ORIGINAL ARTICLE

Arterial Hypertension and Risk of Recurrent Event in Young Ischemic Stroke Patients

Petra Divišová, Daniel Šaňák, Jan Václavík, Michal Král, Martin Hutyra, Jana Zapletalová, Andrea Bártková, David Franc, Tomáš Dorňák, Tomáš Veverka, Miloš Táborský, Petr Kaňovský

ABSTRACT: ***Introduction:*** In young patients, the cause of ischemic stroke (IS) remains often cryptogenic despite presence of traditional vascular risk factors (VRFs). Since arterial hypertension (AH) is considered the most important one, we aimed to evaluate the impact of AH and blood pressure (BP) levels after discharge on risk of recurrent IS (RIS) in young patients. ***Methods:*** The study set consisted of acute IS patients < 50 years of age enrolled in the prospective Heart and Ischemic STrOke Relationship studY registered on ClinicalTrials.gov (NCT01541163). Cause of IS was assessed according to the ASCOD classification. ***Results:*** Out of 319 enrolled patients <50 years of age (179 males, mean age 41.1 ± 7.8 years), AH was present in 120 (37.6%) of them. No difference was found in the rates of etiological subtypes of IS between patients with and without AH. Patients with AH were older, had more VRF, used more frequently antiplatelets prior IS, and had more RIS (10 vs. 1%, $p = 0.002$) during a follow-up (FUP) with median of 25 months. Multivariate logistic regression stepwise model showed the prior use of antiplatelets as only predictor of RIS ($p = 0.011$, OR: 6.125; 95% CI: 1.510–24.837). Patients with elevated BP levels on BP Holter 1 month after discharge did not have increased rate of RIS during FUP (3.8 vs. 1.7%, $p = 1.000$). ***Conclusion:*** AH occurred in 37.6% of young IS patients. Patients with AH had more frequently RIS. Prior use of antiplatelets was found only predictor of RIS in young IS patients with AH.

RÉSUMÉ : Hypertension artérielle et risque de récurrence chez des patients âgés de moins de 50 ans qui ont été victimes d'un accident ischémique. ***Introduction*** **:** Chez les patients âgés de moins de 50 ans, l'étiologie des accidents ischémiques (AI) demeure souvent indéterminée malgré la présence de facteurs de risque vasculaire (FRV) traditionnels. Compte tenu que l'hypertension artérielle (HA) est considérée comme le facteur de risque le plus important, nous avons cherché à évaluer son impact ainsi que l'impact des valeurs de pression artérielle sur le risque de récurrence des AI une fois que des patients ont obtenu leur congé. ***Méthodes*** **:** Cette étude a reposé sur un groupe de patients âgés de moins de 50 ans ayant été victimes d'un AI aigu. Ces patients avaient été inclus préalablement dans une étude prospective (*Heart and Ischemic Stroke Relationship Study* ou HISTORY) enregistrée sur le site ClinicalTrials.gov (NCT01541163). Précisons que la cause des AI a été évaluée en fonction du système de classification ASCOD. ***Résultats*** **:** Sur un total de 319 patients âgés de moins de 50 ans (179 de sexe masculin ; âge moyen : 41,1 ± 7,8 ans), 37,6 % d'entre eux (n = 120) avaient été victimes d'un AI. Aucune différence n'a été constatée entre les patients souffrant d'HA et les autres n'en souffrant pas en ce qui regarde les taux de sous-types étiologiques des AI. Outre un risque de récurrence d'AI plus élevé (10 % contre 1% ; $p = 0{,}002$), les patients souffrant d'HA et rencontrés lors d'un suivi médian 25 mois plus tard étaient plus âgés, donnaient à voir plus de FRV et utilisaient davantage d'antiagrégants plaquettaires (AAP) avant leur AI. Un modèle de régression logistique multivariée par étapes (*multivariate logistic regression stepwise model*) a montré que l'utilisation antérieure d'AAP ne permettait que de prédire le risque de récurrence des AI ($p = 0{,}011$; RC : 6,125 ; IC 95 % 1,510-24,837). Les patients dont les valeurs de pression artérielle mesurées avec un appareil Holter étaient élevées un mois après leur congé n'ont pas montré un risque de récurrence des AI plus élevé au moment de leur suivi (3,8 % contre 1,7 % ; $p = 1{,}000$). ***Conclusion*** **:** Des manifestations d'HA ont été notées chez 37,6 % des patients à l'étude. Ces derniers ont aussi montré un plus grand risque de récurrence des AI. En somme, une utilisation antérieure d'AAP est apparue comme le seul prédicteur du risque de récurrence des AI chez des patients âgés de moins de 50 ans victimes d'un AI et souffrant d'HA.

