

**Recommendation 6** 

# **Learning Objectives**



At the send of this section participants should be able to:

- Describe the role of MRI in the evaluation of patients with UPIA
- Describe the role of ultrasound in the evaluation of patients with UPIA

## **Learning Objectives**

At the send of this section participants should be able to:

- •Describe the role of MRI in the evaluation of patients with UPIA
- •Describe the role of ultrasound in the evaluation of patients with UPIA

## **Recommendation 6**



There is insufficient evidence to recommend the routine use of MRI and US for diagnosis or prognosis in UPIA [5, D]; in UPIA and suspicion of RA, MRI of hands and wrists could be considered for diagnosis [2b, B].

## Recommendation 6

There is insufficient evidence to recommend the routine use of MRI and US for diagnosis or prognosis in UPIA [5, D]; in UPIA and suspicion of RA, MRI of hands and wrists could be considered for diagnosis [2b, B].

This recommendation had an agreement of 8.2/10.

64% of rheumatologists felt that this recommendation was already implemented in their practice, and 18% felt it would change their practice.

# Undifferentiated Arthritis Undifferentiated Arthritis Early stage of classifiable disease Part of an overlap of disease Partial form of a defined disease Disease of unknown origin

UA envelops a heterogeneous group of recent onset arthritides that are not classifiable within established criteria sets such as those of the American College of Rheumatology (ACR) and The European League Against Rheumatism (EULAR).

UA may represent an early stage of a classified form of arthritis that will eventually be definable; an overlap of more than one disease; a partial form of a defined disease; or a disease of unknown origin. UA overall has a better prognosis than RA as it encompasses a spectrum of self-limited disorders. As compared to RA, a patient with UA usually presents with fewer affected joints, less radiographic erosions, better functional ability, and a greater likelihood of being seronegative. Patients with UA are also less likely than patients with RA to require treatment that involves the use of corticosteroids (such as Prednisone) or DMARDs and a substantial proportion of UA patients remit spontaneously.

Hitchon CA, Peschken CA, Shaikh S, El-Gabalawy HS. Early undifferentiated arthritis. *Rheum Dis Clin N Am.* 2005;31:605-626.

## **MRI**



- · Highly sensitive
- Non-invasive
- · Can detect:
  - Synovitis and tenosynovitis
  - Erosions
  - Bone marrow edema
- · Drawbacks: Cost, time, availability

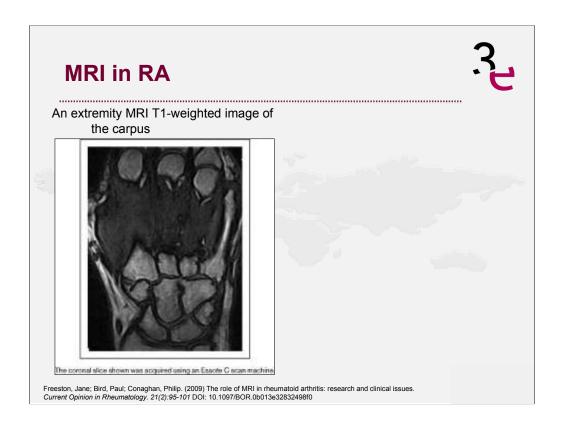
## MRI

-Highly sensitive -Can detect: synovitis and tenosynovitis, erosions, bone marrow edema

-Non invasive -Drawbacks: Cost, time, availability

MRI has a number of advantages in the imaging of inflammatory arthritis. It is highly sensitive and can provide a wide range of information. Drawbacks are listed above.

Freeston, Jane; Bird, Paul; Conaghan, Philip. The role of MRI in rheumatoid arthritis: research and clinical issues. Current Opinion in Rheumatology. 21(2):95-101, March 2009.



This is an image of an MRI of the wrist.

