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A narrative review of new trends in the diagnosis of myofascial trigger points: diagnostic ultrasound imaging and biomarkers

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Myofascial pain syndrome (MPS) is one of the most common conditions of chronic musculoskeletal pain encountered by primary healthcare practitioners on a daily basis. It is generally accepted amongst the broad profile of healthcare practitioners treating MPS that the presence of discrete, palpable and tender nodules within the muscle, known as myofascial trigger points (MTrP), is necessary to confirm the diagnosis of MPS. Manual palpation is currently the most common technique used to detect MTrP, however, previous research has shown that the reliability of manual palpation for detecting MTrP is poor, and in our opinion unacceptably poor, leading to inconsistent diagnosis of MPS and poor patient outcomes. There are currently no objective accepted diagnostic criteria for the clinical detection of MTrP, nor are there standardized diagnostic criteria for MPS. Two promising areas of research with potential

Le syndrome algique myofascial (SAM) est l'une des conditions les plus fréquentes de douleurs musculo-squelettiques chroniques rencontrées par les praticiens de soins de santé primaires tous les jours. Il est généralement admis, parmi un large segment de professionnels de la santé traitant le SAM, que la présence de nodules discrets, palpables et tendres dans le muscle, connus sous le nom de points déclencheurs myofasciaux (PDM), est nécessaire pour confirmer le diagnostic de SAM. La palpation manuelle est actuellement la technique la plus couramment utilisée pour détecter les PDM. Cependant, des recherches antérieures ont montré que la fiabilité de la palpation manuelle pour détecter les PDM est faible, et à notre avis inacceptable, ce qui se traduit par des diagnostics incohérents du SAM et de mauvais résultats pour les patients. Actuellement il n'y a aucun critère diagnostique objectif accepté pour la détection clinique des PDM, ni de critères diagnostiques normalisés pour le SAM. Deux domaines prometteurs de recherche ayant un potentiel

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for enhancing the diagnosis of MPS include the use of diagnostic ultrasound and biomarkers. Further research is needed to advance the development of composite diagnostic criteria employing ultrasound imaging, biomarker assessments and physical assessment to enhance the accuracy and objectivity of MTrP detection and diagnosis of chronic MPS disorder.

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pour améliorer le diagnostic du SAM comprennent l'utilisation de l'échographie diagnostique et les biomarqueurs. D'autres recherches sont nécessaires pour faire avancer le développement de critères de diagnostic composites employant l'échographie, l'évaluation des biomarqueurs et l'évaluation physique pour améliorer l'exactitude et l'objectivité de la détection des PDM et le diagnostic de troubles de SAM chronique.

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MOTS CLÉS : chiropratique, syndrome algique myofascial, point déclencheur myofascial, échographie diagnostique, biomarqueur

Introduction

Myofascial pain syndrome (MPS) is one of the most common conditions of chronic musculoskeletal pain[1], with a prevalence of 15% of patients in general medical practice and up to 85% in pain management centres[2,3]. Despite its prevalence in general medical practice, there is very little research describing the prevalence of myofascial pain in general chiropractic practice. A recent study of Australian chiropractors reported that 60% of patient encounters were related to musculoskeletal conditions[4] while recent survey data collected from chiropractors in Ontario, Canada indicate that 97% of chiropractors encounter myofascial pain in their practice on a daily basis.[5] Given the aging societal demographic[6], MPS is poised to become one of the greatest clinical challenges for the chiropractic profession.

A commonly accepted key diagnostic criterion for MPS amongst practitioners in the field of musculoskeletal pain is the presence of one or more hypersensitive nodule(s), referred to as myofascial trigger points (MTrP), within a taut band(s) of skeletal muscle.[7] Prevailing thought amongst practitioners in the field of musculoskeletal pain accepts that active MTrP are defined by the presence of spontaneous pain at rest as well as being associated with the induction of a local muscular twitch response and/or pain referral with manual or intramuscular needle provocation.[8] In contrast, it is also accepted that latent MTrP are typically asymptomatic at rest, eliciting pain only after manual or needle provocation.[9]

