

SUPPLEMENTARY MATERIAL

Table S1. ICD10 codes used to identify vascular risk factors and comorbidities as secondary diagnosis in each case included in the Spanish Minimum Basic Hospital Discharge Dataset.

Condition	ICD10 codes (including subgroups)
Arterial hypertension	I10
Diabetes mellitus	E10, E11
Dyslipidaemia	E78
Smoking (current or former)	Z72.0; Z87.891; F17
Cocaine	F14; T40.5- T40.5X5S
Cannabis	F1; T40.7- T40.7X5S
Enolism	F10
Obesity	E66
Migraine	G43
Hypothyroidism	E03
Hyperthyroidism	E05.5 – E05.91
Cancer	C00-C96
Ischemic heart disease	I20; I25
Atrial fibrillation	I48
Non-congenital cardiopathy (all)	I42
Dilated cardiomyopathy	I42.0
Heart failure	I13; I50
Valvulopathy (non-rheumatic)	I34; I35; I36; I37
Valvulopathy (rheumatic)	I05; I06; I07; I08; I09
PFO	Q21.1
Chronic renal failure	I12; N18
COPD	J44
OSAH	G47.3
Intracranial atherosclerosis, n (%)	I67.2
Fibromuscular dysplasia, n (%)	I77.3
Arterial dissection (intracranial)	I67.0
Arterial dissection (carotid)	I77.71
Arterial dissection (vertebral)	I77.74
Thrombophilia	D68.5-D68.9
Antiphospholipid syndrome, n (%)	D68.61; D68.62
Systemic vasculitis (all)	M31
Moyamoya disease	I67.5

Sick cell disease, n (%)	D57.0-D57.819
Fabry disease	E75.21
Endocarditis	I33
Cardiac prosthesis infection	T82.7
Brain herniation, n (%)	G93.5
Seizures, n (%)	G40.909; R56.9
Acute coronary syndrome n (%)	I21
Urinary tract infection, n (%)	N39.0
Acute renal failure, n (%)	N17
Broncoaspiration	J69
Pneumonia	J18

PFO: Patent foramen oval, COPD: Chronic obstructive pulmonary disease; OSAH: Obstructive sleep apnea-hypopnea syndrome.

