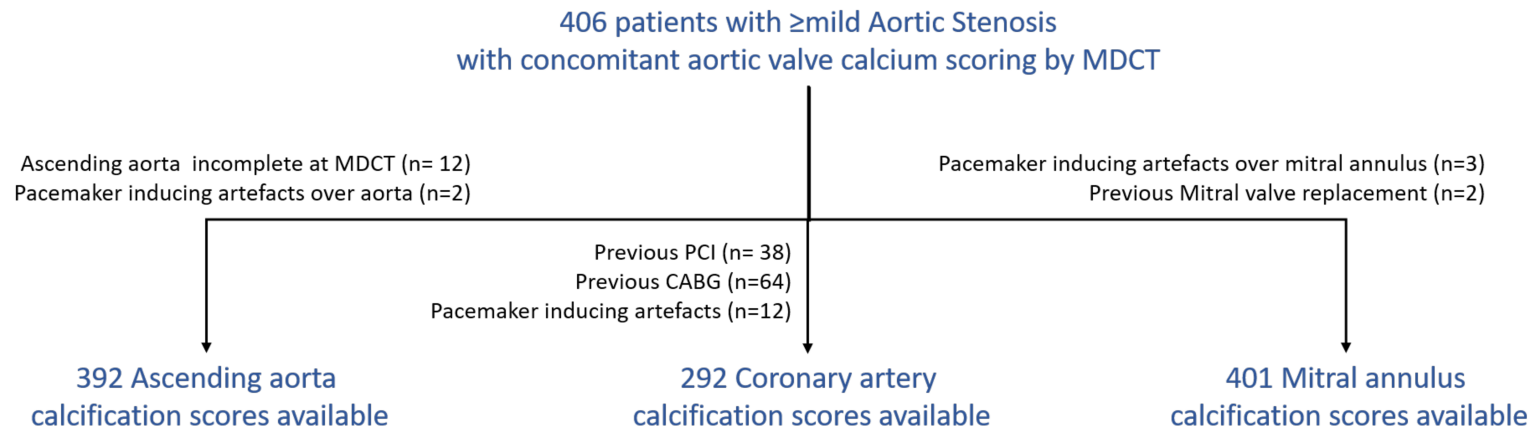


## **Online supplementary material for the article**

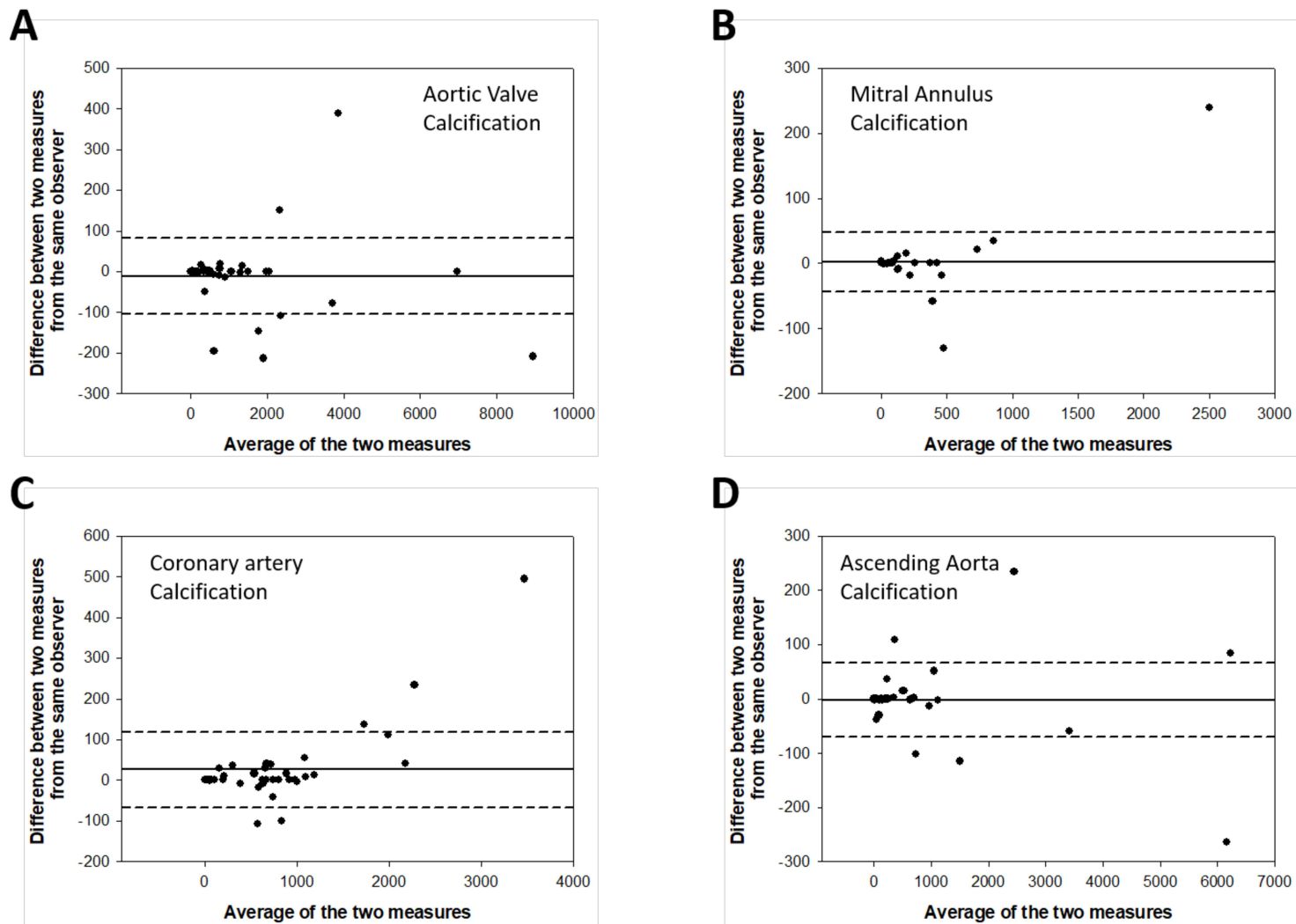
