Neurosurgical Review (2019) 42:599–601
https://doi.org/10.1007/s10143-019-01099-z

LETTER TO THE EDITOR

Gamma Knife radiosurgery for trigeminal neuralgia: when?

Alfio Spina[1] · Nicola Boari[1] · Filippo Gagliardi[1] · Michele Bailo[1] · Sandro Iannaccone[2] · Pietro Mortini[1]

Received: 15 January 2019 / Revised: 14 March 2019 / Accepted: 26 March 2019 / Published online: 1 April 2019

Keywords Trigeminal neuralgia · Gamma Knife radiosurgery · Microvascular decompression · Craniofacial pain

Dear Editor,

As widely known, classic trigeminal neuralgia (TN) represents one of the most common craniofacial pain syndromes [9, 15]. Medical therapy, as first-line treatment, is effective in controlling pain in a high percentage of cases at short-time period; however, this rate does significantly decrease over time [15]. Microvascular decompression (MVD) represents historically the reference technique [15].

Despite several other therapeutic options, almost half of the patients may experience pain recurrence, negatively affecting their quality of life (QoL) [2, 14, 15].

Stereotactic radiosurgery (SRS), such as Gamma Knife radiosurgery (GKRS), has increasingly become a popular treatment for TN, for the lack of treatment-related toxicity and mortality, less invasiveness, and good pain control rates [2, 14–16]. However, the right timing for GKRS or MVD is still a great matter of debate and data in literature are uneven [15]. Other SRS techniques, such as LINAC based SRS, namely, Cyberknife and Novalis, have been adopted for TN, with similar outcome of GKRS [15]. For those patients who are not operable and need a quick minimal invasive treatment, percutaneous techniques can be considered, such as glycerol or radiofrequency rhizotomy and balloon compression, with high rates of immediate pain relief that are, however, not maintained over time [15].

A long history of pain is usually related to a higher probability of pain recurrence after both MVD and GKRS [4, 10, 16].

Mousavi reported a shorter interval to pain relief, a longer interval of pain relief off medication, and a longer duration of pain control in those patients undergoing GKRS for TN within 3 years of pain onset [10].

Conversely, Lee et al. recently found that, even if early performed (< 5 vs. > 5 years), GKRS was related to a better outcome and a shorter latency before pain relief; pain history > 5 years was not related to treatment failure [4].

These data suggest that GKRS seems to be more effective when performed at the early stage of TN. Affected trigeminal nerves usually appears flattened and atrophic especially with a longstanding history of TN [8]. Longer pain history is likewise associated with nervous microstructural changes on diffusion tensor imaging studies, such as demyelination and loss of axon, conditioning minor pain response to surgical therapy [5]. In TN, as for epilepsy and chronic pain, the kindling of second-order sensory neurons into the brainstem, may negatively affect outcome after therapies targeting first-order sensory neurons, such as GKRS and MVD [4, 5, 10]. Accordingly, these two surgical modalities should be carried out early, to improve pain control on short- and long-term periods [4, 10, 16].

Based on these findings, another issue comes out in the selection of the best strategy: which one must be undertaken first? Clinical outcome after GKRS and MVD is frequently better in those patients without history of previous therapies; nevertheless, this relationship seems to affect GKRS more than MVD [1, 2, 7, 15, 16]. For classic TN, outcome after GKRS is worse in those patients who underwent MVD before GKRS, leading to a lower probability of initial pain cessation but similar probability of maintaining pain relief without medication at 10 years [16].

Six studies comparing MVD to GKRS outcomes have been published to date [3, 6, 11–13, 18]. In their prospective non-randomized trial, Linskey and coworkers reported significant better results in MVD patients in terms of pain control; hence, they suggested to perform MVD to younger and healthy patients, while GKRS to those older or when surgery is contraindicated [6].

