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# Cerebrovascular events — from transient ischemic attack and transient global amnesia to transient ischemic attack with MRI-DWI lesions

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## ABSTRACT

**Aim of study**: To compare transient ischemic attack (TIA), transient global amnesia (TGA), and transient ischemic attack with lesions found in magnetic resonance imaging/diffusion-weighted imaging (MRI-DWI) scans, in order to find similarities and differences in their clinical picture.

**Clinical rationale for study**: Magnetic resonance imaging scans account for a substantial part of the financial burden associated with cerebrovascular events. Finding initial clinical features that differentiate transient brain ischemic events will be useful in developing standardized procedures for selecting patients who require further radiological imaging, thereby reducing overall costs.

**Material and methods**: A total of 9701 patients hospitalized in two major tertiary hospitals in the Silesian voivodeship in Poland between January 2016 and July 2024 with a diagnosis of TGA, TIA, and ischemic stroke were analyzed. The final group consisted of 947 patients, who were further divided into three categories: 425 TIA (44.87%), 125 TGA (13.19%), and 387 TIA with MRI-DWI lesions (41.92%). The data of patients were statistically analyzed.

**Results**: Patients with transient focal symptoms and confirmed DWI lesions in MRI scans were significantly older. They were more likely to have coronary heart disease, had higher C-reactive protein (CRP) levels, more severe symptoms, and were less likely to receive antiplatelet treatment than TGA and TIA patients. Transient global amnesia patients had higher systolic blood pressure on admission compared to other groups.

**Conclusions**: The presence of DWI-MRI lesions is associated with a higher initial clinical burden. Our results confirm that the lack of stroke prevention therapies may have determined the more severe course of the vascular event. This study supports a sudden rise in blood pressure being a contributing factor in TGA patients.

**Clinical implications**: Older patients with TIAs, having several vascular risk factors, but lacking prevention therapies are likely to present with cerebral lesions on DWI-MRI. These patients should undergo additional imaging procedures.

**Keywords:** transient ischemic attack, transient global amnesia, stroke, diffusion-weighted imaging, stroke

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## Introduction

Transient ischemic attack (TIA) is a sudden emergence of neurological focal symptoms lasting typically no longer than one hour without concomitant neural tissue damage in radiological imaging. It has been proven to be a potential presage to an ischemic stroke especially in the first 48 hours after onset. Its etiology is similar to that of ischemic stroke and consists of large and small artery disease, cardiac embolism, and some less common causes such as inflammatory and structural vessel disease [1–4]. In recent years, due to an increasing access to neuroimaging possibilities, in particular magnetic resonance imaging (MRI), a shift is observed in the approach to diagnosing of this phenomenon, with more emphasis on structural tissue damage rather than classic time-oriented clinical diagnosis [4]. The growing number of patients with transient symptoms who underwent MRI scans that showed tissue damage particularly in diffusion-weighted imaging (DWI) sequences has encouraged efforts to adequately categorize these patients. Previous studies have shown that DWI changes in clinically appropriate locations are present in about one-third of patients with transient neurological symptoms, suggesting that the 24-hour criterion may allow the inclusion of patients with an acute ischemic stroke.

Different approaches were pursued, most commonly labeling them as transient ischemic attack plus (TIA+) interchangeably with DWI-positive TIA. According to current guidelines, those patients are not differentiated from stroke patients in general regardless of the presence of focal symptoms. Nevertheless, when considering stroke as a clinical diagnosis, patients with transient symptoms represent a unique group which would not be diagnosed as such if they not had been screened with MRI beforehand [2–5]. Studies have shown that the presence of small ischemic lesions in DWI-MRI in patients with transient symptoms may be related to more severe symptoms of longer duration and higher risk of subsequent stroke [2, 3, 6].

