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CLINICAL ARTICLE - VASCULAR

Terson syndrome in aneurysmal subarachnoid hemorrhage—its relation to intracranial pressure, admission factors, and clinical outcome

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Abstract
Background A large number of reports have not been able to clarify the pathophysiology of Terson syndrome (TS) in aneurysmal subarachnoid hemorrhage (aSAH).
Methods Prospective single-center study on aSAH patients. Fundoscopic and radiological signs of TS were assessed. The opening intracranial pressure (ICP) in patients who required a ventriculostomy was recorded with a manometer.
Results Six out of 36 included patients had TS (16.7 %), which was associated with unfavorable admission scores. Twenty-nine patients (80.5 %) required ventriculostomy; TS was associated with higher ICP (median, 40 vs. 15 cm cmH_2O, $p = .003$); all patients with TS had pathological ICP values of >20 cmH_2O. Patients with a ruptured aneurysm of the anterior cerebral artery complex were ten times as likely to suffer from TS (OR 10.0, 95 % CI 1.03–97.50). Detection of TS on CT had a sensitivity of 50 %, a specificity of 98.4 %, a positive predictive value of 83.3 %, and a negative predictive value of 92.4 %. Mortality was 45 times as high in patients with TS (OR 45.0, 95 % CI 3.86–524.7) and neurologic morbidity up until 3 months post-aSAH was significantly higher in patients with TS (mRS 4–6; 100 vs. 17 %; $p = .001$).
Conclusions Our findings demonstrate an association between raised ICP and the incidence of TS. TS should be ruled out in aSAH patients presenting comatose or with raised ICP to ensure upfront ophthalmological follow-up. In alert patients without visual complaints and a TS-negative CT scan, the likelihood for the presence of TS is very low.

Keywords External ventricular drain · Intracranial pressure · Ocular hemorrhage · Retinal hemorrhage · Subarachnoid hemorrhage · Terson syndrome · Vitreous hemorrhage

Introduction

Terson syndrome (TS), initially reported by the French ophthalmologist Albert Terson [1], is nowadays defined as subhyaloid (pre-retinal), retinal, and/or vitreous hemorrhage in the context of aneurysmal subarachnoid hemorrhage (aSAH). The underlying pathophysiological mechanism has not been satisfactorily investigated. So far, two explanatory models have been suggested: Following aneurysm rupture, (1) blood in the subarachnoid space between the optic nerve and its sheath extravasates directly into the eye [2] or (2) retinal venous hypertension and disruption takes place secondary to raised intracranial pressure (ICP) [3–10]. Even though the pathophysiological theory of raised ICP [2–11] is widely favored, only a few studies [12, 13] have provided direct ICP measurements in aSAH patients with TS besides two case reports of iatrogenic ICP elevation causing TS [14, 15]. It was the aim of the current study to further investigate the role of raised ICP in the genesis of TS by directly measuring the opening ICP in aSAH patients who required an external ventricular drain (EVD).

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Materials and methods

All patients consecutively admitted alive for spontaneous SAH were screened for study participation between May 2013 and February 2015. Only patients with aneurysmal SAH confirmed by computed tomographic angiography (CTA) and/or cerebral angiography were included. Patients with non-aneurysmal perimesencephalic SAH as well as moribund patients with absent brain stem reflexes and bilateral fixed mydriasis unlikely to survive until completion of further assessments were excluded.

Patient management

Patients with and without TS received the same management in accordance with current guidelines [16]. Acute hydrocephalus was treated by ventriculostomy right after admission. Aneurysms were occluded within 48 h whenever possible by surgical clipping or endovascular coiling/stenting. Cerebral vasospasm (CVS) prophylaxis with nimodipine was installed. Daily transcranial Doppler (TCD; EZ-Dop, Compumedics, Singen, Germany) served as surrogate markers for CVS [17, 18]. Accelerated mean blood flow velocity (mBFV) of the middle or anterior cerebral artery of >140 cm/s and an increase in mBFV of >50 cm/s/24 h or a Lindegaard index >3 was considered indicative of CVS. CVS was defined by arterial narrowing confirmed by CTA or cerebral angiography [17, 18]. Delayed ischemic neurological deficit (DIND) was defined as the occurrence of a new neurologic deficit or a decrease of at least two GCS points that was not apparent immediately after aneurysm occlusion and lasted at least 1 h after other causes had been ruled out [17, 18]. The occurrence of new cerebral infarctions on CT or MRI not present on imaging between 24 and 48 h after aneurysm occlusion and not attributable to other causes was regarded as delayed cerebral ischemia (DCI) [17, 18]. In cases of symptomatic CVS refractory to hypertensive therapy, endovascular rescue procedures were applied. Decompressive hemicraniectomy was performed in patients presenting with severe brain edema during surgical aneurysm treatment or to alleviate refractory ICP >20 cmH_2O. Chronic hydrocephalus was treated with a ventriculoperitoneal (VP) shunt. Surviving patients were seen for clinical follow-up in neurosurgical clinics. In case of TS, a follow-up visit was scheduled in ophthalmological clinics or in private practice for vision testing and re-evaluation of ophthalmic surgery.