Table S2. Demographic and clinical characteristics by age range

Variable	ALL ISCHEMIC STROKE PATIENTS												
	18-24 N=163	25-29 N=274	30-34 N=573	35-39 N=1230	40-44 N=2485	45-49 N=4437	50-54 N=7332	55-59 N=10846	60-64 N=13561	65-69 N=17271	70-74 N=21928	75-79 N=25155	>= 80 N=81232
Demographic data													
vascular risk factors and comorbidities													
Male, n (%)	81 (49.7%)	134 (48.9%)	300 (52.4%)	773 (62.8%)	1593 (64.1%)	2993 (67.5%)	5290 (72.1%)	8014 (73.9%)	9699 (71.5%)	11556 (66.9%)	13332 (60.8%)	13607 (54.1%)	32036 (39.4%)
Arterial hypertension (%)	8 (4.9%)	16 (5.8%)	55 (9.6%)	216 (17.6%)	695 (28%)	1746 (39.4%)	3481 (47.3%)	5623 (51.8%)	7482 (55.2%)	10064 (58.3%)	13110 (59.8%)	15006 (59.3%)	45461 (56%)
Diabetes mellitus, n (%)	2 (1.2%)	3 (1.1%)	14 (2.4%)	58 (4.7%)	222 (8.9%)	665 (15%)	1530 (15.5%)	3003 (27.7%)	4364 (32.2%)	6048 (35%)	8025 (36.6%)	9013 (35.8%)	24610 (30.3%)
Dyslipidaemia, n (%)	4 (2.5%)	21 (7.7%)	69 (12%)	251 (20.4%)	627 (25.2%)	1445 (32.6%)	2918 (39.8%)	4704 (43.4%)	6117 (45.1%)	8150 (47.2%)	10319 (47.5%)	11457 (45.5%)	30054 (37%)
Smoking, n (%)	43 (26.4%)	103 (37.6%)	239 (41.7%)	543 (44.1%)	1151 (46.3%)	2329 (52.2%)	4262 (58.1%)	6206 (57.2%)	6770 (49.9%)	6865 (39.7%)	6538 (29.8%)	5251 (20.9%)	8157 (10%)
Cocaine, n (%)	10 (6.1%)	24 (8.8%)	45 (7.9%)	85 (6.9%)	134 (5.4%)	183 (4.1%)	170 (2.3%)	112 (1%)	56 (0.4%)	36 (0.2%)	7 (0%)	3 (0%)	0 (0%)
Cannabis, n (%)	14 (8.6%)	33 (12%)	45 (7.9%)	84 (6.8%)	98 (3.9%)	124 (2.8%)	150 (2%)	122 (1.1%)	54 (0.4%)	34 (0.2%)	9 (0%)	2 (0%)	3 (0%)
Enolism, n (%)	4 (2.5%)	12 (4.4%)	29 (5.1%)	80 (6.5%)	241 (9.7%)	498 (11.2%)	1074 (14.5%)	1738 (16%)	1945 (14.3%)	2021 (11.7%)	1676 (7.6%)	1207 (4.8%)	1248 (1.5%)
Cancer diagnosis, n (%)	0 (0%)	3 (1.1%)	3 (0.5%)	18 (1.5%)	38 (1.5%)	81 (1.8%)	195 (2.7%)	424 (3.9%)	659 (4.9%)	872 (5%)	1197 (5.5%)	1318 (5.2%)	3623 (4.5%)
Obesity, n (%)	12 (7.4%)	16 (5.8%)	32 (5.6%)	131 (10.7%)	290 (11.7%)	626 (14.1%)	951 (13%)	1325 (12.2%)	1491 (11%)	1944 (11.3%)	2037 (9.3%)	2003 (8%)	4002 (4.9%)
Ischemic heart disease, n (%)	4 (2.5%)	11 (4%)	18 (3.1%)	51 (4.1%)	124 (5%)	250 (5.6%)	484 (6.6%)	903 (8.3%)	1258 (9.3%)	1849 (10.7%)	2523 (11.5%)	3009 (12%)	9403 (11.6%)
Atrial fibrillation, n (%)	2 (1.2%)	3 (1.1%)	12 (2.1%)	24 (2%)	104 (4.2%)	201 (4.5%)	420 (5.7%)	997 (9.2%)	1910 (14.1%)	3320 (19.2%)	5543 (25.3%)	7912 (31.5%)	33977 (41.8%)
Non-congenital cardiomyopathy, n (%)	1 (0.6%)	10 (3.6%)	17 (3%)	34 (2.8%)	51 (2.1%)	127 (2.9%)	205 (2.8%)	307 (2.8%)	334 (2.5%)	452 (2.6%)	492 (2.2%)	549 (2.2%)	1339 (1.6%)
Dilated cardiomyopathy, n (%)	0 (0%)	4 (1.5%)	7 (1.2%)	15 (1.2%)	26 (1%)	62 (1.4%)	110 (1.5%)	151 (1.4%)	172 (1.3%)	227 (1.3%)	233 (1.1%)	278 (1.1%)	598 (0.7%)