Transient global amnesia (TGA) is a syndrome defined by sudden onset of predominantly anterograde, and to a lesser extent retrograde memory loss, which persists for less than 24 hours. This episode cannot be explained by other neurological causes. Unlike the aforementioned ischemic diseases, TGA etiology remains not entirely explained. Many researchers suggest that vascular changes, intracranial venous pathology, circulatory, epileptic, and migraine might contribute to TGA occurrence [7, 8]. Vascular etiology of TGA remains controversial, as epidemiological studies indicate discrepancies in the prevalence of cardiovascular risk factors between TGA (with less prevalent cardiovascular risk factors) and ischemic stroke or TIA, which typically shares a similar risk factor profile. The presence of punctate foci located mostly uni- or bilaterally in the hippocampal region in DWI-MRI sequence found in TGA patients initially suggested a vascular etiology similarly to that of stroke and TIA patients; however, additional studies showed them to be of transient nature, generally present between 24–72 hours after onset of symptoms, without persistent tissue damage as seen in stroke and TIA+ patients [7–19].

In this study, we aimed to assess similarities and differences between TGA, TIA, and TIA+ regarding the risk factors profile and the clinical, laboratory, and neuroimaging findings. Our study was performed on a fairly large cohort of patients from two tertiary university hospitals located in the same city, and covering the population of over 300,000 citizens.

## Clinical rationale for the study

Magnetic resonance imaging scans account for a substantial part of the financial burden associated with cerebrovascular events. Finding initial clinical features that differentiate transient brain ischemic events will be useful in developing standardized procedures for selecting patients who require further radiological imaging, thereby reducing overall costs. This study adds to the understanding of TGA etiology by providing further evidence that a sudden rise in blood pressure is a contributing factor.

## Material and methods

This was a retrospective cross-sectional study performed in two major tertiary hospitals in the Silesian voivodeship in Poland. Medical data of the initial group, i.e., 9701 patients hospitalized in those centers between January 2016 and July 2024 with diagnoses of transient global amnesia (TGA), TIA, and ischemic stroke, were analyzed. Inclusion criteria were availability of head MR results (1.5 T or 3.0 T) taken during hospitalization, within 5 days after symptoms onset, diagnosis of TGA, defined according to Hogdes and Warlow criteria [7], TIA defined as the presence of transient focal symptoms lasting < 24 hours and without cerebral tissue damage [1], and TIA+ meaning patients with focal symptoms with a complete resolution in less than 24 hours and with clinically appropriate lesions present in DWI-MRI. Ischemic stroke was defined according to ASA 2013 guidelines [20]. Exclusion criteria were the presence of focal symptoms at discharge, treatment with rtPA during hospitalization, other acute diseases that could influence patients' results, or incomplete documentation data that made analysis impossible. From the initial group of 9701 patients, 8530 were excluded because of the lack of an MRI scan during hospitalization or clinical diagnosis of stroke, resulting in 1171 patients subjected to further analysis. 224 patients were then excluded mainly due to the presence of focal symptoms at discharge and not meeting diagnostic criteria of TIA or TGA. Incomplete data were reported in 27 (12.05%) excluded patients who had undergone an MRI scan. The final group consisted of 947 patients, 56.9% of whom were woman, with a mean age of 65.8 ± 13.3 years. They were further divided

