

Diagnostic challenges in bilateral thalamic infarction: national series of cases

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Abstract

Objective: To describe the acute care of patients with bilateral thalamic infarctions in primary and advanced stroke centers in different regions of Colombia. **Methods:** Multicenter retrospective descriptive study of a series of cases of patients with an imaging diagnosis of bilateral thalamic infarction, in Colombia. 14 hospitals located in seven cities of the country participated. **Results:** 28 cases were registered, the mean age was 66.8 years with 53.6% men and 96.3% had a favorable previous mRs (0-2). Mean NIHSS at admission was 14 points, the most frequent clinical presentation was altered mental status in 82.1%. The most compromised structure was the bilateral anterior region of the thalamus in 12 patients (42.85%). The most common etiology was undetermined cause (39.3%). 1 patient underwent reperfusion therapy with intravenous thrombolysis (3.6%). Mean hospital stay was 19 days. **Conclusions:** Bilateral thalamic infarcts are a diagnostic challenge in the emergency department, due to their low reported incidence and the variable clinical presentations, stroke and research centers should be strengthened to contribute to clinical outcomes.

Keywords: Altered level of consciousness. Posterior cerebral arteries. Stroke. Thalamus (MeSH).

Retos diagnósticos en el infarto talámico bilateral: serie nacional de casos

Resumen

Objetivo: Describir la atención aguda de pacientes con infartos bilaterales del tálamo en centros de atención primaria y avanzada de ataque cerebrovascular en diferentes regiones de Colombia. **Métodos:** Estudio descriptivo retrospectivo multicéntrico de serie de casos de pacientes con diagnóstico por imágenes de infarto talámico bilateral, en Colombia. Participaron 14 hospitales ubicados en siete ciudades del país. **Resultados:** Se registraron 28 casos, la edad promedio fue de

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66.8 años con un 53.6% género masculino; el 96.3% tenía un mRS previo favorable (0-2). La escala NIHSS al ingreso promedio de 14 puntos; la presentación clínica más frecuente fue el estado mental alterado en un 82.1%. La estructura más comprometida fue la región anterior bilateral del tálamo en 12 pacientes (42.85%). La etiología más común fue de causa indeterminada (39.3%). Un paciente recibió terapia de reperfusión con trombólisis intravenosa (3.6%). Estancia hospitalaria promedio de 19 días. **Conclusiones:** Los infartos talámicos bilaterales representan un desafío diagnóstico en el departamento de emergencias, debido a su baja incidencia reportada y la variabilidad en las presentaciones clínicas. Se debe fortalecer la capacidad de los centros de atención de ataques cerebrovasculares e investigación, para contribuir a los resultados clínicos.

Palabras clave: Alteración del nivel de conciencia. Arterias cerebrales posteriores. Accidente cerebrovascular. Tálamo (MeSH).

Introduction

The anatomical variant known as the Percheron artery originates from the posterior cerebral artery (PCA). Gerard Percherón described it in 1973 as a solitary common trunk arising from the proximal portion (P1 segment) of the PCA¹. Occlusion of this artery can lead to bilateral thalamic infarctions that may or may not involve the mesencephalon^{2,3}. This anatomical variation is present in 4-12% of the global population⁴ and represents 0.6% of vascular territories affected by ischemic cerebrovascular events^{2,5,6}.

Bilateral thalamic infarction, with or without mesencephalic involvement due to Percheron artery occlusion, can manifest with diverse symptoms. Seven clinical patterns have been previously described, including disturbances in consciousness, behavioral amnesic deterioration, aphasia or dysarthria, ocular movement disorders, motor deficits, cerebellar signs, and others. Among the others, a wide range of neurological and neuropsychological symptoms exists²⁻⁷, ranging from seizures² to hypersexuality. It is a rare and prevalent condition with diffuse symptoms depending on its pathological anatomy, often presenting a diagnostic challenge. There are limited case series reported in the literature from Latin America. Our objective is to describe the acute care of patients with bilateral thalamic infarctions in primary and advanced stroke centers in different regions of Colombia.

