Osteonecrosis of Femoral Head – The Asian Perspective

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Socioeconomic Impact of ONFH

- Disabling disease affecting young adults
- A major indication for total hip replacement (THR) in Asians

ONFH cases/total THR cases

- Taiwan: 46.9%
- Japan/Korea: >40%
- USA: 5~12%
- Sweden: 2.2–3%
- Norway: 0.8%

Journal of Orthopaedic Surgery and Research
Research article
Incidence of hip replacement among national health insurance enrollees in Taiwan
Yu-Shu Lai, Hung-Wen Wei and Cheng-Kung Cheng*1,2
2008
Etiology of ONFH

Trauma–associated ONFH

Secondary ONFH

ONFH with associated risk factors
- Corticosteroids (SLE, SARS…)
  - The most common cause
  - 5–25% of patients who receive medication
  - Usually administered for more than 1 month
- Alcohol use
- Gaucher’s disease, Rheumatic disease, Dysbarism, Pancreatitis, Hyperuricemia, Radiotherapy, Renal failure, HIV, Smoking…

Idiopathic (primary) ONFH
- 10%–15% of all people who develop osteonecrosis are otherwise well
Pathogenesis of ONFH

Not fully understood

Etiology
- Trauma
- Intravascular coagulation
- Alcohol
- Corticosteroids
- Fat emboli
- Extravascular compression

Pathogenesis
- Vasular interruption
- Thrombotic occlusion
- Decreased blood flow
- Ischemia
- Osteocyte necrosis
- Repair
- Loss of structural integrity
- Collapse

Genetic predisposition may contribute to the development of ONFH

Histopathology

The adult hip, p.457
Lippincott-Raven, 1998
Genetic Etiology of ONFH

- Zalavras et al. (2002)
  - Gene: Methylene–tetrahydrofolate reductase gene
- Asano et al. (2003)
  - Gene: Cytochrome P450
- Chao et al. (2003)
  - Gene: ADH2, ALDH2
- Asano et al. (2003)
  - Gene: Multidrug resistance gene 1 (ABCB1, MDR1)
- Dilley et al. (2004)
  - Gene: Beta fibrinogen gene
- Bjorkman et al. (2004)
  - Gene: Factor V Leiden, Prothrombin gene
- Koo et al. (2006)
  - Gene: Nitric oxide synthase
- Hong et al. (2007)
  - Gene: Hypoxia inducible factor 1 alpha
- Hirata et al. (2007)
  - Gene: Apolipoprotein B gene
- Kerachian et al. (2010)
  - Gene: Alpha–2–macroglobulin (A2M)
Identification of the ONFH Disease Gene

- First report of hereditary ONFH (excluding thrombophilia and hypofibrinolysis)
- Positional candidate gene approach
  - Whole genome scan by microsatellite marker mapped the ONFH disease gene to a 15 cM region on chromosome 12q13
    
  - Resequencing the candidate genes detected mutations in type II collagen gene (COL2A1)
    
Does COL2A1 mutation cause ONFH in other ethnic groups?

Shiro Ikegawa (University of Tokyo, Japan)
Mutation: G3508A
Repair and regeneration

A recurrent mutation in type II collagen gene causes Legg-Calvé-Perthes disease in a Japanese family

Yoshinari Miyamoto · Tatsuo Matsuda · Hiroshi Kitoh · Nobuhiko Haga · Hirofumi Ohashi · Gen Nishimura · Shiro Ikegawa

ORIGINAL INVESTIGATION
Early Diagnosis of ONFH

*Extremely important, especially in Asia where there is a higher incidence of ONFH*

- Positive risk factors
- Positive symptom over groin area or medial thigh
- Radiography
- Scintigraphy
  - No longer widely performed
- Computed Tomography
  - In patients for whom MRI is contraindicated (pacemaker, aneurysm clip, etc.)
- **Magnetic Resonance Imaging**
  - *The most accurate modality*
Non-operative Treatment of ONFH