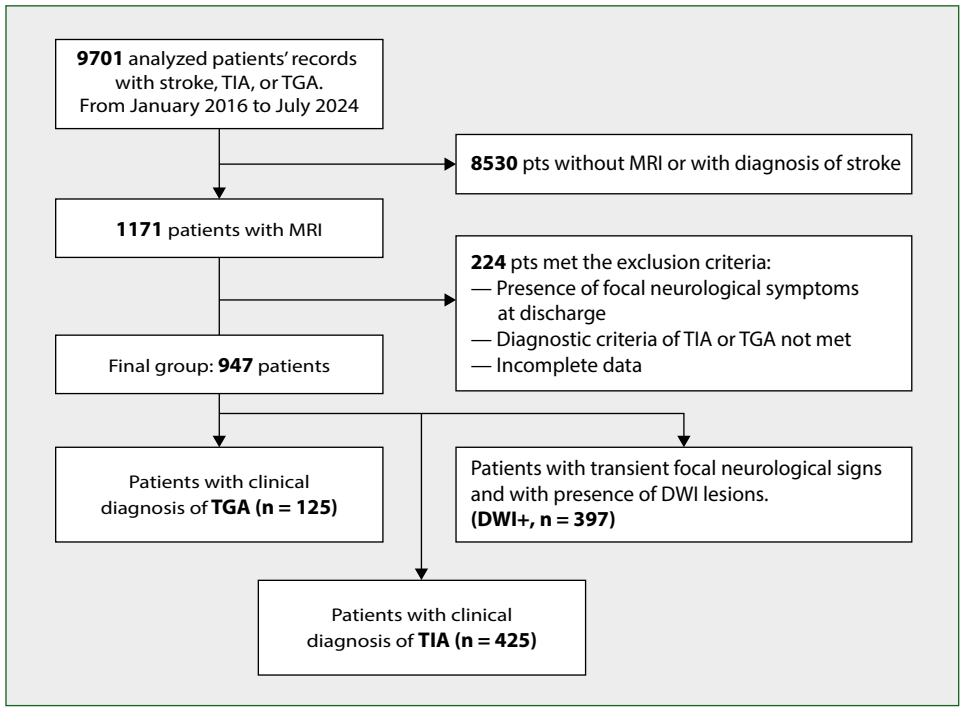



**Figure 1.** The study group creation proces. DWI — diffusion-weighted imaging; MRI — magnetic resonance imaging; TGA — transient global amnesia; TIA — transient ischemic attack

into three categories according to the diagnosis based on the aforementioned criteria. The final group comprised 425 TIA patients (44.87%), 125 patients with TGA (13.19%), and 387 TIA+ (41.92%) patients. The study group creation process is visualized in Figure 1.

Multiple variables from the patients' reports were collected including cardiovascular risk factors, demographics, and antiplatelet, anticoagulant, and statin treatment before and after discharge. Systolic, diastolic, and mean blood pressure records at admission, laboratory findings including glucose level at admission, C-reactive protein (CRP), glycated hemoglobin (HbA1c), thyroid stimulating hormone (TSH), free T4 and free T3 levels, troponin-T, total cholesterol, triglycerides, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) levels were collected. Additionally, the Fazekas scale [21] (0–3) was used to assess the intensity of microangiopathy in patients from all groups. Patients were also assessed by the presence of singular or multiple DWI lesions. They were also stratified based on the time between onset of symptoms and MRI scan. Patients included in our study were examined with cervical Doppler ultrasound to determine the presence of precranial artery stenosis, cardiac monitoring for detection of atrial fibrillation, neurological exam, and assessment with the National Institutes of Health stroke scale (NIHSS). Cardiac examination including cardiac ultrasound was performed for heart failure assessment. Severity of focal neurological deficits at admission in TIA and TIA+ was assessed with the NIHSS scale. [22] Comparison analysis was performed between these 3 groups.

Statistical analysis was performed using Statistica 13.3 [TIBCO Software Inc. (2017) Statistica (data analysis software system, version 13., http://statistica.io)]. Quantitative variables are presented as arithmetic mean and standard deviation (normally distributed variables) or median and interquartile range (variables with abnormal/skewed distribution). Normality of distribution was assessed using the Shapiro-Wilk test. Qualitative variables are reported as absolute values and percentages.

Differences between groups for quantitative variables were assessed using the Kruskal–Wallis test (for variables with abnormal/skewed distribution) or ANOVA (for variables with normal distribution), with post hoc type analysis. Fisher's exact test or chi-squared test was used for qualitative variables.

Due to the retrospective nature of the analysis and the anonymization of the data, the Ethics Committee of the Medical University of Silesia waived the requirement to obtain ethical approval for this study.

## Results

### Risk factors of cardiovascular diseases

Coronary heart disease was reported more often in patients in the TIA and TIA+ than in the TGA group. (22.3% vs. 12.1% vs. 8.8%; p = 0.0002). There were no differences in the prevalence of chronic arterial hypertension, diabetes mellitus, dyslipidemia, heart failure, presence of atrial fibrillation, nicotine addiction, obesity, and large precranial artery stenosis in the study group. Detailed data are summarized in Table 1.

