Effectiveness of Gamma Knife Radiosurgery in Improving Psychophysical Performance and Patient's Quality of Life in Idiopathic Trigeminal Neuralgia

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■ OBJECTIVE: **To assess effectiveness of Gamma Knife Radiosurgery (GKRS) in improving quality of life (QoL) in patients with idiopathic trigeminal neuralgia (TN).**

■ METHODS: **Between January 2001 and October 2013, 166 patients with medically resistant TN were treated at our institution with GKRS. Patients were divided into 2 groups: patients with typical TN (TTN) and patients with atypical TN (ATN).**

All patients underwent clinical evaluation using Marseille and Barrow Neurological Institute pain and numbness scales; in addition, they completed the Short-Form 36 Health Survey, Activities of Daily Living, and Excellent Good Fair Poor questionnaires and underwent psychological and neurologic examination.

■ RESULTS: **Mean follow-up time was 64.7 months. All Short-Form 36 domains were significantly improved in both groups after treatment, with an evident trend to reach the median values of healthy Italian population. Mean postoperative Activities of Daily Living score in the TTN group and ATN group were 5.8 and 5.4, respectively, and Karnofsky Performance Status increased to 94.2 and 86.4, respectively.**

Pain recurrence negatively affected patients' QoL and psychofunctional performance without reaching statistical significance. At the last follow-up, 73% of patients were clustered in the pain-relief group.

■ CONCLUSIONS: **GKRS significantly improves QoL and functional and psychosocial performance of patients with idiopathic trigeminal neuralgia. A trend was observed toward a more favorable outcome in patients with TTN, compared with patients with ATN, without reaching a statistically significant distinction.**

INTRODUCTION

Trigeminal neuralgia (TN) is a common pain syndrome characterized by short and intense pain attacks in the somatosensory distribution area of the fifth cranial nerve.[1,2] According to the cause, TN is classified into 2 main categories: classic and symptomatic.[3]

Idiopathic cases as well as those caused by neurovascular conflict are classified as classic[3]; on the other hand, symptomatic TN, which accounts for the minority of cases, is instead the result of either secondary trigeminal nerve compression caused by space-occupying lesions or demyelination of the root entry zone in case of multiple sclerosis.[2-5] According to clinical patterns, TN has been further classified in the literature as typical (TTN) (TN1) or atypical (ATN) (TN2); as described by Eller et al., TN1 is defined as short attacks of intense, stabbing pain in the distribution area of the trigeminal nerve as a response to definite triggers, whereas TN2 is diagnosed if the painful sensation is burning or aching and present more than 50% of the time over the day.[6]

Key words
- Gamma Knife
- Quality of life
- Radiosurgery
- Trigeminal neuralgia

Abbreviations and Acronyms
ADL: Activities of Daily Living
ATN: Atypical trigeminal neuralgia
BNI: Barrow Neurological Institute
BP: Body pain
GKRS: Gamma Knife radiosurgery
KPS: Karnofsky Performance Status
MH: Mental health
MVD: Microvascular decompression
PF: Physical function
QoL: Quality of life
RE: Role limitation due to emotional problems
RP: Role limitation due to physical problems
SF: Social function
TN: Trigeminal neuralgia
TTN: Typical trigeminal neuralgia
VT: Vitality

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TN per se, as well as side effects of drugs, and the failure of standard therapeutic options are used to dramatically affect patients' quality of life (QoL).[3,7,8] Patients with TN usually experience a worsening of their social functioning, which results in a poor work performance and in consequent high social costs.[3,7]

Medical therapy is often insufficient in achieving pain control and many patients are unable to endure drug-related side effects, seeking other types of treatment.[1,3,4,7]

For idiopathic TN caused by neurovascular conflict, microvascular decompression (MVD) represents the most widely accepted treatment[9]; pain-control rate after MVD is >98%, which decreases to 50%–70% in the long-term, with a recurrence rate of about 3.5%/year.[3,5,10] The rate of complication related to surgical decompression and the rate of recurrence are not negligible, with a mortality of 0.2%–0.5% of cases, recurrence in 22%–42% of cases at more than 5 years follow-up, and new onset of hearing loss in about 10% of cases.[11,12]

