Terson’s Syndrome—Rate and Surgical Approach in Patients with Subarachnoid Hemorrhage

A Prospective Interdisciplinary Study

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Objectives: To analyze the need for surgical intervention in Terson’s syndrome (TS) and the rate of TS, as well as the effect of pars plana vitrectomy (PPV) with or without internal limiting membrane (ILM) peeling, complications, correlations between TS and sex, and the influence of the severity of subarachnoid hemorrhage (SAH) expressed by Glasgow Coma Scale (GCS) score and Hunt and Hess grade on the occurrence of TS.

Design: Prospective, uncontrolled, interdisciplinary study.

Participants: A total of 102 patients with SAH over a period of 24 months.

Methods: Patients were examined on days 1 and 14. A PPV was indicated in cases of nonresorbing vitreous hemorrhage (VH). Peeling of the ILM was performed with the help of ILM-BLUE (DORC, Zuidland, The Netherlands) using end-gripping ILM forceps.

Main Outcome Measures: Effect of PPV on visual acuity (VA) and timing of intervention in cases of nonclearing VH.

Results: The rate of TS was 19.6% (20/102). The mean age of the patients was 52.1±11.8 years. Patients presenting with an initial GCS of less than 8 or with high Hunt and Hess grades were more affected by TS. Eight (9 eyes) of the 20 patients with TS (40% of the patients with TS) underwent a PPV for nonclearing vitreous bleeding. In 4 patients (4 eyes; 20% of patients with TS), ILM peeling was considered necessary because of sub-ILM bleeding. The mean interval between SAH and PPV was 4.4 months (range, 3–5 months). Postoperative follow-up was 6.4 months. Visual acuity improved in all patients. Best-corrected VAs at first and at last presentations were 2.2 and 0.0625 logarithm of the minimum angle of resolution (logMAR), respectively. For patients who underwent ILM peeling, these values were 1.725 and 0.05 logMAR, respectively.

Conclusions: Pars plana vitrectomy and ILM peeling have beneficial effects on the visual rehabilitation of patients with nonclearing VH after TS. We did not identify any safety concerns after PPV in our patients with dense nonclearing hemorrhage that persisted for more than 3 months. Ophthalmology 2014;121:1628-1633 © 2014 by the American Academy of Ophthalmology.

Although Terson’s syndrome (TS) was first described by Litten in 1881,1 it was subsequently named after the French ophthalmologist Albert Terson in 1900.1 Today, TS is commonly defined as the occurrence of an intraocular hemorrhage associated with a subarachnoid hemorrhage (SAH).1,2 Clinically, intraocular hemorrhage may be subretinal, intraretinal, preretinal, subhyaloid, or intravitreal, and, at present, any type of intracranial hemorrhage accompanied by vitreous or retinal hemorrhage is known as TS.3-8 According to the literature, TS also may be caused by intracerebral hemorrhage, subdural or epidural hematoma, severe brain injury, or intraventricular hemorrhage. The mechanism causing intracranial bleeding remains unclear, but the prevailing hypothesis is that TS is the result of retinal venous hypertension caused by displaced blood that is forced into the liquor spaces of the optic nerve and causes obstruction of the central retinal vein and choroidal anastomosis6-8 under high intracranial pressure.

A broad variation in the rate of TS, between 10.5% and 46%, can be found in the literature. This can be attributed to the fact that the definition of TS has shifted in clinical practice from being solely a vitreous hemorrhage (VH) to including any type of VH or retinal hemorrhage (vitreous, intraretinal, preretinal, subhyaloidal);1,3,4 VH is found in 3% to 5% of cases.1,3,4,11 There is an association among intracranial hemorrhage, the severity of intracranial hemorrhage, and the mortality rate. Patients with higher Hunt and Hess grades exhibit a higher frequency of intracranial bleeding and mortality rate.