Keywords: Young ischemic stroke, Arterial hypertension, Stroke recurrence, Secondary prevention, Vascular risk factors

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Introduction

Arterial hypertension (AH) is the most important risk factor for stroke and occurs approximately in 70% of ischemic stroke (IS) patients[1] and most IS patients have elevated blood pressure (BP) at stroke onset.[2] Current evidence shows a strong positive association between a reduction of BP and risk of recurrent IS (RIS).[3–5]

From the Comprehensive Stroke Center, Department of Neurology, Palacký University Medical School and Hospital, Olomouc, Czech Republic (PD, DS, MK, AB, DF, TD, TV, PK); Department of Cardiology, Palacký University Medical School and Hospital, Olomouc, Czech Republic (JV, MH, MT); and Department of Biophysics and statistics, Palacký University Medical School, Olomouc, Czech Republic (JZ)

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Correspondence to: Daniel Šaňák, MD, PhD, FESO, Comprehensive Stroke Center, Department of Neurology, Palacký Medical School and University Hospital, I. P. Pavlova 6, 77520 Olomouc, Czech Republic. E-mail: daniel.sanak@centrum.cz

The incidence of IS among young adults increases as reported recent studies[6–8] and represents approximately 20% of all IS.[9–13] A cause of IS in young patients remains often unclear or differ from elderly patients,[13–15] but one-third of them may be affected by a recurrent vascular event.[16–18] Furthermore, traditional vascular risk factors (VRFs) including AH becoming more prevalent in young IS patients during the last years, especially in those with unhealthy life style.[14,19] This corresponds to the more than twice increased prevalence of AH in the common young adult population during the last 20 years.[20]

Data about AH in young IS patients and about antihypertensive treatment in secondary prevention are limited, since few of them were enrolled in clinical trials or studies. A recent retrospective registry-based study showed that young IS patients, users of antihypertensives, had a lower risk of RIS and mortality compared to the non-users.[21] Another study showed that higher admission systolic and diastolic BP were independently associated with the risk of RIS, while 24-hour BP levels were not.[2]

We aimed to assess prospectively the incidence of AH in young IS patients and evaluate the impact of BP compensation after patients' discharge on the risk of RIS using outpatient BP Holter. Furthermore, we aimed to analyze possible associations among the presence of AH and poor BP compensation after discharge and presence of other risk factors and conditions.

Subjects and Methods

We analyzed consecutive young IS patients <50 years of age, who were enrolled in the prospective single-center observational Heart and Ischemic STrOke Relationship studY (HISTORY) registered on ClinicalTrials.gov (identifier NCT01541163) between years 2011 and 2019.[22] The study protocol was published in detail previously,[22] and thus, we present here a part, which was essential for this study.

All enrolled patients underwent an identical diagnostic protocol, which involved computed tomography (CT) or magnetic resonance imaging (MRI) including CT or MRI angiography, ultrasound of cervical and cerebral arteries, transoesophageal echocardiography (TEE) with the use of contrast agent for a bubble test, ultrasound of veins of both upper and lower limbs in patients with the TEE finding of right–left shunt to exclude present or previous deep vein thrombosis.[23] In all patients without presence of AF at the admission or during a hospital stay at stroke unit, a 24-hour electrocardiogram (ECG) Holter and 3- or 4-week ECG Holter monitoring were performed.

