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ORIGINAL PAPER

# ASSOCIATION BETWEEN BRAIN FOG, CARDIAC INJURY, AND QUALITY OF LIFE AT WORK AFTER HOSPITALIZATION DUE TO COVID-19

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**Abstract**

**Background:** To evaluate incidence and search for possible predictors of brain fog and quality of life at work (QoL-W) among low-to-moderate risk subjects previously hospitalized due to COVID-19. **Material and Methods:** Participants aged ≥18 retrospectively reported 8 brain fog symptoms pre-COVID-19, at 0–4, 4–12 and >12 weeks post-infection via validated clinical questionnaire. The QoL-W was assessed with a 4-point Likert scale where 0, 1, 2, and 3 meant no, mild, moderate, and severe impairment in performing activities at work, respectively. Data on age, sex, comorbidities, and laboratory results (including first in-hospital high-sensitivity cardiac troponin I [hs-cTnI] measurement) were gathered. **Results:** The study included 181 hospitalized subjects (age Me = 57 years), 37.02% women. Most had low disease severity (*Modified Early Warning Score* = 1, 77.90%) and low comorbidity (Charlson Comorbidity Index 0: 28.72%, 1–2: 34.09%), with no intensive care unit treatment needed. COVID-19 led to almost 3-fold increased brain fog symptoms, with incidence of 58.56%, 53.59%, and 49.17% within 4, 4–12, and >12 weeks, respectively ($p < 0.001$). First in-hospital hs-cTnI levels were 47.3% higher in participants who later presented with brain fog at median follow-up of 26.7 weeks since the diagnosis of the SARS-CoV-2 infection. Individuals who experienced at least one brain fog symptom at follow-up, had elevated hs-cTnI, less often presented with atrial fibrillation, and used anticoagulants during initial hospitalization due to COVID-19. The hs-cTnI >11.90 ng/l predicted brain fog symptoms in multivariable model. COVID-19 was associated with 3.6-fold, 3.0-fold, and 2.4-fold QoL-W deterioration within 4, 4–12, and >12 weeks post-infection ($p < 0.05$). Subjects with QoL-W decline >12 weeks were younger, mostly women, had more brain fog symptoms, and higher platelet counts. Multivariable models with self-reported brain fog symptoms (responding coherently and recalling recent information), age, and sex exhibited good discriminatory power for QoL-W impairment (area under the receiver operating characteristic curve 0.846, 95% CI: 0.780–0.912). **Conclusions:** This study highlighted that in non-high-risk subjects hospitalized during the first 2 pandemic's waves: 1) brain fog was common, affecting nearly half of individuals, and impacting QoL-W >12 weeks after initial infection, 2) after 3 months of COVID-19 onset, the decline in QoL-W was primarily attributed to brain fog symptoms rather than demographic factors, health conditions, admission status, and laboratory findings, 3) components of brain fog, such as answering in an understandable way or recalling new information increased the likelihood of significantly lower QoL-W up to tenfold, 4) biochemical indicators, such as the first hs-cTnI level, might predict the risk of experiencing brain fog symptoms and indirectly decreased QoL-W >12 weeks after COVID-19 onset. Occupational medicine practitioners should pay particular attention to younger and female subjects after COVID-19 complaining of problems with answering questions in understandable way or recalling new information as they have an increased risk of QoL-W impairment. Med Pr Work Health Saf. 2024;75(1):3–17

**Key words:** quality of life, predictor, troponin, COVID-19, brain fog, long COVID

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## INTRODUCTION

The spread of coronavirus disease 2019 (COVID-19) resulted in a significant burden of long-term complications worldwide, including the phenomenon called "brain fog" [1,2]. Residual symptoms after an initial severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, mostly affecting cognition and quality of life, also decreased an ability to perform activities at work [3]. To date, most studies on COVID-19 focused on detailed description of symptoms, including neuropsychiatric sequelae, but only a minority aimed to assess their influence on quality of life at work (QoL-W) [4].

What is more, controversies still exist regarding potential predictors of developing brain fog symptoms after the acute phase of the SARS-CoV-2 infection. Previous studies pointed to female sex [5] and comorbidities, such as depression [6] as possible factors associated with persistence of neurocognitive disturbances, including symptoms of the brain fog. On the contrary, in a recent study of 222 patients previously hospitalized in Aruba who participated in a survey at least 1 year after the onset of infection, neither demographics such as age or sex, nor obesity or concomitant respiratory diseases were predictors of post-COVID cognitive impairment [7]. Unclear remains also the prognostic role of laboratory parameters, such as increased troponin level, that has been shown to increase the risk of death [8] or hospitalization due to cardiovascular disease within 12 months after the SARS-CoV-2 infection [9]. However, the role of troponin as a possible predictor or marker of developing post-COVID syndrome, presenting with fatigue or brain fog, has not been accurately studied so far and therefore deserves more attention [10].

