Underutilization of Neurodiagnostic Resources in Drug-Resistant Epilepsy

Epilepsy Currents
2024, Vol. 24(5) 339–341

DOI: 10.1177/15357597241280486
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Use of Recommended Neurodiagnostic Evaluation Among Patients With Drug-Resistant Epilepsy

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Importance: Interdisciplinary practice parameters recommend that patients with drug-resistant epilepsy (DRE) undergo comprehensive neurodiagnostic evaluation, including presurgical assessment. Reporting from specialized centers suggests long delays to referral and underuse of surgery; however, longitudinal data are limited to characterize neurodiagnostic evaluation among patients with DRE in more diverse US settings and populations. Objective: To examine the rate and factors associated with neurodiagnostic studies and comprehensive evaluation among patients with DRE within 3 US cohorts. Design, setting, and participants: A retrospective cross-sectional study was conducted using the Observational Medical Outcomes Partnership Common Data Model including US multistate Medicaid data, commercial claims data, and Columbia University Medical Center (CUMC) electronic health record data. Patients meeting a validated computable phenotype algorithm for DRE between January 1, 2015, and April 1, 2020, were included. No eligible participants were excluded. Exposure: Demographic and clinical variables were queried. Main outcomes and measures: The proportion of patients receiving a composite proxy for comprehensive neurodiagnostic evaluation, including (1) magnetic resonance or other advanced brain imaging, (2) video-electroencephalography, and (3) neuropsychological evaluation within 2 years of meeting the inclusion criteria. Results: A total of 33 542 patients with DRE were included in the Medicaid cohort, 22 496 in the commercial insurance cohort, and 2741 in the CUMC database. A total of 31 516 patients (53.6%) were women. The proportion of patients meeting the comprehensive evaluation main outcome in the Medicaid cohort was 4.5% ($n = 1520$); in the commercial insurance cohort, 8.0% ($n = 1796$); and in the CUMC cohort, 14.3% ($n = 393$). Video-electroencephalography (24.9% Medicaid, 28.4% commercial, and 63.2% CUMC) and magnetic resonance imaging of the brain (35.6% Medicaid, 43.4% commercial, and 52.6% CUMC) were performed more regularly than neuropsychological evaluation (13.0% Medicaid, 16.6% commercial, and 19.2% CUMC) or advanced imaging (3.2% Medicaid, 5.4% commercial, and 13.1% CUMC). Factors independently associated with greater odds of evaluation across all 3 data sets included the number of inpatient and outpatient nonemergency epilepsy visits and focal rather than generalized epilepsy. Conclusions and relevance: The findings of this study suggest there is a gap in the use of diagnostic studies to evaluate patients with DRE. Care setting, insurance type, frequency of nonemergency visits, and epilepsy type are all associated with evaluation. A common data model can be used to measure adherence to best practices across a variety of observational data sources.

Commentary

Drug-resistant epilepsy (DRE) kills more than 10% of affected patients in 2 years.[1] This mortality is higher than that caused by many forms of cancer. Unfortunately, patients with DRE do not receive the same attention and care that patients diagnosed with cancer do. It has been clearly demonstrated that once a patient is diagnosed with DRE, seizure improvement with further changes or addition of antiseizure medications (ASMs) is dismal.[2] A randomized trial has established that surgery for temporal lobe epilepsy (the most common DRE) is far superior to treatment with ASMs, leading to better seizure control, mortality reduction, and better quality of life.[3] More research confirmed these findings and extended them to other forms of focal onset epilepsy. The evidence was so strong that the American Academy of Neurology (AAN) published a practice parameter that recommended that patients with DRE be referred for evaluation of candidacy to epilepsy surgery.[4] The International League Against Epilepsy (ILAE) Surgical Therapies Commission recently issued an Expert Consensus Recommendation stating that:

> Referral for a surgical evaluation should be offered to every patient with drug-resistant epilepsy (up to 70 years of age), as

> soon as drug resistance is ascertained, regardless of epilepsy duration, sex, socioeconomic status, seizure type, epilepsy type (including epileptic encephalopathies), localization, and comorbidities (including severe psychiatric comorbidity like psychogenic nonepileptic seizures [PNES] or substance abuse) if patients are cooperative with management.[5]

Even though not all patients with DRE can ultimately be treated with resective surgery, referral to a center that does perform such surgeries often leads to overall better care. This can be achieved in the form of better diagnosis. For instance, clarification of nonepileptic events in patients with or without epileptic seizures, or diagnosis of monogenic forms of epilepsy that can be amenable to precision therapy. It can also lead to other forms of treatment (such as neuromodulation or diet) that will ultimately improve seizure control and consequently quality of life. Patients referred to a surgical evaluation often have at least 3 pieces of investigation: brain magnetic resonance imaging (MRI), video-electroencephalography (v-EEG), and neuropsychological evaluation. These 3 basic pillars of surgical candidacy investigation can serve as a surrogate to determine if patients with DRE are being managed as per ILAE and AAN recommendations. And this is what Spotnitz et al[6] did: investigated whether patients with DRE were being referred for surgical candidacy evaluations, using these 3 diagnostic tests.

