The impact of hypotension due to the trigeminocardiac reflex on auditory function in vestibular schwannoma surgery

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Object. Surgical manipulation of the fifth cranial nerve during its intra- or extracranial course may lead to bradycardia or even asystole as well as arterial hypotension, a phenomenon described as the trigeminocardiac reflex (TCR). The authors studied the impact of this reflex on postoperative auditory function in patients undergoing vestibular schwannoma (VS) surgery.

Methods. One hundred patients scheduled for VS surgery were studied prospectively for parameters influencing the postoperative auditory function. The evaluation included sex, age, pre- and postoperative auditory function, preoperative mean arterial blood pressure, preoperative medical diseases or medication (for example, antiarrhythmia drugs), tumor size and localization, and the intraoperative occurrence of the TCR.

The TCR, which occurred in 11% of the patients, influenced the postoperative hearing function in the patients with Hannover Class T3 and T4 VSS.

With an overall hearing preservation of 47%, 11.1% of the patients in the TCR group and 51.4% of those in the non-TCR group experienced preserved hearing function postoperatively. In cases involving larger tumors (Hannover Class T3 and T4), an intraoperative TCR was associated with a significantly worse postoperative hearing function during VS surgery (p = 0.005).

Conclusions. The hypotension following TCR is a negative prognostic factor for hearing preservation in patients undergoing VS surgery. Patients’ knowledge of this can be increased pre- and postoperatively. Further study of this phenomenon will advance the understanding of the underlying mechanisms and may help to improve hearing preservation by controlling the occurrence of the TCR.

KEY WORDS • trigeminocardiac reflex • bradycardia • vestibular schwannoma • acoustic neuroma • auditory function • semisitting position

The trigeminocardiac reflex, a phenomenon consisting of bradycardia or even asystole in conjunction with arterial hypotension, can be elicited by surgical manipulation of the trigeminal nerve during its intra- or extracranial course. When the ophthalmic division of the trigeminal nerve is surgically stimulated by manipulation of ocular and periocular structures, the OCR may occur.26 Related reflexes during eye surgery are the blepharocardiac reflex, the oculo-respiratory reflex, and sudden infant death syndrome.51

The TCR may also be elicited by stimulating the maxillary and mandibular divisions of the trigeminal nerve during craniomaxillofacial surgeries,23,40 as described for temporomandibular joint arthroscopies,35 maxillary tuberosity cuttings,9 Le Fort I osteotomies,34 nasal fracture reconstructions,29 zygomatic arch fracture elevations,29,43 and midface disimpactions.36

In neurosurgery, the TCR is described to as occurring during stimulation of the trigeminal ganglion,8,13,21 as well as during procedures such as trigeminal sensory root rhizotomy60 or dorsal root entry zone radiofrequency thermocoagulation of the trigeminal nucleus caudalis.12

In 1999, Schaller, et al.,42 were the first to report the occurrence of a TCR during tumor surgery in the CPA. They observed this reflex in 11% of their cases.

To our knowledge, no study has been conducted to analyze the influence of hypotension due to the TCR on postoperative hearing outcome in VS surgery. Therefore, we designed a study to evaluate the impact of the TCR on the postoperative auditory function in the treatment of such lesions.

Clinical Material and Methods

One hundred patients with VS underwent surgery at the International Neuroscience Institute, Hannover, between
June 2001 and July 2002; data were evaluated prospectively to determine parameters influencing postoperative auditory function.

The study included the following parameters: sex, age, pre- and postoperative auditory function (according to the Hannover classification), preoperative MABP, preoperative medical diseases or medication usage (for example, antiarrhythmic drugs), tumor size (according to the Hannover classification, [T1–T4]) and localization, and the intraoperative occurrence of the TCR.

**Definition of TCR**

The most common manifestation of the TCR is the OCR, which has been described as sinus bradycardia elicited by ocular manipulation, pressure on the globe, or traction of extraocular muscles, especially the medial rectus muscle. Other possible arrhythmias induced through this reflex include junctional rhythm, atrioventricular block, multifocal premature ventricular contractions, ectopic beats, ventricular tachycardia, ventricular fibrillation, and asystole. Because the efferent limb of the TCR is vagal, it causes a 10 to 50% decrease in heart rate in most cases.

