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Year: 2021

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## **The impact of the disease burden on the quality of life of cluster headache patients**

Pohl, Heiko ; Gantenbein, Andreas R ; Sandor, Peter S ; Schoenen, Jean ; Andrée, Colette

**Abstract:** Background: Cluster headache cannot be cured, and not all attacks can be aborted or prevented. Nevertheless, therapeutic guidelines focus solely on the attacks and ignore reverberations of the disorder on patients' lives. However, it is likely that not only pain reduces patients' quality of life (QoL). Objective: To investigate whether the interictal burden independently influence the QoL of subjects suffering from cluster headache. Methods: In this cross-sectional study, we asked patients with a self-reported cluster headache diagnosis to answer a modified EUROLIGHT questionnaire that included the EURO-HIS QoL scale. We built a generalised linear model and included the QoL as the dependent variable. Independent variables comprised both the ictal and the interictal burden. Results: The data of 625 participants entered the analysis. Several aspects of the interictal burden independently reduced the QoL. Among them were fear of pain, self-concealment, and private life difficulties due to the disorder. Conclusion: Both the ictal and the interictal burden of cluster headache independently reduce patients' QoL. We advocate adopting a more holistic approach to cluster headache management extending the focus towards the afflicted person and their QoL, which would generate novel therapeutic goals and strategies, complementary to treating and preventing cluster headache attacks.

DOI: <https://doi.org/10.1177/25158163211029909>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-209819>

Journal Article

Published Version



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Originally published at:

Pohl, Heiko; Gantenbein, Andreas R; Sandor, Peter S; Schoenen, Jean; Andrée, Colette (2021). The impact of the disease burden on the quality of life of cluster headache patients. *Cephalalgia Reports*, 4:251581632110299.

DOI: <https://doi.org/10.1177/25158163211029909>

# The impact of the disease burden on the quality of life of cluster headache patients

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## Abstract

**Background:** Cluster headache cannot be cured, and not all attacks can be aborted or prevented. Nevertheless, therapeutic guidelines focus solely on the attacks and ignore reverberations of the disorder on patients' lives. However, it is likely that not only pain reduces patients' quality of life (QoL).

**Objective:** To investigate whether the interictal burden independently influence the QoL of subjects suffering from cluster headache.

**Methods:** In this cross-sectional study, we asked patients with a self-reported cluster headache diagnosis to answer a modified EUROLIGHT questionnaire that included the EURO-HIS QoL scale. We built a generalised linear model and included the QoL as the dependent variable. Independent variables comprised both the ictal and the interictal burden.

**Results:** The data of 625 participants entered the analysis. Several aspects of the interictal burden independently reduced the QoL. Among them were fear of pain, self-concealment, and private life difficulties due to the disorder.

**Conclusion:** Both the ictal and the interictal burden of cluster headache independently reduce patients' QoL. We advocate adopting a more holistic approach to cluster headache management extending the focus towards the afflicted person and their QoL, which would generate novel therapeutic goals and strategies, complementary to treating and preventing cluster headache attacks.

## Keywords

Patient-centred care, ictal burden, interictal burden, study endpoint

Date received: 19 April 2021; Received revised June 5, 2021; accepted: 9 June 2021

## Introduction

Excruciating pain is the most prominent symptom of cluster headache (CH) attacks,<sup>1</sup> but it is not the only way the disorder inflicts suffering. For instance, in the interictal period, many are frightened of future attacks, unable to work, or disappointed by other's lack of understanding.<sup>2</sup> Nevertheless, therapeutic guidelines focus solely on aborting and preventing headache spells.<sup>3–6</sup>

Attacks are a sine qua non of the disorder,<sup>7</sup> and treating them is crucial. However, acute medication does not abort, and prophylaxis does not prevent every attack—CH can be managed but not cured.<sup>8,9</sup> So, it would be reasonable to

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**Table 1.** Results of the generalised linear model assessing the influence of the interictal burden on quality of life

Item	Number of participants who answered "yes"	P-value	Estimated odds ratio	95% CI
"Do you avoid telling people that you have headaches?"	329/625 (52.6%)	0.018	0.703	0.525 to 0.942
"Do you feel that your family and friends understand and accept your headaches?"	482/625 (77.7%)	<0.001	2.490	1.756 to 3.530
"On the last day when you did not have a headache, were you anxious or worried about your next headache episode?"	429/625 (68.6%)	0.002	0.600	0.434 to 0.831
"On the last day when you did not have a headache, was there anything you could not do or did not do because you wanted to avoid getting a headache?"	332/625 (53.1%)	0.014	0.679	0.499 to 0.924
"During the last three months, have your headaches caused difficulties in your love life?"	396/625 (63.4%)	<0.001	0.416	0.306 to 0.567

The answer "no" is the reference value. An odds ratio >1 suggests that the answer "yes" is associated with an increase in quality of life, whereas a ratio <1 suggests that it is associated with a decrease. CI, confidence interval.

endorse further therapeutic goals, to prioritise lightening its impact on life. For instance, we might ask how we can help patients thrive and obtain a desirable life position despite the disorder.