### **SEX-SPECIFIC CORRELATES OF VALVULAR AND ARTERIAL CALCIFICATION**

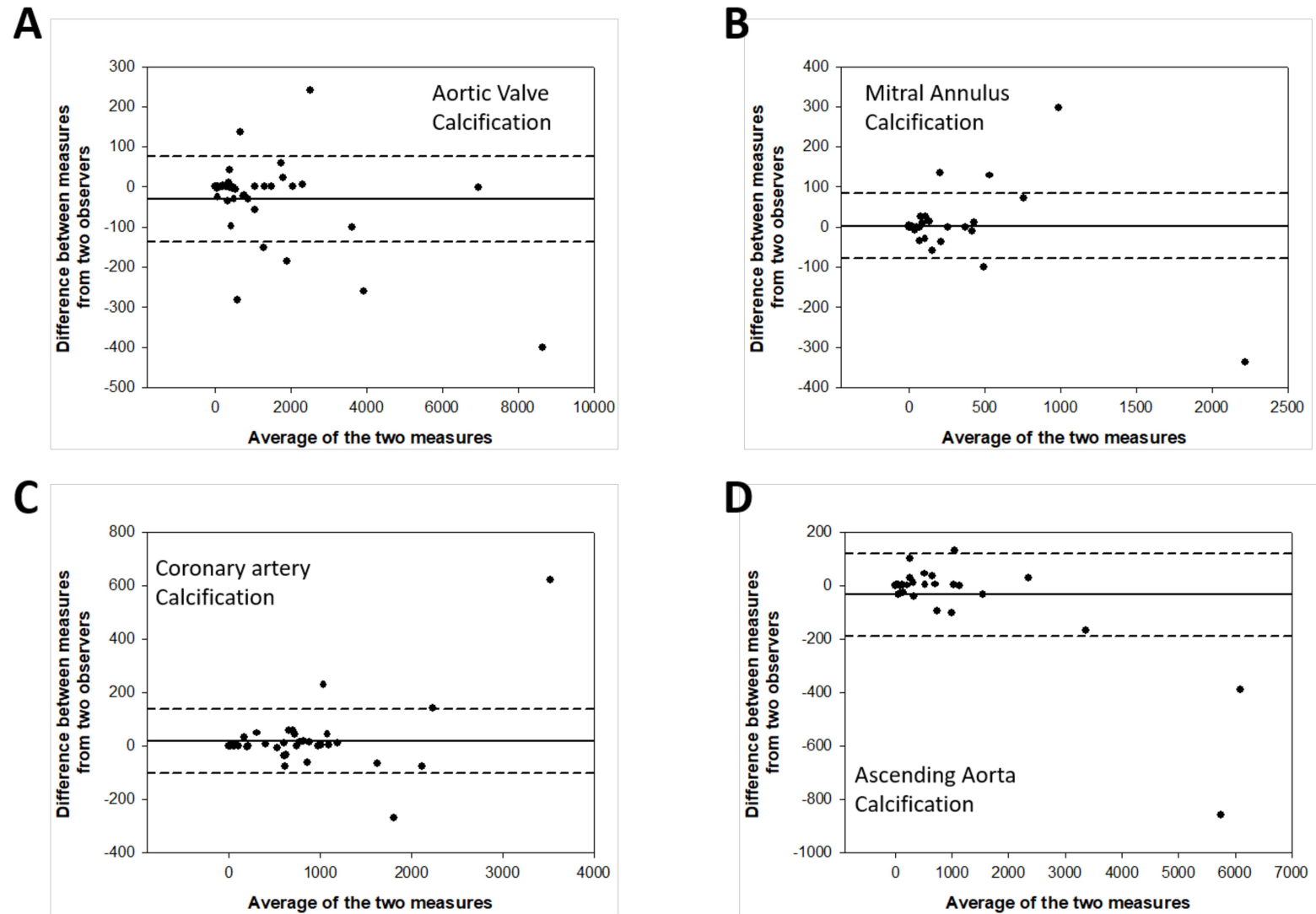
### **BURDEN IN PATIENTS WITH MODERATE AORTIC STENOSIS**