Currently, there are no clear guidelines for the timing of ophthalmological interventions.3,9,14-16 Spontaneous clearance of VH may be expected within 10 to 12 months, but vitreous
surgery can expedite this process, especially in cases of nonclearing hemorrhage. This may prevent some of the severe complications, including epiretinal membrane formation, macular holes, proliferative vitreoretinopathy (PVR), retinal detachment, hemosiderosis, optic atrophy, and development of amblyopia in younger patients.10,11,16–18 Proliferation of glial cells and elements of the retinal pigment epithelium are capable of causing retinal distortion and fibrotic adhesion.18

The aim of our interdisciplinary study was to analyze the need for surgical intervention in TS, the effect of vitrectomy with or without internal limiting membrane (ILM) peeling, the appearance of complications (intraoperative or postoperative), the rate of TS, the correlations between TS and sex, and the influence of severity of SAH expressed by Glasgow Coma Scale (GCS) score and Hunt and Hess grade on the occurrence of TS. All of our patients were hospitalized for SAH.

Methods

This uncontrolled interdisciplinary prospective study was approved by the local ethics committee of the medical council of the state of Hamburg (PV3611 and PV4079). All patients with SAH admitted to our hospital over a period of 24 months were screened for TS if written consent was signed by the patient or legal representative. In total, 102 patients were included in this study. Ophthalmological examination (OE) was performed on days 1 and 14, including best-corrected visual acuity (BCVA); in patients sufficiently responsive to following standardized OE, anterior chamber evaluation and fundoscopy (assessment of optic nerve head, macula, and peripheral retina) were performed after medical mydriasis (Mydriaticum Stulln) and pupillary reaction. The examination on day 14 was performed to detect TS developing after a delay of several days, which has been described elsewhere. In cases of VH in which retinal examination was not possible, B-scan ultrasonography was performed. All patients with TS were asked to come back to the ophthalmology department for a follow-up visit after 3 months or as soon as they were discharged from the rehabilitation centers.

In cases of nonresorbing VH lasting at least 3 months (mean interval between SAH and vitrectomy was 4.4 months; range, 3–5 months), a standard 23-gauge 3-port pars plana vitrectomy (PPV) was performed (9 eyes of 8 patients) using an Accurus system (Alcon, Fort Worth, TX). If sub-ILM deposits of blood or puckering of the ILM was observed during surgery (after clearing the dense VH), an additional peeling of the ILM was performed (4 cases). The ILM was stained with the help of ILM-BLUE (DORC, Zuidland, The Netherlands) and peeled with end-gripping ILM forceps. All patients underwent a complete OE preoperatively and postoperatively and optical coherence tomography (OCT) examination (Cirrus OCT; Carl Zeiss Meditec, Dublin, CA) postoperatively to evaluate the effect of the vitrectomy and the ILM peeling.

Statistics

Statistical analyses of the data were performed using a Student t test, chi-square test, or trend tests (Mantel–Haenszel chi-square), depending on the scale of the measurements, to examine correlations between the parameters using SPSS Statistics 21 (IBM, Chicago, IL). For statistics, visual acuity (VA) values were transformed to a logarithm of the minimum angle of resolution (logMAR) scale and compared using a Student t test. The level of statistical significance was set at P<0.05. For figures, the VA scores were used on a decimal scale for better visualization.

Results

The rate of TS was 19.6% (20/102) with a predominance among female patients (16/66 female patients, 4/36 male patients; P = 0.113). The mean age of the patients was 52.1 ± 11.8 years (range, 23–87 years). Patients presenting initially with a GCS score of less than 8 (chi-square = 13.328; df = 1; P = 0.001), a high Hunt and Hess grade (chi-square = 23.622; df = 1; P<0.001), and a high Fisher grade (chi-square = 9.389; df = 1; P = 0.002) were more often effected by TS. As a consequence of the lower initial GCS score, the higher Hunt and Hess grade, and higher Fisher grade, patients with TS had a statistically significantly worse Glasgow Outcome Scale score after 3 months (chi-square = 12.706; df = 1; P = 0.001) (Table 1).

