ABSTRACT

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Effect of awake craniotomy in glioblastoma in eloquent areas (GLIOMAP): a propensity score-matched analysis of an international, multicentre, cohort study.

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BACKGROUND: Awake mapping has been associated with decreased neurological deficits and increased extent of resection in eloquent glioma resections. However, its effect within clinically relevant glioblastoma subgroups remains poorly understood. We aimed to assess the benefit of this technique in subgroups of patients with glioblastomas based on age, preoperative neurological morbidity, and Karnofsky Performance Score (KPS).

METHODS: In this propensity score-matched analysis of an international, multicentre, cohort study (GLIOMAP), patients were recruited at four tertiary centres in Europe (Erasmus MC, Rotterdam and Haaglanden MC, The Hague, Netherlands, and UZ Leuven, Leuven, Belgium) and the USA (Brigham and Women's Hospital, Boston, MA). Patients were eligible if they were aged 18-90 years, undergoing resection, had a histopathological diagnosis of primary glioblastoma, their tumour was in an eloquent or near-eloquent location, and they had a unifocal enhancing lesion. Patients either underwent awake mapping during craniotomy, or asleep resection, as per treating physician or multidisciplinary tumour board decision. We used propensity-score matching (1:3) to match patients in the awake group with those in the asleep group to create a matched cohort, and to match patients from subgroups stratified by age (<70 years vs ≥70 years), preoperative National Institute of Health Stroke Scale (NIHSS) score (score of 0-1 vs ≥2), and preoperative KPS (90-100 vs ≤80). We used Cox proportional hazard regressions to analyse the effect of awake mapping on the primary outcomes including postoperative neurological deficits (measured by deterioration in NIHSS score at 6 week, 3 months, and 6 months postoperatively), overall survival, and progression-free survival. We used logistic regression to analyse the predictive value of awake mapping and other perioperative factors on postoperative outcomes.

FINDINGS: Between Jan 1, 2010, and Oct 31, 2020, 3919 patients were recruited, of whom 1047 with tumour resection for primary eloquent glioblastoma were included in analyses as the overall unmatched cohort. After propensity-score matching, the overall matched cohort comprised 536 patients, of whom 134 had awake craniotomies and 402 had asleep resection. In the overall matched cohort,

awake craniotomy versus asleep resection resulted in fewer neurological deficits at 3 months (26 [22%] of 120 vs 107 [33%] of 323; p=0·019) and 6 months (30 [26%] of 115 vs 125 [41%] of 305; p=0·0048) postoperatively, longer overall survival (median 17·0 months [95% CI 15·0-24·0] vs 14·0 months [13·0-16·0]; p=0·00054), and longer progression-free survival (median 9·0 months [8·0-11·0] vs 7·3 months [6·0-8·8]; p=0·0060). In subgroup analyses, fewer postoperative neurological deficits occurred at 3 months and at 6 months with awake craniotomy versus asleep resection in patients younger than 70 years (3 months: 22 [21%] of 103 vs 93 [34%] of 272; p=0·016; 6 months: 24 [24%] of 101 vs 108 [42%] of 258; p=0·0014), those with an NIHSS score of 0-1 (3 months: 22 [23%] of 96 vs 97 [38%] of 254; p=0·0071; 6 months: 27 [28%] of 95 vs 115 [48%] of 239; p=0·0010), and those with a KPS of 90-100 (3 months: 17 [19%] of 88 vs 74 [35%] of 237; p=0·034; 6 months: 24 [28%] of 87 vs 101 [45%] of 223, p=0·0043). Additionally, fewer postoperative neurological deficits were seen in the awake group versus the asleep group at 3 months in patients aged 70 years and older (two [13%] of 16 vs 15 [43%] of 35; p=0·033; no difference seen at 6 months), with a NIHSS score of 2 or higher (3 months: three [13%] of 23 vs 21 [36%] of 58; p=0·040) and at 6 months in those with a KPS of 80 or lower (five [18%] of 28 vs 34 [39%] of 88; p=0·043; no difference seen at 3 months). Median overall survival was longer for the awake group than the asleep group in the subgroups younger than 70 years (19·5 months [95% CI 16·0-31·0] vs 15·0 months [13·0-17·0]; p<0·0001), an NIHSS score of 0-1 (18·0 months [16·0-31·0] vs 14·0 months [13·0-16·5]; p=0·00047), and KPS of 90-100 (19·0 months [16·0-31·0] vs 14·5 months [13·0-16·5]; p=0·00058). Median progression-free survival was also longer in the awake group than in the asleep group in patients younger than 70 years (9·3 months [95% CI 8·0-12·0] vs 7·5 months [6·5-9·0]; p=0·0061), in those with an NIHSS score of 0-1 (9·5 months [9·0-12·0] vs 8·0 months [6·5-9·0]; p=0·0035), and in those with a KPS of 90-100 (10·0 months [9·0-13·0] vs 8·0 months [7·0-9·0]; p=0·0010). No difference was seen in overall survival or progression-free survival between the awake group and the asleep group for those aged 70 years and older, with NIHSS scores of 2 or higher, or with a KPS of 80 or lower.

INTERPRETATION: These data might aid neurosurgeons with the assessment of their surgical strategy in individual glioblastoma patients. These findings will be validated and further explored in the SAFE trial (NCT03861299) and the PROGRAM study (NCT04708171).

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