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**Figure S1: Flow chart and available calcification scores for each territory**

Legend: CABG: Coronary artery bypass graft; MDCT: Multidetector computed tomography; PCI: Percutaneous coronary intervention

**Figure S2: Bland-Altman representation of intra-observer variability**

**Figure S3: Bland-Altman representation of intra-observer variability**

**Table S1: Multivariate analysis of ascending aorta calcification load in the whole cohort, in women and in men**

	Whole Cohort				Women		Men	
	Coef.	Std. Err.	Beta	p	Beta	p	Beta	p
Male sex	-149.91	151.33	-0.07	0.32	-	-	-	-
Age (per year)	5.96	5.51	0.07	0.28	0.11	0.32	-0.002	0.98
Body surface area (per m <sup>2</sup> )	47.4	309.77	0.01	0.88	0.11	0.23	-0.05	0.54
Diabetes	51.82	137.57	0.02	0.71	0.1	0.37	-0.02	0.81
Hyperlipidemia	<b>287.57</b>	<b>137.04</b>	<b>0.13</b>	<b>0.04</b>	0.12	0.24	0.15	0.06
eGFR<60 ml/min	150.11	158.92	0.06	0.35	-0.08	0.45	0.14	0.08
Vitamin K antagonist	<b>390.44</b>	<b>168.03</b>	<b>0.14</b>	<b>0.02</b>	<b>0.24</b>	<b>0.01</b>	0.02	0.76
Bisphosphonate	296.35	211.55	0.1	0.16	0.17	0.14	0.003	0.97
Calcium and/or Vitamin D	-48.87	82.29	-0.04	0.55	-0.12	0.26	0.05	0.57
CAC (per AU)	<b>0.16</b>	<b>0.06</b>	<b>0.18</b>	<b>0.004</b>	0.13	0.21	<b>0.22</b>	<b>0.01</b>
MAC (per AU)	-0.02	0.04	-0.02	0.70	-	-	-	-

*CAC*, coronary artery calcification; *eGFR*, estimated glomerular filtration rate; *MAC*, mitral annular calcification.