Methods

A multicenter retrospective descriptive case series study was conducted on patients diagnosed with Percheron artery infarction based on imaging findings. Cases were identified through a call from the vascular committee of the Colombian Association of Neurology to stroke centers between 2014 and 2021. Fourteen hospitals in seven cities (Bogotá, Medellín, Cali, Armenia, Cúcuta, Piedecuesta, and Rionegro) participated, with

data collection using a standardized format and manuscript development consent. Furthermore, the information was sourced from the hospital registry, subject to continuous and rigorous auditing processes.

Demographic variables included origin, age, gender, and cardiovascular risk factors (hypertension, diabetes, dyslipidemia, heart diseases, atrial fibrillation, and smoking). Other data collected encompassed hospital stay, intensive care unit (ICU) stay, hemorrhagic transformation, and pharmacological secondary prevention therapy at discharge. The severity of ischemic events was assessed using the National Institutes of Health Stroke Scale (NIHSS). Functional outcome at hospital discharge was evaluated using the modified Rankin Scale (mRS), considering a favorable outcome as ≤ 2 and unfavorable as ≥ 3 . As the participating centers were stroke centers, they included in their care protocol the follow-up of patients three months after the hospital discharge, through phone contact to assess functional outcomes using mRS. Symptom classification was based on Arauz et al., and Stamm et al.^{4,8} categories, including altered mental status, aphasia or dysarthria, ocular movement disorders, motor deficits, cerebellar signs, and others. Diagnosis of bilateral thalamic infarction secondary to Percheron artery occlusion was confirmed through non-contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI), and/or magnetic resonance angiography.

A univariate analysis was conducted to assess the characteristics of both numerical and categorical variables.; The normality of the variables was determined through the Shapiro-Wilk test and those with a $p > 0.05$ were considered to have a normal distribution and are presented with means and standard deviation, and those that are not normal are presented with median and interquartile ranges. For the statistical analysis, we utilized the SPSS version 21 program (IBM Corporation, USA). Measures of central tendency and descriptive statistics were computed to report the key demographic and clinical characteristics of the patients and the treatment times.

As this was a risk-free study with anonymous data, informed consent was not required. A non-systematic literature search on PubMed, LILACS, Clinical Key, and Google Scholar was conducted for result discussion, using keywords “Bilateral thalamic infarction” “Percheron artery” and “Percheron artery infarction.”

The only missing data were the 3-month follow-up of seven patients which were declared in limitations.

Results

A total of 28 cases of bilateral thalamic infarction were recorded in 14 hospitals across seven cities. The mean age was 66.8 years, and 53.6% of patients were male. Additional demographic characteristics are presented in [Table 1](#). Most cases were reported in Bogotá (42.9%) and Medellín (17.9%), with the majority in 2021 (67.9%). The most common comorbidity was hypertension (64.3%), followed by diabetes (57.1%), structural heart disease (25%), including reduced left ventricular ejection fraction (10.7%), patent foramen ovale (PFO) (7.1%), other atrial septal defects (3.6%), valvular diseases (3.6%), and atrial fibrillation (14.3%). Cigarette smoking was reported in four patients (14.3%). The hospital stay was 19 days, with a median of 10 days (IQR 2-140 days). In addition, 42.9% of patients were hospitalized in the ICU, and 10.7% in the emergency department throughout their hospitalization.

Categorizing the included patients, 96% showed a mRS status of 0-2 before the occurrence. On admission to the emergency department, patients had a median NIHSS score of 12 points (IQR 1-40). The most frequent clinical presentation was altered mental status in 82.1%, followed by ocular movement disorders in 39.3%, motor deficits in 10.71%, headache in 10.71%, and incontinence in 3.6%. No patients exhibited cerebellar signs. The majority of patients presented a combination of the previously described clinical manifestations (64.28%). One patient tested positive for SARS-CoV-2 infection using PCR (Polymerase Chain Reaction).