**Table 1.** Cerebrovascular risk factors

| Study group | TIA+ | TIA | TGA | p-value |
|---|---|---|---|---|
| Arterial hypertension: n (%) | 308 (77.58) | 320 (72.3) | 85 (68) | 0.09577 |
| Diabetes mellitus: n (%) | 76 (19.1) | 110 (25.9) | 19 (15.2) | 0.01097 |
| Dyslipidemia: n (%) | 91 (22.9) | 124 (29.1) | 34 (27.2) | 0.23848 |
| Coronary heart disease: n (%) | 48 (12.1) | 95 (22.4) | 11 (8.8) | 0.00002 |
| Chronic heart failure: n (%) | 76 (19.1) | 110 (25.9) | 19 (15.2) | 0.01097 |
| Atrial fibrillation: n (%) | 20 (5.0) | 17 (4.0) | 3 (2.4) | 0.42092 |
| Obesity: n (%) | 43 (10.8) | 48 (11.3) | 5 (4.0) | 0.04972 |
| Precranial artery sclerosis: n (%) | 9 (2.3) | 15 (3.5) | 2 (1.6) | 0.38045 |
| Atherosclerosis: n (%) | 13 (3.3) | 25 (5.9) | 1 (0.8) | 0.02293 |

TGA — transient global amnesia; TIA — transient ischemic attack; TIA+ — transient ischemic attack plus

## Demographic data

The TGA and TIA groups consisted mainly of females (69.6% and 59.1%, respectively, p = 0.0005), and in the TIA+ group it was close to equal (50.6% were female patients). Patients with TGA were younger than patients with a diagnosis of TIA or TIA+ (TGA: 63.2 ± 10.5 years versus TIA: 66.2 ± 14.8 years and TIA+: 66.2 ± 12.4 years; p = 0.0025).

## Clinical symptoms

The NIHSS score measured on admission was higher in TIA+ patients when compared to the TIA group (1.1 ± 1.6 points vs. 4.8 ± 3.8 points, p ≤ 0.0001). The TGA group was characterized by higher systolic (158.9 ± 24.0 mmHg vs. 153.1 ± 24.3 mmHg and 154.3 ± 23.2 mmHg; p = 0.031) and diastolic (87.2 ± 14.7 mmHg vs. 87.9 ± 42.2 mmHg vs. 87.2 ± 14.7 mmHg; p = 0.042) blood pressure measured on admission.

## Laboratory testing and neuroimaging

The transient ischemic attack plus group was characterized by a higher level of CRP, which was lower in TIA patients and the lowest in TGA patients (9.42 ± 24.3 mg/L vs. 9.0 ± 20.41 mg/L vs. 4.0 ± 2.31 mg/L; p < 0.0001). Higher glucose levels on admission were seen in the TIA+ and TIA groups in comparison to TGA (130.5 ± 52.3 mg/dL and 122.9 ± 39.2 mg/dL vs. 115.1 ± 28.6 mg/dL; p = 0.0118). Furthermore, patients in TIA+ had lower serum high-density lipoprotein (HDL) levels (48.4 ± 14.0 mg/dL vs. 51.9 ± 15.8 mg/dL and 51.4 ± 11.3 mg/dL; p = 0.0036). Statistically insignificant differences were also found in levels of TSH, thyroxine (fT4), triiodothyronine (fT3), troponin-T, glycated hemoglobin, total cholesterol, triglycerides, and LDL level.

The presence of multiple DWI lesions (n = 114) when compared to singular (n = 308) and none (n = 153) was assessed. Detailed data are provided in Supplementary Material.

Mean Fazekas scoring was significantly higher in TIA and TIA+ than in TGA patients (1.3 ± 0.8 points vs. 1.2 ± 0.9 points vs. 1.1 ± 0.8 points). In the TIA and TIA+ groups it was also higher in patients with multiple lesions (2 ± 1.2 points vs. 1 ± 1.2 points vs 1 ± 1.2 points).

The findings of the subgroup analysis of patients with MRI scans performed within 24 hours of the onset of symptoms and more than 24 hours after the onset of symptoms are consistent with those of the original study group.

Patients with > 1 lesion in MRI-DWI were older and more often presented with coronary heart disease and atrial fibrillation. They also had lower NIHSS scale score and were more likely to receive stroke prevention therapies. Detailed data for subgroup analysis are provided in Supplementary Material and summarized in Table 2.