In bold statistically significant results

**Table S2: Univariable analysis of aortic valve calcification load in the whole cohort, in women and in men**

	Whole Cohort				Women		Men	
	Coef.	Std. Err.	Beta	p	Beta	p	Beta	p
Male Sex	<b>784.15</b>	<b>159.61</b>	<b>0.24</b>	<b>&lt;0.0001</b>	-	-	-	-
Age (per year)	<b>23.54</b>	<b>6.78</b>	<b>0.17</b>	<b>0.001</b>	<b>0.29</b>	<b>0.001</b>	<b>0.19</b>	<b>0.002</b>
Body surface area (per m <sup>2</sup> )	466.04	331.5	0.07	0.16	<b>-0.20</b>	<b>0.02</b>	-0.03	0.66
Hypertension	342.78	204.95	0.08	0.10	0.08	0.34	0.1	0.11
Hyperlipidemia	266.01	191.09	0.07	0.17	-0.01	0.90	0.08	0.17
Diabetes	-157.71	163.53	-0.05	0.34	-0.02	0.82	<b>-0.06</b>	<b>0.36</b>
Coronary artery disease	<b>420.62</b>	<b>155.01</b>	<b>0.13</b>	<b>0.01</b>	0.07	0.41	0.13	0.03
eGFR<60 ml/min	<b>406.41</b>	<b>192.23</b>	<b>0.1</b>	<b>0.04</b>	<b>0.23</b>	<b>0.01</b>	0.1	0.10
Current smoker	-142.51	237.25	-0.03	0.55	0.005	0.96	-0.05	0.44
Bicuspid Aortic Valve	<b>680.15</b>	<b>195.11</b>	<b>0.17</b>	<b>0.001</b>	0.01	0.92	<b>0.19</b>	<b>0.001</b>
ACE inhibitor	194.22	166.37	0.06	0.24	0.11	0.21	0.01	0.87
ARB	-110.06	163.62	-0.03	0.50	-0.15	0.09	0.003	0.96
Vitamin K antagonist	6.46	210.64	0.002	0.98	0.05	0.59	0.02	0.70
Statin	210.45	179.61	0.06	0.24	-0.09	0.32	0.08	0.19
Bisphosphonate	-344.07	238.6	-0.07	0.15	-0.005	0.96	-0.01	0.89
Calcium and/or vitamin D	<b>-325.29</b>	<b>103.87</b>	<b>-0.15</b>	<b>0.002</b>	-0.03	0.69	-0.003	0.96
CAC	<b>0.17</b>	<b>0.09</b>	<b>0.11</b>	<b>0.05</b>	<b>0.22</b>	<b>0.02</b>	0.05	0.51
MAC	<b>0.26</b>	<b>0.05</b>	<b>0.25</b>	<b>&lt;0.0001</b>	<b>0.37</b>	<b>&lt;0.0001</b>	<b>0.27</b>	<b>&lt;0.0001</b>
Asc. aorta calcification	-0.07	0.07	-0.06	0.27	0.01	0.93	-0.06	0.32

Asc., ascending; ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; AVC, aortic valve calcification; CAC, coronary artery calcification; eGFR, estimated glomerular filtration rate; MAC, mitral annular calcification. In bold, statistically significant results.

