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Hepatomusculoskeletal Disorders: Coining a new term might improve the management of the musculoskeletal manifestations of chronic liver disease

Hepatomusculoskeletal Disorders

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Abstract

+ADw-html+AD4APA-p+AD4-Chronic liver disease can affect many body systems including the musculoskeletal system. The pathogenetic crosstalk between the liver and organs such as the brain and the kidneys has already been described with compound terms merging the organs affected by the pathology, such as the hepatorenal syndrome. Nevertheless, the musculoskeletal manifestations of chronic liver disease have not been coined with such a term to date. Because of this shortage, documenting the musculoskeletal implications of chronic liver disease in both research and clinical practice is challenging. To fill this gap, the authors propose the term +ACI-hepatomusculoskeletal disorders+ACI-, a compound term of Greek origin that encompasses all the body structures involved in the aforementioned pathologic crosstalk.+ADw-/p+AD4APA-/html+AD4-

Key Words: chronic liver disease; hepatomusculoskeletal disorders; musculoskeletal system; hepatology; pathophysiology; osteodystrophy

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Core Tip: The authors recommend coining the umbrella term “hepatomusculoskeletal disorders” (HD) in response to the need to expand knowledge about chronic liver disorders and capitalize it in the form of practice guidelines

TO THE EDITOR

Chronic liver disease (CLD) is the 11th leading cause of mortality globally accounting for up to 2% of disability-adjusted life years worldwide(1). It encompasses ailments of infectious (viral hepatitis) and non - infectious (alcohol abuse, non - alcoholic

steatohepatitis, cancer) origin leading to progressive structural and functional depletion of hepatic physiology in the form of liver cirrhosis. CLD is associated with multisystem complications involving the kidneys, the heart, the nervous system and the musculoskeletal system(2). Research in the field has recently sought hematological and electrocardiographic CLD biomarkers addressing CLD's extrahepatic manifestations as a potential standpoint for the management of the disease and for the identification of novel therapeutic targets(3),(4),(5). Nevertheless, research regarding the musculoskeletal implications of CLD remains limited. Action is needed to expand the existing knowledge and its clinical applications.

The impact of CLD on the musculoskeletal system has been better understood during the last years(6). The musculoskeletal manifestations can be classified into two categories according to their etiology: a) on the causative disease which insults the liver b) on the type and the degree of liver disease. In more detail, Hepatitis C is frequently associated with rheumatologic phenomena. Polyarthralgia either in the context of mixed cryoglobulinemia triad of purpura, fatigue and arthralgia or alone as HCV-induced arthritis is documented frequently(7),(8). Overt arthritis and fibromyalgia are less frequently diagnosed in parallel with HCV infection. Polyarthritis and polyarthralgia are commonly presented as manifestations of HBV,HAV and HEV infections(7) while erosive arthritis is encountered in anti-CCP positive type I AIH (9). As regards the alcoholic liver disease, ethanol exerts direct cytotoxic effects into the muscular system causing alcoholic myopathy while affects bone metabolism causing matrix decomposition and suppression of bone synthesis(10). Nonalcoholic fatty liver disease (NAFLD) is frequently associated with low bone mineral density(11) while in diseases characterized by defective metabolism of metals (e.g copper in Wilson's disease and iron in haemochromatosis), arthritis, chondrocalcinosis and muscle stiffness and pain are regularly noticed(7),(12). On the other side, the severity of liver disease impacts the musculoskeletal health. Alterations in endogenous steroids metabolism and the use of proton pump inhibitors and diuretics results in fluctuations of mineral

metabolism which result in hepatic osteodystrophy (HO)(13). The defective immune responses due to poor complement system and opsonization sufficiency, portosystemic shunt and bacterial intestinal overgrowth render the patients prone to infections like septic arthritis, osteomyelitis, cellulitis and necrotizing fasciitis(14). Finally, sarcopenia(15),non-traumatic osteonecrosis(16) and higher rate of periprosthetic complications(17) are manifestations from musculoskeletal system that compromise severely the quality of patient's life.

On these grounds, healthcare professionals specializing in the management of musculoskeletal conditions (rheumatologists, orthopedic surgeons, physiatrists, physiotherapists etc) can substantially contribute to CLD management. Prevention - wise, patients with CLD history can benefit from regular screening for osteopenia and osteoporosis and from falls' prevention training(18). Similarly, physiotherapy to maintain muscle mass, improve patients' functionality and prevent sarcopenia-associated injury and disability can be also provided(19). Treatment - wise, orthopedists and rheumatologists need to be alarmed for septic arthritis in CLD patients presenting with joint pain, and for spondylodiscitis and vertebral tuberculosis - in regions where the disease is endemic - in CLD patients presenting with low back pain(20),(21),(22). Performing orthopedic surgery should also entail special consideration in CLD patients. Given their 3.5-fold higher risk for periprosthetic infections, cellulitis and necrotizing fasciitis, conservative management of fractures or osteoarthritis can be prioritized. In case of surgery, the patients and their formal and informal caregivers need to be instructed about the risk of infection and the need to carefully inspect surgical wounds and areas of plaster casting and seek medical attention when appropriate(23).

To contribute towards this end, musculoskeletal healthcare professionals need updated practice guidelines and relevant training. Developing concrete guidelines in turn requires systematic research in the field, with large scale observational studies and clinical trials confirming the existing knowledge and optimizing the recommended

interventions. Currently, it appears that research in the field is heterogeneous, with the majority of studies being observational and having been conducted independently in inconsistent time intervals.

A search for relevant publications on Medline, Scopus and other databases reveals a plethora of terms used to describe CLD musculoskeletal implications. The wording is often alternating (musculoskeletal disorders in patients with CLD, hepatic osteodystrophy) and rather descriptive addressing particular alterations associated with CLD (sarcopenia, osteosarcopenia, skeletal muscle mass) rather than the phenomenon as a whole(2), (24), (25) ,(26). A term grouping all the aforementioned together has not been included in the Medical Subject Headings (MeSH) thesaurus and in the International Disease Classification (ICD10) system to date. To the best of the authors' knowledge no relevant term can be found in hospital records and documentation systems as well. Therefore, the lack of a consistent nomenclature poses significant obstacles to the appraisal of the existing knowledge, let alone its expansion.

The authors recommend coining the umbrella term "hepatomusculoskeletal disorders" (HD) in response to the need to expand relevant knowledge and capitalize it in the form of practice guidelines. The term is a compound word of Greek origin. It emphasizes the implications of liver conditions (hepato-) on muscles (musculo-), bones and connective tissue (skeletal). The composition of the term is similar to other relevant clinical terms such as the hepatorenal or the cardiorenal syndrome. In both these examples, the organs whose pathologies affect each other (liver, heart and kidneys respectively) are merged in a single term. Coining the new term in a similar linguistic format to other terms that are established in clinical practice makes it easily comprehensible to physicians and researchers. Therefore, the proposed term can benefit future research, clinical practice and medical education. Certainly, to address the musculoskeletal implications of CLD sufficiently several steps involving clinicians, researchers, health bodies, healthcare administrators and stakeholders are required. Nonetheless, the new

term can hopefully serve as common ground underlining the need to take relevant action.

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