# **Supplementary Material**

**Orthostatic Hypotension: An Important Risk Factor for Clinical Progression to Mild Cognitive Impairment or Dementia. The Amsterdam Dementia Cohort**

**Supplementary Table 1.** Baseline characteristics in older adults included (n=476) and not included (n=1,406) in the longitudinal analyses.

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|  | **Subjects included in longitudinal analyses (n=476)** | **Subjects not included in longitudinal analyses (n=365)** | **p** |
| **Demographics** |  |  |  |
| Age, y (mean, SD) | 63.3 (7.4) | 59.8 (9.2) | 0.00 |
| Gender (% female) | 36.3 | 37.8 | 0.66 |
| **CV risk factors** |  |  |  |
| BMI (mean, SD) | 26.4 (4.2) | 27.1 (4.4) | 0.03 |
| Current smoker (%) | 14.9 | 19.8 | 0.18 |
| Hypertension (%) | 29.0 | 26.0 | 0.34 |
| Diabetes (%) | 12.0 | 11.8 | 0.93 |
| Hypercholesterolemia (%) | 11.1 | 8.5 | 0.21 |
| SBP (mean, SD) | 147 (19) | 145 (20) | 0.09 |
| DBP (mean, SD) | 85 (10) | 84 (10) | 0.10 |
| **Cardiovascular disease** |  |  |  |
| Stroke, TIA | 8.4 | 7.1 | 0.49 |
| Coronary artery disease | 8.0 | 6.3 | 0.35 |
| Medication |  |  |  |
| Total number of drugs (mean, SD) | 2.4 (2.6) | 2.4 (2.6) | 0.90 |
| **CVRM drugs** |  |  |  |
| Antihypertensive drugs (%) | 35.3 | 32.9 | 0.43 |
| Lipid lowering drugs (%) | 29.6 | 22.2 | 0.02 |
| Antidiabetic drugs (%) | 10.3 | 9.9 | 0.84 |
| **OH-inducing drugs** |  |  |  |
| Antipsychotics (%) | 2.9 | 0.8 | 0.03 |
| Antidepressant drugs (%) | 10.1 | 10.1 | 0.98 |
| Alpha-blockers (%) | 4.2 | 4.1 | 0.95 |
| Long-acting nitrates (%) | 1.1 | 0.8 | 0.74 |

CV, cardiovascular; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TIA, transient ischemic accident; CVRM, cardiovascular risk management; OH, orthostatic hypotension.

**Supplementary Table 2.** Number (%) of subjects with SCD or patients with MCI converting to MCI and/or dementia.

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| --- | --- | --- | --- | --- | --- |
|  | **MCI** | **AD** | **FTD** | **VaD** | **DLB** |
| **Subjects with SCD** | 13 (7.3%) | 8 (3.8%) | 1 (0.6%) | 1 (0.6%) | 0 |
| **Patients with MCI** | - | 44 (21.2%) | 7 (3.4%) | 2 (1%) | 1 (0.3%) |

SCD, subjective cognitive decline; MCI, mild cognitive impairment; AD, Alzheimer’s disease; VaD, vascular dementia; FTD, frontotemporal dementia; DLB= Lewy body dementia.

**Supplementary Table 3a.** Odds (95% CI) of having orthostatic hypotension (OH) in subjects with MCI, and patients with dementia compared to subjects with SCD. Stratified according to diagnosis of hypertension and/ or use of OH-inducing drugs.

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| --- | --- |
|  | **Model 1a** |
|  | Patients **with** hypertension and/or taking OH-inducing drugs (n=791) | Patients **without** hypertension and not taking OH-inducing drugs (n=1,090) |
| **Subjects with SCD**  | 1.0 (reference) | 1.0 (reference) |
| **MCI**  | 1.5 (0.9-2.5) | 1.3 (0.9-2.1) |
| **AD**  | 1.7 (1.1-2.6) | 1.7 (1.2-2.5) |
| **FTD**  | 1.6 (0.9-3.1) | 1.7 (1.0-3.1) |
| **VaD**  | 2.1 (1.0-4.7) | 3.1 (1.1-8.7) |
| **DLB** | 5.2 (2.4-11.3) | 5.1 (2.6-9.7) |

SCD, subjective cognitive decline; MCI, mild cognitive impairment; AD, Alzheimer’s disease; VaD, vascular dementia; FTD, frontotemporal dementia; DLB, Lewy body dementia.

a Adjusted for age, sex.

