Patients with AF and dementia are undertreated for their AF and cardiovascular comorbidities: results from the GARFIELD-AF registry

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Funding Acknowledgements: Type of funding sources: Private grant(s) and/or Sponsorship. Main funding source(s): Thrombosis Research Institute

Background: Oral anticoagulation (OAC) is key in preventing stroke in patients with atrial fibrillation (AF). However, patients with AF and dementia pose practical therapeutic challenges, such as compliance and haemorrhagic complications, resulting in possible underuse of cardiovascular (CV) treatment.

Purpose: The aim of this study is two-fold: a) to determine whether AF patients with dementia are undertreated for stroke prevention with OAC and for their CV comorbidities and b) to assess the risks and benefits of OAC in AF patients with dementia.

Methods: Analyses were conducted in newly diagnosed AF patients enrolled in GARFIELD-AF, the largest multinational prospective AF registry. Medical history of dementia was recorded at enrolment. Guideline-directed medical therapy (GDMT), defined according to ESC guidelines, was explored for coronary artery disease (CAD), diabetes, heart failure (HF), hypertension, and peripheral vascular disease (PVD). Propensity score weighting was applied to obtain estimates of OAC effect on all-cause mortality and stroke within two-year follow-up. Major bleeding occurrence is simply reported due to the low number of events.

Results: The study comprised 764 (1.5%) AF patients with dementia and 50,966 (98.5%) without dementia. Patients with dementia were more often female (58% vs 44%), older (median age 82 vs 71) and had higher prevalence of comorbidities, resulting in higher CHA2DS2-VASc (excl. sex; median 5.0 vs 3.0) and HAS-BLED score (median 2.0 vs 1.0) compared to patients without dementia. The proportion anticoagulated was lower among those with dementia (60% vs 70%), with fewer patients receiving VKA (27% vs 42%) (Fig. 1). Despite the increase in NOAC use among patients with dementia (17% in 2010-2013 vs 48% in 2015-2016), 35% remained non-anticoagulated in 2015-2016. Appropriate GDMT was lower among patients with dementia for the five considered comorbidities combined (35% vs 45%), with substantial differences observed for HF (35% vs 50%), CAD (27% vs 39%) and PVD (36% vs 48%) compared to patients without dementia.

In patients with dementia, OAC usage was associated with lower all-cause mortality (HR 0.69; 95% CI 0.48-1.00). In contrast to patients without dementia, no evidence of a stroke risk reduction with OAC was observed among patients with dementia (HR 1.10; 95% CI 0.50-2.43) (Fig. 2). This finding might be explained by the higher proportion of patients with dementia receiving a reduced NOAC dose (73% vs 39% of NOAC receivers) and their lower VKA quality control (37% vs 46%, defined as time in therapeutic range >65%). Seven (1.6%) and eight (2.7%) major bleeding events occurred among patients with dementia who were on or not on OAC, respectively.

Conclusions: Despite their high risk of stroke, patients with AF and dementia are often undertreated for their AF and CV comorbidities. Our results support the use of OAC and should help inform treatment decisions in this vulnerable population.
**Figure 1.** Baseline treatment distribution by dementia at baseline in patients with CHA₂DS₂-VASc ≥2 (excl. sex)

<table>
<thead>
<tr>
<th>Treatment Proportion (%)</th>
<th>Without Dementia (N = 39543)</th>
<th>With Dementia (N = 729)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>9.6</td>
<td>13.8</td>
</tr>
<tr>
<td>AP only</td>
<td>20.3</td>
<td>25.8</td>
</tr>
<tr>
<td>NOAC + AP</td>
<td>5.5</td>
<td>5.9</td>
</tr>
<tr>
<td>NOAC only</td>
<td>22.4</td>
<td>27.6</td>
</tr>
<tr>
<td>VKA + AP</td>
<td>10.8</td>
<td>7.8</td>
</tr>
<tr>
<td>VKA only</td>
<td>31.4</td>
<td>19.1</td>
</tr>
</tbody>
</table>

AP, antiplatelet; NOAC, non-VKA oral anticoagulant; VKA, vitamin K antagonist
Figure 2. Propensity-weighted\textsuperscript{1} hazard ratios comparing OAC vs No OAC (reference) baseline treatment through two years of follow-up by dementia at baseline

\textbf{Without dementia}

- All-cause mortality
- Non-haemorrhagic stroke/SE

\textbf{With dementia}

- All-cause mortality
- Non-haemorrhagic stroke/SE

\begin{tabular}{lcc}
& HR (95\% CI) & \\
Without dementia & & \\
All-cause mortality & 0.78 (0.71-0.85) & \\
Non-haemorrhagic stroke/SE & 0.72 (0.61-0.85) & \\
With dementia & & \\
All-cause mortality & 0.69 (0.48-1.00) & \\
Non-haemorrhagic stroke/SE & 1.10 (0.50-2.43) & \\
\end{tabular}

\textsuperscript{1}Obtained using an overlap-weighted Cox model. Variables included in the weighting scheme are: country and cohort enrolment, sex, age, ethnicity, type of AF, care setting speciality and location, congestive heart failure, vascular disease, carotid occlusive disease, prior stroke/TIA/SE, prior bleeding, VTE, hypertension, hypercholesterolemia, diabetes, cirrhosis, moderate to severe CKD, hyperthyroidism, hypothyroidism, current smoking, heavy alcohol consumption, BMI, heart rate, systolic and diastolic blood pressure at diagnosis, and baseline antiplatelet use. OAC, oral anticoagulation, TIA, transient ischemic attack, SE, systemic embolism, VTE, venous thromboembolism, BMI, body mass index, CKD, chronic kidney disease.