Gamma Knife radiosurgery (GKRS) (Elekta, Stockholm, Sweden) represents a less invasive treatment for TN, with a lower rate of complications and pain recurrence, compared with other ablative treatments, such as balloon percutaneous rhizotomy.[3,5,10-13] The use of GKRS is widely validated as a safe treatment option even in young patients, as already reported in the literature in large series.[14]

In the last decades, GKRS has proved to be an effective therapeutic approach to TN both as a primary treatment and as a secondary option in medically and surgically refractory syndromes.[13-30] The mechanism of action remains unclear, although there is some evidence that postradiation demyelination of trigeminal sensory fibers may play an important role in the therapeutic effect.[31]

There are many reports regarding the clinical outcome of GKRS in TN treatment[20,25,29,30]; however, data on long-term efficacy of GKRS on the improvement of patients' QoL are still limited.[3,7,8]

This report is focused on the effectiveness of GKRS in improving both clinical outcome and QoL of patients with TN, based on the positive impact on their mental and physical status as well as psychosocial well-being.

METHODS

Study Setting and Participants

Medical records and follow-up data of patients with intractable idiopathic TN undergoing GKRS at our institution were retrospectively reviewed. Only patients fulfilling criteria of the International Headache Society were included.[32,33] Patients were further classified based on typical or atypical pain manifestations.

At hospital admission, each patient signed a written consent for treatment and collection of personal data. All procedures were performed in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Radiosurgical Technique

The Gamma Knife 4C unit (Elekta AB) was used before 2007. The following treatments were performed using the Gamma Knife Perfexion unit.

Gamma Knife treatment started with Leksell stereotactic frame application (Elekta) on the patient's head under local anesthesia. After frame fixation, magnetic resonance imaging was used for treatment planning, which was performed by Leksell GammaPlan software (Elekta).

One single shot with a 4-mm collimator was placed on the anterior part of the cisternal portion of the trigeminal nerve, as shown in Figure 1. The theoretic aim of the primary treatment was to deliver a dose of 45 Gy at the 50% isodose line (90 Gy as the maximal dose), which was modified in some cases because of brainstem proximity.

Variables and Data Measurement

Patients continued their medication unchanged for at least 3 months after treatment and then they started tapering it depending on clinical response.

Follow-up examination was performed at 3, 6, and 12 months after GKRS and yearly thereafter. Degree and latency interval of pain relief, the need for further procedures, the use of medications, and the development of new signs and symptoms were evaluated by an independent neurologist. At follow-up, all patients underwent interviews by a team of psychologists to assess the impact on mental status and personal satisfaction.

Pain was assessed using the Barrow Neurological Institute (BNI) pain scale, a self-reported index on pain control and medication use, both before and after treatment.[26] The Marseille scale, a validated score to assess the clinical outcome after GKRS for TN, was contextually applied to assess pain relief after treatment.[14]

Patients' functional performance was evaluated in all cases by the Karnofsky Performance Status (KPS) and the Activities of Daily Living (ADL), both at hospital admission and at follow-up.[34,35] Recurrence was defined as an increase of BNI score during follow-up after a positive pain response to GKRS.

All patients completed the Short-Form 36 (SF-36) health survey as a self-reported survey of health before and after treatment. The questionnaire is composed of 36 items on physical and mental health, assessing 8 dimensions of QoL: physical function (PF), role limitation due to physical problems (RP), body pain (BP), general health, vitality (VT), social function (SF), role limitation due to emotional problems (RE), and mental health (MH). The raw subscale scores are standardized and range from 0 ± 100, where 0 implies the worst possible health status and 100 the best possible. The scores represent the percentage of the total possible score achieved. SF-36 data were compared with normative data profiles in a healthy Italian population.[36]

Facial numbness after treatment was evaluated using the BNI facial numbness score.[26]

Statistical Methods

Statistical analysis was performed using SPSS software, version 21.0 (IBM Corp., Armonk, New York, USA). To evaluate the functional outcome, the time-to-event was estimated using the Kaplan-Meier method. The log-rank method was selected to detect differences between the curves late in the period of the study; the Breslow test was performed to look for early differences, and the Tarone-Ware test was used as an intermediate strategy. A probability value of <0.05 was considered as significant.

Nonparametric tests were used to compare data (Mann-Whitney and Wilcoxon signed ranks).