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Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure





Physicians' beliefs about brain surgery for drug-resistant epilepsy: A global survey

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ARTICLE INFO

ABSTRACT

Keywords: Brain Epilepsy Purpose: To investigate the opinions of physicians about brain surgery for drug-resistant epilepsy worldwide.

The authors conducted the statistical analyses.

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https://doi.org/10.1016/j.seizure.2022.10.012

Received 12 August 2022; Received in revised form 20 September 2022; Accepted 9 October 2022 Available online 10 October 2022

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Seizure Surgery Treatment *Methods*: Practicing neurologists, psychiatrists, and neurosurgeons from around the world were invited to participate in an online survey. The survey anonymously collected data about demographics, years in clinical practice, discipline, nation, work setting, and answers to the questions about beliefs and attitudes about brain surgery for drug-resistant epilepsy.

Results: In total, 1410 physicians from 20 countries and different world regions participated. The propensity to discuss brain surgery with patients, who have drug-resistant seizures, was higher among men (versus women) [Odds Ratio (OR) 1.67, 95% CI 1.20–2.31; p=0.002]. In comparison to neurologists, psychiatrists were less likely (OR 0.28, 95% CI 0.17–0.47; p<0.001) and neurosurgeons were more likely (OR 2.00, 95% CI 1.08–3.72; p=0.028) to discuss about it. Survey participants working in Africa, Asia, the Middle East, and the Former Union of Soviet Socialist Republics showed a lower propensity to discuss epilepsy surgery with patients.

Conclusion: This study showed that on an international level, there is still a knowledge gap concerning epilepsy surgery and much needs to be done to identify and overcome barriers to epilepsy surgery for patients with drugresistant seizures worldwide.

1. Introduction

Epilepsies are a common chronic brain disorder affecting about 70 million people globally [1]. Antiseizure medications (ASMs) are the mainstay of treatment for epilepsy; however, about 30% of people with epilepsy (PWE) have drug-resistant epileptic seizures [2]. Ongoing epileptic seizures are associated with increased risks of morbidity and mortality for PWE [3–7]. Epilepsy surgery is a valuable therapeutic option to increase the likelihood of achieving seizure freedom, improving the quality of life of PWE [8]. Although the benefits associated with epilepsy surgery are undisputable and consistent around the world, it remains widely underutilized [8].

Previous studies have shown that PWE, who could benefit from epilepsy surgery, should be referred for presurgical assessments as soon as possible, as patients with a shorter duration of epilepsy are more likely to benefit from surgical treatments [9]. However, there is often a long delay in the referral to presurgical evaluation and epilepsy surgery, which can be due to several factors [10]; these may include difficult access to care, various opinions and misconceptions about surgery by patients and their caregivers, as well as by physicians, and socio-economic barriers, among others [10–15].

In the current study, we aimed to investigate the physicians' beliefs about brain surgery for drug-resistant epilepsy in a global survey.

2. Materials and methods

Practicing neurologists, psychiatrists, and neurosurgeons (selfdeclared) (adults and pediatrics for all disciplines) from around the world were invited to participate in an online survey. On 5th January 2022, we (AAP, ET, and FB) emailed an invitation including a questionnaire (using Google forms) to the members of the International Research in Epilepsy (IR-Epil) Consortium [16]. The IR-Epil consortium includes 53 persons (lead physicians with epilepsy expertise) from 53 countries, representing all the continents and all the International League Against Epilepsy (ILAE) regions. Only one person per nation was primarily contacted. We asked the lead persons to share the survey with as many of their colleagues (neurologists, psychiatrists, and neurosurgeons) as possible in their corresponding nations. A reminder was sent once a week. In many places in the world only neurologists and neurosurgeons take care of patients with epilepsy (specifically, on the issue of brain surgery for drug-resistant epilepsy), but in some places psychiatrists do, as there is scarcity of neurologists. Therefore, we investigated these three groups. The survey was distributed among all these three disciplines by the lead person in each country, but we did not have any power to control the participation of the recipients of the survey. The study was closed on 1st May 2022. The survey anonymously collected data about demographics, years in clinical practice, discipline (neurology, psychiatry, neurosurgery), nation, work setting (academic or not), and answers to the questions about beliefs and attitudes about brain surgery for drug-resistant epilepsy (i.e., whether participants discuss the possibility of surgical option with their patients; when they consider doing (or referring for) presurgical workup) (Appendix 1). Fellows and residents were not included. There was no compensation for the participation. The survey was conducted in English, Russian, and Kazakh languages. This study was conducted with the approval of the Shiraz University of Medical Sciences Institutional Review Board.

