



The effects of coronavirus disease 2019 (COVID-19) pandemic on people with epilepsy (PwE): an online survey-based study

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Abstract

During the unprecedented COVID-19 pandemic in 2020, the whole world faced an unusual health emergency. Medical care of chronic neurological diseases, such as Epilepsy, is being neglected. In this survey, we aimed to evaluate the impact of the COVID-19 pandemic on the care of people with Epilepsy (PwE) and to identify their risk factors for seizure worsening to direct better future medical care. We administered a web-based survey (submitted on August 5, 2020). It included socio-demographic, Epilepsy-related, and psychometric data (The Depression, Anxiety, and Stress Scale—21 Items(DASS21) and The Pittsburgh Sleep Quality Index (PSQI). Regression analysis identified predictors of seizure worsening. We collected responses from an online survey of PwE during the pandemic. Out of 151 responders, 71 patients complained of issues related to Epilepsy management and all of whom reached the treating physician and solved their problems. Sleep quality was compromised in 84 patients (55.6%). Two-thirds of the patients in our cohort (66.2%) reported depression, 72.2% reported anxiety, and 75.5% reported stress. Eight patients (5.3%) got COVID-19 infection, and only one patient suffered from mild worsening of the seizure. The main concerns were shortage of medications for 46 (30.5%) patients, getting Coronavirus infection for 67 (44.4%) patients, and seizure worsening for 32 (21.3%) patients. Thirty-five patients (23.2%) reported seizure worsening, which was best explained by retirement or jobless state, having moderate or severe stress, poor sleep quality, vagus nerve stimulation (VNS), fear of getting COVID-19 infection, fear of worsening of seizures, or shortage of medication. During the current COVID-19 pandemic, a significant percentage of PwE experienced worsening of their seizures. This unusual, challenging experience clarifies the urgent need to establish telemedicine services and home-based management of Epilepsy, including ambulatory EEG, home video, and medication delivery to patients' homes to provide continuous medical care.

Keywords Epilepsy · COVID-19 · Pandemic · Seizure worsening · Sleep · Stress

Introduction

Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease (COVID-19) [1]. SARS-CoV-2 primarily targets the human respiratory system, resulting in various symptoms, including fever, cough, and fatigue, but it also has neuroinvasive capabilities [2]. Some patients present mainly with neurologic symptoms such as

anosmia, ageusia, dizziness, headache, or cerebrovascular events [3].

On March 11, 2020, the World Health Organization declared COVID-19 as a pandemic [4]. To sustain personal protective equipment (PPE), minimize exposure among health care staff, and allow the reemployment of medical personnel to provide care where shortages exist, elective surgeries and non-essential medical procedures have been postponed [5]. Though worrying about their safety, medical practitioners unexpectedly found themselves faced with seeking new ways of providing medical care.

The pandemic resulted in an extraordinary change for all patients. People with Epilepsy have a neurological condition that is frequently associated with other comorbidities, risk of breakthrough seizures, and daily use of medicine, rendering them especially susceptible to pandemic-induced changes in health care delivery [6].

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As a result of the COVID-19 pandemic, our hospital limited admissions to the Epilepsy monitoring unit. Besides, inpatient and outpatient EEGs performance was substantially reduced to decrease near the EEG technologist's contact with patients. The system of home delivery of the medication was adapted.

This survey aimed to understand the real impact of the COVID-19 pandemic on PwE by examining patients' seizure frequency, needs, and behaviors to identify potential risk factors for worsening seizures and thus plan better Medical Care strategies.

Methods

Setting and participants

It is a cross-sectional survey designed to assess PwE's impact during the epidemic of COVID-19 using an anonymous online questionnaire that was submitted on 1/08/2020 till 10/08/2020) including socio-demographic, Epilepsy-related, and psychometric variables (DASS 21) and PSQI. Regression analysis identified predictors of seizure worsening.

An online survey was created using Google Forms.

The survey was written in English, then translated into Arabic, then back-translated into English to check for discrepancies. It was reviewed by two independent physicians and pretested on 20 PwE for validation.

