Algorithmic Screening for Axial Spondyloarthritis – Efficacy and Health Economic Analysis Cost-Effective Screening for Early Axial Spondyloarthritis

Edit Vereckei, Dorottya Nagy D and László Hodinka*

National Institute of Rheumatology and Physiotherapy, Hungary

Received: May 12, 2018; Published: May 22, 2018

*Corresponding author: László Hodinka, National Institute of Rheumatology, Budapest, Hungary, H-1023 Budapest Frankel Leóju. 25-29

Abstract

Background: Spondyloarthritis is a non-infectious autoinflammatory disease affecting the spine, peripheral joints and may be associated with skin, enteral and eye manifestations. Progressive vertebral inflammation is dominant in this heterogeneous clinical picture which develops with different frequency and severity in genetically predisposed persons expressing the HLA B27 histocompatibility antigen. Classical bone erosions and fusions can be demonstrated by X-ray, however in a longer latent clinical phase. The correct diagnosis and starting innovative biological treatment is crucial in prevention of the late changes. In order to avoid delay diagnostic criteria and screening tools have been developed for the early clinical phase defined as non-radiographic axial spondyloarthritis. In the hierarchy of screening steps the clinical signs, i.e. typical inflammatory back pain and other manifestations are the basis; rationally followed a traditional X-ray image of the sacroiliac joints and the HLA B27 typing is the rational sequence. However, according to an international multi-center survey preference of MR imaging is common just in the screening phase.

Method: The aim of our study was the health economic analysis of screening non-radiographic axial spondylarthritis with the assumption that the cost of the proper diagnosis of a case is lower following the algorithmic sequence is lower compared to that on MRI basis. Simplified cost minimization, cost-effectiveness and cost-utility calculations have been performed using case numbers of two published and our own patient populations.

Results and Conclusion: Moderate cost reductions as 209 or 503 euros savings and 103 Cost-Effectiveness Ratio (ICER) or cost-utility ratios may be achieved using the recommended algorithms.

Keywords: Axial Spondyloarthritis; Algorithmic Screening; Cost-Effectivity

Abbreviations: ASAS: Assessment of Spondylo Arthritis International Society; CRP: C-Reactive Protein; HLA B27: Histocompatibility Antigen B27; ICER: Incremental Cost Effectivity Ratio; IBD: Inflammatory Bowel Disease; MAXIMA: Management of Axial SpA International and Multicentric Approaches study; MRI: Magnetic Resonance Imaging; PAMP: Pathogen Associated Molecular Pattern; SPACE: SpondyloArthritis Caught Early study; TNF: Tumor Necrosis Factor

Introduction

Spondyloarthritides represents a musculoskeletal disease group characterized by sterile inflammation in the structures connecting vertebrae, cartilaginous and synovial joints and ligamental insertions, called entheses. The inflammation is induced by alive pathogens, pathogen associated molecular structures (PAMPs) or self-tissue destruction and is maintained primarily by intercellular messengers, cytokines. A strong genetic association and risk for the development of the disease was found with the histocompatibility antigen HLA B27 or similar structures playing a role in the recognition of pathogens. A similar pathological process is involved in skin (psoriasis), bowel (inflammatory bowel diseases, IBD) and eye (uveitis) diseases, which are frequently associated with spondyloarthritides [1]. Several diagnostic and classification criteria for the spondyloarthritis, or seronegative spondylarthritis entity have been developed based on the very heterogeneous clinical pictures in the last decades. This entity includes classicalankylosing spondylitis, peripheral inflammatory arthritides, as psoriatic arthritis or spondylitis and postinfective/reactive arthritides and criteria.
for their identification were reviewed, summarized and evaluated recently [2].

The relatively slowly progressing vertebral inflammation (axial manifestation) may remain unidentified for years and this causes a delay of the appropriate and nowadays effective treatment with biologicals [3]. The main cause of the delay that there exists a long period from the first symptoms till the development the characteristic X-ray changes which is defined as non-radiographic axial spondyloarthritis. Today it is generally accepted that this includes a more heterogeneous group of patients with mild disease who never develop the classical axial disease and cases with a long-lasting early phase. The spondyloarthritis concept and development of ASAS criteria (Assessment of SpondyloArthritis international Society, for peripheral and axial spondyloarthritis) significantly decreased the delay in the diagnosis of axial spondyloarthritis (axSpA), from 8-14 years to 5-6 years [4,5]. The key of the early diagnosis is the proper screening by all physicians, who are aware of the relevant phenomena of spondyloarthritides [6-8].

