Article

Not peer-reviewed version

Predictors of Quality of Life in Adults with Migraine After rTMS

Robert Zgarbura , Leea Cristescu Rizea , Alexandru Pavel * , Catalina Tudose

Posted Date: 13 February 2026

doi: 10.20944/preprints202602.1051.v1

Keywords: quality of life; rTMS; migraine

 doi:10.20944/preprints202602.1051.v1

Article

Predictors of Quality of Life in Adults with Migraine After rTMS

Robert Zgarbura [1], Leea Cristescu Rizea [2], Alexandru Pavel [3,*] and Catalina Tudose [4]

[1] "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
[2] "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
[3] FutureMeds, Bucharest, Romania; PAX Clinic, Bucharest, Romania
[4] "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
* Correspondence: alexnpavel@yahoo.com

Abstract

Background: Migraine is a chronic neurological disorder associated with significant functional impairment and reduced quality of life (QoL). Repetitive transcranial magnetic stimulation (rTMS) represents a non-pharmacological treatment option, yet predictors of QoL improvement following rTMS remain poorly understood. **Methods:** In this exploratory observational study, 32 adults with migraine underwent 10–40 rTMS sessions. QoL was assessed at baseline and post-intervention using the WHOQOL-BREF and Migraine-Specific Quality of Life Questionnaire (Migraine-QoL). Anxiety, depression, headache impact, and disability were evaluated using HAMA, HAMD, HIT-6, and MIDAS. Changes in QoL were calculated as post-treatment minus baseline scores. Paired t-tests assessed pre–post changes, Spearman correlations explored associations with baseline variables, and linear regression identified independent predictors. **Results:** Both overall QoL and Migraine-QoL improved significantly following rTMS ($p<0.001$). Antipsychotic use was associated with greater improvement in overall QoL ($p=0.026$). Higher baseline HIT-6 and HAMA scores correlated with greater improvements in Migraine-QoL. In regression analyses, higher baseline headache severity and younger age independently predicted Migraine-QoL improvement, explaining 53.1% of the variance. **Conclusions:** rTMS was associated with meaningful QoL improvements in migraine. Baseline headache burden and age may help identify patients most likely to benefit. Larger controlled studies are needed to confirm these findings.

Keywords: quality of life; rTMS; migraine

1. Introduction

Migraine is a chronic neurological disorder characterized by recurrent attacks of moderate to severe headache, typically pulsating, often unilateral, and commonly associated with nausea, vomiting, photophobia, and phonophobia, with attacks lasting 4–72 hours and causing significant functional impairment [1]. Migraine most often begins at puberty and generally affects those aged between 35 and 45 years. It is more common in women, possibly because of hormonal influences [2].

Several mechanisms have been proposed to explain migraine, and a wide range of risk factors have been identified. These include advanced age, head trauma, lower socioeconomic status, stress, sleep disturbances, obesity, chronic pain syndromes, caffeine or medication overuse, and pro-inflammatory or pro-thrombotic states. Chronic migraine, a distinct subtype, is additionally associated with ineffective acute migraine treatment and sustained medication overuse. Demographic characteristics such as sex and race, along with lifestyle factors including excessive caffeine consumption, weight gain, and sleep disorders, further contribute to migraine risk. Moreover, migraine may be linked to several related syndromes—such as somnambulism, cyclic vomiting, abdominal migraine, benign paroxysmal vertigo, benign paroxysmal torticollis, and

 doi:10.20944/preprints202602.1051.v1

confusional migraine—each characterized by distinct clinical features, durations, and prevalence patterns [3].

Migraine headache has a strong influence on disability, functional impairments, and psychological effects. The majority of the physicians fail to address the degree and extent of impediment caused by a migraine, which contributes to low quality of life and disability [4]. The recurrent attacks cause functional impairments, which can involve both physical and psychological effects, which might happen during or after a migraine attack [5–8]. Comparing migraine sufferers and non-migraine sufferers, migraine sufferers have worse subjective well-being and lower quality of life [4]. The clinical burden of migraine is increasingly recognized as a continuous state rather than a series of isolated events. Patients frequently experience an "interictal burden," characterized by anticipatory anxiety, cognitive "fog" and perceived stigma, which persists even between attacks [9]. The burden of migraine and the challenge in managing it are increased by the comorbid psychiatric conditions that occur in association with it.