A 3-month clinical outcome was assessed by an experienced certified neurologist and using the modified Rankin Scale with a score of 0–2 for a good outcome. All patients used antiplatelets or anticoagulants in the secondary prevention according to the stroke etiology. Most enrolled patients were followed through a clinical or phone controls at least once a year in the follow-up (FUP).

Causes of strokes were classified and graded according to the ASCOD classification.[24] All patients with the ASCOD score other than "grade 1" (potentially causal) were classified as cryptogenic.[24]

AH was defined according to the World Health Organization criteria.[25] All patients had admission BP measurement (emergency room) followed with regular measurements performed each hour during the stay at stroke intensive care unit (at least the first 24 hours). BP measurements continued in a regimen of regular three measurements per day during the remaining hospital stay. All BP measurements were performed by a fully automatic arm BP monitors in the laying patient.

Outpatient BP Holter (Spacelabs™ model 90217A) was performed 1 month after the discharge in consecutive young IS patients between the years 2017 and 2019. The evaluation and interpretation of recorded levels of BP were done by a blinded experienced and certified cardiologist in the Center for Hypertension affiliated to Department of Cardiology in our hospital.

The study protocol was in a compliance with the Declaration of Helsinki (1975) and was approved by the Ethical Committee of our hospital. All patients gave an informed consent to participate in the study.

Statistical analysis SPSS software (version 22.0; SPSS, Chicago, Illinois) was used for the statistical analysis. Normality of distribution was checked using the Shapiro–Wilk test. All parameters with non-normal distributions are presented as means ± SD, medians, and interquartile ranges. The Mann–Whitney test was used for non-parametric values, and the chi-square test and Fisher's exact test were used for parametric values. Univariable and multivariable logistic regression analyses (LRA) were used to evaluate analyzed demographic, baseline and clinical parameters, and VRFs as possible predictors of RIS in patients with AH. Multivariate regression stepwise model was adjusted for potential confounders. All tests used an α-level of 0.05 for significance.

Results

We enrolled 319 young IS patients <50 years of age (179 males, mean age 41.1 ± 7.8 years) in the prospective HISTORY between years 2011 and 2019 and 229 (71.8%) of them were classified as cryptogenic according to ASCOD. Patients' demographic, baseline, and clinical characteristics are shown in Table 1. AH was present in 120 (37.6%) of IS patients and 75 (62.5%) of them used antihypertensives.

Patients with AH had more frequently RIS during the FUP with a median of 25 months (10 vs. 1%, $p = 0.002$) (Table 1), were older (44.1 ± 6.0 vs. 39.8 ± 8.1 years, $p < 0.0001$), had more frequently diabetes mellitus (14.2 vs. 2.0%, $p < 0.0001$), hyperlipidemia (56.7 vs. 27.1%, $p < 0.0001$), atherosclerotic (AS) changes in carotid arteries (42.5 vs. 17.6%, $p < 0.0001$), more frequently smoked (45.0 vs. 30.2%, $p = 0.006$), and used more frequently antiplatelets prior IS (10.8 vs. 2.5%, $p = 0.002$) (Table 1). Patients with AH had also higher admission systolic and diastolic BP, higher admission glycemia, total and LDL cholesterol, and had more frequently elevated serum troponin T at admission (Table 1). More patients with AH died within the first 3 months after IS (4.2 vs. 0.5%, $p = 0.030$) (Table 1). Number of patients with cryptogenic stroke did not differ between patients with and without AH, as well as the other etiological stroke subtypes (Table 1).

Patients with AH and RIS were older (47.3 ± 3.4 vs. 43.6 ± 5.9 years, $p = 0.005$), more frequently used antiplatelets prior IS (33.3 vs. 8.3%, $p = 0.026$), had higher admission glycemia (6.8 vs. 6.0 mmol/L, $p = 0.022$), and had more frequently the etiological stroke subtype "large vessels disease" according to ASCOD classification (16.7 vs. 0%, $p = 0.009$) (Table 2).

