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Ultrasound-assisted resection of insular gliomas

Patrick Murithi Kaberia[1*], Ahmed Hafez Farhoud[1], Mahmoud Abbassy[1], Anwar Hamed Heikal[1] and Ahmed AbdelAziz Fayed[1]

Abstract

Background Insular gliomas' management challenges are attributed to their complex shape, proximity to critical vasculature, and organization. However, cytoreductive surgery's role in maximal extent of resection (EOR) improves survival. Intraoperative ultrasound (IOUS) aids in defining tumor border, detecting residual, and guiding access.

Aim The aim of this study was to assess the impact of using intraoperative ultrasound on the extent of resection of insular gliomas, and the postoperative outcomes in a prospective cohort of 20 patients operated at Alexandria main university hospital and followed up for a period of at least 3 months.

Results The Near total resection rate was 45% with 70% of patients having no neurological morbidity postoperatively. The median EOR was 81% with a range of 44 to 96%. The mean duration of IOUS setup was 19.6 ± 5.04 min, while the additional resection rate following IOUS assessment for residual tumor was 65% ($n=13$). In addition, there was a significant increase in Karnofsky Performance Status (KPS) from the preoperative through to the 90-day follow-up period ($p=0.012$). Finally, following multivariate linear regression analysis, the EOR was identified as having a statistically significant correlation with the postoperative KPS ($p=0.004$).

Conclusion Intraoperative ultrasonography is a valuable modality for strategizing the most efficient route to the tumor, promptly detecting any remaining tumor tissue, and optimizing the extent of resection for insular gliomas, while taking into consideration the phenomenon of brain shift.

Keywords Intraoperative ultrasound, Insular glioma, Extent of Resection

Introduction

The challenges in management of insular gliomas have in the past been attributed to the complex shape, proximity to critical vasculature, functional significance, and organization of the insular cortex [1]. However, over the past two decades, a greater understanding of the role of cytoreductive surgery have shown the importance of maximal extent of resection (EOR) in improving the overall and progression-free survival [1–4].

*Correspondence:
Patrick Murithi Kaberia
patrickaberia@gmail.com
[1] Neurosurgery Department, Alexandria University, Champollion Street, Alexandria 5372066, Egypt

Over the last 2 decades, intraoperative magnetic resonance imaging (IOMRI) has been used to verify that maximizing the extent of resection in glioma surgery is associated with a longer overall survival. However, IOMRI is still limited in its utilization due to the high cost, complicated surgical arrangements, and prolonged operation time [5, 6].

Recently, intraoperative ultrasound (IOUS) has increased in popularity as an imaging modality with useful clinical applications in neurosurgery [5, 7]. IOUS has been shown to aid in maximizing the extent of resection while preserving brain function [5]. It can be utilized with other complimentary technologies to enhance surgical anatomic orientation [7, 8]. The IOUS's real-time imaging, progressive image quality improvement, probe size reduction, repeatability, portability, and low cost make it a realistic, cost-effective tool that augments any neurosurgical operating room [5–11].

Methods

This was a prospective study of 20 consecutive patients with insular gliomas who had surgical excision at the Alexandria main university hospital's neurosurgery department. The study received approval from the Institutional Ethics Committee, as well as informed consent from all patients participating. The research included adult patients [18 years old] with newly diagnosed and recurrent insular gliomas but excluded individuals for whom surgery is contraindicated due to substantial comorbidities, as well as those who had a history of cranial irradiation.

Preoperatively patients' demographic data, neurological examination and Karnofsky Performance Status (KPS) [12] were assessed as well as neuroimaging studies, namely, computerized tomography (CT) and magnetic resonance imaging (MRI). Lastly, preoperative volumetric assessment was done using preoperative imaging.

In this study, all patients were operated under general anesthesia. Intraoperatively, after dural opening, ultrasonography was used to determine the shortest route to the tumor and then after completing the tumor excision it was used to detect tumor residual. The re-resection rate after ultrasound-guided assessment as well as time taken to acquire ultrasound images were documented.

Finally, in the postoperative period, neurological examination, KPS and neuroimaging studies were done in the immediate postoperative and 3-month period. Postoperative volumetric assessment was done using postoperative images, and biopsy samples taken intraoperatively were taken for histopathologic analysis.