There are also discrepancies related to the quality of life of patients after COVID-19 and its possible predictors. One prospective study using online anonymous survey showed that quality of life among patients with long COVID deteriorated in comparison to physical education and physiotherapy students, and was related to role limitation, social functioning, and mental health [11]. Similar conclusions came from a recent observation of 112 patients after mild to moderate SARS-CoV-2 infection who exhibited decreased quality of life in mental health domain compared to general Swiss population; interestingly, women scored significantly lower in the areas of physical functioning, role limitation, and bodily pain [12]. In a Japanese study of 349 patients after COVID-19, it was revealed instead that no specific factors were associated with decreased quality of life after the acute phase of infection, except for ongoing prolonged symptoms, whereas male sex and systemic use of steroids acted as possible protective variables [13]. Recently, Korean researchers showed that besides improvement over time, 1/4 and 1/3 of patients experienced concentration difficulties and decreased neuropsychiatric quality of life, respectively, 24 months after the SARS-CoV-2 infection [14].

Therefore, the aim of this study was to evaluate incidence and search for possible predictors of brain fog and work-related QoL-W among subjects previously hospitalized due to COVID-19.

## MATERIAL AND METHODS

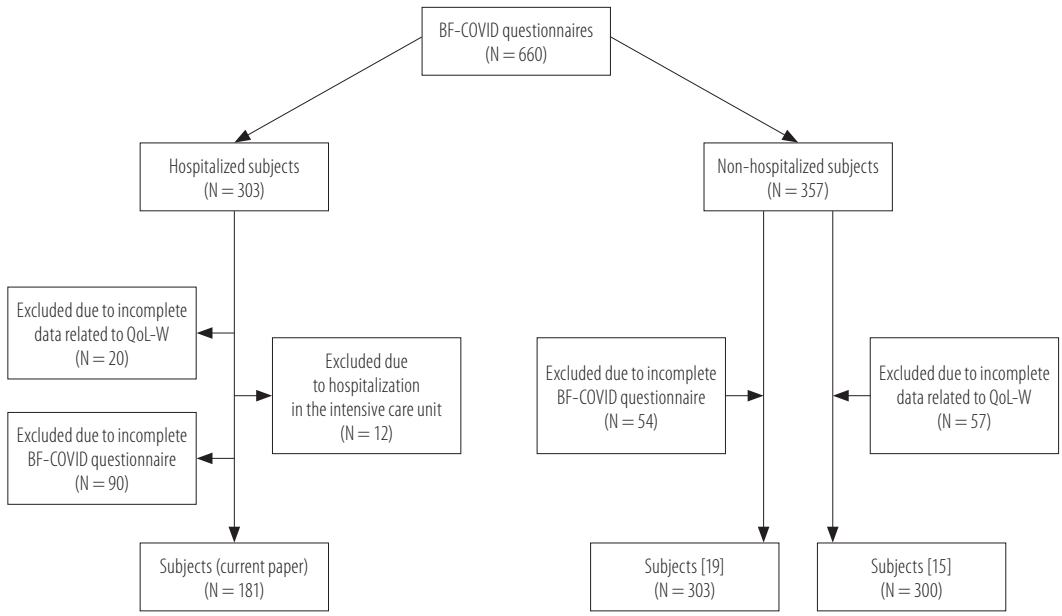
### Participants and assessment of brain fog

Methodology of the current study was presented in details in authors' previously published paper [15]. In brief, included were individuals who fulfilled the following criteria: ≥18 years of age, >3 months since the onset of COVID-19 that was confirmed by detecting viral RNA with the use of reverse transcription polymerase chain reaction from a nasopharyngeal swab, hospitalization due to the SARS-CoV-2 infection in the acute phase of illness, and ability to read and write. The criteria for excluding individuals encompassed acute coronary syndrome, acute heart failure, pulmonary embolism, notable valvular heart disease, and the requirement for intensive care intervention.

For brain fog evaluation, a previously validated clinical questionnaire named *Post-COVID Brain Fog* (BF-COVID) was used [15]. The corrected Cronbach's α of 0.833 indicated satisfactory internal consistency of the questionnaire [15]. Participants were retrospectively asked if they encountered problems with [15]:

- writing, reading, and counting,
- answering questions in understandable or unambiguous way,
- communicating of thoughts during conversation in a manner that others can understand,
- performing several tasks simultaneously (multitasking),
- recalling new information,
- remembering information from the past,
- determining current date and naming days of the week,
- finding right way in a familiar place.

