as are all doctors, and stressful experiences genuinely affect us even when we do not notice.

Heart palpitations afforded me more than insight into my stressful reality. They granted me the experience of being a patient. During that time, the body that I had instinctively trusted for so many years had become no longer trustworthy. I was uncertain about the nature of my palpitations and the future of my health.

As a medical student, I have encountered many patients in similar circumstances. The uncertainty in their eyes and worry on their faces feels familiar as I participate in their care. The occasional PVC subtly reminds me of my experience and sparks a swell of empathy. As I continue in my career, I intend to have grace for myself and for others, for stress or distress, high-stakes exams, or unhappy patients. I would encourage readers to do the same.

John Coggins, BS
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REFERENCES

1. Pedrinazzi C, Durin O, Bonara D, Inama L, Inama G. Epidemiology, classification and prognosis of palpitations. *G Ital Cardiol (Rome)*. 2010 Oct;11(10 Suppl 1):5S–8S.

FROM THE PRESIDENT'S DESK



Mind, Body and Spirit: What Makes Osteopathic Medicine is 'Hands-on'

Bruce R. Williams, DO, FACOFP

What's the difference between a DO and an MD? Have you ever been asked this question? How did you reply? If you're like me, it was answered neither in a simple phrase nor one sentence. It became a discussion—and perhaps a complicated discussion, at that. What if the same question were asked of your patient? What would their response be? "I was listened to." "I was cared for." "My concerns were addressed." "I was a person, not a condition." What if the question were asked of a colleague? "The doctor was thorough." "The doctor was prepared." "The doctor had done the work-up."

What does it mean to be an osteopathic physician? We know who we are. Our patients know who we are. Our colleagues know who we are. But how do we articulate this? How do we tell others what osteopathic medicine is, in a way that illustrates how we are different from other types of physicians and from alternative medicine? Notice, I did not say every *other* alternative medicine, because osteopathic medicine is not alternative medicine. So what makes an MD and a DO different?

In most, cases, that response is not black or white, but gray instead. And that's not a bad thing. Over the past 150 years, both philosophies of medicine have evolved. But there are differences. Allopathy is defined as the treatment of disease by conventional means, that is, with medication that counters the symptoms. The osteopathic philosophy of medicine, in contrast, sees an interrelated unity in all systems of the body, each working with the other to heal when illness occurs. Allopathic medicine treats disease, whereas osteopathic medicine treats dysfunction. Find the disease and stop it, or find the dysfunction and reverse it. That's the fundamental difference between the philosophies and, hence, the foundation of our training.

A great deal of overlap, right? Especially as we learn more about disease and dysfunction.

What else? Early on in our osteopathic education, we, as osteopathic medical students, are taught how to be patients. We entered an OMT lab and let a perfect stranger put their hands on us, touch us, look for tissue texture changes, asymmetry, restriction, tenderness—dysfunction. We placed our trust in that person, and when it was time to correct the dysfunction, we trusted that same person—our classmate—to do what was necessary to help us. This not only taught us OMT but also taught us to communicate with our patients, to grow that physician-patient relationship that is so vital. If a patient allows us to perform manipulation,

“For the osteopathic physician, that idea of not becoming attached gets tossed out the window. We are engaged, we take the extra steps: we write the letters, make the phone calls, fill out the forms, do whatever needs to be done to help patients get better—because these patients are our family.”

they will trust us to do a comprehensive evaluation, make evidence-based recommendations, and help them. Why? Because there is almost nothing else you can give your patient that will make them feel better when they leave your office than when they came in. It is disappointing that this gift of OMT bestowed on us in osteopathic medical school is not always given to our patients. And, if it is given, it is documented, it is coded, it is billed, it will grace the physician and the practice as well. But most importantly, it helped our patient!

Our training has instilled in us a culture of networking, fellowship, and family. When attending conferences, we're motivated more by seeing our friends and colleagues than by earning CMEs. Sure, we get the education, but it's renewing and strengthening our relationships that feels more important. We embrace each other genuinely. Relationships matter to the osteopathic physician. And the relationships we have with each other are deepened by the relationships we have with our patients.

We see our patients as our family. We have all been told not to get too emotionally attached to our patients. For the osteopathic physician, that idea of not becoming attached gets tossed out the window. We are engaged, we take the extra steps: we write the letters, make the phone calls, fill out the forms, do whatever needs to be done to help patients get better—because these patients are our family. Does this mean MDs don't treat their patients this way? Absolutely not! The difference is in the way DOs go about it.

Every physician. Every provider begins with the goal of being trained to help their fellow human being. We all enter our professional course to help, especially those who can't help themselves. And, for the most part, we've all realized that goal. Have we experienced discouragements along the way? Sure. But ultimately, healthcare is a noble profession, entered into by noble people, people who seek to do what will help their fellow man. We want to see our patients healthy, happy and successful. When it comes to our patients, we seek to see the whole picture of their health: like all healthcare workers, we strive to take everything into account. The difference is in how we see our role and our philosophy to that end.

Osteopathic distinctiveness? It is "hands-on." We listen, we learn their histories. We touch and perform the exam. We will see,

evaluate all the available information and make a diagnosis. We speak with our patients in terms they understand and agree to.

Osteopathic medicine is mind, body and spirit. Understanding all three, in tandem, is the key.

Osteopathically yours,



Bruce R. Williams, DO, FACOFP
2022-23 ACOFP President

CALENDAR OF EVENTS

MARCH 29-APRIL 2, 2023

ACOFP 60th Annual Convention & Scientific Seminars
American College of Osteopathic Family Physicians
Orlando, FL & Virtual
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APRIL 20-23, 2023

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JUNE 9-11, 2023

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JUNE 15-18, 2023

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JUNE 23-25, 2023

ACOFP Future Leaders Conference
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JULY 27-30, 2023

Michigan Summer Family Medicine Update
Michigan Association of Osteopathic Family Physicians
Grand Rapids, MI

JULY 28-29, 2023

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AUGUST 2-6, 2023

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AUGUST 4-6, 2023

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AUGUST 11-13, 2023

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REVIEW ARTICLE

COVID-19 FATIGUE: DIAGNOSIS AND TREATMENT FOR THE OSTEOPATHIC PHYSICIAN

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KEYWORDS

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ABSTRACT

The novel coronavirus disease 2019 (COVID-19) has given rise to a global pandemic, as well as a multitude of long-term sequelae that continue to perplex physicians around the world, including in the United States. Among the most common and impactful long-haul symptoms experienced by survivors is COVID-19 fatigue. This review will use long COVID-19, post-acute COVID-19 syndrome (PCS), and Post-Acute Sequelae of COVID-19 (PASC) as synonymous terms to refer to the chronic symptomatology; chronic fatigue associated with PASC will be referred to as COVID-19 fatigue. While the knowledge and research on the exact pathophysiological mechanisms involved in the disease is still limited, parallels have been drawn between fatigue as a component of long COVID-19 and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Current studies suggest applying principles of pathophysiology, diagnosis, and treatment similar to those for ME/CFS in order to aid in managing chronic fatigue in COVID-19 survivors, particularly in the primary care setting. The osteopathic family physician can use the proposed pharmacologic agents, along with osteopathic manipulative treatment (OMT), as therapeutic modalities that can be tailored to each patient's unique case. Nevertheless, research on proven successful treatments is still scarce. For that reason, it is essential that COVID-19 fatigue is recognized early, especially since its longitudinal impacts may be debilitating for many. This review of the available literature on COVID-19 fatigue aims to help provide quality care and lessen the disease burden experienced by patients.

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), quickly became a worldwide pandemic following its discovery in 2019.^{1,2} As of April 2022, the worldwide number of confirmed cases reached 500 million and over 6 million reported deaths.³ Patients diagnosed with COVID-19 can experience symptoms ranging from cough, fever, sore throat, nausea and vomiting to septic shock, severe pneumonia, and acute respiratory distress syndrome (ARDS).^{4,5}

Long COVID-19, post-acute COVID-19 syndrome (PCS), or Post-Acute Sequelae of COVID-19 (PASC) are synonymous terms defining the persistence of symptoms or other sequelae following acute COVID-19.⁶⁻⁹ For this review, we will use long COVID-19, PCS,

and PASC interchangeably to describe symptom continuation for more than 12 weeks after acute infection. Chronic multisystem symptoms include fatigue, dyspnea, anosmia, dysgeusia, arthralgia, amnesia, and difficulty concentrating.^{6,7,10} Various studies suggest that chronic fatigue affects 28%–47% of all survivors (Figure 1).^{6,7,10}

Fatigue can be defined as acute or chronic and is associated with multiple disease states.^{11,12} Interestingly, fatigue prevalence in long COVID-19 patients does not depend on the severity of the acute illness and is one of the most commonly reported symptoms.^{6,7,10} Since this PASC symptomatology is very similar to myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), patients may fit ME/CFS diagnostic criteria.^{12,13} Although there may be instances where ME and CFS occur independently, our focus will be on the ME/CFS complex illness. This review will refer to the diagnosis of fatigue associated with PASC as COVID-19 fatigue.

In the pediatric population, PASC fatigue can be a direct sequela of multisystem inflammatory syndrome in children (MIS-C), which has been associated with SARS-CoV-2 infection. Presenting symptoms of MIS-C are persistent fever, systemic inflammation, and related multi-organ involvement, such as abdominal pain, conjunctival injection, rash, and arthralgias.¹⁴

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Although fatigue can be a symptom of MIS-C secondary to COVID-19, this article focuses on COVID-19 fatigue in adults.

Since long COVID-19 involves various symptoms, the treatment methods must be individualized.¹⁵ As for COVID-19 fatigue, there is currently no proven treatment. With this in mind, this review aims to consolidate the current research on diagnostic criteria, pathophysiology, and potential therapeutic approaches, including pharmacologic options and osteopathic manipulative treatment (OMT).

DIAGNOSIS

Post-infectious, or in this case, COVID-19 fatigue seems to bear a striking resemblance to ME/CFS due to the constellation of symptoms found in both conditions.¹⁶ Because of the similarities in presentation and suggested etiology, the diagnosis of chronic fatigue as a component of PCS is approached using the current knowledge about ME/CFS, once the initial criterion of a laboratory proven COVID-19 infection has been met. Chronic fatigue has an extensive differential diagnosis with various etiologies, summarized in Table 1.^{12,17} It is crucial to rule out common conditions, such as primary sleep disorders, diabetes mellitus, hypothyroidism, and vitamin deficiencies, before attributing fatigue to long COVID-19.

The National Academy of Medicine (NAM) introduced new diagnostic clinical criteria for ME/CFS in 2015. According to the report, a thorough history, physical examination, and targeted laboratory workup are necessary for diagnosis.¹⁸ The NAM requires patients to have post-exertional malaise (PEM), unrefreshing sleep, and substantial impairment in function due to fatigue that does not improve with rest. PEM is an immediate or delayed exacerbation of symptoms and functional decline following a minor physical or mental exertion with intensity and duration disproportionate to the magnitude of the trigger.^{17,19} Patients are also required to have either cognitive impairment or orthostatic intolerance with symptoms present at least 50% of the time for more than 6 months with moderate, substantial, or severe intensity.¹⁷ Additionally, multiple types of pain, such as headaches, arthralgia or myalgia, gastrointestinal and genitourinary problems, and influenza-like symptoms (sore throat and tender axillary/cervical lymph nodes), sensitivity to external stimuli, respiratory and thermoregulatory issues may support a diagnosis of ME/CFS.^{17,18}

Clinicians should elicit a history consistent with ME/CFS and rule out other medical conditions. Questions regarding the severity and duration of symptoms as chronic, frequent, and moderate or severe are required to distinguish ME/CFS from other illnesses.¹⁸ In addition, physicians should inquire regarding fatigue, functional or cognitive impairment, post-exertional malaise, lack of restful sleep or sleep disturbances, and orthostatic intolerance.¹⁸ Patients may describe symptoms without a clear understanding of the illness; for example, cognitive impairment may be described as “brain fog,” “difficulty concentrating,” or “absentmindedness.” Key questions should include implications on instrumental activities of daily living (iADLs), such as household management and career, and activities of daily living (ADLs), like personal hygiene and ambulation.¹⁸

Physical examination may elicit nonspecific abnormal findings or may be unremarkable. Nonspecific signs and symptoms include low-grade fever, inability to maintain cognitive focus, abdominal tenderness, multiple tender joints without redness, warmth or swelling and allodynia/hyperalgesia.¹⁷ The physical examination may also suggest comorbid conditions associated with ME/CFS. Those can include fibromyalgia, myofascial pain syndrome, temporomandibular joint syndrome, irritable bowel syndrome, interstitial cystitis, irritable bladder syndrome, Raynaud’s phenomenon, prolapsed mitral valve, migraine, allergies, multiple chemical sensitivities, Sicca syndrome, obstructive or central sleep apnea, and reactive depression or anxiety.¹⁸

No single laboratory test can be used to diagnose ME/CFS; instead, testing is used to rule out other medical causes of fatigue that would reject the diagnosis of ME/CFS.¹² Laboratory testing can include complete blood count with differential, comprehensive metabolic panel, antinuclear antibody, C-reactive protein, erythrocyte sedimentation rate, ferritin, rheumatoid factor, thyroid-stimulating hormone, free thyroxine, vitamin B12, vitamin D 25-dihydroxy, four-point salivary cortisol, and urinalysis.¹⁷ Like ME/CFS, COVID-19 fatigue is a diagnosis of exclusion.

