OSTEOARTHRITIS & FALLS

Unveiling the science behind OA and falls- linking biomarkers with physical, psychological and imaging markers.

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(PhD candidate)
Ageing and Age-associated Disorder Research group
OUTLINE

- Motivation
- Strategy
- Biomarker study
  - Introduction
  - Method
  - Results
  - Conclusion
MOTIVATION
High Prevalence

50% 

Falls consequences
Death, Hip fractures, injuries, QoL

“an event where the individual comes to rest on the ground or other lower level.”

Falls is costly!
~$24 billion

Multifactorial event

1- World Health Organization 2008
2- Murray 2015
3- Rubeinstein 2006
4- Centers for Disease Control and Prevention., 2005
5- Heinrich et al, 2010
US

Unintentional Fall death rates US (2005-2014)
Source: http://www.cdc.gov/homeandrecreationalsafety/falls/adultfalls.html

Malaysia

Kaplan–Meier survival curve of 10-year mortality for men and women who presented to the emergency room after a fall. (MP Tan et al, 2015)
Asymmetrical joint space narrowing from loss of articular cartilage

The medial (inside) part of the knee is most commonly affected by osteoarthritis.

Most prevalent arthritis
>80% in elderly

Has significant impact on HRQoL

Conflicting result on the association with falls

Challenges: Uncomprehend aetiology & variety of definition

1. Lawrence RC et al 2008
3. Ng CT & Tan MP 2013
“How is OA associated with falls among older adults in terms of biochemical, physical, clinical, imaging and psychological aspects?”
STRATEGY
Comply all definition of OA

OA & Falls

Postural study

Biomarker

Imaging marker

Functional & psycho-social aspect
ASSOCIATIONS OF OA BIOMARKERS AND FALLS AMONG OLDER ADULTS WITH KNEE OA
INTRODUCTION

- Objective: to determine contribution of OA serum candidate biomarkers to falls
- Candidate biomarker:
  - Inflammation
  - Anti-catabolic
  - Psychological/ emotion state
Osteoarthritis

FALLS

TIMP 1
TIMP 2

Catabolic

IL6

Inflammation

NPY

Psychological state

Pain

Fear of falling

Balance

FALLS

Figure 1 Theoretical framework
METHODOLOGY

Participants

- Age ≥65 years
- Knee OA (KL-grade 2-4)
- 15 Fallers and 15 non-fallers

Baseline assessment

- MRI knee
- Postural balance
- WOMAC- symptoms
- Short FES-I- Fear of falling

Biomarker analysis

- ELISA assay
  - TIMP1-R&D
  - TIMP2-R&D
  - NPY-Abcam
  - IL-6-Abcam

Baseline assessment

- ELISA assay
  - TIMP1-R&D
  - TIMP2-R&D
  - NPY-Abcam
  - IL-6-Abcam
### RESULTS  Table 1: Demographic Characteristic

<table>
<thead>
<tr>
<th></th>
<th>Fallers (n=13)</th>
<th>Non-fallers (n=14)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years, mean (SD)</strong></td>
<td>73.8 (5.1)</td>
<td>70.5 (4.0)</td>
<td>0.076</td>
</tr>
<tr>
<td><strong>Gender, female n (%)</strong></td>
<td>12 (92.3)</td>
<td>10 (71.4)</td>
<td>0.326</td>
</tr>
<tr>
<td><strong>BMI, kgm², mean (SD)</strong></td>
<td>25.9 (4.2)</td>
<td>24.4 (3.9)</td>
<td>0.324</td>
</tr>
<tr>
<td><strong>Comorbidities, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>4 (30.8)</td>
<td>3 (21.4)</td>
<td>0.678</td>
</tr>
<tr>
<td>Heart disease</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>NA</td>
</tr>
<tr>
<td>Hypertension</td>
<td>8 (61.5)</td>
<td>7 (50.0)</td>
<td>0.547</td>
</tr>
<tr>
<td>Stroke</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>NA</td>
</tr>
<tr>
<td>Visual Impairment</td>
<td>5 (35.5)</td>
<td>1 (7.1)</td>
<td>0.077</td>
</tr>
<tr>
<td>TABLE 2: CLINICAL CHARACTERISTIC</td>
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<td>----------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>WORMS score (MRI), mean (SD)</strong></td>
<td>Fallers (n=13)</td>
<td>Non-fallers (n=14)</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td>108.46 (32.7)</td>
<td>90.79 (38.29)</td>
<td>0.211</td>
</tr>
<tr>
<td><strong>WOMAC score, median (IQR)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain (0-500)</td>
<td>60 (0-150)</td>
<td>50 (0-150)</td>
<td>0.870</td>
</tr>
<tr>
<td><strong>Short FES-I score, Mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fear of falling</td>
<td>14.31 (6.51)</td>
<td>11.71 (4.29)</td>
<td>0.230</td>
</tr>
<tr>
<td><strong>Postural sway, Mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standing balance</td>
<td>1.15 (0.33)</td>
<td>1.05 (0.31)</td>
<td>0.974</td>
</tr>
</tbody>
</table>
COMPARISONS OF OA BIOMARKERS LEVEL IN FALLERS AND NON-FALLERS
ANTI CATABOLIC MARKERS - TIMP1 & 2

