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Research Article

Volume and Visual Field Defects in Occipital Stroke: The NOR-OCCIP Study

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Introduction. The majority of patients with occipital infarcts display homonymous visual field defects (VFD), with negative implications on activities of daily living and quality of life. To overcome the disability, better prognostic markers in the acute phase, as well as more targeted rehabilitation, would be useful. The aim of the current study was to present an overview of the topographic distribution of occipital infarcts and to investigate whether lesion volume can predict VFD at baseline and after six months. *Materials and Methods*. Multicenter, prospective study including patients with acute occipital infarcts (NOR-OCCIP project). All patients were examined by a neurologist in the acute phase, admitted to a stroke unit, and further assessed by an ophthalmologist within two weeks. Topographic and volumetric data from brain imaging in 72 patients were analyzed and computed by an experienced neuroradiologist. *Results*. A majority (81%) had occipital infarcts with involvement of the primary visual cortex, and VFD were detected on perimetry in 80% of the examined patients. Higher infarct volume led to more severe VFD at baseline ($p = 0.019$); this was more evident if the infarct was located on the right side ($p = 0.001$). The odds for VFD improvement after six months were higher the larger the infarcts were ($p = 0.020$). There was a statistically significant association between volume of infarcts and atrial fibrillation ($p = 0.016$), previous myocardial infarction ($p = 0.023$), and modified Rankin Scale at three months ($p = 0.007$). *Conclusion*. Higher infarct volumes led to more severe VFD at baseline. More than half of the patients (54%) experienced improvement of their VFD at six months; a higher grade of improvement was seen in patients with larger occipital infarcts. Large infarcts were more common in patients with cardiovascular disease, strengthening the argument for secondary prevention.

1. Introduction

Visual impairment is a common finding after acute ischemic cerebral stroke (AIS) and may include impaired central vision, visual field defects (VFD), eye movement disorders, visual perception disorders, and visual inattention [1].

Occipital infarcts due to occlusion of the posterior cerebral artery (PCA) represent less than 10% of all ischemic strokes [2]. Initial neurological deficits following occipital stroke are predominantly VFD, which are found to have negative implications on stroke recovery in general [3], mortality [4], and vision-related quality of life [5].

Previous studies have confirmed the retinotopic map of the human occipital cortex by correlating magnetic resonance imaging (MRI) findings with visual field defects in patients with occipital lobe infarcts [6, 7]. However, only a few studies attempt to correlate the exact lesion location and volume with visual field defects and file prognosis in patients with acute occipital infarcts [8, 9]. We wanted to examine this closer in a Norwegian population.

The NOR-OCCIP project is a prospective, multicenter, population-based cohort study using data from the Norwegian Stroke Registry. One of the aims of the NOR-OCCIP project is to establish an effective multidisciplinary diagnostic pathway for patients with VFD and AIS.

Visual impairment is often not acknowledged despite the fact that it affects more than half of AIS survivors [10] and could interfere with the rehabilitation process. In our previous study, we found that VFD reduce multiple aspects of vision-related quality of life substantially [5]. The aim of the present study was to present an overview of the topographic distribution of acute occipital infarcts and to investigate whether lesion volume can predict VFD at baseline and after six months.

2. Materials and Methods

Between August 2013 and December 2014, all patients >18 years with acute occipital infarcts admitted to three university hospitals in Norway (the University Hospital of St. Olav, Haukeland University Hospital, and Stavanger University Hospital) were considered for inclusion (http://www.clinicaltrials.gov/ct2/show/NCT02307981). Patients were included within seven days of admittance, and written consent was obtained from all patients. Previous stroke or simultaneous acute infarcts in other cerebral lobes were not exclusion criteria. Patients with severe cognitive impairment and/or preexisting conditions with severely affected eyesight were excluded.

The NOR-OCCIP study was approved by the Regional Committee for Medical and Health Research Ethics in Western Norway (2012/2307).