Patient data

Patient baseline characteristics, pre-ictal neurological status (modified Rankin Scale, mRS), and health-related quality of life (hrQoL) using the Euro-Qol (EQ5D), as well as common risk factors for aSAH were recorded. The admission status included the GCS, World Federation of Neurological Surgeons (WFNS) score, and Hunt and Hess grade. Disease-specific parameters such as aneurysm location and multiplicity, dome and neck size were documented. In patients requiring an EVD, the opening ICP was measured with a manometer (Rocketmedical, Washington, England) at the level of the external auditory meatus. The neurological outcome was assessed at discharge and 3 months, respectively. The neuropsychological and hrQoL outcome were recorded 3 months after aSAH using the Montreal Cognitive Assessment (MoCA) and Euro-Qol (EQ5D) questionnaire as part of a standardized national outcome assessment in Switzerland [19].

Ophthalmological examination

The ophthalmological history was taken with respect to previous ophthalmological diseases or eye surgeries. Within the first 72 h upon admission, all patients received an indirect dilated fundus examination by an ophthalmologist who was blinded to the CT and patient data. For pupil dilation, a mix of 25 mg phenylephrine hydrochloride and 5 mg tropicamide in 1 ml solution of 0.9 % saline, sodium edetate, distilled water, and 0.01 % benzalkonium chloride was used. TS was defined as either intravitreous hemorrhage (IVH) or subhyaloid hemorrhage (SHH), or both. Intraocular pressure (IOP) in mmHg was measured with the Tono-Pen Avia applanation tonometer (Reichert, Inc., Depew, NY, USA).

Radiological examination

CT was performed using a second-generation dual-source CT (Somatom Definition Flash, Siemens Healthcare) with a tube voltage of 120 kVp and a tube current–time product of 380 mAs. Images were reconstructed with a slice thickness of 1.0 mm and a slice increment of 0.7 mm using a soft tissue convolution filter (J40). The presence or absence of TS in all CTs performed within the first 72 h after aSAH was assessed by an experienced radiologist (S.L.). He was blinded for the results of the ophthalmological examination and patient data.

Statistical methods

Study groups were arranged with regard to the presence or absence of TS. Admission, treatment, and outcome factors were compared between the two study groups. For categorical variables, Pearson's Chi-square tests were used or Fisher's exact tests if a single cell value was ≤5. Mann–Whitney *U* tests were used to analyze the group differences for continuous parameters. To estimate effect sizes of relationships, a logistic regression analysis was performed. Results were expressed in odds ratios (OR) with 95 % confidence intervals (CI). A probability index < .05 was considered statistically

significant. Stata v.14 (College Station, TX, USA) was used for analysis.

Results

During the study period, 84 patients admitted for spontaneous SAH were screened for study participation and 45 patients (53.6 %) were found to have SAH due to a ruptured aneurysm and be eligible. Seven patients/next of kin refused to consent to participation and for two patients the ophthalmological exam could not be obtained due to death shortly after admission in one case and logistic reasons in another. Thus, a remainder of $n = 36$ patients was analyzed. A flow-chart demonstrating the distribution of study patients into the TS and non-TS group, as well as the obtained ICP measurements is shown in Fig. 1.

Ophthalmological findings

TS was diagnosed in six (16.7 %) out of 36 patients (Table 1). When considering each of the 12 eyes separately, pure IVH occurred in one eye (8.3 %) and pure SHH in six eyes (50 %). Combined IVH and SHH occurred in three eyes (25 %). In two patients, only the left eye was affected. In the remaining four patients, TS occurred bilaterally. IOP of patients with TS (median, 15.0 mmHg ± 1.7, SE)) did not differ from IOP of patients without TS (median, 14.0 mmHg ± 0.5; $p = .111$).