**Supplementary Table 3b.** Odds (95% CI) of having early or delayed orthostatic hypotension (OH) compared to subjects without OH in subjects with MCI, and patients with dementia. Stratified according to diagnosis of hypertension and/ or use of OH-inducing drugs.

|  |  |  |
| --- | --- | --- |
|  | Patients **with** hypertension and/or taking OH-inducing drugs (n=791) | Patients **without** hypertension and not taking OH-inducing drugs (n=1,090) |
|  | Early OH | Delayed, prolonged OH | Early OH | Delayed, prolonged OH |
| **Subjects with SCD**  | 1.0 (reference) | 1.0 (reference) | 1.0 (reference) | 1.0 (reference) |
| **MCI**  | 1.0 (0.2-5.2) | 1.7 (0.9-3.0) | 1.0 (0.2-5.2) | 1.4 (0.8-2.4) |
| **AD**  | 0.8 (.02-3.8) | 1.7 (1.0-2.9) | 0.8 (0.2-3.8) | 1.9 (1.2-3.0) |
| **FTD**  | 0.7 (0.2-2.5) | 2.2 (1.1-4.4) | 0.7 (0.2-2.5) | 2.2 (1.2-4.2) |
| **VaD**  | 0.8 (0.2-3.8) | 2.9 (1.2-6.9) | 1.5 (0.8-2.9) | 4.1 (1.4-12.5) |
| **DLB** | 1.0 (0.2-5.3) | 7.8 (3.4-17.7) | 1.3 (0.6-2.8) | 7.9 (4.0-15.8) |

SCD, subjective cognitive decline; MCI, mild cognitive impairment; AD, Alzheimer’s disease; VaD, vascular dementia; FTD, frontotemporal dementia; DLB, Lewy body dementia.

a Adjusted for age, sex.

**Supplementary Table 4a.** Risk (hazard ratio, 95% confidence interval) of clinical progression to mild cognitive impairment or dementia in patients with orthostatic hypotension (OH) at baseline compared to patients without OH at baseline. Stratified according to diagnosis of hypertension and/ or use of OH-inducing drugs.

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| --- | --- | --- |
|  | **Model 1a** |  |
|  | Patients **with** hypertension and/or taking OH-inducing drugs (n=195) | Patients **without** hypertension and not taking OH-inducing drugs (n=281) |
| **Subjects without OH** | 1.0 (reference) | 1.0 (reference) |
| **OH\*** | 2.0 (1.0-3.9) | 1.1 (0.6-2.0) |

\*OH (≥20 mmHg drop in systolic BP and/or ≥10 mmHg drop in diastolic BP) at 1 and/or 3 minutes after standing.

a Adjusted for age, sex.

**Supplementary Table 4b.** Risk (hazard ratio, 95% confidence interval) of clinical progression to mild cognitive impairment or dementia in patients with orthostatic hypotension (OH) at baseline compared to subjects without OH at baseline. Stratified according to diagnosis of hypertension and/ or use of OH-inducing drugs.

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| --- | --- | --- |
|  | **Model 1a** |  |
|  | Patients **with** hypertension and/or taking OH-inducing drugs (n=195) | Patients **without** hypertension and not taking OH-inducing drugs (n=281) |
| **Subjects without OH** | 1.0 (reference) | 1.0 (reference) |
| **Early OH\*** | 2.0 (0.6-7.0) | 0.4 (0.1-1.7) |
| **Delayed, prolonged OH\*\*** | 2.0 (1.0-4.0) | 1.5 (0.8-2.8) |

\*OH (≥20 mmHg drop in systolic BP and/or ≥10 mmHg drop in diastolic BP) at 1 minute after standing, \*\*OH at (1 and) 3 minutes after standing.

a Adjusted for age, sex.