Table 1. Characteristics of Patients with Subarachnoid Hemorrhage (Aneurysmal and Perimesencephalic Subarachnoid Hemorrhage)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No TS</th>
<th>With TS</th>
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<tbody>
<tr>
<td>Sex</td>
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<tr>
<td>Male</td>
<td>32</td>
<td>4</td>
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<tr>
<td>Female</td>
<td>88.9%</td>
<td>11.1%</td>
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<tr>
<td>Female</td>
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<td>16</td>
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<tr>
<td>Female</td>
<td>75.8%</td>
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<tr>
<td>GCS score at admission</td>
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<tr>
<td>≥8</td>
<td>73</td>
<td>11</td>
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<td>&lt;8</td>
<td>18</td>
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<td>&lt;8</td>
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<td>9</td>
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<td>&lt;8</td>
<td>50.0%</td>
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<td>Hunt and Hess grade</td>
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<td>I</td>
<td>34</td>
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<td>II</td>
<td>94.4%</td>
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<td>III</td>
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<tr>
<td>III</td>
<td>92.3%</td>
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<tr>
<td>III</td>
<td>13</td>
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<tr>
<td>IV</td>
<td>72.2%</td>
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<td>IV</td>
<td>10</td>
<td>4</td>
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<tr>
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<td>V</td>
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<tr>
<td>V</td>
<td>12.5%</td>
<td>87.5%</td>
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<td>Fisher grade at admission</td>
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<td>1</td>
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<td>3</td>
<td>90.9%</td>
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<td>4</td>
<td>69.0%</td>
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<td>GOS after 3 mos</td>
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<td>1</td>
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<td>1</td>
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<tr>
<td>3</td>
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<td>4</td>
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<td>5</td>
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<td>5</td>
<td>90.9%</td>
<td>9.1%</td>
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GCS = Glasgow Coma Scale; GOS = Glasgow Outcome Scale; TS = Terson’s syndrome.
The first OE was performed on the day that written consent was obtained, a mean of 7.26 days after SAH (standard error of the mean ± 37.28). In 57 patients (59.9%), OE was repeated 14 days after the first OE (15.56±:10.46 days). The second examination was performed in every patient who was still admitted to our hospital. Because of ethic committee regulations, no changes to the usual clinical course were allowed. The third OE was planned to be performed 3 months after the onset of the SAH. A total of 15 of the 20 patients (75%) with TS returned for OE after 3 months or as soon as possible after discharge from the rehabilitation unit (135.53±:56.85 days after SAH).

Patients with SAH without TS had no ocular pathologies or monocular visual impairment. Several patients had binocular double vision due to motoric nerve palsy.

Of the 20 patients with TS, 8 (9 eyes; 40% of the patients with TS) underwent a standard 3-port, 23-gauge PPV because of non-clearing vitreous bleeding. In 4 patients (4 eyes; 20% of patients with TS), ILM peeling was necessary because of sub-ILM bleeding or puckering of the ILM. The mean interval between SAH and vitrectomy was 4.4 months (range, 3–5 months). All procedures were performed by a single surgeon (L.W.). The type of anesthesia was chosen in consultation with patients, but general anesthesia was used only if there were no neurologic or other systemic safety concerns. Seven operations were performed under general anesthesia, and 2 operations were performed with retrobulbar block. The mean time for PPV was 33.9±:5.6 minutes (range, 20–60 minutes). None of the patients were pseudophakic at the time of vitrectomy. One procedure was combined with retrobulbar block, and 2 patients (3 eyes) who developed cataracts received an intraocular lens implantation during the postoperative follow-up. Cryotherapy was performed in 4 patients (50%) because of the intraoperative detection of retinal lesions (e.g., lattice degenerations, no retinal breaks) in the outermost periphery to reduce the risk of postoperative retinal complications while putting the lens at as low a risk as possible. In the case requiring combined cataract surgery and vitrectomy, a hexafluoroethane gas tamponade and laser treatment had to be used because of a peripheral retinal detachment that was not noted during the preoperative echography but was seen as soon as the retina became visible during surgery. Optic nerve atrophy was not observed in any of the patients. No intraoperative complications were observed, and except for the 3 cases of cataract surgery, no patients had to undergo a subsequent reoperation because of complications (e.g., PVR, retinal detachment, or epiretinal membranes).