Migraine is strongly associated with many psychiatric disorders, involving depression, anxiety, and bipolar disorders [10]. This cumulative toll results in a profound erosion of Health-Related Quality of Life (HRQoL), affecting professional productivity, social participation, and psychological well-being [11]. For decades, migraine management relied on repurposed medications such as beta-blockers, tricyclic antidepressants, and anticonvulsants. While effective for some, these "traditional" preventives are often limited by poor adherence due to systemic side effects like fatigue, weight gain, and cognitive impairment [12]. The therapeutic landscape underwent a paradigm shift with the elevation of Calcitonin Gene-Related Peptide (CGRP) targeted therapies—including monoclonal antibodies (e.g., erenumab, fremanezumab) and small-molecule "gepants" (e.g., atogepant, rimegepant)—to first-line status. Unlike older drugs, these agents were designed specifically for migraine pathophysiology and offer a rapid onset [12], dual action (acute relief and prevention) and an improved safety (minimal vasoconstrictive risk, making them safer for patients with cardiovascular contraindications compared to traditional triptans) [13]. Despite these advances, approximately 30–40% of patients remain refractory to CGRP-targeted therapies or prefer non-pharmacological interventions to avoid systemic medication [12]. This has led to the integration of non-invasive neuromodulation, most notably Repetitive Transcranial Magnetic Stimulation (rTMS). By delivering magnetic pulses to modulate cortical excitability—targeting areas such as the primary motor cortex (M1) for pain processing or the dorsolateral prefrontal cortex (DLPFC) for mood and frequency regulation—rTMS offers a localized treatment with a unique safety profile. Recent clinical evidence suggests that high-frequency rTMS protocols (10–20 Hz) not only reduce headache frequency but also provide superior improvements in patient-reported QoL metrics, by addressing the emotional and functional dimensions of the disease [2,14].

Our aim is to analyze which baseline predictors influence QoL in participants with migraine undergoing rTMS sessions as an exploratory analysis.

2. Materials and Methods

Between August 2023 and December 2025 we included participants diagnosed with migraine who presented at a local neurology clinic for rTMS sessions and collected socio-demographic and clinical data. The study obtained approval from the local ethics committee. All participants signed informed consent before inclusion. The study was conducted in accordance with the Declaration of Helsinki [15].

Participants underwent 10 to 40 sessions of rTMS performed by a trained clinician. The recomended protocol was intermitent Theta Burst Stimulation with 5-10Hz (pps), 20 pulses per train, 20 trains, 2s of stimulation, 8s pause between each train. The specific magnetic stimulation machine was a MagVenture MagPro R20, figure of 8 coil for the per se stimulation and either round or parabolic coil was used to determine the motor threshold/motor evoqued potential. Stimulation intensity for each patient was at 120% of the motor evoqued potential.

 doi:10.20944/preprints202602.1051.v1

Clinical data collected included: current use of psychiatric (antidepressant and antipsychotic) or migraine medication, current psychotherapy and number of previous rTMS trials. The scales applied included: Hamilton Anxiety Scale (HAMA) [16] , Hamilton Depression scale (HAMD) [17], WHOQOL-Bref (QoL) [18], Migraine Quality of Life (Migraine-QoL) [19], Headache Impact Test (HIT-6) [20], Migraine Disability Assessment Test (MIDAS) [21]. All scales were applied at baseline and at the end of rTMS sessions by a licensed psychiatrist. The same rater scored both baseline and end of trial scales and was different than the clinician conducting the rTMS sessions.

HAMA is a clinician administered scale with 14 items measuring anxiety symptoms. Each item is scored on a scale of 0 (not present) to 4 (severe) with a total score range of 0-56. Higher scores represent worse anxiety levels.