PATHOPHYSIOLOGY

Although a lot is yet to be discovered about the specific pathophysiology of PCS, the long-lasting symptom of fatigue has been compared to ME/CFS due to its chronicity and often debilitating impact on ADLs. The proposed mechanisms underlying COVID-19 fatigue include dysregulated immune response, excess oxidative stress, changes in DNA methylation patterns, impediment of cerebrospinal fluid (CSF) outflow, and indirect neuropsychiatric insults.

It is suggested that the high inflammation caused by acute COVID-19 engages the immune system in a robust response involving various cytokines. The result is persistent dysregulation of signaling mediators even after the initial illness subsides, leading to an ongoing cycle of continuous immune overactivity.²⁰ Another inflammatory pathway to chronic fatigue involves oxidative stress the body cannot overcome. Physiologic changes during viral illness lead to increased reactive oxygen species, such as superoxide, as a defense mechanism. However, prolonged COVID-19 can imbalance free radicals and antioxidants, including vitamin E and coenzyme Q10 (CoQ10). This may cause further cell injury by damaging DNA and protein.²¹ As a key source of reactive oxygen species, mitochondria are particularly vulnerable. Therefore, the central nervous system (CNS), where mitochondria dependence is crucial to meet energy demand, has increased susceptibility to oxidative stress. As a result, patterns of damage and chronic fatigue may be perpetuated. DNA methylation is an epigenetic process that usually silences gene expression on the molecular level. Alteration in methylation patterns has been linked to various conditions, including autoimmunity, cancer, and neurodegenerative disease.²² Although the number of studies is limited, hypomethylation has been found in cases of ME/CFS. It is suggested that COVID-19 fatigue may follow a similar pattern of decreased epigenetic silencing, ultimately resulting in increased synthesis of inflammatory proteins.

An additional proposed mechanism involves the glymphatic system, which plays a crucial role in the fluid clearance of the CNS. Its impairment is suggested to underlie multiple neurologic conditions, including Alzheimer's disease.²³ COVID-19 has a tropism for lymph endothelial cells, leading to fewer olfactory sensory neurons. It is hypothesized that the decrease in nerve cells impedes the low-resistance pathway of CSF outflow through the cribriform plate.²⁴ The disrupted drainage of fluid may result in stasis and lingering inflammatory mediators, precipitating continuous CNS immune response and subsequently post-acute fatigue. This theory is further supported by multiple studies suggesting a positive correlation between ME/CFS and elevated intracranial pressure.²⁵

COVID-19 fatigue may be considered a byproduct of the biopsychosocial impact of disease in addition to being a symptom of PASC. The lack of association between symptom burden and chronic fatigue has led researchers to consider that neuropsychiatric insults of non-viral etiology may be the primary culprit for this long-haul manifestation.²⁶ Regardless of acute viral illness severity, a correlation between psychiatric history and COVID-19 fatigue appears to be present. In a 2020 study exploring persistent fatigue, patients with a past diagnosis of anxiety or depression represented a significant proportion of those complaining of the long-haul symptom.²⁷

The multiple pathophysiological phenomena likely involved in COVID-19 fatigue can help guide the approach to management and treatment.

TREATMENT

Current research on COVID-19 fatigue therapeutics is limited. However, literature on ME/CFS suggests several options that appear to have shown effectiveness in some patients. Functional improvement of chronic fatigue has been observed for nicotinamide adenine dinucleotide hydride (NADH), probiotics, high cocoa polyphenol rich chocolate, and a combination of NADH and CoQ10.²⁸ Herbal supplements and pharmacologic agents, such as aripiprazole, have also shown benefits. Nevertheless, potential side effects need to be considered when prescribing treatment. One instance is minocycline, associated with nausea

and dizziness necessitating discontinuation in multiple patients.²⁹ There is limited evidence that dietary modifications may relieve ME/CFS.²⁸ Researched treatments are summarized in Table 2.^{17,28,30-37} An additional tool that may help fill the gap, where traditional therapeutics fall short, is OMT.

Osteopathic Treatment Considerations:

OMT may also help address the symptomatology of COVID-19 fatigue. Considering biomechanics, neural pathways, circulation, metabolism/energy expenditure, and psychosocial factors, OMT can be utilized to target the different ways disease impacts the body. Proposed modalities focus on fatigue and indirect approaches promoting the body's natural healing response. For instance, based on osteopathic principles, the Perrin technique, which involves manually stimulating fluid motion to optimize drainage, is one method of normalizing neuro-lymphatic flow.²⁴ Table 3 describes further how the five models of osteopathic medicine may provide a more holistic approach to targeting both somatic dysfunctions and fatigue symptoms in COVID-19 survivors.^{24,29,38-42}

CONCLUSION

COVID-19 fatigue affects as many as 47% of patients following acute infection, making it a significant health care burden and a commonly encountered complaint for family practitioners.^{6,43} The family medicine physician may be the first provider to interact with a patient suffering from long COVID-19 or MIS-C fatigue secondary to a SARS-CoV-2 infection. PCS fatigue is a diagnosis of exclusion; therefore, a thorough history is critical to making the diagnosis, and ruling out other serious diseases with similar symptoms. Considering how signaling molecules, epigenetic changes, oxidative damage, and neurological changes may work together to perpetuate inflammatory response and prolong COVID-19 fatigue, a number of treatment methods can be used in primary care to alleviate the burden of disease. Learning more about PCS pathophysiology can widen physicians' perspectives. Family medicine physicians can optimize patient care and improve public health outcomes by applying that knowledge to treat persistent fatigue pharmacologically or by using OMT.

TABLE 1:
 Differential Diagnosis for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome^{12,17}

| CARDIOVASCULAR | ENDOCRINE | GASTROINTESTINAL | HEMATOLOGIC |
|---------------------------------|------------------------------|---|------------------------------|
| Arrhythmia | Addison disease | Celiac disease | Anemia |
| Cardiomyopathy | Adrenal insufficiency | Food intolerance/allergy | Iron overload |
| Coronary artery disease | Cushing disease | Inflammatory bowel disease | Primary malignancy |
| Pulmonary hypertension | Diabetes mellitus | Small intestinal bacterial overgrowth | Secondary malignancy |
| Valvular heart disease | Hypercalcemia | | |
| | Hyperthyroidism | | |
| | Hypothyroidism | | |
| INFECTIOUS | NEUROLOGIC | PSYCHIATRIC | RHEUMATOLOGIC |
| Coccidioidomycosis | Cerebrospinal fluid leak | Anxiety | Dermatomyositis |
| Epstein-Barr virus | Chiari malformation | Bipolar disorder | Fibromyalgia |
| Giardiasis | Cranio cervical instability | Eating disorder | Polymyalgia rheumatica |
| Hepatitis B/C | Dementia | Major depressive disorder | Polymyositis |
| Human immunodeficiency virus | Multiple sclerosis | Schizophrenia | Rheumatoid arthritis |
| Lyme disease | Myasthenia gravis | Somatoform disorder | Sjögren syndrome |
| Parvovirus B19 | Narcolepsy | Substance use | Systemic lupus erythematosus |
| Q fever | Parkinson disease | | Temporal arteritis |
| Syphilis | Seizure disorder | | |
| Tuberculosis | Spinal stenosis | | |
| West Nile Virus | Traumatic brain injury | | |
| SLEEP | TOXIC SUBSTANCE EXPOSURE | OTHER | |
| Narcolepsy | Gulf War illness | Asthma | |
| Periodic limb movement disorder | Heavy metals (lead, mercury) | Athletic overtraining syndrome | |
| Sleep apnea | Medication adverse effect | Chronic obstructive pulmonary disease | |
| | Mold/mycotoxins | Overwork | |
| | | Severe obesity (BMI >40 kg/m ²) | |
| | | Vitamin deficiency | |

TABLE 2:
COVID-19 Fatigue Researched Treatments Summary

| TREATMENT | NO. SUBJECTS | PERTINENT RESULT OF STUDY | ADDITIONAL NOTES |
|---|--------------|---|---|
| Q-14 (Hua Shi Bai Du herbal supplement) | 204 | Improved symptoms including fatigue, fever, cough, and chest discomfort after COVID-19 infection. ³⁰ | Effective additive to traditional treatment. |
| Traditional Chinese medicine Bufeihuoxue (BFHX) capsule | 129 | Improvement in a 6-minute walk distance relative to a baseline group; Significantly lower Fatigue Assessment Inventory (FAI). | Rate of adverse effects (liver injury and diarrhea) was higher in the BFHX group than in the placebo group. ³¹ |
| High-dose zinc and ascorbic Acid | 214 | Does not significantly improve the severity of COVID fatigue. ³² | N/A |
| Cognitive-behavioral therapy (CBT) | 114 | In clinical trials at The ReCOVER Study for severe COVID fatigue. ³³ | The trial aims to assess if CBT may significantly decrease the severity of post-COVID fatigue. |
| Cardiopulmonary rehabilitation | 40 | In clinical trials at the COVID-Rehab study | The COVID-Rehab study aims to assess the effectiveness of optimizing functional capacity through improving cardiorespiratory fitness in patients suffering from post-COVID-19 sequelae, including fatigue; caution needs to be exercised and rehabilitation program individually tailored, as exercise that is too intense may lead to post-exertional malaise and worsen fatigue symptoms. ³⁷ |
| <i>Pacing*</i> (activity management) | N/A | Building stamina, alleviating the amount of exertion that would lead to PEM. Sometimes establishing a new functional baseline. | Patients counseled to reserve, balance, and understand their energy, especially after an episode of PEM. |
| Minocycline* | 100 | Shown to be a neural anti-inflammatory in animal models. ³⁴ | One mechanism to ME/CFS is increased neural inflammation. ¹⁷ |
| Aripiprazole* | 101 | Shown to have some utility in decreasing ME/CFS symptoms. ³⁵ | Dopamine agonist, also known to reduce inflammation. |
| Low-dose naltrexone (LDN)* | 18 | Improvement in impaired thought, concentration and cognitive overload, immune disturbances symptoms (sore throat, enlarged or tender lymph nodes, and susceptibility to colds/ influenza) | Acts at TRPM3 and opioid receptors in NK cells. ³⁶ |
| CoQ10 and NADH supplementation* | 73 | Significant improvement in fatigue impact scale total score versus placebo, as well as improved biochemical parameters. ²⁸ | N/A |

*researched for ME/CFS

TABLE 3:**Osteopathic Manipulative Medicine Integration.** Osteopathic manipulative techniques organized by each one of the five models of osteopathic medicine

| OSTEOPATHIC MEDICINE MODEL | TREATMENT | PROPOSED MECHANISM | RELATED PATHOPHYSIOLOGY |
|----------------------------|--|--|---|
| Biomechanical | Indirect and direct (if tolerated) OMT techniques directed to key somatic dysfunctions of the spine, thoracic cage, pelvis and extremities | Removes somatic restrictions to reduce structural impediments and therefore, optimize biomechanics, and improve function ²⁹ ; early intervention during the acute phase of illness may prevent buildup of restrictions leading to dysfunction and minimize occurrence of long-haul COVID-19 symptoms, including fatigue | Inflammatory state resulting in persistent functional restrictions (somatic dysfunctions) and ultimately dysfunctional movement of the body; altered regional motion and tissue compliance can interfere with the function of vascular, lymphatic and neurologic components ⁴² |
| Neurologic | Suboccipital release, OA decompression, rib raising, sacral/pelvic techniques | Normalizes sympathetic and parasympathetic nervous system activity by decreasing soft tissue and muscle tone in order to modulate paravertebral ganglia and vagal tone ³⁸ | Increased stress on the body due to a prolonged state of inflammation and immune dysregulation; continuous overactivation of the sympathetic nervous system leading to facilitation and viscerosomatic reflexes |
| Respiratory-Circulatory | Perrin technique/Thoracic pump/Pedal pump | Optimizes lymphatic drainage and promotes the body's natural healing response by normalizing neuro-lymphatic flow ²⁴ | Continuous chronic inflammation due to stagnant lymph, inducing persistent neuro-inflammation |
| | Venous sinus drainage | Removes impediments from venous channels in the cranium and improves clearance of the CNS ³⁹ | Glymphatic system impairment and disrupted CNS drainage |
| | Myofascial release of the thoracic inlet and thoracic diaphragm (doming) | Decreases inlet and diaphragm hypertonicity and improves lymphatic return ⁴⁰ | Increased state of inflammation of the body due to dysregulated signaling mediators; increased number of mediators fostering prolonged inflammation |
| Metabolic-Energetic | Articulatory techniques, Indirect techniques targeting musculoskeletal (MSK) somatic dysfunctions | Removes MSK restrictions throughout the body to improve movement and function allowing conservation of energy, as well as improving the body's efficiency and ability to adapt in response to stressors ⁴² | Increased energy demand of the body and CNS as a result of prolonged inflammatory and disease state |
| Behavioral | Compression of the 4th ventricle (CV4) | Likely reduces anxiety and induces general relaxation ⁴¹ | Biopsychosocial impact of disease leading to long-haul COVID-19 fatigue |

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REVIEW ARTICLE

THE VIRTUES OF OSTEOPATHIC MANIPULATIVE TREATMENTS IN PATIENTS WITH OPIOID USE DISORDER

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KEYWORDS

Opioid use disorder

OMT

Trauma

Pain management

ABSTRACT

As America continues to face the opioid epidemic, numerous people have made great strides in receiving formal treatment for their opioid use disorder (OUD). This research seeks to examine the effects of providing osteopathic manipulative treatment (OMT) along with traditional OUD pharmacological methods in providing results for patients. By using prior research on OMT techniques, we were able to uncover how effective OMT can be in reducing the time and discomfort associated with seeking opioid recovery. Osteopathic manipulative treatment, in combination with traditional pharmacology, was associated with reduction of somatic pain, higher success with medication-assisted treatment and lower costs. This research also highlights the importance of OMT in the era of COVID-19 social distancing, as well as special considerations when treating those with trauma histories associated with their disorder. We argue the benefit of OMT in combination with pharmacological methods can be successful at reducing the overall burden of prior OUDs.