## Initial stroke prevention therapies

### *Prior to admission:*

Patients diagnosed with TIA or TGA were more likely to receive single antiplatelet medication compared to TIA+ patients (77.2% vs. 58.2% vs. 81.7%, p ≤ 0.0001). Anticoagulant treatment was more common in patients with TIA than in those with TIA+ and TGA (9.8% vs. 5.8% vs. 2.44%, p ≤ 0.0001). There were no differences in treatment of dyslipidemia before the incident. Double antiplatelet therapy was more common in TIA than in TIA+ patients (1.91% vs. 0.76%). Low molecular weight heparin was more common in TIA than in TIA+ patients (0.72% vs. 0.25%). Oral anticoagulants [OAC (vascular dose)] with single antiplatelet medication were more common in TIA than in TIA+ patients (0.72% vs. 0.25%). Vitamin K antagonists (VKA) were more common in TIA than in TIA+ patients (0.95% vs. 0.25%). None of the TGA patients received DAPT, LMWH, OAC (vascular dose) + single antiplatelet medication, or VKA prior to the vascular event.

Lack of oral stroke prevention medication intake prior to admission was more common in TIA+ then in TGA patients, while the TIA group was receiving any form of primary prevention therapy significantly more often (81.86% vs. 77.24% vs. 58.23%).

**Table 2.** Demographics, and laboratory and clinical testing

| | TIA+ | TIA | TGA | p-value |
|---|---|---|---|---|
| Age [years] Mean ± SD | 66.2 ± 12.4 | 65.8 ± 13.3 | 63.15 ± 10.45 | 0.0025 |
| Gender n (%) | | | | |
| Female | 201 (50.63) | 251 (59.06) | 87 (69.6) | 0.0005 |
| Male | 38 (30,4) | 174 (40.94) | 196 (49.37) | 0.0005 |
| SBP [mmHg] | 154.3 ± 23.2 | 153.1 ± 24.26 | 158.9 ± 24 | 0.0545 |
| DBP [mmHg] | 87.2 ± 14.7 | 87.9 ± 42.3 | 90 ± 15.24 | 0.0918 |
| CRP [mg/L] | 9.4 ± 24.3 | 9 ± 20.41 | 4 ± 2.3 | < 0.0001 |
| TCh [mg/dL] | 176.8 ± 50.6 | 175.7 ± 46.5 | 182 ± 44.8 | 0.3732 |
| HDL [mg/dL] | 48.4 ± 14 | 51.9 ± 15.8 | 51.4 ± 11.3 | 0.0036 |
| LDL [mg/dL] | 104.1 ± 45.2 | 99 ± 42.4 | 107.2 ± 42.7 | 0.1518 |
| TG [mmol/L] | 130.2 ± 88.3 | 135 ± 98.3 | 127.6 ± 70.4 | 0.8869 |
| Glucose [mg/dL] | 130.6 ± 52.3 | 123 ± 39.2 | 115.1 ± 28.6 | 0.0118 |
| HbA1c [%] | 7.4 ± 5.1 | 8 ± 8.6 | 5.8 ± 0.4 | 0.1583 |
| FAZEKAS Mean ± SD | 1.3 ± 0.8 | 1.2 ± 0.9 | 1.1 ± 0.8 | 0.0134 |
| NIHSS Mean ± SD | 4.8 ± 3.8 | 1.1 ± 1.6 | — | < 0.0001 |
| TSH [mlU/L] | 1.99 ± 3.90 | 2.01 ± 1.92 | 1.82 ± 1.38 | |
| Ft3 [pmol/L] | 2.84 ± 0.48 | 2.89 ± 0.48 | 2.82 ± 0.61 | |
| Ft4 [pmol/L] | 1.29 ± 0.24 | 1.2 ± 0.23 | 1.29 ± 0.25 | |
| Troponin-T [ng/L] | 3.22 | 4.98 ± 7.02 | 5.57 ± 11.8 | |

CRP — C-reactive protein; DBP — diastolic blood pressure; FAZEKAS — Fazekas scale; Ft3 — triiodothyronine; Ft4 — thyroxine; HbA1c — glycated hemoglobin; HDL — high density lipoprotein; LDL — low density lipoprotein; NIHSS — National Institutes of Health Stroke Scale; SBP — systolic blood pressure; TCh — total cholesterol; TG — triglycerides; TGA — transient global amnesia; TIA — transient ischemic attack; TIA+ — transient ischemic attack plus