## **MRI in UPIA**



- Bone marrow edema was found to be an independent predictor of the future development of RA from UPIA (1)
- The presence of MRI synovitis and erosion pattern with the involvement of several hand joints but not the first carpometacarpal joint increased the probability of developing RA (2)

### **MRI in UPIA**

- •Bone edema was found to be an independent predictor of the future development of RA from UPIA (1)
- •The presence of a distinct MRI synovitis and erosion pattern with the involvement of several hand joints but not the first carpometacarpal joint also increased the probability of developing RA (2)
- 1) Tamai M, Kawakami A, Uetani M, Takao S, Arima K, Fujikawa K, et al. Anti-cyclic citrullinated peptide antibody and magnetic resonance imaging-detection of bone marrow oedema are most important predictors in classification as well as prognostic evaluation of undifferentiated arthritis. Ann Rheum Dis. 2007; 66(Suppl II):338.
- 2) Duer A, Ostergaard M, Horslev-Petersen K, Vallo J. Magnetic resonance imaging and bone scintigraphy in the differential diagnosis of unclassified arthritis. Ann Rheum Dis. 2008 Jan; 67(1):48-51.

## **Ultrasound**



- More sensitive than physical exam or plain radiographs
- Non-invasive
- · Dynamic, real-time imaging
- · Can detect:
  - Synovitis and tenosynovitis
  - Erosions
  - NOT Bone marrow edema
- Drawbacks: Operator dependence, time, availability

## **Ultrasound**

More sensitive than physical exam or plain radiographs

Non-invasive

Dynamic, real-time imaging

Can detect:

Synovitis and tenosynovitis

**Erosions** 

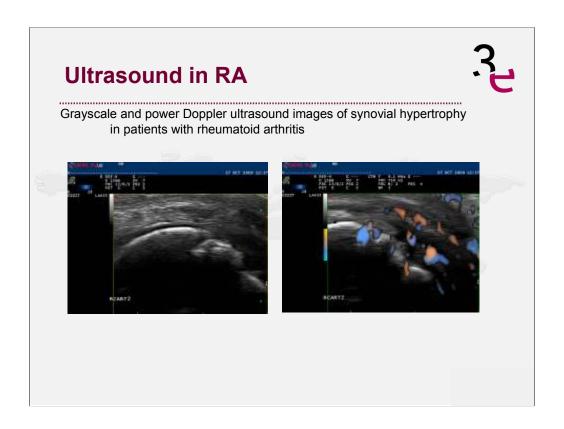
NOT Bone marrow edema

Drawbacks: Operator dependence, time, availability

Ultrasound has several advantages and some disadvantages, as listed above.

Brown, A. K. Using ultrasonography to facilitate best practice in diagnosis and management of RA

Nat. Rev. Rheumatol. 2009. 5; 698-706.



**Figure 1** Grayscale and power Doppler ultrasound images of synovial hypertrophy in patients with RA

# **Ultrasound (U/S) in UPIA**



 2 studies, using mixed populations revealed US-PD signal and US-GS synovitis as potential candidates for future studies in UPIA (1,2)

### U/S in UPIA

2 studies, using mixed populations revealed US-PD signal and US-GS synovitis as potential candidates for future studies in UPIA.

There was limited evidence on the role of U/S in UPIA, however 2 did provide support for a potential role for US – grey scale, and US-power doppler.

- 1. Freeston J, Wakefield R, Conaghan P, Hensor E, Emery P. Ultrasound at Presentation Predicts Clinical Outcome in Very Early Inflammatory Patients Arthritis Rheum. 2007; 56(12).
- 2. Scire C, Montecucco C, Epis O, Eleonora B, Codullo V, Bugatti S, et al. Residual Disease Activity Assessment by Muskoloskeletal Utrasounds in Early Arthritis. Arthritis Rheum. 2008; 58(9):S408.

# Expert consensus regarding U/S and MRI in UPIA



- Data is still too scarce to recommend the routine use of any of these imaging tools
- This recommendation does not dispute the fact that compared to physical examination and radiographs, both MRI and US may offer important advantages through more sensitive depiction of inflammatory and destructive disease manifestations

## Expert consensus regarding U/S and MRI in UPIA

- •Data is still too scarce to recommend the routine use of any of these imaging tools
- •This recommendation does not dispute the fact that compared to physical examination and radiographs, both MRI and US may offer important advantages through more sensitive depiction of inflammatory and destructive disease manifestations

The current recommendation pertains only to the diagnostic and prognostic value of these imaging tools in UPIA.