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Table 1: Comparison of demographic, baseline clinical characteristics and outcomes between patients with and without AH

	Patients with AH	Other patients	*p*
N	120	199	
Males (n, %)	70 (58.3)	109 (54.8)	0.481
Age (year, mean ± SD)	44.1 ± 6.0	39.8±8.1	<0.0001
IS in anterior circulation (n, %)	90 (75.0)	139 (69.8)	0.266
IHD (n, %)	6 (5.0)	1 (0.5)	0.182
DM (n, %)	17 (14.2)	4 (2.0)	<0.0001
Hyperlipidemia (n, %)	68 (56.7)	54 (27.1)	<0.0001
BMI ≥25 (n, %)	93 (77.5)	106 (53.3)	<0.0001
Obesity (BMI > 30, n, %)	49 (40.8)	27 (13.6)	<0.0001
AS changes in carotid arteries (n, %)	51 (42.5)	35 (17.6)	<0.0001
Smoking (n, %)	54 (45.0)	60 (30.2)	0.006
Prior use of antiplatelets (n, %)	13 (10.8)	5 (2.5)	0.002
Admission NIHSS (median, range)	4 (1–35)	4 (1–37)	0.325
Cryptogenic IS (n, %)	89 (74.2)	140 (70.4)	0.309
Cardio-embolic IS (n, %)	12 (10.0)	24 (12.1)	0.666
Large vessels disease IS (n, %)	2 (1.7)	3 (1.5)	1.000
Small vessels disease IS (n, %)	3 (2.5)	0	0.052
Arterial dissection IS (n, %)	7 (5.8)	15 (7.5)	0.561
IV thrombolysis (n, %)	35 (29.2)	78 (39.2)	0.078
Mechanical thrombectomy (n, %)	17 (14.2)	41 (20.6)	0.158
Admission SBP (mm Hg, median)	150	136	<0.0001
Admission DBP (mm Hg, median)	88	80	<0.0001
Admission GLY (median, range, mmol/L)	6.1 (3.7–29.4)	5.7 (3.7–21.0)	0.008
Total CH (median, range, mmol/L)	4.8 (2.9–8.2)	4.5 (1.0–8.3)	0.002
LDL-CH (median, range, mmol/L)	2.8 (0.8–6.6)	2.4 (0.5–4.9)	0.003
NT-pro BNP > 125 ng/L (n/N[a], %)	39/97 (40.2)	48/150 (32.0)	0.208
Troponin > 14 ng/L (n/N[a], %)	13/104 (12.5)	5/170 (2.9)	0.002
Three-month clin. outcome (mRS, median)	0	0	0.029
Good 3-month clin. outcome (mRS 0–2)	98 (81.7)	177 (88.9)	0.103
Three-month mortality (n, %)	5 (4.2)	1 (0.5)	0.030
Follow-up (median, range, months)	25 (1–106)	23 (1–121)	0.104
Recurrent IS (n, %)	12 (10.0)	2 (1.0)	0.002

AH = arterial hypertension; AS = atherosclerotic; BMI = body mass index; CH = cholesterol; DBP = diastolic blood pressure; DM = diabetes mellitus; GLY = glycemia; IHD = ischemic heart disease; IS = ischemic stroke; IV = intravenous; mRS = modified Rankin Scale; NIHSS = National Institute of Health Stroke Scale; SBP = systolic blood pressure.

Univariate LRA showed age and prior use of antiplatelets as predictors of RIS in patients with AH (Table 3) and multivariate stepwise model showed the prior use of antiplatelets as only predictor of RIS ($p = 0.011$, OR: 6.125; 95% CI: 1.510–24.837).

