Cavernous malformations

To The Editor: We read with great interest the article written by Cheng-Chia Lee and colleagues2 (Lee CC, Pan DHC, Chung WY, et al: Brainstem cavernous malformations: the role of Gamma Knife surgery. Clinical article. J Neurosurg 117 Suppl:164–169, December 2012). The authors retrospectively reviewed the efficacy and safety of Gamma Knife surgery (GKS) in patients with brainstem cavernous malformations (CMs). Forty-nine patients with symptomatic CMs were treated by GKS between 1993 and 2010. The mean age in these patients was 37.8 years. There were 118 episodes of hemorrhage during the pre-GKS observation period. The authors calculated the pre-GKS hemorrhage rate in 49 patients who experienced more than 2 bleeding episodes. After excluding the first hemorrhage (118 – 49 = 69 episodes), the authors calculated the annual hemorrhage rate to be 31.3% (69 episodes in 220.3 patient-years). Forty-five patients (91.8%) underwent regularly scheduled follow-up MRI examinations and were available for study; the mean follow-up duration was 40.6 months and the overall observation period consisted of 172.4 patient-years. Six episodes of hemorrhage in 6 patients were documented during this period. Three of these episodes occurred within 2 years after GKS, and 3 episodes occurred more than 2 years after GKS.

Lee et al.2 calculated the annual hemorrhage rate during the first 2 years after GKS to be 3.33% (3 hemorrhages/90.0 patient-years), which was not difficult to understand. However, they calculated the annual hemorrhage rate after the initial 2-year follow-up to be 1.74% (3 hemorrhages/172.4 patient-years). We examined several other studies1,3–5 in which annual hemorrhage rates were calculated. We found the method used by Lee et al. to determine the annual hemorrhage rate after the initial 2-year follow-up period to be quite different from the method used in those studies. We therefore recalculated the annual hemorrhage rate for this period and found it to be 3.64% (3 hemorrhages/[172.4 – 90.0] patient-years) rather than 1.74% (3 hemorrhages/172.4 patient-years) as described by Lee et al. We did this because 172.4 patient-years was the overall observation period and 82.4 patient-years (172.4 – 90.0 patient-years) was the precise observation period after the initial 2-year follow-up. The calculation method used in the study by Lee et al. to determine the post-GKS annual hemorrhage rate after the initial 2-year follow-up is not quite reasonable. It reduces the annual hemorrhage rate after 2 years and leads to a misunderstanding of the effectiveness of GKS on CMs. Using our method of calculation, the annual hemorrhage rate after the initial 2-year period (3.64%) was higher than that during the first 2 years (3.33%). This finding can be contrasted with the conclusions of the study by Lee et al., which state that the annual hemorrhage rate decreased within the first 2 years and further decreased after those 2 years.

In recent years, the positive therapeutic effect of GKS on intracranial CMs, including brainstem CMs, has been confirmed by many studies.1,3–6 In a future study, a randomized controlled prospective multicenter trial is recommended to compare the effectiveness between different treatment methods—surgery and GKS—and observation with close follow-up evaluation.

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Disclosure

The authors report no conflict of interest.

References


Response: We appreciate the efforts that Dr. Da Li and Dr. Jun-Ting Zhang took to read and recalculate our
statistics, and we thank them for sharing their thoughts with the *Journal of Neurosurgery* readers and us. We are pleased to have the opportunity to revise our data and continue to provide important information on CM therapies.

The point raised in the comments by Drs. Li and Zhang is related to the method we used to calculate the post-GKS annual hemorrhage rate. To clarify the problem, we returned to our original data and recalculated the hemorrhage rate more than 2 years post-GKS. We found, however, that the real problem lies in the way in which we calculated patient-years during the initial 2 years of follow-up.

Indeed, 29 patients were followed up for more than 2 years, and 16 were followed up for less than 2 years. Therefore, we cannot simply use 90 for the number of patient-years (45 patients × 2 years) in the initial 2 years. Please refer to the following recalculated data (Fig. 1):

Initial 2 years post-GKS: 70.0 patient-years = (29 patients × 2 years) + (16 patients × various follow-up periods)

After the initial 2 years post-GKS: 82.4 patient-years = (29 patients × various follow-up periods) – (29 patients × 2 years)

So, the recalculated annual hemorrhage rates after GKS are:

Initial 2 years post-GKS: 4.29% = 3 hemorrhage episodes/70.0 patient-years

After the initial 2 years post-GKS: 3.64% = 3 hemorrhage episodes/82.4 patient-years

We are preparing an erratum notice that will reflect changes throughout our article. The original Figure 2 showing changes over time in the post-GKS annual hemorrhage rate has been revised (Fig. 2) and is shown below.

We still can conclude that GKS is effective in reducing the rate of recurrent hemorrhage in patients with brainstem CMs. In our study, the annual hemorrhage rate decreased from 31.3% to 4.29% within 2 years and further decreased to 3.64% after 2 years.

Certainly, we agree that the positive therapeutic effect of GKS on intracranial CMs has been confirmed by many studies, and that a randomized controlled prospective multicenter trial is necessary to compare the effec-

**Fig. 1.** Chart showing breakdown of patient follow-up and timing of hemorrhage episodes after GKS. In this series, 3 hemorrhage episodes occurred within the first 2 years of follow-up and 3 hemorrhage episodes occurred after that time. The number of patient-years in the first 2 years of follow-up totaled 70 and the number of patient-years in the later period was 82.4. FU = follow-up; H = hemorrhage; pt = patient.

**Fig. 2.** Bar graph demonstrating changes in the annual hemorrhage rate following GKS (within 2 years and beyond 2 years). There was a decreasing trend in the hemorrhage rate after GKS. In most patients, hemorrhage was controlled, and the patient did not suffer any further neurological deterioration.