Individuals once only responded either "yes" or "no" to the above mentioned questions regarding brain fog symptoms and assessed their presence in 4 time periods,




BF-COVID – *Post-COVID Brain Fog*, QoL-W – quality of life at work.

**Figure 1.** Details of the recruitment process in the study of brain fog and quality of life at work among people previously hospitalized for COVID-19 (April–August 2021, University Hospital in Kraków)

i.e., before the SARS-CoV-2 infection, within 0–4 weeks (acute phase), 4–12 weeks (post-acute phase), and >12 weeks post-infection (chronic phase). Additionally, subjects evaluated their QoL-W using a 4-point Likert scale, where 0, 1, 2, and 3 meant no, mild, moderate, and severe impairment at work, respectively [15]. Therefore, individuals who scored 0 in a 4-point Likert scale did not encounter any difficulties in performing professional activities, whereas the score of 3 meant that these subjects were not able to work at all [16,17].

Between April and August 2021, a paper version of the BF-COVID questionnaire was completed by subjects attending the post-COVID ambulatory in the University Hospital in Kraków, Poland. Additionally, anonymous electronic questionnaires were collected online through links either posted on Facebook or sent via mass email to the University Hospital employees. Received questionnaires were then matched with electronic hospital database in order to gather data on age, sex, concomitant diseases, results of the first laboratory tests since hospital admission, and date of the confirmed SARS-CoV-2 infection. The severity of comorbidities was classified into 3 grades based on the Charlson Comorbidity Index (CCI): mild (scores of 1–2), moderate (scores of 3–4), and severe (scores of ≥5) [18]. Finally, 181 BF-COVID questionnaires were included in the analysis after further exclusion of these with incomplete data (Figure 1). All study participants actively performed their job before the diagnosis of COVID-19.

**Laboratory investigations**

Complete blood count, C-reactive protein, creatinine, D-dimers, interleukin-6, N-terminal pro-B-type natriuretic peptide (NT-proBNP), procalcitonin, and myoglobin were assayed by standard laboratory methods. The high-sensitivity cardiac troponin I (hs-cTnI) levels were evaluated using the ARCHITECT i1000SR system (Abbott Laboratories, USA).

**Ethics approval and subject consent**

This study was conducted in accordance with Declaration of Helsinki as a part of the CRACoV-HHS project (CRAcow in CoVid pandemics – Home, Hospital, and Staff) [15,19]. Approval from the Jagiellonian University Bioethics Committee was received [15,19]. Participants who attended ambulatory for post-COVID subjects in the University Hospital in Kraków, Poland signed written informed consent before filling out a paper version of the BF-COVID questionnaire [15,19]. In accordance with Polish law, no written consent was required from individuals who completed an online anonymous version of the BF-COVID questionnaire, however, full information regarding purpose of the study was introduced to them [15,19,20].

**Statistical analysis**

The normality of the quantitative variables was assessed using the Shapiro-Wilk test. The data was then presented as mean ± standard deviation, medians, and interquartile

ranges (IQRs). For the comparison of 2 groups, either the Student's t-test or the Mann-Whitney U test was employed. Furthermore, comparisons involving >2 groups were analyzed utilizing the Kruskal-Wallis test and Friedman's ANOVA, followed by Dunn's *post hoc* test when appropriate. Regarding qualitative variables, they were presented as numbers and proportions. To compare these variables, the $\chi^2$ test and the Cochran Q test for dependent variables were used when appropriate. The Bonferroni correction was implemented for pairwise comparisons, where a significance level of <0.008 was considered. For other comparisons, a p-value <0.05 was utilized.

Deterioration in QoL-W was defined as a decrease of at least 1 level on a 4-point Likert scale compared to the pre-COVID-19 value. The quartiles for hs-cTnI were categorized as follows: <3.00 ng/l (N = 46), 3.01–6.07 ng/l (N = 47), 6.08–11.98 ng/l (N = 40), and >11.98 ng/l (N = 48).

### Multivariate models assessing the occurrence of brain fog symptoms following COVID-19 and a decline in work-related quality of life

All variables demonstrating a link with the presence of brain fog symptoms or the decline in QoL-W >12 weeks after COVID-19 in the univariate model (with a significance level of $p < 0.05$ and correlation coefficient with other independent variables $r < 0.7$), were incorporated into multivariable models. The multivariable models adjusted for age and sex were constructed using a stepwise backward elimination approach and demonstrated as odds ratios (OR) and 95% confidence intervals (CI). Moreover, the calibration of the models was carried out with the Hosmer-Lemeshow test, and the evaluation of the models' suitability was conducted using the Akaike information criterion. For the model's discrimination ability, the authors used receiver operating characteristic curves.