For the diagnosis of bilateral thalamic infarction, non-contrast CT was performed in 82.1% and cerebral MRI in 75%, with both neuroimaging modalities in 60.71% ([Fig. 1](#)). The most affected thalamic regions were the bilateral anterior regions in 42.85%, followed by bilateral medial regions in 21.42%. In 17.8% of patients, different regions were affected in the same patient, with one thalamus having anterior involvement and the other complete involvement. Complete bilateral involvement occurred in 7.14% of patients, and only one patient had posterior bilateral involvement (3.57%),

Table 1. Demographic and clinical characteristics

Characteristics	n (%)
Gender	
Male	15 (53.6)
Female	13 (46.4)
Age	67*
City	
Bogotá	12 (42.9)
Medellín	5 (17.9)
Rionegro	4 (14.3)
Cali	3 (10.7)
Piedecuesta	2 (7.1)
Cúcuta	1 (3.6)
Armenia	1 (3.6)
Diagnostic year	
2014	2 (7.1)
2016	1 (3.6)
2019	2 (7.1)
2020	4 (14.3)
2021	19 (67.9)
Medical background	
Hypertension	18 (64.3)
Diabetes mellitus	16 (57.1)
Atrial fibrillation	4 (14.3)
Cardiopathy	7 (25)
Smoking	4 (14.3)
Clinical manifestations	
Altered consciousness	24 (85.7)
Headache	2 (7.1)
Motor deficit	2 (7.1)
Dysarthria	1 (3.6)
NIHSS	12* IQR (1-40)
Hospitalization	
ICU	14 (50)
Ward	11 (39.3)
Emergency room	3 (10.7)
mRs Discharge	
Favorable (0-2)	11 (39.3)
Unfavorable (3-6)	17 (60.7)
mRs follow-up (90 days)	
Favorable (0-2)	13 (61.9)
Unfavorable (3-6)	8 (38.1)

*Median.

while another had medial region involvement (3.57%). The mesencephalon was compromised in 53.5% of patients, and the pons in 1 patient (3.6%).

Only one patient underwent intravenous thrombolysis as reperfusion therapy (3.6%). In all patients, stratification studies were performed to evaluate possible etiology of the stroke. Among the tests performed, there was echocardiography, carotid imaging, lipid profile laboratories, and hematologic profile. An undetermined cause