The questionnaire contained the following sections:

- Introduction with a brief description of the aim of the study.
- Informed consent (mandatory).
- Demographic and social data (age, sex, marital state, working status, and comorbid medical diseases).
- Changes in working activities during the COVID-19 period.
- Epilepsy-related variables (the type of seizure, number of medications, frequency of seizure before and after the pandemic, history of status epilepticus before or during the pandemic, and compliance with the medication).
- Pandemic impacts {sleep pattern during the pandemic, hours of exposure to screen[(Television (T.V.), Cell Phone, Computer], mean concern during the pandemic and if the patient had COVID-19 infection}.
- How did the patient access the medical service during the pandemic.
- Depression, Anxiety, and Stress Scale (DASS-21) and calculation of scores were based on the previous study [7]. Questions 3, 5, 10, 13, 16, 17 and 21 formed the depression subscale. The total depression subscale score was divided into normal (0–9), mild depression (10–12),

moderate depression (13–20), severe depression (21–27), and extremely severe depression (28–42). Questions 2, 4, 7, 9, 15, 19, and 20 formed the anxiety subscale. The total anxiety subscale score was divided into normal (0–6), mild anxiety (7–9), moderate anxiety (10–14), severe anxiety (15–19), and extremely severe anxiety (20–42). Questions 1, 6, 8, 11, 12, 14, and 18 formed the stress subscale. The total stress subscale score was divided into normal (0–10), mild Stress (11–18), moderate Stress (19–26), severe Stress (27–34), and extremely severe Stress (35–42). The Arabic version of DASS 21 was validated [8]. The DASS was previously used in research related to SARS [9].

- PSQI [10] is a 19-item, self-rated questionnaire designed to measure sleep quality and disturbance over the past month in clinical populations. The 19 items are grouped into 7 components, including (1) sleep duration, (2) sleep disturbance, (3) sleep latency, (4) daytime dysfunction due to sleepiness, (5) sleep efficiency, (6) overall sleep quality, and (7) sleep medication use.

Each of the sleep components yields a score ranging from 0 to 3, with 3 indicating the most significant dysfunction. The sleep component scores are summed to produce a total score ranging from 0 to 21, with a higher total score (referred to as global score) indicating worse sleep quality.

In distinguishing good and poor sleepers, a global PSQI score > 5 yields a sensitivity of 89.6% and a specificity of 86.5%. Validation of the Arabic version of PSQI was done before [11].

- No personally identifiable information was collected.
- The survey link was distributed electronically to patients registered in the Epilepsy Unit through the Whatsapp application. It was also posted on medical social media accounts in Kuwait (Instagram). In this survey, the primary outcome variable was the change in seizure frequency during the pandemic compared to the 3-month pre-pandemic onset. We aim to explore the risk factors associated with worsening of seizure frequency.

We set a convenience sample of at least 150 PwE. Subjects younger than 18 years old were excluded from the survey since the psychological questionnaire scales are validated for adults only. The survey was closed at 23:59, August 10, 2020.

Statistical analysis

Data were analyzed using SPSS statistical software version 21.0. We used proportions and standard deviations (S.D.s) to summarize the distribution of variables. Differences between groups were described with Chi-square for frequencies. Univariate logistic regression was used to determine

the association between the different studied variables and the worsening of seizures. Statistically significant variables were analyzed with a multivariate logistic regression model to detect independently associated factors with seizure worsening. The multivariate model contained variables that were associated with $p < 0.1$ in univariate analysis. The significance of the obtained results was set at $p < 0.05$ level.

Ethical considerations

Ethical approval was obtained from the research committee at Ibn Sina Hospital, Kuwait.

Result

Demographic and patients characteristics

Table 1 displays the demographics of the survey. A total of 151 respondents. Most of our patients were females, 64.9%, younger than 50 years, 91.4%, and singles (65.6%). Thirty-eight patients (25.2%) were working from home during the pandemic. Only 21 patients (13.9%) had other comorbidities.

