Treatment Patterns of Antihypertensive Medications Among Alzheimer's Disease Patients in United States and France

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AcornAI by Medidata, a Dassault Systèmes Company, Boston, MA

PRESENTED AT:

Virtual ISPOR Europe 2020
16-19 November
BACKGROUND & OBJECTIVES

Background

- Cardiovascular disease (CVD) has been shown to be a risk factor for cognitive decline among patients with Alzheimer’s Disease (AD) [1,2]
- Treatments for CVD, including antihypertensives, may reduce cognitive decline among these patients [3–7]
- Due to differences in payment structures between the United States (US) and France, we expect there to be regional variation in compliance to medication

Objectives

- The objective of this study was to examine treatment patterns of antihypertensive medication use and clinical characteristics among patients with AD in the US and France
DATA SOURCES

US

- Patient data were extracted from HealthVerity™ Marketplace longitudinal ambulatory electronic medical record (EMR) dataset between Jan 1, 2014 and Dec 31, 2018
  - HealthVerity™ has the most complete coverage of United States healthcare, consumer, and purchase data, with access to over 330 million patients and 30 billion transactions [8]. HealthVerity™ Marketplace is a self-service cloud solution allowing users to build patient and provider cohorts from more than 60 unique data sources.

France

- Patient data was extracted from the The Health Improvement Network® (THIN®) France database between July 1, 2016 and June 30, 2019
  - THIN® is an anonymized EMR powered by Cegedim Health Data®-division. THIN® is a large European database, collecting data at the physicians’ level.

All data were converted to the Observational Medical Outcomes Partnership (OMOP) Common Data Model, version 5 [9].

Analyses were conducted in Aginity Workbench for Redshift v4.9.3.2873 and R v1.1.456.
STUDY DESIGN

- Patients with AD (identified by International Classification of Diseases [ICD]-9 code 331.0 or ICD-10 code G30.*) and ≥ 2 years of continuous observation were selected from de-identified electronic medical records in the US between 1/1/2014 and 11/30/2018, and in France between 7/1/2016 to 6/30/2019 (Figure 1).

- The following treatment patterns of antihypertensive medication use, including thiazide-type diuretics angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and calcium channel blockers (CCBs), were assessed:
  - Adherent, assessed over 1-year after the patient’s earliest antihypertensive medication record (index date) using the novel method described in Biederman et al. (2019) [10]
  - Non-adherent, assessed over 1-year after the patient’s earliest antihypertensive medication record (index date)
  - Non-users, defined as having no evidence of antihypertensives use in the first 2 years of observation (index date = observation start date)

Figure 1. Selection Criteria and Patient Attrition

Demographic and clinical characteristics (listed in Table 1) were identified using ICD-9-CM, ICD-10-CM, Anatomical Therapeutic Chemical (ATC), and RxNorm codes for each antihypertensive use category and were assessed during the 1st year post-index date

- Patient characteristics of antihypertensive medication users were compared to non-users using chi-squared (for categorical variables) and Student’s t tests (for continuous variables)
RESULTS

- In the US population, 50.9% of patients had ≥ 1 record for an antihypertensive; among these patients, 30.1% were adherent while 69.9% were non-adherent (Figure 2)
- In the France population, 12.7% of patients had ≥ 1 record for an antihypertensive; among these patients, 71.9% were adherent while 28.1% were non-adherent (Figure 2)

Figure 2. Adherence Distribution, By Country

In the US,

- Adherent patients had a mean age of 76.34 years, a mean Quan’s Charlson Comorbidity Index score (QCI) of 1.83, and were using a mean of 2.34 distinct concomitant medications (Table 1)
- Non-adherent patients had a mean age of 77.08 years, a mean QCI of 1.58, and were using a mean of 1.99 distinct concomitant medications
- Non-users of antihypertensives had a mean age of 76.89 years, a mean QCI of 1.05, and were using a mean of 1.45 distinct concomitant medications
- Across the antihypertensives users and non-users, the top three most common comorbid conditions assessed were depression (adherent: 23.9%; non-adherent: 19.1%; non-users: 19.3%), coronary artery disease (adherent: 18.5%; non-adherent: 15.1%; non-users: 9.6%), and hypothyroidism (adherent: 17.0%; non-adherent: 14.0%; non-users: 14.0%)
- Approximately one-third of patients were male (adherent: 34.5%; non-adherent: 37.1%; non-users: 36.2%)
- Among antihypertensives users, in both adherent and non-adherent patients, ACE inhibitors were the most commonly prescribed antihypertensives, followed by thiazide diuretics, ARBs, and CCBs