### *Stroke prevention therapies on discharge*

In all groups, the most commonly prescribed secondary stroke prevention therapy was antiplatelet medication, while double antiplatelet therapy was second (TGA: 80.5% vs. 10.6%; TIA: 57.5% vs. 22.0%; TIA+ 77.8 vs. 10.1%; $p \leq 0.0001$). OAC therapy was prescribed at discharge more often in TIA and TIA+ patients than in TGA patients (13.2% vs. 10.6% vs. 1.6%; $p \leq 0.0001$). OAC (vascular dose) + single antiplatelet medication was prescribed more commonly in TIA than in TIA+ and TGA patients (2.6% vs 1.0% vs 0.8%). LMWH was prescribed in the TIA group (1.18%) but was not prescribed in any of the TGA and TIA+ patients. VKA were prescribed most commonly in the TIA group, followed by the TIA+ group (0.71% vs. 0.51%), and they were not prescribed in the TGA group. Lack of secondary stroke prevention on discharge was more common in the TGA than in the TIA group (6.5% vs. 2.6%). All of the TIA+ patients received secondary stroke prevention therapy.

Statins were prescribed more frequently on discharge in the TIA+ group than in the TIA and TGA groups (99.2% vs. 90.3% vs. 85.3%).

Detailed data are summarized in Table 3.

## Discussion

Recently, vascular events have begun to be understood as a spectrum rather than a collection of separate diagnoses such as stroke, TIA, and TGA. Ortiz-Garcia et al. [2] in their recent study compared cerebral events with those affecting coronary vessels, which, if applied to our research, would suggest that our study groups could be classified and compared as follows: TIA to unstable angina and TIA+ to non-STEMI (NSTEMI) myocardial infarction. In this context DWI-MRI lesions would be a representation of tissue damage, likewise elevated troponin T levels during an NSTEMI event indicate damage to the heart muscle. Absence of DWI-MRI lesions with focal symptoms without permanent tissue damage as seen in TIA would be compared to unstable angina, where we see clinical symptoms without elevated troponin T levels and thereupon heart muscle damage. Such an approach has little to no coverage in previous studies and is a valuable contribution the knowledge of acute cerebrovascular syndromes.

In addition, the comparison of disease entities presented in our study may be important in distinguishing specific clinical scenarios that require additional radiological imaging. The

**Table 3.** Antiplatelets and anticoagulants taken by patients on admission and on discharge, and statin treatment at discharge

| Study group | TIA+ | TIA | TGA | p-value |
|---|---|---|---|---|
| Stroke prevention therapy on admission: n (%) | | | | < 0.0001 |
| None | 325 (81.86) | 244 (58.23) | 95 (77.24) | |
| SAPT | 43 (10.83) | 115 (27.45) | 25 (20.33) | |
| DAPT | 3 (0.76) | 8 (1.91) | 0 (0.00) | |
| OAC | 23 (5.79) | 41 (9.79) | 3 (2.44) | |
| LMWH | 1 (0.25) | 4 (0.95) | 0 (0.00) | |
| OAC (vascular dose) + single antiplatelet medication | 1 (0.25) | 3 (0.72) | 0 (0.00) | |
| VKA | 1 (0.25) | 4 (0.95) | 0 (0.00) | |
| Stroke prevention therapy on discharge: n (%) | | | | < 0.0001 |
| None | 0 (0.00) | 11 (2.60) | 8 (6.50) | |
| SAPT | 308 (77.78) | 243 (57.45) | 99 (80.49) | |
| DAPT | 40 (10.10) | 93 (21.99) | 13 (10.53) | |
| OAC | 42 (10.61) | 56 (13.24) | 2 (1.63) | |
| OAC (vascular dose) + single antiplatelet medication | 4 (1.01) | 11 (2.60) | 1 (0.81) | |
| LMWH | 0 (0.00) | 5 (1.18) | 0 (0.00) | |
| VKA | 2 (0.51) | 3 (0.71) | 0 (0.00) | |
| Statin treatment on discharge: n (%) | 105 (85.37) | 382 (90.31) | 392 (92.24) | < 0.0001 |

DAPT — double antiplatelet therapy; LMWH — low molecular weight heparin; OAC — oral; SAPT — single anti-platelet therapy, anticoagulants; TGA — transient global amnesia; TIA — transient ischemic attack; TIA+ — transient ischemic attack plus; VKA — vitamin K antagonists

identification of clinical features that predict the occurrence of lesions seen on DWI-weighted MRI scans may in the future be used by clinicians to optimize costs by targeting chosen patients for brain MRI imaging using standardized screening procedures, because these scans account for significant part of the financial burden of stroke and TGA. Differences in symptoms severity and prognosis may be important in developing more specific clinical approaches and treatments [2–4, 23, 24].

