**The impact of renal denervation procedure on use of antihypertensive drugs in the real-life setting**

Federico REA 1,2, Gabriella MORABITO 1, Laura SAVARé 1,3,4, Giovanni CORRAO 1,2, Giuseppe MANCIA 5

1 National Centre for Healthcare Research & Pharmacoepidemiology, at the University of Milano-Bicocca Milan, Italy

2 Laboratory of Healthcare Research & Pharmacoepidemiology, Unit of Biostatistics, Epidemiology and Public Health, Department of Statistics and Quantitative Methods, University of Milano-Bicocca, Milan, Italy

3 MOX - Laboratory for Modeling and Scientific Computing, Department of Mathematics, Politecnico di Milano, Milan, Italy

4 CADS - Center for Analysis Decisions and Society, Human Technopole, Milan, Italy

5 University of Milano-Bicocca (Emeritus Professor), Milan, Italy

**SUPPLEMENTARY MATERIAL**

**Supplementary Table S1**. Non-antihypertensive drugs prescribed in the year before the index admission and during the 3 years after the index discharge

|  |  |  |  |
| --- | --- | --- | --- |
| Medications | Before(N=136) | After | p-trend |
| 6 months(N=134) |  1 year(N=132) | 2 years(N=130) | 3 years(N=125) |
| Digitalis glycosides | 1 (0.7%) | 3 (2.2%) | 2 (1.5%) | 3 (2.3%) | 2 (1.6%) | 1.000 |
| Organic nitrates | 21 (15.4%) | 20 (14.9%) | 13 (9.9%) | 18 (13.9%) | 16 (12.8%) | 0.172 |
| Antiarrhythmics | 11 (8.1%) | 12 (10.0%) | 9 (6.8%) | 9 (6.9%) | 10 (8.0%) | 0.509 |
| Lipid-lowering agents | 83 (61.0%) | 90 (67.2%) | 77 (58.3%) | 81 (62.3%) | 76 (60.8%) | 0.060 |
| Antiplatelets | 81 (59.6%) | 93 (69.4%) | 75 (56.8%) | 71 (54.6%) | 67 (53.6%) | <0.001 |
| Anticoagulants agents | 12 (8.8%) | 14 (10.4%) | 13 (9.9%) | 15 (11.5%) | 17 (13.6%) | 0.241 |
| Antidiabetic drugs | 59 (43.6%) | 60 (44.8%) | 55 (41.7%) | 58 (44.6%) | 54 (43.2%) | 0.179 |
| NSAIDs | 7 (5.2%) | 11 (8.2%) | 11 (8.3%) | 12 (9.2%) | 9 (7.2%) | 0.555 |
| Anti-gout drugs | 18 (13.2%) | 19 (14.2%) | 13 (9.9%) | 22 (12.9%) | 25 (20.0%) | 0.114 |
| Drugs for respiratory diseases | 11 (8.1%) | 10 (7.5%) | 13 (9.9%) | 11 (8.5%) | 14 (11.2%) | 0.400 |
| Antidepressants | 11 (8.1%) | 13 (9.7%) | 12(9.1%) | 16(12.3%) | 17 (13.6%) | 0.085 |

**Supplementary Table S2**. Baseline characteristics of patients who underwent renal denervation and of the corresponding controls

|  |  |  |
| --- | --- | --- |
|  | Renal denervation group(N=130) | Controls(N = 130) |
| Age: median [IQR] | 68 [60-75] | 67 [61-75] |
| Men | 88 (67.7%) | 88 (67.7%) |
| Clinical status § |  |  |
| Good | 44 (33.9%) | 44 (33.9%) |
| Intermediate | 35 (26.9%) | 35 (26.9%) |
| Poor | 31 (23.8%) | 31 (23.8%) |
| Antihypertensive drugs |  |  |
| α-blockers | 95 (73.1%) | 95 (73.1%) |
| β-blockers | 106 (81.5%) | 106 (81.5%) |
| Diuretics | 124 (95.4%) | 124 (95.4%) |
| Angiotensin-converting enzyme inhibitors | 78 (60.0%) | 78 (60.0%) |
| Angiotensin II receptor blockers | 93 (71.5%) | 93 (71.5%) |
| Calcium channel blockers | 121 (93.1%) | 121 (93.1%) |
| Renin-inhibitors | 8 (6.2%) | 8 (6.2%) |

IQR: interquartile range

§ The clinical status was assessed by the Multisource Comorbidity Score (MCS) according to the hospital admission and the drugs prescribed in the 3-year period before the index admission. Four categories of clinical status were considered: good (0 ≤ score ≤ 4), intermediate (5 ≤ score ≤ 9), poor (10 ≤ score ≤ 14), and very poor (score ≥ 15).

**Supplementary Table S3**. Number of antihypertensive drug classes prescribed in the year before the index admission and in the 3 years after the index discharge, considering patients who were prescribed at least 3 antihypertensive drugs

|  |  |  |
| --- | --- | --- |
| Antihypertensive drugs | Before(N=163) | After |
| 6 months(N=161) | 1 year(N=159) | 2 years(N=156) | 3 years(N=151) |
| 0 | - | 3 (1.5%) | 5 (3.1%) | 4 (2.6%) | 2 (1.3%) |
| 1 | - | 3 (0.0%) | 4 (2.5%) | 5 (3.2%) | 6 (4.0%) |
| 2 | - | 11 (6.0%) | 13 (8.2%) | 13 (8.3%) | 21 (13.9%) |
| 3 | 27 (16.6%) | 37 (17.2%) | 45 (28.3%) | 40 (25.6%) | 38 (25.2%) |
| 4 | 51 (31.3%) | 45 (30.6%) | 39 (24.5%) | 43 (27.6%) | 47 (31.1%) |
| 5 | 61 (37.4%) | 51 (36.6%) | 45 (28.3%) | 42 (26.9%) | 34 (22.5%) |
| 6 | 24 (14.7%) | 10 (6.1%) | 8 (5.0%) | 9 (5.8%) | 3 (2.0%) |
| 7 | 0 (0.0%) | 1 (0.6%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |

**Supplementary Table S4**. Antihypertensive drug classes prescribed in the year before the index admission and in the 3 years after the index discharge, considering patients who were prescribed at least 3 antihypertensive drugs

|  |  |  |  |
| --- | --- | --- | --- |
| Antihypertensive drugs | Before(N=163) | After | p-trend |
| 6 months(N=161) |  1 year(N=159) | 2 years(N=156) | 3 years(N=151) |
| α-blockers | 109 (66.9%) | 94 (58.4%) | 84 (52.8%) | 83 (53.2%) | 73 (51.7%) | <0.001 |
| β-blockers | 123 (75.5%) | 108 (67.1%) | 103 (64.8%) | 107 (68.6%) | 97 (64.2%) | <0.001 |
| Diuretics | 144 (88.3%) | 133 (82.6%) | 125 (78.6%) | 125 (80.1%) | 118 (78.2%) | <0.001 |
| Loop diuretics | 60 (36.8%) | 58 (36.0%) | 55 (34.6%) | 58 (37.2%) | 55 (36.4%) | 0.588 |
| Furosemide | 55 (33.7%) | 54 (33.5%) | 51 (32.1%) | 53 (34.0%) | 53 (35.1%) | 0.836 |
| Mineral corticoid receptor antagonists | 37 (22.7%) | 34 (21.1%) | 37 (23.3%) | 35 (22.4%) | 25 (16.6%) | 0.089 |
| Spironolactone | 6 (3.7%) | 4 (2.5%) | 6 (3.8%) | 6 (3.9%) | 4 (2.7%) | 0.751 |
| Angiotensin-converting enzyme inhibitors | 96 (58.9%) | 83 (51.6%) | 78 (49.1%) | 71 (45.5%) | 63 (41.7%) | <0.001 |
| Angiotensin II receptor blockers | 107 (65.6%) | 94 (58.4%) | 86 (54.1%) | 86 (55.1%) | 79 (52.3%) | <0.001 |
| Calcium channel blockers | 139 (85.3%) | 114 (70.8%) | 109 (68.6%) | 112 (71.8%) | 104 (68.9%) | <0.001 |
| Renin-inhibitors | 16 (9.8%) | 12 (7.5%) | 9(5.7%) | 3(1.9%) | 4 (2.7%) | <0.001 |

**Supplementary Table S5**. Number of antihypertensive drug classes prescribed to control patients in the year before the index admission and in the 3 years after the index discharge of the corresponding patient who underwent the renal denervation, considering patients who were prescribed at least 3 antihypertensive drugs

|  |  |  |
| --- | --- | --- |
| Antihypertensive drugs | Before(N=155) | After |
| 6 months(N=154) | 1 year(N=153) | 2 years(N=150) | 3 years(N=145) |
| 0 | - | 1 (0.7%) | 2 (1.3%) | 1 (0.7%) | 2 (1.4%) |
| 1 | - | 0 (0.0%) | 0 (0.0%) | 5 (3.3%) | 4 (2.8%) |
| 2 | - | 6 (3.9%) | 7 (4.6%) | 6 (4.0%) | 11 (7.6%) |
| 3 | 25 (16.1%) | 37 (24.0%) | 44 (28.8%) | 40 (26.7%) | 39 (26.9%) |
| 4 | 48 (31.0%) | 38 (24.7%) | 37 (24.2%) | 38 (25.3%) | 37 (25.5%) |
| 5 | 59 (38.1%) | 49 (31.8%) | 48 (31.4%) | 43 (28.7%) | 36 (24.8%) |
| 6 | 23 (14.8%) | 23 (14.9%) | 15 (9.8%) | 17 (11.3%) | 16 (11.0%) |

**Supplementary Table S6**. Number of antihypertensive drug classes prescribed in the year before the index admission among the whole cohort members and those who survived at the 3rd year after renal denervation

|  |  |  |
| --- | --- | --- |
| Antihypertensive drugs | Whole cohort members(N=136) | Patients alive at the 3rd year(N=125) |
| 4 | 51 (37.5%) | 49 (37.5%) |
| 5 | 61 (44.9%) | 56 (44.9%) |
| 6 | 24 (17.7%) | 20 (16.0%) |
| p-value | 0.067 |

**Supplementary Table S7**. Antihypertensive drug classes prescribed in the year before the index admission among the whole cohort members and those who survived at the 3rd year after renal denervation

|  |  |  |  |
| --- | --- | --- | --- |
| Antihypertensive drugs | Whole cohort members(N=136) | Patients alive at the 3rd year(N=125) | p-value |
| α-blockers | 100 (73.5%) | 93 (74.4%) | 0.438 |
| β-blockers | 111 (81.6%) | 101 (80.8%) | 0.407 |
| Diuretics | 128 (94.1%) | 118 (94.4%) | 0.659 |
| Angiotensin-converting enzyme inhibitors | 83 (61.0%) | 72 (57.6%) | 0.006 |
| Angiotensin II receptor blockers | 95 (69.9%) | 87 (69.6%) | 0.829 |
| Calcium channel blockers | 124 (91.2%) | 113 (90.4%) | 0.347 |
| Renin-inhibitors | 12 (8.8%) | 12 (9.6%) | 0.282 |