In the neurosurgical literature, the TCR has been defined as the onset of bradycardia with a heart rate lower than 60 beats/minute accompanied by a drop in MABP of 20% or more caused by intraoperative manipulation or traction of the trigeminal nerve. Heart rate and the MABP are expected to return spontaneously to normal levels with cessation of manipulation or traction.

Given the aforementioned definition, the occurrence of bradycardia alone without signs of hypotension, even during trigeminal nerve manipulation, was not considered a TCR in this study.

**Tumor Classification and Resection**

Tumor extension was described as follows: Class T1, purely intrameatal; T2, intra- and extrameatal; T3a, filling the cerebellopontine cistern; T3b, reaching the brainstem; T4a, compressing the brainstem; and T4b, severely dislocating the brainstem and compressing the fourth ventricle. The tumor classes T1 and T2 were considered to represent small lesions, and the T3 and T4 classes were considered to represent large tumors.

All patients underwent a suboccipital craniectomy while in the semisitting position; the technique has been described previously in detail. Intraoperative monitoring of somatosensory evoked potentials, AEP, and electromyography of the facial nerve was performed routinely in all cases, except AEP monitoring was not undertaken in patients with preoperative deafness. Complete tumor resection was achieved in all cases.

**Hearing Tests**

Hearing tests were performed before surgery and 1 to 2 weeks postoperatively in each case. Preoperative and postoperative auditory function was analyzed using the Hannover classification (Table 1), as follows: H1 (normal hearing), 0 to 20 dB and 95 to 100% SDS; H2 (useful hearing), 21 to 40 dB and 70 to 94% SDS; H3 (moderate hearing), 41 to 60 dB and 40 to 69% SDS; H4 (poor hearing), 61 to 80 dB and 10 to 39% SDS; and H5 (no functional hearing), > 80 dB and 0 to 9% SDS. Each patient’s best SDS was taken for classification of speech discrimination.

**Anesthesia Protocol**

After oral premedication with midazolam, anesthesia was induced by administration of propofol and subsequent sufentanil and rocuronium. Anesthesia was maintained with propofol, and when it seemed clinically necessary, a bolus of sufentanil and rocuronium was administrated. After tracheal intubation, the lungs were mechanically ventilated.
ventilated by moderate hyperventilation (PaCO$_2$ 35 mm Hg) with a mixture of air and oxygen (FiO$_2$ 0.35).

In the operating room, patients underwent routine monitoring including electrocardiography and urine bladder temperature monitoring.

The central venous catheter was located in the right atrium so as to aspirate any invaded air during embolism. For early recognition of air embolism, precordial Doppler ultrasonography (2.2 MHz) was initiated. A radial artery catheter was inserted to allow continuous invasive blood pressure monitoring.

**Intraoperative Monitoring**

Hemodynamic parameters (systolic and diastolic heart rate, MABP, and right atrial pressure) were monitored continuously during surgery, and their values were recorded. Electrocardiography, pulse oximetry, capnography with end-tidal CO$_2$, and transcutaneous electrical stimulation of the left ulnar nerve (using the train-of-four method) were routinely monitored in all patients. Arterial blood gas analyses were performed every 1 to 2 hours.

**Intraoperative Management of the TCR**

When the TCR occurred, the anesthesiologist immediately informed the surgeon, who stopped preparation of the tumor and interrupted the eliciting mechanism. The cessation of surgical stimulation was followed by a normalization of the hemodynamic parameters in all cases. Intravenous administration of vagolytics such as atropine was not necessary to control the TCR in any of these cases. Surgery was then continued without further occurrence of the TCR. Postoperatively for at least 24 hours continuous monitoring of the hemodynamic and respiratory parameters and repeated neurological examinations were performed in the intensive care unit.

**Statistical Analysis**

The influence of the studied parameters on postoperative auditory function was analyzed using the SPSS statistical package (SPSS, Chicago, IL) using a stepwise logistic regression with a likelihood-ratio test. The level of significance was set at a probability value of less than 0.05.

**Results**

Of 100 patients with VS evidence of the TCR during tumor resection was found in 11 (11%).