HAMD is a clinician administered scale with 17 items measuring depressive symptoms with higher scores representing more severe depression.

WHODAS-QOL-Bref is a validated scale with 26 items used to measure quality of life acros 4 domains: physical health, psychological health, social relationships and environment. Higher score show higher quality of life.

Migraine QoL is a 13-item scale used to evaluate quality of life specifically in participants diagnosed with migraine. It consists of 3 subscales: Role Restrictive, Role Preventive and Emotional Functioning. Higher scores indicate better quality of life.

HIT-6 is a patient reported questionnaire which measures the intensity of headache and its impact on daily functioning. It consists of 6 questions covering pain severity, social functioning, role functioning (work/home), cognitive functioning (concentration), vitality (energy levels) and psychological stress. Higher scores represent higher headache severity.

MIDAS is a short, self-administered questionnaire used to evaluate the disability of due to headache during the previous 3 months. Questions cover days missed from school/work and reduced activity during free time. Higher scores show more disability.

Statistical Analysis

Descriptive statistics were used to characterize the sample. Categorical variables were presented as N (%), while continuous variables as mean (SD).

We computed the ΔQoL and ΔMigraine-QoL as the differences in total scores between end-of-intervention timepoint and baseline. Higher delta scores translated as more improvement in QoL between the two timepoints. For the QoL variables we also applied a paired sample t-test to evaluate if the changes between timepoints were statistically significant. These scores were used in Spearman correlations (non-normal distribution) to identify which scales from baseline correlate with changes in QoL. The mean delta score for each QoL scale was individually compared between all the categorical variables to establish predictors. All significant variables were included in a linear regression analysis to identify possible confounders. All analyses were conducted with SPSS Statistics v26 and significance threshold was $p<0.05$.

3. Results

The total sample included was N=32 participants, 71.9% were female, the mean age was 41.88±15.94, 87.5% were from urban area. At baseline, participants had mild anxiety and depression. The full description of the sample is presented in Table 1.

Table 1. Social and demographic characteristics.

	rTMS participants (N=32)
Gender	
Male	9 (28.1%)
Female	23 (71.9%)
Age	41.88 (15.94)

 doi:10.20944/preprints202602.1051.v1

Urban area	28 (87.5%)
Rural area	4 (13.5%)
Education	
Highschool	15 (46.9%)
University	17 (53.1%)
Occupational status	
Unemployed	9 (28.1%)
Employed	23 (71.9%)
In a relationship	18 (56.3%)
Single	14 (43.7%)
Number of previous rTMS trials	1.84 (1.85)
Currently on antidepressant medication	25 (78.1%)
Currently on antipsychotic medication	7 (21.9%)
Currently in psychotherapy	8 (25%)
Currently on migraine medication	11 (34.4%)
Migraine QOL baseline	51.56 (15.74)*
Migraine QOL after	72.75 (9.14)*
QOL baseline	53.56 (11.46)*
QOL after	66.84 (8.09)*
HAMA baseline	17.69 (3.16)
HAMD baseline	15.41 (4.25)
MIDAS baseline	16.22 (4.31)
HIT6 Baseline	49.44 (12.58)

*paired sample t-test p<.001.

After computing the ΔQoL scores for both QoL scales and comparing socio-demographic and clinical characteristics we found that the presence of antipsychotic was significantly associated with improvement in overall QoL (ΔQoL 18.57±5.86 vs 11.80±7.37, p=.026), while baseline HIT-6 and HAMA were significantly correlated with improved Migraine-QoL (p=.001 for HIT-6 and p=.013 for HAMA). The full comparisons are presented in Tables 2 and 3.

Table 2. Comparison between ΔQol/ΔMigraine-QoL and categorical socio-demographic and clinical variables.