Adopting a more holistic approach to health requires study endpoints with a broader perspective. Quality of life (QoL) may be a concept wide enough to meet this requisition and sufficiently clearly delineated for use in scientific studies. The World Health Organization defines it as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns."<sup>10</sup>

Studies measuring CH patients' QoL found it, generally, poor.<sup>11–13</sup> However, the development of therapeutic measures intended to increase the QoL requires a more differentiated analysis of what lowers it. If we identified aspects of the interictal burden that affect the QoL *independently* from the attacks, we could attempt to tackle the disorder's impact on different fronts. However, it is currently unknown if the interictal period has such weight or if the ictal burden alone determines the QoL.

We refer to stresses and strains associated with the disease and present in the absence of a headache attack as interictal burden.<sup>2</sup>

This study investigates whether potentially modifiable aspects of the in-bout interictal burden—i.e. the interictal burden present during the in-bout period—independently influence the QoL of CH patients.

## Methods

This study is a secondary analysis of data collected for the EUROLIGHT CH project. We discussed the data collection method and the study design in a previous paper.<sup>14</sup> In brief, from May to August 2012, we asked people with a self-reported CH diagnosis to complete anonymously and online a modified version of the EUROLIGHT questionnaire, which has been published elsewhere.<sup>14</sup> Then, we

validated the diagnosis based on the reported symptoms. Only data of patients whose symptoms met the criteria for episodic or chronic CH according to the diagnostic criteria published in the International Classification of Headache Disorders, version 3 beta<sup>15</sup> were taken for further analysis.

The inclusion criteria were participation consent and CH diagnosis. We excluded participants whose diagnosis could not be validated and patients with episodic CH outside the active phase of their headache disorder ("out-bout"). Hence, only the data of patients with a chronic CH or an episodic CH in the active phase ("in bout") entered further analysis. We decided to focus on patients in the active period, because quality of life strongly increases during the out-bout period.<sup>11</sup> Besides, we excluded patients if they had not answered all items required for the analysis detailed below.

The available data determined the sample size. The National Ethics Committee (CNER) Luxembourg approved the study (CNER N° 201206/13).

## Modelling QoL

We measured QoL with the EURO-HIS QoL scale<sup>16</sup> that consists of eight items to which participants state the extent of accordance on five-point Likert scales. Summating the scores of the individual items yields the total score. The lowest possible total score of the EURO-HIS QoL is eight, and the highest is 40, with higher values indicating a better QoL.<sup>16</sup> Previously published standard values<sup>17</sup> allowed the transformation of the total scores into percentiles.

To answer the research question, we built a generalised linear model and included the total score of the EURO-HIS QoL as an ordinal-scaled dependent variable together with the independent variables listed in Table 1. Given that age and sex influence the EUOR-HIS QoL score,<sup>17</sup> we entered these variables likewise into the model. Furthermore, we included attack frequency and the CH-type (episodic vs chronic) as covariate and cofactor, respectively, into the model.

The Test of Parallel Lines investigated whether the proportional odds assumption held; Pearson's chi-square statistic assessed the goodness of fit. Pseudo R-squared Nagelkerke indicated the proportion of the variability of the dependent variable explained by the independent variables.

Odds ratios (OR), including their 95% confidence interval (CI), indicate the influence of individual variables on the QoL. In dichotomous variables, we chose the answer "no" as the reference category. So, an  $OR > 1$  implies that participants who answered "yes" to the variable in question have greater odds of having a higher QoL than patients who answered "no". Conversely, an  $OR < 1$  implies that participants who answered "yes" have smaller odds of having a higher QoL than patients who answered "no".

### Further statistical analyses

We report interval scaled variables as means and standard deviations and categorical variables as frequencies. The statistical analysis was performed at the university hospital of Zurich using IBM SPSS version 25 (IBM, USA). The significance level was 0.05.

### Data availability statement

The data collected and analysed for this study are available from the corresponding author on reasonable request.

## Results

Seven hundred seventy-four participants met the inclusion criteria, of whom 625 had responded to all variables included in the regression model and entered further analysis. Their mean age was  $42 \pm 10$  years; 68.5% (428/625) were male, and 32.6% (204/625) suffered from chronic CH.

Participants reached an average score of  $27 \pm 6$  points (range: 9 to 40 points) on the EURO-HIS QoL scale. We used standard values published by Brähler et al. to translate the total scores into percentiles;<sup>17</sup> 72.2% of the participants (451/625) had values below the median and 57% (356/625) below the lower quartile. Only 12.2% (76/625) reached a score above the upper quartile.

Table 1 summarises the parameter estimates of variables representing the interictal burden. Furthermore, age ( $P = 0.002$ ), attack frequency ( $P = 0.003$ ), and CH-type ( $P < 0.001$ ) influenced the QoL statistically significantly, while—despite a noticeable trend—sex ( $P = 0.089$ ) did not. The estimated odds ratio of the variable "age" was 1.022 (95% CI 1.008 to 1.037), indicating that higher values are associated with an increased QoL. The variable "attack frequency during the last 30 days" had an odds ratio of 0.976 (95% CI 0.960 to 0.992), suggesting that a higher attack frequency is associated with decreasing QoL. Finally, the odds ratio of 0.497 (95% CI 0.361 to 0.684)

imply that compared with episodic CH, chronic CH is associated with a significantly lower QoL.