In the TCR group, the mean age was 52.45 years (range 35–68 years) compared with 47 years (range 18–74 years) in the non-TCR group. There were three male (27.3%) and eight female (72.7%) patients compared with 52 male (58.4%) and 37 female (41.6%) patients, and the tumor side was left in eight cases (72.7%) and right in three cases (27.3%) compared with left in 50 cases (56%) and right 39 cases (44%) in the TCR and non-TCR groups, respectively.

The preoperative MABP was 96.9 mm Hg (range 81–120 mm Hg) in patients in whom a TCR was observed and 102.6 mm Hg (range 76–138 mm Hg) in those in whom one was not. In the TCR group the maximal intraoperative MABP was 91.7 mm Hg (range 81–12 mm Hg) and the minimal was 46.2 mm Hg (range 39–66 mm Hg), whereas in the non-TCR group a maximal intraoperative MABP was 94.6 mm Hg (range 74–136 mm Hg) and the minimal MABP was 59.6 mm Hg (range 46–79 mm Hg).

There were no significant differences between the TCR and the non-TCR groups with regard to sex, age, tumor side, MABP, and preoperative medical disease or medication (Table 2).

In the TCR group, 81.8% of the tumors were large (T3 and T4 classes).

Of the 11 patients with a TCR, nine (81.8%) harbored large (T3–T4) tumors (three cases of T3a, one of T3b, and five of T4a), and two (18.2%) harbored small (T1–T2) tumors (two cases of T2). Among these 11 patients, two were deaf preoperatively, and both had large (T4a) tumors.

Of the 89 patients without a TCR, 75 (84.3%) harbored large (T3–T4) tumors (20 cases of T3a, 12 of T3b, 40 of T4a, and three of T4b) and 14 (15.7%) harbored small (T1–T2) tumors (two cases of T1 and 12 of T2). Of these 89 patients, 15 were preoperatively deaf (14 with large tumors and one with a small VS). The distribution of the preoperative hearing status among patients in both groups is summarized in Tables 1 and 3.

Eighty-three of the 100 patients had preoperatively functional hearing; 74 of these 83 had no TCR intraoperatively whereas a TCR occurred in nine during surgery. With an overall hearing preservation rate of 47% (39 of 83 patients with preoperative Hannover Classes H1–H4), 11.1% (one of nine patients) in the TCR group and 51.4% (38 of 74 patients) in the non-TCR group showed preserved hearing function postoperatively (Table 4 and Fig. 1).

Comparison of tumor sizes and postoperative hearing preservation revealed some intergroup differences.

Of the 61 patients with larger (T3–T4) tumors in the non-TCR group, 27 (44.3%) had auditory function preserved.
In the TCR group, the overall preservation rate was 11.1% (one of nine patients). In the one case of preserved hearing in the TCR group the VS class was T2. As there were no Class T1 tumors in this group, there is a lack of homogeneity within the small tumors between the TCR group and the non-TCR group. This inconsistency in small tumors limits the possibility of correlating the occurrence of the TCR with the incidence of hearing preservation in this group.

Therefore, the large VSs were analyzed separately. Sixty-eight of the 84 patients with large (Class T3 and T4) tumors had preoperatively functional hearing; 61 of them had no TCR intraoperatively; and in seven a TCR occurred during surgery. With an overall hearing preservation rate of 39.7% (27 of 68 patients with preoperative Classes H1–H4), 0% in the TCR group and 44.3% (27 of 61 patients) in the non-TCR group showed preserved hearing function (Class H1–H4) postoperatively.

Restricting the analysis of large (Class T3 and T4) tumors to hearing Classes H1 to H3 revealed the following results: TCR intraoperatively was absent in 46 and present in five during surgery. With an overall hearing preservation rate of 19.6% (10 of 51 patients with preoperative Classes H1–H3), 0% in the TCR group and 21.7% (10 of 46 patients) in the non-TCR group showed preserved hearing function (Class H1–H3) postoperatively.

In summary, the TCR and the tumor size influenced postoperative hearing function in patients with larger tumors (Class T3 and T4). In this group, patients with an intraoperative TCR suffered significantly worse postoperative hearing function than those in whom a TCR was not observed during VS surgery (p = 0.005).