Outpatient BP Holter 1 month after discharge was performed in 84 consecutive patients (39 males, mean age 42.8 ± 6.0 years) and elevated BP levels were detected in 26 (31.0%) of them (Table 4). Patients with abnormal BP levels after discharge on BP Holter were more frequently males, had more frequently AH (53.8 vs. 31.0%, $p = 0.047$) and higher admission diastolic BP, and had more frequently AS plaques in carotid arteries (50.0 vs. 24.1%, $p = 0.019$). The number of RIS did not differ between both subgroups (3.8 vs. 1.7%, $p = 1.000$) during FUP (Table 4).

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Table 2: Comparison of demographic, baseline clinical characteristics and outcomes between patients with AH and RIS and without RIS

	Patients with RIS	Other patients	*p*
N	12	108	–
Males (n, %)	8 (66.6)	63 (58.3)	0.759
Age (year, mean ± SD)	47.3 ± 3.4	43.6 ± 5.9	0.005
IS in anterior circulation (n, %)	11 (91.6)	80 (74.1)	0.289
IHD (n, %)	1 (8.3)	5 (0.5)	0.476
DM (n, %)	4 (33.3)	13 (12)	0.067
Hyperlipidemia (n, %)	7 (58.3)	63 (58.3)	1.000
BMI ≥25 (n, %)	12 (100)	81 (75.0)	0.067
Obesity (BMI > 30, n, %)	8 (66.7)	41 (38.0)	0.070
AS changes (n, %)	8 (66.7)	43 (39.8)	0.079
Smoking (n, %)	8 (66.7)	46 (42.6)	0.157
Prior use of antiplatelets (n, %)	4 (33.3)	9 (0.8)	0.026
Prior use of antihypertensives (n, %)	10 (83.3)	65 (60.1)	0.103
Admission NIHSS (median, range)	3 (1–15)	4 (1–35)	0.659
Cryptogenic IS (n, %)	7 (58.3)	82 (75.9)	0.294
Cardio-embolic IS (n, %)	1 (8.3)	11 (10.2)	1.000
Large vessels disease IS (n, %)	2 (16.7)	0	0.009
Small vessels disease IS (n, %)	0	3 (2.8)	1.000
Arterial dissection IS (n, %)	0	7 (6.5)	1.000
IV thrombolysis (n, %)	2 (16.7)	33 (30.6)	0.505
Mechanical thrombectomy (n, %)	0	17 (15.7)	0.212
Admission SBP (mm Hg, median)	160	150	0.469
Admission DBP (mm Hg, median)	90	88	0.746
Admission GLY (median, range, mmol/L)	6.8 (5.3–14.7)	6.0 (3.7–29.4)	0.022
Total CH (median, range, mmol/L)	4.9 (2.9–6.7)	4.7 (2.9–8.2)	0.562
LDL-CH (median, range, mmol/L)	2.7 (0.8–4.9)	2.8 (1.1–6.6)	0.670
NT-pro BNP > 125 ng/L (n/N[a], %)	3/10 (30.0)	36/87 (41.4)	0.735
Troponin > 14 ng/L (n/N[a], %)	2/11 (18.2)	11/93 (11.8)	0.625
Three-month clin. outcome (mRS, median)	1	0	0.473
Good 3-month clin. outcome (mRS 0–2)	9 (75)	90 (83)	0.439
Three-month mortality (n, %)	1 (8.3)	4 (3.7)	0.415
Follow-up (months, median)	26	24	0.103

AH = arterial hypertension; AS = atherosclerotic; BMI = body mass index; DBP = diastolic blood pressure; DM = diabetes mellitus; GLY = glycemia; IHD = ischemic heart disease; CH = cholesterol; IS = ischemic stroke; IV = intravenous; mRS = modified Rankin Scale; NIHSS = National Institute of Health Stroke Scale; RIS = recurrent ischemic stroke; SBP = systolic blood pressure.

