



Synovitis in Haemophilia: A Factor Think Tank Podcast Series

Episode 2. Diagnosis
Slide summary

Disclaimer

- The Factor Think Tank is an educational activity funded by Sobi. Synovitis in Haemophilia: A Factor Think Tank Podcast Series was developed by the Factor Think Tank working group and the accompanying slide deck is only intended for healthcare professionals
- Slides 6–11 summarise content from the e-Delphi consensus article by Mancuso et al.;¹ wording closely resembles that of the article to reflect the e-Delphi consensus discussions
- All views and opinions expressed in the podcast are those of the participants only
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Synovitis in Haemophilia: A Factor Think Tank Podcast Series (1)

- Findings from the e-Delphi consensus study on synovitis and joint health in haemophilia have been published in [Haemophilia](#) and provide the basis for the podcast series

HAEMOPHILIA

Synovitis and joint health in patients with haemophilia:
Statements from a European e-Delphi consensus study

*Maria Elisa Mancuso, Katharina Holstein, James S. O'Donnell,
Sébastien Lobet, Robert Klamroth, the FVIII Think Tank Study Group*

Synovitis in Haemophilia: A Factor Think Tank Podcast Series (2)

- The e-Delphi consensus examined five key domains relevant to synovitis in haemophilia:
 - Definition and pathophysiology
 - Diagnosis
 - Impact on joint health
 - Monitoring and follow-up
 - Prevention and treatment
- Based on these key domains an educational [series of five podcasts](#), featuring lead author Dr Maria Elisa Mancuso and co-authors or expert guest speakers, is available to healthcare professionals

This slide deck provides supporting information for [Episode 2. Diagnosis](#) of the podcast series on synovitis in haemophilia



An overview of synovitis in haemophilia

- Synovitis is defined as inflammation of synovial tissue within the joint¹
- It is common in patients with haemophilia in response to blood within joints and is the first step towards the development of chronic arthropathy¹
- One bleeding episode can initiate synovial inflammation, which may develop into chronic synovitis if bleeds recur frequently and are not adequately prevented²
- Synovitis is highly relevant to joint health in haemophilia; however, knowledge gaps exist regarding definition, pathophysiology, diagnosis, prevention, follow-up and treatment³
- Delphi methodology, which is often used to produce best-practice guidelines where evidence is missing, was employed to conduct a European e-Delphi consensus study on synovitis in haemophilia³

1. van Vulpen L, et al. Haemophilia. 2021;27(Suppl. 3):96–102; 2. van Vulpen L, et al. Osteoarthritis Cartilage. 2015;23:63–9;
 3. Mancuso M, et al. Haemophilia. 2023;29:619–28

e-Delphi consensus article

Domain: Diagnosis of synovitis (statements 5–8)

Diagnosis of synovitis in haemophilia e-Delphi consensus statements 5–8: Background

- Overt synovitis can be clinically detected by assessing signs of joint inflammation, e.g., swelling, warmth, limited motion and pain (also symptoms of acute haemarthrosis)^{1–3}
 - Tingling or tightness around the joint may precede such symptoms
- Detection of synovitis in joints that appear free from clinically relevant bleeds is challenging, especially in early childhood⁴
- The HJHS was developed to assess joint status to identify early signs of joint involvement in children with haemophilia;⁴ however, it is not sensitive enough for early detection of synovitis⁵
- Imaging assessment is highly recommended, and is useful to define the severity of synovial hyperplasia and follow its progression over time⁶
- MRI is considered to be the most sensitive ‘gold standard’ imaging technique, allowing direct analysis of soft tissue, joint effusions, cartilage and haemosiderin⁷

HJHS, Haemophilia Joint Health Score; MRI, magnetic resonance imaging

1. Srivastava A, et al. Haemophilia. 2020;26(Suppl. 6):1–158; 2. Krüger S, et al. Haemophilia. 2018;24:657–66; 3. Querol F, et al. Blood Coagul Fibrinolysis. 2019;30:S7–10; 4. Hilliard P, et al. Haemophilia. 2006;12:518–25; 5. Kuijlaars I, et al. Haemophilia.

