Online supplement

Higher risk of future events, mortality, and greater healthcare use among patients with increasingly recurrent atherosclerotic cardiovascular disease events in Taiwan: a retrospective cohort study

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Supplement 1 (Figure). Definition of subsequent events

Patients with an index event (population A), were further defined into subsets if they experienced a first recurrent event (population B) and a second recurrent event (population C). Post-event mortality was calculated and compared between each of these populations.

(Size of the circles is not proportional to the number of actual data)
Supplement 2 (Figure). Selection flow of study population

(a) Patients with new-onset CHD

Patients hospitalized with diagnosis of **CHD** during 2012–2014
N=111,399

Exclude:
1. Patients hospitalized with any diagnosis of ASCVD during 2-year baseline period before index date (n=13,033)
2. Patients aged under 20 years (n=60)
3. Patients with CBVD or PAD event in index hospitalization (n=985)

Patients aged 20 years and older with newly diagnosed CHD during 2012–2014
N=97,321

(b) Patients with new-onset CBVD

Patients hospitalized with diagnosis of **CBVD** during 2012–2014
N=133,538

Exclude:
1. Patients hospitalized with any diagnosis of ASCVD during 2-year baseline period before index date (n=11,356)
2. Patients aged under 20 years (n=200)
3. Patients with CHD or PAD event in index hospitalization (n=1,068)

Patients aged 20 years and older with newly diagnosed CBVD during 2012–2014
N=120,914
(c) Patients with new-onset PAD

Patients hospitalized with diagnosis of **PAD** during 2012–2014
N=21,572

Exclude:
1. Patients hospitalized with any diagnosis of ASCVD during 2-year baseline period before index date (n=6,411)
2. Patients aged under 20 years (n=14)
3. Patients had CBVD or CHD event in index hospitalization (n=353)

Patients aged 20 years and older with newly diagnosed PAD during 2012-2014
N=14,794

CBVD, cerebrovascular disease; CHD, coronary heart disease; PAD, peripheral artery disease
Supplement 3 (Figure). Recurrent event types by index events type

Patients with index CHD
N = 97,321

1st recurrent ASCVD
N = 21,902

2nd recurrent ASCVD
N = 5,601

3rd recurrent ASCVD
N = 1,731

Patients with index CBVD
N = 120,914

1st recurrent ASCVD
N = 25,337

2nd recurrent ASCVD
N = 6,644

3rd recurrent ASCVD
N = 2,153

Patients with index PAD
N = 14,794

1st recurrent ASCVD
N = 5,951

2nd recurrent ASCVD
N = 2,463

3rd recurrent ASCVD
N = 1,073

ASCVD: atherosclerotic cardiovascular disease; CBVD: cerebrovascular disease; CHD: coronary heart disease; PAD: peripheral artery disease
Supplement 4 (Table). Probability of survival estimated by Kaplan–Meier method

<table>
<thead>
<tr>
<th>Condition</th>
<th>Patients, n</th>
<th>Deaths, n</th>
<th>(%)</th>
<th>Probability of survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6 mo</td>
</tr>
<tr>
<td><strong>Coronary heart disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Index event</td>
<td>97,321</td>
<td>21,773</td>
<td>(22.4)</td>
<td>0.889</td>
</tr>
<tr>
<td>First recurrent event</td>
<td>21,902</td>
<td>4,769</td>
<td>(21.8)</td>
<td>0.887</td>
</tr>
<tr>
<td>Second recurrent event</td>
<td>5,601</td>
<td>1,376</td>
<td>(24.6)</td>
<td>0.856</td>
</tr>
<tr>
<td><strong>Cerebrovascular disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Index event</td>
<td>120,914</td>
<td>32,125</td>
<td>(26.6)</td>
<td>0.899</td>
</tr>
<tr>
<td>First recurrent event</td>
<td>25,337</td>
<td>6,540</td>
<td>(25.8)</td>
<td>0.881</td>
</tr>
<tr>
<td>Second recurrent event</td>
<td>6,644</td>
<td>1,528</td>
<td>(23.0)</td>
<td>0.884</td>
</tr>
<tr>
<td><strong>Peripheral artery disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Index event</td>
<td>14,794</td>
<td>6,217</td>
<td>(42.0)</td>
<td>0.842</td>
</tr>
<tr>
<td>First recurrent event</td>
<td>5,951</td>
<td>2,412</td>
<td>(40.5)</td>
<td>0.821</td>
</tr>
<tr>
<td>Second recurrent event</td>
<td>2,463</td>
<td>924</td>
<td>(37.5)</td>
<td>0.817</td>
</tr>
</tbody>
</table>

mo, months.
Supplement 5 (Table). Cumulative incidence rate of recurrent events considering competing risk estimated by Fine and Gray method