Admission status

There was no difference in age, gender, risk factors for aSAH, pre-ictal status, or time interval between aSAH and admission to hospital (Table 2). The incidence of sentinel headache in this study cohort has been reported previously [20]. The ophthalmological history revealed cataract in three patients (one with TS, two without TS), glaucoma in one patient without TS, and previous eye surgery in two patients without TS. The GCS was significantly lower in patients with TS (median GCS 3 vs. 14, $p < .001$). All patients with TS compared to 20 % patients without TS presented comatose and intubated (100 vs. 20 %, $p < .001$). TS was also associated with unfavorable clinical grading as determined by the WFNS and the Hunt and Hess scale (Table 2).

Aneurysm characteristics and treatment

There was an association between location of the ruptured aneurysm in the anterior cerebral artery complex (A1, A2, and Acom) and TS (Table 3). Patients with a ruptured aneurysm of the anterior cerebral artery complex were ten times as likely to suffer from TS than patients with aneurysms in other locations (OR 10.0, 95 % CI 1.03–97.50, $p = .048$). Aneurysm laterality, as well as dome and neck sizes were comparable in both groups. Patients with TS were less likely to be clipped (0 %) compared to patients without TS (46.7 %; Pearson Chi-square 4.58, $p = .032$). In four patients with TS, the aneurysm was secured by

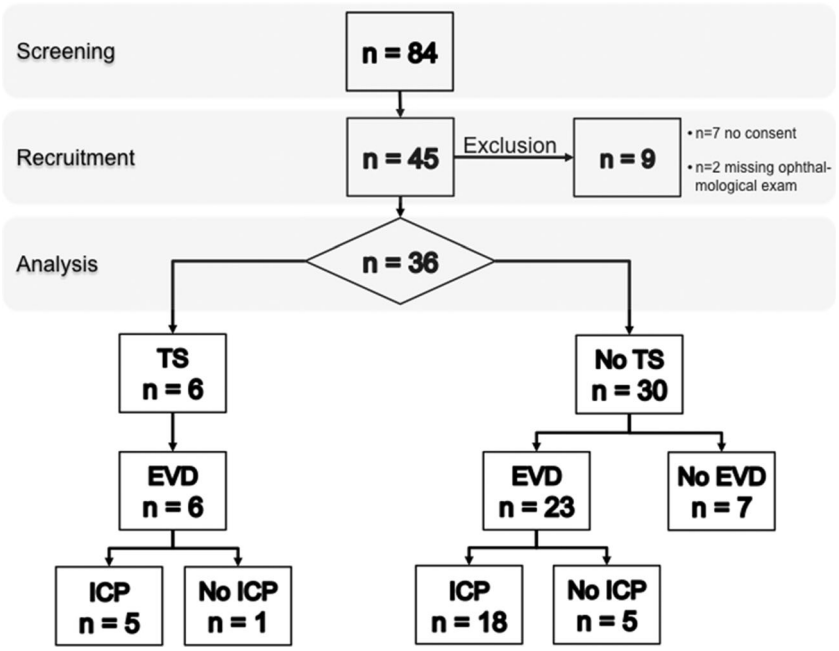

Fig. 1 Flow chart of $n = 36$ patients with aneurysmal subarachnoid hemorrhage with or without Terson syndrome (TS) that were included in the current study and received an external ventricular drain (EVD) or not. Note that intracranial pressure (ICP) measurement was not feasible in the emergency situation in $n = 6$ patients with EVD because a manometer was not at hand immediately

Table 1 Case descriptions with ophthalmological findings in six patients with Terson syndrome (TS)

Patient		Aneurysm	Left eye IVH, SHH, IOP	Right eye IVH, SHH, IOP	Aneurysm occlusion	3-month outcome
1	F, 69 years	13.3 × 4.9 mm, A1	IVH, − , 20	- , − , 22	–	Dead
2	M, 51 years	7.0 × 2.5 mm, ICA	IVH, SHH, 14	- , − , 14	Coiling	Vegetative state
3	M, 53 years	7.0 × 5.0 mm, Acom	IVH, SHH, 15	IVH, SHH, 15	Coiling	Dead
4	F, 45 years	4.0 × 1.0 mm, A2	- , SHH, 15	- , SHH, 15	–	Dead
5	F, 49 years	6.0 × 2.0 mm, Acom	- , SHH, 10	- , SHH, 8	Coiling	Dead
6	F, 54 years	8.1 × 4.0 mm, Acom	- , SHH, 17	- , SHH, 31	Coiling	Dead

IOP intraocular pressure (as measured by tonometry; in mmHg), *IVH* intravitreous hemorrhage, *F* female, *M* male, *SHH* subhyaloid hemorrhage, *A1* precommunicating segment of anterior cerebral artery, *A2* postcommunicating segment of anterior cerebral artery, *Acom* anterior communicating artery, *ICA* internal carotid artery

endovascular coiling. In two patients with TS, no aneurysm occlusion was done in light of their unfavorable neurological status. Patients with TS were more likely to receive decompressive hemicraniectomy as an ICP salvage treatment (OR 14.5, 95 % CI 1.06–198.8, $p = .045$).