INTRODUCTION

Patients who have opioid use disorder (OUD) are often labeled or misrepresented as “addicts,” a one-dimensional, negative connotation that neglects to capture the important aspects of a person’s identity and behavior.¹ A physician’s multidimensional consideration of the person not only reflects empathy but also can lead to a more accurate medical assessment of the patient, guiding the most appropriate treatment.

Osteopathic medical practice focuses on four main tenets, namely, that (1) the body is a unit, (2) the body is capable of self-regulation, (3) structure and function are reciprocally related, and (4) rational treatment is based on the basic principles of the body unit, each of which recognizes the importance of the body as a whole.² These tenets can be applied in the context of OUD, a complex, multisystem disorder in which there are changes in the structure and function of the brain and other organs due to the chronic use, misuse, and abuse of opioids.³

In any individual person, there are many factors, for example, the nature of the addictive substance and genetic predisposition, that play a role in the development of a substance abuse disorder.

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In one research study, for example, multiple genetic codes were discovered to be linked with an increased risk of having an OUD.⁴ “Addictive” rewards, which are positive experiences or sensations that reinforce the continued use of opioids, such as euphoria, “highs,” or weightlessness seen in patients with OUD, are linked with the disruption of dopamine homeostasis, leading to the dysregulation of the brain’s reward mechanisms.⁵ One of the primary goals of osteopathic manipulation is to promote the body’s natural inclination toward homeostasis. In patients with OUD with disruption in homeostatic mechanisms, both physiologically and somatically, osteopathic manipulative treatment (OMT) can be used to restore the proper balance and enhance recovery.^{3,5}

Along with losing the positive reward associated with substance use, patients with substance use disorders often experience extreme withdrawal symptoms, including vomiting, fatigue, sweats, insomnia, and delirium. We propose that there are multiple OMT techniques that can target these specific dysfunctions:

- Stomach pain, discomfort, and tenderness can be mitigated by using Chapman’s points.
- Lymphatic technique can be used to address withdrawal-related headache and congestion.
- The physician can practice osteopathic cranial manipulative medicine to help lessen the withdrawal side effects of insomnia and delirium.

For most patients with OUD, withdrawal symptoms serve as a large obstacle for overcoming their disorder. They thus continue using opioids, thereby reinforcing this negative behavior.⁶ By providing OMT that may help to ease these symptoms, physicians can foster disuse. A more comfortable recovery process increases the chances that patients will seek recovery treatment.

When using opioid medications, patients with OUD have an exaggerated reward response via dopaminergic pathways that can reinforce repeated opioid use and lead to the associated maladaptive behaviors.⁷ We theorize that a similar reward response can be elicited while receiving OMT. By stimulating dopaminergic pathways through the viscerosomatics of OMT, we predict general improvements in each patient's health, including their overall physical and mental well-being.

In addition to traditional and standard pharmacological treatment of OUD, we propose that using OMT in OUD patients can achieve significant benefits, including but not limited to (1) the reduction of subjective pain, (2) fewer titration trial doses, and (3) reduced costs.

1. The Reduction of Subjective Pain

Often withdrawal symptoms can be linked with a heightened sympathetic body response.⁸ Autonomic-centered osteopathic manipulative treatments normalize the sympathetic or parasympathetic response.

Some possible OMT treatments that have been suggested for conditions like anxiety or elevated heart rate include, but are not limited to, the following:

- Occipitoatlantal (OA) release, rib raising, trapezius muscle release
- Osteopathic cranial manipulative medicine
- Cervical/thoracic/lumbar soft tissue (ST) or myofascial release (MFR)

These treatments normalize parasympathetic and sympathetic tones and address somatic dysfunctions in the spine and can benefit an OUD patient because they help normalize negative withdrawal symptoms. In OUD patients experiencing withdrawal, sympathetic overdrive leads to elevated heart rate, blood pressure, and temperature.⁸ By implementing techniques that negate these sympathetic symptoms, patients will be less subjected to withdrawal symptoms.

For instance, clonidine as a central alpha-2 antagonist is often used to reduce sympathetic overdrive or facilitation in acute opioid withdrawal. By performing OA release on the patient, a technique that increases the parasympathetic tone, this would give the patient relief that parallels that of the patient taking clonidine. In addition, treatment for withdrawal symptoms like diarrhea and emesis can also be considered, which could include OA release, Chapman's reflex for stomach and esophagus, celiac ganglion MFR, and thoracic/lumbar ST or MFR.⁹

Another nonpharmacological option in patients with OUD who are experiencing discomfort is the OMT technique of "laying on

of hands." The perception of touch can elicit positive physical and emotional responses in patients with OUD, as mediated by a variety of neurotransmitters. In a study of patients with chronic pain who were treated with OMT, biomarkers such as beta endorphin increased from pre- to posttreatment.¹⁰ Beta endorphins are associated with positive affect, mood, and sense of well-being. By stimulating these same pathways, the patient may feel a familiar sense of comfort and release. This release of dopamine, along with pharmacological treatments targeting withdrawal symptoms, commonly alleviates the negative symptoms associated with withdrawal.

2. Fewer Titration Trial Doses

Many OUD patients seek and receive medication-assisted treatment (MAT), including methadone and buprenorphine, to achieve remission and recovery.¹¹ In one study, it was found that patients on MAT were able to remain addiction-free 60% of the time while on the medication as compared to those OUD patients on placebos.¹² Additionally, it was quantitatively found that OUD patients on MAT had higher treatment retention.¹²

Despite the effectiveness of MAT, finding the correct dosage for patients can be a time-consuming, elongated process, which proves painful and uncomfortable for patients as withdrawal symptoms heighten.¹² Osteopathic manipulative treatment techniques are designed to improve lymphatic flow and circulatory mechanisms. By improving lymphatic flow, patients may feel fewer severe withdrawal effects.¹³ Lymphatic techniques can help clear the body of toxins and inflammation, and when used in conjunction with MAT in patients experiencing withdrawal, they can reduce the risk of harboring infection.¹³ Additionally, lymphatic techniques can reduce the time and dosage of MAT necessary to obtain the most beneficial outcomes for OUD patients.

Both MAT and OMT are successful as monotherapies and are symbiotic in nature. Together, they can be used without interfering with the benefit of the other. Patients on MAT who must go daily to a methadone clinic or require regular follow-up with a specialized prescriber are already used to frequent, recurring appointments with healthcare providers. This is similar to what they can expect with OMT. Thus, adding additional appointments will not deter most OUD patients from continuing OMT support.

3. Reduced costs

Food, massages, concerts, shows, and the like are all activities that can boost and enhance a person's pleasure pathways. While all these activities are readily available, they can prove cost prohibitive. In contrast, OMT is an option for all patients, regardless of socioeconomic status, which can be performed in the office with no equipment and is often covered by insurance.

Additionally, OMT is widely accepted in literature as a legitimate treatment option and represents a cost-friendly alternative to activating pleasure pathway responses.

Osteopathic manipulative treatment can also be used in combination with accepted pharmacological treatments. In the Guidelines for the Chronic Use of Opioid Analgesics, a recently

adopted policy by the Federation of State Medical Boards, the recommendation for a pain treatment plan includes both pharmacologic and nonpharmacologic methods, such as OMT. In a pilot study that evaluated the effect of OMT on the brains of patients with chronic low back pain, the researchers found significant changes in circulatory pain biomarkers posttreatment with OMT.¹⁴ Osteopathic manipulative treatment adds to the primary care physician's (PCP's) tool kit and offers a noninvasive, low-cost, and low-risk option for patients.

Another study conducted demonstrated that osteopathic manipulation along with traditional pharmaceuticals is one of the top 10 most common complementary health approaches among adults.¹⁰ Applying the osteopathic approach for the treatment of psychiatric conditions can be traced back to 1914, when the Still-Hildreth Sanatorium (SHS) was opened. The treatment protocol at SHS included OMT at least three times per week, healthy diet and exercise, group and social activities, and managing the physical environment. While there were limitations in data in an SHS chart review, the study found that many patients recovered or improved with the treatment at SHS, more so than they might have with pharmaceuticals alone.¹⁵

SPECIAL CONSIDERATIONS

Patients with trauma histories

Many patients who suffer with substance use disorders also have comorbid trauma histories and special consideration needs that must be heeded when touching patients who have experienced any kind of physical or sexual trauma in their pasts.¹⁶ In one study comparing people with OUD to those without it, the former suffered with statistically significant symptoms of posttraumatic stress disorder (PTSD), depression, and anxiety.¹⁷ A study conducted in Australia determined that one-third of people with OUD meet the criteria for PTSD.¹⁸

Before performing OMT on OUD patients, careful consideration of previous physical and emotional trauma to touch must be considered. Special attention must be paid to the high comorbidity of PTSD and OUD, possibly triggering a PTSD reaction.^{19,20} By being aware of touch as a trigger, we highlight various techniques to help ease the patient into comfort during the visit.²¹

In the OMT treatment setting, securing a trauma history results in a more comprehensive understanding of the patient. Some are open and comfortable discussing their traumatic experiences, having processed them through psychotherapy and, in turn, having developed resilience and insight; however, others continue to experience dissociative and emotional reactivity symptoms relating to their past trauma that need to be explored and addressed before they can be touched for OMT. It is important for the OMT provider to appreciate how the trauma has affected the patient and how this might impact the OMT treatment, rather than granular details pertaining to the trauma itself.

To best understand potential triggers of trauma for your patient, we reference the American Psychiatric Association guidelines for best practices in addressing trauma with sensitivity. It is important to initiate trauma evaluation compassionately by gently asking about the following parameters:²²

1. Screening for exposure to traumatic event
2. Potential triggers for trauma
3. Symptoms associated with trauma (fear, horror, etc.)
4. Detailed understanding of exposure
5. Full psychiatric evaluation screening for PTSD, suicidal ideation, and risk assessment

The first step in approaching patients with OUD and trauma history is describing in lay language exactly how and where you are going to touch them, with what pressure, and the manner in which you are going to diagnose their somatic dysfunction. It is vital to ask and receive the patient's permission before touching them. Once the somatic dysfunction is found, the next step is to again discuss with the patient exactly what technique you are going to use, where your hands are going to be, what level of pressure you plan to use, and how it should feel during the treatment. You should also invite patients to stop the treatment at any time they feel uncomfortable and let them know that if they want to retry, then a slower, more gentle approach can be employed.

Given that many patients are highly sensitive to touch and hypervigilant in situations where they feel physically vulnerable, the most appropriate OMT techniques to start with are those that are soft and gentle.²¹ So-called "soft techniques," including suboccipital release, cradling with traction, or prone traction, are beneficial for both helping with the sympathetic overdrive and other distressing symptoms related to withdrawal from opioids, as well as with PTSD-related symptoms. These techniques allow a more holistic approach to simultaneously treating hyperactive elements of both PTSD and OUD. Soft techniques, when explained and employed in a compassionate manner, have been deemed to be wholly salutary.¹⁶

Along with emphasizing soft, gentle touches, other advantageous techniques may be employed. We suggest creating a provider checklist that can be used at every office visit with any patient. By taking the time to assess patient boundaries and comfort, providers are able to better foster patient-physician connections that can help aid in the path to healing. Suggestions include the following:

1. *Communication.* Using plain language, make sure the patient knows the nature of the technique and the area of the body being worked on.
2. *Model.* Use models and safe skin areas to demonstrate pressure, temperature, and any assistive devices associated with the technique utilization. Consider having another person present in the room, such as a medical assistant, resident, or family member, upon whom the technique can be performed in order to let the patient watch and feel more comfortable.
3. *Boundaries.* Set clear expectations with your patient before any touching about areas they want you to avoid. Discuss sensitive touching areas and how they should be handled.
4. *Witness.* During the duration of the treatment, have a healthcare worker who is the same gender as the patient present in the room.

5. *Time option.* Offer multiple shorter sessions for the patient to help ease them into the process and new stimulation.
6. *Soft techniques.* Any soft tissue should be handled with pressure in accordance with the patient's comfort level.
7. *Discussion.* Throughout and on completion of the treatment, assess the patient's emotional state and treatment tolerance. Be sure to express that the patient, at any time, is able to voice areas of concern or discomfort. Open discussions with the patient to assess the mental and physical feelings that emerge from treatment.
8. *Interpersonal.* Refer patients with trauma for both medical management as well as eye movement desensitization and reprocessing, cognitive behavioral therapy, and other types of psychotherapy. Provide a list of resources for the patient to seek additional forms of treatment, support, and comfort for their OUD.