We descriptively summarized the demographic variables and responses from the whole cohort. Values were presented as median (interquartile range) for continuous variables and number (percent) of subjects for categorical variables. Univariate comparisons were made through the Mann-Whitney U test or Chi-squared test, as appropriate. The associations between baseline characteristics of the survey participants and the response to the selected question 'Do you discuss the possibility of brain surgery with your patients with epilepsy who have drug-resistant seizures?' were determined by logistic regression entering all the variables with p < 0.05 from the univariate comparison into a multivariate model. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated. Results were considered significant for p values < 0.05 (two-sided). Data analysis was performed using STATA/IC 13.1 (StataCorp LP, College Station, TX, USA).

Availability of data and material: The data will be shared upon request.

3. Results

In total, 1410 physicians from different regions of the world participated in the study (Appendix 2). The median age of the respondents was 43 (35–53) years, and most of the participants were women (53.5%). The majority of the respondents were active as neurologists (84.2%) and reported visiting 10 to 50 patients with epilepsy per month (47.0%). The demographic and baseline characteristics of the participants are summarized in Table 1.

The participants who answered 'Yes' to the question 'Do you discuss the possibility of brain surgery with your patients with epilepsy who have drug-resistant seizures?' were 1126 (79.9%). They were older [44 (36–54) versus 39 (32–49) years; p < 0.001] and had longer clinical experience [15 (7–24) versus 10 (4.5–20) years in practice; p < 0.001] in comparison to the participants who answered 'No'. Men reported discussing the possibility of brain surgery with their patients more often than women (85.8% versus 74.7%; p < 0.001). Neurologists and neurosurgeons reported discussing this issue more commonly than psychiatrists. Across the world regions, the respondents working in Europe, North America, and South America were more likely to discuss epilepsy surgery with their patients. Further, when countries of the world are classified according to their economic condition (https://www.un.org/e n/development/desa/policy/wesp/wesp_current/2014wesp_country classification.pdf), the respondents working in the developed economies reported to discuss epilepsy surgery with their patients more

commonly than physicians practicing in economies in transition or

developing economies [234/260 (90.0%) versus 877/1132 (77.5%); p

Table 1Baseline characteristics of the participants.

| Characteristics | Participants ($N = 1410$) |
|--|-----------------------------|
| Age, years | |
| N ^a | 1354 |
| Median | 43 (35–53) |
| Sex | |
| N^a | 1406 |
| Male | 654 (46.5) |
| Female | 752 (53.5) |
| Discipline | |
| N^a | 1404 |
| Neurology | 1182 (84.2) |
| Psychiatry | 85 (6.0) |
| Neurosurgery | 137 (9.8) |
| Years in practice | |
| N^a | 1360 |
| Median | 14 (6-23) |
| World regions | |
| N^a | 1392 |
| Europe | 158 (11.4) |
| Africa | 46 (3.3) |
| Asia | 70 (5.1) |
| Middle East | 374 (26.9) |
| North America | 103 (7.4) |
| South America | 335 (24.1) |
| Former Union of Soviet Socialist Republics | 306 (22.0) |
| Country classification | |
| N^a | 1392 |
| Developed economies | 260 (18.7) |
| Economies in transition/Developing economies | 1132 (81.3) |
| Work setting | |
| N^a | 1403 |
| Academic | 453 (32.3) |
| Not academic | 421 (30.0) |
| Both | 529 (37.7) |
| Patients with epilepsy seen per month | |
| N^a | 1405 |
| <10 | 523 (37.2) |
| 10–50 | 660 (47.0) |
| >50 | 222 (15.8) |

Data are median (interquartile range) for continuous variables and n (%) for categorical variables.