Table 1 Demographics of survey respondents ($N = 151$)

Variables	Mean \pm SD/number (%)
Mean age in years	31.11 \pm 11.69
Range in years	18–62
Age group	
Younger than 50 years	138 (91.4)
50 year or old	13 (8.6)
Gender	
Male	53 (35.1)
Female	98 (64.9)
Marital state	
Single	99 (65.6)
Married	39 (25.8)
Divorce	12 (7.9)
Widow	1 (0.7)
Occupation	
Full-time job	38 (25.2)
Part-time job	9 (6.0)
Student	49 (32.5)
Retired	8 (5.3)
Not working	47 (31.1)
Working from home	38 (25.2)
Not working	113 (74.8)
Comorbidity	
No	130 (86.1)
Yes	21 (13.9)

Epilepsy

Table 2 shows the characteristics of patients' Epilepsy in this survey.

Two-thirds of the patients (66.2%) have Epilepsy for more than 5 years.

51% of the patients have focal Epilepsy (35.8% have focal Epilepsy with impaired consciousness, 15.2% have focal Epilepsy without loss of consciousness). Thirty-five patients (23.2%) reported worsening of their seizures during the pandemic. The cohort was on antiseizure medications (ASMs), either monotherapy or polytherapy, and the minority of the cohort needed additional therapy such as VNS 3.3% or surgery 5.3%.

The Impact of the COVID-19 Pandemic on PwE:

Table 3: 71 patients (47%) contacted their treating physicians during the pandemic due to issues related to Epilepsy.

Only eight patients (5.3%) got COVID-19 infection, and one only suffered from mild worsening of the seizure.

Table 2 The characteristics of Epilepsy

Disease duration	
Less than 1 year	6 (4)
One to 5 years	54 (29.8)
More than 5 years	100 (66.2)
Seizure type	
Generalized	29 (19.2)
Focal with loss of consciousness	54 (35.8)
Focal without loss of consciousness	23 (15.2)
Absence	14 (9.3)
Myoclonus	10 (6.6)
Unknown onset	21 (13.9)
Antiseizure medications	
Monotherapy	79 (52.3)
Polytherapy	72 (47.7)
Other treatment modalities	
VNS	5 (3.3)
Surgery	8 (5.3)
Time of the last seizure before the pandemic	
Less than 3 months	58 (38.4)
More than 3 months	93 (61.6)
Worsening of seizures during the pandemic	
Yes	35 (23.2)
No	116 (76.8)
Last medical review before the pandemic	
Less than 3 months	49 (32.5)
Three months or earlier	102 (67.5)

Table 3 The impact of COVID-19 pandemic on patients with Epilepsy

Contact with treating doctor	
No Contact	80 (53.0)
Contact at clinic	29 (19.2)
Contact on phone	24 (15.9)
Contact on social media	18 (11.9)
Compliant on ASMs during the pandemic	
Yes	145 (96.0)
No	6 (4.0)
Shortage of ASMs	
No	133 (88.1)
Yes	18 (11.9)
Increase in the time of your exposure to screen	
Yes	119 (78.8)
No	32 (21.2)
The main concern during the pandemic	
Shortage of ASMs	46 (30.5)
To get Coronavirus infections	67 (44.4)
Seizure worsening	32 (21.3)
To loss job	6 (4.0)
Coronavirus infection	
Yes	8 (5.3)
No	143 (94.7)
Worsening of seizure during Coronavirus infection	1/8 (12.5)

Psychological factors and sleep Quality during the pandemic (Table 4)

100 patients (66.2%) suffered from different degrees of depression according to the DASS21 scale.

Eighty-four patients (55.6%) of the patients reported low quality of their sleep, according to PSQI.

Correlation

Table 5 Relation between the worsening of seizures and different demographic and clinical factors. There was a statistically significant association between increased seizures during the pandemic and history of status epilepticus before the pandemic ($p=0.001$), occupation (retirement and not working, a full-time job, a part-time job and being a student (62.5%, 15.8%, 11.1%, and 18.4%, respectively, $p=0.031$), having VNS for Epilepsy ($p < 0.045$), having seizure within the last 3 months before the pandemic vs. earlier, 29.7% vs. 12.9%, $p < 0.001$), having medical review within the last 3 months before the pandemic vs. earlier (36.7% vs. 16.7, $p < 0.006$), shortage of ASMs (34, 25.6% vs. 1, 5.6%, $p < 0.046$), depression (145 patient, 88.2% vs. 6 patients, 11.8%, $p < 0.039$), poor sleep quality (26 patients, 31.0% vs 9 patients 13.4%, $p < 0.012$), concern regarding seizure worsening (13 patients, 40.6%, $p < 0.028$).