OSTEOPATHIC MANIPULATIVE TREATMENTS IN THE COVID-19 ERA AND ITS AFTERMATH

In the ongoing and current pandemic, depending on the COVID-19 infection rate in any particular region, social distancing is still of high priority in certain indoor and outdoor settings. At the beginning of the pandemic, social distancing led to abrupt cessation of many people's joyful outlets for stress and coping, including concerts, dinner with friends, and even work-related activities. In addition, many healthcare office practices shifted to a telehealth model. In this time of isolation, with people staying home, working remotely, and losing their access to other means of stress relief, the substance use rates have increased significantly. Several months into the pandemic, a June 2020 study evaluated the impact of COVID-19 and substance use on more than 5,000 adults.²³ The study found that more than 13% of respondents abused a substance, such as alcohol or opioids.²³ In this same study, one in 10 subjects were found to start or increase substance use as compared to before the pandemic.²³

Osteopathic manipulative treatment can only be performed in person and requires repeated treatments. These repeated office visits galvanize the patient-doctor trust alliance. Furthermore, such office visits allow patients the chance to leave their homes and have human interaction. In one study, it was determined that patients who harbored trust in their doctors responded more positively to their advice.²⁴ This trust likely emanated from personal interactions between the doctor and patient, including frequent and longer one-on-one contact.²⁴

DISCUSSION

There are multiple OMT techniques, and each osteopathic PCP should determine a treatment plan based on their clinical judgment and an individual patient's needs. Five key models serve as the basis for osteopathic treatments: biomechanical, respiratory-circulatory, neurological, metabolic-energy, and behavioral.¹⁵ Osteopathic PCPs can select OMT treatments that address one or more of these models alone or in combination.

Our research team hopes to start a deeper investigation of many of our claims. In such studies, we hope to better compare MAT alone versus OMT in combination with MAT on traditional measures of withdrawal. By conducting more in-depth studies of the effectiveness of OMT in OUD patients, we hope to raise continued awareness of the importance of implementing OMT in daily practice with OUD patients.

CONCLUSION

An osteopathic approach in the care of OUD patients can help remediate this multidimensional condition. It enables the osteopathic PCP to provide care for the whole patient, not simply their addiction. Further research is required to determine the extent of the effects of OMT on the OUD patient. We predict that OMT combined with pharmacological treatment, as compared to pharmacological treatment alone, on the OUD patient can lead to better outcomes—for example, a decreased MAT maintenance dose, lower rate of relapse, lower admissions rates to rehabilitation programs, and improved compliance with MAT. Medication-assisted treatment has been found to be successful as monotherapy, but we suggest higher success rates when used in conjunction with OMT. Overall, OMT targets the same pathways that the abused drug might, improves circulatory effects, and is widely recognized and accepted both in literature and by the insurance industry, offering a cost-effective method that, when combined with pharmacological treatments, can provide the patient with maximal care.

Opioid use disorder is not a new problem. It is essential that doctors take into consideration the best ways to help patients overcome their OUD, especially with comorbid conditions, such as PTSD. Our research highlights the importance that OMT in combination with traditional pharmacology can have on OUD recovery. Additionally, we have set forth the essential guidelines for how to make patients feel comfortable whenever and wherever OMT is performed. Especially in the up-and-coming telemedicine era, it is essential that doctors, if able, provide a hands-on approach to help expedite the healing process of OUD patients.

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REVIEW ARTICLE

PROSTATE CANCER WITH A PRESENTING SYMPTOM OF LOWER THORACIC BACK PAIN

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KEYWORDS

Prostate cancer

Back pain

Aggressive pathology

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ABSTRACT

Back pain is a common complaint addressed by family physicians. This is an uncommon case of a patient presenting with back pain and subsequent workup revealing a new diagnosis of metastatic prostate cancer with bone metastasis. This case can be used to highlight an unusual presentation and to facilitate inclusion of prostate cancer in the differential diagnosis. A review of the literature calls attention to the clinical features that make such a scenario likely and guides the discussion of the current understanding of the mechanisms leading to such a presentation. Underlying risk factors of obesity, diabetes, and chronic kidney disease (CKD) may increase this risk. A high Gleason score with poorly differentiated features also increases the risk of de novo metastatic presentation.

INTRODUCTION

Prostate cancer generally presents with asymptomatic prostate-specific antigen (PSA) elevation or symptoms of prostatism, which include increasing frequency of urination, nocturia, increased urgency, urinary hesitancy, and incomplete bladder emptying.¹ This case highlights an uncommon presentation of prostate cancer. Back pain is not a common presenting symptom in early prostate cancer patients.² This highlights the need for primary care physicians to keep prostate cancer in the differential diagnosis for new and sudden onset of back pain without any previous history.

HISTORY

A 62-year-old white male, with a history of obesity, type 2 diabetes mellitus, hypertension, and chronic kidney disease (CKD), presented to his primary care physician with worsening lower thoracic back pain. The pain began worsening a week before the initial visit. The patient ranked the pain a 5 out of 10. The pain was aggravated by any activity and alleviated with oral acetaminophen. There were no other associated symptoms.

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There was no prior history of cancer, nor did the patient have any family history of cancer. He also did not have any autoimmune disorders or immune deficiencies. The patient had retired from his career as a physician before his initial complaint of back pain. A colonoscopy was performed a month before his initial visit and was normal. The patient had been monitoring his PSA annually and it was within normal limits a year prior to presentation. On physical examination, his temperature was 98.3°F, pulse 80 bpm, respirations 18 breaths/min, and blood pressure 145/85 mm Hg. On palpation, his lower thoracic spine was tender. His lungs were clear, his heart was regular, and the HEENT exam was normal. The patient declined a rectal prostate exam. Laboratory examination revealed a PSA of 9.9 ng/mL, creatinine of 5.3 mg/dL, and eGFR of 11 mL/min. A creatinine study done one month prior was at the same level. On the first visit, the patient was treated with acetaminophen and hydrocodone for symptomatic pain control. Follow-up plain radiographs did show a compression defect at the T12 vertebrae.

On a follow-up visit, one week later, he reported his back pain was 3 out of 10 with the prescribed pain medications. A CT scan with contrast was not performed because of the patient's history of CKD. Magnetic resonance imaging (MRI) of the thoracic spine revealed a compression fracture of the T12 vertebrae. The patient was referred for kyphoplasty, which showed metastatic prostate adenocarcinoma. A base-of-skull-to-upper-midhigh positron-emission tomography (PET)

INTRODUCTION

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A 62-year-old white male, with a history of obesity, type 2 diabetes mellitus, hypertension, and chronic kidney disease (CKD), presented to his primary care physician with worsening lower thoracic back pain. The pain began worsening a week before the initial visit. The patient ranked the pain a 5 out of 10. The pain was aggravated by any activity and alleviated with oral acetaminophen. There were no other associated symptoms. There was no prior history of cancer, nor did the patient have any family history of cancer. He also did not have any autoimmune disorders or immune deficiencies. The patient had retired from his career as a physician before his initial complaint of back pain. A colonoscopy was performed a month before his initial visit and was normal. The patient had been monitoring his PSA annually and it was within normal limits a year prior to presentation. On physical examination, his temperature was 98.3°F, pulse 80 bpm, respirations 18 breaths/min, and blood pressure 145/85 mm Hg. On palpation, his lower thoracic spine was tender. His lungs were clear, his heart was regular, and the HEENT exam was normal. The patient declined a rectal prostate exam. Laboratory examination revealed a PSA of 9.9 ng/mL, creatinine of 5.3 mg/dL, and eGFR of 11 mL/min. A creatinine study done one month prior was at the same level. On the first visit, the patient was treated with acetaminophen and hydrocodone for symptomatic pain control. Follow-up plain radiographs did show a compression defect at the T12 vertebrae.

On a follow-up visit, one week later, he reported his back pain was 3 out of 10 with the prescribed pain medications. A CT scan with contrast was not performed because of the patient's history of CKD. Magnetic resonance imaging (MRI) of the thoracic spine revealed a compression fracture of the T12 vertebrae. The patient was referred for kyphoplasty, which showed metastatic prostate adenocarcinoma. A base-of-skull-to-upper-midthigh positron-emission tomography (PET) scan showed hypermetabolic osseous metastases in the T12 vertebrae with kyphoplasty changes but with no other evidence of distant metastases. It also showed mild prostatomegaly with fluorodeoxyglucose (FDG) uptake along the right side of the prostate. The usage of both an MRI and PET scan allowed for the integration of the structural findings from an MRI into the functional findings of a PET scan. These findings, along with the immunohistochemistry profile detailed below, indicated metastatic adenocarcinoma suggestive of primary prostate cancer. Thoracic spine biopsies showed tumor cells positive for

AE1/AE3 and CAM5², which are both epithelial markers, as well as NKX3¹, which is a prostate cancer marker.³ The biopsies were negative for CK7 (a lung and upper GI marker), CK20 and CDX2 (lower GI markers), TTF1 (a lung marker), and GATA3 (a bladder marker).³ Prostate biopsies showed adenocarcinoma with a Gleason score of 9 (4 + 5) in 8 out of 12 cores.

Most prostate cancers will present with a Gleason score of 6 to 7 consistent with low-risk cancer, however, his score indicated poorly differentiated and highly aggressive cancer with a predilection for metastasis.⁴ He was first started on combined androgen blockade therapy with a combination of leuprolide acetate and bicalutamide, which is the standard of care for hormone-sensitive metastatic prostate cancer. Leuprolide acetate is a GnRH agonist that suppresses the production of testosterone through a feedback mechanism when given continuously. However, when first started, leuprolide acetate causes a temporary increase in testosterone levels that is blocked by concurrent use of bicalutamide, a direct testosterone antagonist.⁵ The patient was referred to radiation oncology for definitive prostate radiation due to the limited metastasis of this patient's cancer to just one vertebral body. After completing this successfully, he received 40 fractions of 200 cGy each, for a total dose of 8000 cGy delivered to the prostate and seminal vesicles. The treatment began a few days after the initial visit and was completed 5 days a week for 8 weeks. His repeat PSA is undetectable (<0.64 ng/mL) and his back pain has resolved. The patient was on a renal transplant list due to end-stage renal disease. However, due to the finding of metastatic cancer, he no longer qualified for a transplant. The patient is currently in remission with no evidence of disease, with PSA levels monitored every 3 months. The patient's prognosis is guarded—although a cure is unlikely, a long-term durable remission is possible. The combination of immunosuppression from CKD and aggressive pathology likely contributed to his metastatic presentation.

DISCUSSION

Prostate-specific antigen, also known as human kallikrein 3, belongs to a family of serine proteases. It is produced primarily in the prostate epithelium, which is why it gets this designation.⁶ Prostate-specific antigen functions principally to allow for sperm motility and also may have some role in breaking down cervical mucus.⁷ Prostate cancer is not the only pathology in which there will be elevated PSA levels; benign prostatic hyperplasia and prostatitis will also cause elevated levels. For this reason, PSA is used only as a screening tool for prostate cancer and requires additional testing for diagnosis. Contrary to what would be expected, in poorly differentiated prostate cancer, PSA levels will be significantly reduced due to the loss of prostate-specific phenotype, as demonstrated by negative PSA staining on immunohistochemistry.⁶ Bonk et al demonstrated in a microarray study of 21,000 tissue samples that low PSA levels were correlated with TMPRSS2:ERG gene translocation and PTEN (phosphatase and tensin homolog) deletions.⁶ Phosphatase and tensin homolog is a tumor suppressor gene that functions to turn off cell-signaling pathways. TMPRSS2:ERG is one of the most common genetic changes found in about half of all prostate cancers previously

example, $3 + 3 = 6$, $4 + 3 = 7$. The total scores or Gleason scores of 6 and 7 are reflective of low and intermediate risk; whereas, Gleason scores of 8 or higher are considered high risk.¹⁶

The primary and secondary histologic pattern of differentiation of cells noted after biopsies are each graded 1 through 5 and then summed together to achieve a Gleason score for the samples, for example, $3 + 3 = 6$, $4 + 3 = 7$. The total scores or Gleason scores of 6 and 7 are reflective of low and intermediate risk; whereas, Gleason scores of 8 or higher are considered high risk.¹⁶

B. Prostate cancer metastasis

Advanced cancers like breast and prostate primarily metastasize to bone causing compression and pathological fractures.³⁷ Metastasis of prostate cancer to bone occurs through hematogenous spread.¹⁷ The release of exosomes from prostate cancer cells into the bloodstream show organotropism for bone, making bone the primary site for prostate cancer metastasis. The identification of organotropism is primarily determined by integrin components and proteins in epithelial-to-mesenchymal transition (EMT).¹⁸ This tropism is determined by the noncollagen proteins found in the bone matrix.¹⁹ Bone matrix is about 95% type I collagen, and the remaining 5% includes proteins like osteopontin, osteonectin, and bone sialoprotein.¹⁹ These proteins are the targets of migratory prostate cancer cells, allowing for metastasis and growth at the bone.¹⁹ In addition to tropism, EMT has been correlated with metastasis and later stages of cancer progression. Liu et al showed that fatty acid binding protein 12 (FABP12) expression was correlated with prostate cancer progression in PC3 cell lines. Fatty acid binding protein 12 acts through the peroxisome proliferator-activated receptor-gamma pathway, which will induce EMT as well as increase prostate cancer reliance on fatty acids for energy production.²⁰ Fatty acids are not only implicated in energy production but also in signal transduction (as second messengers).²¹ Tumor growth factor-beta is also implicated in EMT progression and bone metastasis.²² The metastasis to bone will result in altered bone density due to the altered activity of osteoblasts and osteoclasts.²²

N-cadherin and E-cadherin expression are also implicated in prostate cancer progression and metastasis. Patients with higher-grade lesions, ie, a Gleason score ≥ 8 , show lower concentrations of E-cadherin and higher concentrations of N-cadherin.¹⁹ The elevated levels of N-cadherin are also implemented in promoting castration resistance, which could potentially be a target to protect against malignancy.²³ MicroRNAs (miRs) are another option for novel therapy for prostate cancers. For instance, miR15/16 are tumor suppressors shown to be downregulated in prostate cancer²⁴; miR15/16 are involved in cell-cycle control mechanisms by binding and inactivating cyclin D1, cyclin E, Bcl-2, c-Myc, and EF2.²⁵ The downregulation of these miRs result in increased cell cycling. Reintroduction of these miRs has been shown to stimulate apoptotic pathways (through Bcl-2), decreased growth, and proliferation.²⁵ Also, miR-145 is implicated in prostate cancer; however, this miR upregulates metastasis of prostate cancer cells by increasing motility through inactivation of the N-cadherin.²⁵ Zaman et al showed that upregulating miR-145 decreases

proliferation of prostate cancer cells and increases apoptotic cells, indicating its use as a therapeutic target.²⁷ Other options are BRCA and poly(ADP-ribose) polymerase, which are both involved in DNA repair mechanisms and are current therapeutic targets of prostate cancer according to the American Cancer Society.