N^a Refers to the total number of the participants for whom data were available.

<0.001). Out of 523 participants who were usual to see less than 10 patients with epilepsy per month, 356 (68.1%) answered to discuss epilepsy surgery with patients with drug-resistant seizures; the corresponding rates in participants who visited 10–50 and more than 50 patients per month were 86.4% and 88.3%. The characteristics of respondents according to the given answer are shown in Table 2.

Among the participants, who reported not discussing brain surgery with patients who have drug-resistant seizures, the main reasons for refraining from discussing were the fear of complications associated with surgery, the high costs of epilepsy surgery, and the belief that surgery is not beneficial for seizure reduction. Among the participants, who reported discussing brain surgery, the presence of a clear lesion detectable in brain neuroimaging study was the most common reason to consider doing (or referring for) presurgical workup in a patient with epilepsy. Additional details about the answers to the survey questions are provided in Table 3.

Associations between the baseline characteristics of the survey participants and the response to the selected question (Do you discuss the possibility of brain surgery with your patients with epilepsy who have drug-resistant seizures?) in regression analysis are reported in Table 4. The propensity to discuss brain surgery with patients, who have drug-resistant seizures, was higher among men (versus women) (OR 1.67, 95% CI 1.20–2.31; p=0.002). In comparison to neurologists, psychiatrists were less likely (OR 0.28, 95% CI 0.17–0.47; p<0.001) and neurosurgeons were more likely (OR 2.00, 95% CI 1.08–3.72; p=0.028) to discuss about it. Survey participants working in Africa, Asia, the

Table 2Baseline characteristics of the participants according to the answer to 'Do you discuss the possibility of brain surgery with your patients with epilepsy who have drug-resistant seizures?'.

| Characteristics | 'Yes' | 'No' | p value |
|--|--------------|--------------|---------|
| Age, years (N ^a =1354) | | | |
| Median | 44 (36-54) | 39 (32-49) | < 0.001 |
| Sex (N ^a =1406) | | | < 0.001 |
| Male | 561/654 | 93/654 | |
| Female | (85.8) | (14.2) | |
| | 562/752 | 190/752 | |
| | (74.7) | (25.3) | |
| Discipline (N ^a =1404) | | | < 0.001 |
| Neurology | 963/1182 | 219/1182 | |
| Psychiatry | (81.5) | (18.5) | |
| Neurosurgery | 38/85 (44.7) | 47/85 (55.3) | |
| | 121/137 | 16/137 | |
| | (88.3) | (11.7) | |
| Years in practice (N ^a =1360) | | | < 0.001 |
| Median | 15 (7-24) | 10 (4.5-20) | |
| World regions (N ^a =1392) | | | < 0.001 |
| Europe | 146/158 | 12/158 (7.6) | |
| Africa | (92.4) | 19/46 (41.3) | |
| Asia | 27/46 (58.7) | 16/70 (22.9) | |
| Middle East | 54/70 (77.1) | 85/374 | |
| North America | 289/374 | (22.7) | |
| South America | (77.3) | 13/103 | |
| Former Union of Soviet Socialist | 90/103 | (12.6) | |
| Republics | (87.4) | 36/335 | |
| | 299/335 | (10.7) | |
| | (89.3) | 100/306 | |
| | 206/306 | (32.7) | |
| | (67.3) | | |
| Work setting (N ^a =1403) | | | 0.372 |
| Academic | 372/453 | 81/453 | |
| Not academic | (82.1) | (17.9) | |
| Both | 331/421 | 90/421 | |
| | (78.6) | (21.4) | |
| | 419/529 | 110/529 | |
| | (79.2) | (20.8) | |
| Patients with epilepsy seen per | | | < 0.001 |
| month (N ^a =1405) | 356/523 | 167/523 | |
| <10 | (68.1) | (31.9) | |
| 10–50 | 570/660 | 90/660 | |
| >50 | (86.4) | (13.6) | |
| | 196/222 | 26/222 | |
| | (88.3) | (11.7) | |