All included patients had acute occipital infarcts confirmed by magnetic resonance imaging (MRI) or computer tomography (CT). A neuroradiologist with 16 years of experience (KDK) classified the lesions with respect to the anatomical characteristics and manually delineated the lesions using the open-source platform 3D Slicer version 4.10.1 (http://www.slicer.org) to calculate lesion volume. Lesion location was categorized into 14 areas affecting the visual pathway: areas 1-6: Brodmann area 17 shown in Figure 1, area 7: posterior pole of the occipital lobe, area 8: Brodmann area 18 (posterior surface of the secondary visual cortex), area 9: Brodmann area 19 (inferior/temporal surface of the secondary visual cortex), area 10: parietal lobe, area 11: temporal lobe, area 12: hippocampus, area 13: thalamus, and area 14: corpus callosum. Acute bilateral occipital infarcts were categorized as two separate infarcts, with separate analysis of topographic distribution, volume, and visual field defects. Acute infarcts in other locations and previous stroke were categorized as frontal, medial, parietal, temporal, brain-
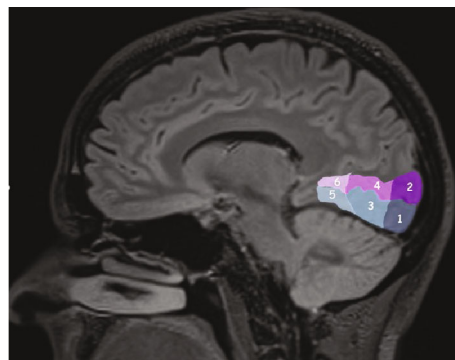

FIGURE 1: Lesion location. Areas 1 to 6 are delineated in a sagittal 3D FLAIR (TE 386 ms, TR 5000 ms, TI 1800 ms, isotropic voxel size 1 m^3, Siemens Skyra 3 T, Siemens Healthineers GmbH, Erlangen, Germany).

stem, cerebellum, multiple locations, occipital, or other locations. We also performed a subanalysis where patients with infarcts solely in areas 8-14, not affecting the primary visual cortex, were excluded.

According to national guidelines [11], all patients received full neurological examination, diagnosis, and treatment at the admitting stroke unit during the acute phase. Demographic variables, lifestyle factors, and information regarding previous diseases and medication were collected from the Norwegian Stroke Registry [12]. Neurological status was assessed using the National Institutes of Health Stroke Scale (NIHSS) in the acute phase [13, 14], and functional outcome at three months was measured using the modified Rankin Scale (mRS) [15].

Ophthalmic examination, including perimetry, was performed using a standardized investigation sheet at baseline (within two weeks) and after six months. The ophthalmic examination included best-corrected visual acuity (Snellen or EDTRS eye charts) and a general eye examination identifying preexisting ocular pathology. The visual field was examined quantitatively by standardised automated perimetry using 30-2 threshold tests on the majority of the patients, whereas eight individuals were tested with full-field 120-point screening. Experienced ophthalmologists evaluated the quality of the results. The same testing strategy was applied to each patient, ensuring the possibility of a direct comparison. The testing was performed separately for each eye. The Octopus 900 perimeter (Haag-Streit Diagnostics, Koeniz, Switzerland) was used at Haukeland University Hospital, the Humphrey Automated Field Analyser II (Carl Zeiss Meditec, Dublin, CA, USA) at St. Olavs Hospital, and Oculus Twinfield 2 perimeter (Oculus, Wetzlar, Germany) at Stavanger University Hospital. The perimetry results were classified as normal, scotoma (<50% of quadrant), quadrantanopia, incomplete hemianopia (<75% of hemifield), hemianopia, or severe bilateral defects.

