Prevalence of Comorbidities among HIV-positive patients in Taiwan

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Comorbidity distribution

THAB0205 Schouten
Comorbidity and ageing in HIV-1 infection: the AGEhIV Cohort Study

Long-term complications of cART

• Hyperlipidemia
• Lipodystrophy
• Hyperglycemia
• Hypertension
• Type 2 diabetes mellitus
• Cardiovascular disease
• Osteonecrosis (not a component of metabolic syndrome)
Prevalence of comorbidities among HIV-positive patients in Taiwan

• A survey conducted among HIV-positive patients regularly seeking HIV care at the national Taiwan University Hospital between May to December 2015
  – 1398 patients on cART were included
    • 95.1% male; 89.0% men who have sex with men
    • Mean age, 39.2 years (SD, 10.9)
    • Current smokers, 31.5%
    • CD4, 590 cells/mm$^3$ (SD, 279)
    • Plasma HIV RNA load, 1.99 (SD, 1.36) log$_{10}$ copies/ml;
      – <50 copies/ml, 89.0%
Antiretroviral therapy regimens

NRTI

3rd agent

nNRTI

PI

Raltegravir

Others

TDF/3TC

AZT/3TC

ABC/3TC

Others

Efavirenz

Nevirapine

Rilpivirine

Atazanavir

ATV/r

KAL

DRV/r

NRTI

3rd agent
Prevalence of comorbidities

Prevalence, %

- DM
- Hypertension hyperlipidemia
- CAD
- HBsAg (+)
- Anti-HCV (+)

Prevalence, %
Risk factors for incident diabetes mellitus among HIV-infected patients receiving combination antiretroviral therapy in Taiwan: a case–control study

- From January 1993 to December 2006
  - 1534 HIV-infected adults seeking HIV care at NTUH
  - The mean duration of follow-up was 4.6 years
  - The cumulative follow-up time was 3829 PYFU
  - 50 patients (6.1%) developed incident DM
    - an incidence rate of 13.1 cases per 1000 PYFU [95% confidence interval (95% CI) 9.8–17.1 cases]

- 100 matched controls
  - sex, age at diagnosis of HIV infection, year of diagnosis of HIV infection, mode of HIV transmission and baseline CD4 lymphocyte count

Associated factors with incident DM in multivariable analysis

- Risk factors for incident DM
  - a family history of DM
    - OR 2.656; 95% CI 1.209–5.834
  - exposure to zidovudine
    - OR 3.168; 95% CI 1.159–8.661
  - current use of protease inhibitors
    - OR 2.528; 95% CI 1.186–5.389

Incidence of DM among ARV-naïve HIV-positive patients, 2003-2013

HIV infection, N=1667 (2004/1/1-2013/12/31)

- Death, n=97
  - <6M, n=62

- Prevalent DM n=25

- Loss to follow up, n=361
  - <6M, n=148

N=1432, including 28 (2%) with incident DM

96.4% male
90% on cART
Mean age, 32.9 (SD, 9.5)
Anti-HCV (+), 6.8%
Follow-up, 5.3 years
Cumulative cART duration, 54.7 m
DM incidence and duration of cumulative exposure to cART

Graph showing the incidence% (PYFU) of diabetes mellitus (DM) over different durations of antiretroviral therapy (ART). The graph includes the following points:

- **<12 mo**: 0%
- **12-24 mo**: 2.7%
- **24-36 mo**: 4%
- **≥36 mo**: 3.9%
DM and cumulative exposure to zidovudine

Incidence

<12 mo 12-24 mo 24-36 mo ≥36 mo

AZT duration

2.6‰ 2‰ 4.3‰ 4.8‰
DM and cumulative exposure to stavudine/didanosine

- Incidence:
  - <12 mo: 8.4%
  - 12-24 mo: 7.7%
  - 24-36 mo: 10%
  - ≥36 mo: 8.3%

- d4T/ddI duration:
  - <12 mo
  - 12-24 mo
  - 24-36 mo
  - ≥36 mo
DM and cumulative exposure to tenofovir

- Incidence:
  - <12 mo: 0.9%
  - 12-24 mo: 1.2%
  - 24-36 mo: 1.3%
  - ≥36 mo: 1.2%

- TDF duration:
  - <12 mo
  - 12-24 mo
  - 24-36 mo
  - ≥36 mo
Prevalence of metabolic syndrome among HIV-positive Taiwanese: Objectives

- To determine the prevalence of metabolic syndrome among HIV-infected patients who received HAART.