The most commonly employed clinical technique used to confirm the presence of a MTrP is manual palpation. Despite this, the sensitivity and/or specificity of manual palpation for detecting MTrP has not been studied because there is presently no known "gold" standard measure for a MTrP locus. Accordingly, the literature has only cited inter and intra rater reliability data. Previous research reports significant inter-observer variability amongst non-expert clinicians in detecting a MTrP, taut band and local twitch response via manual palpation[10,11], whereas elicitation of referred pain during physical examination was only marginally reliable[12]. Hsieh *et al*.[12] further emphasized that training did not meaningfully improve inter-rater reliability, concluding that "among non-expert physicians, physiatric or chiropractic, trigger point palpation is not reliable for the detection of a taut band and local twitch response, and only marginally reliable for referred pain following training."[12] As a result, no consensus or validated guidelines exist for the clinical diagnosis of MPS.

Several key factors appear to influence the poor reliability of the physical assessment and clinical diagnosis of MTrP and MPS, the most prominent of which being the lack of consensus amongst practitioners on their diagnostic criteria.[13] One contributing factor may be the disparity in training between practitioners. Previous literature shows that insufficient training exists amongst medical physicians in the physical assessment of MTrP and pain

management[14]; similar studies have not yet been performed with chiropractors. The location of the MTrP site may also be a significant determinant for reliability, given that MTrP often form deep within the paravertebral muscles, making them very challenging to detect using manual palpation alone.[12,15] Even when palpable, manual provocation of tender MTrP regions may elicit reactive tension, spasm and/or withdrawal responses from some patients, adding greater variability in detection between subjects. Indeed, existing studies differ in terms of the anatomic location in which MTrP were studied, bringing to question the reliability of these studies in determining the utility of manual palpation for different anatomic regions.

Given the variation in the clinical presentation of chronic musculoskeletal pain and the challenges in reliably detecting MTrP, chronic musculoskeletal pain is inconsistently diagnosed, resulting in inadequate treatment and poor patient outcomes. To this extent, no objective diagnostic tool(s) or universally accepted diagnostic criteria currently exist for the clinician to objectively assess the the MTrP locus[13], nor is there an accepted list of objective and validated gold standard criteria for the diagnosis of MPS. Two promising areas of research aiming to address this gap include ultrasonography and biomarkers.

Diagnostic Ultrasound

Ultrasound is defined as a sound wave greater than 20,000 Hz.[16] Diagnostic ultrasound specifically employs waveform frequencies within the range of 1-30 MHz which are reflected in varying degrees to form high resolution images, called sonograms.[17] As a result, diagnostic ultrasound is an imaging technique that has been used extensively in musculoskeletal imaging. Although not routinely employed in the clinical assessment of MTrP, the accumulating body of research suggests that diagnostic ultrasound may have the potential to significantly contribute to the identification of MTrP within skeletal muscle.

Several investigators have pioneered the use of diagnostic ultrasound imaging to characterize MTrP and distinguish between active and latent MTrP loci from normal tissues. These studies have employed brightness-modulation (B-mode), elastography and Doppler imaging methods.[15,18-22]

B-mode Imaging

Previous research using B-mode ultrasound has suggested that MTrP present as spherical, elliptical and/or even band-like hypoechoeic (dark gray) regions.[18,21] This presentation contrasts with typical normal muscle appearing as a hypoechoic background of muscle fascicles separated by clearly demarcated linear hyperechoic strands representing fibroadipose septa–perimysium. The unique hypoechogenicity of a MTrP region suggests a difference in local tissue density featuring abnormal reduction in echoes visualized by ultrasonography.[18,19,23] A leading explanation for this may be the accumulation of fluid or local tissue edema resulting from acute inflammatory exudate combined with blood or, in a chronic state, residual inflammatory by-products after the inflammatory process has subsided.[23]

Despite the emerging research suggesting that MTrP may present as distinct hypoechoic loci within muscle tissue, research has yet to resolve the association between ultrasound imaging and manual palpation. A recent pilot study found no correlation between the manual detection of active MTrP and tissue characteristics visualized on ultrasound imaging.[24] In contrast, one case study reported contrasting findings of hyperechoic regions within areas of palpable tenderness in a single patient.[25] These inconsistencies may be explained by the fact that obtaining quality images with ultrasound is highly dependent on technique and operator experience. A significant limitation to the cited studies is that they do not clearly describe where within the muscle the ultrasound images were recorded from, nor do they disclose operator experience. In addition, they do not adequately characterize their samples in the context of clinical acuity, extent of pain, physical examination abnormalities and/or whether the MTrP was palpable, active or latent.