Association of TS and ICP

A total of $n = 29$ patients required ventriculostomy for acute hydrocephalus (80.5 %), among those were all six patients with TS. The opening ICP was measured in 5/6 (83.3 %) patients with TS and in 18/23 patients without TS (78.3 %; Fig. 1). TS was associated with a higher opening ICP (median 40 vs. 15 cmH_2O, $p = .003$; Fig. 2). When dichotomized for 'pathologically raised' ICP of >20 cmH_2O at the time of ventriculostomy, patients with TS were more likely to have pathologically raised ICP as patients without TS (100 vs. 56.7 %; OR 27.0, 95 % CI 1.26–576.4, $p = .008$). However, some patients that presented with high ICP did not develop TS (Fig. 3).

Clinical course and outcome

There were no differences in neurological (re-bleed, CVS, DIND, DCI, epilepsy) or general (infectious, cardiac, or electrolyte) complications between patients with and without TS, but there were marked differences in mortality and neurological outcome. Mortality (OR 45.0, 95 % CI 3.86–524.7, $p = .002$) and neurologic morbidity (mRS 4–6; 100 vs. 17 %; Pearson Chi-square 22.50, $p = .001$; Table 4) at 3 months post-aSAH was considerably higher in patients with TS as compared to those without TS. Severe brain injury was the reason of death in four and pulmonary embolism in one patient with TS. In patients without TS, death was attributable to severe brain injury, cardiac arrest, and pulmonary embolism in each case, respectively. For the only surviving patient with TS, the family refused ophthalmological follow-up in light of her reduced neurological status and absence of subjective visual complaints.

CT detection of TS

The presence or absence of TS on the first 72 h CTs (Fig. 4) was assessed in 72 eyes (Table 5). TS was correctly detected in five out of ten eyes (true positive rate). In 61 out of 62 eyes without TS, the absence of TS was correctly rated on CT (true negative rate). Five eyes with TS diagnosed by the ophthalmological examination were missed on CT (false negative rate). In one eye, the radiologist detected TS, which was not confirmed in the ophthalmological examination (false positive rate). This translates into a sensitivity of 50 %, a specificity of 98.4 %, a positive predictive value of 83.3 %, and a negative predictive value of 92.4 % for the CT.

Discussion

In this prospective study on 36 patients with aSAH, we assessed various aspects of TS such as its incidence, association with clinical grading, aneurysm location, raised ICP, and clinical outcomes including mortality.

The study primarily aimed at shedding more light on the role of ICP in the pathophysiology of TS. We here demonstrate a positive correlation between the incidence of TS and raised opening ICP in patients with aSAH measured by ventriculostomy (Fig. 2). In a previous series [13], a tendency for higher ICP in aSAH patients with TS was observed, but could not be proven due to a low number of patients with available data (TS $n = 4$; mean, 27.5 cmH_2O; range, 20–40 cmH_2O vs. non-TS $n = 8$; 22.0 cmH_2O; range, 5–40 cmH_2O; $p = .573$). Similarly, in the current study, it was not feasible to obtain opening ICP in every case as emergency ventriculostomy in comatose patients was not delayed when a manometer was not at hand immediately. Our current findings are in keeping with Medele et al. [12] who noted extremely raised ICP (>30 mmHg) during EVD placement in seven out of ten patients with TS (mean initial ICP 26 ± 6.9 mmHg vs. non-TS 15 ± 5.8 mmHg). However, their patient sample was heterogeneous because it comprised aSAH patients and

Table 2 Basic demographic parameters and admission status of patients with and without Terson syndrome (TS)

