

How to Assess, Detect, and Manage Joint Involvement in the Era of Transformational Therapies in Hemophilia: Role of Point-of-Care Ultrasound

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Introduction

Repeated joint bleeding is the main clinical manifestation in Patients with Hemophilia (PwH) [1]. Early detection of joint alterations is essential for guiding appropriate patient care [2]. Hemophilic arthropathy pathophysiology is complex, including both inflammatory and degenerative mechanisms [1,3]. On this hand, synovial hypertrophy - the main consequence of joint bleeding - is one of the earliest manifestations of hemophilic arthropathy [4-6]. Early detection of synovial hypertrophy may enable patients and caregivers to initiate prevention strategies to reduce joint damage and prevent physical disability. Current approaches for assessing joint status in patients with hemophilia include clinical examination, Magnetic Resonance Imaging (MRI) and Point of Care Ultrasound (POCUS). In the era of novel treatments for hemophilia, the use of reliable, objective measures of joint health is important in the long-term follow-up of patients. POCUS is a frequently used imaging approach because it is rapid, noninvasive, and relatively inexpensive [3,7,8]. However, ultrasound results can be impacted by the level of experience of the physician and inter-user variability.

POCUS is an easy-to-use method to assess hemophilic arthropathy and is useful for the detection of acute intra-articular problems (i.e., hemothrosis), signs of disease activity (i.e., synovial hypertrophy) and irreversible degenerative joint changes (i.e., osteochondral damage) [9,10]. In detail, POCUS is useful for monitoring subclinical bleeding events and synovial proliferation as markers of occult disease activity or progression and can differentiate acute pain related to a bleeding event or an arthritis-mediated pain [11-15]. Differentiation of the source of acute pain and identification of a joint bleeding episode may be useful in planning appropriate treatment (i.e., factor replacement therapy to stop the bleeding or medication for pain control) [12]. Significant osteochondral changes (i.e., cartilage echo textural changes, cartilage thickness loss, subchondral bone irregularities) may also be detected, even though the ultrasound beam cannot access and visualize osteochondral surfaces located centrally in the joint cavity [11-15]. Despite this limitation, there is a high correlation between ultrasound and the gold standard technique MRI for the quantification of hemophilic arthropathy [7,16,17] and high specificity and sensitivity were reported for synovitis in the main joints (knees, ankles, and elbows) [9,17]. In addition, MRI has some disadvantages, including high cost, limited availability, and long waiting lists, need for contrast agent administration to distinguish synovial proliferation, and need for sedation for young children [18]. The routine use of MRI for the screening of the six joints of interest in PwH can be both time and cost prohibitive.

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In contrast, POCUS does not require sedation, is less expensive than MRI, does not require a contrast agent to assess synovial vasculature, and it is more readily available than MRI [7]. Ultrasound is sensitive for soft-tissue abnormalities (synovial hypertrophy) in hemophilic joints [16], for which swelling can also be used as an indicator for chronic synovial proliferation. Ultrasound detects even minimal amounts of synovial or blood effusion in the joint recesses [19-21]. Different from MRI, ultrasound is valuable in revealing initial osteochondral damage and synovial hypertrophy in joints that are otherwise asymptomatic when an MRI examination is not planned, and can, therefore, be proposed as a screening modality. Furthermore, several evidence suggested that POCUS was able in revealing synovial hypertrophy in joints judged as totally normal according to clinical examination [22].

In summary, hemophilic arthropathy is a complex, serious complication of hemophilia, and integrating new methods of joint assessment that are easily accessible in the clinical setting may help both the patient and the health care provider to obtain timely information to optimize treatment and manage acute issues. POCUS is useful for the diagnosis of acute bleeding, early detection of joint damage, monitoring disease progression, and evaluating treatment regimens. Future large-scale studies demonstrating that POCUS-guided interventions improve patient outcomes may help to establish the role of POCUS as a complementary assessment tool for physicians managing the care of PwH.

Disclosure

Rita Carlotta Santoro served as a consultant for Bayer, Novo Nordisk, Roche, Sobia, Takeda, BioMarin, CSL-Behring. Matteo Nicola Dario Di Minno has received research funding from and served as a consultant for Bayer, Pfizer, Novo Nordisk, Roche, Sobia, and Takeda.

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