Migraine and Cryptogenic Ischemic Stroke

Valentina Mazzoleni, MD,[1]
Mario Grassi, PhD,[2] Corrado Lodigiani, MD, PhD,[3]
Maurizia Rasura, MD,[4] Marialuisa Zedde, MD,[5]
Carlo Gandolfo, MD,[6] Andrea Zini, MD,[7]
Maria Luisa DeLodovici, MD,[8] Maurizio Paciaroni, MD,[9]
Massimo Del Sette, MD,[10] Antonella Toriello, MD,[11]
Rossella Musolino, MD,[12] Rocco Salvatore Calabrò, MD,[13] Paolo Bovi, MD,[14] Alessia Giossi, MD,[15]
Alessandro Adami, MD,[16] Giorgio Silvestrelli, MD,[17]
Anna Cavallini, MD,[18] Simona Marcheselli, MD,[19]
Domenico Marco Bonifati, MD,[20]
Nicoletta Checcarelli, MD,[21] Lucia Tancredi, MD,[22]
Alberto Chiti, MD,[23] Elisa Giorli, MD,[24]
Debora Pezzini, MD,[1] Martina Locatelli, MD,[1]
Sonia Bonacina, MD,[1] Giacomo Giacalone, MD,[25]
Giorgio Dalla Volta, MD,[26] Mauro Magoni, MD,[27]
Paolo Cerrato, MD,[28] Valeria Bignamini, MD,[29]
Giuseppe Micieli, MD,[30] Maurizio Melis, MD,[31]
Sandro Sanguigni, MD,[32] Massimiliano Braga, MD,[33]
Alessandro Padovani, MD, PhD,[1] and
Alessandro Pezzini, MD,[1]
Italian Project on Stroke in Young Adults Investigators

The available evidence on the relationship between migraine and cryptogenic ischemic stroke (CIS) is scarce. Hence, whether patients with CIS might be an appropriate target for studies on the link between migraine and cerebral ischemia is not definitively proven.

Using data from the international prospective multicenter case–control Searching for Explanations for Cryptogenic Stroke in the Young: Revealing the Etiology, Triggers, and Outcome (SECRETO) study, Martinez-Majander and coworkers recently

TABLE. ORs and 95% CIs from Conditional Logistic Regression on the Association between Migraine and Cryptogenic Ischemic Stroke

	Cases/Controls n (%)	OR (95% CI)[a]	OR (95% CI)[b]
Entire group			
No migraine	1,196 (73.3)/1,348 (83.0)	1	1
Any migraine	436 (26.7)/284 (17.0)	1.86 (1.56–2.22)	1.65 (1.37–1.99)
Migraine without aura	264 (16.4)/213 (12.9)	1.51 (1.23–1.85)	1.43 (1.15–1.78)
Migraine with aura	167 (10.4)/59 (3.6)	3.56 (2.59–4.89)	2.65 (1.90–3.70)
Men			
No migraine	684 (81.9)/776 (89.2)	1	1
Any migraine	152 (17.9)/94 (10.8)	1.85 (1.38–2.47)	1.50 (1.09–2.05)
Migraine without aura	89 (10.7)/69 (7.9)	1.41 (0.99–2.00)	1.22 (0.83–1.78)
Migraine with aura	62 (7.4)/25 (2.9)	3.23 (1.97–5.30)	2.31 (1.36–3.92)
Women			
No migraine	494 (63.8)/606 (77.7)	1	1
Any migraine	284 (36.3)/186 (23.5)	1.87 (1.48–2.35)	1.78 (1.40–2.27)
Migraine without aura	175 (22.6)/140 (17.9)	1.54 (1.18–2.01)	1.57 (1.19–2.07)
Migraine with aura	105 (13.6)/34 (4.4)	3.80 (2.50–5.78)	3.03 (1.96–4.67)

Although age was a criterion for matching, the cases were, on average, 2.1 years older than the controls, which resulted in a small but significant age effect. Thus, all multivariate analyses were adjusted for age. Interaction between migraine and sex as well as between migraine and cardiac interatrial right-to-left shunt were studied including interaction terms in the model. Thirty-six cases had missing data in the variable "any migraine"; 70 participants (58 cases and 12 control subjects) had missing data in the variables "migraine without aura" and "migraine with aura."

[a]Adjusted for hypertension, diabetes, hypercholesterolemia, and current smoking.

[b]Adjusted for hypertension, diabetes, hypercholesterolemia, current smoking, and cardiac right-to-left shunt.

CI = confidence interval; OR = odds ratio.

showed that migraine, especially the subtype with aura (MA), was associated with CIS in both women and men, independently of concomitant vascular risk factors and patent foramen ovale.[1] Because of their potential implications for future research, we think these findings should be confirmed and expanded in independent datasets, to increase evidence of the association of migraine with CIS. We, therefore, analyzed data from 1,668 patients with first-ever CIS aged 18 to 45 years, as part of the multicenter prospective Italian Project on Stroke in Young Adults (IPSYS), and 1,668 control subjects with no known history of vascular diseases, matched with cases by age (±3 years), sex, and ethnic background, selected from the staff members of participating hospitals. The recruitment period was January 2000 through December 2018. CISs were defined as cerebral infarcts that did not meet the criteria for a defined etiologic category, according to an etiological classification based on the Trial of Org 10172 in Acute Stroke Treatment criteria, accommodated and validated for stroke in the young.[2] All participants underwent cardiac interatrial right-to-left shunt (RLS) assessment by transcranial Doppler sonography with intravenous injection of agitated saline.[2] We performed logistic regression analyses and calculated odds ratios (ORs) with 95% confidence intervals with adjustment for potentially disease-modifying variables.