Calculation of the extent of resection (EOR) [13]:

$$\begin{aligned}\text{EOR} = &\left[(\text{PreOperative Volume} - \text{PostOperative Volume})\right.\\ &\left./\text{PreOperative Volume}\right] \times 100\\ &> 90\% \ (\text{Near Total Resection})\\ &50 - 90\% \ (\text{Partial Resection})\\ &< 50\% \ (\text{Biopsy})\end{aligned}$$

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) (Qualitative data were described using number and percent. The Shapiro–Wilk test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). The significance of the obtained results was judged at the 5% level. The tests used were Friedman test and Post Hoc Test (Dunn's), Student t-test, and linear regression analysis.

Results

This study included 20 patients, 14 (70%) males and 6 (30%) females. The age ranged from 36.0 to 73.0 years, with a mean of 55.20 ± 11.45 years. Out of the total of 20 patients included in the study, 75% ($n = 15$) exhibited high grade tumors. Specifically, 50% ($n = 10$) of the high-grade glioma patients were diagnosed with WHO grade IV glioblastoma, while 25% ($n = 5$) had grade III anaplastic glioma. Furthermore, the remaining 25% ($n = 5$) were diagnosed with grade II diffuse low-grade gliomas. The distribution of preoperative clinical presentation is shown in Table 1 below.

In this study, near total resection (NTR) was achieved in 45% of cases ($n = 9$) while 50.0% of cases ($n = 10$) had partial resection. In addition, 5% ($n = 1$) were classified as biopsy. Additionally, the mean EOR was 78.60 ± 13.87, with a range of 44.0 to 96.0 and a median of 80.50.

The transcortical approach was the primary method employed, accounting for 90% ($n = 18$) of cases, while the transsylvian approach was utilized in only 10% ($n = 2$) of cases. The duration (mins) required to set up the IOUS was 19.6 ± 5.04 and an additional resection following assessment of the tumor bed for residual was required in 65.0% ($n = 13$).

Motor deficits constituted the primary complication during both the immediate postoperative period 30.0% ($n = 6$) and the 90-day follow-up period 10% ($n = 2$). The median EOR for those without morbidity was 90, range 70–96, while the median EOR for those with morbidity was 59, range 44–78. A comparison of the means of the 2 groups was statistically significant ($p = 0.001$) as shown in Table 2.

Table 1 Distribution of the studied population according to clinical findings and duration of symptoms

Variables	Total	
Main symptom	No	%
Headache	8	40.0
Seizures	11	55.0
Language deficits	5	25.0
Motor deficits	7	35.0
Cognitive decline	1	5.0
Incidental	2	10.0
Duration of symptoms (months)		
Min.–Max	1.0–3.0	
Mean ± SD	2.0 ± 0.79	
Median	2.0	

Table 2 Comparison of EOR according to morbidity in the study population

EOR				t	P
No morbidity		Morbidity			
Median (Min.–Max.)	Mean ± SD	Median (Min.–Max.)	Mean ± SD		
90 (70–96)	84.83 ± 8.78	59 (44–78)	60.0 ± 15.06	4.118*	0.001*

t: Student *t*-test

p: *p* value for comparison between cases with and without morbidity

* Statistically significant at $p \leq 0.05$

Table 3 presents a comparative analysis of the three examined study periods based on the Karnofsky Performance Status (KPS). The mean KPS during the preoperative phase was 64 ± 16.98, ranging from 30.0 to 90.0, with a median value of 70.0. During the postoperative phase, the mean KPS was 68.50 ± 19.54, exhibiting a range of 30.0–90.0, and a median value of 80.0. Finally, in the follow-up period, the mean was 72.50 ± 13.42, exhibiting a range of 50.0–90.0 and a median of 70.0. Statistical analysis revealed a significant difference among the three study periods ($p = 0.012$).

Finally, following univariate linear regression analysis, the WHO grade ($p = 0.040$) and the KPS ($p < 0.001$) exhibited statistical significance. The analysis also revealed that the EOR had an inverse correlation with WHO high-grade glioma (coefficient of − 16.255). In addition, multivariate analysis further showed that the EOR had the strongest statistically significant correlation with the postoperative KPS ($p = 0.004$) (Figs. 1, 2, 3).