- To evaluate the association between different drug class and its exposure duration and metabolic syndrome.
Materials & Methods

• Cross-section study design
  – 2008.5.20-2009.5.31 questionnaire survey
    • age, gender, smoking, family history of DM, CVD, hypertension, height, weight, waist circumference, systolic blood pressure, diastolic blood pressure

• Inclusion criteria
  – HIV-infected adults seeking HIV care at NTUH
  – Outpatient clinics
  – Age>18 years

• Exclusion criteria
  – Pregnant women
  – Medical chart not available
Definition of Metabolic syndrome


– 3 of the 5 measures

1. Waist circumference:
   ≥90 cm in men; ≥80 cm in women

2. Triglycerides:
   ≥150 mg/dl or receipt of treatment

3. HDL-C:
   <40 mg/dl in men; <50 mg/dl in women

4. Blood pressure:
   SBP ≥130 mmHg; DBP ≥85 mmHg
   or receipt of anti-hypertensives

5. Fasting glucose level:
   ≥100 mg/dl; or receipt of treatment
Metabolic syndrome in HIV-infected Taiwanese

- A cross-sectional survey in 877 HIV-infected patients, aged 36-44 years
- Metabolic syndrome was diagnosed in 210 patients (26.2%)
- 24.3% with a family history of DM
- 26.2% overweight
- 20.4% with glucose >100 mg/dl
- 3.5% were receiving OHA or insulin replacement

Duration of exposure to antiretroviral therapy and prevalence of hyperlipidemia

![Graph showing duration of exposure to antiretroviral therapy and prevalence of hyperlipidemia. The x-axis represents different time intervals of exposure (0 month, <12 month, 12-35 month, 36-71 month, ≥72 month), and the y-axis represents the percentage of cases with hyperlipidemia. The graph includes data for different drug classes: HAART, PI, NRTI, NNRTI, and with different lipids levels (TG ≥250, T-CHO ≥240).]
Main findings

- Factors associated with metabolic syndrome in multivariate analysis
  - protease inhibitors [PI]: odds ratio (OR), 1.63 (95% CI, 1.10-2.43)
  - exposure to PI for ≥3 years: OR, 1.96 (95% CI, 1.13-3.42),
  - exposure to HAART for ≥6 years: 1.78 (95% CI, 1.03-3.07)
  - exposure to NRTIs for ≥6 years and 1.91 (95% CI, 1.11-3.30)
NRTI duration and metabolic syndrome (adjusted for age, gender, BMI, smoking, family history, and use of antidiabetics lipid-lowering agents and antihypertensives)

<table>
<thead>
<tr>
<th>NRTI duration</th>
<th>95% CI LOW</th>
<th>OR</th>
<th>UP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;12 month</td>
<td>0.56</td>
<td>1.14</td>
<td>2.32</td>
</tr>
<tr>
<td>12-35 month</td>
<td>0.78</td>
<td>1.50</td>
<td>2.86</td>
</tr>
<tr>
<td>36-71 month</td>
<td>1.06</td>
<td>2.05</td>
<td>3.97</td>
</tr>
<tr>
<td>≥ 72 month</td>
<td>1.43</td>
<td>2.78</td>
<td>5.38</td>
</tr>
</tbody>
</table>
nNRTI duration and metabolic syndrome (adjusted for age, gender, BMI, smoking, family history, and use of antidiabetics lipid-lowering agents and antihypertensives)

### NNRTI duration

<table>
<thead>
<tr>
<th>Duration</th>
<th>95% CI LOW</th>
<th>OR</th>
<th>UP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;12 month</td>
<td>0.56</td>
<td>1.10</td>
<td>2.15</td>
</tr>
<tr>
<td>12-35 month</td>
<td>0.87</td>
<td>1.62</td>
<td>3.05</td>
</tr>
<tr>
<td>36-71 month</td>
<td>0.70</td>
<td>1.30</td>
<td>2.43</td>
</tr>
<tr>
<td>≥ 72 month</td>
<td>1.08</td>
<td>2.01</td>
<td>3.76</td>
</tr>
</tbody>
</table>
PI duration and metabolic syndrome (adjusted for age, gender, BMI, smoking, family history, and use of antidiabetics lipid-lowering agents and antihypertensives)