Our study showed that TGA patients were younger, less burdened by risk factors for ischemic events, had lower glycemia levels and had lower microangiopathy scores when compared to TIA and TIA+ subjects, which is generally consistent with data regarding this topic in the literature [7, 9, 10, 13, 26]. This supports the current understanding of TGA pathogenesis being broader than of purely ischemic origin.

Lackova et al. [27] in their recent study found that lipoprotein(a) [Lp(a)] concentration is an independent risk factor for ischemic stroke when compared to patients with no history of cerebrovascular events. Patients with TIA and TGA were excluded from their study, which can potentially be taken into consideration when designing future trials focusing on Lp(a) levels.

## Blood pressure

According to Anisetti et al. [28], long-term variability in systolic blood pressure (SBP) in patients with or without arterial hypertension is correlated with increased occurrence of cardiovascular events. In addition, major theories regarding the pathophysiology of TGA attribute the acute increase in blood pressure attributed to both physiological, emotional, and vascular events as a direct cause of this condition, at least in some patients. In this context, the higher systolic blood pressure on admission in TGA patients found in our study may be explained [1, 3, 28]. It is worth noting that in these studies TGA patients were less likely to receive medication for chronic hypertension than TIA and stroke patients, further supporting these claims [9, 13, 29]. It has also been found in other studies that results may differ when compared between the sexes, with women showing higher levels of systolic blood pressure, which may be attributed to the more common cause of hypertension crisis being a result of acute mental stress and emotional disturbance, which have longer lasting and more severe effects when compared to physical activity in men [9]. Our study supports the recommendation for prolonged systemic blood pressure monitoring in TGA patients in the causative diagnostic process.

In accordance with the meta-analysis by Elsaid et al. [30], sympathetic nervous system activation caused primarily by stress is an important risk factor for the development of chronic hypertension. This may lead to a breakdown of the blood brain barrier and impaired autoregulation, leading to vessel damage and increased risk of cerebrovascular events [30]. Acute mental stress is also believed to be a factor in endothelial disfunction through hypothalamic-pituitary-adrenal

axis involvement [31]. In several studies clinical association was found between self-perceived psychological stress and cerebrovascular events such as ischemic stroke and TIA. However, it is difficult to assess the extent to which sympathetic nervous system activation influences the occurrence of TIA, especially when compared to TGA, in which sympathetic involvement is considered a major clinical factor [32–34].

It is necessary to further investigate the complex relationship between hypertension and cognitive function, especially by assessing the previous cognitive status of patients with cerebrovascular events, which was not included in our study.

## Radiological findings

Lesions in the hippocampal region in TGA patients have led some to define DWI-positive TGA cases as hippocampal strokes, treating them as equal to other vascular events. This approach may not yet be accepted because of a lack of adequate follow-up studies to exclude the temporary nature of radiological DWI-MRI findings in TGA, which would distinguish them from those of permanent ischemic origin. The burden of diabetes mellitus was higher among the TIA and TIA+ patients in comparison with TGA patients. The structural and functional microangiopathy with endotheliopathy may play a key role in clinical presentation of transient neurological deficit. Higher microangiopathy scores in the TIA and TIA+ groups in our study support these claims, suggesting a potentially different origin of DWI findings other than small vessel disease in TGA patients [8–10, 35–37]. In addition, DWI lesions outside the hippocampal region have been reported in patients with typical TGA symptoms [16, 23, 38]. Nevertheless, the high occurrence of ischemic lesions in TGA patients, which is comparable to the incidence of similar radiological findings in TIA groups, may indicate the need for MRI screening in these conditions until specific criteria are developed [2, 3, 9–11, 15]. It is worth noting that the incidence of hippocampal lesions depends on the use of 1.5 T, 3.0 T, or 7.0 T MRI scanners, with higher magnetic field strength being consistent with more accurate findings. This needs to be taken into account in future research [39]. Some studies have found differences in risk factors such as intracranial and precranial arterial stenosis. Although similar to our results, most other studies, particularly those with larger study groups, show no differences in the presence of risk factors in respect to the incidence of DWI lesions [9, 11, 13]. Patients with multiple DWI lesions were older, had more comorbidities, were primarily male, and had higher microangiopathy scores. The clinical course in patients with multiple DWI lesions was milder than in those with singular DWI lesions, as determined by lower NIHSS scale score on admission, which can be explained by them being more likely to receive stroke prevention therapies and possibly collateral circulation.