C. Reasons for unusual presentation

The development of Type 1 and Type 2 diabetes may be related to our body's immune function.²⁸ In Type 1 diabetes, the immune cells, such as the T cells and macrophages, proliferate abnormally and produce numerous proinflammatory markers that may also be defective in diabetic patients with increased glucose levels in blood.²⁹ Certain receptors on the immune cells that recognize pathogens are defective in patients with sustained high glucose levels, leading to an overall immunosuppression and increased susceptibility to various diseases.³⁰ There are also studies that show that blood from patients who do not have diabetes, when subjected to increased glucose levels, had reduced cytokines. Cytokines are biomarkers produced to recruit more immune cells when pathogens invade our body.³¹

The human body has two types of immunity, namely innate and adaptive. When a patient has end-stage renal disease, the increased activation of the innate immune cells leads to increased inflammation and oxidative stress on the kidney cells. This, in turn, activates the adaptive immunity, persistently leading to more inflammation.³² Dysregulation of immunity in CKD may contribute to increased risk of malignancy.³³

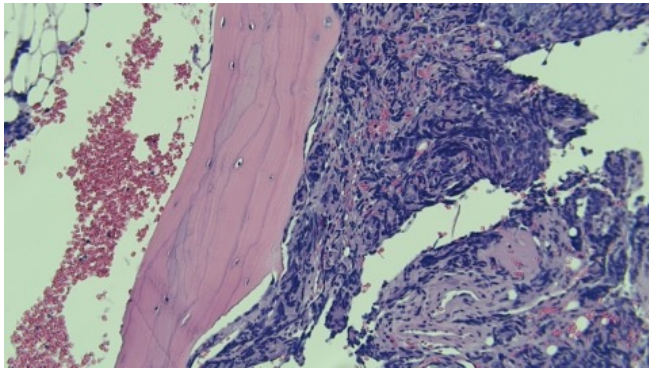
Excess body weight and obesity happen when the total body energy expenditure is less than the consumption, making elevated amounts of adipose tissue deposit in various areas of the body. Therefore, adiposity plays a major role in development of diseases affecting the heart and body metabolism.³⁴ There is also increased evidence that obesity may lead to higher risk for different kinds of cancer, such as breast, thyroid, gastric, colorectal, gallbladder, and multiple myeloma.³⁵ Obesity and excess body weight are determined by measuring the body mass index. According to the World Cancer Research Fund Report, obesity's role in prostate cancer is probable but not investigated. There were restrictions such that imaging without contrast had to be performed due to CKD and renal insufficiency, but PET and MRI helped with identification of bone metastases.³⁶

CONCLUSION

There is a need for inclusion of back pain as risk scoring for prostate cancer. As a standard of care, worsening low thoracic pain is usually not tested for prostate cancer. There is also a need for active surveillance as standard of care, not only for patients with a high PSA level, but also for patients who may not have a high PSA level but do have other indications such as aggressive Gleason score patterns and MRI imaging results.³⁸ There is literature available that points toward hereditary factors leading to an increased risk of prostate cancer as an outcome; therefore, a genetic risk evaluation via a polygenic risk score may help with early identification of such cases.³⁹

FIGURE 1:

Low- and high-power view of decalcified bone show extensive involvement by solid sheets of carcinoma cells with prominent nucleoli.

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REVIEW ARTICLE

OSTEOPATHIC CONSIDERATIONS IN PAIN MANAGEMENT

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KEYWORDS

Pain management

Chronic pain

Myofascial release

Counterstrain

Tenderpoint

ABSTRACT

Chronic pain is defined as pain that has persisted for greater than 6 months. This type of pain may last longer than 6 months and can continue even after the injury or illness that has caused it has healed or resolved. Pain signals can remain active in the nervous system for weeks to months and even years. Individuals with a chronic pain syndrome can experience severe negative effects on their activities of daily living and their mental well-being. The osteopathic philosophy and osteopathic manipulative treatment (OMT) set the osteopathic physician up to provide a comprehensive treatment plan to manage patients with chronic pain. To direct osteopathic techniques to address pain, it is imperative to understand the anatomy and physiology of the way pain is signaled to the central nervous system. Pain can also be classified into multiple categories based on the origin of the signal, which is essential to decipher to direct therapy. The goal of osteopathic care in chronic pain syndrome is to relieve musculoskeletal somatic dysfunctions and to normalize sympathetic and parasympathetic neural tone. This would create the optimal environment to induce the body's own self-healing capabilities.

INTRODUCTION

Chronic pain is defined as persistent pain signals that continue to fire in the nervous system from weeks, months, to even years as defined by the National Institute of Neurological Disorders and Stroke¹. Chronic pain persists even after the causative injury or illness has resolved or healed. While acute pain subsides within 3–6 months, some people may develop chronic pain without any causative or past injury that can last more than 6 months². Chronic pain often interferes with work or other activities of daily living. The stress on the body from chronic pain may cause physical conditions, such as tense muscles, limited range of motion, decreased energy, and even changes in appetite. The Institute of Medicine reports that chronic pain is a biopsychosocial condition that often requires a multifaceted and integrated approach in which all the components should be evidence-based.³

EPIDEMIOLOGY

The US Centers for Disease Control and Prevention (CDC) reports that an estimated 20.4% (50 million) of US adults have chronic pain and 8.0% of US adults (19.6 million) have high-impact chronic pain with higher prevalence associated with advancing age.⁴

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PRINCIPLES OF OSTEOPATHY

Approaching chronic pain from an osteopathic perspective allows for physicians to not only address the patient's physiologic concerns but also their psychosocial apprehensions. The four tenets of osteopathic medicine allow the osteopathic physician to understand pathology, not only as a medical problem affecting human anatomy and physiology but also affecting the body as a whole unit considering the body's innate ability to self-regulate.⁵ The four tenets of osteopathy are: the body is a unit, the body is capable of self-healing and regulation, structure and function are reciprocally interrelated, and treatment is based upon the previous three tenets.⁶

Osteopathic physicians should also consider the interrelationship of structure and function to best direct the treatment modality. Conventional medical therapies for chronic pain generally consist of medications and treatments targeting the physiologic aspects of the pain and neglect the psychosocial aspects that are clearly affected by this pathology.

In osteopathic medicine, therapy can be targeted through different models of illness. Osteopathy teaches the treatment of the body as a whole unit through the application of these five models: biomechanical, neurological, respiratory-circulatory, metabolic, and behavioral.⁷ When treating chronic pain, the most beneficial model for therapy would be the biomechanical lens, which aims to alleviate muscular and structural somatic dysfunctions, thus allowing the body to restore its function and facilitate its innate ability to self-heal. This, however, does not mean that the other

models cannot be used as supplementary therapy for chronic pain. All five models should be used to facilitate the most effective and well-rounded treatment for chronic pain.

The biomechanical model of osteopathy teaches that there are correct positions for each structure in the body, allowing for the body to maintain homeostasis. Any change in these positions would cause changes in alignment and interrupt the homeostasis of the physiology in that structure. Due to this, external forces that can be applied with precision can return the body to proper alignment of the structure. This would restore homeostasis and allow the body's innate ability to heal itself.⁸

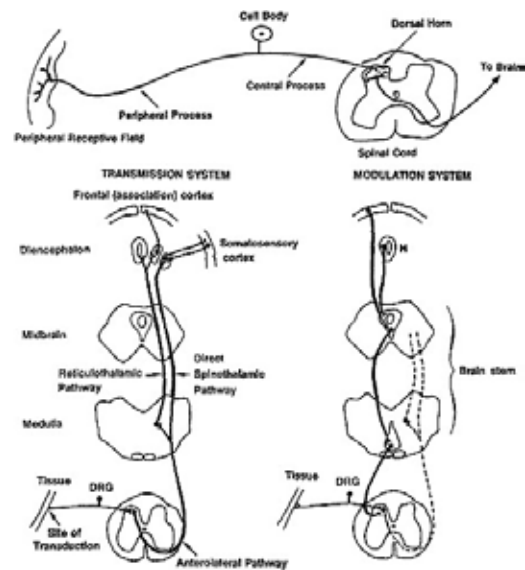
PATHOPHYSIOLOGY

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Pain serves to prevent tissue damage and protect the body while it is healing. Painful stimuli are detected by nociceptors, which are free nerve endings located in tissues and organs. They have high thresholds and, under normal circumstances, only respond to noxious stimuli. There are two types of nociceptors: High threshold mechanoreceptors, which stimulate small myelinated fast-conducting Aδ fibers that transmit a well-localized sharp or pricking sensation that lasts as long as the stimulus, and polymodal nociceptors that stimulate small unmyelinated slow-conducting C fibers.⁹ C fibers are unmyelinated slow-conducting fibers that transmit a less well-localized, persistent aching pain that lasts after the initial stimulus has gone. Aβ fibers conduct low-intensity mechanical stimuli that convey touch and not pain; however, in chronic pain states, they are involved in the transmission of pain.¹⁰

The transmission of pain involves a pathway by which an inciting injury or stimulus excites nociceptors on peripheral nerve endings. This triggers a cascade of chemical reactions and impulses that are directed toward the central nervous system (CNS). This is the route by which the CNS is informed of impending or actual tissue damage. Its peripheral process runs in peripheral nerves, and its peripheral terminals are present in most body structures. These terminals are sensitive to noxious heat, mechanical stimulation, and or pain-producing chemicals. The central process enters the spinal cord via the dorsal root and terminates on central pain-transmission cells that relay the information to higher centers. Both peripheral and central processes are maintained by the cell body in the dorsal root ganglion, which is near, but not in, the spinal cord.

FIGURE 1:

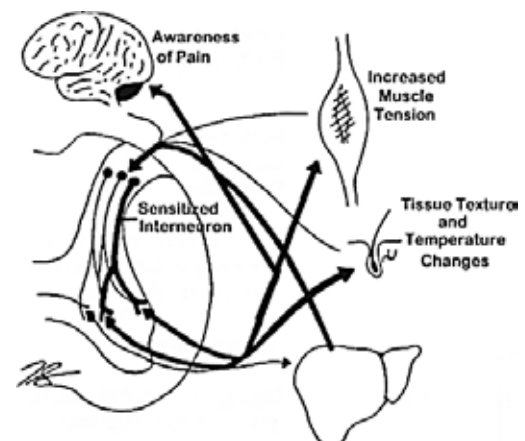
Adapted from Institute of Medicine (US) Committee on Pain, Disability, and Chronic Illness Behavior; Osterweis M, Kleinman A, Mechanic D, eds. *Pain and Disability: Clinical, Behavioral, and Public Policy Perspectives* Figure 7-1 showing a diagrammatic outline of the major neural structures relevant to pain.³



To direct osteopathic manipulation using the biomechanical model, osteopathic physicians must understand the concept of facilitation. Facilitation is the maintenance of a pool of neurons (premotor neurons, motor neurons of preganglionic sympathetic neurons in one or more segments of the spinal cord) in a state of partial or subthreshold excitation.¹¹ In this state, less afferent stimulation is required to trigger the discharge of impulses, therefore causing pain without any substantial triggers or inciting events. Facilitation may be due to a sustained increase in afferent input or changes in the affected neurons themselves. Once this has been established, facilitation can be sustained by normal CNS activity (Figure 1).

FIGURE 2:

Adapted from Savarese RG. *OMT Review* 3rd edition depicting the process of spinal segmental facilitation.¹²



If this form of facilitation occurs at an individual spinal level, it is termed segmental facilitation. To determine how a segment becomes facilitated, physicians must address the areas from which a spinal cord segment can receive neurologic input. These areas are the brain, the viscera via sympathetic or parasympathetic visceral afferents, and from somatic afferents (muscle spindles, Golgi tendons). Any abnormal stimuli from these areas can cause the neurons of the spinal cord to become sensitive to the stimulus and can therefore become “facilitated” if the signal is persistent or large in magnitude. (Figure 2). This facilitated pool of neurons can then affect the initiating site of the stimulus or any surrounding areas such as the neighboring muscles and/or organs via autonomic afferents.¹³

An example of this is a trapezius muscle strain that can cause facilitation of the spinal segments of C1–C6. When a patient strains his or her trapezius muscle, abnormal and continuous sensory input from the overstretched muscle spindle sensitizes the interneurons of the C1–C6 spinal levels. This reflex causes muscle tension, pain, and tightness at the area of the trapezius, which will result in restriction of motion and tenderness upon palpation. Prolonged muscle tension causes continuation of the stimulus and therefore maintains the facilitation of these segments. Muscle tension of the trapezius causes nociceptor activation in the neighboring areas and a release of prostaglandins, bradykinin, and other cytokines. These chemicals can cause local vasodilation and tissue texture changes. This cycle of sensitization of these facilitated segments can cause increased muscle tension of the local paraspinal muscles. The increased tension of the paraspinal muscles can cause the cervical spinal segments to rotate and side bend, which can cause asymmetry. This asymmetry can cause the dysfunction and strain of more muscle groups that can then, in turn, cause further facilitation of more distal spinal segments.