7 2017;23:934–40; 6. Mancuso ME, et al. Haemophilia. 2023;29:619–28; 7. Doria A, et al. Haemophilia 2010;16(Suppl. 5):107–14

Diagnosis of synovitis in haemophilia e-Delphi consensus statements 5–8: Background

- MRI has a number of limitations^{1,2}
 - Bloody vs non-bloody effusions not clear; joint fluid only distinguished with contrast
 - Not universally available
 - Time-consuming and costly
 - Sedation may be required for children
- POC-MSKUS has been developed for use in clinical practice, in response to the challenges with MRI^{3–5}
 - Good visualisation of joint structures
 - Affordable bedside joint health monitoring
 - Simple scoring systems can facilitate detection of synovitis by non-specialist healthcare professionals
 - Enables patient involvement in treatment decisions, which may improve prophylaxis adherence

MRI, magnetic resonance imaging; POC-MSKUS, point-of-care musculoskeletal ultrasound

1. Doria A, et al. Haemophilia. 2010;16(Suppl. 5):107–14; 2. van Vulpen L, et al. Haemophilia. 2018;24(Suppl. 6):44–9; 3. Martinoli C, et al. Thromb Haemost. 2013;109:1170–9; 4. Volland LM, et al. J Ultrasound Med. 2019;38:1569–81; 5. Hermans C, et al. Blood Rev.

2022;52:100890

Diagnosis of synovitis in haemophilia e-Delphi consensus statements 5–8: Background

- Different scanning protocols have been proposed to standardise joint evaluation across treatment centres and countries, the most commonly used being HEAD-US and JADE^{1,2}
- Both protocols evaluate the presence/absence of synovial hypertrophy, cartilage integrity and bony changes^{1,2}
- The quantitative and more detailed protocols utilising power Doppler may be better suited to research and clinical trials than for routine clinical practice³

HEAD-US, Haemophilia Early Arthropathy Detection with Ultrasound Score; JADE, Joint Tissue Activity and Damage Examination protocol; POC-MSKUS, point-of-care musculoskeletal ultrasound

1. Martinoli C, et al. *Thromb Haemost.* 2013;109:1170–9; 2. Volland L, et al. *J Ultrasound Med.* 2019;38:1569–81; 3. Bakeer N, et al. *Res Pract Thromb Haemost.* 2021;5:e12531

Diagnosis of synovitis in haemophilia e-Delphi consensus statements 5–8

5 HJHS 2.1 as a clinical assessment tool is not sensitive enough to detect synovitis

6 POC-MSKUS assessment using standardised protocols is a sensitive tool to detect and monitor synovitis and early joint changes

7 The added value of power Doppler imaging during MSKUS assessment to detect markers of disease activity needs to be confirmed

Diagnosis of synovitis in haemophilia e-Delphi consensus statements 5–8

8.1 The use of MRI is more accurate than POC-MSKUS to detect, quantify and monitor synovitis*

8.2 The use of POC-MSKUS is enough to detect, quantify and monitor synovitis*

*The statement, 'The MRI scale of the IPSPG is recommended to quantify, detect and monitor synovitis', was split into two amended statements following a second e-Delphi round
IPSPG, International Prophylaxis Study Group; MRI, magnetic resonance imaging; MSKUS, musculoskeletal ultrasound; POC-MSKUS, point-of-care musculoskeletal ultrasound

Podcast discussion points

Synovitis in Haemophilia: A Factor Think Tank Podcast Series
Episode 2. Diagnosis

Episode 2. Diagnosis

- This episode focuses on five topics relevant to the diagnosis of synovitis in haemophilia:
 - Clinical assessment of synovitis
 - Use of MRI for diagnosis
 - Limitations of MRI
 - Alternative diagnostic imaging techniques
 - Guidance available for ultrasound imaging
- Host Dr Maria Elisa Mancuso leads the discussion with guest Professor Dario Di Minno



Dr Maria Elisa Mancuso is Senior Haematology Consultant at the Center for Thrombosis and Hemorrhagic Diseases of IRCCS Humanitas Research Hospital in Rozzano, Milan, Italy



Professor Dario Di Minno is Full Professor of internal medicine at the Department of Clinical Medicine and Surgery of Federico II University of Naples, Italy, and Head of the Center for Thrombosis and Hemorrhagic Diseases