Despite these limitations, the emerging literature suggests that MTrP may present as discrete hypoechoic regions within muscle tissues as visualized by ultrasonography. The next phase of studies should investigate the association between manual palpation and sonography to better understand the characteristics of the underlying tissues detectable via manual palpation within the underlying muscle.

Elastography

Ultrasound elastography is a technique employed to qualitatively and quantitatively assesses the mechanical properties of soft tissues.[26,27] Elastography is based on the

principle that local contraction and/or pathology alters tissue elastic properties (Young's modulus) resulting in changes in the velocity of ultrasound propagation through the tissue. This technique has been used to assess local tissue properties of MTrP with the expectation that local contractures lead to greater tissue stiffness relative to surrounding normal tissue.

Spectral Doppler analysis has demonstrated that vibration amplitudes are 27% lower on average within a MTrP region compared with surrounding healthy tissue.[27] A recent study employing elastography supported these findings further by reporting a reduction in local stiffness which correlated with palpable reduction in stiffness at the MTrP site after dry needling.[28] Using elastography, the investigators measured significant reductions in shear modulus post-needling ($p<0.01$), corresponding with a decrease in local palpable hypertonicity.

The reason for the decreased wave propagation velocities measured through localized, hypoechoic regions within the muscle is unclear. Future studies should aim to further elucidate the elastographic features of local contraction vs. inflammation to enhance our understanding of the underlying pathophysiologic mechanisms contributing to these observations.

Doppler Imaging

Ultrasound Doppler flow is an imaging technique used to measure the Pulsatility Index (PI). The PI is calculated as [(peak systolic velocity – minimum diastolic velocity)/ mean velocity] and is used as a measure of downstream resistance to blood flow in tissues.[29] An increased PI is physiologically interpreted as increased resistance to blood flow. Previous research has reported higher PI at active MTrP loci versus normal tissue sites, while no differences in PI have been reported between latent MTrP and normal tissue.[19,20] Peak systolic velocities at active MTrP sites are typically greater than latent MTrP or normal tissue sites while, in contrast, minimum diastolic velocities are significantly lower than latent MTrP and/or normal tissue sites.[20]

Retrograde diastolic blood flow has also been reported at the MTrP site. Using Doppler flow waveform analysis and computational modeling to study the vascular environment, the researchers have suggested that these collective observations could be explained by the presence of increased blood volume and stasis within the vascular bed of the MTrP as a result of increased outflow resistance subsequent to vasoconstriction.[20] It has also been postulated by this group that the high pulsatile blood flow at the site of MTrP may be the result of increased compliance and volume of the vascular compartment combined with increased outflow resistance due to local muscle fiber contraction leading to inflammatory-induced vasoconstriction and/or compression of the local capillary bed. Additionally, anatomical determinants and/or external pressure of the ultrasound transducer may have also contributed to these findings, given that the force of the transducer was not reported or controlled for in the methodology and/or analysis. These collective observations point to the possibility that edema and vasoconstriction at the outflow-blood vessels of a MTrP may reduce local perfusion and contribute to the distinctive sonographic features of the MTrP, including the characteristic hypoechoicity.

Post-Acquisition Image Enhancement

Post-acquisition image enhancement techniques have also been used in the evaluation of MTrP. Turo *et al*.[23] introduced the concept of entropy to MTrP image analysis. Entropy is a statistical measure of the probability distribution of grey pixel values on B-mode imaging, creating a score that quantifies the homogeneity of the region of interest within tissue. The lower the score the more homogeneous the tissue, with a score of zero depicting complete homogeneity. Hypoechoic tissues characterized by edema and or hyper-vascularity present with lower entropy scores while tissues containing fat or scar/fibrosis show higher entropy scores. The combination of entropy and vibration elastography has experimentally demonstrated 69% sensitivity and 81% specificity at detecting the MTrP site as determined by manual palpation. A limitation to this technique, however, is that it involves post-image acquisition processing making image results unavailable for immediate clinical decision-making. If found to be useful, developing ultrasound devices in the future with the capability for real-time entropy image analysis would be a valuable addition to the clinician's toolbox for enhancing the reliability of MTrP identification.

