Psoriasis and it’s Comorbidities
A Dermatology Perspective

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The Pollinization Effect
Dermatologists & Rheumatologists

Derm 

PS PSA 

Rheums
Psoriasis / Psoriatic Arthritis

Severe Psoriasis

Psoriasis arthritis hands
Disclosures

- Dr. Charles Lynde
- Consultant/Speaker/Principal Investigator:
  - Abbive
  - Amgen
  - Janssen
  - Merck
  - LEO
  - Takeda
  - Pfizer
  - Celgene
  - Eli Lilly
  - Novartis
Learning Objectives

- Recognize the common comorbidities associated with psoriasis and
- Identify psoriasis treatment impact on comorbidities
Dermatologists pride themselves on their ability to see when others cannot
Severe Psoriasis

- Obese
- Hypertensive
- Diabetic
- CAD
- Depressed
- PSA

Where were our eyes?
Eyes become open and we started to see!
Psoriasis Arthritis

Eyes become opened and we started to see
Which one do you think most common in Psoriasis?

According to a systematic literature review and random-effects meta-analysis of existing data (79 studies), which comorbidity has the highest prevalence in psoriasis?

- Psoriatic arthritis
- Hypertension
- Obesity
- Anxiety
Seriously, its Anxiety

According to a systematic literature review and random-effects meta-analysis of existing data (79 studies), which comorbidity **has the highest prevalence in psoriasis**?

- Psoriatic arthritis – 24%
- Hypertension – 21%
- Obesity – 11%
- Anxiety – 30%
The Spectrum of Psoriasis 2015: Multifaceted, Comorbid, Systemic, Inflammatory Disease

Psoriasis: A systemic inflammatory condition

- Disease severity plaques
- Scalp Pso
- Nail Pso
- Pso Arthritis
- Metabolic comorbidities
- Low quality of life
- Psychological comorbidities
Common Comorbidities Among Patients with Psoriasis

- Systemic inflammation
- Arthritis, spondylitis
- Cardiovascular disease
- Metabolic syndrome and its components (central obesity, hyperglycemia, hyperlipidemia, high blood pressure)
- Inflammatory bowel diseases
- Uveitis
- Anxiety, depression, low QOL, erroneous lifestyle
Psoriasis and its Comorbidities
High prevalence of major comorbidities among patients with psoriasis

Based on a systematic literature review and random-effects meta-analysis of existing data (79 studies)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Studies (N)</th>
<th>Pooled prevalence (%)</th>
<th>95% CI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>11</td>
<td>30.2</td>
<td>21.7–38.8</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>34</td>
<td>24.1</td>
<td>19.3–29.0</td>
</tr>
<tr>
<td>Depression</td>
<td>21</td>
<td>21.7</td>
<td>15.1–28.3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>20</td>
<td>21.2</td>
<td>19.2–23.3</td>
</tr>
<tr>
<td>Obesity</td>
<td>9</td>
<td>11.9</td>
<td>7.2–16.8</td>
</tr>
<tr>
<td>Cardiovascular diseases</td>
<td>12</td>
<td>10.2</td>
<td>7.7–12.8</td>
</tr>
<tr>
<td>Diabetes</td>
<td>21</td>
<td>8.5</td>
<td>7.4–9.6</td>
</tr>
<tr>
<td>Hyperlipidemia, dyslipidemia, hyperglycemia</td>
<td>7</td>
<td>7.4</td>
<td>6.5–8.4</td>
</tr>
<tr>
<td>IBD, Crohn’s disease, ulcerative colitis</td>
<td>3</td>
<td>0.8</td>
<td>0.1–1.4</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>5</td>
<td>0.2</td>
<td>0.1–0.3</td>
</tr>
</tbody>
</table>
What impact can psoriasis–associated systemic inflammation have on the rest of the body’s systems?
Clinical Scenario

A 45 yr old man with diabetes (HbA1C = 10.5) hypertension (BP 150/100) and longstanding psoriasis presents for treatment. Know fatty liver. Baseline LFts are 2x ULN. On antihypertensive already. Prior UVB – no response. MTX prior caused LFTs to increase to 5X ULN so stopped
Metabolic Syndrome, Obesity, and High CV Risk