Discussion

The impact of microsurgical resection on the progression of gliomas is actively being reevaluated in light of tumor genetics [14]. In cases of low-grade glioma, a proactive approach to resection has been linked to positive outcomes such as seizure remission, reduced likelihood of malignant transformation, and enhanced overall survival [15–17]. Likewise, in high-grade glioma, a higher extent of resection has been demonstrated to improve overall survival, and even a resection threshold as low as 80% may yield significant advantages [18, 19].

In this study, the overall median EOR was 81% (44–96%) with the highest EOR noted among low-grade gliomas with a median EOR of 90% (80–96%). This finding is consistent with previous studies reporting a median EOR ranging from 80 to 86% [1, 3, 20–22]. Li-Feng et al. established that IOMRI-assisted surgery significantly increased the median EOR from 79% (58–100%) when using neuronavigation alone to 96% (86–100%) after utilization of the IOMRI, in patients with residual tumors ($p < 0.001$) [23]. Furthermore, prior to Li-Feng et al. latter EOR findings, Skrap et al. [22] established a median EOR of 80% while using cortical-subcortical stimulation and neurophysiological monitoring, while Sanai et al. [3] found that the median EOR for high-grade insular gliomas was 81% (range 47–100%) and 82% (range 31—100%) for low-grade gliomas.

Intraoperatively, the mean time (minutes) taken to set up the IOUS was 19.6 ± 5.04. This was significantly shorter than the average time taken to set up the IOMRI, which has been documented as ranging from 30 min to 3 h [24, 25]. Furthermore, an additional resection of identified residual following IOUS assessment was done in 65% patients ($n = 13$).

Simon et al. [26] conducted a study on a substantial group of patients diagnosed with insular glioma of WHO grade II–IV. WHO grade IV, advanced age, and low preoperative KPS were indicators of poor outcome. In the univariate analysis, being diagnosed at a younger age (below 40 years), having WHO grade I, II, or III histology, Yaşargil type 5A/B glioma, and an EOR greater

Table 3 Comparison between the three studied periods according to KPS

KPS	Preoperative	Postoperative	Follow-up	Fr	P
Min.–Max	30.0–90.0	30.0–90.0	50.0–90.0	8.882*	0.012*
Mean ± SD	64.0 ± 16.98	68.50 ± 19.54	72.50 ± 13.42		
Median (IQR)	70.0 (60.0–70.0)	80.0 (60.0–80.0)	70.0 (65.0–85.0)		
Sig. bet. Periods	$p_1 = 0.042^*$, $p_2 = 0.724$, $p_3 = 0.093$				

Fr: Friedman test, Significance between study periods was done using post hoc test (Dunn's)

