Overall survival benefit from surgical resection in treatment of recurrent glioblastoma

ESMO Clinical Practice Guidelines on high-grade gliomas dismiss impact of surgical resection on overall survival (OS) in treatment of recurrent glioblastoma (GBM), citing two pooled analyses as evidence of no effect. Neither analysis considered one critical factor in analyzing efficacy of re-resection—the extent of resection (EOR)—known to be important at first surgery. Furthermore, only 12% (37/300) and 27% (208/758) of patients underwent any surgery at all, respectively [1, 2]. Even if surgery had an effect on OS in these series, obvious imbalance, small numbers, and surgical heterogeneity would hardly provide sufficient power to detect any difference. Several recent series with higher numbers of patients, accounting EOR at surgery for recurrent GBM, demonstrate role of not only EOR in treatment efficacy, but also that more complete second resection can compensate for incomplete first resection [3–5].

Bloch et al. reported that 30% (107/354) GBM resections during their study period were for treatment of recurrent disease—all patients underwent postoperative MRI to estimate EOR. Impact of EOR, classified as gross total resection (GTR) or subtotal resection (STR), at both initial surgery and surgery for recurrence was analyzed. Median survival for patients with GTR followed by GTR was 20 months; for STR followed by GTR 19 months, and for STR followed by STR 15.9 months. STR at recurrence in patients with initial STR demonstrated significantly decreased survival compared with GTR at recurrence (15.9 versus 19 months, $P = 0.004$). For patients with initial STR, survival following repeat resection significantly increased with GTR compared with STR: 16.7 versus 7.4 months, $P = 0.001$.

Oppenlander et al. analyzed 170 consecutive patients and demonstrated EOR threshold for recurrent GBM. Significant improvement in OS was attained beyond 80% EOR—efficacy notably similar to newly diagnosed GBM. Median PFS following re-resection was 5.2 months, median OS 19 months for re-resection population, and remarkable 30 months in subset with EOR $\geq 97\%$. Cox proportional hazards analysis showed age, Karnofsky Performance Scale score, and EOR predictive of survival following repeat resection ($P = 0.0001$).

Quick et al. achieved radiologically confirmed complete resection in 29/40 patients (72%). Median survival after re-resection was 15 months for volumetric EOR $\geq 95\%$ and 9 months for lesser; significantly correlating with survival after re-resection in multivariate analysis [3].

Surgical series have patient selection and segregating surgery versus tumor influence on EOR is difficult. Adequate studies comparing resection versus observation are hard. An ANOCEF trial randomizes elderly patients with good performance status to GTR or biopsy. With advances in imaging and surgical techniques the number of patients able to undergo resection for recurrent GBM is increasing [3]. Role of surgery in recurrent GBM cannot be simply dismissed, trivializing seems harmful to many patients. Moreover, ignoring it, e.g. as a stratification factor in randomized clinical trials leads to imbalances in treatment arms and misleads. In single-arm studies with near complete resection as eligibility criterion, effect of added experimental treatment likely gets inflated. ESMO should consider all available and published data at next revision of the guidelines noting necessary caveats.

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