Table 4 Psychological factors, and sleep quality during the pandemic

DASS 21—Depression during the pandemic	
No depression	51 (33.8)
Mild depression	20 (13.2)
Moderate depression	21 (13.9)
Severe depression	42 (27.8)
Extremely severe depression	17 (11.3)
DASS 21—Anxiety during the pandemic	
No anxiety	42 (27.8)
Mild anxiety	33 (21.9)
Moderate anxiety	2 (1.3)
Severe anxiety	38 (25.2)
Extremely severe anxiety	36 (23.8)
PSQI—Sleep during the pandemic	
Impaired sleep quality	84 (55.6)
Good sleep quality	67 (44.4)
DASS-21 Stress during the pandemic	
No feeling of stress	37 (24.5)
A mild feeling of stress	25 (16.6)
A moderate feeling of stress	19 (12.6)
A severe feeling of stress	24 (15.9)
Extremely feeling of stress	46 (30.5)
PSQI—Sleep during the pandemic	
Impaired sleep quality	84 (55.6)
Good sleep quality	67 (44.4)

Logistic regression

The logistic regression model was statistically significant for the five variables surviving after stepwise selection (Table 6): retirement and jobless state AOR = 1.78 (95% C.I. 1.25–2.54), $p=0.0018$, having moderate stress AOR = 1.01 (95% C.I. 0.72–1.81), $p=0.045$ or severe stress AOR = 1.66 (95% C.I. 1.20–2.27), $p=0.009$, having VNS AOR = 2.54 (95% C.I. 0.47–13.68), $p=0.006$, PSQI AOR = 2.89 (95% C.I. 1.25–6.70), $p=0.013$. The concern during the pandemic [shortage of the medications AOR 3.87 (95% CI 1.37–9.09), Getting Covid 19 infection AOR 3.08 (95% CI 1.23–7.73) and seizure worsening AOR 1.19 (95% CI 0.41–2.41) $p=0.001$ in all].

Discussion

This survey was conducted 5 months after WHO declared COVID-19 as pandemic when there were still restrictions on mobility, work, and public services.

We aimed at investigating the impact of the pandemic on PwE care, which is crucial in planning the future form of medical care.

Table 5 Relation between the worsening of seizures and different demographic and clinical factors (N = 35)

Variables	Frequency of worsening of seizure N (%)	<i>p</i>
Occupation		
Full-time job	6 (17.1)	0.031*
Part-time job	1(2.9)	
Student	9 (25.7)	
Not working/retired	19 (54.3)	
Other treatment modalities		
VNS	3 (8.6)	0.045*
Surgery	0	
Time of the last seizure before the pandemic		
Less than 3 months	23 (29.7)	0.001*
More than 3 months	12 (12.9)	
Last medical review before the pandemic		
Less than 3 months	18 (36.7)	0.006*
Three months or earlier	17 (16.7)	
DASS 21—Depression during the pandemic		
No depression	6 (11.8)	0.039*
Mild depression	6 (30.0)	
Moderate depression	5 (23.8)	
Severe depression	13 (31.0)	
Extremely severe depression	5 (29.4)	
PSQI—Sleep during the pandemic		
Impaired sleep quality	26 (31.0)	0.012*
Good sleep quality	9 (13.4)	
The concern during the pandemic		
Shortage of ASMs	8 (17.4)	0.028*
To get Coronavirus infections	14 (20.9)	
Seizure worsening	13 (40.6)	
To loss job	0	

*Statistically significant at $p \leq 0.05$

All the respondents are from Kuwait. By the last day of the survey on 10/8/2020, the total number of COVID-19 cases in Kuwait was 72,400 [12]. During the survey, there was a partial lockdown from 5 pm till 6 am, and people from countries with a high incidence of COVID-19 cases were banned from Kuwait entry [13].

In our sample, about two-thirds of the respondents are female, and most of them are young with a mean of 31.11 ± 11.69 years, subgroups known to be heavy net users. Two-thirds of the respondents have focal Epilepsy, which matches the fact that focal seizures are the most prevalent type of seizure [14].

About one in two PwE of the whole sample complained of Epilepsy-related problems requiring neurologist's intervention.