p: *p* value for comparing between the three studied periods

p_1: *p* value for comparing between pre and postoperative

p_2: *p* value for comparing between preoperative and follow up

p_3: *p* value for comparing between postoperative and follow up

*: Statistically significant at $p \leq 0.05$

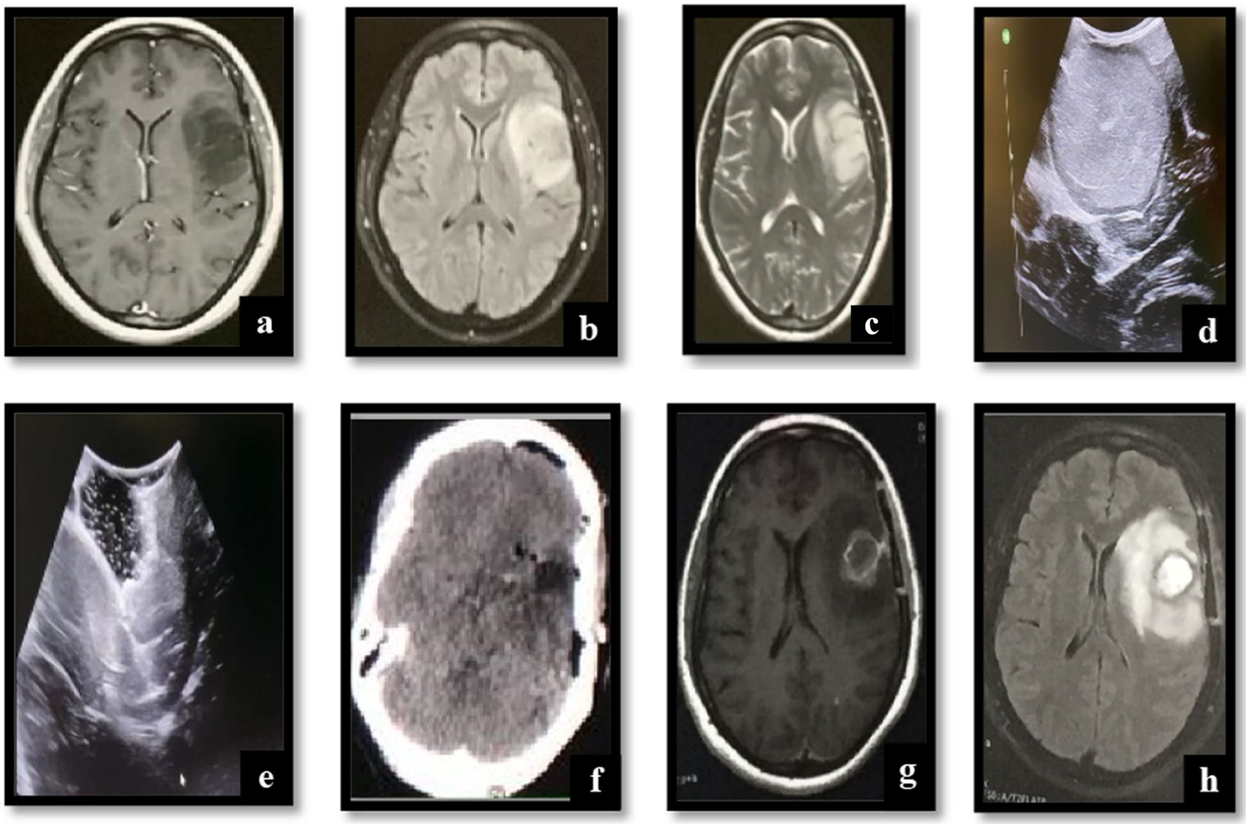

Fig. 1 A 38-year-old female patient who presented with a 1-month history of headache. **a**–**c** Preoperative Imaging showing Left sided low-grade insula glioma with frontal and temporal extension. **d and e** Intraoperative ultrasound (IOUS) images showing hyperechoic pre-resection image of the glioma and postresection saline-filled cavity. **f**–**h** Postoperative CT and 90 day follow-up MRI showing post-resection cavity and associated perilesional edema within the left insula region

than 90% were associated with a "favorable" outcome [1, 26]. These findings were also replicated in this study. We also observed that in cases without morbidity, the median EOR was 90%, while in those with morbidity had an EOR of 59%.

Univariate linear regression analysis conducted on our study sample revealed that the EOR had a statistically significant correlation with the postoperative KPS and WHO grade. Subsequent multivariate analysis further revealed that the EOR had a greater correlation with the postoperative KPS. This data further highlights the predictive value of the EOR, KPS and WHO grade in prognostication following insular glioma resection. [1, 25, 26]

This study also established a statistically significant rise in KPS from preoperative [64.0(30–90)] to postoperative [68.5(30–90)] and 90-day follow-up [72.5(50–90)]. However, our 90-day follow-up KPS was significantly lower than the KPS in studies conducted using other image-guided systems such as IOMR-assisted [90(70–100)] and neuronavigation systems [80(60–100)]. This may imply a superior advantage of the combination of image guided systems in enhancing quality of life [25].

We can therefore conclude that the utilization of IOUS can result in marginal improvement in EOR among patients with insular gliomas. Furthermore, despite being a cheaper and less time consuming real-time intraoperative tool, it did not move the needle when compared with other image guided systems such as IOMRI-assisted surgeries.

