

| Variables                           | Overall Sample | No MCR         | MCR            | p     | Effect Size*                  | No MCR         | MCR Global Function | p     | Effect Size*                  | No MCR         | MCR Structured SCC | p     | Effect Size*                  | No MCR         | MCR SCC & Global Function | p     | Effect Size*                  |
|-------------------------------------|----------------|----------------|----------------|-------|-------------------------------|----------------|---------------------|-------|-------------------------------|----------------|--------------------|-------|-------------------------------|----------------|---------------------------|-------|-------------------------------|
| Proportions (%)                     |                | 1026 (90.20)   | 112 (9.80)     |       |                               | 1097 (96.40)   | 41 (3.60)           |       |                               | 1099 (96.60)   | 39 (3.40)          |       |                               | 1117 (98.20)   | 21 (1.80)                 |       |                               |
| Age (years)                         | 74.51 ± 6.11   | 74.4 ± 6.09    | 75.57 ± 6.16   | 0.06  | -0.19 (-0.39, 0.01)           | 74.39 ± 6.08   | 77.83 ± 5.97        | <0.01 | <b>-0.57 (-0.88, -0.25)</b>   | 74.39 ± 6.07   | 77.85 ± 6.12       | <0.01 | <b>-0.57 (-0.89, -0.25)</b>   | 74.47 ± 6.12   | 76.57 ± 4.71              | 0.06  | -0.34 (-0.78, 0.09)           |
| Sex                                 |                |                |                |       |                               |                |                     |       |                               |                |                    |       |                               |                |                           |       |                               |
| Male                                | 552 (48.50)    | 504 (49.10)    | 48 (42.90)     | 0.24  | 6.27 (-3.40, 15.93)           | 536 (48.90)    | 16 (39.00)          | 0.21  | 9.84 (-5.39, 25.06)           | 535 (48.70)    | 17 (43.60)         | 0.53  | 5.09 (-10.75, 20.93)          | 543 (48.60)    | 9 (42.90)                 | 0.60  | 5.76 (-15.61, 27.12)          |
| Female                              | 586 (51.50)    | 522 (50.90)    | 64 (57.10)     |       |                               | 561 (51.10)    | 25 (61.00)          |       |                               | 564 (51.30)    | 22 (56.40)         |       |                               | 574 (51.40)    | 12 (57.10)                |       |                               |
| BMI (Kg/m <sup>2</sup> )            | 28.37 ± 4.78   | 28.31 ± 4.73   | 28.95 ± 5.22   | 0.25  | -0.13 (-0.33, 0.06)           | 28.3 ± 4.73    | 30.43 ± 5.66        | 0.01  | -0.45 (-0.76, -0.14)          | 28.32 ± 4.74   | 29.86 ± 5.56       | 0.06  | -0.32 (-0.64, 0.01)           | 28.36 ± 4.75   | 29.15 ± 6.32              | 0.83  | -0.17 (-0.60, 0.27)           |