# **Summary**



 MRI and ultrasound may be useful in the evaluation of patients with UPIA, but evidence to date is insufficient to support a general recommendation

## **Summary**

MRI and ultrasound may be useful in the evaluation of patients with UPIA, but evidence to date is insufficient to support a general recommendation.

## References



- Nell VP, Machold KP, Stamm TA, Eberl G, Heinzl H, Uffmann M, et al. Autoantibody profiling as early diagnostic and prognostic tool for rheumatoid arthritis. Ann Rheum Dis. 2005 Dec; 64(12):1731-1736.
- Schellekens GA, Visser H, de Jong BA, van den Hoogen FH, Hazes JM, Breedveld FC, et al. The diagnostic properties of rheumatoid arthritis antibodies recognizing a cyclic citrullinated peptide. Arthritis Rheum. 2000 Jan; 43(1):155-163.
- Nielen MM, van der Horst AR, van Schaardenburg D, van der Horst-Bruinsma IE, van de Stadt RJ, Aarden L, et al. Antibodies to citrullinated human fibrinogen (ACF) have diagnostic and prognostic value in early arthritis. Ann Rheum Dis. 2005 Aug; 64(8):1199-1204.
- Vittecoq O, Incaurgarat B, Jouen-Beades F, Legoedec J, Letourneur O, Rolland D, et al. Autoantibodies recognizing citrullinated rat filaggrin in an ELISA using citrullinated and non-citrullinated recombinant proteins as antigens are highly diagnostic for rheumatoid arthritis. Clin Exp Immunol. 2004 Jan; 135(1):173-180.
- Goldbach-Mansky R, Lee J, McCoy A, Hoxworth J, Yarboro C, Smolen JS, et al. Rheumatoid arthritis associated autoantibodies in patients with synovitis of recent onset. Arthritis Res. 2000; 2(3):236-243.
- Narvaez J, Sirvent E, Narvaez JA, Bas J, Gomez-Vaquero C, Reina D, et al. Usefulness of magnetic resonance imaging of the hand versus anticyclic citrullinated peptide antibody testing to confirm the diagnosis of clinically suspected early rheumatoid arthritis in the absence of rheumatoid factor and radiographic erosions. Semin Arthritis Rheum. 2008 Oct; 38(2):101-109.



- Tamai M, Kawakami A, Uetani M, Takao S, Rashid H, Tanaka F, et al. Early prediction of rheumatoid arthritis by serological variables and magnetic resonance imaging of the wrists and finger joints: results from prospective clinical examination. Ann Rheum Dis. 2006 Jan; 65(1):134-135.
- van der Helm-van Mil AH, Verpoort KN, Breedveld FC, Huizinga TW, Toes RE, de Vries RR. The HLA-DRB1 shared epitope alleles are primarily a risk factor for anti-cyclic citrullinated peptide antibodies and are not an independent risk factor for development of rheumatoid arthritis. Arthritis Rheum. 2006 Apr; 54(4):1117-1121.
- van der Helm-van Mil AH, le Cessie S, van Dongen H, Breedveld FC, Toes RE, Huizinga TW.
   A prediction rule for disease outcome in patients with recent-onset undifferentiated arthritis: how to guide individual treatment decisions. Arthritis Rheum. 2007 Feb; 56(2):433-440.
- Verpoort KN, Jol-van der Zijde CM, Papendrecht-van der Voort EA, Ioan-Facsinay A, Drijfhout JW, van Tol MJ, et al. Isotype distribution of anti-cyclic citrullinated peptide antibodies in undifferentiated arthritis and rheumatoid arthritis reflects an ongoing immune response. Arthritis Rheum. 2006 Dec; 54(12):3799-3808.
- Boire G, Cossette P, de Brum-Fernandes AJ, Liang P, Niyonsenga T, Zhou ZJ, et al. Anti-Sa antibodies and antibodies against cyclic citrullinated peptide are not equivalent as predictors of severe outcomes in patients with recent-onset polyarthritis. Arthritis Res Ther. 2005; 7(3):R592-603.