MRI, magnetic resonance imaging

Topic 1. Clinical assessment of synovitis

- While some cases of synovitis may be clinically overt, with pain or swelling, many cases can be asymptomatic, leading to missed diagnosis of underlying synovitis
- Clinical assessments, such as the Gilbert Score and the HJHS, were designed to detect the early stages of arthropathy
 - Both instruments include the presence of swelling as the main sign of effusion or hypertrophic synovium
- However, a proportion of cases with underlying disease may be still be missed by the Gilbert Score or HJHS; imaging tools such as MRI can be used to complete diagnosis

“The most important thing is that in several cases synovitis can be totally asymptomatic”

HJHS, Haemophilia Joint Health Score; MRI, magnetic resonance imaging
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Topic 2. Use of MRI for diagnosis

- MRI is recognised as the ‘gold standard’ imaging tool for joint assessment in patients with haemophilia, and can be used to assess all stages of clinical arthropathy
- It can detect alterations in both the joint and the surrounding tissues, including the presence of hypertrophic synovium and effusion
- MRI is more applicable to research settings than to daily clinical practice:
 - Scans need to be performed and interpreted by radiology departments
 - MRI scoring tools, for example IPSPG, are geared towards research rather than daily clinical practice
 - MRI can provide more information than is necessary for daily clinical practice

“MRI is really sensitive for the assessment of joints in haemophilic patients”

IPSPG, International Prophylaxis Study Group; MRI, magnetic resonance imaging
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Topic 3. Limitations of MRI

- Limited availability of MRI machines (~one per hospital, with some centres having none) means long waiting lists and delay between clinical questions and answers
- Long acquisition time means that only a maximum of two joints can be measured per session, rather than all six index joints (i.e., elbows, knees and ankles)
- Sedation is needed for children
- Several factors can limit the interpretation of MRI images, including artefacts (e.g., from hemosiderin), and difficulty distinguishing blood-related vs non-blood-related findings

“For all these reasons we have to think about some alternatives”

MRI, magnetic resonance imaging

Topic 4. Alternative diagnostic imaging techniques

- There has been a great effort to implement POC-MSKUS into clinical examination during the past 10–15 years
- POC-MSKUS is widely available, affordable, quick and reproducible
- It provides clear images that are easy to interpret
- It is more akin to a clinical assessment than a radiological examination
- POC-MSKUS images can be used in discussions with patients to support their understanding, which is important for treatment compliance

“We are using something similar to a stethoscope for the joints”

POC-MSKUS, point-of-care musculoskeletal ultrasound

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Topic 5. Guidance available for ultrasound imaging

- Scanning protocols currently used in the EU and USA aim to standardise the ultrasound approach, and generally focus on two main dimensions to provide a complete assessment of joint status and judge how prophylaxis or other treatment is performing:
 1. Degenerative alterations (changes in cartilage and subchondral bone)
 2. Disease activity (presence of hypertrophic synovium and joint effusions)
- There is >90% agreement between POC-MSKUS and MRI for the assessment of degenerative alterations and disease activity
- Use of colour and power Doppler is currently being discussed; colour Doppler may be beneficial for visualising hypervascular hypertrophic synovium, but is more relevant for research than clinical settings

“POC-MKUS, being easy, reliable, cheap and available is a good choice to assess our patients on a routine basis”

MRI, magnetic resonance imaging; POC-MSKUS, point-of-care musculoskeletal ultrasound

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Conclusions

- Synovitis can be clinically silent; dedicated imaging is important
- MRI represents the ‘gold standard’; however, there are limitations preventing its widespread use, such as issues around availability, feasibility and cost
- POC-MKUS is a good alternative
 - It can detect and quantify relevant biomarkers of disease activity
 - It has comparable sensitivity to MRI for detecting synovial hypertrophy
 - It is sensitive enough to detect osteochondral changes

Listen to the whole series

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More in the series

- If you enjoyed this podcast and want to find out more about the Factor Think Tank, please visit the website: www.factorthinktank.com
- All episodes in the series can be found here:
 - Episode 1. Definition and pathophysiology (Dr Maria Elisa Mancuso and Dr Robert Klamroth)
 - Episode 2. Diagnosis (Dr Maria Elisa Mancuso and Prof Dario Di Minno)
 - Episode 3. Impact on joint health (Dr Maria Elisa Mancuso and Dr Sébastien Lobet)
 - Episode 4. Monitoring and follow-up (Dr Maria Elisa Mancuso and Dr Katharina Holstein)
 - Episode 5. Prevention and treatment (Dr Maria Elisa Mancuso and Dr Gianluigi Pasta)