| Education (years)                   | 7.11 ± 3.76    | 7.2 ± 3.72     | 6.29 ± 4.05    | <0.01 | 0.24 (0.05, 0.44)             | 7.23 ± 3.75    | 4.02 ± 2.44         | <0.01 | <b>1.31 (0.99, 1.63) §</b>    | 7.11 ± 3.73    | 6.97 ± 4.69        | 0.15  | 0.04 (-0.28, 0.36)            | 7.17 ± 3.75    | 3.67 ± 2.31               | <0.01 | <b>0.94 (0.51, 1.37)</b>      |
| Smokers (Yes)                       | 91 (8.00)      | 84 (8.20)      | 7 (6.20)       | 0.47  | -1.94 (-6.72, 2.85)           | 90 (8.20)      | 1 (2.4)             | 0.24  | <b>-5.77 (-10.76, -0.77)</b>  | 90 (8.20)      | 1 (2.60)           | 0.36  | <b>-5.63 (-10.84, -0.41)</b>  | 91 (8.10)      | —                         |       | 0.40                          |
| MMSE                                | 26.94 ± 2.75   | 27 ± 2.72      | 26.42 ± 2.98   | 0.04  | 0.21 (0.02, 0.41)             | 27.13 ± 2.59   | 21.81 ± 1.51        | <0.01 | <b>3.54 (3.19, 3.88) §</b>    | 26.96 ± 2.74   | 26.49 ± 2.86       | 0.34  | 0.17 (-0.15, 0.49)            | 27.05 ± 2.66   | 21.49 ± 1.56              | <0.01 | <b>3.57 (3.11, 4.02) §</b>    |
| RAVLTi                              | 35.03 ± 7.48   | 35.0 ± 7.35    | 35.0 ± 8.60    | 0.52  | 0.01 (-0.18, 0.21)            | 35.26 ± 7.43   | 29.05 ± 6.46        | <0.01 | <b>0.84 (0.53, 1.15)</b>      | 35.1 ± 7.47    | 33.21 ± 7.83       | 0.16  | 0.25 (-0.07, 0.57)            | 35.19 ± 7.42   | 26.89 ± 6.24              | <0.01 | <b>1.12 (0.69, 1.55)</b>      |
| RAVLTd                              | 6.83 ± 2.57    | 6.85 ± 2.58    | 6.68 ± 2.55    | 0.72  | 0.07 (-0.13, 0.26)            | 6.89 ± 2.54    | 5.44 ± 3.07         | <0.01 | 0.56 (0.25, 0.88)             | 6.85 ± 2.57    | 6.3 ± 2.62         | 0.29  | 0.22 (-0.10, 0.54)            | 6.87 ± 2.56    | 4.84 ± 2.52               | <0.01 | <b>0.79 (0.36, 1.23)</b>      |
| CDT                                 | 10.63 ± 2.76   | 10.7 ± 2.74    | 9.96 ± 2.87    | <0.01 | 0.27 (0.08, 0.47)             | 10.73 ± 2.69   | 8.02 ± 3.35         | <0.01 | <b>0.81 (0.49, 1.12) §</b>    | 10.66 ± 2.74   | 9.61 ± 3.01        | 0.02  | 0.38 (0.06, 0.70)             | 10.69 ± 2.72   | 7.43 ± 3.12               | 0.02  | <b>1.20 (0.76, 1.63)</b>      |
| Slowness (Yes)                      | 232 (20.40)    | 120 (11.70)    | 112 (100.00)   | <0.01 | <b>88.30 (86.34, 90.27)</b>   | 191 (17.40)    | 41 (100.00)         | <0.01 | <b>82.59 (80.34, 84.83)</b>   | 193 (17.60)    | 39 (100.00)        | <0.01 | <b>82.44 (80.19, 84.69)</b>   | 91 (8.10)      | 21 (100.00)               | <0.01 | <b>81.11 (78.81, 83.41)</b>   |
| Interleukin 6 (pg/ml)               | 3.28 ± 5.1     | 3.14 ± 4.92    | 4.58 ± 6.36    | <0.01 | -0.23 (-0.42, -0.03) §        | 3.13 ± 4.76    | 7.29 ± 9.99         | <0.01 | -0.42 (-0.73, -0.10) §        | 3.24 ± 5       | 4.47 ± 7.26        | 0.19  | -0.24 (-0.56, 0.08)           | 3.2 ± 4.9      | 7.95 ± 10.75              | 0.29  | -0.44 (-0.87, -0.01) §        |