Postoperatively, patients were followed up for 6.4 months (range, 3–12 months). The postoperative OCT scans showed no signs of epiretinal membranes, macular edema, or other signs of pathology.

Visual acuity improved in all patients. The BCVAs at first presentation and last presentation were 2.2 and 0.0625 logMAR, respectively. The BCVAs at the first and last presentations of the patients undergoing ILM peeling were 1.725 and 0.05 logMAR, respectively (all patients [n = 9], P<0.001; with ILM peeling [n = 4], P = 0.029; without ILM peeling [n = 5], P<0.001) (Table 2).

**Discussion**

The prevalence of TS, defined as any kind of intraocular hemorrhage, is between 10.5% and 46%, and VH may be associated with 3% to 5% of the cases.9–13 Our study showed a rate of TS of 19.6% (20/102) and a higher rate of VH in these patients with TS (40%). Prevalence often may be underestimated because of the severity of the underlying condition, and if neurosurgical centers do not perform an OE routinely, only a minority of patients will be diagnosed at the time of SAH.14,19 The presence of vitreous bleeding is a sign of the severity of the disease, as clearly demonstrated by our results. According to Frizzell et al.,1 the higher rate of VH in our study may be related to improved survival rates of the patients and may be a sign of improved interdisciplinary treatment regimens.

The precise mechanism of TS remains obscure and has been under debate for many years. Manschot13 hypothesized that a spontaneous subarachnoid bleeding causes sudden intracranial hypertension and that blood is forced under high pressure into the subarachnoid space of optic nerves. This was challenged by Hedges and Walsh10 on the grounds that pressure is not transmitted down the sheath space because there is no connection between the subarachnoid space and intraocular structures and that VH occurs through a rapid increase of intracranial pressure transmitted throughout the venous channels into the orbital veins. Michalewska et al.,5 using spectral domain OCT, suggested that blood may enter the vitreous cavity around the retinal vessels near the optic disc. Inside the eye, the blood may spread inretinally, below the ILM, or along retinal vessels.

Vitrectomy for visual rehabilitation after VH in patients with TS accelerates visual recovery, but there is still controversy10,12 as to the optimal timing for surgical intervention. Several factors need to be considered. Early vitrectomy...
can lead to substantial rehabilitation of VA and reduces the risks for complications that can occur if surgery is delayed (e.g., PVR, retinal detachment, ghost cell glaucoma, and epiretinal membrane formation). However, some authors suggest performing a vitrectomy only after failure of spontaneous resorption of hemorrhage.17,21

The time course for spontaneous resorption is variable and may take years to complete,11,21 although clearance rates of 10 to 12 months have been reported.11,16 Current recommendations suggest 3 to 6 months of observation after the acute event. Vitrectomy should follow if there is no resorption of hemorrhage or improvement of VA by this time.24,25 The vitrectomy technique has evolved enormously over the last few decades (higher cutting rates, shorter operation time, less trauma because of smaller gauge trocars, and lower complication rates). This fact could also argue for earlier intervention. Augsten et al,26 describing 6 eyes from 3 patients, concluded that for patients with bilateral TS without spontaneous resorption, surgery should be performed in at least 1 eye no later than 4 to 8 weeks after SAH. Daus et al27 suggested delaying vitrectomy in patients with unilateral hemorrhage and early vitrectomy in patients with bilateral vitrectomy. The time span in our study between SAH occurrence (diagnosis of TS) and surgical intervention was 4.4 months. This interval was used because rehabilitating measures for all of our patients were planned to take place after discharge from the hospital, and sometimes patients were in a poor general state of health. If the ensuing OE showed no signs of resorption, surgical intervention was scheduled. Our data show that all of our patients benefited from surgery, with a significant increase in BVCA (preoperative 2.2 and postoperative BCVA 0.0625 logMAR) (Fig 1A). We observed no intraoperative complications.