	TS		No TS		*p value*
Age in years (median ± SE)	52.5 ± 3.4		56.2 ± 2.5		0.625[a]
Sex					
Male	2	33 %	18	60 %	0.230[b]
Female	4	67 %	12	40 %	
GCS (median ± SE)	3 ± 0.0		14 ± 0.7		<0.001[a]
Hunt and Hess score					
2	–	0 %	13	43 %	0.009[b]
3	1	17 %	9	30 %	
4	–	0 %	3	10 %	
5	5	83 %	5	17 %	
WFNS score					
1	–	0 %	4	13 %	0.003[b]
2	–	0 %	14	47 %	
3	–	0 %	4	13 %	
4	–	0 %	3	10 %	
5	6	100 %	5	17 %	
Fisher score					
2	–	0 %	1	3 %	0.809[b]
3	6	100 %	28	94 %	
4	–	0 %	1	3 %	
Intubated					
Yes	6	100 %	6	20 %	<0.001[b]
No	–	0 %	24	80 %	
aSAH to hospital admission (in hours; median ± SE)	2.5 ± 2.1		3.5 ± 6.7		0.524[a]
Systolic blood pressure (in mmHg; median ± SE)	157.5 ± 17.1		156.0 ± 4.5		0.768[a]
Risk factors*					
Smoking	1	25 %	16	62 %	0.178[b]
Arterial hypertension	3	60 %	12	43 %	0.478[b]
Alcohol abuse	1	20 %	5	19 %	0.968[b]
Illegal drugs	–	0 %	2	8 %	0.566[b]
Previous aSAH	–	0 %	1	4 %	0.701[b]
Sentinel headache	1	25 %	6	22 %	0.901[b]
Genetic predisposition	–	0 %	1	4 %	0.696[b]
mRS before aSAH					
0	5	83 %	28	93 %	0.418[b]
≥ 1	1	17 %	2	7 %	
EQ5D index before aSAH (median ± SE)	.889 ± .064		1.000 ± .023		0.609[a]
Ophthalmological history					
Previous eye surgery	–	0 %	2	7 %	>.999[c]
Cataract	1	17 %	2	7 %	.431[c]
Glaucoma	–	0 %	1	3 %	>.999[c]
Glasses	–	0 %	7	23 %	.317[c]
Reading glasses	1	17 %	9	30 %	.654[c]
Total patients	n = 6	100 %	n = 30	100 %	

[a] two-tailed Mann–Whitney test, [b] Pearson Chi-square test, [c] Fisher's exact test

* Missing data present (in patients arriving in a coma without possibility to obtain data from next of kin). *EQ5D* Euro-Qol questionnaire, *mRS* modified Rankin Scale, *SE* standard error

patients with severe traumatic brain injury alike. Interpreting the present results in view of the available literature, raised ICP seems to be a significant contributing factor to the pathogenesis of TS. A median ICP of 40 cmH_2O in our patients with TS suggests an ICP cut-off that lies well above the commonly accepted threshold of >20 cmH_2O with which

Table 3 Disease-specific parameters and treatment details of patients with and without Terson syndrome (TS)

	TS	No TS	*p* value		
Aneurysm location					
Acom/ACA	5	83 %	10	33 %	0.120[a]
ICA/Pcom	1	17 %	6	20 %	
MCA	–	0 %	10	33 %	
Posterior circulation	–	0 %	4	14 %	
Aneurysm laterality					
Left	3	50 %	9	30 %	0.203[a]
Middle	3	50 %	10	33.3 %	
Right	–	0 %	11	36.7 %	
Dome size in mm (median ± SE)	7.0 ± 1.3		6.9 ± 0.5		0.864[b]
Neck size in mm (median ± SE)	3.3 ± 0.7		3.0 ± 0.3		0.920[b]
Multiple aneurysms					
Yes	–	0 %	10	33 %	0.096[a]
No	6	100 %	20	67 %	
Treatment					
Surgical occlusion	–	0 %	14	47 %	0.032[a]
Endovascular occlusion	4	67 %	16	53 %	0.549[a]
Ventriculostomy	6	100 %	23	76.7 %	0.187[a]
Ventriculoperitoneal shunt	2	33 %	9	30 %	0.817[a]
Lumbar drain	–	0 %	4	13 %	0.343[a]
Decompressive hemicraniectomy	2	33 %	1	3 %	0.015[a]
Time in hours - aSAH to EVD (median ± SE)	4.0 ± 2.2		7.0 ± 2.2		0.059[b]
Opening ICP (in cmH_2O; median ± SE)*	40.0 ± 4.2		15.0 ± 1.8		0.003[b]
Total patients	n = 6	100 %	n = 30	100 %	

[a] Pearson Chi-square test; [b] two-tailed Mann–Whitney test

Acom anterior communicating artery, *EVD* external ventricular drain, *ICA* internal communicating artery, *ICP* intracranial pressure, *MCA* middle cerebral artery, *Pcom* posterior communicating artery, *SE* standard error. *Measurements available in five patients with TS and 18 patients without TS (Fig. 1)

56.7 % of our patient sample still had no TS. This is also illustrated in Fig. 3, which plots opening ICP against the neurological outcome at 3 months for patients with and without TS. It is evident from these results that in the TS group, all patients with high ICP had unfavorable outcomes. It is also important to note that there were some patients who had high initial ICP, had no TS, and had favorable outcomes. Results from post-mortem examinations in deceased patients with TS would be required to fully prove this hypothetical cascade (elevated ICP leading to retinal venous disruption). We are aware that TS could have occurred the first days following SAH. We wanted to assess a direct association between the incidence of TS and raised opening ICP when inserting an EVD at admission, and a second exam at a later point in time could have camouflaged a causal effect. Therefore, we designed the study without a second ophthalmological exam. It currently remains unclear whether a sudden ICP peak or a long-standing raised ICP causes TS.