The patients were divided into the following subgroups: (1) Normal visual field, (2) Mild VFD (scotoma or quadrantanopia), and (3) severe VFD (hemianopia or severe bilateral defects). Improvement of VFD after 6 months was defined as a mean deviation improvement of ≥2.0 on 30-2 threshold
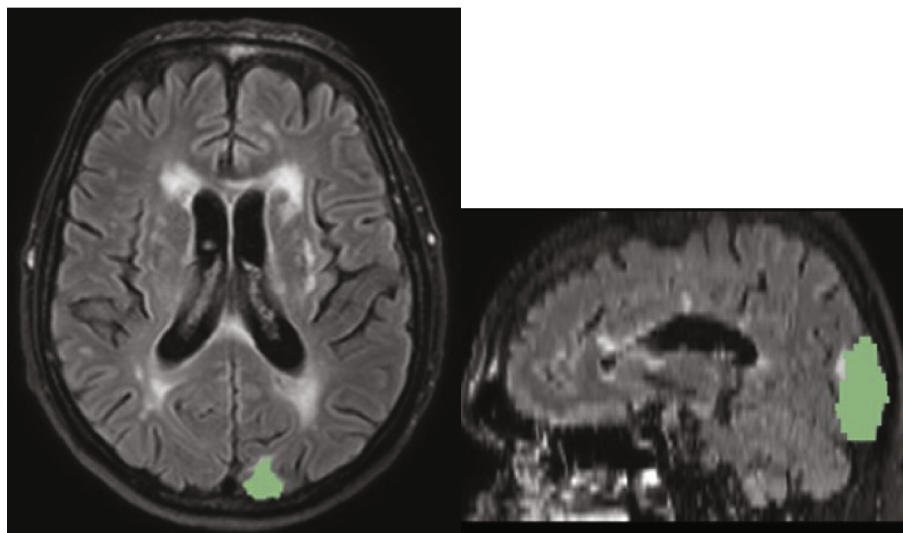
FIGURE 2: 2D FLAIR volumetric mapping of acute infarct in the left occipital lobe in a 62-year-old male with an infarct volume of 37 cc, coloured with green overlay.

tests for all perimeters compared to baseline results or ≥3 continuous point improvement on full-field 120-point screening for The Humphrey Automated Field Analyser II.

Descriptive statistics are presented as counts and percentages for categorical data and as medians and interquartile ranges (IQR) for continuous data. Comparisons of categorical variables between groups were performed using Pearson's chi-squared test or Fisher's exact test. Due to skewed distributions, comparisons of continuous data between groups were performed with Mann–Whitney U test. Data analysis was performed with statistical package for social sciences, version 26 (IBM Corp., Armonk, NY). Estimated p values <0.05 were considered statistically significant.

3. Results

Overall, 76 patients with acute occipital infarcts were included (31 patients from Haukeland University Hospital, 21 patients from St. Olavs University Hospital, and 24 patients from Stavanger University Hospital). For detailed information about inclusion and drop-outs, we refer to our first paper in the NOR-OCCIP project [5]. In the current paper, four patients were excluded from further analysis: one because by not obtainable MRI/CT scans, one because AIS was not found on MRI on reevaluation, one as the AIS was deemed not to affect the visual pathways, and one as a glioma was diagnosed later in the course.

Among the remaining 72 patients, cerebral MRI was obtained in 67 patients and cerebral CT in five patients. The occipital stroke was right-sided in 26, left-sided in 39, and bilateral in seven patients. Acute bilateral occipital infarcts were categorized as two separate infarcts, resulting in a total number of 79 occipital infarcts. Simultaneous AIS in other cerebral lobes was found in 19 patients. Previous stroke was found in 20 patients, five of which were located in the occipital lobe. Figure 2 shows a 2D FLAIR vol-

TABLE 1: Stroke distribution; affected areas: right/left hemisphere ($n = 79$).

Area 1*	19/22
Area 2	11/17
Area 3	17/22
Area 4	12/20
Area 5	11/20
Area 6	6/18
Posterior pole of the occipital lobe	5/4
Secondary visual cortex, Brodmann area 18	12/16
Secondary visual cortex, Brodmann area 19	8/18
Parietal lobe	6/7
Temporal lobe	3/4
Hippocampus	4/2
Thalamus	2/1
Corpus callosum	3/0

Areas 1-6: primary visual cortex, Brodmann area 17.

umetric mapping of acute infarct in the left occipital (patient 4), TE 140 ms, TR 10 000 ms, TI 2750 ms, slice thickness 3 mm, matrix 256 × 256, Philips Intera 1,5 T, Philips Medical Systems, Best, The Netherlands.

The majority of the patients had involvement of one or more of the areas 1-6 (Brodmann area 17) in the occipital lobe (81%). Furthermore, 12% had involvement of the posterior pole of the occipital lobe, 35% of Brodmann area 18, 33% of Brodmann area 19, 16% of the parietal lobe, 9% of the temporal lobe, 8% of the hippocampus, 4% of the thalamus, and 4% of the corpus callosum (Table 1).