<table>
<thead>
<tr>
<th>PI duration</th>
<th>95% CI LOW</th>
<th>OR</th>
<th>UP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;12 month</td>
<td>0.83</td>
<td>1.42</td>
<td>2.43</td>
</tr>
<tr>
<td>12-35 month</td>
<td>0.74</td>
<td>1.24</td>
<td>2.10</td>
</tr>
<tr>
<td>36-71 month</td>
<td>0.71</td>
<td>1.35</td>
<td>2.60</td>
</tr>
<tr>
<td>≥ 72 month</td>
<td>1.03</td>
<td>2.30</td>
<td>5.15</td>
</tr>
</tbody>
</table>
Summary

• Main findings
  - The prevalence of metabolic syndrome in HIV-positive patients was 26.2%
  - Exposure to PI $\geq$ 3 years; to HAART $\geq$ 6 years; and to NRTI $\geq$ 6 years were statistically significantly associated with metabolic syndrome

• Clinical implication
  - Long-term metabolic complications of HAART
Odds of osteoporosis (T-score ≤ −2.5) in patients with HIV compared with HIV-uninfected controls

- Both the ASSERT and ACTG 5224s studies showed more rapid BMD loss with TDF/FTC vs. ABC/3TC at both the hip and spine\(^1\),\(^2\)

- The ACTG 5224s study also showed more rapid BMD loss at the spine (but not at the hip) with ATV/r vs EFV\(^2\)

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ameil (2004)</td>
<td>5.03 (91.47, 17.27)</td>
</tr>
<tr>
<td>Brown (2004)</td>
<td>4.26 (0.22, 82.64)</td>
</tr>
<tr>
<td>Bruera (2003)</td>
<td>4.51 (0.26, 79.27)</td>
</tr>
<tr>
<td>Dolan (2004)</td>
<td>2.11 (0.54, 8.28)</td>
</tr>
<tr>
<td>Huang (2002)</td>
<td>3.52 (0.15, 81.92)</td>
</tr>
<tr>
<td>Knobel (2001)</td>
<td>5.13 (1.80, 14.60)</td>
</tr>
<tr>
<td>Loiseau-Peres (2002)</td>
<td>4.28 (0.46, 39.81)</td>
</tr>
<tr>
<td>Madeddu (2004)</td>
<td>29.84 (1.80, 494.92)</td>
</tr>
<tr>
<td>Tebas (2000)</td>
<td>3.40 (0.19, 61.67)</td>
</tr>
<tr>
<td>Teichman (2003)</td>
<td>17.41 (0.97, 313.73)</td>
</tr>
<tr>
<td>Yin (2005)</td>
<td>2.37 (1.09, 5.16)</td>
</tr>
<tr>
<td>Overall (95% CI)</td>
<td>3.68 (2.31, 5.84)</td>
</tr>
</tbody>
</table>

Figure redrawn from Brown TT and Qaqish RB. AIDS 2006;20:2165–74.
1. Stellbrink HJ, et al., 12th EACS 2009, Cologne, Germany. Abstract PS10/1;
Methods

- March 2002 – February 2006
- Prospective observational cohort
- HIV-1 infected male patients with at least one dual-energy X-ray absorptiometry (DXA) scan of the lumbar spine
- A standardized case report form
  - demographic data
  - smoking habit; physical exercise
  - body mass index (BMI)
  - comorbid conditions (including kidney disease or coinfection with hepatitis); concomitant medication (including hormone treatments, bisphosphonates, and calcium)
  - time with HIV-1 infection
  - current and previous antiretroviral regimens
  - plasma viral load; CD4 T-cell count
Definitions

• DXA scan: normal values, osteopenia or osteoporosis
• Low BMD: osteopenia or osteoporosis
• Progression of low BMD was defined as a normal lumbar T score in the first scan that progressed to osteopenia or osteoporosis; or osteopenia that progressed to osteoporosis

WHO classification

**Osteopenia**: a T score of between -1 and -2.5 SD
**Osteoporosis**: a T score <-2.5 SD

T score L1–L4 quantitatively evaluate trabecular bone tissue
Methods

• A first DXA measurements analysis determine the prevalence of bone demineralization and to define factors related to low BMD

• A longitudinal analysis evaluate the rate of loss of BMD and related factors

• Statistical analysis
  – DXA scan results and clinical and demographic characteristics
  – Cross-sectional study, ordinal logistic regression models were applied to correlate the effect of the independent variables
  – Longitudinal analysis
  – SAS 9.2
Results