Mont et al. reported that >80% of affected hips progress to femoral head collapse by 4 years after the diagnosis

Hernigou et al. reported that 88% hips became symptomatic and 73% hips demonstrated collapse at a mean of 11 years

- Restricted weight-bearing
- High-energy shock wave
- Hyperbaric oxygen
- Pulsed electromagnetic fields
- Medication
  - Bisphosphonate
  - Anticoagulant
  - Lipid-lowering agents
  - Vasodilator
Non-operative Treatment of ONFH

- **High-energy shock wave**
  - Ludwig J et al. (Germany, 2001) & Wang CJ et al. (Taiwan, 2005 & 2009)
    - Harris Hip Score was significantly improved
    - Some favorable results
  - Alves et al. (Brazil, 2009)
    - Systematic review from 1966 to 2009
    - Only 5 articles
    - No controlled and double-blinded studies
Non–operative Treatment of ONFH

**Medication**
- Bisphosphonate
  - Lai et al. 2005, Taiwan
  - Agarwala et al. 2005 & 2009, India
  - Improvement in clinical function
  - Reduction in the rate of femoral head collapse and requirement for THR
- Anticoagulant
- Lipid–lowering agents
- Vasodilator
  - Iloprost (Prostacyclin analogue, PGI2)
  - Meizer R et al. 2005 & 2009, Austria
  - Jager M et al. 2008, Germany
  - Treatment of bone marrow edema or early stage of ONFH
Other Medications or Food Supplements in Asia

- **Japan**
  - Vitamin E (Alpha-tocopherol-supplemented diet) reduced the incidence of ON (5/21 rabbits vs. 14/20 rabbits, p=0.004)
  - [Acta Orthopaedica. 2010](#)

- **China**
  - **Chinese drugs**
    - Promoting blood circulation
    - Eliminating blood stasis on vascular endothelial growth factor (VEGF) expression in rabbits with steroid–induced ONFH
  - [J Tradit Chin Med. 2009](#)

- **Thailand**
  - Core decompression + **Menatetrenone (Vitamin K2)**
Operative Treatment of ONFH

- Core decompression ±
  - Cancellous bone graft
  - Fibular or iliac bone graft (vascularized or non-vascularized)
  - Multipotential stem cells
  - Bone morphogenic protein
  - Tantalum rod

- Osteotomy

- Hip arthroplasty
  - THR?
  - Hemiarthroplasty?
  - Resurfacing arthroplasty?
Pre-collapse Disease

Nowadays core decompression is still one of the safest and most commonly used procedures in treating pre-collapse stage of ONFH

Variable results
Operative Treatment of ONFH

- **Core decompression +**
  - Cancellous bone graft
  - Fibular or iliac bone graft (vascularized or nonvascularized)
  - Multipotential stem cells
  - Bone morphogenic protein
  - Tantalum rod
Core decompression combined with trochanteric cancellous bone grafting – through a single 1.5 cm wound
## Results

(110 patients, mean fu time of 87 months)

<table>
<thead>
<tr>
<th></th>
<th>Group A (51)</th>
<th>Group B (59)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Core decompression only</td>
<td>Core decompression + trochanteric BG</td>
</tr>
<tr>
<td>Ficat stage I</td>
<td>66.7%</td>
<td>80.0%</td>
</tr>
<tr>
<td></td>
<td>(p=0.08)</td>
<td></td>
</tr>
<tr>
<td>Ficat stage IIA</td>
<td>20.6%</td>
<td>61.8%</td>
</tr>
<tr>
<td></td>
<td>(p=0.001)</td>
<td></td>
</tr>
<tr>
<td>Ficat stage IIB</td>
<td>9.1%</td>
<td>57.9%</td>
</tr>
<tr>
<td></td>
<td>(p=0.023)</td>
<td></td>
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<tr>
<td>Overall</td>
<td>23.5%</td>
<td>61.0%</td>
</tr>
<tr>
<td></td>
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<td>(p=0.021)</td>
</tr>
</tbody>
</table>