Table 6 Multivariate logistic analysis to identify independent variables affecting seizure worsening (N = 151)

Variables	AOR (95%CI)	<i>p</i> value
Occupation		
Full-time job	0.61(0.15–2.47)	0.739
Part-time job	0.33 (0.05–2.13)	0.423
Student	0.56 (0.15–2.05)	0.372
Not working/retired	1.78 (1.25–2.54)	0.0018*
Other treatment modalities		
VNS	2.54 (0.47–13.68)	0.006*
Time of the last seizure before the pandemic		
Less than 3 months	0.22 (0.10–0.50)	0.068
More than 3 months	0	
Last medical review before the pandemic		
Less than 3 months	0.96 (0.34–2.72)	0.166
Three months or earlier	0	
Shortage of ASMs	0.17 (0.22- 1.34)	0.09
Depression during the pandemic		
No depression	3.13 (0.81–12.02)	0.10
Mild depression	0.97 (0.24–4.00)	
Moderate depression	1.33 (0.31–5.67)	
Severe depression	0.93 (0.27–3.18)	
Extremely severe depression	0	
Impaired sleep during the pandemic	2.89 (1.25–6.70)	0.013*
Stress during the pandemic		
No feeling of stress	2.80 (0.90–8.70)	0.75
A mild feeling of stress	1.75 (0.55–5.61)	
A moderate feeling of stress	1.01 (0.72–1.81)	0.045*
A severe feeling of stress	1.66 (1.20–2027)	0.009*
Extremely feeling of stress	0	
The concern during the pandemic		
Shortage of medications	3.87 (1.37–9.09)	0.001*
To get Coronavirus infections	3.08 (1.23–7.73)	
Seizure worsening	1.19 (0.41–2.41)	

AOR Adjusted odds ratio, CI confidence interval

*Statistically significant at $p \leq 0.05$

In an Italian study, 37% of the cohort needed neurologists' help, but only 71% of them managed to contact their physicians [15].

According to a WHO (World Health Organization) survey of 155 countries about the rapid assessment of service delivery for chronic diseases during the COVID-19 pandemic, the main finding is that health services have been disrupted in many countries (31–63%) [16].

Most of the patients (96%) are compliant with their ASMs, which may be related to staying at home due to pandemic restriction and medication availability. The Ministry of Health (MOH) in Kuwait established a system of home delivery of medications during the lockdown. A 93% compliance rate was reported in an Italian study [15]. A 93.5%

compliance rate was reported in the Saudi study [17]. A lower compliance rate was reported in India, which may be related to a shortage of medications [18].

The seizure rate worsening in PwE reported here (23.2%) is comparable to international and regional studies.

In April 2020, an Italian study surveyed individuals with and without Epilepsy found that 18% of those with Epilepsy had worsened seizures, particularly those who are chronically taking more ASMs and having low sleep quality [15].

In a Saudi study that included 158 patients during the pandemic, 29.5% reported increased seizure frequency. This increase was associated with noncompliance with medications, altered sleep patterns, and increased self-reported stress [17].

While in a Spanish study, which included 255 patients, 25 (9.8%) patients reported an increase in seizure frequency. This increase was associated with drug-resistant Epilepsy, insomnia, fear of Epilepsy, and income reduction [18].

In our study, worsening of seizures was observed in retired or jobless patients and those who have impaired sleep quality, VNS, moderate or severe stress, fear of worsening in the seizure control, getting COVID-19, infection, or lacking their ASMs.

Seizure control worsening associated with the retirement or jobless state of some patients could be explained by their severe baseline Epilepsy, which affects their chance of getting a job [19].

In our sample, 55.6% of the patient-reported low sleep quality, matching with the findings of similar studies; for example, 47% of the patients in the Italian study [15] and 71.2% in the Saudi study [17] experienced a significant change in their sleep. While in the Spanish study, 28.2% had insomnia [18].

Sleep quality impairment could be associated with several factors such as reduced exposure to sunlight, decreased physical activity, psychological distress during the total lockdown, the lack of regular life routines (regular work schedules, social activities, and changes in living conditions), and increased exposure to the screen [20–22].

The overall impairment of sleep quality during the COVID-19 pandemic, mainly sleep fragmentation and sleep deprivation, may affect PwE, which may increase seizure worsening even through an increase in brain excitability [23].