Newer ASAS-endorsed screening algorithms recommend sequencing identification of the inflammatory character of back pain (IBP, nocturnal pain relieving by movement) and other SpA features of skin, gut or eye, then performing sacroiliac X-rays and in the case it is negative, HLA B27 testing (SPACE) [6,9]. Authors developed in parallel but in independently a very similar algorithmic screening with consecutive steps of recommended pre-screening at general practitioner level (low back pain, inflammatory back pain and serum C-reactive Protein, CRP), collaborating specialists’ level (gastroenterology, ophthalmology, dermatology, if necessary) and confirmative steps at rheumatologist level including X-ray imaging and HLA B27 typing, (Figure 1) [10]. However, the international MAXIMA survey showed, that academic and practicing rheumatologists report over 90 percent use of MRI compared to the less preferred X-rays and HLA B27 testing [11]. We initiated the study reported here with the working hypothesis that sequential screening based on inflammatory clinical features, and then standard sacroiliac X-ray followed by HLA B27 and MRI only after, the clinical arm is cheaper and cost-effective. In order to prove this we tested our screening algorithm and performed a simplified health economic analysis of identifying non-radiographic axial spondylarthritis cases.

Methods

Patients: Out of 49 patients with suspected inflammatory back pain 18 were classified as axial spondylarthritis cases on clinical IBP and elevated CRP in our previous study testing our screening algorithm [12]. Definite ankylosing spondylitis was diagnosed by erosive X-ray SI changes. Ten patients had more SpA features with negative SI X-ray classified as non-radiographic axial spondylarthritides cases. Three of them was HLA B27 positive. However, four patients showed consistently low level CRP.

Health Economy Calculations: Cost minimization, cost-effectiveness and cost-minimization calculations have been performed. The calculations were made in a model using the case numbers reported in the MAXIMA study [11], in the SPACE cohort for the ASAS criteria modification [6] and in our cohort. Costs have been calculated by pricing of the interventions in the mentioned surveys resulting one nonrad-axSpA diagnosis as the effectivity/utility measure as this opens access to biological therapy. For the comparison nonrad-axSpA diagnoses have been projected to 100-100 screened persons, respectively. Comparative costs have been based on the Hungarian prices of interventions containing amortisation and work costs expressed in euros. For calculations of Incremental Cost Effectiveness Ratio (ICER) the usual formula was used as Cb-Ca/Eb-Ea, where C is Cost, E is Effectivity, a is the MAXIMA, b is the SPACE or our own screening system. Utility measure was the same, as savings are identical for cost-utility calculation.

Results

In the SPACE model 209, in our one 523 euros may be saved for an identified axSpA case. In incremental cost-effectiveness (ICER)
calculations, access to a TNF inhibitor was used as a theoretical effect measure, and acceptable ICERs have been found in the SPACE model and in our own (103 and 80, respectively). In cost-utility calculations utility measure was the theoretical mean health gain of a three-month anti-TNF treatment of a nr-axSpA case, and similar results have been found.

**Discussion**

Cross-sectional studies have shown that among the identified axial spondyloarthritis cases there is a less progressive subpopulation, probably an early phase or milder subtype: non-radiographic axial spondyloarthritis, i.e. without structural changes in the spine. However they are also candidates of anti-TNF therapy as the other classical cases [13,14]. The screening algorithms differentiate a heterogeneous axial spondyloarthritis population with characteristic back pain, absence of structural changes on imaging, with or without clear inflammatory signs on sacroiliacal MRI, with or without an elevated CRP, less impaired functional capacity, higher female and lower HLA B27 prevalence. (Significant part of them, diagnosed mainly on the clinical arm, show no progression into ankylosing spondylitis even for years. A recent and continuous debate discuss whether the entity is an independent one or it is a developmental stage on the progression of ankylosing spondylitis [15,16].

However, the disease burden on non-radiographic axial spondyloarthritis is comparable to the radiographic axial spondyloarthritis or evento ankylosing spondylitis and a biological treatment is beneficial. Because of the better functional state, less comorbidity and additional costs anti-TNF treatment of non-radiographic axSpA patients is more cost-effective [17,18]. Referral studies show that general practitioners, gastroenterology, dermatology and ophthalmology and even rheumatology specialists present limited awareness on screening modalities [19].

We matched the numbers and prices of the reported diagnostic interventions for an effective diagnosis in the MAXIMA survey, the ASAS SPACE cohort and our screening and used the cost-minimization, cost-effectivity and cost-utility calculations. Our conclusion is, that moderate, however real cost reduction may be achieved when clinical signs, sacroiliacal X-rays and HLA B27 testing are used for identifying axial spondyloarthritis cases, even non-radiographic phase. Extensive sacroiliacal and vertebral MRI is recommended for the judgment of state and progression of axial spondylarthritis, rather than for screening. Asnr-axSpA patients clinically are usually eligible for starting anti-TNF therapy their follow up for progression into ankylosing spondylitis and determining the real health gain receiving the biological is recommended.