In addition to facilitation, understanding the mechanisms of viscerosomatic and somatovisceral reflexes is crucial to directing osteopathic therapy. A viscerosomatic reflex occurs when a visceral stimulus of some sort can produce a response to its related spinal segments and surrounding somatic structures.¹⁴ Conversely, a somatovisceral response is one where a somatic stimulus of some sort can produce a response in segmentally related visceral structures.¹⁵ An example of a viscerosomatic reflex would be how the pain of acute cholecystitis may present as right-sided thoracic back pain. This is because the segmental sympathetic innervation of the gallbladder and upper gastrointestinal tract come from the T5–T9 spinal cord levels. An example of a somatovisceral reflex would be the concept of trigger points. A trigger point located at the right side of the chest between the fifth and sixth ribs can cause tachyarrhythmias.¹²

TYPES OF CHRONIC PAIN SYNDROMES

Chronic pain can be subdivided into two broad categories: nociceptive and neuropathic. Nociceptive pain is caused by short-lasting noxious stimuli in intact tissue in the absence of peripheral or central sensitization. In chronic pain, these nociceptors can malfunction and remain turned on. This therefore causes the sensation of pain even though the inciting injury has resolved. Neuropathic pain results from nerve injury.¹⁶ Instead of an injury

to an organ causing receptors to fire pain signals, neuropathic pain occurs when the nerve itself is damaged. Examples of neuropathic pain include diabetic neuropathy, multiple sclerosis, herpes zoster, and spinal injuries. Unlike nociceptive pain, neuropathic pain may not respond as effectively to conventional pain-relieving medicines such as anti-inflammatories or opiates.¹⁷ In neuropathy, since the damage is to the nerve itself, different modalities must be used to alleviate the symptoms. As mentioned earlier, these types of pain signaling pathways are not mutually exclusive and therefore warrant a more holistic approach to their management.

Since chronic pain can be so diverse in its presentation and location, osteopathic therapy should be tailored to the entire autonomic nervous system in addition to the musculoskeletal system. Knowing the information about the sympathetic innervations and segmental facilitation, osteopathic physicians are equipped with treatment modalities that can normalize sympathetic tone by focusing on specific segments and areas of the body that may be the cause of abnormal nervous signaling. Besides addressing the sympathetic nervous system, osteopathic physicians can also direct therapy to regulate the parasympathetic nervous system. This entails regulating parasympathetic tone by normalizing the vagus nerve and the pelvic splanchnic innervation. Deciphering where the pain is located and where it originates from can help indicate which part of the parasympathetic nervous system should be targeted for therapy.

MUSCULOSKELETAL OSTEOPATHIC TREATMENTS

Patients suffering from chronic pain often have somatic dysfunctions. Whether it results from facilitated segments that cause referred pain to the surrounding musculature or from the actual site of injury, osteopathic manipulation has shown to be effective in relieving or decreasing the intensity of the pain after the intervention. A randomized controlled trial of osteopathic treatment techniques was performed in 2012 on military personnel with acute low back pain. The results of the trial showed that the patients reported significantly less pain during the osteopathic treatment visits and with every subsequent follow-up visit compared to patients who only received allopathic treatment.¹⁸

Myofascial release (MFR) includes several types of osteopathic manipulative treatment (OMT) to stretch and release muscular and fascial restrictions. Myofascial release can be direct, indirect, active, or passive. This treatment can be performed anywhere on the body, especially on the cervical, thoracic, or lumbar paraspinal musculature. To successfully execute this technique, it is important to localize and palpate a restriction. A restriction can present as muscle tension, decreased range of motion, or tenderness. Once the restriction is identified, the physician must decide what type of MFR to perform, whether it be direct, indirect, passive, or active (Table 1). If the patient being evaluated is elderly with multiple comorbidities or other skeletal pathology, such as osteoporosis or arthritis, a more indirect and passive approach may be preferred. In an indirect approach to MFR, the physician should move the myofascial structures away from the restrictive

barrier. This can be done by using either the upper or lower limbs as a lever or by using compression along the long axis of the muscle being treated.¹⁹ In a direct approach to MFR, the physician should move the myofascial tissues toward a restrictive barrier or by using traction along the long axis of the muscle being treated.

This treatment modality may be more suited to an otherwise healthy individual with no other comorbidities and with acute musculoskeletal complaints. Physicians can also fine-tune MFR by adding a twisting component in a clockwise or counterclockwise fashion to the affected muscle. Transverse forces perpendicular to the long axis of the muscle can also aid in the fine-tuning aspect of MFR. Physicians may also ask the patient to breathe or to make certain eye movements in conjunction with the MFR to enhance the treatment. For example, the physician may increase the force of the traction on the muscle incrementally, with each exhalation that the patient might take. The goal of the treatment is to serve in both a diagnostic and therapeutic role. The physician must continue to palpate for restrictions as the technique is being performed to feel for muscle tension release, changes in temperature, or changes in color due to increased blood flow. All these changes can indicate restoration of the musculoskeletal system's functional balance. A recent study in January 2022 examined breast cancer survivors who had upper torso misalignment and muscular imbalance after surgical intervention. The study showed that patients who had MFR earlier postop experienced improvement in their torso malalignment and increased range of motion.²⁰

TABLE 1:

| TREATMENT | INDIRECT | DIRECT | ACTIVE | PASSIVE |
|---------------|----------|--------|--------|---------|
| MET | | x | x | |
| MFR | x | x | | x |
| Counterstrain | x | | | x |

Counterstrain is a passive indirect technique in which the tissue being treated is positioned at a point of balance or slightly away from the restrictive barrier. Moving the muscles into a position of ease for a certain period can “reset” the affected muscles into their normal state as opposed to the inflamed or hypertonic state. Counterstrain, much like MFR, can be performed anywhere on the body and can also serve as a very effective treatment modality for patients in which MFR might be too intense. Patients who are elderly and have chronic musculoskeletal pain may benefit from a less-intense and indirect treatment such as counterstrain. In order to perform counterstrain, the identification of tenderpoints is crucial. Tenderpoints are small hypertense areas of tenderness that can usually be found in the region of the patient's complaint. Tenderpoints usually reside near bony attachments of ligaments, tendons, or in the belly of the affected muscle.²¹ After the physician has located the tenderpoint, they must palpate the tenderpoint with the fingertip and maintain contact with the tenderpoint to monitor it throughout the entirety of the treatment. Once a tenderpoint is palpated, a new pain scale must be established. Usually, the physician must explain that the tenderpoint being palpated and causing pain while the patient is in a neutral position will now be referred to as a 10/10 or a dollar's worth of pain. The

goal is for the physician to tell the patient that they will try to move the patient to the position where the tenderpoint becomes at least a 3/10 pain level, with the ultimate goal of having no pain at all or a 0/10 pain level. Once the patient has understood the goal of treatment, the physician can now maneuver the surrounding musculature and bony structures of the tenderpoint to the position of most relief. While maintaining light contact with the tenderpoint, the physician makes a gross adjustment to shorten the muscle being treated. If the technique is effective, no more than 30% of the tenderness should remain. There are many tenderpoints that can be present on a patient; however, the one that is most tender should be treated first. Usually, if the first tenderpoint is treated effectively, the subsequent tenderpoints can be relieved as well.

Muscle energy is traditionally an active and direct technique. However, it can also be used as an indirect form, although this is rare. As a result, patients who have more acute musculoskeletal complaints and are otherwise healthy may benefit more from this technique as opposed to an elderly patient with chronic complaints and multiple comorbidities. There are two main forms of muscle energy, which are the post-isometric relaxation and the reciprocal inhibition techniques. The post-isometric relaxation technique is the more commonly used technique. This involves the diagnosis of somatic dysfunctions in the area the physician is about to treat. For example, a correct and accurate vertebral spinal somatic dysfunction must be established in order for the treatment to be efficacious. The treatment is effective when the physician rechecks the somatic vertebral dysfunction and notes an improvement in the position along with improved range of motion of the spinal segment. Reciprocal inhibition muscle energy is a technique that utilizes the reflex mechanism of reciprocal inhibition when antagonist muscles are contracted.²² By contracting the antagonistic muscle, signals are transmitted to the spinal cord through the reciprocal inhibition reflex arc, therefore forcing the agonist muscle to relax. A recent study has shown that muscle energy techniques have improved musculoskeletal nonspecific neck pain. The study has shown that the technique improved cervical range of motion in patients with chronic pain and reduced the intensity of the pain in people with neck pain as well.²³

SYMPATHETIC NERVOUS SYSTEM TREATMENTS

In addition to directing osteopathic treatment toward the musculoskeletal system, OMT can also be directed toward the autonomic system using the neurologic model of treatment. Specifically, in chronic pain, the autonomic nervous system can be in a hypersympathetic state where facilitated segments can cause increased neuronal firing. This would then cause increased sensation of pain that would not necessarily respond to purely musculoskeletal treatment modalities. To address the hypersympathetic tone of the autonomic nervous system, there are osteopathic treatments that can be directed toward the sympathetic chain ganglion and Chapman's points in order to normalize sympathetic tone. Most of these techniques can be repeated multiple times until a soft tissue release is felt or when sympathetic tone has been normalized.²⁴

One of the techniques that may be used to normalize sympathetic tone is rib raising. The thoracic ganglia are located anterior to the corresponding rib. Anterior pressure on the rib head will put pressure on the ganglia, causing a short-term increase in sympathetic activity, followed by a long-term decrease in sympathetic activity.²⁵

The upper lumbar sympathetic ganglia are also continuous with the thoracic paraspinal sympathetic ganglia. However, due to the lack of ribs, a technique known as direct paraspinal inhibition can also be used to produce the same autonomic response as that of rib raising. This is achieved by applying anterior pressure to the paraspinal area of the upper lumbar region. By doing this, the upper lumbar sympathetic ganglia can be stimulated in an effort to normalize sympathetic tone.²⁶

Several treatment modalities can be employed to treat the sympathetic tone to the head and neck structures. Treatment such as paraspinal inhibition, muscle energy, and MFR can also be applied to the C1–C3, which comprise the superior ganglia, C6–C7, which comprise the middle ganglia, and C7–T1, which comprise the inferior ganglia.

Chapman points are small ganglion form contractions that present as smooth, firm, palpable nodules that are approximately 2 to 3 millimeters in diameter. A Chapman's point represents the somatic manifestation of its visceral dysfunction.²⁷ Therefore, treating Chapman's points or Chapman's reflexes can also decrease sympathetic tone to the associated visceral tissues. Chapman's points are treated by using a small circular motion with the fingertip either in a clockwise or counterclockwise fashion over the point itself. The treatment is completed once either the point is no longer tender or sympathetic tone is normalized.

PARASYMPATHETIC NERVOUS SYSTEM TREATMENTS

Since the parasympathetic nervous system is primarily found via vagal tone or through sacral innervation, most of the osteopathic treatment modalities that treat the parasympathetic nervous system are aimed at manipulating cranial structures or sacral structures.

Cranial manipulation techniques, such as condylar decompression, can help free parasympathetic responses to structures stimulated by cranial nerves IX and X by freeing the passage through the jugular foramen.²⁸ For example, people who may have chronic migraines may benefit from condylar decompression as it can normalize parasympathetic firing of the nervous system with the added benefit of MFR to the surrounding musculature. Manipulation of the occipito-atlantal, atlantoaxial, and the C2 joints can also influence parasympathetic tone via the vagus nerve. Treatment of sacral somatic dysfunctions with sacral inhibition can also normalize hyperparasympathetic tone such as pain from constipation. A recent comparative study in 2013 evaluated the efficacy of OMT on postop ileus patients. The study found that patients who had OMT performed on them had decreased time to flatus and a decreased hospital length of stay.²⁹ As well as normalizing parasympathetic tone, both these techniques would

also enable myofascial stretching to the surrounding musculature, which would, in turn, decrease pain.

CONCLUSION

Chronic pain is a condition that affects millions of people throughout the US and the world. It requires a multifactorial approach to treatment and alleviation of pain. Doctors of osteopathic medicine are presented with a unique opportunity to implement their osteopathic training and principles to patients with chronic pain. A fundamental understanding of chronic pain and the different types of chronic pain is essential to direct therapy.

In addition to traditional medical therapy, osteopathic physicians can use multiple models of treatment to direct their therapy toward musculoskeletal dysfunctions as well as neurologic autonomic nervous system imbalances. Due to the variety of modalities present in osteopathic medicine, it can serve as an effective supplement to conventional therapy in the treatment of chronic pain.

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REVIEW ARTICLE

THE USE OF OSTEOPATHIC MANIPULATIVE TREATMENT AS A THERAPY FOR MENTAL HEALTH DISORDERS: A REVIEW

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KEYWORDS

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OMT
Mental illness
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ABSTRACT

There is historical and modern evidence for the use of osteopathic manipulative treatment (OMT) to treat patients with mental health disorders. The first section of this article examines the historical perspective, focusing intently on the Still-Hildreth Sanatorium. This hospital specialized in the osteopathic treatment of mental illnesses. While it was open, it saw patients with diverse mental disorders and reported exceptional recovery rates. However, some data from this institution were destroyed, so this perspective is incomplete. The second part of this article examines modern osteopathic research into this topic. Although there is some literature supporting the use of OMT for mental disorders, overall, it is underwhelming. Few mental illnesses have been researched, and for those that have been, there are too few studies to reliably assess the outcomes. Moreover, these studies have limited sample sizes, further affecting their credibility. To accurately gauge the benefits of OMT, future work should overcome these limitations.

