

# Preserving quality of life is not incompatible with increasing overall survival in diffuse low-grade glioma patients

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In this issue of *Acta Neurochirurgica*, Brennum et al. [3] suggest that it could be acceptable to give patients with diffuse low-grade glioma (DLGG) the choice of more substantial surgical resection, leading to permanent neurological deficits, including with regard to motor and language functions.

Although the intention of the authors is laudable, the message here is too simplistic—and potentially dangerous—to be currently adapted to routine practice.

First of all, it has clearly been demonstrated that the extent of surgical resection has a significant impact on overall survival in DLGG patients [5, 17, 22, 23]. As a consequence, as recommended by the European guidelines, early surgery is currently the first treatment option to consider in DLGG [24]. This is the reason why some authors have achieved “supratotal” resection (i.e., extended resection with a margin beyond MR imaging-defined abnormalities) [25], especially in asymptomatic patients with incidental discovery of DLGG [8, 18]. Thanks to the use of intraoperative functional mapping at both the cortical and subcortical level, favorable oncological and functional outcomes have been obtained [6]. Indeed, intrasurgical tasks can be adapted to the quality of life (QoL) of each patient, according to his or her job, hobbies and habits, including sensorimotor, visual, language, cognitive and even behavioral functions [13, 15]. These results led to the recent proposal of a screening policy for DLGG [19]. However, it is worth noting that the aim of surgery is not (yet) to cure

patients, but to avoid anaplastic transformation and thus induce a shift from a tumor that will become malignant if no treatment is administered (ultimately leading to death) to a chronic disease controlled by serial treatments [12]. By applying the concept of preventive surgery, overall survival is now estimated at around 15 years since the first symptom—as recently shown in more than 1,000 DLGGs [5, 22].

In this setting, due to the long survival of these patients, it is crucial to preserve or even improve their quality of life. According to the European guidelines, the surgical goal is to maximally remove the tumor whenever possible while minimizing the postoperative morbidity [24]. In other words, the aim is not only to increase the extent of resection, but also to maximize the benefit-to-risk ratio of surgery, i.e., to maximize the onco-functional balance by improving both QoL and survival [11, 20]. Indeed, it could be ethically acceptable to propose to a patient to voluntarily generate a permanent neurological deficit if it were possible to cure him or her. Nonetheless, even in cases of supratotal resection for DLGG located outside eloquent areas, whereas no malignant transformation has been observed yet, tumor relapse has already occurred [25]. Therefore, why elicit disabling sequelae by maximizing the resection for DLGG involving functional structures, knowing that the glioma will inescapably recur? Such a proposal might also let the patients believe that they could be cured by the surgery, which is currently impossible.

Rather, it would be more honest to explain to the patient and his or her family that alternative strategies can be considered in the near future. First, it is possible to reoperate on recurrent DLGG without functional worsening, with an additional reduction of the tumor volume and an increased delay before malignant transformation [21]. Indeed, subsequent surgeries may be performed with preservation of QoL, even for gliomas located within eloquent structures, thanks to mechanisms of neuroplasticity [7, 14]. Such functional reorganization has been extensively demonstrated in DLGG because of

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the slow growth of this tumor [10]. Thus, why generate a permanent deficit following a first surgery rather than preserving a normal QoL for many years and reoperating later with *in fine* the same oncological impact thanks to an improvement of the extent of resection during the second surgery—in a patient enjoying a normal family, social and professional life? Second, if the tumor migrates along the white matter tracts, knowing that the plastic potential is very low at the subcortical level (preventing large resection) [10, 16], chemotherapy can be administered. Of note, chemotherapy may preserve QoL, including cognitive functions [2], while significantly increasing survival [4]. Furthermore, chemotherapy can also induce shrinkage of the glioma, making possible a (re-)operation while preserving the functional status [1]. Such a multistage and individualized therapeutic approach enables solving the classical dilemma in DLGG (primo non nocere versus maximum survival), namely, to be more ambitious by improving both QoL and survival [12].

In summary, because it is not possible for a patient (and an expert) to imagine what it really means living with neurological disabilities, and because results from new personalized management strategies—dealing with the interactions between the course of this chronic disease, reaction brain remapping and onco-functional modulation elicited by serial treatments—have been improved [9, 12], it is today ethically questionable to propose generating a permanent motor or language impairment in patients with (still) incurable DLGG.

**Conflicts of interest** None.

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