<table>
<thead>
<tr>
<th>Condition</th>
<th>Event</th>
<th>Patients, n</th>
<th>Events, n</th>
<th>(%)</th>
<th>Event rate 6 mo</th>
<th>12 mo</th>
<th>18 mo</th>
<th>24 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coronary heart disease</strong></td>
<td>Index event</td>
<td>97,321</td>
<td>21,902</td>
<td>(22.5)</td>
<td>0.104</td>
<td>0.147</td>
<td>0.175</td>
<td>0.194</td>
</tr>
<tr>
<td></td>
<td>First recurrent event</td>
<td>21,902</td>
<td>5,601</td>
<td>(25.6)</td>
<td>0.134</td>
<td>0.196</td>
<td>0.237</td>
<td>0.263</td>
</tr>
<tr>
<td></td>
<td>Second recurrent event</td>
<td>5,601</td>
<td>1,731</td>
<td>(30.9)</td>
<td>0.196</td>
<td>0.273</td>
<td>0.327</td>
<td>0.360</td>
</tr>
<tr>
<td><strong>Cerebrovascular disease</strong></td>
<td>Index event</td>
<td>120,914</td>
<td>25,337</td>
<td>(20.9)</td>
<td>0.110</td>
<td>0.140</td>
<td>0.162</td>
<td>0.180</td>
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<tr>
<td></td>
<td>First recurrent event</td>
<td>25,337</td>
<td>6,644</td>
<td>(26.2)</td>
<td>0.169</td>
<td>0.216</td>
<td>0.245</td>
<td>0.268</td>
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<tr>
<td></td>
<td>Second recurrent event</td>
<td>6,644</td>
<td>2,153</td>
<td>(32.4)</td>
<td>0.242</td>
<td>0.298</td>
<td>0.333</td>
<td>0.351</td>
</tr>
<tr>
<td><strong>Peripheral artery disease</strong></td>
<td>Index event</td>
<td>14,794</td>
<td>5,951</td>
<td>(40.2)</td>
<td>0.241</td>
<td>0.301</td>
<td>0.338</td>
<td>0.367</td>
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<tr>
<td></td>
<td>First recurrent event</td>
<td>5,951</td>
<td>2,463</td>
<td>(41.4)</td>
<td>0.259</td>
<td>0.341</td>
<td>0.383</td>
<td>0.413</td>
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<tr>
<td></td>
<td>Second recurrent event</td>
<td>2,463</td>
<td>1,073</td>
<td>(43.6)</td>
<td>0.281</td>
<td>0.376</td>
<td>0.428</td>
<td>0.470</td>
</tr>
</tbody>
</table>

mo, months.
Supplement 6 (Figure). Percentage of patients having cardiovascular-related healthcare use following each event.

(a) Coronary heart disease

(b) Cerebrovascular disease

(c) Peripheral artery disease

0–6 months

CV OPD visits  CV ER visits  CV Admission

82.0% 84.3% 80.7%
16.7% 20.3% 25.2%
25.8% 28.5% 34.7%

Index event  1st recurrent event  2nd recurrent event

0–12 months

CV OPD visits  CV ER visits  CV Admission

80.9% 82.6% 78.7%
12.7% 15.1% 19.3%
39.4% 20.4% 26.3%

Index event  1st recurrent event  2nd recurrent event

0–18 months

CV OPD visits  CV ER visits  CV Admission

83.2% 85.2% 81.6%
19.6% 23.7% 28.4%
30.0% 33.3% 39.3%

Index event  1st recurrent event  2nd recurrent event

CV, cardiovascular disease; ER, emergency room; OPD, outpatient department.
Supplement 7 (Figure). Percentage of patients prescribed with statin following each event

CBVD: cerebrovascular disease; CHD: coronary heart disease; PAD: peripheral artery disease.