All statistical analyses were performed using Statistica 13.0 software.

## RESULTS

Data that confirms results of this study is obtainable from the corresponding author upon reasonable request.

### Baseline characteristics

The study involved 181 subjects who were admitted to hospital, with age Me = 57 years and 37.02% of them being women (Table 1). Upon admission, the severity of the disease was evaluated using a *Modified Early Warning Score* (MEWS), indicating that the majority of patients had low to moderate disease severity (77.90% with a score of 1 and 15.62% with a score of 2). None of individuals required treatment in an intensive care unit. Upon admission, almost 7 out of 10 patients (approx. 68.51%) required oxygen therapy, with the most common method being the use of a nasal cannula followed by a simple face mask. Most of the subjects in the study had either no comorbidities or low comorbidity, as indicated by the following CCI scores: 0 in 28.72%, 1–2 in 34.09%, and 3–4 in 23.20% of study participants, respectively.

The median duration of hospitalization for patients was 1.4 weeks, with an interquartile range of 1.1 to 2.0 weeks. The median follow-up period from diagnosis of the SARS-CoV-2 infection was 26.7 weeks (IQR 22.3–31.1 weeks).

### Brain fog symptoms after COVID-19

Before the emergence of COVID-19, 21.0% (N = 38) of individuals indicated experiencing any symptoms of brain fog. COVID-19 exhibited an association with an almost 3-fold increase (to 58.56%, 53.59%, and 49.17%) in the incidence of any brain fog symptoms within 4 weeks, 4–12 weeks, and >12 weeks ($p < 0.001$ for all intervals) (Table 2).

An increase in occurrence of moderate or severe brain fog symptoms was observed across all time periods following the SARS-CoV-2 infection: 30.94% (N = 56) within 0–4 weeks, 23.76% (N = 43) within 4–12 weeks, and 15.46% (N = 28) >12 weeks, in contrast to 4.42% (N = 8) prior to diagnosis of the SARS-CoV-2 infection ($p < 0.001$ for all comparisons).

Subjects who experienced any symptom of brain fog within weeks following the onset of COVID-19 displayed a lower prevalence of atrial fibrillation, undergoing treatment with an anticoagulant, and having elevated hs-cTnI level in comparison to other participants (as detailed in Table 1).

### Association between cardiac troponin levels and brain fog symptoms

The first in-hospital cardiac troponin I level measurement had a median value of 6.07 ng/l, with an IQR spanning from 3.00 to 11.97 ng/l. The hs-cTnI levels surpassing the 99th percentile threshold (28 ng/l [Abbott-Architect]) [21] were detected in 6.08% (N = 11) of the study cohort. Patients within the highest quartile of hs-cTnI levels (>11.90 ng/l) exhibited elevated

**Table 1.** Baseline characteristics according to brain fog symptoms >3 months post-infection among subjects hospitalized due to COVID-19 at University Hospital in Kraków (2020–2021)

