

## The Effectiveness of Gamma Knife Surgery in the Treatment of Trigeminal Neuralgia: A Systematic Review

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### ABSTRACT

**Introduction:** Gamma knife surgery is one of the stereotactic surgery which recently used in the treatment of trigeminal neuralgia due to its minimally invasive nature. The short-term effectiveness of gamma knife surgery in a reduction of pain episodes among patients with trigeminal neuralgia are reported by several studies. However, few studies elaborated the long-term effectiveness of gamma knife surgery.

**Objective:** This review aimed at evaluating the effectiveness of gamma knife surgery by reviewing of pain relief rates and recurrence rates reported by the included studies.

**Methods:** The electronic search was conducted in Medline, EmBase and Science direct databases using the key words of (Gamma knife surgery AND trigeminal neuralgia). The search of the literature, after exclusion of irrelevant, duplicated and review studies revealed 8 studies met the inclusion criteria. The data extraction conducted using data extraction sheet regarding characteristics such as duration of symptoms, number of trigeminal divisions involved, lack of sensation or surgery before surgery, anatomical results in the operation, the rate of pain relief and pain recurrence rate.

**Results:** The history of surgery and medications before gamma knife radio surgery was assessed by included studies. It was found that only one study used gamma knife surgery as their first treatment of choice with no prior surgery. The pain relief rate ranged from 73.8% to 96% while pain recurrence rate, which reported in four included studies ranged from 2% to 26.3%.

**Conclusions:** The gamma knife surgery was not the first surgical choice of treatment in most of the studies. The reported pain relief rates associated with this new technique were generally high while pain recurrence rates were low. As the worst reported scenario found about a quarter of patients complained of pain recurrence following gamma knife surgery.

**Keywords:** Gamma knife; Trigeminal neuralgia; Neurosurgery; Pain management.

### INTRODUCTION

Trigeminal neuralgia is a characteristic pain syndrome which presents clinically with sharp severe electrical-shock like pain episodes distributed according to the divisions of the trigeminal nerve <sup>(1)</sup>. Treatment of trigeminal neuralgia is mainly pharmacological with antiepileptic or antidepressant drugs to reduce pain episodes <sup>(2)</sup>. Invasive surgical treatment is only used in refractory trigeminal neuralgia when medications are no longer effective. The micro-vascular decompression and thrombotic ablation surgery have been the interventions of choice for surgical treatment of trigeminal neuralgia <sup>(3)</sup>.

Stereotactic radio surgery is a new way to treat well-defined targets in the brain, causing the destruction of cells, blockage of blood vessels or certain functional changes. It is one of the fastest growing fields of neurosurgery <sup>(4)</sup>. Gamma knife surgery (GKS) is one of the

stereotactic surgery which recently used in the treatment of trigeminal neuralgia (TN) due to its minimally invasive nature <sup>(5)</sup>. Although GKS has an immediate high success rate, there are still some patients in whom GKS fails to provide pain relief. Additionally, about 50% of patients may develop recurrent refractory pain within 3-5 years of follow-up <sup>(6)</sup>.

Gamma Knife Surgery is a four-step neurosurgery procedure including the treatment planning, the application of the stereotactic frame to the patient's head, the acquisition of holographic images, and radiation exposure <sup>(7)</sup>. The system allows the stereoscopic acquisition of images from MRI, cerebral angiography, positron emission tomography and computed tomography. Applications for GKS include treatment of benign and malignant tumors well defined from the head, cerebral vascular malformations and treatment of certain pain

cases such as trigeminal neuropathy as well as treatment of some movement and mental disorders <sup>(8)</sup>.

The pain relief rate published in patients who underwent GKS is often variable, ranging from 35% to 65% in 5 years to 20% to 45% in 10 years <sup>(9)</sup>. Studies found postoperative complications of GKS were accompanied with prognostic factors such as patient's gender, age, duration of symptoms, side of the face where the symptoms occurred, number of trigeminal divisions involved, the performance of the partial trigeminal fraction, and the presence of trigger points <sup>(10)</sup>. The short-term effectiveness of GKS in the reduction of pain episodes among patients with trigeminal neuralgia are reported by several studies <sup>(11-14)</sup>. However, few studies elaborated the long-term effectiveness of GKS <sup>(15, 16)</sup>. This review aimed at evaluating the effectiveness of GKS by reviewing of pain relief rates and recurrence rates reported by the included studies.

**METHODS**

The electronic search was conducted in Medline, EmBase (Pubmed) and Sciencedirect databases using the key words of (Gamma knife surgery AND trigeminal neuralgia). The search of the literature resulted in 175 eligible articles and after exclusion of irrelevant, duplicated and review studies, 8 studies met the inclusion criteria (table 1).

The data extraction conducted using data extraction sheet regarding characteristics such as sample size, duration of symptoms, history of surgery before surgery, the rate of pain relief, pain recurrence rate and complication rate.

The study was done after approval of ethical board of Jazan university.

**RESULTS**

**Table (1): Search Findings**

Search Engine	Search Terms	Eligible	Included
PubMed (Medline and Embase)	Gamma knife surgery AND trigeminal neuralgia (clinical trials)	31	6
Science Direct	Gamma knife surgery AND trigeminal neuralgia (1997-2017) (Only journals) (topics: gamma knife, trigeminal neuralgia)	144	2
Total		175	8

The search of the literatures, after exclusion of irrelevant, duplicated and review studies revealed 8 studies met the inclusion criteria. Included studies aimed to evaluate the effect of Gamma knife radio-surgery in patients with trigeminal neuralgia (table 2). These studies recruited different numbers of participants ranged from 23 patients in a study of **Kondziolka et al.**<sup>(17)</sup> to 106 in a study conducted by the same author <sup>(18)</sup>.