Complete ophthalmic examination (including perimetry) within two weeks after admittance was obtained in 64 patients (89%). After six months, 53 of these (83%) underwent a follow-up ophthalmic examination. Perimetry revealed a VFD in 51 patients (80%) at the first examination

TABLE 2: Demographics.

	Valid n	All ($n = 72$)
Age (years), median (IQR)	64	69.7 (57.3, 77.6)
Females	72	27 (38%)
Hypertension	71	37 (52%)
Hypercholesterolemia	71	24 (34%)
Atrial fibrillation	71	18 (25%)
Previous stroke	71	12 (17%)
Previous TIA	69	6 (9%)
Myocardial infarction	71	12 (17%)
Diabetes	71	6 (8.0%)
Cigarette smoking	67	27 (40%)
NIHSS score, median (IQR)	66	2.0 (0.0, 4.0)
mRS score 3 months, median (IQR)	59	2.0 (1.0, 3.0)

IQR: interquartile range; TIA: transient ischemic attack; NIHSS: National Institutes of Health Stroke Scale; mRS: modified Rankin Scale.

and in 41 (77%) at follow-up. Among those with VFD, improvement of VFD after six months was found in 54%.

The median age was 69.7 years (57.3-77.6) and the majority of patients (62%) were men. As for previous illnesses, arterial hypertension was the most common (52%), whereas 25% had a history of atrial fibrillation (Table 2).

No significant differences in age, sex, or premorbidity could be found between the group with normal visual field and the group with VFD in the acute phase. The median scores of the National Institute of Health Stroke Scale (NIHSS) at baseline and the modified Rankin Scale (mRS) after three months were significantly higher in the visual field defect group compared to the group with normal visual field ($p = 0.001$).

A previous myocardial infarction was significantly associated with a larger stroke volume ($p = 0.023$). This was also the case for atrial fibrillation ($p = 0.016$). No significant association was found between volume and NIHSS, age, gender, hypertension, hypercholesterolemia, previous stroke/TIA, diabetes, or smoking. However, we found a statistically significant association between infarct volume and a higher score of mRS at three months ($p = 0.007$).

The relation between the volume of occipital infarcts and VFD is shown in Table 3. A higher infarct volume increased the risk for severe visual field defects (VFD) compared to normal visual field (NVF), $p = 0.019$. Similar results were not found comparing mild VFD to NVF, $p = 2.31$. A subanalysis where infarcts that were solely located in areas 8-14 were excluded ($n = 54$), showed a significant difference in the effect of volume on the severity of VFD in infarcts in the right vs. left occipital lobe; $p = 0.011$. In the right occipital lobe, the effect of infarct volume on the severity of VFD was significant ($p = 0.001$ for severe VFD and $p = 0.022$ for mild VFD). A similar effect of volume on the severity of VFD was not found in infarcts in the left occipital lobe.

Perimetric VFD improvement after six months was more frequent in infarcts with higher volumes ($p = 0.057$). This finding was more evident in the performed subanalysis where infarcts solely in areas 8-14 were excluded, $p = 0.020$.

This implies that the larger the infarct volume, the larger the chance of VFD to improve over time.

Hemispatial neglect was examined by line bisection test, and results were available for 46 patients (63.9%). Hemispatial neglect was found in five of these patients (10.9%), of which three were left-sided and two were right-sided. A subanalysis where infarcts that were solely located in areas 8-14 were excluded ($n = 36$), hemispatial neglect was found in four patients, of which three were left-sided. The numbers were too low for statistical analysis adjusting for neglect.

4. Discussion

The current study presents an overview of the topographic distribution of acute occipital infarcts and shows a correlation between lesion volume and the severity of visual field defects in the acute phase and after six months. Furthermore, we also examined the effect of cardiovascular and other risk factors for stroke in the territory of the PCA.

We have previously shown that VFD after stroke has a negative impact on quality of life, whereas other researchers have described increased morbidity and mortality [3–5]. It was thus encouraging that 54% of the patients with VFD after occipital stroke experienced partial improvement of their visual field loss after six months, and the odds for improvement were higher the larger the VFD were. In addition, only 80% of the 64 patients examined by perimetry in the acute phase had VFD, indicating that 20% experienced a full spontaneous recovery before baseline testing within two weeks. The frequency of VFD improvement in this study is in agreement with the level reported from similar stroke studies [16, 17]. As for spontaneous VFD recovery, the likelihood decreases with increasing time poststroke, and after three months, the prognosis for spontaneous recovery is poor [3].