~Randomized patient selection for different surgical procedures
Osteotomy in Treating ONFH

- Transtrochanteric rotational osteotomy (Sugioka’s osteotomy)
- Posterior rotational osteotomy
  - Atsumi et al. 2010, Japan
- Curved intertrochanteric osteotomy
  - Hasegawa et al. 2010, Japan

Several Japanese studies:
  Effective for delaying the progression of ONFH with extensive lesions

European and American studies:
  Disappointing results
  Increase the difficulty of THR in the future
Hip Replacement Surgery

- **Total hip arthroplasty?**
  - Ficat stage IV with damage of acetabular cartilage
    - Metal-on-Metal?
    - Ceramic-on-Ceramic?
    - Ceramic-on-HCPE?
    - Metal-on-HCPE?

- **Bipolar hemiarthroplasty or femoral head resurfacing arthroplasty?**
  - Ficat stage III (no acetabular involvement)
  - Femoral head collapse >2mm
  - A combined necrotic angle >200° or >30% involvement

Mont, 2006
Total Hip Arthroplasty for ONFH

- Varying results
- Relatively young patients with high activity
- Inferior to THR for OA?
ONFH (Age for THR in Taiwan)

Mean 49 years in 12,466 hips
1997-2004
Survival Curve of THR for ONFH
(12,466 hips, 1997–2004, Taiwan)

- Median: 98.14%
- Range: 99.87-94.71%

94.71% at end of 8th year
Survival Curve of THR for ONFH vs Osteoarthritis

<table>
<thead>
<tr>
<th>Total Hip Arthroplasty</th>
<th>Available N</th>
<th>Median survival rate (%) (Range: 1 – 8 years)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ONFH</td>
<td>12,466</td>
<td>98.14 (99.87–94.71)</td>
<td>0.4791</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>18,515</td>
<td>98.41 (99.80–95.04)</td>
<td></td>
</tr>
</tbody>
</table>
Hemiarthroplasty for ONFH

- **Variable success rate**
  - Amstutz et al. 1994, Grevitt & Spencer, 1995, Chan & Shih, 2000...
    - Preserve acetabular bone stock for the young patients
    - Satisfactory outcome
  - Takaoka et al. 1992, Sanjay & Moreau, 1996, Yamano et al. 2003...
    - High rate of acetabular degeneration and protrusio
### Bipolar Hemiarthroplasty for ONFH

(7,407/19,873 hips arthroplasty, 37.3%, 1997–2004, Taiwan)

#### Osteonecrosis of femoral head

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Available N</th>
<th>Median survival rate (%) (Range: 1 – 8 years)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>THR</td>
<td>12,466</td>
<td>97.11 (98.94–94.71)</td>
<td></td>
</tr>
<tr>
<td>Hemiarthroplasty</td>
<td>7,407</td>
<td>97.02 (99.27–94.94)</td>
<td>0.071</td>
</tr>
</tbody>
</table>

94.94% at end of 8th year
THR vs Hemiarthroplasty for ONFH

Which one is better???:

Osteolysis

OK

10Y  12Y

48/M
Resurfacing Hemiarthroplasty for ONFH

- Varying success
- Time-buying surgery
  - Adili & Trousdale, 2003
    - HSS: from 48.1 to 79.3
    - Survival rate: 75.9% at 3 years
  - Sharma & Cheng, 2007
    - Survival rate: 72.6% at 4 years

Role in treating ONFH????
Conclusion

Osteonecrosis of Femoral Head – The Asian Perspective

- High Incidence in Asia
  - A lot of basic and clinical researches
    - Exploring pathogenesis
    - Developing new or alternative treatment modalities
  - Genetic research for early diagnosis and prevention
Thanks for your attention !!!