The Test of Parallel Lines confirmed the proportional odds assumption ( $P = 0.243$ ), and Pearson's Chi-square statistic indicated a good model fit ( $P > 0.999$ ). Pseudo R-squared Nagelkerke was 0.293.

## Discussion

Generally, the QoL was poor in this sample of CH patients. Various influencing factors in both the ictal and the interictal period had an independent negative impact. Families' and friends' lack of understanding and difficulties in the love life weighed particularly heavily. Notably, not all patients experienced every aspect of the interictal burden, suggesting that none is an inevitable consequence of the disorder.

Many could not avert the disease's impact on their social network and endured difficulties in their partnerships, implying that CH does not affect them alone. Instead, it seems that the disease makes it difficult for them to be in a relationship with others and for others to be in a relationship with them. Nevertheless, the momentous negative consequences of others' lacking acceptance highlight that CH does not reduce the need for love and support.

Research in other disorders suggests that partners are a great source of strength and support. However, they also suffer together with their significant other and may feel emotionally overwhelmed by the imposed disability, too. Notably, psychological interventions may help couples cope, increase the QoL, and reduce distress.<sup>18</sup> Consequently, when treating CH patients, it is worth considering the importance of their partners as well.

CH is on patients' minds—even in the absence of pain. Concealing the disorder, trying to prevent, and worrying about the next headache spell, all indicate fear.<sup>19,20</sup> Patients likely are frightened by the prospect of future attacks and the envisioned reaction of their social circle to disclosing their disorder.

Fear of pain is associated with anxiety and depression, leads to avoidance and hypervigilance, and correlates with self-reported disability.<sup>21–23</sup> It is unknown whether therapeutic interventions can reduce this type of fear in patients with CH. However, cognitive-behavioural therapy was effective in this regard in patients with other pain disorders,<sup>24</sup> suggesting that fear may likewise not be invariable among CH sufferers.

The tendency to hide from others information perceived as distressing refers to the concept of "self-concealment" that Larson and Chastain introduced in 1990.<sup>20</sup> Self-concealment is associated with anxiety and depression<sup>20</sup> and prevents patients from seeking help.<sup>25</sup> However, Luoma et al. reported that treating individuals with substance abuse according to Acceptance and Commitment Therapy (ACT) principles significantly reduces self-concealment.<sup>26</sup>

Consequently, concealment is probably neither invariable nor necessary in patients with CH, too.

Overall, our analysis confirms that the interictal burden independently reduces the QoL, and—albeit yet to be proved—therapeutic measures can likely alleviate the interictal burden and increase the QoL. Hence, though there is no interictal burden without an ictal burden, focusing solely on the latter implies missing an opportunity to relieve distress because drugs cannot prevent or abort all attacks.<sup>8,9</sup>

Based on these findings, we advocate broadening the therapeutic goals and attempting to maximise the QoL. This approach embraces the idea of patient-centred care, which holds that considering patients' families in the personalised care plan may facilitate meeting the objective of emotional—not just physical—well-being.<sup>27</sup>

Finally, putting the patient—instead of the disorder—in the centre of therapeutic efforts seconds Sir William Osler's famous quote, "The good physician treats the disease; the great physician treats the patient who has the disease."<sup>28</sup>

### Strengths and limitations

The large sample included in the analysis is a strength of this study. We have already discussed limitations due to the study design and the algorithm used to validate the diagnosis elsewhere.<sup>14</sup> A further limitation is that the list of interictal burdens analysed in this study is not exhaustive. It is possible—and even likely given the Pseudo R-square of 0.293—that other, yet to be described types of burden, such as access to health care<sup>29</sup> and life-style related comorbidities<sup>30</sup> exert an additional influence on CH patients' QoL.

### Conclusion

Therapeutic goals need to accommodate the therapeutic possibilities. When confronted with a disorder that, like CH, cannot be cured, efforts should focus on controlling symptoms. However, symptoms of CH are not just pain but also difficulties to cope, difficulties in love life, and difficulties that arise from others' lack of understanding. We advocate shifting the focus towards the afflicted person and their QoL, because then, besides treating and preventing the attacks, additional therapeutic goals and options emerge.

### Key findings

- The QoL is poor in patients with chronic CH or episodic CH in the active period.
- Various factors in both the ictal and the interictal period influence independently and negatively the QoL.
- Given that not only the ictal burden but also the interictal burden can potentially be modified, we advocate focusing not solely on aborting and preventing headache spells.

### Authors' contributions

CA collected the data. HP analysed the data and drafted the first version of the manuscript. AG, CA, PS, and JS contributed to the development of the manuscript by revising it critically for important intellectual content. All authors read and approved the final version.

### 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.

### Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The study received financial support by the patient association Migraine Action Switzerland as well as the Swiss Headache Society. HP was funded by the Werner Dessauer Stiftung. PSS received financial support from the Research Fund of the Reha-Clinic group. The funding sources had no influence role in the study design or analysis.

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