2014 Update on the CRA/SPARCC Treatment Recommendations for the Management of Spondyloarthritis

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Learning Objectives

• Learn about proposed principles of the management of SpA in Canada

• Learn about specific management recommendations for the management of SpA in Canada

• Discuss barriers to the implementation of these recommendations
Disclosures

- Advisory boards/advisory groups: Abbvie, Amgen, Janssen, Pfizer, UCB
- Travel grants: Abbvie, Amgen
- Unrestricted grants: Pfizer, Amgen
Background

• SPARCC has partnered with the CRA to create treatment recommendations for the management of spondyloarthritis (SpA)
  • Initial guidelines published in 2003\(^1\)
  • Guidelines updated in 2007\(^2\)

• Since 2007, continued rapid evolution of the management and monitoring of SpA
  • Role of traditional DMARDs tenuous\(^3\)
  • NSAIDs may be disease-modifying\(^4\)
  • Newer biologic agents
  • Role of MRI and recognition of non-radiographic axial SpA (nr-axSpA)\(^5\)

\(^{1}\)Maksymowych WP 2003
\(^{2}\)Maksymowych WP 2007
\(^{3}\)Chen J 2013, Chen J 2006, van Denderen JC 2005, Haibel H 2005
Methods

- Participants in the CRA/SPARCC Guidelines working group included:
  - SPARCC Executive Committee
  - Rheumatologist leaders from SPARCC collaborating sites
  - Canadian rheumatologists from across the country with a special interest in SpA
    - Both academic and community practice
  - Canadian juvenile SpA expert
  - PGY-5 rheumatology trainee with special interest in SpA
  - Epidemiologist/health services researcher
  - Member of the CRA Executive
  - Member of the CRA Therapeutics Committee
  - Patient representative from the Canadian Spondylitis Association

- Pharmaceutical/industry representatives had no role in the process at any point
Methods

• Late 2012: need to update recommendations recognized
  • 2007 document reviewed to identify issues requiring further discussion
• January 2013: teleconference of SPARCC EC for first draft of proposed guidelines
• April 2013: web-based survey distributed to Working Group (WG)
  • Evaluation of new items on 5-point Likert scale
• May 2013: Survey results discussed in detail by WG in afternoon session of SPARCC Investigators’ Meeting
• June and July 2013: Revised drafts of proposed guidelines submitted to WG
• July 2013 – January 2014: Literature review
Methods

• January 2014: draft paper completed, WG asked to vote on each recommendation to comprise an “Expert Opinion” rating

• February 2014: recommendations presented at CRA AGM as part of “National Update”

• February-March 2014: recommendation disseminated to and reviewed by CRA Therapeutics Committee

• March 2014: Therapeutics Committee requests survey of entire CRA membership to ensure that recommendations based on “expert opinion” match the opinion of its members

• May 2014: Survey of CRA disseminated
An Important Note

• These recommendations are not intended for the diagnosis or classification of SpA
  • Diagnosis of SpA made based upon physician clinical judgment
  • Suggest previously proposed classification criteria (ASAS or CASPAR)
An Important Note

Recommendaotns will be divided into two parts:

• Part I: Principles of the Management of SpA in Canada
  • Optimal management of SpA in Canada and barriers to implementation
  • Largely derived from expert opinion

• Part II: Specific Management Recommendations
  • Specific recommendations for SpA treatment with larger body of literature support
Patient Population

Axial SpA

Peripheral SpA

nr-axSpA
Non-radiographic axial SpA (nr-axSpA):

Axial SpA lacking diagnostic SI joint changes on X-ray but having diagnostic MRI findings

1Rudwaleit M 2009, Rudwaleit M 2009
## Grading Evidence

<table>
<thead>
<tr>
<th>Level of Evidence (LOE)</th>
<th>Strength of Recommendation (SOR)</th>
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<tbody>
<tr>
<td><strong>I</strong>: Meta-analysis, systematic reviews of RCT’s, or an individual RCT</td>
<td><strong>A</strong>: Strong recommendation:</td>
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<td>• Direct level 1 evidence</td>
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<td><strong>II</strong>: Meta-analysis, systematic reviews of observational studies (cohort/case control</td>
<td><strong>B</strong>: Moderate recommendation:</td>
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<td>studies), or individual observational studies</td>
<td>• Direct level 2 or extrapolated level 1 evidence</td>
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<td>OR</td>
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<td>RCT subgroup/post-hoc analysis</td>
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<td><strong>III</strong>: Non analytic studies (case reports, case series)</td>
<td><strong>C</strong>: Weak recommendation:</td>
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<td>• Direct level 3 or extrapolated level 2 evidence</td>
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<td><strong>IV</strong>: Expert opinion</td>
<td><strong>D</strong>: Consensus recommendation:</td>
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<td></td>
<td>• Expert opinion based on very little evidence</td>
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<td><strong>NR</strong>: Recommendation is not linked to evidence</td>
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Algorithm for Assessment of SpA
Algorithm for Assessment of SpA