This cross-sectional retrospective study used 3 large electronic databases that were normalized by the Observational Medical Outcomes Partnership Common Data Model: a US multistate Medicaid, a Commercial Claims and Encounters (CCAE), and the Columbia University Medical Center (CUMC) electronic health record data. Patients with DRE were identified as well as the types of diagnostic tests they did. The inclusion criterion was a diagnosis of DRE at or before an index encounter between January 2015 and April 2020. DRE was defined as intractable epilepsy and exposure to 2 or more unique nongabapentinoid ASMs for 90 days or more each.[7] As a side note, this group had previously demonstrated 93.7% specificity of DRE identification in electronic database compared to manual chart review.[8] The study then evaluated the proportion of patients in each cohort receiving a composite proxy for a comprehensive neurodiagnostic evaluation within 2 years of meeting the inclusion criterion. This comprehensive evaluation includes: (1) brain MRI or other forms of advanced brain imaging (positron emission tomography, single photon emission computed tomography, etc), (2) v-EEG, and (3) neuropsychological evaluation.

A total of 58 779 patients were included in the study, 53.6% of them were female. A total of 33 542 patients were in the Medicaid, 22 496 in the CCAE, and 2741 in the CUMC cohorts. Their findings showed that overall, only a very small proportion of patients with DRE had a comprehensive neurodiagnostic evaluation. Patients in the CUMC had greater use of all neurodiagnostic studies (14.3%) than those in the CCAE (8%), with those in the Medicaid cohort having the lowest (4.5%). Out of the 3 investigation modalities, brain MRI was most commonly done in the Medicaid (35.6%) and CCAE (43.4%) cohorts, although a higher proportion of patients had brain MRI at the CUMC (52.6%). Advanced brain imaging was done in only 3.2% of the Medicaid cohort, 5.4% of the CCAE cohort, and 13.1% of the CUMC cohort. v-EEG was the second most used neurodiagnostic modality in the Medicaid (24.9%) and CCAE (28.4%) cohorts, but the most used by patients in the CUMC cohort (63.2%). Finally, neuropsychological evaluation was done in only 13% of Medicaid, 16.6% of CCAE, and 19.2% of CUMC cohorts.

Multivariable logistic regression testing association with the composite comprehensive evaluation shows that the number of outpatient and nonemergency inpatient visits in the year preceding the index date were consistently associated with a comprehensive evaluation. Interestingly, an incrementally increasing number of ASMs was associated with greater odds of complete evaluation only in the CCAE cohort. As expected, patients with generalized epilepsy were less likely to have received a complete neurodiagnostic evaluation in all 3 cohorts. Evaluation of race and ethnicity was limited by missing data. However, from the data available, cases with unreported ethnicity and race had lower odds of receiving a comprehensive evaluation at the CUMC and Medicaid cohorts. Hispanics in the CUMC cohort also had lower odds of comprehensive evaluation. The CCAE does not report race or ethnicity.

Adults older than 65 years had lower odds of being evaluated, while those between 18 and 39 were more likely to be evaluated than adults between 40 and 64 years old in any of the cohorts. Overall, adults were less likely to be investigated in the Medicaid and CCAE cohorts compared to the CUMC cohort.

The study had some limitations, as noted by the authors, and included: (1) all data used had been coded for billing purposes and have variable sensitivity and specificity; (2) there are limitations when comparing electronic health records (available for the CUMC cohort) to insurance claims data; the CUMC database had an open cohort and longer observation times. This might have underestimated the number of patients that did complete a presurgical investigation; (3) patients with focal and generalized onset were included, as long as they had DRE. This may limit the number of complete investigations, since patients with generalized DRE often have other comorbidities that may preclude the complete investigation, such as intellectual disability and autism, as well as decrease the need for neuropsychological tests in patients that will not undergo a resective surgery.

This study shows a sad reality: DRE is not managed as it should be in the vast majority of patients, in several different groups, and especially outside specialized epilepsy centers. Unfortunately, this poor management perpetuates the burden of seizures, low quality of life, and increased mortality seen in these patients. Socioeconomic factors are important, but even in a universal health system only a very small fraction of patients receive appropriate care.[1] More needs to be done, urgently. Perhaps the first step would be better education of medical students, so they can incorporate this important knowledge into their practices. Another piece might be empowering

patients, so they know how to advocate for themselves. Studies like this one are important to help us see what happens in the real world and help us devise new ways of getting the care patients with DRE need and deserve.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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