| Variable | Participants (N = 181) | | | p |
|---|---|---|---|---|
| | total | no brain fog symptom (N = 68) | any brain fog symptom (N = 113) | |
| Demographics | | | | |
| age [years] (Me (IQR)) | 57 (46–66) | 57 (46–66) | 58 (47–66) | 0.731 |
| female sex [n (%)] | 67 (37.02) | 20 (29.41) | 47 (41.59) | 0.100 |
| Comorbidities [n (%)] | | | | |
| diabetes mellitus | 29 (16.02) | 9 (13.24) | 20 (17.70) | 0.427 |
| hypertension | 78 (43.09) | 29 (42.65) | 49 (43.36) | 0.924 |
| hypercholesterolemia | 37 (20.44) | 18 (26.47) | 19 (16.81) | 0.118 |
| obesity | 66 (36.46) | 32 (32.35) | 44 (38.94) | 0.372 |
| smoking | 54 (29.83) | 21 (30.88) | 33 (29.20) | 0.811 |
| atrial fibrillation | 12 (6.62) | 9 (13.24) | 3 (2.65) | 0.006 |
| chronic heart failure | 7 (3.87) | 2 (3.33) | 5 (4.72) | 0.670 |
| ischemic heart disease | 16 (8.83) | 4 (5.88) | 12 (10.62) | 0.276 |
| previous stroke | 9 (4.97) | 2 (2.94) | 7 (6.19) | 0.330 |
| asthma or chronic obstructive pulmonary disease | 18 (9.94) | 5 (7.35) | 4 (3.54) | 0.131 |
| chronic kidney disease | 4 (2.21) | 2 (2.94) | 2 (1.77) | 0.631 |
| depression | 19 (10.49) | 8 (11.76) | 11 (9.73) | 0.667 |
| previous neoplasm | 10 (5.52) | 6 (8.82) | 13 (11.50) | 0.366 |
| Treatment before admission [n (%)] | | | | |
| antidepressant | 21 (11.60) | 7 (10.29) | 14 (12.39) | 0.669 |
| anticoagulant | 15 (8.28) | 10 (14.71) | 5 (4.42) | 0.015 |
| benzodiazepine | 4 (2.20) | 0 (0.00) | 4 (3.54) | 0.298 |
| neuroleptics | 6 (3.31) | 1 (1.47) | 5 (4.42) | 0.412 |
| COVID-19 symptoms on admission [n (%)] | | | | |
| anosmia | 35 (19.34) | 16 (23.53) | 19 (16.81) | 0.268 |
| cough | 121 (66.86) | 56 (82.35) | 95 (84.07) | 0.763 |
| dyspnea | 63 (34.81) | 44 (64.71) | 77 (68.14) | 0.634 |
| fever | 151 (83.43) | 58 (85.29) | 94 (83.19) | 0.708 |
| gastrointestinal | 63 (34.81) | 22 (32.35) | 41 (36.28) | 0.591 |
| COVID-19 severity on admission – MEWS score [pts] (M±SD) | 1.28±0.57 | 1.23±0.55 | 1.31±0.58 | 0.447 |
| Oxygen therapy [n (%)] | | | | |
| not required | 23 (12.71) | 10 (14.71) | 13 (11.50) | 0.634 |
| nasal cannula | 124 (68.51) | 48 (70.59) | 76 (67.26) | |
| simple face mask | 34 (18.84) | 6 (8.82) | 17 (15.04) | |
| Laboratory tests | | | | |
| hs-cTnI [ng/l] (Me (IQR)) | 6.07 (3.00–11.97) | 4.48 (2.75–9.46) | 6.60 (2.80–13.68) | 0.022 |
| NT-proBNP [ng/l] (Me (IQR)) | 144 (60–333) | 124 (48–273) | 157 (69–523) | 0.213 |

**Table 1.** Baseline characteristics according to brain fog symptoms >3 months post-infection among subjects hospitalized due to COVID-19 at University Hospital in Kraków (2020–2021) – cont.

| Variable | Participants (N = 181) | | | p |
|---|---|---|---|---|
| | total | no brain fog symptom (N = 68) | any brain fog symptom (N = 113) | |
| Laboratory tests – cont. | | | | |
| CRP [mg/l] (Me (IQR)) | 72 (33–113) | 77.9 (28.9–117) | 71.9 (37–106) | 0.751 |
| procalcitonin [mg/l] (Me (IQR)) | 0.09 (0.05–0.17) | 0.08 (0.04–0.16) | 0.09 (0.05–0.19) | 0.188 |
| IL-6 [ng/l] (Me [IQR) | 32.27 (14.6–53.89) | 34.9 (16.4–49.9) | 30.0 (12.2–55.4) | 0.700 |
| D-dimers [mg/l] (Me (IQR)) | 0.79 (0.51–0.28) | 0.84 (0.48–1.11) | 0.79 (0.56–1.41) | 0.596 |
| myoglobin [mg/l] (Me (IQR)) | 57.5 (35.9–111) | 57.1 (35.5–88.9) | 59.1 (36.1–116.7) | 0.713 |
| creatinine [μmol/l] (M±SD) | 80.07±40.17 | 78.84±37.69 | 80.82±41.74 | 0.922 |
| platelets [$\times 10^9$/l] (Me (IQR)) | 196 (146–282) | 197 (152–269) | 196 (141–286) | 0.793 |

CRP – C-reactive protein, hs-cTnI – high-sensitivity cardiac troponin I, IL-6 – interleukin-6, MEWS – *Modified Early Warning Score*, NT-proBNP – N-terminal pro-B-type natriuretic peptide.

NT-proBNP levels (Me = 310 [IQR 80–682] ng/l vs. Me = 99 [IQR 48–145] pg/ml, p = 0.006), increased D-dimers (Me = 1.07 [IQR 0.64–1.89] mg/l vs. Me = 0.72 [IQR 0.47–1.08] mg/l, p = 0.026), and a higher prevalence of ischemic heart disease (15.38% vs. 2.17%, p = 0.033), neuroleptic treatment (9.62% vs. 0.00%, p = 0.038), oxygen therapy (90.38% vs. 80.43%, p = 0.047), alongside a reduced prevalence of anticoagulant treatment (0.00% vs. 8.70%, p = 0.045), when compared to patients within the first quartile. The independent predictors of hs-cTnI within the top quartile were NT-proBNP concentrations (OR = 0.996, 95% CI: 0.994–0.998 per ng/l, p = 0.001).