Heart failure, n (%)	0 (0%)	0 (0%)	7 (1.2%)	9 (0.7%)	26 (1%)	61 (1.4%)	121 (1.7%)	240 (2.2%)	360 (2.7%)	503 (2.9%)	835 (3.8%)	1265 (5%)	7397 (9.1%)
Valvulopathy (non-rheumatic), n (%)	1 (0.6%)	1 (0.4%)	6 (1%)	10 (0.8%)	19 (0.8%)	50 (1.1%)	59 (0.8%)	122 (1.1%)	189 (1.4%)	400 (2.3%)	644 (2.9%)	930 (3.7%)	3789 (4.7%)
Valvulopathy (rheumatic), n (%)	0 (0%)	3 (1.1%)	7 (1.2%)	18 (1.5%)	32 (1.3%)	44 (1%)	86 (1.2%)	148 (1.4%)	249 (1.8%)	395 (2.3%)	567 (2.6%)	763 (3%)	2834 (3.5%)
PFO, n (%)	41 (25.2%)	60 (21.9%)	96 (16.8%)	167 (13.6%)	268 (10.8%)	312 (7%)	292 (4%)	271 (2.5%)	150 (1.1%)	185 (1.1%)	146 (0.7%)	109 (0.4%)	127 (0.2%)
OSA, n (%)	1 (0.6%)	0 (0%)	10 (1.7%)	30 (1.7%)	95 (3.8%)	230 (5.2%)	428 (5.8%)	693 (6.4%)	863 (6.4%)	1160 (6.7%)	1365 (6.2%)	1226 (4.9%)	1861 (2.3%)
Intracranial atherosclerosis, n (%)	1 (0.6%)	2 (0.7%)	3 (0.5%)	11 (0.9%)	46 (1.9%)	92 (2.1%)	274 (3.7%)	448 (4.1%)	588 (4.3%)	734 (4.2%)	964 (4.4%)	1083 (4.3%)	3074 (3.8%)
Unusual causes													
Fibromuscular dysplasia, n (%)	2 (1.2%)	0 (0%)	0 (0%)	0 (0%)	2 (0.2%)	5 (0.2%)	6 (0.1%)	5 (0.1%)	5 (0%)	0 (0%)	3 (0%)	3 (0%)	3 (0%)
Arterial dissection (all), n (%)	10 (6.1%)	10 (3.6%)	29 (5.1%)	90 (7.3%)	118 (4.7%)	144 (3.2%)	176 (2.4%)	107 (1%)	89 (0.7%)	62 (0.4%)	53 (0.2%)	44 (0.2%)	56 (0.1%)
Arterial dissection intracranial, n (%)	1 (0.6%)	1 (0.4%)	3 (0.5%)	13 (1.1%)	9 (0.4%)	5 (0.1%)	10 (0.1%)	7 (0.1%)	9 (0.1%)	4 (0%)	4 (0%)	4 (0%)	7 (0%)
Arterial dissection (carotid), n (%)	5 (3.1%)	4 (1.5%)	10 (1.7%)	42 (3.4%)	60 (2.4%)	101 (2.3%)	130 (1.8%)	71 (0.7%)	63 (0.5%)	44 (0.3%)	31 (0.1%)	25 (0.1%)	33 (0%)
Arterial dissection (vertebral), n (%)	5 (3.1%)	5 (1.8%)	18 (3.1%)	35 (2.8%)	50 (2%)	38 (0.9%)	40 (0.5%)	29 (0.3%)	19 (0.1%)	14 (0.1%)	18 (0.1%)	15 (0.1%)	16 (0%)
Thrombophilia, n (%)	12 (7.4%)	14 (5.1%)	23 (4%)	27 (2.2%)	76 (3.1%)	109 (2.5%)	117 (1.6%)	137 (1.3%)	114 (0.8%)	111 (0.6%)	98 (0.4%)	90 (0.4%)	183 (0.2%)
Vasospasm, n (%)	1 (0.6%)	3 (1.1%)	3 (0.5%)	1 (0.1%)	5 (0.2%)	7 (0.2%)	9 (0.1%)	12 (0.1%)	8 (0.1%)	9 (0.1%)	3 (0%)	13 (0.1%)	14 (0%)
Arteritis, n (%)	0 (0%)	1 (0.4%)	2 (0.3%)	2 (0.2%)	4 (0.2%)	4 (0.1%)	6 (0.1%)	9 (0.1%)	7 (0%)	7 (0%)	5 (0%)	10 (0%)	15 (0%)
Systemic lupus erythematosus, n (%)	2 (1.2%)	2 (0.7%)	8 (1.4%)	9 (0.7%)	20 (0.8%)	24 (0.5%)	13 (0.2%)	28 (0.3%)	25 (0.2%)	22 (0.1%)	24 (0.1%)	19 (0.1%)	31 (0%)
Endocarditis, n (%)	0 (0%)	1 (0.4%)	1 (0.2%)	1 (0.1%)	9 (0.4%)	4 (0.1%)	8 (0.1%)	18 (0.2%)	20 (0.1%)	22 (0.1%)	27 (0.1%)	32 (0.1%)	61 (0.1%)
Outcome													
In-hospital mortality, n (%)	3 (1.8%)	4 (1.5%)	14 (2.4%)	31 (2.5%)	77 (3.1%)	124 (2.8%)	278 (3.8%)	498 (4.6%)	770 (5.7%)	1071 (6.2%)	1766 (8.1%)	2517 (10%)	16410 (20.2%)