| Tumor Necrosis Factor alpha (pg/ml) | 2.80 ± 3.85    | 2.77 ± 3.76    | 3.08 ± 4.58    | 0.10  | -0.08 (-0.28, 0.11)           | 2.78 ± 3.86    | 3.42 ± 3.46         | <0.01 | -0.17 (-0.48, 0.15)           | 2.81 ± 3.9     | 2.64 ± 1.85        | 0.26  | 0.04 (-0.28, 0.36)            | 2.8 ± 3.88     | 2.82 ± 1.07               | 0.06  | -0.06 (-0.44, 0.43)           |
| C Reactive Protein (mg/dl)          | 0.58 ± 0.81    | 0.57 ± 0.83    | 0.64 ± 0.71    | 0.06  | -0.08 (-0.28, 0.11)           | 0.58 ± 0.82    | 0.54 ± 0.59         | 0.50  | 0.05 (-0.26, 0.36)            | 0.57 ± 0.82    | 0.75 ± 0.69        | 0.06  | -0.21 (-0.53, 0.11)           | 0.58 ± 0.82    | 0.62 ± 0.73               | 0.66  | -0.05 (-0.48, 0.38)           |
| FBG (Fasting Blood Glucose) (mg/dl) | 105.19 ± 28.79 | 104.7 ± 27.17  | 109.69 ± 40.6  | 0.17  | -0.17 (-0.37, 0.02)           | 105.16 ± 28.98 | 106.07 ± 23.41      | 0.80  | -0.03 (-0.34, 0.28)           | 104.75 ± 27.16 | 117.49 ± 57.67     | 0.08  | -0.04 (-0.35, 0.27) §         | 105.19 ± 28.92 | 105.1 ± 20.73             | 0.82  | 0.03 (-0.43, 0.44)            |
| Total Cholesterol (mg/dl)           | 184.83 ± 36.84 | 184.86 ± 36.38 | 184.54 ± 40.92 | 0.93  | 0.01 (-0.19, 0.20)            | 185.18 ± 36.75 | 175.49 ± 38.39      | 0.10  | 0.26 (-0.05, 0.58)            | 184.81 ± 36.76 | 185.49 ± 39.35     | 0.98  | -0.02 (-0.34, 0.30)           | 184.98 ± 36.79 | 176.86 ± 39.19            | 0.41  | 0.22 (-0.21, 0.65)            |
| HDL Cholesterol (mg/dl)             | 49.42 ± 13     | 49.30 ± 12.80  | 50.10 ± 15.00  | 0.90  | -0.05 (-0.24, 0.15)           | 49.52 ± 12.95  | 46.76 ± 14.02       | 0.11  | 0.21 (-0.10, 0.52)            | 49.43 ± 12.87  | 49.1 ± 16.42       | 0.44  | 0.20 (-0.11, 0.51)            | 49.44 ± 13     | 48.38 ± 13.14             | 0.60  | 0.08 (-0.35, 0.51)            |
| LDL Cholesterol (mg/dl)             | 114.03 ± 31.2  | 114.00 ± 31.00 | 111.00 ± 33.40 | 0.40  | 0.10 (-0.09, 0.30)            | 114.27 ± 31.14 | 107.61 ± 32.67      | 0.15  | 0.21 (-0.10, 0.53)            | 114.11 ± 31.2  | 111.54 ± 31.68     | 0.85  | 0.08 (-0.24, 0.40)            | 114.12 ± 31.12 | 109.19 ± 36               | 0.52  | 0.16 (-0.27, 0.59)            |
| Triglycerides (mg/dl)               | 103.04 ± 60.19 | 103.1 ± 59.98  | 102.53 ± 62.36 | 0.48  | 0.01 (-0.19, 0.20)            | 102.96 ± 60.5  | 105.37 ± 51.77      | 0.45  | -0.04 (-0.35, 0.27)           | 102.58 ± 59.76 | 116.18 ± 70.99     | 0.40  | -0.23 (-0.55, 0.09)           | 103.24 ± 60.57 | 92.57 ± 33.26             | 0.86  | 0.18 (-0.25, 0.61)            |
| SBP (mmHg)                          | 133.45 ± 14.55 | 133.19 ± 14.59 | 135.85 ± 14.03 | 0.06  | 0.02 (-0.17, 0.22)            | 133.31 ± 14.56 | 137.2 ± 14.14       | 0.06  | -0.27 (-0.58, 0.05)           | 133.39 ± 14.58 | 135.13 ± 13.93     | 0.45  | -0.12 (-0.44, 0.20)           | 133.39 ± 14.57 | 136.9 ± 13.46             | 0.19  | -0.24 (-0.67, 0.19)           |