✉ Alfio Spina
spina.alfio@hsr.it

[1] Department of Neurosurgery and Gamma Knife Radiosurgery, I.R.C.C.S. San Raffaele Scientific Institute, Vita-Salute University, Via Olgettina 60, 20132 Milan, Italy

[2] Department of Rehabilitation and Functional Recovery, I.R.C.C.S San Raffaele Scientific Institute, Vita-Salute University, Milan, Italy

Similar results were reported by Pollock in 2010 and Inoue in 2017, while Oh and co-workers reported similar pain recurrence rates between MVD and GKRS patients [3, 6, 12, 13]. It has to be noted that in all these studies, the GKRS group was statistically significant older than MVD group. Nanda et al. reported a higher rate of no pain-no medication outcome for MVD with no difference in terms of initial pain relief and recurrence when compared to GKRS; age in the two groups was similar [11].

In a recent series, despite better results of MVD in terms of pain control, preservation of pain tolerance, and recurrence, complications were reported in 11% of patients, while 0% of treatment-related complications were experienced by patients undergoing GKRS ($p < 0.001$) [18]. GKRS was performed once again in older patients with a longer history of pain (48 vs. 84 months; $p < 0.001$); MVD patients with partial response underwent also rhizotomy, as further treatment, to obtain adequate pain control [18]. These data prevent to date to draw definitive conclusions.

Generally, MVD is able to provide faster pain relief than GKRS with similar rates of recurrence at long follow-up periods; however, it has to be noted that MVD is related to the risk of postoperative facial palsy, deafness, CSF leak, meningitis and wound infections, and perioperative death; on the other hand, even if the rate of facial numbness is similar after GKRS, no other major complications were reported [1, 14–16].

No contraindications in performing MVD after a failure of one or two previous GKRS procedures have been reported, while it can be more difficult to target the nerve in GKRS after MVD due to volume nerve reduction or other postoperative anatomic changes that may negatively affect treatment efficacy [8, 16].

According to the abovementioned issues, GKRS as first and early procedure seems to be reasonable in the era of minimally invasive neurosurgery. Patients, who respond to a less invasive technique, such as GKRS, would have been spared from much higher risks; while those who need an MVD have had the right *surgery escalation* therapy. Treatment selection is usually related to the physicians' or patients' confidence and not to an effective risk/benefit analysis, and a definitive treatment algorithm for TN is still lacking [15]. As recently pointed out, MVD still represents the reference technique for TN; however; radiosurgery can be performed safe and effective even as a first line treatment [17]. Future studies should be focused no more on the comparison of different therapies but on distinctive treatment algorithms, in order to individualize the treatment on patients' and pain features.

Compliance with ethical standard

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this type of study, formal consent is not required.