PFO: Patent foramen oval, COPD: Chronic obstructive pulmonary disease; OSAH: Obstructive sleep apnea-hypopnea syndrome.

Table S3. Demographic and clinical characteristics of the included patients by sex and age group.

Variable	All patients			18-50 y.o.			> 50 y.o.		
	Men (N=99408)	Women (n=87079)	p	Men (N=5874)	Women (n=3288)	p	Men (N=)	Women (n=)	p
<i>Demographic data, vascular risk factors and comorbidities</i>									
Mean age (SD), years	71.6 (13.1)	78.4 (12.8)	< 0.001	43.03 (5.7)	41.7 (6.74)	0.000	73.36 (11.2)	79.79 (10.6)	< 0.001
Arterial hypertension, n (%)	53540 (53.9)	49423 (56.8)	< 0.001	1941 (33%)	795 (24.2)	0.000	51599 (55.2)	48628 (58%)	< 0.001
Diabetes mellitus, n (%)	31971 (32.2)	25586 (29.4)	< 0.001	707 (12%)	257 (7.8%)	0.000	31264 (33.4)	25329 (30.2)	< 0.001
Dyslipidaemia, n (%)	40898 (41.1)	35238 (40.5)	0.003	1772 (30.2)	645 (19.6)	0.000	39126 (41.8)	34593 (41.3)	0.02
Smoking, n (%)	39953 (40.2)	8504 (9.8%)	< 0.001	3016 (51.3)	1392 (42.3)	0.000	36937 (39.5)	7112 (8.5%)	< 0.001
Cannabis, n (%)	683 (0.7%)	89 (0.1%)	< 0.001	334 (5.7%)	64 (1.9%)	0.000	349 (0.4%)	25 (0%)	< 0.001
Cocaine, n (%)	764 (0.8%)	101 (0.1%)	< 0.001	411 (7%)	70 (2.1%)	0.000	353 (0.4%)	31 (0%)	< 0.001
Enolism, n (%)	10806 (10.9)	967 (1.1%)	< 0.001	763 (13%)	101 (3.1%)	0.000	10043 (10.7)	866 (1%)	< 0.001
Hypothyroidism, n (%)	2417 (2.4%)	7814 (9%)	< 0.001	100 (1.7%)	229 (7%)	0.000	2317 (2.5%)	7585 (9.1%)	< 0.001
Hyperthyroidism, n (%)	463 (0.5%)	1053 (1.2%)	< 0.001	29 (0.5%)	34 (1%)	0.003	434 (0.5%)	1019 (1.2%)	< 0.001
Cancer diagnosis, n (%)	5393 (5.4%)	3038 (3.5%)	< 0.001	65 (1.1%)	78 (2.4%)	0.000	5328 (5.7%)	2960 (3.5%)	< 0.001
Obesity, n (%)	7167 (7.2%)	7693 (8.8%)	< 0.001	672 (11.4%)	435 (13.2)	0.012	6495 (6.9%)	7258 (8.7%)	< 0.001
Ischemic heart disease, n (%)	13159 (13.2)	6728 (7.7%)	< 0.001	316 (5.4%)	142 (4.3%)	0.025	12843 (13.7)	6586 (7.9%)	< 0.001
Atrial fibrillation, n (%)	23869 (24%)	30556 (35.1)	< 0.001	252 (4.3%)	95 (2.9%)	0.001	23618 (25.3)	30461 (36.4)	< 0.001
Non-congenital cardiomyopathy, n (%)	2622 (2.6%)	1296 (1.5%)	< 0.001	185 (3.1%)	55 (1.7%)	0.000	2437 (2.6%)	1241 (1.5%)	< 0.001
Dilated cardiomyopathy, n (%)	1411 (1.4%)	472 (0.5%)	< 0.001	96 (1.6%)	18 (0.5%)	0.000	1315 (1.4%)	454 (0.5%)	< 0.001
Enolitic cardiomyopathy, n (%)	153 (0.2%)	7 (0%)	< 0.001	14 (0.2%)	0 (0%)	0.005	139 (0.1%)	7 (0%)	< 0.001
Heart failure, n (%)	4413 (4.4%)	6411 (7.4%)	< 0.001	74 (1.3%)	29 (0.9%)	0.10	4339 (4.6%)	6382 (7.6%)	< 0.001
Valvulopathy (all), n (%)	4726 (4.8%)	6233 (7.2%)	< 0.001	101 (1.7%)	84 (2.6%)	0.006	4625 (4.9%)	6149 (7.3%)	< 0.001
Valvulopathy (non-rheumatic), n (%)	3055 (3.1%)	3165 (3.6%)	< 0.001	52 (0.9%)	35 (1.1%)	0.39	3003 (3.2%)	3130 (3.7%)	< 0.001
