# Trigemino-cardiac reflex

The trigeminocardiac reflex (TCR) is defined as the sudden onset of parasympathetic dysrhythmia, sympathetic hypotension, apnea or gastric hypermotility during stimulation of any of the sensory branches of the trigeminal nerve [1) 2) 3)].

Initial reports were based on animal experiments; however, TCR in neurosurgical patients was first elaborated by Schaller et al. in 1999 [4) 5) 6) 7)].

## Epidemiology

The incidence of the TCR in neurosurgical procedures involving or near the trigeminal nerve vicinity was reported to be about 10–18% [8) 9)].

The sensory nerve endings of the trigeminal nerve send neuronal signals via the Gasserian ganglion to the sensory nucleus of the trigeminal nerve, forming the afferent pathway of the reflex arc. This afferent pathway continues along the short internuncial nerve fibers in the reticular formatio to connect with the efferent pathway in the motor nucleus of the vagus nerve.

## Classification

TCR was classified according to morphophysiological aspects involved with reflex elicitation.

575 patients were included in a study. TCR was found in 8.9% of patients. The reflex was more often triggered by interventions made within the anterior cranial fossa. The maxillary branch (type II in the new classification) was the most prevalent nerve branch found to trigger the TCR. Heart rate (HR) and mean arterial blood pressure (MABP) were similarly altered ($p = 0.06$; $F = 0.3912809$), covaried with age ($p = 0.012$; $F = 9.302$), and inversely correlated to each other ($r = -0.27$).

TCR is a critical cardiovascular phenomenon that must be quickly identified, efficiently classified, and should trigger vigilance. Prompt therapeutic measures during neurosurgical procedures should be carefully addressed to avoid unwanted complications. Accurate categorization using the new classification scheme will help to improve understanding and guide the management of TCR in the perioperative period [10)].

## Etiology

The work of Meuwly et al. is the first systematic review about TCR and demonstrates clear evidence for TCR occurrence and a more severe course of the TCR in slight anesthesia underlying the importance of skills in anesthesia management during skull base surgery [11)].

### Clinical Features

Clinically, the trigemino-cardiac reflex has been reported to occur during craniofacial surgery, balloon-compression rhizolysis of the trigeminal ganglion, and tumor resection in the cerebellopontine angle. Apart from the few clinical reports, the physiological function of this brainstem-reflex has not yet been fully explored. From experimental findings, it may be suggested that the trigemino-cardiac reflex represents an expression of a central neurogenic reflex leading to rapid cerebrovascular vasodilatation generated from excitation of oxygen-sensitive neurons in the rostral ventrolateral medulla oblongata. By this physiological response, the adjustments of the systemic and cerebral circulations are initiated to divert blood to the brain or to increase blood flow within it. As it is generally accepted that the diving reflex and ischemic tolerance appear to involve at least partially similar physiological mechanisms, the existence of such endogenous neuroprotective strategies may extend the actually known clinical appearance of the TCR and include the prevention of other potentially brain injury states as well. This may be in line with the suggestion that the TCR is a physiological, but not a pathophysiological entity [12)].

### After surgery for pituitary neuroendocrine tumors

In a retrospective observational study, 19 out of 338 (8%) enrolled adult patients demonstrated a TCR during transsphenoidal/transcranial surgery for pituitary neuroendocrine tumors. The 2 subgroups (TCR vs non-TCR) had similar patient's characteristics, risk factors, and histology. Preoperatively, there was a similar distribution of normal pituitary function in the TCR and non-TCR subgroups. In this TCR subgroup, there was a significant decrease of that normal pituitary function after operation (37%) compared to the non-TCR group (60%) ($P<0.03$). The TCR subgroup therefore demonstrated a 3.15 times (95%CI 1.15-8.68) higher risk for non-normalizing of postoperative pituitary function compared with the non-TCR subgroup ($P<0.03$).It is presented, for the first time, an impact of TCR on the functional hormonal outcome after pituitary surgery and strongly underline again the importance of the TCR in clinical daily practice. As a consequence, TCR should be considered as a negative prognostic factor of hormonal normalization after surgery for pituitary neuroendocrine tumors that should be included into routine practice [13)].

## Treatment

The TCR can be successfully managed by the cessation of the stimulus producing the TCR. Decision support tools are needed to make static predictive analysis dynamic and useful for a single patient and to make (skull base) surgery still safer [14)].

## Prevention

The risk factors already known to increase the incidence of TCR include: Hypercapnia; hypoxemia; light general anesthesia; age (more pronounced in children); the nature of the provoking stimulus (stimulus strength and duration); and drugs: Potent narcotic agents (sufentanil and alfentanil); beta-blockers; and calcium channel blockers. Because of the lack of full understanding of the TCR physiology, the current treatment options for patients with TCR include: (i) risk factor identification and modification; (ii) prophylactic measures; and (iii) administration of vagolytic agents or

sympathomimetics [15].

Another factor represents certainly the awareness and capability of the surgeon to perform the (micro)surgical preparation with smooth and slow tractions around the trigeminal nerve or 1 of its branches [16]

2 patients with recurrent and profound bradycardia due to Trigemino-cardiac reflex during endovascular Onyx™ embolization for a dural arteriovenous fistula. Prophylactic intra-arterial injection of lidocaine (10-20 mg) effectively and safely blocked the recurrence and potential occurrence of TCR. These 2 patients had reduced heart rate with either hypotension or hypertension during their TCR episodes, suggesting that stimulating a distinct cerebral artery (occipital artery versus vertebral artery branch) can initiate TCR by provoking the vagus nerve via the common neuronal pathway while simultaneously inhibiting or exciting the sympathetic pathway. Intra-arterial injection of lidocaine during endovascular procedures can be recommended as an effective prophylactic approach for use in the treatment of the cerebrovascular disorder where there is high risk of embolization-induced TCR [17].

## Case reports

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