Subjects who exhibited any symptom of brain fog from the onset of COVID-19 displayed a 47.3% higher level of hs-cTnI compared to those without brain fog (p = 0.022, as detailed in Table 1 and Figure 2a). Moreover, the highest quartile of hs-cTnI was associated with an increased number of brain fog symptoms >12 weeks from COVID-19 diagnosis (1 [0–3] vs. 0 [0–1], p < 0.027) as compared to the lowest hs-cTnI quartile.

In the multivariable model, which was adjusted for age and sex, the presence of brain fog symptoms after diagnosis of the SARS-CoV-2 infection was solely predicted by the highest quartile of hs-cTnI (>11.90 ng/l), as indicated in Table 3.

## Quality of life at work following the onset of COVID-19

Prior to occurrence of COVID-19, 9.95% (N = 18) of participants reported an impairment in QoL-W, with 8.84% (N = 16) reporting mild impairment and 1.11% (N = 2) moderate or severe.

The COVID-19 was associated with a 3.6-fold, 3.0-fold, and 2.4-fold increase in occurrence of QoL-W impairment within 4 weeks, 4–12 weeks, and >12 weeks (p < 0.05 for all time periods). A decline in QoL-W was noted in all the time periods after the SARS-CoV-2 infection: 35.91% (N = 65) within 0–4 weeks, 29.44% (N = 53) within 4–12 weeks, and 24.15% (N = 43) >12 weeks (p < 0.001 for all) (Table 4).

Noteworthy, a subgroup of individuals, comprising 4.42% (N = 8) within the 4–12 week interval, and 1.69% (N = 3) >12 weeks, reported an improvement in their QoL-W compared to the period before the emergence of COVID-19.

Subjects who experienced a prolonged decline in QoL-W for >12 weeks following the diagnosis of the SARS-CoV-2 infection were characterized by being younger (52 [IQR 39–60] years vs. 59 [IQR 47–68] years, p < 0.001), more frequently identifying as women (51.16% vs. 31.11%, p = 0.019), and having a higher prevalence of brain fog symptoms (88.37% vs. 53.33%, p < 0.001), and a higher platelet count (208 [IQR 160–324] vs. 192 [IQR 138–271] $\times 10^9$/l, p = 0.025), in comparison to other participants.

## Quality of life at work and brain fog symptoms

Subjects who experienced any impairment in QoL-W following COVID-19 had a higher median count of brain fog symptoms in various time intervals: within 4 weeks (3 [IQR 1–4] vs. 0 [IQR 0–2]), 4–12 weeks

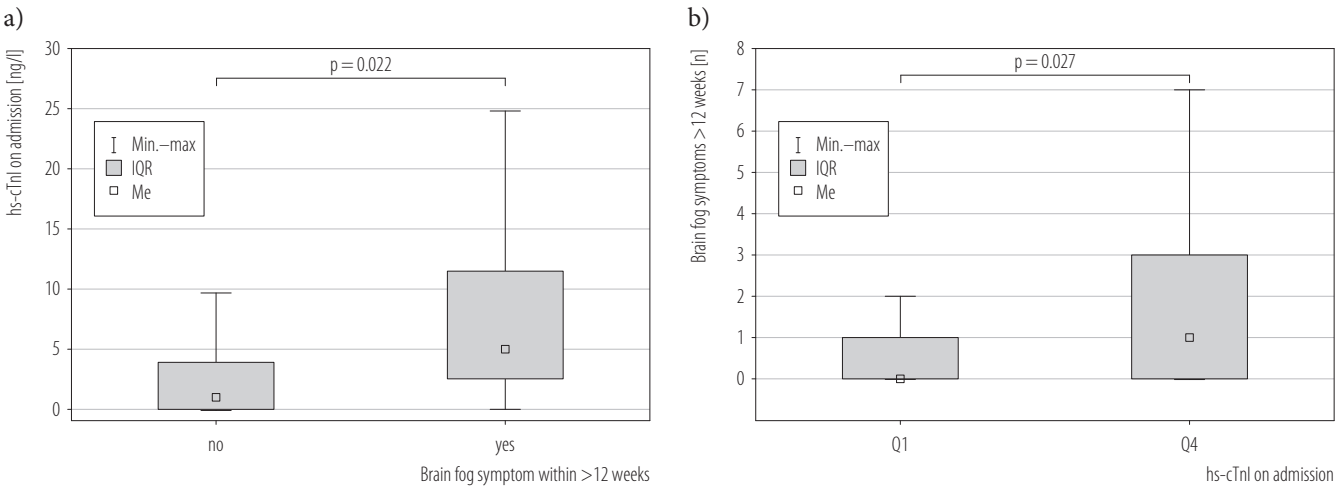
**Table 2.** Elements of brain fog in low-risk hospitalized patients before and after COVID-19