Discussion

AH was present in 37.6% of young IS patients < 50 years of age in our study and this finding corresponds to previous report of presence of AH in 39.2% of young IS patients from the Helsinki Registry.[2] In our study, patients with AH had significantly more RIS during the FUP than those without AH (Table 1). The multicenter INTERSTROKE case-control study showed stronger association between AH and stroke in younger patients (< 45 years) than older (≥45 years).[26]

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Table 3: Univariate logistic regression analysis for identification of independent predictors of recurrent ischemic stroke; subgroup analysis of patients with AH

Variable	*p*	OR	95% CI
Age	0.040	1.277	1.010–1.614
IS in anterior circulation	0.792	1.066	0.661–1.718
IHD	0.582	1.873	0.200–17.50
DM	0.057	3.654	0.963–13.85
Hyperlipidemia	1.000	1.000	0.298–3.352
BMI ≥25	0.998	–	–
Obesity (BMI > 30)	0.069	3.220	0.911–11.37
AS changes in carotid arteries	0.090	2.977	0.843–10.50
Smoking	0.167	2.435	0.689–8.600
Cryptogenic IS	0.195	0.444	0.129–1.517
Cardio-embolic IS	0.840	0.802	0.094–6.813
Large vessels disease IS	0.999	–	–
Small vessels disease IS	0.999	–	–
Arterial dissection IS	0.999	–	–
Admission SBP (median)	0.675	1.006	0.979–1.032
Admission DBP (median)	0.663	0.990	0.945–1.036
Prior use of antiplatelets	0.016	5.500	1.382–21.87

AH = arterial hypertension; AS = atherosclerotic; BMI = body mass index; DBP = diastolic blood pressure; DM = diabetes mellitus; IHD ischemic heart disease; IS = ischemic stroke; IV = intravenous; mRS = modified Rankin Scale; SBP systolic blood pressure.

Table 4: Comparison of demographic, baseline clinical characteristics and outcomes between patients with elevated blood pressure on BP Holter and with normal levels

	Elevated BP	Normal BP	*p*
N	26	58	
Males (n, %)	19 (73.1)	20 (34.5)	0.001
Age (years, mean ± SD)	43.9±5.6	41.3±6.1	0.068
IS in anterior circulation (n, %)	18 (69.2)	39 (67.2)	0.857
AH (n, %)	14 (53.8)	18 (31.0)	0.047
IHD (n, %)	1 (3.8)	0	1.000
DM (n, %)	1 (3.8)	2 (3.4)	1.000
Hyperlipidemia (n, %)	11 (42.3)	23 (39.7)	0.819
Peripheral arterial disease (n, %)	0	0	–
BMI ≥25 (n, %)	13 (50.0)	36 (62.1)	0.300
Obesity (BMI > 30, n, %)	6 (23.1)	11 (19.0)	0.665
AS changes in carotid arteries (n, %)	13 (50.0)	14 (24.1)	0.019
Smoking (n, %)	14 (53.8)	19 (32.8)	0.067
Cryptogenic IS (n, %)	22 (84.6)	47 (81.0)	0.768
Admission SBP (mm Hg, median)	148	141	0.148
Admission DBP (mm Hg, median)	90	85	0.013
IV thrombolysis (n, %)	9 (34.6)	22 (37.9)	0.771
Mechanical thrombectomy (n, %)	4 (15.4)	9 (15.5)	1.000
Three-month clin. outcome (mRS, median)	0	0	0.170
Good 3-month clin. outcome (mRS 0–2)	25 (96.2)	58 (100)	0.310
Three-month mortality (n, %)	0	0	–
Follow-up (median, range, months)	15 (9–36)	15 (7–30)	0.352
Recurrent IS (n, %)	1 (3.8)	1 (1.7)	1.000
Patients on AH medication (n, %)	10 (38.5)	17 (29.3)	0.406

AH = arterial hypertension; AS = atherosclerotic; BMI = body mass index; BP, blood pressure; DBP = diastolic blood pressure; DM = diabetes mellitus; IHD = ischemic heart disease; IS = ischemic stroke; IV = intravenous; mRS = modified Rankin scale; SBP = systolic blood pressure.