**Table S3: Univariable analysis of mitral annular calcification load in the whole cohort, in women and in men**

	Whole Cohort					Women		Men	
	Coef.	Std. Err.	Beta	p		Beta	p	Beta	p
Male Sex	<b>-301.61</b>	<b>160.84</b>	<b>0.09</b>	<b>0.05</b>		-	-	-	-
Age (per year)	<b>25.27</b>	<b>6.62</b>	<b>0.19</b>	<b>&lt;0.0001</b>		<b>0.28</b>	<b>0.001</b>	<b>0.12</b>	<b>0.05</b>
Body surface area (per m <sup>2</sup> )	-1.51	326.76	0.0002	1.00		0.03	0.71	0.07	0.24
Hypertension	<b>446.06</b>	<b>199.81</b>	<b>0.11</b>	<b>0.03</b>		0.16	0.07	0.09	0.16
Hyperlipidemia	198.49	187.06	0.05	0.29		0.15	0.10	0.01	0.88
Diabetes	<b>483.77</b>	<b>159.1</b>	<b>0.15</b>	<b>0.001</b>		<b>0.18</b>	<b>0.04</b>	<b>0.14</b>	<b>0.02</b>
Coronary artery disease	<b>320.84</b>	<b>153.07</b>	<b>0.1</b>	<b>0.04</b>		<b>0.25</b>	<b>0.004</b>	0.04	0.50
eGFR<60 ml/min	<b>512.48</b>	<b>189.07</b>	<b>0.13</b>	<b>0.01</b>		0.09	0.30	<b>0.15</b>	<b>0.01</b>
Current smoker	-328.93	233.46	-0.07	0.16		-0.12	0.17	-0.04	0.49
ACE inhibitor	10.1	163.88	0.003	0.95		0.07	0.43	-0.01	0.89
ARB	271.26	160.37	0.08	0.09		-0.02	0.83	<b>0.14</b>	<b>0.03</b>
Vitamin K antagonist	<b>514.42</b>	<b>208.31</b>	<b>0.12</b>	<b>0.01</b>		-0.01	0.90	<b>0.19</b>	<b>0.001</b>
Statin	-95.56	176.56	-0.03	0.59		-0.13	0.14	0.04	0.49
Bisphosphonate	<b>578.17</b>	<b>231.96</b>	<b>0.12</b>	<b>0.01</b>		0.1	0.25	0.11	0.07
Calcium and/or vitamin D	<b>242.22</b>	<b>102.76</b>	<b>0.12</b>	<b>0.02</b>		0.16	0.06	<b>0.19</b>	<b>0.002</b>
CAC	0.14	0.08	0.1	0.08		<b>0.29</b>	<b>0.002</b>	0.06	0.42
Asc. aorta calcification	0.12	0.07	0.09	0.07		0.14	0.12	0.04	0.49
AVC	<b>0.24</b>	<b>0.05</b>	<b>0.25</b>	<b>&lt;0.0001</b>		<b>0.37</b>	<b>&lt;0.0001</b>	<b>0.27</b>	<b>&lt;0.0001</b>

Asc., ascending; ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; AVC, aortic valve calcification; CAC, coronary artery calcification; eGFR, estimated glomerular filtration rate. In bold, statistically significant results.

**Table S4: Univariable analysis of coronary artery calcification load in the whole cohort, in women and in men**

	Whole Cohort				Women		Men	
	Coef.	Std. Err.	Beta	p	Beta	p	Beta	p
Male Sex	<b>370.36</b>	<b>130.75</b>	<b>0.16</b>	<b>0.005</b>	-	-	-	-
Age (per year)	<b>27.34</b>	<b>5.03</b>	<b>0.3</b>	<b>&lt;0.0001</b>	<b>0.45</b>	<b>&lt;0.0001</b>	<b>0.3</b>	<b>&lt;0.0001</b>
Body surface area (m <sup>2</sup> )	629.68	102.88	0.09	0.12	0.03	0.77	0.02	0.82
Hypertension	<b>598.24</b>	<b>152.9</b>	<b>0.22</b>	<b>&lt;0.0001</b>	<b>0.31</b>	<b>&lt;0.0001</b>	<b>0.22</b>	<b>0.003</b>
Hyperlipidemia	<b>414.97</b>	<b>142.57</b>	<b>0.17</b>	<b>0.004</b>	<b>0.32</b>	<b>&lt;0.0001</b>	0.12	0.11
Diabetes	252.32	142.22	0.1	0.08	<b>0.21</b>	<b>0.03</b>	0.08	0.29
Coronary artery disease	<b>677.78</b>	<b>123.86</b>	<b>0.3</b>	<b>&lt;0.0001</b>	<b>0.34</b>	<b>&lt;0.0001</b>	<b>0.3</b>	<b>&lt;0.0001</b>
eGFR<60 ml/min	303.8	167.74	0.11	0.07	0.15	0.12	0.11	0.14
Current Smoker	-67.12	192.19	-0.02	0.73	-0.07	0.48	-0.01	0.87
ACE inhibitor	<b>414.03</b>	<b>144.37</b>	<b>0.17</b>	<b>0.004</b>	<b>0.21</b>	<b>0.03</b>	0.14	0.06
ARB	147.51	137.74	0.06	0.29	0.13	0.18	0.05	0.48
Vitamin K antagonist	204.39	178.36	0.07	0.25	0.18	0.06	0.06	0.44
Statin	<b>346.73</b>	<b>136.51</b>	<b>0.15</b>	<b>0.01</b>	<b>0.21</b>	<b>0.03</b>	0.12	0.10
Bisphosphonate	54.78	198.72	0.02	0.78	<b>0.24</b>	<b>0.01</b>	-0.03	0.64
Calcium and/or vitamin D	-51.58	76.27	0.04	0.50	<b>0.22</b>	<b>0.02</b>	-0.08	0.27
MAC	0.08	0.04	0.04	0.08	<b>0.29</b>	<b>0.002</b>	0.06	0.42
AVC	<b>0.08</b>	<b>0.04</b>	<b>0.1</b>	<b>0.05</b>	<b>0.22</b>	<b>0.02</b>	0.05	0.51
Asc. aorta calcification	<b>0.25</b>	<b>0.06</b>	<b>0.11</b>	<b>&lt;0.0001</b>	<b>0.29</b>	<b>0.002</b>	<b>0.24</b>	<b>0.001</b>