Data are median (interquartile range) for continuous variables and n (%) for categorical variables.

N^a Refers to the total number of the participants for whom data were available.

Table 3 Answers to the survey questions.

| ⁸ If you do not discuss the possibility of brain surgery with your patients with epilepsy who have drug-resistant seizures, what are your reasons? | |
|---|-----------|
| N = 284 | |
| I am afraid of the complications (personality change, cognitive | 105 |
| problems, hemorrhage, etc.) of brain surgery | (37.0) |
| Financial reasons (the cost of surgery is high) | 77 (27.1) |
| I do not believe that epilepsy surgery is beneficial for patients (for seizure reduction) | 34 (12.0) |
| I do not want to lose my patient to another center | 19 (6.7) |
| I do not see patients with drug-resistant seizures | 18 (6.3) |
| Limited access to facilities for presurgical work-up/epilepsy surgery | 13 (4.6) |
| Other | 8 (2.8) |
| ^a When do you consider doing (or referring for) presurgical work-up | |
| in a patient with epilepsy? | |
| N = 1126 | |
| After the second anti-seizure medicine has failed | 679 |
| | (60.3) |
| When there is a clear lesion detectable in brain neuroimaging | 776 |
| | (68.9) |

Data are n (%).

^a More individual answers were allowed.

Table 4Logistic regression analysis: characteristics of the participants according to the answer to 'Do you discuss the possibility of brain surgery with your patients with epilepsy who have drug-resistant seizures?'.

| Variable | Odds ratio(95% confidence interval) | P value |
|--|-------------------------------------|---------|
| Age | 1.01 (0.98–1.05) | 0.545 |
| Male sex | 1.67 (1.20-2.31) | 0.002 |
| ^a Discipline | | |
| Psychiatry | 0.28 (0.17-0.47) | < 0.001 |
| Neurosurgery | 2.00 (1.08-3.72) | 0.028 |
| Years in practice | 1.00 (0.97-1.04) | 0.873 |
| ^b World regions | | |
| Africa | 0.14 (0.05-0.35) | < 0.001 |
| Asia | 0.23 (0.10-0.57) | 0.001 |
| Middle East | 0.30 (0.15-0.59) | 0.001 |
| North America | 0.60 (0.24-1.46) | 0.259 |
| South America | 0.75 (0.36-1.55) | 0.433 |
| Former Union of Soviet Socialist | 0.33 (0.16-0.67) | 0.002 |
| Republics | | |
| ^c Patients with epilepsy seen per month | | |
| 10–50 | 2.50 (1.77-3.54) | < 0.001 |
| >50 | 2.56 (1.53-4.29) | < 0.001 |

^a Reference is neurology. ^bReference is Europe. ^cReference is less than 10.

Middle East, and the Former Union of Soviet Socialist Republics showed a lower propensity to discuss epilepsy surgery with patients. The number of patients seen per month greater than 10 was also independently associated with a higher probability to discussing surgical therapeutic options with PWE.

4. Discussion

This study was a large international survey aimed at exploring the attitudes of healthcare personnel involved in the care of PWE from 20 countries and different world regions. As expected, we found that physicians from different world regions have different opinions and attitudes on this issue. This should be an important area for advocacy and education to improve the knowledge and attitudes of physicians and healthcare personnel involved in the epilepsy field.