The main limitations of this study were a small sample size, no control group, and a short follow-up time. Furthermore, limited resources hindered our capacity to acquire immediate postoperative MRI's, integrate neuronavigation and ultrasound

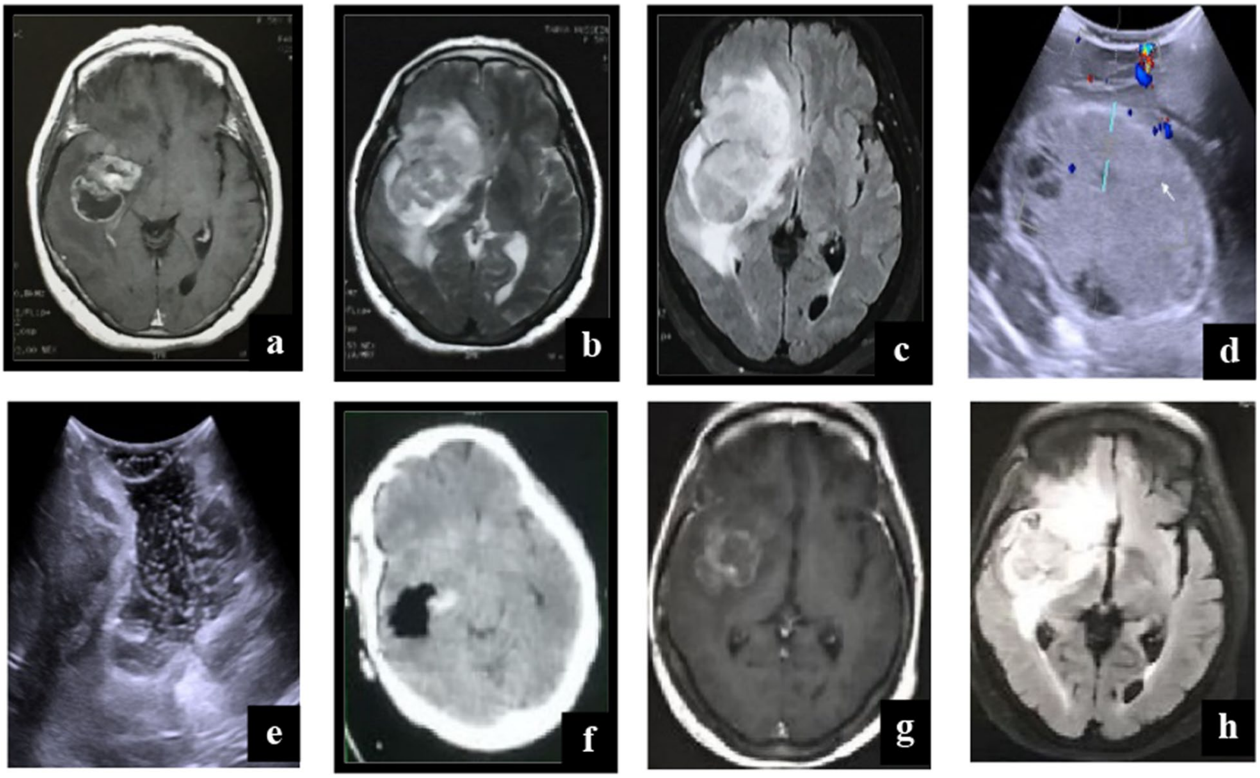

Fig. 2 A 63-year-old female presented with a 3-month history of seizures and left sided weakness. **a**–**c** Preoperative Imaging showing right sided high-grade insula glioma with parietal and temporal extension. **d and e** Intraoperative ultrasound (IOUS) showing hyperechoic pre-resection image with intralesional fluid voids and post-resection saline filled cavity. **f**–**h** Postoperative CT showing resection cavity and 90 day follow-up MRI showing tumor recurrence and extensive perilesional edema within the right insula region

technology, perform frequent awake craniotomies and cortical/subcortical mapping. Therefore, it is imperative to do more advanced research to align technology and resources, with the goal of optimizing the extent of resection and the overall outcome.

Conclusion

In resource limited settings, the utilization of IOUS can be a real-time, cost-effective, feasible, time-efficient, and easily accessible technological approach to enhance the extent of resection of insular gliomas. Furthermore, the extent of resection and the postoperative KPS are dependable indicators of outcome after surgical resection of insular gliomas.

Finally, IOUS is a valuable imaging modality for strategizing the most efficient route to the tumor, promptly detecting any remaining tumor tissue, and optimizing the extent of resection for insular gliomas, while taking into consideration the phenomenon of brain-shift.