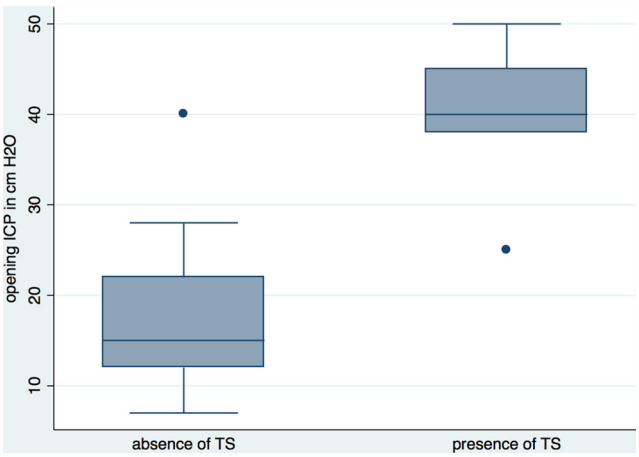

Fig. 2 Box plot demonstrating that the opening intracranial pressure (ICP) was significantly higher in patients with Terson syndrome (TS) than in patients without TS (median, 40 vs. 15 cm cmH_2O, $p = .003$). The median with the 25th–75th percentile (*box*), the upper and lower adjacent values (*whiskers*) and outliers (*dots*) are displayed

Incidence of TS

The incidence of TS in the current series was 16.7 %, which is in line with the incidence reported in other prospective studies of 8 % [21], 11 % [22], 12.1 % [23], 16.7 % [24], 17 % [25], 18.3 % [13], 20.9 % [26], 21.7 % [27], 27 % [28] and 28 %

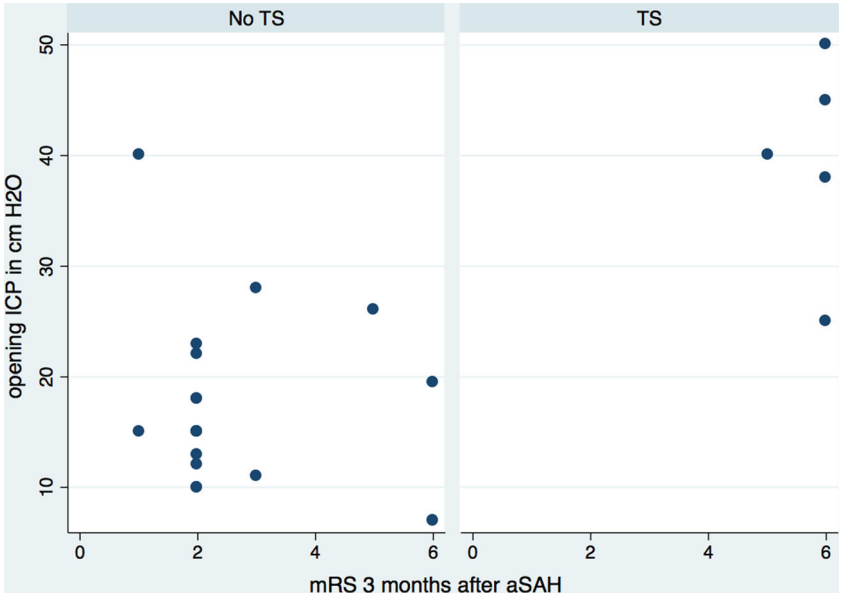

Fig. 3 Graph plotting the opening intracranial pressure (ICP) in cmH_2O against neurological outcome at 3 months (modified Rankin Scale, mRS) in patients with Terson syndrome (TS) and without TS. Note that ICP is generally high and outcome unfavorable in patients with TS, whereas individual patients with high ICP have no evidence of TS and acceptable outcomes

[29]. As a tertiary center, we recognize referral bias as a number of moribund patients were not transferred or died before reaching the hospital. Possibly, the incidence of TS would have been higher if non-referred patients and those who died before the ophthalmological exam ($n = 1$ in the current study) could have been considered.