In many places in the world, along with neurologists, psychiatrists and neurosurgeons also take care of PWE (sometimes as their primary care physicians, especially when there is scarcity of neurologists). We found that characteristics of participants reflecting more intense or direct involvement with PWE (i.e., working as a neurologist or neurosurgeon, a longer clinical practice, and visiting a higher number of PWE per month) were associated with a higher probability to discussing surgery as a therapeutic option for drug-resistant epilepsy. These results are consistent with a systematic review of the literature including 11 studies, showing that neurologists with formal epilepsy education, surgical exposure during training, high epilepsy practice, or experience in surgical referral are more prone to discuss epilepsy surgery and to refer patients for surgical evaluation [17].

Working in Europe, North America, and South America was also directly associated with a higher propensity to discuss epilepsy surgery with patients, probably reflecting a wider availability of resources and this therapeutic option. This is further suggested by the greater attitude of discussing epilepsy surgery (with patients) by physicians working in the developed economies than those from economies in transition or developing countires.

Our study has also highlighted some possible barriers to the effective implementation of epilepsy surgery. As our survey reveals, there are still some prejudices, misbeliefs, and fears surrounding referral for epilepsy surgery in the medical community. They include fear of complications and perceived lack of or insufficient efficacy for seizure control. Some of these beliefs may simply reflect local socio-economical or public health peculiarities and individual attitudes, and should not be generalized. When performed in experienced centers, the morbidity and mortality

associated with epilepsy surgery are low [18], and its antiseizure efficacy depends on several preoperative predictors that need to be carefully evaluated before considering a surgical approach [19,20]. With regard to these aspects, the most common reasons for thinking of or referring to epilepsy surgery were the presence of a clear lesion detectable in brain neuroimaging study or after the failure of the second ASM. Hence, participants tend to agree that a surgical approach is considered for patients with drug-resistant epilepsy and with neuroimaging-identified lesions.

Several prior studies have evaluated the attitudes of physicians toward epilepsy surgery, but on a more regional level [17]. Our study shows that worldwide healthcare professionals involved in the field of epilepsy have variable opinions and attitudes toward surgical approaches for this condition, reflecting heterogeneity in knowledge and the need for more focused educational interventions in the medical community to increase the referral to surgical options. Despite a large and continuously growing evidence supporting the benefits of epilepsy surgery in selected patients with drug-resistant epilepsy, surgery remains underutilized [21], often as a consequence of physician-specific barriers, such as inadequate knowledge about the selection of appropriate surgery candidates, negative or ambivalent attitudes toward approaches alternative to ASM, inadequate risk-benefit assessment of epilepsy surgery, poor communication practices with patients and their relatives, and complex and expensive presurgical evaluations [17,21]. However, there are also some barriers related to the socio-economic characteristics of local public health systems. As an example, in our survey, financial reasons and limited access to facilities for presurgical work-up/epilepsy surgery were listed among the causes for insufficient or lack of epilepsy surgery referrals. Furthermore, participants from low and middle-income countries had a lower propensity to discuss epilepsy surgery with their patients. One of the reasons for this is the scarcity or simply the absence of specialized centers for epilepsy surgery, especially in low- and middle-income countries. There is a treatment gap with a high proportion of people with active epilepsy who are devoid of access to the most appropriate treatment as a result of limited access to treatment due to socio-economic inequalities across the world countries [22]. A recent systematic review has estimated that, currently, 10.1 million PWE may be candidates for surgical treatment, with 1.4 million more cases per year; the highest global volume of surgically treatable epilepsy is found in Africa, the Middle East, and Latin America, regions with the lowest healthcare resources [23]. From a public health perspective, this may have extremely serious consequences and further increase inequalities in the future, unless the allocation of global healthcare resources is revised.