| Brain fog element | Participants (N = 181) [n (%)] | | | | | | |
|---|---|---|---|---|---|---|---|
| | before COVID–19 | 0–4 weeks after the COVID-19 onset | p[a] | 4–12 weeks after the COVID-19 onset | p[a] | >12 weeks after the COVID-19 onset | p[a] |
| 1. Problems with writing, reading, and counting | | | | | | | |
| none | 178 (98.34) | 144 (79.56) | <0.001 | 152 (84.44) | <0.001 | 161 (90.45) | <0.001 |
| mild | 3 (1.66) | 22 (12.15) | | 21 (11.67) | | 15 (8.43) | |
| moderate | 0 (0.00) | 9 (4.97) | | 7 (3.89) | | 1 (0.56) | |
| severe | 0 (0.00) | 6 (3.32) | | 0 (0.00) | | 1 (0.56) | |
| 2. Problems with an answer in an understandable or unambiguous way | | | | | | | |
| none | 178 (98.34) | 144 (79.56) | <0.001 | 155 (86.11) | <0.001 | 160 (89.89) | <0.001 |
| mild | 2 (1.11) | 22 (12.15) | | 16 (8.89) | | 14 (7.87) | |
| moderate | 1 (0.55) | 7 (3.87) | | 9 (5.00) | | 4 (2.25) | |
| severe | 0 (0.00) | 8 (4.42) | | 0 (0.00) | | 0 (0.00) | |
| 3. Problems with thoughts communication during a conversation | | | | | | | |
| none | 176 (97.24) | 140 (77.78) | <0.001 | 152 (85.40) | <0.001 | 165 (91.16) | 0.001 |
| mild | 5 (2.76) | 23 (12.78) | | 17 (9.55) | | 11 (6.08) | |
| moderate | 0 (0.00) | 16 (8.89) | | 7 (3.93) | | 4 (2.21) | |
| severe | 0 (0.00) | 1 (0.56) | | 2 (1.12) | | 1 (0.55) | |
| 4. Problems with performing several independent tasks simultaneously | | | | | | | |
| none | 165 (91.16) | 106 (58.57) | <0.001 | 122 (67.78) | <0.001 | 138 (77.53) | <0.001 |
| mild | 11 (6.08) | 44 (24.31) | | 33 (18.33) | | 24 (13.48) | |
| moderate | 4 (2.21) | 16 (8.84) | | 16 (8.89) | | 11 (6.18) | |
| severe | 1 (0.55) | 15 (8.29) | | 9 (5.00) | | 5 (2.81) | |
| 5. Problems with recalling new information | | | | | | | |
| none | 161 (88.95) | 101 (55.80) | <0.001 | 110 (61.11) | <0.001 | 125 (70.22) | <0.001 |
| mild | 17 (9.39) | 47 (25.97) | | 41 (22.78) | | 32 (17.98) | |
| moderate | 2 (1.10) | 18 (9.95) | | 20 (11.11) | | 16 (8.99) | |
| severe | 1 (0.55) | 15 (8.23) | | 9 (5.00) | | 5 (2.81) | |
| 6. Problems with remembering information from the past, e.g., recognizing people or remembering events | | | | | | | |
| none | 159 (87.85) | 123 (67.96) | <0.001 | 123 (68.33) | <0.001 | 136 (76.40) | <0.001 |
| mild | 18 (9.94) | 35 (19.33) | | 41 (22.78) | | 32 (17.98) | |
| moderate | 2 (1.10) | 17 (9.39) | | 12 (6.67) | | 8 (4.45) | |
| severe | 2 (1.10) | 6 (3.31) | | 4 (2.22) | | 2 (1.12) | |
| 7. Problems with determining the current date and days of the week | | | | | | | |
| none | 177 (97.80) | 151 (83.43) | <0.001 | 156 (86.67) | <0.001 | 162 (91.01) | 0.001 |
| mild | 4 (2.20) | 20 (11.04) | | 18 (10.00) | | 11 (6.18) | |
| moderate | 0 (0.00) | 5 (2.76) | | 6 (3.33) | | 5 (2.81) | |
| severe | 0 (0.00) | 5 (2.76) | | 0 (0.00) | | 0 (0.00) | |