### Discussion

The TCR is a phenomenon of hemodynamic instability due to a decrease in cardiac output. This reflex can be elicited by stimulating either the trigeminal nerve itself or any structure innervated by this nerve. After stimulation, neuronal signals are sent to the sensory nucleus of the trigeminal nerve, constituting the afferent pathway of the reflex arc.

Through short internuclear fibers to the motor nucleus of the vagus nerve, the efferent pathway is activated. Some of these efferent fibers terminate in the myocardium and act as cardioinhibitors, leading to hypotension, bradycardia, asystole, and ventricular fibrillations through coronary vasospasm. Other efferent fibers induce apnea or gastric hypermotility.

Removing the triggering factor can cause cessation of the reflex, raising hemodynamic parameters to normal levels.

### Predicting the Occurrence of the TCR

The most important factor involved in the occurrence of the TCR is the stimulation intensity during manipulation of the trigeminal pathway. Traction is more likely to elicit the TCR when performed rather abruptly and sustained than when undertaken smoothly and gently. Even intracranial manipulation of the trigeminal nerve is possible without inducing the reflex when this maneuver is performed gently. In terms of CPA surgery, Schaller, et al., reported the influence of preoperative medication (beta-blockers and calcium channel blockers) on the occurrence of the TCR. This correlation was not found in the present study.

In the present series, more than 80% of the TCRs occurred in patients harboring larger tumors of Classes T3 and T4. This can be explained by the close anatomical relationship of large VSs to the course of the trigeminal nerve in the CPA, as well as by the necessity for more traction and manipulation of the trigeminal nerve during tumor preparation in these cases.

### Patient Positioning and the TCR

For VS surgery, both the supine and the semisitting positions are possible options. Because of several significant advantages, the semisitting position is a favorable approach during CPA surgery. Complete exposure and visualization of all structures in the posterior fossa and the possibility of operating continuously in a clean field are most advantageous for the surgeon and patient. The use of irrigation with the help of “the third hand” maintains a clear surgical field and reduces the necessity for suction, which otherwise might traumatize the neurovascular structures of the posterior fossa.

Conversely, the sitting position may be associated with complications such as venous air embolism and postural hypotension. These disadvantages can be reduced by modifying the sitting position to that of the semisitting (lounging) position.

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**TABLE 4**

Rates of postoperative hearing preservation

<table>
<thead>
<tr>
<th>Postop Hearing Status</th>
<th>Patients w/ TCR</th>
<th>Patients w/o TCR</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preservation</td>
<td>1 (11)</td>
<td>38 (51.4)</td>
<td>39 (47)</td>
</tr>
<tr>
<td>Deafness*</td>
<td>8 (88.9)</td>
<td>36 (48.6)</td>
<td>44 (53)</td>
</tr>
</tbody>
</table>

* Patients with preoperative deafness were excluded.
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Black, et al. described hypotensive reactions as occurring equally as often in patients in the supine position as for those in the semisitting position. Therefore, a major influence of patient positioning on cardiovascular parameters in the observed group seems to be unlikely. In addition, attempts were made to reduce hypotensive reactions during patient positioning by the following measures: semisitting instead of sitting position, slow elevation during the positioning procedure, sufficient infusion of plasma expanders and electrolytic solutions, and application of compression stockings. Schaller, et al. observed a TCR in 14 (11%) of their 125 patients who underwent CPA tumor surgery while in the supine position. In our study, all patients were in the semisitting position for surgery. Nonetheless, we observed the same incidence of the TCR in our series (11 [11%] of 100 patients) as Schaller and colleagues did. Moreover, the minimal intraoperative MABP found in both studies for the TCR group was very similar (44 mm Hg in that by Schaller, et al., and 46.2 mm Hg in our series).

Because an identical definition of the TCR was applied in both studies, these findings indicate that a patient’s intraoperative positioning seems not to be a relevant factor influencing the occurrence of the TCR.

Treatment and Morbidity Associated With the TCR

Interrupting the eliciting mechanism is the principal treatment modality for the TCR. Cessation of trigeminal nerve manipulation is followed by a normalization of the hemodynamic parameters.

Some authors have recommended the use of atropine to treat the TCR and to prevent new episodes. In our series, however, the symptoms disappeared within 20 seconds after ceasing of the manipulation, and medication was not required. In all cases, the surgery could be continued without further problems while the surgical maneuvers (traction intensity and/or area of manipulation) were modified.