Many patients with visual disturbances after stroke are unable to go through visual assessment including standard perimetry examination, with reliable results [1, 10]. The main challenge is that perimetry relies highly on the patient's ability to cooperate, and the results may also be influenced by the coexistence of hemispatial neglect. We found an interesting correlation between a higher infarct volume and the severity of VFD, more evident with infarcts in the right occipital lobe. These results might be helpful in the clinical evaluation of visual disturbances in patients unable to participate in perimetry. Whereas the location of the infarct in the brain is a key point regarding symptoms, little is known about the prognostic value of topography, volume, and the affected brain structures in a broad perspective. While perimetry cannot reveal the exact location of the damage in the visual pathway [18], brain MRI provides a high level of detail regarding the location and extension of the damage.

In the present study, the topographic distribution of the brain lesions was categorized into 14 different locations. A large number of patients with AIS in the visual pathways had involvement of one or more of the areas 1-6 in the primary visual cortex (81%), but the majority also had additional involvement of at least one of the areas 7-14. Beh

TABLE 3: Relation between volume (cc) of occipital infarcts and visual field defects.

	n = 79*	Mean volume (cc)	SD	Median volume (cc)	Interquartile range (IQR)
Normal VF	14	13.8	22.6 (0.4-75)	5.15	1.1-14.0
Mild VFD	15	55.1	130.2 (0.2-508)	9.3	4.1-36.0
Severe VFD	41	43.4	62.6 (0.1-369)	30.1	10.5-48.2
Perimetry missing	9	88.0	89.4 (7.8-296)	50.9	39.6-84.8

VF: visual field; VFD: visual field defect. *Acute bilateral occipital infarcts in 7 of the 72 included patients were categorized as two separate infarcts.

et al. demonstrated on a small sample of patients how information from different brain imaging modalities provided a more complete picture of vision loss [9]. Visual field maps were derived from fMRI, the lesions were delineated on anatomical scans, and white matter tracts from diffusion-weighted MRI data. The fused maps from all imaging techniques were useful in the clinical setting to find residual functional activity in parts of the visual brain representing VFDs on perimetry. However, as the radiological correlation is complicated and ischemic lesions may affect several retinotopic areas, studies with larger samples of patients are needed to expand our understanding of the relationship between radiological findings in the visual pathways and visual field deficits.

Posterior circulation (PC) strokes share many clinical and pathogenic features with anterior circulation strokes. The clinical PC ischemic syndrome frequently includes sensory, motor, and neuropsychological deficits in addition to the well-known homonymous hemifield VFD, which is more specific to involvement of the posterior cerebral artery [19]. In the present study, men were more frequently affected than women, which is in accordance with other studies on PC strokes [20, 21]. Diabetes and hypertension are more common in posterior vs. anterior circulation disease [21, 22]. We found that previous myocardial infarction and atrial fibrillation were significantly associated with a larger stroke volume. Larger infarct volumes were significantly related to higher mRS scores at three months poststroke, reflecting a higher degree of disability. These findings highlight the importance of secondary prevention of stroke among patients suffering from myocardial infarction and atrial fibrillation.

The limitation of the present study is at first some diversity in imaging protocols. The majority of patients underwent MRI, while five patients underwent CT scans at admission. MRI may be more appropriate for predicting lesion-based prognosis compared to CT as it provides a more detailed structure of the brain. Secondly, there is a relatively low number of patients included in this study, reflecting the low population density in Norway, despite of involving three large university hospitals in the NOR-OCCIP study.

5. Conclusions

We describe how radiological assessment in addition to clinical investigations can lead to more accurate knowledge about the extent and prognosis of VFD among occipital stroke patients. Based on our findings, prevention of stroke

in patients with atrial fibrillation and those after myocardial infarction should be of uttermost importance. The association between VFD and location of stroke in the territory of the posterior cerebral artery is so far poorer understood than lesion location and function in the anterior circulation. Further studies should thus be conducted in order to meet these patients with swift and standarized investigations, a better assessment of the prognosis, and tailored rehabilitation.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Acknowledgments

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