



# The WHO CNS 5th Edition: A Quandary for the Surgical Neurooncologist and Adult Diffuse Glioma Patients in LMICs

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The 2021 World Health Organization (WHO) classification of brain tumors,<sup>1</sup> as a follow-up to the 2016 update, incorporates validated molecular markers to previously established histomorphological features and has led to a significant shift in the diagnosis and management of adult diffuse gliomas. The classification provides a distinction between astrocytoma Isocitrate Dehydrogenase (IDH) mutant grade 4 and the IDH-wildtype glioblastoma, which is also a grade 4 tumor, while also making provision for an entity regarded as molecular glioblastoma. Oligodendroglioma must now be defined as an IDH mutant and 1p 19q co-deleted tumor. The inability to perform a molecular typing of the tumors now necessitates the addition of the suffix; not otherwise stated in the diagnosis of the tumor.

The new classification is part of concerted efforts over the years, directed at pushing the frontier of care for glioma patients. These undertakings are in the background of seemingly disappointing results at improving the overall survival in adult diffuse gliomas particularly in the high-grade gliomas. Remarkable clinical and basic research efforts are generating new opportunities in the care of adult gliomas in the fields of surgery, radiation therapy, chemotherapy, and immunotherapy. Surgical neurooncology is now focused on providing an individualized operative approach, developed through comprehensive preoperative imaging evaluation, utilizing radiogenomics where applicable and available, with the clear goal of achieving satisfactory oncofunctional outcomes, within the context of the patient's expectations. Surgery is, therefore, directed at achieving safe, maximal tumor resection, aimed at leveraging on the established positive influence of maximal resection<sup>2</sup> without a compromise of the quality of life of the patients. The surgical neurooncologist is, therefore, saddled with the responsibility of providing representative and adequate amount of tissue required to determine the anatomic

histology and molecular diagnosis of the tumor, which impacts on the postoperative treatments that will be offered the patient. In low- and middle-income countries (LMICs), postoperative treatments are also dependent on the availabilities of radiation therapy and chemotherapeutic agents.

The 2021 classification is a potential game changer in the care of adult diffuse gliomas, with the tendency that the adoption of these diagnostic guidelines in the LMICs, can significantly impact on the care of the patients, as well as become a veritable tool in providing data for research into the possible peculiarities of these tumors in specific LMICs.<sup>3</sup> It has, however, thrown up a huge challenge for the LMICs in terms of capacity for making these diagnoses as well as the availability of the diagnostic facilities. Thus, there is a tendency to widening the disparity in the care of glioma patients between the high-income countries (HICs) and LMICs. To mitigate this tendency, there should be domestication of these guidelines, rather than outright adoption, within the context of what resources are available and the financial burden of care to be borne mainly by the patients and their relatives, due to the lack of medical insurance coverage in most instances. This can be achieved to varying extents and in different ways, though the predisposition of the Indian Society of Neurooncology in setting its own guidelines regarding the molecular typing of gliomas following the release of the 2016 classification<sup>4</sup> can provide a guide to other LMICs in the adaptation of the new classification. It may be pertinent for each LMIC to decide, for example, how important fluorescence in situ hybridization will be to the final diagnosis of oligodendrogliomas in addition to the classic oligodendroglial morphology on histology, considering the cost. How important will sequencing for IDH mutation be in the context of an inconclusive immunohistochemistry for the mutation? It

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might also be beneficial that regional workup laboratories within countries congregate their efforts and maximize opportunities. Collaboration with centers in HICs to support in-country trainings and analysis of samples may also be helpful. Funded research and participation in clinical trials will also serve to augment these efforts.

In LMICs, the surgical neurooncologists remain pivotal to the optimization of the care of glioma patients, often being the first specialist physician in contact with the patient, which may include the basic requisition for brain imaging, followed by the planning and execution of tumor resections guided by established guidelines for the achievement of maximal onco-functional. All of the above within the constraints of available resources. The surgical neurooncologists will also usually serve as either the coordinators or cocoordinators of the brain tumor boards in the places where this crucial element is available. It is, therefore, important that LMICs move to empower the available surgical neurooncologists such that they are conversant with the changing guidelines in the care of adult diffuse glioma patients and also lean in the direction of starting/strengthening subspecialty training in surgical neurooncology to develop a critical mass of surgeons who will evolve into leaders in the clinical care of these patients as

well as in clinical and basic translational research. This will have a multiplier effect in ensuring the patients in LMICs have access to the best care possible and also engender collaboration that will further push the frontiers in these countries.

#### Conflict of Interest

None declared.

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