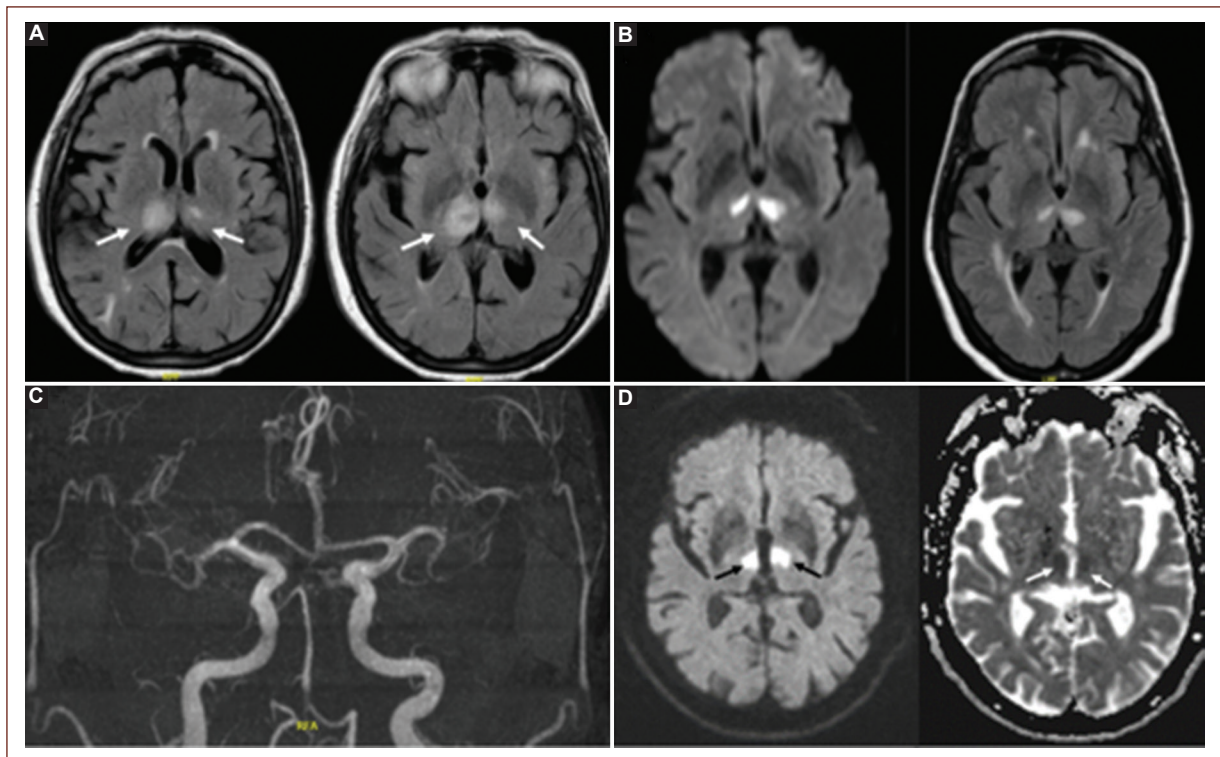


Figure 1. Bilateral thalamic infarction. **A:** asymmetric bilateral thalamic hyperintensity on FLAIR sequence. **B:** bilateral thalamic infarction in brain MRI with Time-of-Flight Angiography. **C:** percheron artery in MR angiography. **D:** restricted diffusion area at bilateral paramedian thalamic level with representation in ADC Maps sequence.

of stroke was identified in 39.3% of cases, 32.1% had a cardioembolic origin, 21.4% exhibited small vessel disease, and 7.1% demonstrated involvement of large vessels. Symptomatic hemorrhagic transformation occurred in 14.3% of patients. One patient underwent closure of a PFO (3.6%). At hospital discharge, 39.3% of patients had a favorable mRS, with a mortality rate of 17.9%. Follow-up at three months was conducted for 21 patients, with a favorable mRS reported in 61.9% (Table 2). As secondary prevention, patients were discharged with Acetyl Salicylic Acid (ASA) in 55.5% of cases, dual antiplatelet therapy (ASA plus clopidogrel) in 7.4%, and oral anticoagulants (direct-acting and VKA anticoagulants) in 11.1%.

Discussion

To the best of our knowledge, this retrospective case series is one of the largest reported in Colombia and Latin America (Table 2). While the prevalence of the Percheron artery remains unknown, it is estimated that this neurovascular variant could be present in up to 33% of the population (Fig. 2)⁹. Infarction of the Percheron

artery accounts for 0.1-2% of all ischemic strokes¹⁰. Bilateral thalamic infarctions are rare, occurring in 22-35% of all thalamic infarctions¹¹, with Percheron artery occlusion being responsible for 4-18% of this type of ischemic lesion^{10,12}.

In our series, the majority of reported cases were diagnosed in the cities of Bogotá and Medellín, reflecting the higher population density and concentration of academic centers with stroke programs compared to other regions in the country¹³. This facilitates greater access to imaging, the development of stroke care protocols, and increased diligence in stroke registries.

Clinical

The diagnosis of Percheron artery infarction has been a challenge due to its extensive clinical variability involving bilateral thalamic compromise with potential extension to the mesencephalon or pons. Occasionally, the irrigation of the rostral region of the mesencephalon depends on the paramedian peduncular artery, which may arise either from the paramedian thalamic artery itself or independently from the basilar artery.

Table 2. Percheron artery case series

Title	Authors	Year	Country	Number of patients
Clinical spectrum of artery of Percheron infarct: clinical-radiological correlations	Antonio Arauz, Hernán M. Patiño-Rodríguez, Juan C. Vargas-González, et al.	2013	México	15
Artery of Percheron Infarct: 12 cases and their complex clinical courses	Brian J. Stamm, Christina M. Lineback, Lesli E. Skolarus, et al.	2018	USA	12
Artery of Percheron infarction: imaging patterns and clinical spectrum	Lazzaro, Wright, Castillo, et al.	2010	USA	37
The time course of acute Percheron artery ischemic coma and imaging: a retrospective cohort study	Dao Ming Tong, Guo-Hong Liu, Yuan-Wri Wang, et al.	2020	China	93
Assessment of Percheron infarction in images and clinical findings	Zhuhua Xu, Lingling Sun, Yang Duan, et al.	2017	China	18