## C-reactive protein

C-reactive protein and other inflammatory agents are important markers associated with inflammation as a contributor to the pathogenesis of vascular events. In numerous studies, CRP levels have been associated with poorer clinical outcomes and higher recurrence rates in patients with TIA and stroke, which prompts scientists to seek potential inflammatory therapies [40–44]. In contrast, in TGA, inflammation is not typically considered by researchers to be a pathophysiological mechanism in this context [7, 8]. Data from other studies is consistent with ours, as we found lower CRP levels in the TGA and TIA groups compared to the TIA+ group [9, 13].

## Stroke prevention

Antiplatelet therapy is proven to be the most efficient secondary prevention of non-cardioembolic cerebrovascular events. Importantly, in our study, patients with DWI-MRI lesions were less likely to receive antiplatelet therapy before the event. In addition, our results show that the course of the event in the TIA+ group was significantly more severe, as shown by a higher NIHSS score on admission. This may mean that if antiplatelet therapy had been administered as a primary or secondary prevention, it may potentially prevented tissue damage. A similar difference is shown in secondary prevention therapies with OACs, where in the TIA group more patients were receiving them before onset compared to the TIA+ group. It is important to note that we did not find a statistically significant difference in atrial fibrillation reported by patients, which may be caused by anticoagulants being taken by patients for other indications and due to under-reporting. The TGA group were less likely to receive anticoagulants before onset, which may be an intermediate indication that cardio-embolism is rarely the cause of this syndrome [44–48].

## Limitations

There are some limitations that need to be mentioned: first of all, this study was conducted in two centers in southern Poland, the patients were Caucasian, and our results might not be generalized. Additionally, due to the retrospective nature of this study, there are some data, especially about the patients' history, which might not be reported in medical records. Thus, we were not able to include some of the risk factors associated with TGA such as migraine, head injury, and specific scenarios occurring before onset of the disease such as Valsalva maneuver or physical exercise. Other risk factors might be underreported (e.g., tobacco usage) because data were gathered based on the patients' testimony. Lp(a) serum levels were not included in this trial. Also, ABCD2 and ABCD3I scores were not included in our study. The researchers did not assess stroke management therapies on admission and during the hospital stay. Furthermore, only patients with MRI scans were included in this analysis, and selection for MR imaging was not based on any unified selection protocol.

Researchers were not able to determine the exact timing between symptom onset and MRI scan due to the exact time of symptom onset not being included in most of the patients' records.

## Clinical implications

Patients with transient focal symptoms and confirmed DWI lesions in MRI scans were significantly older. They were more likely to have coronary heart disease, had higher CRP levels and more severe symptoms, and were less likely to receive antiplatelet treatment than TGA and TIA patients. Our results confirm that lack of stroke prevention therapies may have determined the more severe course of the vascular event. Our study may be used by researchers to develop standardized procedures such as scales, expert recommendations, and guidelines for selecting patients who need additional radiological imaging. The study provides further evidence that a sudden rise in blood pressure is a contributing factor in TGA patients.

## Article information

**Data availability statement:** *The data for this study are available on request from the authors.*
**Ethics statement:** *Ethical approval is not applicable for this article.*
**Author contributions:** *KD — data curation, formal analysis, writing — original draft, writing — review & editing. TC — methodology, formal analysis, writing — review & editing. MT-G — data curation, writing — original draft, writing — review & editing. AC-F — data curation, writing — review & editing. SP — data curation, writing — review & editing. AD — data curation, writing — review & editing. AK-B — writing — review & editing. AL-B — methodology, writing — original draft, writing — review & editing, project administration, supervision. JS — conceptualization, methodology, writing — original draft, writing — review & editing, project administration, supervision.*
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