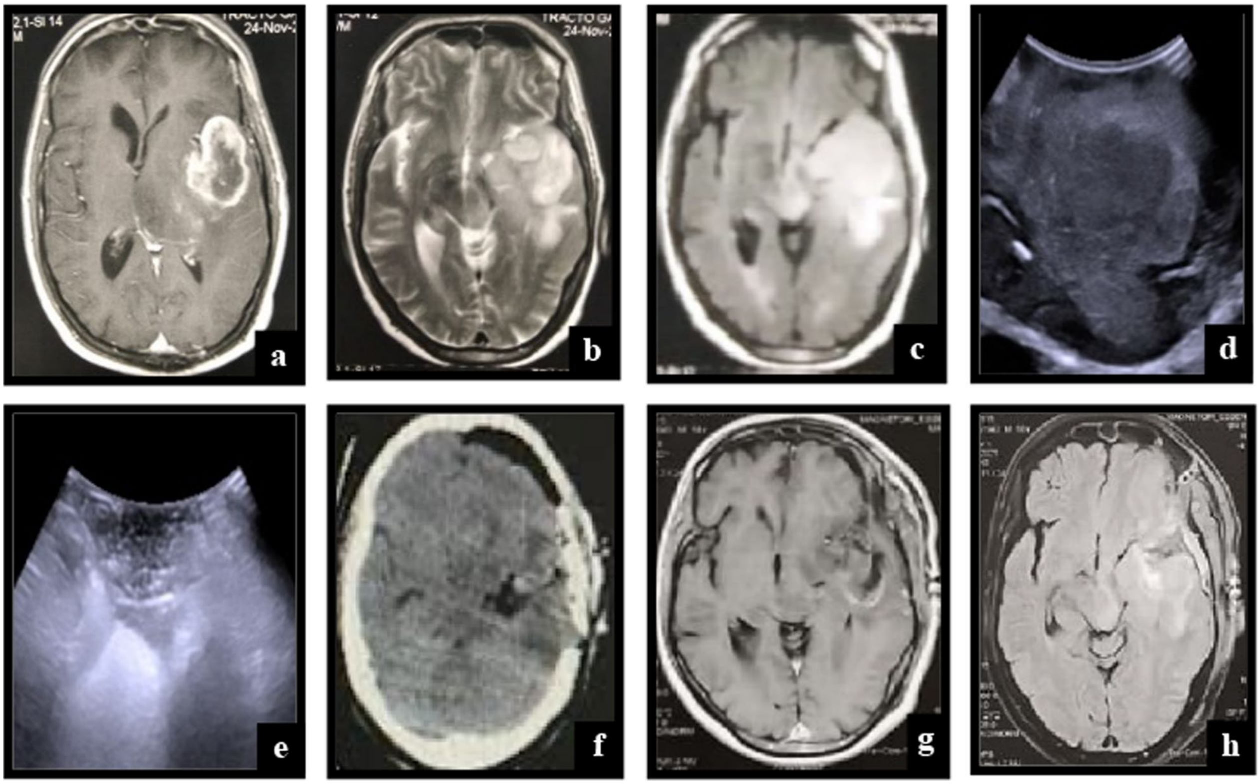

Fig. 3 A 57-year-old male presented with a 3-month history of headache and dysphasia. **a**–**c** Preoperative Imaging showing left sided high-grade insula glioma with frontal and temporal extension. **d and e** Intraoperative ultrasound (IOUS) showing hyperechoic pre-resection image of the glioma and postresection saline filled cavity. **f**–**h** Postoperative CT and follow-up MRI resection cavity with small residual and minimal perilesional edema within the left insula region

Abbreviations

EOR	Extent of resection
IOMRI	Intraoperative magnetic resonance imaging
MRI	Magnetic resonance imaging
IOUS	Intraoperative ultrasound
CT	Computerized tomography
WHO	World Health Organization
NTR	Near total resection
KPS	Karnofsky Performance Status/Scale

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Author contributions
PK analyzed and interpreted the patients' data regarding the perioperative details and clinical outcomes. All authors performed English editing. All authors performed clinical evaluation of patients, and surgical interventions, helped in reviewing and editing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The data sets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate.
The research protocol was approved by the ethical committee in the faculty of medicine at Alexandria University in its monthly session. Informed written consent was obtained from each patient. The reference number is: Member of ICLAS, http://iclas.org/members-list, https://www.hhs.gov/ohrp/assurances/index.html. IRB No: 00007555-FWA No: 00018699, Serial No: 0304260.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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