Table 4 In-hospital follow-up, complications, and outcome of patients with and without Terson syndrome (TS)

	TS		No TS		*p* value
ICU days (median ± SE)	9.5 ± 4.5		14 ± 1.6		0.815[a]
Complications					
Re-bleed	1	17 %	1	3 %	0.193[b]
CVS	4	67 %	14	47 %	0.371[b]
DIND	1	17 %	9	30 %	0.506[b]
DCI	2	33 %	4	13 %	0.230[b]
Infection	2	33 %	11	37 %	0.877[b]
Cardiac complication	1	17 %	2	7 %	0.418[b]
Electrolyte disorder	2	33 %	8	27 %	0.739[b]
Epileptic seizure	–	0 %	2	7 %	0.515[b]
mRS at discharge					
Favorable (mRS 0–1)	–	0 %	12	40 %	0.0001[b]
Moderate (mRS 2–3)	–	0 %	13	43 %	
Unfavorable (mRS 4–5)	1	17 %	2	7 %	
Death (mRS 6)	5	83 %	3	10 %	
mRS at 3 months					
Favorable (mRS 0–1)	–	0 %	13	43 %	0.0001[b]
Moderate (mRS 2–3)	–	0 %	13	43 %	
Unfavorable (mRS 4–5)	1	17 %	1	3 %	
Death (mRS 6)	5	83 %	3	10 %	
EQ5D index at 3 months (median ± SE)*	.000 ± .026		.722 ± .065		0.001[a]
MoCA at 3 months (median ± SE)*	.0 ± .17		22.5 ± 1.8		0.001[a]
Total patients	n = 6	100 %	n = 30	100 %	

[a] two-tailed Mann–Whitney test; [b] Pearson Chi-square test

CVS cerebral vasospasm, *DCI* delayed cerebral ischemia, *DIND* delayed ischemic neurological deficit, *EQ5D* Euro-Qol 5D, *ICU* intensive care unit, *MoCA* Montreal cognitive assessment, *mRS* modified Rankin Scale, *SE* standard error. *for statistical analysis dead patients were counted as 0 points

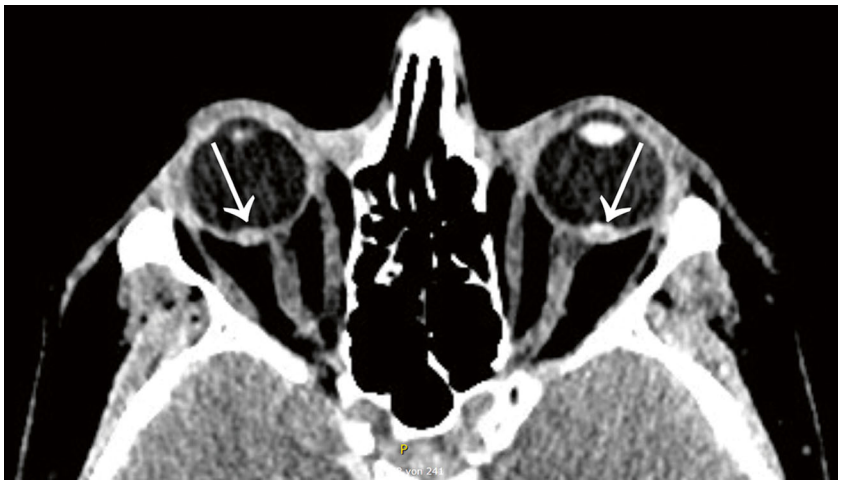

Fig. 4 CT confirming the diagnosis of Terson syndrome by the presence of bilateral hyperdense nodules (*arrows*) on the temporal retinal surface in a patient with aneurysmal subarachnoid hemorrhage

Clinical grading at admission

In accordance with earlier reports [13, 23, 26, 27, 29], there was a marked difference in the clinical admission status between the study groups (Table 2). In the present cohort, 100 % of patients with TS arrived comatose and intubated. In prior studies, coma on admission varied from 21.4 % [30], 43.8 % [26], 85.7 % [23], 90 % [12], 90.9 % [13], up to 100 % of patients [3, 21, 25]. The diagnostic significance of a history of transient or prolonged coma with respect to TS has been previously discussed [13, 21, 25, 31]. Hunt and Hess grades 3–5 were recorded in 83 % of the present patient sample with TS as compared to 42.8 % [30], 62.5 % [21], 70.0 % [24], 75.0 % [26], 83.3 % [28], 95.2 % [23], up to 100 % in prior reports [13]. Poor neurological condition in our six aSAH patients with TS resulted in no treatment in two and endovascular coiling in the other four cases (Table 3). It is our treatment protocol to defer surgical clipping and opt for early endovascular coiling in patients with Hunt and Hess grade 4 and 5 unless an intraparenchymal hematoma requires urgent evacuation [32].