Only two studies reported the mean age of onset for trigeminal neuralgia. It was 64 years old in a study of **Dellaretti et al.**<sup>(12)</sup> and 67 years old in another study conducted by **Kondziolka et al.**<sup>(18)</sup>. The duration of trigeminal neuralgia symptoms was ranged from 9 months in two studies conducted by **Chang et al.**<sup>(19)</sup> and **Han et al.**<sup>(20)</sup>, to 19.8 months reported by **Young et al.**<sup>(21)</sup>.

The history of surgery and medications before gamma knife radio surgery was positive in all studies except a study conducted by **Young et al.**<sup>(21)</sup> where the gamma knife surgery was the first treatment with no prior intervention. Five studies reported past history of surgery aimed to treat trigeminal neuralgia <sup>(12, 17, 20, 22, 23)</sup>.

The percentage of patients felt pain relief rate was also assessed by included studies, it was ranged from 73.8% which reported by **Nicol et al.**<sup>(23)</sup>, to 96% in another study conducted by **Kondziolka et al.**<sup>(17)</sup>. Regarding pain recurrence rate, it was reported in four included studies and ranged from 2% in a study of **Han et al.**<sup>(20)</sup>, to 26.3 reported by **Dellaretti et al.**<sup>(12)</sup>. Only four included studies reported significant complications mainly changes in sensation in the facial region. The incidence of such sensory changes ranged from 8% in a study conducted by **Chang et al.**<sup>(19)</sup> to 21% reported by **Dellaretti** and his colleagues<sup>(12)</sup>.

**Table (2): Summary of the findings**

<b>Study citation (Author-Year)</b>	<b>Sample size</b>	<b>Mean age group of the patients</b>	<b>duration of symptoms</b>	<b>Past history of surgery</b>	<b>pain relief rate</b>	<b>Pain recurrence rate</b>	<b>Complications</b>
<b>Dellaretti <i>et al.</i> 2008</b>	76	64 years old	6 to 42 months (mean 20.3)	30 patients had undergone past surgery	83.1%	26.3%	21% reported worsen outcomes 8 of these patients described some facial numbness
<b>Kondziolka <i>et al.</i> 1997</b>	106	67 years old	11 months	All patients with refractory trigeminal neuralgia	80%	10%	10% reported sensory changes
<b>Kondziolka <i>et al.</i> 1998</b>	23	66 years old	12 months (range 5–33 months)	Non-reported	96%	Non-reported	Non-reported
<b>Nicol <i>et al.</i> 2000</b>	42	Non-reported	14 months	30 patients had undergone no prior treatments.	73.8%	Non-reported	16.7% reported increased facial paresthesia
<b>Chang <i>et al.</i> 2000</b>	53	Non-reported	9 months	Non-reported	86.7%	Non-reported	8% reported facial sensory change
<b>Young <i>et al.</i> 1998</b>	110	Non-reported	19.8 months	No prior surgical intervention	95.5%	3.3%	Non-reported
<b>Kondziolka <i>et al.</i> 1996</b>	51	Non-reported	9.6 months	44 patients had undergone prior surgery	86%	Non-reported	Non-reported
<b>Han <i>et al.</i> 1999</b>	43	Non-reported	9 months	Non-reported	81%	2%	Non-reported

## DISCUSSION

Throughout the last two decades, gamma knife surgery was used to treat refractory trigeminal neuralgia. The present study is a review of clinical trials carried out to evaluate the effectiveness of gamma knife radio surgery in the treatment of trigeminal neuralgia. Radio surgery is the least invasive procedure for trigeminal neuralgia and early results were encouraging with acceptable rates of pain relief as shown by the studies included in this review.

The rate of pain relief was found high by the included studies and varied in the narrow range from 73.8% to 96%. This narrow variation could

be justified by different specifications of knife surgery techniques such as the magnitude of dose and the target localization. The most known assumptions interpret the cause of trigeminal neuralgia referring it to vascular compression on the origin of the trigeminal nerve.

The irradiation located during gamma knife surgery may decompress the vessels around the nerve root and leads to pain relief. However, no evidence of vascular compression in trigeminal neuralgia was detected in contrast to facial hemispasm where vascular occlusion was demonstrated<sup>[22, 24]</sup>.

There was a low incidence of complications following gamma knife surgery, which was mainly sensory changes in the facial region, with a maximum incidence of 21% reported by **Dellaretiet al.**<sup>(12)</sup>

This low complication rate reflected the safety of gamma knife surgery in the treatment of trigeminal neuralgia. Moreover, this complication rate of 21% reported by **Dellaretiet al.**<sup>(12)</sup> can be explained by longer duration of symptoms associated with trigeminal neuralgia in comparison with other reported studies. It was postulated that some nerve injury might be necessary to achieve pain relief following gamma knife surgery, this theory was supported by experiments conducted on baboons<sup>(25)</sup>.

Only four included studies reported recurrence rate of pain and it varied from 2% in a study of **Han et al.**<sup>(20)</sup> to 26.3% reported by **Dellaretti et al.**<sup>(12)</sup>. This variation can be explained by different definitions of pain recurrence and duration of follow up after surgery among included studies. All included studies used pre- and post-interventional designs which were appropriate for assessment of pain relief after gamma knife surgery.

## CONCLUSIONS

The gamma knife surgery was not the first surgical choice of treatment in most of the included studies. The reported rates of pain relief, associated with this new technique, were generally high while pain recurrence rates were low. As the worst reported scenario found about a quarter of patients complained of pain recurrence following gamma knife surgery.

## CONFLICT OF INTEREST

The authors stated no conflicts of interest or financial sponsoring was received.

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