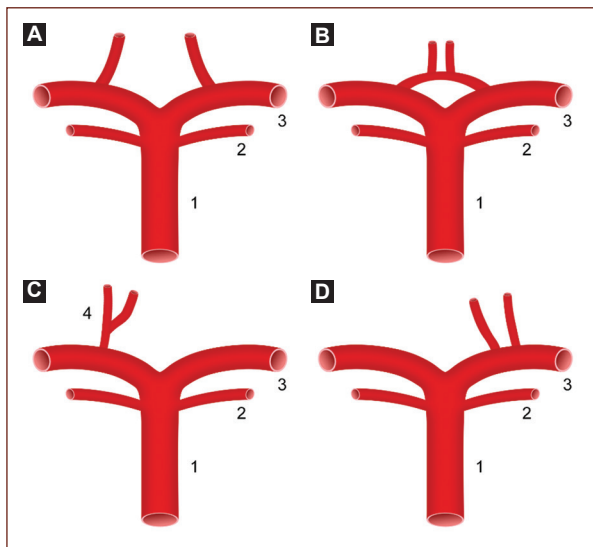


Figure 2. Anatomical variants of the thalamic paramedian arteries. 1. Basilar Artery. 2. Superior Cerebellar Artery. 3. Posterior Cerebral Artery (PCA). 4. Percheron Artery. **A:** paramedian arteries independent of the PCA (Usual). **B:** paramedian loop arteries. **C:** paramedian artery of Percheron (originates unilaterally in the P1 segment and then bifurcates, supplying the bilateral paramedian thalamus and rostral midbrain). **D:** both paramedian arteries originate from the P1 segment.

This variability explains the existence of thalamic infarctions without mesencephalic involvement and the possible asymmetry of mesencephalic extension in bilateral thalamic infarctions¹⁴. In our series, 53.5% of patients exhibited mesencephalic involvement, a percentage consistent with previous reports^{4,15}, while 3.6% showed extension to the pons.

On emergency admission, patients were assessed using the NIHSS scale, with an average of 12 points (IQR 1-40), comparable to the findings of Xu et al.'s case series¹⁶ and higher than that reported by Stamm et al.⁸, where an average of 7.3 points was recorded. Most patients presented altered mental status (82.1%), aligning with the analyses of Arauz et al., Saida et al., and Honig et al.^{4,12,23}, attributed to the involvement of the ascending reticular activating system^{16,17}, followed by ocular movement disorders (39.3%).

Within the patients with mesencephalic extension, 100% exhibited altered mental status, 75% had ocular abnormalities, 16.6% experienced motor disturbances, and 16.6% presented with hypoesthesia. The patient with pontine extension displayed an altered mental status characterized by somnolence and headache, presenting a less severe clinical picture than a previously reported case¹⁸, where stupor and pupil changes were observed.

Special cases

A patient with a history of diabetes mellitus and valvular heart disease, diagnosed with bilateral thalamic infarction and testing positive for COVID-19 during hospitalization, was recorded. This individual entered with a sudden coma, ineligible for reperfusion therapies. After 10 days in the ICU, the patient succumbed to pulmonary complications. Two case reports of patients with COVID-19 and Percheron artery infarction were found in the literature. In both instances, the patients were discharged with a favorable mRS. The patient in Wilson et al.'s case¹⁹ underwent thrombolytic therapy, while Pantovic et al.'s case²⁰ was managed with intrahospital anticoagulation due to the COVID-19 diagnosis.

The etiology of the infarction in one patient was attributed to a PFO. Closure of the PFO with an Amplatzer device was performed without complications, resulting in a favorable clinical outcome during follow-up. To the best of our knowledge, only one other published report of PFO and Percheron artery exists, although the specific management was not described²¹.

Imaging

During the hyperacute and acute phases, cerebral MRI demonstrates superior diagnostic performance compared to plain head CT for detecting thalamic infarctions. Francioni et al.,²² emphasize the early availability of cerebral MRI with Fluid Attenuation Inversion Recovery and Diffusion Weighted Image sequences, allowing for the diagnosis of hyperacute infarctions. In our series, five patients were diagnosed with head CT, while 23 underwent cerebral MRI or both imaging modalities.