Suspect axial SpA: chronic back pain, age of onset <45

Suspect peripheral SpA

If appropriate, MRI whole spine and pelvis

Assessed by rheumatologist for presence of SpA

Within 3 months

Within 6 weeks
Wait Time

Recommendations

• Axial SpA suffers a diagnostic delay of 5-10 years\textsuperscript{1}

• In PsA, a diagnostic delay of just 6 months results in poorer outcomes\textsuperscript{2}

• Timely MRI access is critical for diagnosing nr-axSpA\textsuperscript{3}

\textsuperscript{1}Rudwaleit M 2012, Ozgocmen S 2012
\textsuperscript{2}Haroon 2013
\textsuperscript{3}Rudwaleit M 2009, Rudwaleit M 2012
Wait Time Recommendations (LOE IV, SOR D):

Early diagnosis and treatment

Leverage change at a government level

Access to rheumatologists and MRI in underserviced areas
Barriers to Implementation

- Limited access to rheumatologists in much of Canada
  - Long wait lists
  - Responsibility of rheumatologist to see emergent cases first
  - Screening all patients <45 with back pain for SpA would overwhelm current workforce
  - Difficult to access MRI in much of the country
  - Imaging of whole spine limited
  - In certain areas, more appropriate to image SI joints first
Algorithm for Assessment of SpA
Algorithm for Assessment of SpA

At baseline visit:

- Screen for Hepatitis B, other chronic infection, liver disease, renal disease and malignancy
Algorithm for Assessment of SpA

At every assessment by rheumatologist, including baseline:

- Patient history
- Relevant clinical exam
  - Axial: include spinal mobility
  - Peripheral: include TJC, SJC, enthesitis
- Assessment for extra-articular manifestations
- Assessment for comorbid conditions associated with inflammatory arthritis
- BASDAI
- Function
- Patient assessment of global well-being
- CRP/ESR
- Drug toxicity
- Appropriate imaging
- Quality of life
Frequency of assessments dependent on disease severity, treatment type and patient preference (LOE IV, SOR D)
Algorithm for Assessment of SpA

Prior to initiating therapy:

- NSAIDs: gastrointestinal and cardiovascular risk
- DMARDs: CBC, liver function, renal function
- Biologic: HIV (if high risk), latent TB, appropriate vaccinations
Algorithm for Treatment of SpA
Algorithm for Treatment of SpA

Diagnosis of SpA
Algorithm for Treatment of SpA

Non-pharmacologic treatment:

- Patient education
- Regular exercise
- Physiotherapy
- Patient associations/self-help groups
- Smoking cessation
- Referral to relevant specialist for extra-articular manifestations, if needed
- Management of comorbid conditions associated with inflammatory arthritis
- Work assessment/counselling
Smoking cessation (LOE II, SOR B):

Smoking associated with radiographic progression in axial SpA\(^1\)

Smoking associated with worse patient-reported outcomes in axial and peripheral SpA\(^2\)

Relationship may be dose-dependent\(^3\)

\(^3\)Mattey DL 2011
Algorithm for Treatment of SpA

**NSAIDs:**
- At least two NSAIDs
- Two week trial of each
- Maximum dosage

**Corticosteroids:**
- Consider injection at local sites of inflammation such as SI joints, peripheral joints and entheses
- Consider short course of systemic steroids

**Inadequate Response**
NSAIDs (LOE I, SOR A):

NSAID use may modify radiographic outcome in axial SpA in certain circumstances\(^1\)

2 week trial of each NSAID is sufficient\(^2\)

Systemic steroids in AS (LOE I, SOR A):

High dose prednisolone over 2 weeks was effective in uncontrolled disease\(^3\)

\(^1\)Wanders A 2005, Kroon F 2012, Poddubnyy D 2012
\(^3\)Haibel H 2014, Ejstrup L 1985, Peters ND 1992
Algorithm for Treatment of SpA

Inadequate Response

Axial SpA

Peripheral SpA

Inadequate Response
Algorithm for Treatment of SpA

Axial SpA

Inadequate Response

TNFi

Inadequate Response after 16 weeks

Switch TNFi

Inadequate Response after 16 weeks
No evidence for the efficacy of DMARDs for the treatment of axial SpA (LOE I, SOR A)\(^1\)

TNFi are efficacious in axial SpA (LOE I, SOR A)\(^2\)

TNFi may prevent radiographic progression in AS\(^3\)


\(^2\)Baraliakos X 2012 and numerous others

\(^3\)Haroon N 2013
Choice of TNFi should incorporate the presence of extra-articular manifestations (LOE I, SOR A)¹