Valvulopathy (rheumatic), n (%)	1823 (1.8%)	3323 (3.8%)	< 0.001	51 (0.9%)	53 (1.6%)	0.001	1772 (1.9%)	3270 (3.9%)	< 0.001
PFO, n (%)	1293 (1.3%)	931 (1.1%)	< 0.001	562 (9.6%)	382 (11.6)	0.002	731 (0.8%)	549 (0.7%)	0.002
Chronic renal failure, n (%)	10219 (10.3)	10002 (11.5)	< 0.001	156 (2.7%)	52 (1.6%)	0.001	10063 (10.8)	9950 (11.9)	< 0.001
COPD, n (%)	8629 (8.7%)	1926 (2.2%)	< 0.001	36 (0.6%)	19 (0.6%)	0.835	8593 (9.2%)	1907 (2.3%)	< 0.001
OSA, n (%)	5873 (5.9%)	2089 (2.4%)	< 0.001	318 (5.4%)	48 (1.5%)	0.000	5555 (5.9%)	2041 (2.4%)	< 0.001
Intracranial atherosclerosis, n (%)	4216 (4.2%)	3104 (3.6%)	< 0.001	122 (2.1%)	33 (1%)	0.000	4094 (4.4%)	3071 (3.7%)	< 0.001
<i>Unusual causes</i>									
Fibromuscular dysplasia, n (%)	14 (0%)	22 (0%)	0.08	6 (0.1%)	8 (0.2%)	0.097	8 (0%)	14 (0%)	0.124
Arterial dissection (all), n (%)	706 (0.7%)	282 (0.3%)	< 0.001	279 (4.7%)	122 (3.7%)	0.020	427 (0.5%)	160 (0.2%)	< 0.001
Arterial dissection intracranial, n (%)	48 (0%)	29 (0%)	0.11	23 (0.4%)	9 (0.3%)	0.359	25 (0%)	20 (0%)	0.706
Arterial dissection (carotid), n (%)	441 (0.4%)	178 (0.2%)	< 0.001	148 (2.5%)	74 (2.3%)	0.422	293 (0.3%)	104 (0.1%)	< 0.001
Arterial dissection (vertebral), n (%)	223 (0.2%)	79 (0.1%)	< 0.001	110 (1.9%)	41 (1.2%)	0.024	113 (0.1%)	38 (0%)	< 0.001
Thrombophilia, n (%)	603 (0.6%)	508 (0.6%)	0.516	127 (2.2%)	134 (4.1%)	0.000	476 (0.5%)	374 (0.4%)	0.057
Vasospasm, n (%)	42 (0%)	46 (0.1%)	0.29	7 (0.1%)	13 (0.4%)	0.007	35 (0%)	33 (0%)	0.833
Systemic vasculitis (all), n (%)	157 (0.2%)	201 (0.2%)	< 0.001	11 (0.2%)	14 (0.4%)	0.036	146 (0.2%)	187 (0.2%)	0.001
Moyamoya disease, n (%)	15 (0%)	17 (0%)	0.466	4 (0.1%)	9 (0.3%)	0.012	11 (0%)	8 (0%)	0.653
Sick cell disease, n (%)	6 (0%)	11 (0%)	0.137	2 (0%)	6 (0.2%)	0.021	4 (0%)	5 (0%)	0.618
Endocarditis, n (%)	116 (0.1%)	88 (0.1%)	0.308	10 (0.2%)	6 (0.2%)	0.893	106 (0.1%)	82 (0.1%)	0.318
Cardiac prosthesis infection, n (%)	178 (0.2%)	157 (0.2%)	0.950	9 (0.2%)	15 (0.5%)	0.006	169 (0.2%)	142 (0.2%)	0.573
<i>In-hospital complications</i>									
Brain herniation, n (%)	494 (0.5%)	559 (0.6%)	< 0.001	49 (0.8%)	38 (1.2%)	0.128	445 (0.5%)	521 (0.6%)	< 0.001
Seizures, n (%)	546 (0.5%)	641 (0.7%)	< 0.001	25 (0.4%)	21 (0.6%)	0.166	521 (0.6%)	620 (0.7%)	< 0.001
Acute coronary syndrome n (%)	428 (0.4%)	351 (0.4%)	0.359	14 (0.2%)	12 (0.4%)	0.274	414 (0.4%)	339 (0.4%)	0.219
Urinary tract infection, n (%)	4124 (4.1%)	9474 (10.9%)	< 0.001	89 (1.5%)	118 (3.6%)	0.000	4035 (4.3%)	9356 (11.2%)	< 0.001
Acute renal failure, n (%)	3524 (3.5%)	3210 (3.7%)	0.103	75 (1.3%)	20 (0.6%)	0.002	3449 (3.7%)	3190 (3.8%)	0.185
Bronchoaspiration, n (%)	3880 (3.9%)	3813 (4.4%)	< 0.001	63 (1.1%)	21 (0.6%)	0.037	3817 (4.1%)	3792 (4.5%)	< 0.001