In our study, patients with AH were older and have more VRFs including the presence of AS changes in carotid arteries and higher level of cholesterol than those without AH (Table 1). These findings may explain the higher frequency of RIS in young IS patients with AH and support the concept of "risk profile" in young IS patients, in whom the prevention is strongly needed. Accumulation of VRF with increasing age among young IS patients was associated with increased risk of atherothrombotic event in future[27] and more of VRF risk were associated with IS in those who were aged 40 to 49 years compared to those who were under 40 years.[28] Recent German nationwide case-control study in young IS patients showed that AH had the second highest adjusted population-attributable risk for IS among VRF.[29] Furthermore, pooled data from 15 hospital-based registries of young IS patients (15–49 years) showed increasing frequency of large vessels AS and small vessels disease with age and higher prevalence of these causes in men.[30]

In our study, patients with AH and RIS were older, more frequently used antiplatelets prior IS, and had higher admission glycemia in comparison with patients without RIS (Table 2). Age and prior use of antiplatelets were found only predictors of RIS in young IS patients with AH in our study in univariate LRA model (Table 3) and multivariate stepwise LRA model showed only the prior use of antiplatelets as predictor of RIS. These findings also support the concept of "risk profile" in young IS patients, who were treated with antiplatelets prior IS for the presence of VRF.

Most (74.2%) of our patients with AH had cryptogenic etiology of IS according to the ASCOD classification and the second most frequent (10%) cause was cardio-embolism

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(Table 1). Patients with AH and RIS had the large vessels disease (16.7%) as the second most frequent cause (after cryptogenic etiology) (Table 2), which was more frequent in comparison with the patients without RIS (0%) (Table 2). Higher frequency of large vessels disease as a cause of stroke in the young patients with AH, who suffered from RIS, may indicate the significant role of atherosclerosis and VRFs in stroke recurrence in these patients.

Elevated levels of BP on outpatient BP Holter 1 month after discharge were present in 31% of our patients (Table 4). Patients with abnormal outpatient BP Holter were older, had more frequently AH and AS changes in carotid arteries, but they had similar rate of RIS during the FUP as those with normal levels (Table 4). A recent report showed suboptimal use of antihypertensive medication in one-third of all young users after IS. Furthermore, young users of antihypertensive medication had lower risk of RIS and mortality compared to non-users after IS.[21]

In our study, 62.5% of patients with AH used antihypertensives prior IS. This rate corresponds to 59.6% of AH users – young IS patients enrolled in the Helsinki Young Stroke Registry.[21] The data from this registry showed a higher proportion of antihypertensive use and better usage in patients with higher age. Furthermore, the higher frequency of use of antihypertensives was associated with presence of VRF.[21]

Our study has limitations. Single-center design was used in our study and was based on the protocol of the prospective HISTORY.[22] A very low number of patients, who underwent the outpatient BP Holter 1 month after discharge, was analyzed and thus, the results of the comparison between the patients with normal and elevated levels of BP were very limited. We did not analyze clinically asymptomatic RIS detected on MRI because not all patients underwent control MRI during the FUP.

In conclusion, AH was frequent in young IS patients and its presence increased the risk of RIS in them, especially in those with presence of other VRF. Abnormal levels of BP on outpatient BP Holter after discharge did not increase the risk of RIS. Despite frequent unknown cause of IS in young patients, targeted prevention in those with AH and other VRF may reduce the IS recurrence.

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Conflict of Interest

All authors have no conflict of interest.

Statement of Authorship

PD and DS: study concept and design, acquisition of data, analysis and interpretation of data; drafting and critical revision of the manuscript for important intellectual content; and final approval of the version to be published. JV and MH: acquisition of data, responsibility for cardiologic part of study, and analysis and interpretation of BP values. JZ: statistical analysis and interpretation of analysis. MK, AB, DF, TD, and TV: acquisition of data and critical revision of the manuscript for important intellectual content. MT and PK: critical revision of the manuscript for important intellectual content.

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