This study has some limitations. The numbers of the participants from different world regions were not homogenous. Furthermore, the actual representativeness of the participants for each nation is not known (the ratio of the participants to the total number of the physicians in each nation); it is possible that physicians with a positive attitude/experience of epilepsy surgery were more likely to participate in such a survey. Furthermore, the structure and language of the survey might have influenced the results. Despite these limitations, with more than 1400 participants from more than 20 countries, this is the largest international survey devoted to epilepsy surgery. It shows that on an international level, there is still a knowledge gap concerning epilepsy surgery and that much needs to be done to identify and overcome barriers to epilepsy surgery.

Funding

This study was supported by Shiraz University of Medical Sciences, Shiraz, Iran.

CRediT authorship contribution statement

Ali A. Asadi-Pooya: Visualization, Data curation, Formal analysis,

Writing – original draft. Francesco Brigo: Visualization, Data curation, Formal analysis, Writing - original draft. Eugen Trinka: Visualization, Data curation, Formal analysis, Writing - original draft. Simona Lattanzi: Visualization, Data curation, Formal analysis, Writing – original draft. Ioannis Karakis: Data curation, Writing - review & editing. Nirmeen Adel Kishk: Data curation, Writing – review & editing. Kette **D. Valente:** Data curation, Writing – review & editing. **Asel Jusupova:** Data curation, Writing – review & editing. Saule T. Turuspekova: Data curation, Writing - review & editing. Anilu Daza-Restrepo: Data curation, Writing - review & editing. Guilca Contreras: Data curation, Writing - review & editing. Mansur A. Kutlubaev: Data curation, Writing - review & editing. Alla Guekht: Data curation, Writing - review & editing. Abbas Rahimi-Jaberi: Data curation, Writing - review & editing. **Ghaieb Aljandeel:** Data curation, Writing – review & editing. Yamile Calle-Lopez: Data curation, Writing – review & editing. Taoufik Alsaadi: Data curation, Writing – review & editing. Abdulaziz Ashkanani: Data curation, Writing - review & editing. Lakshmi Narasimhan Ranganathan: Data curation, Writing – review & editing. Abdullah Al-Asmi: Data curation, Writing – review & editing. Samson G. Khachatryan: Data curation, Writing - review & editing. David Gigineishvili: Data curation, Writing – review & editing. Boulenouar Mesraoua: Data curation, Writing - review & editing. Naluca Mwendaweli: Data curation, Writing - review & editing.

Declaration of Competing Interest

Ali A. Asadi-Pooya: Honoraria from Cobel Daruo, Ronak, and RaymandRad; Royalty: Oxford University Press (Book publication); Grant from the National Institute for Medical Research Development.

Eugen Trinka has received personal fees from Arvelle/Angelini, Argenix, UCB, Eisai, Bial, Böhringer Ingelheim, Medtronic, Everpharma, Epilog, GSK, Biogen, Takeda, Liva-Nova, Newbridge, Novartis, Sanofi, Sandoz, Sunovion, GW Pharmaceuticals, Marinus; grants from Austrian Science Fund (FWF), Österreichische Nationalbank, European Union, GSK, Biogen, Eisai, Novartis, Red Bull, Bayer, and UCB; other from Neuroconsult Ges.m.b.H., outside this work.

Simona Lattanzi has received speaker's or consultancy fees from Angelini, Eisai, GW Pharmaceuticals, and UCB Pharma, and has served on advisory boards for Angelini, Arvelle Therapeutics, Bial, EISAI, and GW Pharmaceuticals.

Abdulaziz Ashkanani: Honoraria as a consultant/advisor & speaker for Novartis, Eli Lilly, NewBridge, and Hikma Co.

Mansur Kutlubaev has received speaker's fees from Eisai.

Yamile Calle-López has received fees as a speaker from UCB Pharma. Others: none.

Acknowledgement

We thank Shiraz University of Medical Sciences.

Supplementary materials

Supplementary material associated with this article can be found, in

the online version, at doi:10.1016/j.seizure.2022.10.012.

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