Non-responders to TNFi may benefit from switching to another TNFi (LOE II, SOR B)²

Algorithm for Treatment of SpA

- Inadequate Response
  - Axial SpA
    - Inadequate Response
  - Peripheral SpA
Algorithm for Treatment of SpA

Peripheral SpA

DMARDs:
• Consider MTX, LEF, SSZ
• Consider DMARD combination therapy

Inadequate Response
DMARD use in peripheral SpA (LOE I, SOR A)\(^1\)

Combination therapy with DMARDs (LOE IV, D):

Consider in those with poor prognostic factors, recent-onset disease and inadequate response to monotherapy\(^2\)

\(^1\)Ash Z, 2012
\(^2\)Sakellariou GT 2013, Fraser AD 2005, Coates LC 2013
DMARDs in Peripheral SpA

• Recent meta-analysis concluded MTX effective for peripheral arthritis in PsA, but did not improve radiographic progression\(^1\)

• Same meta-analysis found SSZ effective, but minimally so
  • SSZ also does not prevent radiographic progression\(^2\)

• Placebo-controlled RCT found LEF useful in PsA\(^3\)
  • Observational study showed improved joint counts, dactylitis and PROs\(^4\)

\(^1\)Ash Z 2012
\(^2\)Rahman P 1998
\(^3\)Kaltwasser JP 2004
\(^4\)Behrens F 2013
DMARDs in Peripheral SpA

• The metric that we chose to evaluate LOR and SOR assigns high levels to meta-analyses and RCTs regardless of potential flaws in study design.

• Authors felt that the effect of DMARDs on peripheral SpA, though positive, was clinically minimal.
Algorithm for Treatment of SpA

Inadequate Response

- TNFi
  - Inadequate Response after 16 weeks
    - Switch TNFi
    - Inadequate Response after 16 weeks
  - Ustekinumab:
    - Consider if concomitant moderate-severe psoriasis
TNFi are efficacious and inhibit radiographic progression in peripheral SpA (LOE I, SOR A)$^1$

TNFi effective for the treatment of refractory enthesitis (LOE I, SOR A)$^2$ and dactylitis (LOE II, B)$^3$

$^1$Ash Z 2012 and numerous others
Choice of TNFi should incorporate the presence of extra-articular manifestations (LOE I, SOR A)\(^1\)

Combination of MTX and TNFi may be associated with prolonged drug response (LOE II, SOR B)\(^2\)

\(^1\)Braun J 2005, Rudwaleit M 2009, Gao X 2012

Ustekinumab use in patients with concomitant moderate-severe psoriasis (LOE I, SOR A): 

Improvement in joint counts, physical function and QoL

Non-responders to TNFi may benefit from switching to another TNFi (LOE II, SOR B)

1McInnes IB 2013, Gottlieb A 2009, Kavanaugh A 2010
Response To Therapy

• In axial SpA, consider changing therapy if 2 or more of:
  • BASDAI>4
  • Elevated acute phase reactants
  • Presence of inflammatory lesions in the SIJ and/or spine on MRI

• In peripheral SpA, consider TNFi if:
  • Persistent inflammation despite of trial of NSAIDs and one DMARD
  • Refractory enthesitis or dactylitis
Juvenile Spondyloarthritis

- Modifications of the CRA-SPARCC recommendations for application to a JSpA population
  - Currently JSpA contains several overlapping subtypes
  - Shared genetic and familial predispositions with adult SpA
    - A continuum of disease?

- Many adult rheumatologists in Canada will manage JSpA patients after the age of 18
Consider whole-body MRI for assessment of widespread enthesial, axial and peripheral disease (LOE IV, SOR D)

Regular physical activity is recommended (LOE I, B)\(^1\)

Use of foot orthotics (LOE I, SOR B)\(^2\)

\(^2\)Powell 2005
Peripheral arthritis is more common in JSpA; use a trial of NSAIDs of 1-2 months duration (LOE IV, SOR D)

TNFi are beneficial in both axial and peripheral predominant JSpA
(LOE I, SOR A IFX)
(LOE II, SOR B ETN, ADA)\(^1\)

Next Steps

• Draft guidelines reviewed by CRA therapeutics committee

• Need to ensure that the recommendations reflect the opinion of the CRA in general rather than only SpA experts

• Publication (long and short versions)
Conclusions

• Guidelines address:
  • Overarching general management principles
  • Ethical considerations
  • Wait time recommendations
  • Monitoring recommendations
  • Specific management recommendations
  • Modifications of the recommendations for application to a JSpA population
  • Barriers to implementation

• Each patient is unique and guidelines cannot be blindly applied to all
  • Clinical judgment and partnership with patients important

• Many clinical questions remain unanswered and require continued study
Thank you.