In 12 patients, bilateral thalamic infarction was observed without extension to other vascular structures. Half of these patients exhibited concurrent extension to the mesencephalon. The medial pattern was evident in six patients, five of whom showed mesencephalic involvement. One patient presented pontine involvement with the posterior right thalamus and anterior left thalamus affected, an infrequent occurrence reported in the literature with subsequent fatal outcomes. However, our patient experienced a favorable clinical outcome with a mRs of 2 at 90 days.

Lazzaro et al., in a retrospective analysis spanning from 2000 to 2009, reported a case series involving 37 patients with infarction secondary to Percheron artery occlusion, identifying four distinct imaging patterns of infarction: (1) bilateral paramedian thalamic infarction with involvement of the rostral mesencephalon (43%), (2) bilateral paramedian thalamic infarction without involvement of the rostral mesencephalon (38%), (3) bilateral paramedian and anterior thalamic infarction with mesencephalic involvement (14%), and (4) bilateral paramedian and anterior thalamic infarction without involvement of the rostral mesencephalon (5%)²³.

Treatment

Although thrombolytic reperfusion therapy is the gold standard for patients within the therapeutic window, only one patient underwent thrombolytic therapy, resulting in an unfavorable mRs of five at discharge. However, at the three-month follow-up, this patient achieved complete recovery (mRs of 0). Unfortunately, due to a lack of clinical suspicion, the non-availability of MRI in all hospital centers,

and the low sensitivity of CT for hyperacute/acute ischemic lesions, the diagnosis of this condition is generally delayed. As a result, both intravenous thrombolytic therapy and endovascular treatment are uncommon, despite significant residual cognitive and neurological deficits²⁴.

Hospitalization and outcomes

In the etiological classification of stroke according to the TOAST, the most frequent etiology was undetermined in 39.3% of cases due to incomplete evaluation, administrative difficulties, or patients being unfit for additional diagnostic tests. Cardioembolic origin was present in 32.1% of patients, followed by small vessel disease in 21.4%, aligning with the case series reported by De la Cruz-Cosme et al.,²⁵ where cardioembolism was identified as the primary cause, and the series by Arauz et al.,⁴ where small vessel disease was the main cause followed by cardioembolism.

In comparison with other case series, the hospital stay for this population was longer, with the most common causes being related to pneumonia and urinary tract infections²⁶. Due to the limited capacity of hospital beds, the majority remained in the emergency area throughout their hospitalization. Only 50% of patients were managed in the ICU despite a critical clinical condition, due to the limited number of stroke units (four in the entire country), hindering optimal care.

Follow-up

The prognosis for patients with Percheron artery infarction is generally favorable^{4,16}. In the study by Hermann and colleagues²⁷, focal neurological deficits recovered in weeks to months after the stroke event. Twelve out of 31 patients persisted with focal neurological impairments after 1 year. In our case series, most patients were discharged with unfavorable mRs (60.7%), of which 17.9% died during hospitalization, all presenting extension to the mesencephalon. As reported by Xu et al.¹⁶, there is a tendency toward unfavorable outcomes when such extension is evident.

Limitations

Given the retrospective nature of the study, there may be information bias in the acquisition of clinical data. It is important to note that the cases presented do not represent the total number of cases reported nationwide during this time, as only centers voluntarily participating in the call for cases were included in this case series. It was not possible to follow-up with all patients for 3 months due to

difficulties in contacting them. Furthermore, it is important to report that the Percheron artery was not documented in all cases with angio CT scan or angio MRI.

Conclusions

Bilateral thalamic infarctions pose a diagnostic challenge in the emergency department due to their reported low incidence and clinical presentation variability. Suspicions should primarily arise in patients with sudden deterioration of consciousness and oculomotor abnormalities. The availability of CT and/or MRI is crucial for defining a diagnosis and promptly initiating management if necessary. Due to the rapidly evolving symptomatology, these patients should be admitted to a stroke unit or ICU for better care and reduced prolonged hospitalization times. The findings should alert us to the need for strengthening stroke care programs in the country's hospitals and maintaining an organized, multicenter stroke registry to achieve better clinical outcomes for patients.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

Use of artificial intelligence for generating text. The authors declare that they have used generative artificial intelligence, specifically (name of the AI in question) in the writing of this manuscript and/or in the creation of images, graphics, tables, or their corresponding captions (please specify in all cases where it has been used).

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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