- Obesity – BMI > 30
  - Twice as common in psoriasis
  - Obese patients have more severe psoriasis
  - More likely to have a fatty liver
    - May predispose to complications from MTX

- Psoriatic children are already more likely to be obese
  - Children also more likely to have central obesity
Metabolic Syndrome, Obesity and High CV Risk

- Metabolic Syndrome
  - 3 or more abdominal obesity, hypertension, hypertriglyceridemia, reduced HDL, insulin resistance
  - High amounts of intraabdominal fat may increase TNFα and IL–6
Metabolic Syndrome, Obesity and High CV Risk

- CV risk
  - Pso linked to increase risk of MI, CVA, Atrial fibrillation

- Risk of Myocardial Infarction in Patients with Pso

- Conclusions: Pso may confer an independent risk of MI. The RR was greatest in young patients with severe pso
Pso Severity and the Prevalence of Major Medical Comorbidity

A population based study

Howa Yeung, BS: Junko Takeshita, MD, PhD: Nehal N. Mehta, MD, MSCE: Stephan E. Kimmel, MD, MSCE: Andrea B. Troxel, ScD: Joel M. Gelfand, MD, MSCE

JAMA Dermatol. Doi:10.100/jamadermatol.2013.5015
Published online Aug 7, 2013
Metabolic Syndrome, Obesity and High CV Risk

- Large population analysis showed positive dose response between pso severity and burden of major medical comorbid disease
- Population based cross section al study in UK (the health improvement network)
- Pso diagnosis confirmed with letter to GP
  - Questionnaire to GP also determined severity (mild, moderate, severe)
Psoriasis associated with:
- Chronic pulmonary disease
- Diabetes
- Myocardial infraction
- Peptic ulcer disease
- Renal Disease
- Rheumatologic disease
Obesity

- ETN: PASI 75 response rates decreased in heavier patients
- ADA: PASI 75 response rates decrease in heavier patients
- UST: two dosing schedules, 45mg q12w standard dosing, 90mg q12w for > 100kg
Obesity

- Using combination therapy with biologic may be more challenging if underlying fatty liver
  - Consider patients on ADA if require MTX to prevent antidrug antibodies OR for secondary failure
Association Between Tumor Necrosis Factor Inhibitor Therapy and Myocardial Infarction Risk in Patients with Psoriasis

Jashin J. Wu, MD; Kwun-Yee T. Poon, MS; Jennifer C. Channual, MD; Albert Yuh-Jer Shen, MS, MD

Published online August 20, 2012.
Doi: 10.1001/archdermatol.2012.2502
Metabolic Syndrome/CVD

- Wu et al looked at Kaiser database
- TNFa treated vs oral/phototherapy vs topical
- Treatment groups were surrogates for severity
- TNFa group associated with 50% reduction in MI risk compared to topical agents
- Stronger effect in those > 60 yrs age
  - Oral/phototherapy group also associated with reduction
Tumor Necrosis Factor Inhibitor Therapy and Myocardial Infarction Risk in Patients With Psoriasis, Psoriatic Arthritis, or Both

Jashin J. Wu MD and Kwun-Yee T. Poon MS
Department of Dermatology, Kaiser Permanente Los Angeles Medical Centre, Los Angeles, CA
Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, CA

J Drugs Dermatol.
2014;13(8):932-934
The effects of tumour necrosis factor inhibitors, methotrexate, non-steroidal anti-inflammatory drugs and corticosteroids on cardiovascular events in rheumatoid arthritis, psoriasis and psoriatic arthritis: a systemic review of meta-analysis

Camille Roubille, Vincent Richer, Tara Starnino, Collette McCourt, Alexandra McFarlane, Patrick Fleming, Stephanie Siu, John Kraft, Charles Lynde, Janet Pope, Wayne Gulliver, Stephanie Keeling, Jan Dutz, Louis Bessette, Robert Bissonnette, Boulos Haraoui

doi:10.1136/annerheumdis-2014-206624
Metabolic Syndrome/CVD

Meta-analysis showed systemic therapy associated with significant decrease in risk of all CVE
Metabolic Syndrome/CVD