	ΔQoL	**p**	**ΔMigraine-QoL**	**p**
Gender				
Male	13.33 (9.29)	.983	22.89 (12.25)	.630
Female	13.26 (6.97)		20.52 (12.15)	
Location				
Urban area	13.25 (7.88)	.937	12.45 (2.35)	.426
Rural area	13.5 (5.26)		8.87 (4.44)	
Education				
Highschool	11.93 (6.26)	.341	21.6 (12.86)	.860
University	14.47 (8.51)		11.64 (2.82)	
Occupational status				
Unemployed	14.78 (4.52)	.377	22.67 (13.57)	.695
Employed	12.7 (8.44)		20.61 (11.65)	
Relationship status				
In a relationship	12.67 (7.65)	.749	12.67 (2.99)	.875
Single	12.79 (7.64)		11.61 (3.10)	
Antidepressant medication				
Yes	14.04 (7.85)	.230	10.25 (3.88)	.531
No	10.57 (5.97)		12.60 (2.52)	

 doi:10.20944/preprints202602.1051.v1

Antipsychotic medication				
Yes	18.57 (5.86)	**.026**	28 (11.31)	.104
No	11.8 (7.37)		19.28 (11.73)	
Psychotherapy				
Yes	15 (6.59)	.431	26.5 (9.43)	.111
No	12.71 (7.87)		19.42 (12.45)	
Migraine medication				
Yes	10.64 (6.61)	.137	19.05 (12.93)	.129
No	14.67 (7.76)		25.27 (9.31)	

Table 3. Correlations between baseline evaluations and ΔQoL/ΔMigraine-QoL.

	Age	**HIT6**	**MIDAS**	**HAMA**	**HAMD**
ΔQoL	-.036, p=.845	-.069, p=.708	-.186, p=.309	.090, p=.625	.068, p=.710
ΔMigraine QoL	-.329, p=.066	.568, **p=.001**	.241, p=.185	.434, **p=.013**	.242, p=.183

In the end we conducted a regression analysis including all significant parameters from previous analyses. The overall model was significant and explained 53.1% of the variance (R^2=.531, p<.001). Baseline severity of headaches (HIT-6) and lower age were associated with larger improvements in Migraine-QoL. The complete model is presented in Table 4.

Table 4. Regression analysis of possible confounders for ΔMigraine-QoL .

	B	**Std. Error**	**95% CI**	**p**
Age	-.204	.100	-.409, 0	**.05**
HIT6	.512	.134	.237, .787	**.001**
HAMA	.852	.534	-.241, 1.945	.122

4. Discussion

In this study, we examined predictors of quality of life (QoL) in patients with migraine undergoing repetitive transcranial magnetic stimulation (rTMS). The use of rTMS in migraine has gained increasing attention as a non-pharmacological neuromodulatory intervention, particularly for patients who are refractory to or intolerant of the available medication. Cortical hyperexcitability and maladaptive plasticity are thought to contribute not only to headache generation but also to sensory hypersensitivity, cognitive complaints, and affective symptoms. Consequently, rTMS may exert benefits that extend beyond pain reduction, potentially influencing QoL through improvements in emotional regulation, cognitive functioning, and perceived disability.

Previous clinical trials and meta-analyses have demonstrated that high-frequency rTMS can reduce headache days and migraine intensity [22]. However, comparatively fewer studies have examined predictors of quality-of-life outcomes, particularly from an exploratory perspective.

Our findings are consistent with prior studies demonstrating that migraine-related disability and QoL impairment are only partially explained by headache frequency alone [22], supporting the exploratory aim of the present study: to identify additional factors that may predict quality-of-life improvement following rTMS in patients with migraine.

Our results suggest participants with migraine receiving antipsychotics had higher improvement in overall QoL following rTMS. It is still not clear how antipsychotics could positively impact migraine, but evidence has shown that some antipsychotics, such as olanzapine, may be effective in pain disorders overall [23].

The regression analysis which evaluated the possible effect of confounders on ΔMigraine-QoL showed that baseline age and HIT6 scores were independently associated with increased improvements. Respectively, lower baseline age and higher headache severity predicted higher improvements in Migraine-QoL after rTMS sessions. Across controlled studies, rTMS has been associated with reductions in headache-related impact as captured by HIT-6, a validated measure

 doi:10.20944/preprints202602.1051.v1

that correlates with QoL and functional impairment in migraine. However, effect sizes vary by protocol, target, and population [24,25]. Baseline affective symptom severity did not significantly impact Migraine-QoL after rTMS sessions.