INTRODUCTION

When A. T. Still created osteopathy, he never intended for it to be separate from allopathy. Rather, he noticed limitations in the current medical field and sought to overcome them. His meticulous work culminated in the establishment of this new medicine.¹ Osteopathy was built on a unique philosophy: the body is a unit; it is capable of self-regulation and self-healing; structure and function are reciprocally interrelated; and rational treatment is based on these principles.² It differed from the current medical field because it emphasized the need for a rational and scientific basis.³ Dr. Still founded an institution to teach this philosophy, and now there are 38 osteopathic medical schools in the United States.

While both teach the standard medical curriculum, there are several distinctions between osteopathic schools and their allopathic counterparts. Perhaps most notable is the educational focus on osteopathic manipulative treatment (OMT). Osteopathic manipulative treatment involves the identification of somatic dysfunctions in the patient and the utilization of specific techniques to correct them. The techniques are highly versatile and can be utilized in the treatment of numerous conditions. For

instance, studies have demonstrated that OMT can reduce back pain and osteoarthritis-associated knee pain.⁴⁻⁶ Research also suggests that OMT can ameliorate symptoms of migraines and reduce their duration.^{7,8} Additionally, it can enhance lymphatic flow in patients to help reduce edema.^{9,10} More recently, OMT has also been shown to improve the symptoms of patients diagnosed with COVID-19.^{11,12} Although research is limited, it is clinically clear that OMT is versatile and effective.

Mental health disorders in the United States are widely prevalent and have an immense economic impact.^{13,14} They have become a focal point of the healthcare field and are potentially as serious as corporeal disorders. They encompass a wide range of conditions with specific diagnostic criteria established by the DSM. An estimated 26% to 32% of American adults suffer from a mental illness, with 6% suffering from a severe disorder.¹³ Moreover, research suggests that only approximately one-third of patients with a serious illness recover.¹⁵ While debilitating disorders like schizophrenia could contribute to these low recovery rates, another possible explanation is that there is a negative stigma surrounding mental health, and it creates a barrier for patients to seek treatment.¹⁶ In the public eye, people with mental health issues are viewed as dangerous.¹⁷ To avoid being branded as violent, they refrain from receiving help for their conditions.

Since OMT has proven effective in managing a plethora of conditions and because mental illnesses are common in our society, the use of the former to help treat the latter has been questioned. The focus of this article is to answer that question, specifically if the use of OMT can aid in the therapy of patients with mental disorders. To effectively review this topic, the

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article will explore two unique perspectives. Initially, it will look at the historical evidence from the time of A. T. Still and the first osteopaths. Afterward, it will examine the research that modern osteopaths have done on the topic. The article will then conclude with a summary of the field and where future endeavors should go.

THE EARLY YEARS OF OSTEOPATHY

Early osteopathy was initially met with considerable allopathic scorn and public skepticism. These feelings created barriers to the growth and credibility of the field. Patients were cautious about being treated by an osteopathic physician and, at a systemic level, laws were established to prevent them from practicing.¹⁸ This discrimination extended to the military, where DOs were not given the same rights as their allopathic counterparts.¹⁹ However, the meticulous work of Dr. Still and his successors was eventually fruitful. To gain a reputation, Dr. Still would publicly demonstrate his ability to treat patients. The field also gained respect when he healed patients forsaken by allopathy.²⁰ In these instances, Dr. Still would examine the body for underlying lesions—areas that were not functioning properly due to a structural misalignment. Upon finding them, he would correct them, often resulting in recovery.²⁰ On occasion, the patients who were discarded from allopathy had mental illnesses. One example was a young girl who had suffered since infancy from extreme nervousness (anxiety). Her condition would cause her to fervently yell, and no efforts to placate her were effective. Dr. Still was able to find an underlying lesion and, upon correcting it, the girl recovered.^{21,22} In another instance, a father sought out Dr. Still's help for his daughter. She was healthy until she fell from a vehicle and was injured. Her condition was so severe that she was placed in a state institution. A. T. Still examined her and found a displaced joint in her upper cervical vertebrae. He amended the lesion, and, in time, the patient recovered her senses.^{21,23}

As alluded to, the osteopathic treatment for mental health diseases was similar to that of other illnesses: find the anatomical abnormality, and, upon rectifying it, mental health should return.²⁴ It was widely believed that the root of mental illness was a vascular or nervous problem. There was a lesion in the body compromising the blood flow or innervation, and correction of this restriction would cause recovery from the mental ailment.²⁴⁻²⁷ In mental health patients, these lesions were commonly found in the cervical or thoracic vertebrae. Often, patients would also present with gastrointestinal problems, so care was taken to examine the kidneys and bowels, too.²⁴ While OMT was the primary osteopathic technique, at times, adjuvant treatments were utilized. For instance, there is a record of the implementation of hydrotherapy to help treat patients with mental disorders.^{26,28} Moreover, osteopathy emphasized the importance of diet on healing and, thus, most patients had a nutritional component to their treatment plans.²⁶

While there was limited record of A. T. Still treating patients with mental health problems, his students would ultimately be the ones to set the example of osteopathic care for mental disorders. Arthur Hildreth was a close friend of Dr. Still and a student in the first graduating class at his medical school.^{29,30} He was an avid

believer in the power of osteopathy and even played a pivotal role in getting osteopathy legalized in Missouri.³¹ Early in his career, Dr. Hildreth saw patients with all kinds of diseases, and, consequently, he had limited experience with mental illnesses. Most notably, he was brought a young girl diagnosed with suicidal mania. He examined her, found restricted vertebrae, and corrected them. After a couple years of therapy, the girl was well enough to be taken home by her mother.³¹

Dr. Hildreth's career changed drastically in 1913 when he was approached by Drs. Harry and Charlie Still, the sons of A. T. Still. They had been propositioned about converting an old military base into an institution for the osteopathic treatment of mental illnesses and wanted Dr. Hildreth to manage it.^{21,31} He quickly accepted, and the Still-Hildreth Sanatorium was founded. The hospital's goal was not just to care for the patients, but also to cure them; Dr. Hildreth used specialized plans for each patient to identify and eliminate the root cause of the problem.³² Similar to the instances mentioned previously, anatomical restrictions were often found in the patients and documented.³³ As mentioned earlier, these lesions were often in the cervical or thoracic vertebrae and correcting them could prove beneficial to the patients.

Within a couple of years, the results at the Still-Hildreth Sanatorium proved to be exceptional. The osteopathic treatment of mental illnesses was effective. This success was quickly disseminated through journals. The hospital was praised as a model example of the capabilities of osteopathic medicine and its accomplishments were celebrated universally in the field.^{34,35} With each successful patient discharge, the osteopathic field gained credibility with the public. Perhaps the main reason that the institution was so widely commended was that it took in patients that the allopathic field could not help and cured them.^{36,37} Previously, conditions such as Bell's mania, schizophrenia, and dementia were considered incurable, but the Still-Hildreth Sanatorium showed the world that recovery was possible.³⁶ A. T. Still was proud of this success and routinely wrote about it. Even his final message before he died praised the work that the sanatorium was doing.²¹

It is beneficial to examine the recovery rates of the patients and the types of patients that the hospital was treating to better understand the achievements of the Still-Hildreth Sanatorium. Throughout the lifetime of the hospital, it reported an average recovery rate of approximately 50%.³⁸⁻⁴⁰ While these averages are for all illnesses that were treated and only at a specific moment in time, they give a general idea of the hospital's capacity to cure patients. Looking more specifically, data from the Museum of Osteopathic Medicine in Kirksville, Missouri, were used to generate multiple tables.⁴¹ Table 1 examines the common disorders of the sanatorium's patients. Most patients were diagnosed with schizophrenia, bipolar disorder, or anxiety disorders. However, there were patients with other conditions as well. Table 2 investigates the outcomes of therapy for the most common mental disorders. Excluding dementia cases, between 30% and 50% of patients had a full recovery, close to the average that the institution, itself, reported. While this value may not seem impressive, the average recovery at a contemporary sanatorium was merely 3%.^{42,43}

While the Still-Hildreth Sanatorium was seemingly successful, certain factors eventually led to its closure in 1968. One crucial component in the institution's decline was the production and increasing availability of psychotropic medications.^{42,44} With the development of promising novel drugs for the treatment of mental health disorders, patients began to opt for this therapy as opposed to osteopathy. Freudian philosophy also contributed to the failure of the sanatorium.^{42,44} This archetype linked touch to sexuality and resulted in reduced use of OMT. This was the principal treatment at the Still-Hildreth Sanatorium, and without it, the ability to treat patients was greatly affected. The hospital tried to adapt. It used new treatments and utilized some drugs. For instance, people with schizophrenia were treated with insulin shock therapy.^{45,46} However, these adaptations were ultimately in vain. The sanatorium merged with the Kirksville College of Osteopathic Medicine and, after neglecting to implement suggested changes, it closed.⁴²

MODERN OSTEOPATHY

Present-day osteopathy has evolved over time. A. T. Still believed that drugs should be reserved for treating poison only, and that in other cases, osteopathic principles yielded the best results.²¹ In contrast, modern osteopathy has acknowledged the benefits that medications can have on patient outcomes, and now most DOs use them as often as their allopathic counterparts. Another distinction is that osteopathic doctors used to practice family medicine, but they are now found in every specialty.⁴⁷ While there have been changes to osteopathy, the core tenets remain, as does the teaching of OMT, although the use of OMT in practicing osteopathic physicians has been declining.^{48,49} Consequently, the literature for the use of OMT to treat mental health disorders is predominately underwhelming.

There has been some research that has looked at the benefits of OMT in the treatment of anxiety. One study recruited people with a primary diagnosis of generalized anxiety disorder and assessed them with the Hamilton Anxiety Rating Scale (HAM-A) and two self-reported questionnaires.⁵⁰ Every participant received five sessions of OMT, after which results were measured by reassessing HAM-A scores and the self-reported questionnaires. While they found a significant reduction in HAM-A scores and one of the questionnaires, there was no change in the other one. The study posited that the questionnaire did not change because it more closely measured the fear of anxiety as opposed to the severity of symptoms and because the scores were already relatively low at the beginning of the study.⁵⁰ Another study using similar criteria also found a significant reduction in the levels of anxiety in patients after several sessions of OMT.⁵¹ These studies demonstrate the potential that OMT has in helping patients with anxiety.

Research has also examined the use of OMT in the treatment of depression. A 2001 study recruited women using the Zung Depression Scale and separated them into an OMT therapy group and a control group.⁵² This study reported that both groups had significant improvement via a reassessment using the Zung

Depression Scale. However, the OMT group reverted to the normal range, or no psychopathology, by the conclusion of the study, while most of the control group still had moderate depression.⁵² A similar study also found a significant decrease in the level of depression in participants after OMT.⁵¹ However, another study that looked at self-reported depression in first-year osteopathic medical students found no significant reduction after treatment with OMT.⁵³ This study has a major confounding variable though, as every participant was a medical school student. Medical school is rigorous, and it is possible that this stressful environment skewed the data and made it seem like OMT is not effective. These results illustrate the need for further research. More thorough studies might elucidate the benefits of OMT on depression.

Some studies have looked at the outcomes of patients with attention deficit hyperactivity disorder (ADHD) following OMT. One study recruited children with a primary diagnosis of ADHD and placed them into two groups.⁵⁴ Both groups received conventional care, that is, drug therapy, but the experimental group was also treated with OMT. Outcomes were primarily measured by the administration of a pre- and post-Biancardi-Stroppa Modified Bell Cancellation Test. The researchers found that the members of the intervention group had statistically significant improvements as measured by posttest, suggesting improved symptoms.⁵⁴ A related study also suggested that OMT has a positive effect on children with ADHD.⁵⁵ These experiments show that OMT can potentially be beneficial in the treatment of patients with ADHD.

While limited, data support the use of OMT for post-traumatic stress disorder (PTSD). In a pilot study, soldiers with PTSD were recruited and given two sessions of OMT prior to receiving any intensive outpatient therapy.⁵⁶ The researchers reported using an array of assessments to measure the results of the study. Almost all the tools used showed a decrease in symptoms and an increase in cognitive ability. Moreover, the self-reported intensity of headaches and anxiety decreased.⁵⁶ Another study has looked at the use of OMT in treating PTSD, but at the time of publication, the data remained under evaluation.⁵⁷ Additionally, other studies have looked at treating stress with OMT, not necessarily PTSD but a crucial component of it. However, the results are varied.^{53,58} Since the literature is conflicting and limited, more studies are needed to assess the benefits of OMT for PTSD.

The modern literature evaluating the value of OMT for mental disorders is limited. Many mental illnesses have not been studied, and those that have are restricted by their limitations. For instance, while obsessive-compulsive disorder, bipolar disorder, schizophrenia, eating disorders, and personality disorders are prevalent in our society, there have been no studies evaluating whether OMT improves their outcomes. Even with mental disorders in which OMT has been studied, there have been too few studies to reliably assert the treatment's benefits. They might suggest that OMT can improve symptoms, but without more studies, it is difficult to definitively ascertain. Also, the studies that do exist have notable shortcomings. They often do not have a control group, making their results weaker, and they universally have a small sample size. Without testing a larger population, it is difficult to apply the outcomes to the general public.