References

1. Berger I, Nayak N, Schuster J, Lee J, Stein S, Malhotra NR (2017) Microvascular decompression versus stereotactic radiosurgery for trigeminal neuralgia: a decision analysis. Cureus 9:e1000. https://doi.org/10.7759/cureus.1000
2. Gagliardi F, Spina A, Bailo M, Boari N, Cavalli A, Franzin A, Fava A, Del Vecchio A, Bolognesi A, Mortini P (2018) Effectiveness of Gamma Knife radiosurgery in improving psychophysical performance and patient's quality of life in idiopathic trigeminal neuralgia. World Neurosurg 110:e776–e785. https://doi.org/10.1016/j.wneu.2017.11.096
3. Inoue T, Hirai H, Shima A, Suzuki F, Yamaji M, Fukushima T, Matsuda M (2017) Long-term outcomes of microvascular decompression and Gamma Knife surgery for trigeminal neuralgia: a retrospective comparison study. Acta Neurochir 159:2127–2135. https://doi.org/10.1007/s00701-017-3325-7
4. Lee CC, Chen CJ, Chong ST, Hung SC, Yang HC, Lin CJ, Wu CC, Chung WY, Guo WY, Hung-Chi Pan D, Wu HM, Lin CP (2018) Early stereotactic radiosurgery for medically refractory trigeminal neuralgia. World Neurosurg 112:e569–e575. https://doi.org/10.1016/j.wneu.2018.01.088
5. Lee CC, Chong ST, Chen CJ, Hung SC, Yang HC, Lin CJ, Wu CC, Chung WY, Guo WY, Pan DH, Wu HM, Sheehan JP, Lin CP (2018) The timing of stereotactic radiosurgery for medically refractory trigeminal neuralgia: the evidence from diffusion tractography images. Acta Neurochir 160:977–986. https://doi.org/10.1007/s00701-017-3449-9
6. Linskey ME, Ratanatharathorn V, Penagaricano J (2008) A prospective cohort study of microvascular decompression and Gamma Knife surgery in patients with trigeminal neuralgia. J Neurosurg 109(Suppl):160–172. https://doi.org/10.3171/jns/2008/109/12/s25
7. Longhi M, Rizzo P, Nicolato A, Foroni R, Reggio M, Gerosa M (2007) Gamma knife radiosurgery for trigeminal neuralgia: results and potentially predictive parameters–part I: idiopathic trigeminal neuralgia. Neurosurgery 61:1254–1260; discussion 1260-1251. https://doi.org/10.1227/01.neu.0000306104.68635.d4
8. Maarbjerg S, Wolfram F, Gozalov A, Olesen J, Bendtsen L (2015) Significance of neurovascular contact in classical trigeminal neuralgia. Brain 138:311–319. https://doi.org/10.1093/brain/awu349
9. Miller JP, Acar F, Burchiel KJ (2009) Classification of trigeminal neuralgia: clinical, therapeutic, and prognostic implications in a series of 144 patients undergoing microvascular decompression. J Neurosurg 111:1231–1234. https://doi.org/10.3171/2008.6.17604
10. Mousavi SH, Niranjan A, Huang MJ, Laghari FJ, Shin SS, Mindlin JL, Flickinger JC, Lunsford LD (2015) Early radiosurgery provides superior pain relief for trigeminal neuralgia patients. Neurology 85:2159–2165. https://doi.org/10.1212/wnl.0000000000002216
11. Nanda A, Javalkar V, Zhang S, Ahmed O (2015) Long term efficacy and patient satisfaction of microvascular decompression and gamma knife radiosurgery for trigeminal neuralgia. J Clin Neurosci 22:818–822. https://doi.org/10.1016/j.jocn.2014.11.028
12. Oh IH, Choi SK, Park BJ, Kim TS, Rhee BA, Lim YJ (2008) The treatment outcome of elderly patients with idiopathic trigeminal neuralgia : micro-vascular decompression versus Gamma Knife radiosurgery. J Korean Neurosurg Soc 44:199–204. https://doi.org/10.3340/jkns.2008.44.4.199

13. Pollock BE, Schoeberl KA (2010) Prospective comparison of posterior fossa exploration and stereotactic radiosurgery dorsal root entry zone target as primary surgery for patients with idiopathic trigeminal neuralgia. Neurosurgery 67:633–638; discussion 638-639. https://doi.org/10.1227/01.neu.0000377861.14650.98
14. Spina A, Boari N, Gagliardi F, Bailo M, Morselli C, Iannaccone S, Mortini P (2017) The emerging role of gamma knife radiosurgery in the management of glossopharyngeal neuralgia. Neurosurg Rev 42: 31–38. https://doi.org/10.1007/s10143-017-0886-0
15. Spina A, Mortini P, Alemanno F, Houdayer E, Iannaccone S (2017) Trigeminal neuralgia: toward a multimodal approach. World Neurosurg 103:220–230. https://doi.org/10.1016/j.wneu.2017.03.126
16. Tuleasca C, Carron R, Resseguier N, Donnet A, Roussel P, Gaudart J, Levivier M, Regis J (2015) Decreased probability of initial pain cessation in classic trigeminal neuralgia treated with Gamma Knife surgery in case of previous microvascular decompression: a prospective series of 45 patients with >1 year of follow-up. Neurosurgery 77:87–94; discussion 94-85. https://doi.org/10.1227/neu.0000000000000739
17. Tuleasca C, Regis J, Sahgal A, De Salles A, Hayashi M, Ma L, Martinez-Alvarez R, Paddick I, Ryu S, Slotman BJ, Levivier M (2018) Stereotactic radiosurgery for trigeminal neuralgia: a systematic review. J Neurosurg 130:1–25. https://doi.org/10.3171/2017.9.jns17545
18. Wang DD, Raygor KP, Cage TA, Ward MM, Westcott S, Barbaro NM, Chang EF (2018) Prospective comparison of long-term pain relief rates after first-time microvascular decompression and stereotactic radiosurgery for trigeminal neuralgia. J Neurosurg 128:68–77. https://doi.org/10.3171/2016.9.jns16149