Future studies should aim to validate these findings in larger, controlled cohorts and to integrate standardized QoL instruments alongside neurophysiological and neuroimaging markers. Stratification based on baseline psychosocial burden, migraine chronification, and psychiatric comorbidity may help to identify patient subgroups most likely to experience meaningful quality-of-life improvements following rTMS.

Limitations

While our study brings the benefits of exploratory analysis there are some limitations. The relatively small sample size may have limited statistical power and warrants replication in larger samples. Also, while widely validated, both HAMA and HAMD are clinician rated scales and the study would benefit from adding patient reported outcomes for affective symptoms as well. Third, although antipsychotics showed a positive impact on overall QoL, it would be useful to further explore this mechanism in order to offer a better understanding of the effect.

5. Conclusions

This section is not mandatory but can be added to the manuscript if the discussion is unusually long or complex.

Author Contributions: Conceptualization, R.Z., C.T. and A.P.; methodology, R.Z and A.P.; validation, R.Z., L.C.R. and C.T.; formal analysis, A.P.; investigation, R.Z..; data curation, A.P. and R.Z.; writing—original draft preparation, R.Z., L.C.R. and A.P.; writing—review and editing, R.Z., L.C.R., A.P. and C.T..; visualization, R.Z.; supervision, C.T. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of Inter Health Systems SRL (based on request nr 1/01.09.2023, resolution on 20.10.2023).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patients to publish this paper.:

Acknowledgments: The authors would like to thank the personnel from Emerald Medical Center for their support.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

rTMS	Repetitive transcranial magnetic stimulation
QoL	Quality of life
HAMA	Hamilton Anxiety Scale
HAMD	Hamilton Depression Scale
HIT-6	Headache Impact Test
MIDAS	Migraine Disability Assessment Test

References

1. Migraine | National Institute of Neurological Disorders and Stroke n.d. https://www.ninds.nih.gov/health-information/disorders/migraine (accessed February 9, 2026).