Pneumonia, n (%)	1387 (1.4%)	1112 (1.3%)	0.027	25 (0.4%)	9 (0.3%)	0.251	1362 (1.5%)	1103 (1.3%)	0.012
Outcome									
In-hospital mortality, n (%)	10133 (10.2%)	13430 (15.4%)	<0.001	168 (2.9%)	85 (2.6%)	0.441	9965 (10.7%)	13345 (15.9%)	<0.001

PFO: Patent foramen oval, COPD: Chronic obstructive pulmonary disease; OSAH: Obstructive sleep apnea-hypopnea syndrome.

Table S4. Prevalence of vascular risk factors in general population by sex and age group (health survey 2014).

Comorbidity, n (%)	≥ 18 (all)			18-50 (young)			> 50 (old)		
	All (22321)	Men (10297)	Women (12024)	All (10669)	Men (5224)	Women (5445)	All (11652)	Men (5073)	Women (6579)
HBP	6023 (27%)	2675 (26%)	3348 (27.8%)	911 (8.5%)	514 (9.8%)	397 (7.3%)	5112 (43.9%)	2161 (42.6%)	2951 (44.9%)
Dyslipidemia	5166 (23.2%)	2310 (22.5%)	2856 (23.8%)	1026 (9.6%)	650 (12.5%)	376 (6.9%)	4140 (35.6%)	1660 (32.9%)	2480 (37.8%)
Diabetes Mellitus	1956 (8.8%)	942 (9.2%)	1014 (8.4%)	191 (1.8%)	103 (2%)	88 (1.6%)	1765 (15.2%)	839 (16.6%)	926 (14.1%)
Smoking	4787 (21.4%)	2629 (25.5%)	2158 (17.9%)	3096 (29%)	1705 (32.6%)	1391 (25.5%)	1691 (14.5%)	924 (18.2%)	767 (11.7%)
Excessive enolic intake	8195 (36.7%)	5304 (51.5%)	2891 (24%)	3891 (36.5%)	2470 (47.3%)	1421 (26.1%)	4304 (36.9%)	2834 (55.9%)	1470 (22.3%)
Obesity (BMI > 30)	2794 (13.7%)	1299 (13.6%)	1495 (13.8%)	943 (9.3%)	516 (10.4%)	427 (8.3%)	1851 (18%)	783 (17.1%)	1068 (18.7%)
Ischemic heart disease	929 (4.2%)	580 (5.6%)	349 (2.9%)	60 (0.6%)	44 (0.8%)	16 (0.3%)	869 (7.5%)	536 (10.6%)	333 (5.1%)