TIMP1 (ng/mL) vs. Fallers vs. Non-fallers

- TIMP1 levels are similar between Fallers and Non-fallers (NS).

TIMP2 (ng/mL) vs. Fallers vs. Non-fallers

- TIMP2 levels are significantly different between Fallers and Non-fallers (p = 0.017).
INFLAMMATORY MARKERS- IL6

EMOTIONS MARKERS- NPY
CORRELATION BETWEEN OA BIOMARKERS AND CLINICAL CHARACTERISTIC IN FALLERS AND NON-FALLERS SUB-GROUP
MRI SCORES: INCREASED IN OA SEVERITY

TIMP1

TIMP2

WORMS score for MRI-Knee OA

Fallers
Non-fallers
MRI SCORES: INCREASED IN OA SEVERITY

**IL6**

- Non-fallers: [Graph showing IL6 levels with a p-value of 0.025]
- Fallers: [Graph showing IL6 levels with a p-value of 0.010]

**NPY**

- Non-fallers: [Graph showing NPY levels with a p-value of 0.010]
- Fallers: [Graph showing NPY levels with a p-value of 0.010]
WOMAC PAIN: INCREASED IN PAIN SEVERITY

IL6

NPY
SHORT FES-I SCORE: FEAR OF FALLING

**IL6**

**NPY**

\[ p : 0.026 \]
MCTSIB TEST: INCREASED IN STANDING SWAY

**TIMP2**

- **p**: 0.038

**NPY**

- **Non-fallers**
- **Fallers**
# TABLE 3: CORRELATIONS SUMMARY

<table>
<thead>
<tr>
<th></th>
<th>ANTI-CATABOLIC</th>
<th>ANTI-CATABOLIC</th>
<th>INFLAMMATORY</th>
<th>EMOTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TIMP1</td>
<td>TIMP2</td>
<td>IL6</td>
<td>NPY</td>
</tr>
<tr>
<td>Fallers</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Non-fallers</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>MRI scores</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>WOMAC Pain</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Fear of falling</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Postural sway</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
</tr>
</tbody>
</table>

*Correlation coefficient

- TIMP1: Transforming growth factor inhibitor (TIMP1) is positively correlated with MRI scores and WOMAC Pain, and negatively correlated with Fear of falling.
- TIMP2: Transforming growth factor inhibitor (TIMP2) is positively correlated with MRI scores and WOMAC Pain, and negatively correlated with Fear of falling.
- IL6: Interleukin 6 (IL6) is positively correlated with MRI scores and WOMAC Pain, and negatively correlated with Fear of falling.
- NPY: Neuropeptide Y (NPY) is positively correlated with MRI scores and WOMAC Pain, and negatively correlated with Fear of falling.

*Correlation coefficient*
STRENGTH AND LIMITATION

- This study represents a proof of concept study.
- Identified potential trends in the association between OA biomarkers and falls.
- Small sample size: Inform future larger studies.
CONCLUSION

- Biomarkers as potential tools
- The anti catabolic marker, TIMP2 α risk of Falls
- Evaluate role for higher disease burden