 doi:10.20944/preprints202602.1051.v1

2. Eldaief MC, Press DZ, Pascual-Leone A. Transcranial magnetic stimulation in neurology: A review of established and prospective applications. Neurol Clin Pract 2013;3:519–26. https://doi.org/10.1212/01.CPJ.0000436213.11132.8e.
3. Straube A, Andreou A. Primary headaches during lifespan. J Headache Pain 2019;20. https://doi.org/10.1186/s10194-019-0985-0.
4. Ghadeer HA Al, AlSalman SA, Albaqshi FM, Alsuliman SR, Alsowailem FA, Albusror HA, et al. Quality of Life and Disability Among Migraine Patients: A Single-Center Study in AlAhsa, Saudi Arabia. Cureus 2021;13:e19210. https://doi.org/10.7759/cureus.19210.
5. Diamond M. The impact of migraine on the health and well-being of women. J Womens Health (Larchmt) 2007;16:1269–80. https://doi.org/10.1089/jwh.2007.0388.
6. Haw NJ, Cabaluna IT, Kaw GE, Cortez JF, Chua MP, Guce K. A cross-sectional study on the burden and impact of migraine on work productivity and quality of life in selected workplaces in the Philippines. J Headache Pain 2020;21. https://doi.org/10.1186/s10194-020-01191-6.
7. Munir F, Leka S, Griffiths A. Dealing with self-management of chronic illness at work: Predictors for self-disclosure. Soc Sci Med 2005;60:1397–407. https://doi.org/10.1016/j.socscimed.2004.07.012.
8. Brandes JL. Migraine and functional impairment. CNS Drugs 2009;23:1039–45. https://doi.org/10.2165/11530030-000000000-00000.
9. Bernstein C, Burstein R. Sensitization of the Trigeminovascular Pathway: Perspective and Implications to Migraine Pathophysiology. J Clin Neurol 2012;8:89. https://doi.org/10.3988/jcn.2012.8.2.89.
10. Hamelsky SW, Lipton RB. Psychiatric comorbidity of migraine. Headache 2006;46:1327–33. https://doi.org/10.1111/j.1526-4610.2006.00576.x.
11. Shapiro RE, Nicholson RA, Seng EK, Buse DC, Reed ML, Zagar AJ, et al. Migraine-Related Stigma and Its Relationship to Disability, Interictal Burden, and Quality of Life: Results of the OVERCOME (US) Study. Neurology 2024;102. https://doi.org/10.1212/WNL.0000000000208074.
12. Hilliard T. Migraine in 2025: an update on management. Med Today 2025:8.
13. Dejulio PA, Perese JK, Schuster NM, Oswald JC. Lasmiditan for the acute treatment of migraine. Pain Manag 2021;11:437–49. https://doi.org/10.2217/pmt-2021-0002.
14. Jiang Y, Yuan C, Sun P, Li C, Wang L. Efficacy and safety of high-frequency repetitive transcranial magnetic stimulation (rTMS) for migraine: a meta-analysis of randomized controlled trials. Acta Neurol Belg 2024;124:1167–76. https://doi.org/10.1007/s13760-024-02570-5.
15. World Medical Association. Declaration of Helsinki, Ethical Principles for Scientific Requirements and Research Protocols. World Medical Association 2013:29–32.
16. HAMILTON M. THE ASSESSMENT OF ANXIETY STATES BY RATING. British Journal of Medical Psychology 1959;32:50–5. https://doi.org/10.1111/j.2044-8341.1959.tb00467.x.
17. Health M, States U, Clinical E, Evaluation D. Chapter 14 The Hamilton Rating Scale for Depression 1986.
18. Harper A, Power M, Orley J, Herrman H, Schofield H, Murphy B, et al. Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. Psychol Med 1998;28:551–8. https://doi.org/10.1017/S0033291798006667.
19. Caproni S, Bianchi E, Cupini LM, Corbelli I, Beghi E, Calabresi P, et al. Migraine-specific quality of life questionnaire and relapse of medication overuse headache. BMC Neurol 2015;15. https://doi.org/10.1186/s12883-015-0339-8.
20. Yang M, Rendas-Baum R, Varon SF, Kosinski M. Validation of the Headache Impact Test (HIT-6™) across episodic and chronic migraine. Cephalalgia 2011;31:357. https://doi.org/10.1177/0333102410379890.
21. Stewart WF, Lipton RB, Kolodner KB, Sawyer J, Lee C, Liberman JN. Validity of the Migraine Disability Assessment (MIDAS) score in comparison to a diary-based measure in a population sample of migraine sufferers. Pain 2000;88:41–52. https://doi.org/10.1016/S0304-3959(00)00305-5.
22. Matharu MS, Silberstein S, Yuan H, Edgar D, Colman R, Schwedt TJ, et al. Migraine-related disability according to headache frequency subclassifications: A systematic review and meta-analysis. Cephalalgia 2025;45. https://doi.org/10.1177/03331024251385965.

 doi:10.20944/preprints202602.1051.v1

23. Jimenez XF, Sundararajan T, Covington EC. A Systematic Review of Atypical Antipsychotics in Chronic Pain Management: Olanzapine Demonstrates Potential in Central Sensitization, Fibromyalgia, and Headache/Migraine. Clin J Pain 2018;34:585–91. https://doi.org/10.1097/AJP.0000000000000567.
24. Leahu P, Bange M, Ciolac D, Scheiter S, Matei A, Gonzalez-Escamilla G, et al. Increased migraine-free intervals with multifocal repetitive transcranial magnetic stimulation. Brain Stimul 2021;14:1544–52. https://doi.org/10.1016/j.brs.2021.10.383.
25. Rendas-Baum R, Yang M, Varon SF, Bloudek LM, DeGryse RE, Kosinski M. Validation of the Headache Impact Test (HIT-6) in patients with chronic migraine. Health Qual Life Outcomes 2014;12. https://doi.org/10.1186/s12955-014-0117-0.