In France,

- Adherent patients had a mean age of 76.05 years, a mean QCI of 1.12, and were using a mean of 1.84 distinct concomitant medications (Table 1)
- Non-adherent patients had a mean age of 75.89 years, a mean QCI of 1.03, and were using a mean of 1.54 distinct concomitant medications
- Non-users of antihypertensives had a mean age of 63.76 years, a mean QCI of 0.64, and were using a mean of 0.86 distinct concomitant medications
- Across the antihypertensives users and non-users, the top three most common comorbid conditions assessed were mild cognitive impairment (100% of all patients), depression (adherent: 19.7%; non-adherent: 11.9%; non-users: 10.5%), and hypothyroidism (adherent: 9.7%; non-adherent: 8.9%; non-users: 5.9%)
Approximately 40% of patients were male (adherent: 42.7%; non-adherent: 43.9%; non-users: 35.5%)

Among antihypertensives users, in both adherent and non-adherent patients, ARBs were the most commonly prescribed antihypertensives, followed by ACE inhibitors, CCBs, and thiazide diuretics.

Table 1. Demographic and Clinical Characteristics By Antihypertensive Use and Country

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</thead>
<tbody>
<tr>
<td>Age (mean, SD)</td>
<td>76.34±7.90</td>
<td>77.08±8.04</td>
<td>76.89±8.89</td>
<td>76.05±10.84</td>
<td>75.89±11.33</td>
<td>63.76±22.23</td>
</tr>
<tr>
<td>Male (n, %)</td>
<td>752 (34.5%)</td>
<td>1,878 (37.1%)</td>
<td>2,877 (36.2%)</td>
<td>473 (34.27%)</td>
<td>192 (34.39%)</td>
<td>2,035 (35.5%)</td>
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Clinical Characteristics

- Queen’s Charlson Comorbidity Index score (mean, SD): 1.83±1.92 vs 1.56±1.86 vs 1.05±1.05 vs 1.12±1.07 vs 1.03±1.02 vs 0.64±0.78
- Number of distinct concomitant medications (mean, SD): 2.34±2.19 vs 2.09±1.85 vs 1.58±1.45 vs 1.84±1.33 vs 1.54±1.33 vs 0.86±1.14
- Atrial fibrillation (n, %): 349 (16.0%) vs 546 (18.9%) vs 665 (8.4%) vs 3 (0.3%) vs 0 (0.0%) vs 8 (0.1%)
- Bipolar disorder (n, %): 19 (0.9%) vs 43 (1.6%) vs 93 (3.2%) vs 1 (0.1%) vs 1 (0.2%) vs 22 (0.3%)  
- Coronary artery disease (n, %): 463 (18.5%) vs 764 (18.1%) vs 762 (9.6%) vs 79 (1.7%) vs 307 (6.9%) vs 118 (1.8%)
- Depression (n, %): 522 (23.9%) vs 968 (19.1%) vs 1559 (19.3%) vs 220 (19.7%) vs 52 (11.9%) vs 779 (10.5%)
- Epilepsy (n, %): 106 (4.8%) vs 172 (7.3%) vs 350 (4.4%) vs 12 (1.1%) vs 6 (1.4%) vs 91 (1.2%)
- Glioma (n, %): 45 (2.1%) vs 87 (3.7%) vs 161 (1.9%) vs 7 (0.6%) vs 4 (0.9%) vs 13 (0.2%)
- Hearing loss (n, %): 106 (4.9%) vs 232 (5.0%) vs 340 (4.3%) vs 14 (1.3%) vs 4 (0.9%) vs 51 (0.7%)
- Hypothyroidism (n, %): 17 (0.8%) vs 27 (0.9%) vs 32 (0.4%) vs 6 (0.5%) vs 4 (0.9%) vs 55 (0.7%)
- Hypothyroidism (n, %): 310 (17.0%) vs 707 (14.0%) vs 1113 (14.0%) vs 108 (9.7%) vs 39 (8.8%) vs 435 (5.9%)
- Mild cognitive impairment (n, %): 95 (4.4%) vs 223 (4.4%) vs 317 (4.0%) vs 1,117 (10.0%) vs 437 (10.0%) vs 7,428 (10.0%)
- Osteoporosis (n, %): 154 (7.1%) vs 320 (8.4%) vs 690 (8.7%) vs 23 (2.1%) vs 6 (1.4%) vs 43 (0.6%)
- Parkinson’s disease (n, %): 41 (1.9%) vs 102 (2.0%) vs 205 (2.6%) vs 17 (1.5%) vs 8 (1.8%) vs 112 (1.5%)
- Pneumonia (n, %): 58 (2.6%) vs 101 (2.0%) vs 133 (1.7%) vs 19 (1.7%) vs 4 (0.9%) vs 65 (0.9%)
- Schizophrenia (n, %): 8 (0.4%) vs 24 (0.4%) vs 61 (0.8%) vs 0 (0.0%) vs 0 (0.0%) vs 3 (0.0%)
- Stroke/Transient ischemic attack (n, %): 158 (7.2%) vs 311 (6.1%) vs 262 (3.7%) vs 57 (5.1%) vs 10 (4.3%) vs 110 (1.5%)