Our findings confirmed the association between migraine and CIS (Table). Although in sensitivity analyses the strength of the association was greater for women and for MA, we did not find interaction between sex and migraine (p for interaction = 0.800) or its subtypes. Migraine without aura (MO) turned out to be associated with CIS both in the entire group and in the subgroup of women. Finally, although findings did not change significantly when cardiac RLS was entered into the model (see Table), this interatrial anomaly had significant interaction with both migraine and MA (p for interaction = 0.018 and 0.001, respectively).

Strengths of our study are the large number of participants, the high level of data completeness, the extensive diagnostic workup, and the diagnosis of migraine made by neurologists on the basis of accepted, validated criteria, which likely reduced misclassification bias.

To sum up, in line with Martinez-Majander and coworkers, we strongly supported the evidence of association between migraine and CIS, especially for the subtype MA and for women, using a different, large, prospective, multicenter, countrywide dataset. Unlike the SECRETO study, which was probably underpowered to detect weak effects, we also found association between MO and CIS, and, in line with some recent studies,[3,4] interaction between RLS and both migraine and MA.

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Author Contributions

V.M. and A.Pe. contributed to the conception and design of the study; all authors contributed to the acquisition and analysis of data; V.M. and A.Pe. contributed to drafting the text.

Potential Conflicts of Interest

Nothing to report.

[1] *Department of Clinical and Experimental Sciences, Neurological Clinic, University of Brescia, Brescia, Italy*
[2] *Department of the Nervous System and Behavior Sciences, Unit of Medical and Genomic Statistics, University of Pavia, Pavia, Italy*
[3] *Thrombosis and Hemorrhagic Diseases Center, IRCCS Humanitas Clinical and Research Hospital, Rozzano-Milan, Italy*
[4] *Stroke Unit, Saint Andrea Hospital, La Sapienza University, Rome, Italy*
[5] *SC Neurology, Arcispedale Santa Maria Nuova–IRCCS, Reggio Emilia, Italy*
[6] *Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, and Maternal–Child Sciences, University of Genoa, Genoa, Italy*
[7] *IRCCS Institute of Neurological Sciences of Bologna, UOC Neurology and Metropolitan Stroke Network, Maggiore Hospital, Bologna, Italy*
[8] *Neurology Unit, di Circolo Hospital, University of Insubria, Varese, Italy*
[9] *Stroke Unit, Division of Cardiovascular Medicine, University of Perugia, Perugia, Italy*
[10] *SC Neurology, Galliera Hospital, Genoa, Italy*
[11] *UOC Neurology, San Giovanni e Ruggi d'Aragona, University of Salerno, Salerno, Italy*
[12] *Department of Neuroscience, Psychiatric and Anesthesiology Sciences, Neurological Clinic, University of Messina, Messina, Italy*
[13] *IRCCS, Bonino-Pulejo "Neurolesi" University Hospital, Messina, Italy*
[14] *UO Neurology, Borgo Trento University Hospital, Verona, Italy*
[15] *UO Neurology, Istituti Ospitalieri, Cremona, Italy*
[16] *Stroke Center, IRCCS Sacro Cuore Don Calabria, Verona, Italy*
[17] *Stroke Unit, UO Neurology, Carlo Poma Hospital, Mantua, Italy*
[18] *Stroke Unit, IRCCS C. Mondino Foundation Institute, Pavia, Italy*
[19] *Emergency Neurology and Stroke Unit, IRCCS Humanitas Clinical and Research Hospital, Rozzano-Milan, Italy*
[20] *UOC Neurology, Cà Foncello Hospital, ULSS 9, Treviso, Italy*
[21] *UOC Neurology, Valduce Hospital, Como, Italy*
[22] *Neurological Clinic III, San Paolo University Pole, ASST Santi Paolo e Carlo, Milan, Italy*
[23] *Neurology, Azienda Ospedaliera Universitaria Pisana, Pisa, Italy*
[24] *Neurology Unit, Sant'Andrea Hospital, La Spezia, Italy*
[25] *Stroke Unit, UO Neurology Clinic, San Raffaele IRCCS, Milan, Italy*
[26] *UO Neurology, Città di Brescia Clinical Institute, Brescia, Italy*
[27] *Stroke Unit, Vascular Neurology, Spedali Civili, Brescia, Italy*
[28] *Department of Neuroscience, Stroke Unit, University of Torino, Torino, Italy*
[29] *Stroke Unit, UO Neurology, Santa Chiara Hospital, Trento, Italy*
[30] *Emergency Neurology, IRCCS C. Mondino Foundation Institute, Pavia, Italy*
[31] *Stroke Unit, G. Brotzu Hospital, Cagliari, Italy*
[32] *Department of Neurology, Madonna del Soccorso Hospital, San Benedetto del Tronto, Italy*

[33]*UOC Neurology, ASST Vimercate, Vimercate, Italy*

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