- Tamai M, Kawakami A, Uetani M, Takao S, Arima K, Fujikawa K, et al. Anti-cyclic citrullinated peptide antibody and magnetic resonance imaging-detection of bone marrow oedema are most important predictors in classification as well as prognostic evaluation of undifferentiated arthritis. Ann Rheum Dis. 2007; 66(Suppl II):338.
- Savolainen E, Kautiainen H, Koivula MK, Luosujarvi R, Risteli J, Kaipiainen-Seppanen O.
  Change of diagnoses and outcome of patients with early inflammatory joint diseases
  during a mean 13-month follow-up. Scand J Rheumatol. 2007 May-Jun; 36(3):194-197.
- van Gaalen FA, Linn-Rasker SP, van Venrooij WJ, de Jong BA, Breedveld FC, Verweij CL, et al. Autoantibodies to cyclic citrullinated peptides predict progression to rheumatoid arthritis in patients with undifferentiated arthritis: a prospective cohort study. Arthritis Rheum. 2004 Mar; 50(3):709-715.
- Bukhari M, Thomson W, Naseem H, Bunn D, Silman A, Symmons D, et al. The performance
  of anti-cyclic citrullinated peptide antibodies in predicting the severity of radiologic
  damage in inflammatory polyarthritis: results from the Norfolk Arthritis Register. Arthritis
  Rheum. 2007 Sep; 56(9):2929-2935.
- Visser H, le Cessie S, Vos K, Breedveld FC, Hazes JM. How to diagnose rheumatoid arthritis early: a prediction model for persistent (erosive) arthritis. Arthritis Rheum. 2002 Feb; 46(2):357-365.
- Visser K, Verpoort KN, van Dongen H, van der Kooij SM, Allaart CF, Toes RE, et al.
   Pretreatment serum levels of anti-cyclic citrullinated peptide antibodies are associated with
   the response to methotrexate in recent-onset arthritis. Ann Rheum Dis. 2008 Aug;
   67(8):1194-1195.



- Ortiz AM, González-Álvaro I, García-Vicuña R, Carvajal I, Castañeda S. Anti-cyclic citrullinated peptide antibodies and high IL-15 serum levels predict better than rheumatoid factor the requirement of intensive treatment in early arthritis patients. Ann Rheum Dis. 2007; 66(Suppl II):593.
- Farragher TM, Goodson NJ, Naseem H, Silman AJ, Thomson W, Symmons D, et al.
   Association of the HLA-DRB1 gene with premature death, particularly from cardiovascular
   disease, in patients with rheumatoid arthritis and inflammatory polyarthritis. Arthritis
   Rheum. 2008 Feb; 58(2):359-369.
- Aho K, Palosuo T, Lukka M, Kurki P, Isomaki H, Kautiainen H, et al. Antifilaggrin antibodies in recent-onset arthritis. Scand J Rheumatol. 1999; 28(2):113-116.
- Devauchelle-Pensec V, Saraux A, Youinou P, Le Goff P. Antiperinuclear factor and antikeratin/antifilaggrin antibodies for differentiating early rheumatoid arthritis from polymyalgia rheumatica. Joint Bone Spine. 2001; 68(4):306-310.
- Quinn MA, Green MJ, Marzo-Ortega H, Proudman S, Karim Z, Wakefield RJ, et al. Prognostic factors in a large cohort of patients with early undifferentiated inflammatory arthritis after application of a structured management protocol. Arthritis Rheum. 2003 Nov; 48(11):3039-3045.
- van der Helm-van Mil AH, Verpoort KN, le Cessie S, Huizinga TW, de Vries RR, Toes RE. The HLA-DRB1 shared epitope alleles differ in the interaction with smoking and predisposition to antibodies to cyclic citrullinated peptide. Arthritis Rheum. 2007 Feb; 56(2):425-432.