Moreover, because the TCR response includes the inhibition of adrenergic vasoconstriction and the activation of vagal cardio-inhibitory fibers, atropine-based cholinergic inhibition of adrenergic vasoconstriction and the activation may also cause serious arrhythmias. Furthermore, Signore, et al. reported observing episodes of bradycardia during VS surgery performed via the translabyrinthine approach, which did not respond to atropine administration but ceased after modulation of surgical maneuvers.

Nonetheless, even transient cardiac arrest may occur in one of 2200 cases of strabismus surgery.

Although even intraoperative death has been reported in association with the TCR, in general the postoperative course is favorable and uneventful, as long as the TCR is recognized early and managed adequately during surgery.

Auditory Function

Because VSs have a vestibular origin, the cause of hearing loss in patients with these tumors is not always obvious. Moreover, patients with intrameatal processes sometimes present with deafness or very poor hearing, whereas patients with large tumors occasionally experience nearly normal hearing. Possible mechanisms of hearing loss are mechanical injury to the cochlear nerve, elevation of the IAC pressure, and/or vascular compromise of the auditory apparatus.

Recordings in the IAC have shown the pressure to be significantly elevated in most patients with VSs, corresponding to tumor extension into the IAC.

In the largest reported series, 27% of all patients with VS presented with deafness preoperatively, and deafness was present postoperatively in another 44%.

Several prognostic factors have already been described for postoperative hearing function in VSs. Male sex, small-to-medium-tumor size, good or moderate preoperative short wave V AEP latency, and tumor origin from the superior part of vestibular nerve have been reported as favorable preoperative factors.

Severe changes of the IAC verified on preoperative bone-window computerized tomography scans are also described as being associated with poor preoperative hearing function, as well as with an unfavorable postoperative preservation. Additionally, the extent of IAC widening and tumor growth in the anterior and caudal directions are significant predictors for postoperative auditory function in patients with large tumors. Somers, et al. evaluated magnetic resonance imaging findings and found that low intralabyrinthine signal intensity documented on gradient echo images was associated with a lower rate of hearing preservation. The authors hypothesized that tumor-induced vascular compression in the IAC was responsible for the decrease in intralabyrinthine signal intensity.

Based on intraoperative electrophysiological monitoring, brainstem AEPs and near-field cochlear nerve action potentials proved to be most useful predictors for hearing preservation, as described by our group in detail elsewhere.

The influence of the TCR on postoperative hearing preservation has not yet been reported. Patients harboring Class T3 and T4 tumors presented with a significantly poorer postoperative auditory function when a TCR occurred during surgery, in comparison with patients in the non-TCR group.

Although no patient with a larger tumor (Class T3 and T4) and an intraoperative TCR sustained functional hearing postoperatively, there was a hearing preservation of 44.3% of patients in the non-TCR group with these large tumors.

An already compromised vascular supply in the IAC due to tumor compression can be further decreased in cases of sudden intraoperative hypotension occurring along with the TCR. This mechanism may lead to decreased auditory function or even deafness, despite morphological preservation of the cochlear nerve during surgery.

In addition, larger tumors may increase pressure in the IAC, thereby enhancing subsequent ischemia of the auditory apparatus. This mechanism would explain the major impact of the TCR on auditory function in cases of larger VSs. Moreover, these tumors are already often subject to more intraoperative manipulations because of their size.

Gentle and smooth manipulations in the region of the trigeminal nerve while avoiding traction have proved to be the most important surgical maneuvers for decreasing the occurrence of the TCR. As soon as this phenomenon has occurred, the surgeon should be informed immediately to give...
him or her the opportunity to cease the surgical maneuver quickly and effectively.

Conclusions

The TCR is a common intraoperative phenomenon and is of major importance as a negative prognostic factor for hearing preservation in patients undergoing VS surgery. Bearing this in mind, the process of informing patients pre- and postoperatively can be improved. For normalization of hemodynamic parameters, a modification of surgical maneuvers is sufficient, without adjuvant medication. Further study of this phenomenon will advance our knowledge of risk factors and our understanding of the underlying physiologic mechanisms. Such studies may help to improve hearing preservation in patients undergoing VS surgery by controlling the occurrence of the TCR.

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