TABLE 1:
Common Diagnoses of Patients at the Still-Hildreth Sanatorium

| PATIENT DIAGNOSIS | PERCENTAGE OF PATIENTS WITH DIAGNOSIS |
|---|---------------------------------------|
| Schizophrenia | 36% |
| Bipolar disorder | 19% |
| Anxiety disorders | 12% |
| Mental disorder due to medical condition/pregnancy | 8% |
| Dementia | 7% |
| Depression | 6% |
| Other conditions (nonpsychiatric, nonmedical, etc.) | 12% |

TABLE 2:
Outcomes of Therapy for Common Mental Illnesses at the Still-Hildreth Sanatorium

| Patient Diagnosis | Recovery | Improvement | No Change/Worse | Death | Unknown |
|--|----------|-------------|-----------------|-------|---------|
| Schizophrenia | 29% | 26% | 36% | 2% | 7% |
| Bipolar disorder | 51% | 25% | 9% | 4% | 11% |
| Anxiety disorders | 48% | 23% | 10% | 1% | 18% |
| Mental disorder due to medical condition/pregnancy | 30% | 18% | 25% | 9% | 19% |
| Dementia | 5% | 15% | 47% | 15% | 18% |
| Depression | 30% | 32% | 16% | 6% | 17% |

CONCLUSION

There have been historical examples of using OMT to treat patients with mental health disorders. As discussed earlier, A. T. Still, himself, had some documented case examples. However, the historical precedent for osteopathic treatment of mental illness was the Still-Hildreth Sanatorium. While it was open, this hospital cared for a diverse population of patients with varying mental disorders. It treated these patients primarily osteopathically and reported exceptional recovery and improvement rates in most cases. However, later in its course, the use of OMT declined due to the public's negative perception of the treatment. Being unable to fully adapt, the sanatorium closed. While an excellent example, there are limitations to the hospital's data. Before the Museum of Osteopathic Medicine in Kirksville, Missouri acquired them, some records were destroyed. In addition, while records do mention somatic dysfunctions, the specific osteopathic techniques utilized are absent from them. Therefore, our historical knowledge is incomplete.

Modern osteopathy has yet to fully explore whether OMT can improve results in the treatment of patients with mental illnesses. While studies have specifically investigated the use of OMT for anxiety, depression, ADHD, and PTSD, there are important constraints in them. The number of studies for each mental disorder is lacking, and they suffer from a small sample size. As a result, there is conflicting evidence in the literature, and the findings are not generalizable to the public. Additionally, there are many mental disorders that have not been the subject of this type of study. Without any research, it is impossible to know if these patients would benefit from this therapy. Future work should seek to overcome these shortcomings by using robust sample sizes to ensure that results are accurate and applicable to the greater society. Moreover, they should pursue research into different mental health conditions to assess the true versatility of OMT. It is hoped that this review will renew interest in the use of OMT as an adjunctive therapy for mental disorders. Demonstrating the benefits of OMT will likely help in the treatment of many patients.

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CLINICAL IMAGE

RIGHT SHOULDER DEFORMITY: CLAVICLE FRACTURE

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A 16-year-old male presented to the emergency department for a chief complaint of right shoulder pain. He was riding a dirt bike prior to his arrival, when he hit a bump that caused the front wheel of his bike to go upward, resulting in the patient falling off his bike and landing on his upper back and right shoulder. He was wearing a helmet and denies head trauma, neck pain, back pain, abdominal discomfort, or other injury. His only complaint was pain in his right shoulder with associated decreased range of motion. On exam, deformity was noted to the right clavicular region with diffuse tenderness to palpation. There were no open wounds or skin tenting. He did have abrasions to the right upper, posterior shoulder. He denied paresthesias or weakness to his right upper extremity. He did not have any past medical problems or surgeries. Upper extremity pulses were 3+ bilaterally. An x-ray was obtained of the right shoulder, which showed the following (Figure 1).

FIGURE 1:

Midshaft clavicle fracture.



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QUESTIONS

1. Which of the following physical exam findings signify need of emergent referral for a clavicular fracture?

- Tenderness to palpation over the fracture site
- Numbness over the area of the arm supplied by the ulnar nerve
- Bruising over the fracture site
- Decreased range of motion

Correct answer:

B. Numbness over the area of the arm supplied by the ulnar nerve

Clavicle fractures typically present with tenderness to palpation, but this finding alone is not emergent.^{1,2,3} The clavicle is in close proximity to neurovasculature, most prominently the brachial plexus.^{3,4} Numbness or loss of motor function over the area supplied by the nerves of the brachial plexus, including musculocutaneous, axillary, median, radial, and ulnar nerves, suggests injury to these nerves and requires emergent referral.^{2,3,5} Bruising and edema are typical physical exam findings and are not necessarily emergent; however, tenting of the skin should be observed for, as this would be an emergent finding.^{2,3,6} Range of motion will likely be decreased secondary to pain, but this also does not signify an emergency.³

2. Which of the following fracture characteristics would necessitate surgical treatment as opposed to conservative management?

- Nondisplaced midshaft clavicle fracture
- Distal third clavicle fracture with intact acromioclavicular joint
- Proximal third clavicle fracture with no intrathoracic complications
- Midshaft clavicle fracture in a patient with decreased distal pulses

Correct answer:

D. Midshaft clavicle fracture in a patient with decreased distal pulses

Several characteristics make clavicle fractures surgical, including open fractures, high risk of nonunion, symptomatic nonunion and malunion, skin tenting, neuromuscular injury, floating shoulder, and multiple traumas.^{1,2,3,6} Nondisplaced clavicle fractures, particularly those in the midshaft, are most commonly treated conservatively as long as the aforementioned findings are not present.^{1,2,3,6,8} Distal third fractures are also managed conservatively if there is no joint involvement, displacement, or any of the aforementioned findings.^{2,6,7} Proximal third fractures are managed conservatively.^{2,6,10} Although midshaft clavicle fractures are most commonly treated

conservatively, neurovascular compromise, such as decreased distal pulses, makes them emergent.^{1,2,3,6}

DISCUSSION

Clavicular fractures are the most common fractures in children, making up 10% to 15% of childhood fractures and 2% to 5% of adult fractures.^{1,2,3} These fractures demonstrate a bimodal age distribution, with the first peak being young adult males and the second peak being older adults.^{2,3} The most common cause of a clavicle fracture is a fall directly onto the shoulder.^{1,2,3} These fractures commonly occur in cyclists and in those who experience motor vehicle accidents.² The middle portion of the shaft of the clavicle is affected in 90% to 95% of pediatric fractures.^{2,3}

The clavicle is a long bone connecting medially to the sternum and laterally to the acromion, thus making it the only bone with a connection to the trunk and the upper extremity.^{4,6} The clavicle also has attachment sites for several muscles and ligaments, allowing it to play a critical role in range of motion of the upper extremity.⁴ Because of the clavicle's muscular, bony, and ligamentous attachments, in addition to its close proximity to subclavian vessels and the brachial plexus, many possible complications can accompany clavicle fractures.^{2,4} Because of this, it is important to recognize clavicle fractures and the presenting signs and symptoms that could make treatment emergent.^{2,3}

Clavicle fractures can occur in the proximal, midshaft, or distal portion of the bone with the most common location being the midshaft.^{1,2,3} This occurs due to the bone being thin in this area and not having muscular or ligamentous support.^{1,11} Young patients will typically present with a history of a fall on the affected shoulder, with pain in the area of the fracture that worsens with movement of the affected arm.^{2,3,6} On physical examination, a deformity may be appreciated, and in midshaft fractures such as this can manifest as the shoulder being depressed and uneven with the other side.² Range of motion of the affected shoulder will be decreased or unable to be assessed because of pain.³ Other typical associated findings can include bruising, tenderness, and swelling over the fracture site.² Physical examination is critical in suspected clavicle fractures to assess for more emergent signs such as skin tenting and neurovascular compromise.^{1,2,3,12} Skin tenting can be observed when a bone fragment tugs on the skin and stretches it.¹² This finding suggests angulation or displacement of the clavicle, which is a risk for an open fracture and may necessitate emergent surgery.^{2,3} Another important component of the physical exam is assessing the neurovasculature.^{2,3} The brachial plexus runs behind the clavicle, and function of these nerves should be assessed.^{2,3} The subclavian vessels also run adjacent to the clavicle; therefore, pulses should be assessed as well.^{2,3} Compromise of neurovasculature would necessitate an emergent referral.^{1,2,6,8} Because the clavicle connects the upper extremity to the trunk, it is also necessary to assess nearby organs and bony attachments.^{2,4} Concomitant scapular or rib fractures may be present, and due to the proximity of the lungs, it is important to assess for pneumothorax or hemothorax.^{2,4}

Imaging can provide a definitive diagnosis of clavicular fracture.^{2,3} First-line imaging consists of a plain film x-ray with two views: anteroposterior (AP) and 45-degree cephalic tilt.^{1,2,3,6} The AP view

allows visualization of the whole clavicle, including its connections to the sternum and acromion.¹³ The cephalic tilt view allows visualization of possible occult fracture.¹³ In the case of shortening or suspected scapular fractures, AP views should be used.⁶ To further assess joint involvement, particularly with proximal and distal fractures, a CT scan may be indicated.² A CT scan is also helpful in assessing displacement in midshaft clavicle fractures as well as shortening, nonunion, malunion, intra-articular involvement, and vascular injury.^{1,2,3} MRI is not a commonly used imaging method for clavicle fractures; however, it can be used to further assess the brachial plexus, soft tissue, joints, and vasculature.¹⁴ Once it has been determined that a fracture is present, it can be classified further based on location, displacement, and articular involvement in order to guide treatment.³ The Allman classification considers middle third fractures to be Group I, distal third fractures to be Group II, and proximal third fractures to be Group III.^{6,7}

TREATMENT

Treatment of clavicle fractures is based on location, presence of displacement, fracture characteristics, and patient needs.^{2,6} All fractures require orthopedic referrals, but knowing the fracture type will help determine the urgency of referral.^{2,6} Midshaft clavicle fractures (Allman Group 1) are the most common type and are typically treated conservatively with a sling or Figure-of-8 splint.^{1,2,3,6,7,8} Conservative treatment of midshaft clavicle fractures seems to have better outcomes if the fracture is nondisplaced.^{2,6,8} Conservative treatment is still used in displaced midshaft clavicle fractures, particularly if shortening and displacement are less than 2 cm; however, the risk of nonunion and malunion is higher.^{2,3,6,8} The risk of nonunion is also increased in smokers, females, patients of increased age, and in fractures with comminution and displacement.^{1,2} Immobilization continues until union occurs, which can typically take up to 6 weeks in children and up to 12 weeks in adults.^{2,6} Range of motion activities for the elbow are encouraged while the sling is in place.⁶ Following union and removal of the sling, shoulder range of motion activities should be completed.⁶ Operative management for midshaft clavicle fractures is indicated with open fractures, those with a higher risk of nonunion, symptomatic nonunion and malunion, skin tenting, neurovascular injury, floating shoulder, or multiple traumas.^{2,3,6}

Distal third clavicle fractures (Allman Group 2) are typically treated with sling immobilization, especially if ligaments are intact and there is no displacement.^{2,6,7,9} Figure-of-8 braces are not used, as they can further displace the fracture.² Conservative versus operative management is complicated by intra-articular fractures, coracoclavicular ligament involvement, AC joint involvement, and displacement.⁶ Operative management is nearly always indicated for open and unstable fractures.⁹

Proximal third fractures (Allman Group 3) are not as common, thus limiting the ability for a treatment consensus, but they are typically managed conservatively.^{7,10} Immobilization with a sling is ideal, and range of motion as tolerated is encouraged.⁶ The worst complications of proximal fractures are most often due to associated injuries, including thoracic injuries, as proximal fractures typically involve significant trauma.^{2,6,10}

The patient in this case presented with right shoulder discomfort and decreased range of motion without any neurovascular compromise, open wounds, or skin tenting. His initial imaging demonstrated a comminuted fracture at the middle third of the clavicle with elevation of the medial component and relation to the distal component by up to 2 cm with an interposed fracture fragment. The acromioclavicular joint was intact and there were no associated rib fractures. The patient underwent open reduction and with internal with internal fixation of the right clavicle with a plate and screws (Figure 2). He was placed in a sling and advised to follow up in 2 weeks. At his follow-up visit, his wound had healed and the sling was discontinued. He was allowed to initiate activity shoulder height and below and advised to return 2 weeks later.

FIGURE 2:

Post-surgical image.



Clavicle fractures are common findings in adults and children.^{1,2,3} These are managed based on multiple characteristics, and it is important to discern emergent signs that necessitate the need for immediate surgical referral versus those that can be managed conservatively.^{2,3,6} Conservatively managed clavicle fractures typically heal in up to 6 weeks in children and up to 12 weeks in adults.^{2,6} Fractures managed conservatively are usually followed up shortly after the event and then every couple of weeks to assess progress and symptoms.⁶ Once symptoms have resolved, range of motion and strengthening exercises are encouraged, with the option to do this under the care of a physical therapist.^{2,3,6} Common complications to be aware of with conservative management are nonunion, malunion, and posttraumatic arthritis.^{2,6} Patients should avoid contact sports until they can demonstrate full range of motion, strength, and lack of tenderness of the injured shoulder.⁶

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