- ETN decreases hsCRP in psoriasis
- ADA improves endothelial cell function
- ADA associated with reduction of hsCRP and reduction of vascular inflammation as measured by FDG-PET (Bissonnette et al)
- TNFa inhibitors associated with reduced CV events in RA in CORRONA registry
Potential mechanism for risk of CDV disease in psoriasis

- Family History
- Smoking
- Hypertension
- Diabetes
- Dyslipidemia
- Obesity
- Others (alcohol)

Conventional risk factors

Higher Prevalence

Common risk factors

Psoriasis

- Immune/inflammatory activity

Cardiovascular Disease

Other potential mechanisms
- Common genetic risk factors
- PsO severity & progression
- PsO therapy
- Under Dx & treatment of CDV disease
Adjusted Relative Risk of MI Patients with PsO based on Patient Age

![Graph showing relative risk of MI patients with PsO based on age. The graph indicates that the relative risk is greatest in young patients with severe PsO.](image)
FDG-PET/CT Imaging reveals inflammation in skin, liver, vasculature and joints
Effects of T-Cell activation on plaque inflammation
TNFα promotes dyslipidaemia and insulin resistance, both of which are traditional risk factors for atherosclerosis. TNFα upregulates adhesion molecules leading to fatty streak formation and the initiation or atherosclerosis, and is involved in the inflammation leading to plaque rupture. TNFα may promote thrombophilia, encouraging thrombotic events. Post-ischaemic event repair may be modified by inflammatory cytokines. Anti-TNFα therapy may exert an influence at any of these stages.
Psoriasis – time course of disease morbidity and mortality

Canadian Dermatology-Rheumatology Comorbidity Initiative Investigators

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McCourt C, Submitted,
McFarlane A, Submitted
Based on literature review
RA
Psoriatic arthritis
Psoriasis