- Verstappen SMM, McCoy MJ, Roberts C, Dale NE, Hassell AB, Symmons DPM. Predictors of poor prognosis in very early inflammatory polyarthritis. Arthritis and Rheumatism. 2008; 58(9):S769-S769.
- Berthelot JM, Maugars Y, Castagne A, Audrain M, Prost A. Antiperinuclear factors are present in polyarthritis before ACR criteria for rheumatoid arthritis are fulfilled. Ann Rheum Dis. 1997 Feb; 56(2):123-125.
- Vittecoq O, Jouen-Beades F, Krzanowska K, Bichon-Tauvel I, Menard JF, Daragon A, et al. Rheumatoid factors, anti-filaggrin antibodies and low in vitro interleukin-2 and interferongamma production are useful immunological markers for early diagnosis of community cases of rheumatoid arthritis. A preliminary study. Joint Bone Spine. 2001 Mar; 68(2):144-153.
- Saraux A, Berthelot JM, Chales G, Le Henaff C, Mary JY, Thorel JB, et al. Value of laboratory tests in early prediction of rheumatoid arthritis. Arthritis Rheum. 2002 Apr 15; 47(2):155-165.
- Jansen LM, van Schaardenburg D, van der Horst-Bruinsma IE, Dijkmans BA. One year outcome of undifferentiated polyarthritis. Ann Rheum Dis. 2002 Aug; 61(8):700-703.
- Kurki P, von Essen R, Kaarela K, Isomaki H, Palosuo T, Aho K. Antibody to stratum corneum (antikeratin antibody) and antiperinuclear factor: markers for progressive rheumatoid arthritis. Scand J Rheumatol. 1997; 26(5):346-349.



- Hitchon CA, Wong K, El-Gabalawy HS. Measurement of baseline serum matrix metalloproteinase levels adds minimal prognostic value over routine clinical parameters in the prediction of radiographic erosions in early inflammatory arthritis Arthritis and Rheumatism. 2008; 58(9):S754-S754.
- Teitsson I, Withrington RH, Seifert MH, Valdimarsson H. Prospective study of early rheumatoid arthritis. I. Prognostic value of IgA rheumatoid factor. Ann Rheum Dis. 1984 Oct; 43(5):673-678.
- Mjaavatten MD, Haugen AJ, Helgetveit K, Sidenvall G, Nygaard H, Kvien TK. High anticyclic citrullinated peptide level is a stronger predictor than low level for persistent joint swelling in patients presenting with arthritis of <=16 weeks duration. Arthritis and Rheumatism. 2008; 58(9):S770-S770.
- Stockman A, Tait BD, Wolfe R, Brand CA, Rowley MJ, Varney MD, et al. Clinical, laboratory
  and genetic markers associated with erosions and remission in patients with early
  inflammatory arthritis: a prospective cohort study. Rheumatol Int. 2006 Apr; 26(6):500-509.
- Tunn EJ, Bacon PA. Differentiating persistent from self-limiting symmetrical synovitis in an early arthritis clinic. Br J Rheumatol. 1993 Feb; 32(2):97-103.
- El Miedany Y, Youssef S, Mehanna AN, El Gaafary M. Development of a scoring system for assessment of outcome of early undifferentiated inflammatory synovitis. Joint Bone Spine. 2008 Mar; 75(2):155-162.
- Reneses S, Pestana L, Fernandez-Suarez A, Criado R, Wichmann I, Garcia A, et al. A recent onset inflammatory polyarthritis register in Spain: factors that predict remission. Scand J Rheumatol. 2007 Sep-Oct; 36(5):378-385.



- Schumacher HR, Jr., Habre W, Meador R, Hsia EC. Predictive factors in early arthritis: long-term follow-up. Semin Arthritis Rheum. 2004 Feb; 33(4):264-272.
- Green M, Marzo-Ortega H, McGonagle D, Wakefield R, Proudman S, Conaghan P, et al. Persistence of mild, early inflammatory arthritis: the importance of disease duration, rheumatoid factor, and the shared epitope. Arthritis Rheum. 1999 Oct; 42(10):2184-2188.
- Goldbach-Mansky R, Lee JM, Hoxworth JM, Smith D, 2nd, Duray P, Schumacher RH, Jr., et al. Active synovial matrix metalloproteinase-2 is associated with radiographic erosions in patients with early synovitis. Arthritis Res. 2000; 2(2):145-153.
- Cunnane G, Fitzgerald O, Beeton C, Cawston TE, Bresnihan B. Early joint erosions and serum levels of matrix metalloproteinase 1, matrix metalloproteinase 3, and tissue inhibitor of metalloproteinases 1 in rheumatoid arthritis. Arthritis Rheum. 2001 Oct; 44(10):2263-2274.