Antihypertensives Medication Use

- Thiazide diuretics: 985 (44.3%) vs 1,664 (33.4%) vs 1,101 (6.0%)
- ARBs: 792 (36.4%) vs 1,533 (30.3%) vs 525 (47.0%)
- CCBs: 363 (16.7%) vs 545 (10.8%) vs 187 (16.7%)
- ACE inhibitors: 1,392 (59.3%) vs 2,724 (53.8%) vs 471 (42.2%)

Comparing the US and France,

- Antihypertensives non-users were over 10 years younger in France compared to in the US
- QCI scores and number of distinct concomitant medications were lower across the antihypertensives users and non-users in France compared to in the US
- The prevalence of comorbidities were lower in France in all conditions (except mild cognitive impairment) and across the antihypertensives users and non-users compared to in the US
  - Notably, atrial fibrillation was observed in 8.4% to 16.0% of patients in the US while between 0.1% and 0.3% were observed in France
  - Mild cognitive impairment was observed in 100% of all patients in France, while it was observed in 4.0% to 4.4% of patients in the US
- Choice of antihypertensives prescribed by providers differed between the two countries; thiazide diuretics were the least prescribed in France (9.0% and 6.0%) while being the second most commonly prescribed in the US (44.3% and 33.4%), and ACE inhibitors were the most commonly prescribed in the US (59.3% and 53.8%) while ARBs were the most prescribed in France (47.0% and 43.7%)
LIMITATIONS

- Studies using EMR data sources assume patients filled and took their medications as prescribed. Using reimbursement claims-based data sources may provide more accurate measurement of patient adherence to antihypertensive medications.
- Patients assessed from France were limited to those with an activity within a pre-specified 3-year period, yielding small sample sizes of antihypertensive users from this population and may not be representative of entire France population of antihypertensive users.
- This study is subject to limitations in accuracy and consistency of medical coding as is common for studies using EMR.
CONCLUSIONS & DISCUSSION

- In the US population, patients prescribed antihypertensives were more likely to be non-adherent, while the opposite was true in the France population, possibly driven by differences in medical practice and access to care.

- Drivers of the lower QCI, number of distinct concomitant medications use, and prevalence of comorbid conditions observed in France may include a generally healthier lifestyle and population in France [11], differences in medical coding and diagnosis practices, and the absence of specialized hospitals in the THIN network; these may also explain the large differences observed in the prevalence of atrial fibrillation and mild cognitive impairment between the two countries.

- Differences were observed in the choice of antihypertensive medications prescribed to patients, suggesting clinical guidelines for antihypertensive treatment may differ between the two countries.

- Further research is needed to identify modifiable characteristics associated with non-adherence of antihypertensives in patients with AD in these countries.
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REFERENCES