Biomarkers

Clinical assessment of biomarkers may also offer an objective tool in the diagnostic workup of MPS. Previous research has shown that an altered biochemical milieu of

pain and inflammatory biomarkers exists within a localized palpable MTrP region of the muscle identified using the criteria established previously by Simons and Travell[30,31]. Shah *et al*. reported increased concentrations of interleukin 1b (IL-1b), interleukin 6 (IL-6), interleukin 8 (IL-8), tumor necrosis factors (TNF-a), bradykinin, calcitonin gene-related peptide (CGRP), substance P and norepinephrine within these regions of the muscle[30,31]. Importantly, it is yet unresolved whether patients with active MTrP may also demonstrate elevated levels of inflammatory biomarkers in remote uninvolved sites. It has been hypothesized that a systemic response characterized by elevated systemic levels of IL-6,IL-8, creatine kinase (CK) and monocyte chemo-attractant protein-1 MCP-1[32,33] may be indicative of skeletal muscle injury and/or ischemia-reperfusion mechanisms commonly linked to the pathophysiology of MPS[34]. Currently, no consensus in the literature exists regarding the association between systemic biomarkers and the physical finding of MTrP on manual palpation. Future studies should explore the reliability (sensitivity, specificity) of biomarkers for MTrP detection in the clinical evaluation of the chronic myofascial pain patient.

A current limitation of this technique is that it cannot provide the practicing clinician with immediate results for use in daily clinical practice, given that blood is typically analyzed off-site. Future research should address this by advancing biomarker assay technology that could be implemented in routine clinical practice, enhancing the clinician's decision making and reduce unnecessary delay in therapeutic intervention.

Conclusion

Myofascial pain is one of the most common chronic pain conditions seen daily by chiropractors, however, the lack of consensus amongst primary care clinicians for the diagnostic criteria is a major limitation to appropriate and timely intervention for suffering patients. The primary challenge in the clinical management of MPS is the need for objective, reliable, gold-standard diagnostic criteria for the identification of MTrP.

Although it is not currently used in routine clinical settings for the diagnosis of MPS, diagnostic ultrasound is a safe, non-ionizing, and portable tool enabling high resolution imaging of soft tissue. Although ultrasound may offer important diagnostic insight into the structural and mechanical properties of MTrP, its sensitivity and specificity for detecting palpable nodules has not yet been studied. It may be particularly valuable in resolving smaller and/or deeper MTrP loci less amenable to palpation. Future research should aim to establish the association between manual palpation and sonographic findings in order to validate these techniques for future clinical application.

Biomarker analysis may further contribute to our understanding of the pathophysiologic changes associated with MPS by enabling the objective quantification of pain and inflammatory biomarkers released subsequent acute and/or chronic myofascial injury. This may be especially important in the early or pre-clinical stage of MPS where palpable MTrP may not be clinically evident. Furthermore, biomarkers may be valuable as confirmatory findings in the case where MTrP may not be palpable or when discrepancies exist between assessors.

The relationship between ultrasound imaging, biomarker outcomes and palpable nodules has not been studied. Given the poor interrater reliability of manual palpation, additional objective outcomes are necessary to enhancing the sensitivity and specificity of MTrP detection. Importantly, research should aim to assess the clinical utility of ultrasound and biomarkers to predict future clinical morbidity (i.e. pain). Although biomarker analysis and diagnostic ultrasound imaging have the potential to provide important additional objective insight into the physical assessment of MTrP and diagnosis of MPS, they are not intended to replace manual palpation. Furthermore, if these technologies are shown to be reliable, future research should strive to advance ultrasound and biomarker technologies to enable the clinician with immediate feedback for use in daily clinical decision-making. Given that diagnostic ultrasound and biomarker assessment technologies are presently featured in routine medical practice, it is feasible that these technologies could be easily integrated into daily chiropractic practice to enhance the clinical assessment of chronic musculoskeletal pain.

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