Based on drugs with data in those areas
Thus data on TNFi are given but not data on other biologics or Tofacitinib
<table>
<thead>
<tr>
<th>Topic</th>
<th>Recommendation</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks of CVD</td>
<td>1. Individuals with RA, PsA, and Pso have a greater risk of CVD than the general population. The diseases themselves and traditional risk factors contribute to this risk. The risk of MI in RA is comparable to that in DM. This should be recognised by healthcare providers and patients.</td>
<td>2b, 3b (RA) 2b (PsA) 2b (Pso)</td>
</tr>
<tr>
<td></td>
<td>2. Traditional modifiable risk factors should be screened for and managed appropriately to reduce the risk of CVD in RA, PsA, and Pso populations.</td>
<td>5</td>
</tr>
<tr>
<td>Impact of treatment on CVD</td>
<td>3. CS use should be minimised in RA, especially in patients with CV risk factors.</td>
<td>2b, 5</td>
</tr>
<tr>
<td></td>
<td>4. In patients with RA or PsA, especially those with additional CV risk factors, the risk and benefits of NSAID use should be weighed.</td>
<td>3b, 5</td>
</tr>
<tr>
<td>Topic</td>
<td>Recommendation</td>
<td>Level of evidence</td>
</tr>
<tr>
<td>------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
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<tr>
<td>Impact of treatment on CVD</td>
<td>Healthcare providers and patients should be aware that MTX and/or TNFi use may decrease the risk of CVE in RA. Their use may help to reduce CS and NSAID use, especially in patients with CV risk factors.</td>
<td>2b, 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Healthcare providers and patients should be aware that MTX and/or TNFi use may decrease the risk of CVD in PsA/Pso.</td>
<td>2b, 5</td>
</tr>
<tr>
<td>Smoking</td>
<td>Statement: Current smoking is associated with an increased prevalence and/or incidence and possibly a negative impact on disease severity in RA, PsA, and Pso. Recommendation: Smoking status should be determined in all patients with RA, PsA, and Pso and smoking cessation should be encouraged.</td>
<td>2b, 5</td>
</tr>
<tr>
<td>Topic</td>
<td>Recommendation</td>
<td>Level of evidence</td>
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<td>-------</td>
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</table>
| Weight| **8.** Statement: Pso severity may be associated with increased BMI and obesity. Increased BMI may be associated with increased disease activity of RA and Pso.  
Recommendation: Healthcare providers should be aware that higher BMI is associated with a reduced treatment response in RA, PsA, and Pso. TNFi may be associated with a mild increase in weight in RA, PsA, and Pso but the clinical relevance is unknown. | 4, 5 (RA)  
3b, 4, 5 (PsA)  
2b, 5 (Pso) |
|       | **9.** Statement: The effects of dietary manipulations on disease activity in RA, PsA, and Pso are still uncertain.  
Recommendation: BMI should be determined in all patients with RA, PsA, and Pso.                                                                                                                                                                                                 | 5 |
<p>|       | <strong>10.</strong> Healthcare workers should encourage normal BMI                                                                                                                                                                                                                                                                          | 5. |</p>
<table>
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<tr>
<th>Topic</th>
<th>Recommendation</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignancies and Infection</td>
<td>11. Patients and health care providers should be aware of increased risk of infection when initiating systemic therapies (biologics, DMARDs, corticosteroids), especially in RA.</td>
<td>2b, 5</td>
</tr>
<tr>
<td></td>
<td>12. Risk of infection should be assessed (including relevant comorbidities) when initiating systemic therapy.</td>
<td>2b, 5</td>
</tr>
<tr>
<td></td>
<td>13. Prior to initiating systemic therapy, additional cancer screening beyond the nationally recommended guidelines for age and sex is not required. Individuals at increased risk for skin cancer may require closer monitoring.</td>
<td>2b, 5</td>
</tr>
<tr>
<td>Topic</td>
<td>Recommendation</td>
<td>Level of evidence</td>
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<td>-------------------------------------------</td>
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<tr>
<td>Risk of cancer recurrence or new cancer</td>
<td>14. In the absence of sufficient data on recurrent cancer, patients with a prior cancer should be informed about a potential risk of new or recurrent cancers when treated for RA, PsA, or Pso with TNFi or some of the DMARDs.</td>
<td>2b, 5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>15. Individual disease–specific risk factors and markers for increased disease severity in RA, PsA, and Pso do not appear to be associated with increased bone loss. Usual profiling with standardised methods should be used to assess risk of osteoporosis and fracture.</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>16. Systemic CS have a negative impact on BMD. Usual CS–induced osteoporosis guidelines for prevention and treatment should be followed.</td>
<td>1b (RA), 5 (PsA, Pso)</td>
</tr>
</tbody>
</table>
Key Messages

- Psoriasis is a chronic systemic immune mediated inflammatory diseases.
- Some psoriasis therapies may help decrease the morbidity and mortality associated with psoriasis and its comorbidities.
- Presence of ECMs may influence choice of therapy. Particular if patient has multiple ECMs (e.g. PsA with AS, IBD, and/or uveitis).
- Other comorbidities also influence treatment choices:
  - e.g. obesity and metabolic syndrome may preclude the use of MTX and CYC and move us up the therapeutic ladder to biologics.
  - In patients who have Pso with or without inflammatory arthritis, anti-TNF treatment may be considered as first line therapy in selected patients.
Psoriasis as an Immune-mediated Inflammatory Disease: Key Messages

- Patients with pso often have one or more concomitant conditions, many of which also have inflammatory pathphysiology
  - e.g., pso arthritis, inflammatory bowel diseases
- The classic features of pso are cutaneous manifestations of a systemic inflammatory disease
  - Current best practice is to treat skin disease to target
  - Certain presentations of pso are more likely to require systemic treatment to reach target
  - Early anti-inflammatory treatment may reduce long term effects of pso and its comorbidities
The Future

- Quality of life
- Decrease inflammation
- Translate into improving comorbidities?
Questions?