VNS is used as an adjunctive treatment in patients with medically refractory Epilepsy, and this would explain our results of poor seizure control even though the sample size was small [24].

Two-thirds of the patients in our study (66.2%) reported depression, 72.2% reported anxiety, and 75.5% reported stress. These results are slightly different from other studies, such as in the Italian study [15], 34.9% of the patients reported depression, and 59.5% reported anxiety. 26.7% of

patients reported confinement-related anxiety, 8.6% depression, and 12.2% in the Spanish study [18]. These differences may be explained by the different timing of the studies to the onset of the pandemic. On the other hand, our results are nearly similar to the Saudi study [17] that reported a 59.4% increase in self-reported stress.

Two studies confirmed the lockdown's negative psychosocial changes, such as sleep disturbances, depression, and anxiety, impacting a patient's well-being [20, 25].

The immediate psychological impact of COVID-19 was the focus of a recent Chinese study, which showed that more than half of the respondents in one rated their psychological impact as moderate-to-severe, and about one-third reported moderate-to-severe anxiety. Females and students had higher stress levels, anxiety, and depression [26].

Moderate and Severe Stress correlate with seizure worsening. Stress is a significant and prevalent precipitant of seizure. Allendorfe et al. demonstrated the cortical and physiological responses, i.e., cortisol level and heart rate, to acute psychosocial stress. They showed a significant relationship between left temporal lobe Epilepsy seizure control and Hypothalamic–Pituitary–Adrenal axis and the fMRI (functional magnetic resonance imaging) reactivity to acute psychosocial stress [27]. Limited prospective studies using general methods of stress reduction have shown promise in improving seizure control [28].

Our results demonstrate an evident disruption in Epilepsy self-management during the pandemic.

Recommendations

- Evaluate the patients for mood, stress, and sleep disorders
- Encourage patients for good drug compliance,
- Establishment of home-based Epilepsy management:
 - 1) Ambulatory EEG.
 - 2) Homemade video.
 - 3) Home delivery of medication.

Conclusion

The COVID-19 pandemic and social distance measures to control have a significant impact on patients with Epilepsy. Many patients experienced an increase in seizure frequency, and a high percentage reported anxiety, stress, depression symptoms, and impaired sleep quality. The retirement or jobless state, having moderate or severe stress, low sleep quality, VNS, and fear of getting COVID-19 infection, seizure worsening, and shortage of medications were risk factors for increased seizure frequency. Special attention should be paid to these factors to

prevent seizure worsening in PwE and to help set up an efficient telemedicine program devoted to Epilepsy care.

Limitations

This web-based survey introduces several biases and provides low strength of scientific evidence. Still, our target was to reach the highest number of PwE nationwide during the pandemic, and the Internet offered the best opportunities to achieve our goal. On the other hand, this did not allow PwE with moderate-severe cognitive impairment; thus, this group of PwE was not explored in our study.

It is an online survey; we cannot verify if the concerns regarding seizure worsening are a cause or consequence of increased seizure frequency, confirm the answers were entered truthfully, or ensure that all persons had Epilepsy according to The international league against Epilepsy (ILAE) criteria.

Most of our responders are females and are young adults who use the Internet the most; thus, our sample could not represent the general prevalence of Epilepsy across the entire lifespan. The reduced number of extreme age people could bias the number of reported seizures, drug resistance rate, and antiepileptic medications.

We measured psychometric scales only during the pandemic, and no pre-pandemic baseline was done. Still, we used them as variables to understand their contribution to seizure changes and not as the primary outcome variable of our study on the pandemic impact on PwE.

Author contributions FA: design and conceptualized the study and wrote the initial draft. SFA, JA: major role in methods creation, statistical analysis, and interpretation. JA, AMH: major role in the acquisition of data. MA: interpreted the data and revised the manuscript for intellectual content. All authors contributed to the article and approved the submitted version.

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Availability of data and materials The data of this study are available on request to the corresponding author.

Compliance with ethical standards

Competing interest All authors disclose no conflict of interest related to this study.

Ethical considerations Ethical approval was obtained from the research committee at Ibn Sina Hospital, Kuwait.

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