Asc., ascending; ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; AVC, aortic valve calcification; CAC, coronary artery calcification; eGFR, estimated glomerular filtration rate; MAC, mitral annular calcification. In bold, statistically significant results.



**Table S5: Univariable analysis of ascending aorta calcification load in the whole cohort, in women and in men**

	Whole Cohort				Women		Men	
	Coef.	Std. Err.	Beta	P>t	Beta	P>t	Beta	P>t
Male Sex	<b>-205.88</b>	<b>121.16</b>	<b>-0.09</b>	<b>0.09</b>	-	-	-	-
Age (per year)	<b>14.61</b>	<b>5.05</b>	<b>0.15</b>	<b>0.004</b>	0.16	0.07	<b>0.12</b>	<b>0.05</b>
Body surface area (per m <sup>2</sup> )	695.26	98.8	-0.04	0.43	0.08	0.37	-0.05	0.39
Hypertension	<b>420.36</b>	<b>149.93</b>	<b>0.14</b>	<b>0.01</b>	<b>0.18</b>	<b>0.04</b>	0.12	0.06
Hyperlipidemia	<b>484.8</b>	<b>139.48</b>	<b>0.17</b>	<b>0.001</b>	<b>0.2</b>	<b>0.02</b>	<b>0.17</b>	<b>0.01</b>
Diabetes	<b>336.3</b>	<b>119.95</b>	<b>0.14</b>	<b>0.01</b>	<b>0.21</b>	<b>0.02</b>	0.1	0.12
Coronary artery disease	<b>467.23</b>	<b>113.78</b>	<b>0.2</b>	<b>&lt;0.0001</b>	<b>0.21</b>	<b>0.01</b>	<b>0.22</b>	<b>&lt;0.0001</b>
eGFR<60 ml/min	<b>411.15</b>	<b>141.43</b>	<b>0.15</b>	<b>0.004</b>	0.15	0.10	<b>0.14</b>	<b>0.02</b>
Current smoker	119.35	173.49	0.03	0.49	-0.01	0.89	0.07	0.25
ACE inhibitor	205.67	123.17	0.08	0.10	0.04	0.62	<b>0.13</b>	<b>0.03</b>
ARB	56.18	121.81	0.02	0.65	0.15	0.09	-0.07	0.25
Vitamin K antagonist	<b>350.55</b>	<b>155.11</b>	<b>0.11</b>	<b>0.02</b>	0.17	0.06	0.06	0.38
Statin	<b>420.57</b>	<b>131.18</b>	<b>0.16</b>	<b>0.001</b>	0.16	0.07	<b>0.18</b>	<b>0.004</b>
Bisphosphonate	308.57	175.81	0.09	0.08	0.05	0.57	0.09	0.14
Calcium and/or vitamin D	115.87	67.49	0.09	0.09	0.07	0.46	0.06	0.35
MAC	0.07	0.04	0.09	0.07	0.14	0.12	0.04	0.49
AVC	-0.04	0.04	-0.06	0.27	0.01	0.93	-0.06	0.32
CAC	<b>0.21</b>	<b>0.05</b>	<b>0.23</b>	<b>&lt;0.0001</b>	<b>0.29</b>	<b>0.002</b>	<b>0.24</b>	<b>0.001</b>

*ACE*, angiotensin-converting enzyme; *ARB*, angiotensin-receptor blocker; *AVC*, aortic valve calcification; *CAC*, coronary artery calcification; *eGFR*, estimated glomerular filtration rate; *MAC*, mitral annular calcification. In bold, statistically significant results.