| DBP (mmHg)                          | 78.02 ± 7.92   | 78.04 ± 8.01   | 77.86 ± 7.09   | 0.75  | -0.18 (-0.38, 0.01)           | 78 ± 7.92      | 78.66 ± 8.06        | 0.65  | -0.27 (-0.58, 0.05)           | 78.07 ± 7.96   | 76.67 ± 6.62       | 0.19  | 0.18 (-0.14, 0.50)            | 78.01 ± 7.93   | 78.81 ± 7.4               | 0.54  | -0.10 (-0.53, 0.33)           |
| MACQ (score)                        | 22.29 ± 1.99   | 22.2 ± 1.97    | 22.8 ± 2.15    | <0.01 | -0.25 (-0.45, -0.06) §        | 22.28 ± 1.99   | 22.41 ± 2.05        | 0.71  | -0.07 (-0.38, 0.24)           | 22.15 ± 1.88   | 26.08 ± 1.35       | <0.01 | <b>-2.11 (-2.44, -1.78)</b>   | 22.27 ± 1.98   | 23.19 ± 2.4               | 0.04  | -0.46 (-0.90, -0.03)          |
| SCC (Yes)                           | 545 (47.90)    | 433 (42.20)    | 112 (100.00)   | <0.01 | <b>57.80 (54.78, 60.82) §</b> | 524 (47.80)    | 21 (52.10)          | 0.60  | 3.45 (-12.13, 19.04)          | 528 (47.10)    | 27 (69.20)         | <0.01 | <b>22.10 (7.31, 36.88)</b>    | 524 (46.90)    | 21 (100.00)               | <0.01 | <b>53.09 (50.16, 56.02)</b>   |
| TMTA (s)                            | 75.70 ± 42.84  | 73.10 ± 40.60  | 99.20 ± 54.20  | <0.01 | -0.48 (-0.68, -0.28) §        | 73.36 ± 39.78  | 138.29 ± 68.17      | <0.01 | <b>-1.58 (-1.90, -1.26) §</b> | 74.67 ± 42.18  | 104.59 ± 51.33     | <0.01 | <b>-0.95 (-1.27, -0.64) §</b> | 74.37 ± 41.52  | 146.48 ± 52.75            | <0.01 | <b>-1.37 (-1.80, -0.93) §</b> |
| TMTB (s)                            | 163.91 ± 99.22 | 160 ± 97.10    | 200 ± 111.00   | <0.01 | -0.36 (-0.55, -0.16) §        | 161 ± 97.84    | 241.85 ± 105.36     | <0.01 | <b>-0.82 (-1.14, -0.51)</b>   | 162.78 ± 98.79 | 195.79 ± 107.18    | 0.05  | -0.33 (-0.65, -0.01)          | 162.09 ± 98.06 | 260.48 ± 114.63           | <0.01 | <b>-1.00 (-1.43, -0.57)</b>   |
| Time of observation (months)        | 62.73 ± 21.37  | 62.64 ± 21.36  | 63.56 ± 21.53  | 0.39  | -0.04 (-0.24, 0.15)           | 63.07 ± 21.26  | 53.66 ± 22.53       | 0.01  | <b>0.44 (0.13, 0.75)</b>      | 62.74 ± 21.35  | 62.38 ± 22.15      | 0.82  | 0.02 (-0.30, 0.34)            | 62.86 ± 21.32  | 55.76 ± 23                | 0.23  | 0.33 (-0.10, 0.76)            |
| Mean Survival Time (months)         | 85.50 ± 19.57  | 85.50 ± 19.57  | 83.40 ± 20.94  | 0.10  |                               | 85.60 ± 19.27  | 77.20 ± 28.42       | <0.01 |                               | 85.50 ± 19.49  | 80.20 ± 3.87       | 0.06  |                               | 85.50 ± 19.49  | 80.20 ± 24.16             | 0.20  |                               |

\*Cohen' delta effect size where not otherwise specified, § Glass' delta effect size and prevalence differences for categorical variables

All data are shown as mean ± sd for continuous variables and as n (%) for proportions .

Medium to large effect size (>0.5) were highlighted in bold

MMSE: Mini Mental Statement Examination; RAVLT: Rey Auditory Verbal Learning Test (i, immediate; d, delayed); CDT: Clock Drawing Test; MAC-Q: Memory Assessment Clinic-Q; SCC: Subjective Cognitive Complaint; TMT: Trail Making Test