349 HIV-infected participants

59 were excluded
- 32 females
- 23 unknown HAART history
- 4 hemophilia

290 participants with 660 DXA measurements

197 participants at least two DXA scan results

## Patient characteristics: 1\textsuperscript{st} DXA

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>n = 290</td>
</tr>
<tr>
<td>Age, median (IQR)</td>
<td>37 (31-43)</td>
</tr>
<tr>
<td>&gt;65 years old (male), n (%)</td>
<td>4 (1.4)</td>
</tr>
<tr>
<td>Time since HIV diagnosis (years)</td>
<td>1.35 (0.38-3.39)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>131 (45%)</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>21.55 (20.03-23.18)</td>
</tr>
<tr>
<td>BMI from 18.6 to 25 kg/m(^2), n (%)</td>
<td>233 (80)</td>
</tr>
<tr>
<td>Hepatitis B/C co-infection, n (%)</td>
<td>77 (27)</td>
</tr>
<tr>
<td>Current CD4 , absolute value (cells/ul)</td>
<td>292 (169-455)</td>
</tr>
<tr>
<td>Suppressed viral load, n (%)</td>
<td>212 (74)</td>
</tr>
<tr>
<td>Naive, n (%)</td>
<td>12 (4)</td>
</tr>
<tr>
<td>Time on ART (years)</td>
<td>1.51 (0.42-3.61)</td>
</tr>
<tr>
<td>Use of protease inhibitors, n (%)</td>
<td>161 (56)</td>
</tr>
</tbody>
</table>
# Prevalence of Low Bone Mineral Density

- **290 patients were enrolled**

<table>
<thead>
<tr>
<th>Category</th>
<th>Overall N=290</th>
<th>First DXA (n=197)</th>
<th>Most recent DXA (n=197)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1–L4 T score median (IQR)</td>
<td>-0.7(-1.3 to 0.1)</td>
<td>-0.8 (-1.3 to 0.1)</td>
<td>-0.8 (-1.4 to 0.3)</td>
</tr>
<tr>
<td>Osteopenia, n (%)</td>
<td>108 (37%)</td>
<td>74 (38%)</td>
<td>76 (39%)</td>
</tr>
<tr>
<td>Osteoporosis, n (%)</td>
<td>9 (3%)</td>
<td>9 (5%)</td>
<td>3 (2%)</td>
</tr>
</tbody>
</table>

- 9 (3%) osteoporosis
- 108 (37%) osteopenia
- 173 (60%) normal
A Low BMI Was Associated with Low BMD

290 patients were enrolled

117 (40%) with low BMD

173 (60%) without low BMD

<table>
<thead>
<tr>
<th>Odds Ratio</th>
<th>95% C.I.</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt;18.6</td>
<td>3.84</td>
<td>1.36-10.86</td>
</tr>
</tbody>
</table>

Age (per 10 years increase)

Smoking

Hepatitis B/C co-infection

Calcium supplement

Suppressed viral load <400 copies/mL

PI exposure

Current CD4 cells counts

Time on ART
Results

349 HIV-infected male patients

59 were excluded
- 32 females
- 23 unknown HAART history
- 4 hemophilia

197 patients at least two DXA scan results

188 patients at risk for progression of low BMD
  114, normal
  74, osteopenia
Progression of BMD Loss

188 patients at risk for progression of low BMD

16 (8.5%) progression of low BMD

172 (91.5%) stable

Age (per 10-year increase)  Smoking
Hepatitis B/C co-infection  BMI
Suppressed viral load <400 copies/mL  PI exposure
Current CD4 cells counts  Time on ART
Summary

• A high proportion (40%) of HIV-infected Taiwanese males showed presence of reduced BMD

• Low BMI was a significant factor related to reduced BMD (odds ratio: 3.84, 95% CI 1.36-10.86)

• 8.6% of patients with follow-up showed progression of reduced BMD
Risk of hip fracture by FRAX (N=2311)

- 18-29 y: N=394
- 30-39 y: N=879
- 40-49 y: N=647
- 50-59 y: N=270
- >=60 y: N=121
Risk of major fracture by FRAX (N=2311)
Ongoing work

- BMD assessment and determinations of Vit D for patients aged 45 years or older
  - Follow-up of Vit D once annually
  - BMD assessment every 2 years
  - Provision of information/education/counseling on bone health
Acknowledgements

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  – Liu WC, Wu PY, Zhang JY, Yang SP, Chang HY, Luo YZ, Chang SY
  – Shih TF (Dept Radiology)

• Far Eastern Memorial Hospital
  – Tsai MS; Yang CJ

• Taiwan CDC
  – Lo YC