Aneurysm location, laterality, and size

Contrary to a previous report [13] on the significant association between TS and the involvement of ICA aneurysms, only one of six patients with TS had an ICA aneurysm in this study cohort. The remaining five patients with TS presented with aneurysms of the ACA complex, resulting in a significant association of TS with this location (OR 10.0, 95 % CI 1.03–97.50, $p = .048$). Previous authors have found a higher incidence of aneurysms of the anterior circulation in patients with TS [28, 33]. Most reports could not identify any specific aneurysm locations that predisposed for TS occurrence [21, 23, 24, 26, 27]. In line with the literature, we found no correlation of TS with laterality [13, 24, 26, 33] or size [23, 26] of the aneurysm. In terms of aneurysm morphology, only Koskela et al. [22] found an association with the occurrence of TS and aneurysm length but not with width.

Table 5 The agreement of CT evidence and the ophthalmological examination for the presence or absence of Terson syndrome (TS) in a prospective series of $n = 36$ patients with 72 eyes

	TS	No TS	
CT +	5	1	PPV 0.83
CT -	5	61	NPV 0.92
	Sensitivity 0.50	Specificity 0.98	

NPV negative predictive value, *PPV* positive predictive value

Clinical outcome

Outcome was devastating in patients with TS in the present series, with five deaths (83.3 % mortality) and one severely disabled survivor. Mortality has been found to be higher in prospective studies that systematically screened patients, regardless of unfavorable clinical admission status and early mortality [34]. Most authors agree that TS is generally associated with elevated mortality and morbidity rates [12, 13, 24, 26, 34]. Bearing this in mind, the presence of TS could potentially aid in estimating the prognosis in comatose SAH patients. It is worth mentioning though, that some aSAH patients suffering from TS may have an acceptable outcome that can range considerably (depending on the study methodology) from as low as 6.3 % [26], 28.6 % [23], 36.4 % [13], 36.6 % [28], 50 % [30], 60 % [12, 27], up to 90 % in previous reports [24], and 43 % in a systematic review [34]. A limitation of the current study is that clinical outcome was interpreted for only six patients with TS. An increasing number of prospective studies, each reporting relatively small patient cohorts with TS, call for a meta-analysis to get more precise estimates of the association between TS and clinical outcome.

Ophthalmological aspects of TS

Usually, early vitrectomy is not necessary in the natural history of non-traumatic SAH-related intraocular hemorrhages according to Stiebel-Kalish et al. [35]. However, the authors propose early vitrectomy in one eye for patients with bilaterally decreased visual acuity. The rationale for early detection of TS in aSAH patients is to ensure upfront ophthalmological follow-up. Recognizing the indication for early vitrectomy is vital to hasten visual recovery [35] and overall rehabilitation in severely disabled patients, especially those who often present comatose or with high ICP, as demonstrated by our data. The only surviving patient with TS in our series did not require ophthalmological surgery.

IOP was found to be similar in patients with TS and without TS. It is important to note, however, that IOP was measured after ICP was lowered by ventriculostomy. From a scientific point of view, it would be interesting to measure IOP before EVD insertion. However, this would be impossible to do since acute hydrocephalus should be treated immediately in the context of a life-threatening condition.

Radiological aspects of TS

The current series of patients revealed a sensitivity and specificity of 50 % and 98.4 %, as well as a positive predictive value of 83.3 % and a negative predictive value of 92.4 % to detect TS in the first 72-h CTs. This compares well to a sensitivity of 42 % and a specificity of 97 % reported by Koskela et al. [22] although the authors partially excluded the orbits by applying standardized radioprotection measures. In the literature, inter-rater agreement was reported to be high [22, 36], but false-negative detection secondary to beam hardening artifacts is not uncommon. [37]

Conclusions

The present study demonstrates a positive correlation between the incidence of TS and raised ICP in patients with aSAH. In patients presenting comatose or with elevated ICP, TS is likely to be present and should be ruled out, preferably by an ophthalmological examination to ensure upfront ophthalmological follow-up. In alert patients without visual complaints and a TS-negative CT scan, the likelihood for the presence of TS is very low. Our results once again confirm the impressive association between TS and increased mortality and suggest TS as a predictor of 3-month mortality.

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Compliance with Ethical Standards All persons provided informed consent prior to their inclusion in the study.

Conflicts of interest The authors declare that they have no conflict of interest. All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Ethical approval All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee St. Gallen, Switzerland (EKSG 13/011/1B).

Informed consent Informed consent was obtained from all individual participants included in the study.

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