**References**

1. De Koning A, Schoones JW, van der Heijde D, van Gaalen FA (2018) Pathophysiology of axial spondyloarthritis: consensus and controversies. Eur J Clin Invest 48(5): e12913.
2. Van Tubergen A (2015) The changing clinical picture and epidemiology of spondyloarthritis. Nat Rev Rheumatol 11: 110-118.
3. Deodhar A, Mittal M, Reilly P, et al. (2016) Ankylosing spondylitis diagnosis in US patients with back pain: identifying providers involved and factors associated with rheumatology referral delay Clin Rheumatol35: 1769-1776.
4. Sepriano A, Landewe R, Van Der Heijde D, et al. (2016) Predictive validity of the ASAS classification criteria for axial and peripheral spondyloarthritis after follow-up in the ASAS cohort: a final analysis. Ann Rheum Dis 75: 1034-1042.
5. Jones A, Harrison N, Jones T, et al. (2014) Time to diagnosis of axial spondyloarthritis in clinical practice: signs of improving awareness. Rheumatology 53: 2126-2127.
6. Van den Berg,De Hooge M, Rudwaleit M, Sieper J, van Gaalen F, et al. (2013) ASAS modification of the Berlin algorithm for diagnosing axial spondyloarthritis: results from the SPondyloArthritis Caught Early (SPACE)-cohort and from the Assessment of SpondyloArthritis international Society (ASAS)-cohort Ann Rheum Dis 73: 1646-1655.
7. Van Hoeven I, Luine J, Han H, et al. (2014) Identifying axial spondyloarthritis in Dutch primary care patients, ages 20-45 years, with chronic low backpain Arthritis Care Res 66: 446-453.
8. Roura JX, Estevez EC, Vazquez FL, et al. (2015) Reccomendations for the detection, study and referral of inflammatory low-back pain in primary care. Reumatol Clin 11: 90-98.
9. Poddubny D, Van Tubergen A, Landewe R, et al. (2015) Assessment of SpondyloArthritis international Society (ASAS): Development of an ASAS-endorsed recommendation for the early referral of patients with a suspicion of axial spondyloarthritis. Ann Rheum Dis 74: 1483.
10. Nagy D, Geher P, SzantoS (2013) Refferal and screening recommendations for the early diagnosis of suspected axial spondyloarthritis (Beutalasi es szuresi javaslatok az axialis spondylarthritisek koraidigosztalazahoz. Hungarian) Magy Reumatol 54: 24-31.
11. Van Der Heijde D, Sieper R, Elewaut D, et al. (2014) Referral patterns, diagnosis, and disease management of patients with axial spondyloarthritis Results of an international survey. J Clin Rheumatol 20: 411-417.
12. Nagy D, Hodinka L, Geher P (2014) Epidemiology and screening of non-radiographic axial spondyloarthritis in a Hungarian population. (Nem-rontgen axialis spondylarthritiss epidemioologai jelemzöneke es szuresi lehetosegeinek vizsgalata Budapesten, Hungarian). Magy Reumatol 55: 131-132.
13. Barakakos X, Braun J (2015) Non-radiographic axial spondyloarthritis and ankylosing spondylitis: what are the similarities and differences? RMD Open 1(Suppl 1): e000053.
14. Wallman JK, Kapetanovicz MC, Petersson I (2015) Comparison of non-radiographic axial spondyloarthritis and ankylosing spondylitis patients - baseline characteristics, treatment adherence, and development of clinical variables during three years of anti-TNF therapy in clinical practice. Arthritis Res Ther 17: 378-389.
15. Deodhar A, Strand V, Kay J Braun J (2016) The term ‘non-radiographic axial spondyloarthritis’ is much more important to classify than to diagnose patients with axial spondyloarthritisAnn Rheum Dis 75: 791-794.
16. Malaviya AN, Rawat R, Agrawal N, Patil NS (2017) The nonradiographic axial spondyloarthritis, the radiographic axial spondyloarthritis, and ankylosing spondylitis: The tangled skein of rheumatology. International Journal of Rheumatology.
17. Boonen A, Sieper J, van der Heijde D, Dougdos M, Bukowski JF, et al. (2015) The burden of non-radiographic axial spondylarthritisis. Seminars in Arthritis and Rheumatism 44: 556-562.
18. Sieper J, Hu X Black CM, et al. (2016) Systematic review of clinical, humanistic, and economic outcome comparisons between radiographic and non-radiographic axial spondyloarthritis. Systematic review of the burden of nr-axSpA versus AS. Seminars in Arthritis and Rheumatism 46: A1-A6.
19. Danve A, Deodhar A (2015) Screening and referral for axial spondyloarthritis-need of the hour. Clin Rheumatol 34: 987-993.