Well-known complications of TS, such as epiretinal membrane formation, PVR, and retinal detachment, are the result of the proliferation of glial cells and elements of the retinal pigment epithelium causing retinal distortion and fibrotic adhesions.18 There are also reports of sub-ILM and subhyaloid hemorrhages. Friedman and Margo28 reported a dissection between the ILM and the underlying Müller cell end plates, and Srinivasan and Kyle29 reported both a sub-ILM and subhyaloid hemorrhage in patients with TS. Yokoi et al30 suggested that as a consequence of the VH and the breakdown of the ILM, glial cell migration and proliferation into the vitreous cavity result in epiretinal membrane formation and PVR. In a case report using immunohistochemistry, Arroyo and Bula31 analyzed a pigmented macular membrane overlying intraretinal blood after performing vitrectomy and membrane peeling. The histologic and immunohistochemical analyses revealed a membrane consistent with the ILM. Another finding of this study was that the dissection plane in TS was between the ILM and the Müller cell end plates.

Figure 1. Comparison of visual acuity (VA) (decimal scale) before and after vitrectomy for dense vitreous hemorrhage (VH) in patients with Terson’s syndrome (TS). A, All patients. B, Patients who underwent operation without internal limiting membrane (ILM) peeling. C, Patients who had an additional ILM peeling.
In cases of vitreous bleeding with or without sub-ILM bleeding, vitrectomy with or without membrane peeling and peeling of the ILM needs to be performed to remove the VH, the epiretinal gliosis, and the sub-ILM bleeding. The combination of new microsurgical instrumentation and different dyes facilitates the peeling and increases the performance and end results of surgery. Garwe and Koerner analyzed the data for 37 patients (45 eyes) with TS and VH in a retrospective 30-year study and concluded that 85% of the patients experienced a rapid and persistent visual recovery. The 4 patients in our study who underwent ILM peeling for sub-ILM bleeding showed an increase in BCVA from 1.725 to 0.05 logMAR (Fig 1C). Postoperatively and during the follow-up period, 3 patients underwent cataract surgery because of the development of lens opacification after vitrectomy. There were no complications after cataract surgery.

For premacular subhyaloid hemorrhages, spontaneous resorption may be slow and may result in long-standing visual impairment. Ulbig et al concluded that puncturing the posterior hyaloid face or the ILM using a pulsed neodymium-doped yttrium aluminum garnet laser is a viable alternative treatment to vitrectomy, provided that the bleeding is not dense enough to block the laser beam. The care of patients after SAH requires an intensive coordination of effort among specialties, from neurosurgeons, neurologists, radiologists, and ophthalmologists to rehabilitating centers. Our 24-month prospective study contributes to the complex management of TS with, to our knowledge, one of the highest numbers of recruited patients and a close interdisciplinary collaboration of ophthalmologists and neurosurgeons.

Study Limitations

One of the limitations of our study is that it is an uncontrolled study. Also, the number of patients, although being one of the most extensive prospective studies of the rate of TS and outcome of vitrectomy in TS, is still not high. Therefore, any conclusions based on the data presented must be drawn with caution.

In conclusion, this prospective uncontrolled study shows that vitrectomy, and ILM peeling if needed, had advantageous effects on the visual rehabilitation of all patients with nonclearing VH after TS. The rate of TS (19.6%) is comparable to that in other reports, but the rate of VH is high (40%). So far, no consensus among vitreoretinal surgeons as to the optimal timing for surgical intervention exists, but in our cases of dense nonclearing hemorrhage that persists for more than 3 months, we did not identify any safety concerns after PPV.

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Footnotes and Financial Disclosures

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Abbreviations and Acronyms:
BCVA = best-corrected visual acuity; GCS = Glasgow Coma Scale; ILM = internal limiting membrane; logMAR = logarithm of the minimum angle of resolution; OCT = optical coherence tomography; OE = ophthalmological examination; PPV = pars plana vitrectomy; PVR = proliferative vitreoretinopathy; SAH = subarachnoid hemorrhage; TS = Terson’s syndrome; VA = visual acuity; VH = vitreous hemorrhage.

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