**Table 2.** Elements of brain fog in low-risk hospitalized patients before and after COVID-19 – cont.

| Brain fog element | Participants (N = 181) [n (%)] | | | | | | |
|---|---|---|---|---|---|---|---|
| | before COVID–19 | 0–4 weeks after the COVID-19 onset | p[a] | 4–12 weeks after the COVID-19 onset | p[a] | >12 weeks after the COVID-19 onset | p[a] |
| 8. Problems with finding the right way in a familiar place | | | | | | | |
| none | 178 (98.34) | 157 (86.74) | <0.001 | 162 (90.00) | <0.001 | 166 (93.36) | 0.008 |
| mild | 3 (1.66) | 21 (11.60) | | 12(6.67) | | 10 (5.62) | |
| moderate | 0 (0.00) | 1 (0.55) | | 6 (3.33) | | 2 (1.12) | |
| severe | 0 (0.00) | 2 (1.10) | | 0 (0.00) | | 0 (0.00) | |

Numbers and proportions of patients who responded to each question in each period.
Data were evaluated with a Friedman ANOVA and Dunn's *post hoc* test.
[a] Versus before COVID-19.




The data were analyzed using the Mann-Whitney U test.
Q1 – first of quartile of hs-cTnI, Q4 – fourth quartile of hs-cTnI.

**Figure 2.** The influence of the first in-hospital high-sensitivity cardiac troponin I (hs-cTnI) measurement on a) the occurrence and b) quantity of brain fog symptoms after COVID-19

(2 [IQR 1–5] vs. 0 [IQR 0–2]), and >12 weeks (2 [IQR 1–5] vs. 0 [IQR 0–1]), in comparison to those who did not experience such impairment ($p < 0.001$ for all intervals) (Figure 3 ).

A positive correlation between the decline in QoL-W and the quantity of brain fog symptoms following COVID-19 was observed: within 4 weeks ($r = 0.415$), 4–12 weeks ($r = 0.381$), and >12 weeks ($r = 0.411$), with all correlations being significant at $p < 0.001$.

Participants who experienced a decrease in QoL-W >12 weeks after COVID-19 displayed a higher prevalence of almost all brain fog symptoms (question 1.1, 1.2, 1.4, 1.5, 1.7, 1.8) compared to those who did not encounter a change in their QoL-W (Table 5). The association between QoL-W and the ability to recall past information (question 1.6) was only observed within the 0–4 week phase (OR = 1.94, 95% CI: 1.02–3.70, $p < 0.001$).

Furthermore, at the 12-week mark after the disease onset, the prevalence of several brain fog symptoms remained notably high in individuals with a sustained decline in QoL-W, including responding coherently (question 1.2; 30.23% vs. 3.70%), conveying thoughts effectively (question 1.3; 34.88% vs. 8.15%), multitasking (question 1.4; 53.49% vs. 12.59%), and recalling recent information (question 1.5; 60.47% vs. 20.0%), in contrast to subjects with normal QoL-W (all with $p < 0.001$).

**Table 3.** Independent predictors of brain fog symptoms after COVID-19 within >12 weeks from COVID-19 onset

| Brain fog predictor | OR (95% CI) | p |
|---|---|---|
| Univariable model | | |
| age (per year) | 0.99 (0.97–1.02) | 0.599 |
| female sex | 1.71 (0.90–3.25) | 0.101 |
| atrial fibrillation | 0.18 (0.05–0.69) | 0.012 |
| anticoagulant | 0.27 (0.09–0.82) | 0.021 |
| hs-cTnI >11.90 ng/l (Q4) | 3.33 (1.40–7.93) | 0.006 |
| Multivariable model | | |
| age (per year) | 0.99 (0.96–1.03) | – |
| female sex | 1.80 (0.70–4.65) | – |
| atrial fibrillation | 0.23 (0.01–5.24) | – |
| anticoagulant | 0.75 (0.03–18.15) | – |
| hs-cTnI >11.90 ng/l (Q4) | 3.20 (1.24–8.23) | 0.016 |
| AUC | 0.674 (0.552–0.896) | |
| Hosmer-Lemeshow test | | 0.560 |

AUC – the area under the curve, hs-cTnI – high-sensitivity cardiac troponin I.

### Determinants of quality of life at work

A reduction in QoL-W >12 weeks following the onset of COVID-19 was independently predicted by age, female sex, and the existence of any brain fog symptom subsequent to COVID-19 (referred to as Model A) (Table 5). When examining components of brain fog, in addition to age and female sex, 2 specific symptoms – responding coherently (question 1.2) and recalling recent information (question 1.5) – predicted a decrease in QoL-W (referred to as Model B) (Table 5).

The models utilizing self-reported brain fog symptoms, age, and self-declared sex displayed a strong discriminatory capability for assessing QoL-W, yielding a median area under the curve (AUC) of 0.846 (95% CI: 0.780–0.912), as outlined in Table 5 and Figure 4. The Akaike Information Criterion (AIC) values for the goodness of fit in models A and B were 89.79 and 149.94, respectively.

## DISCUSSION

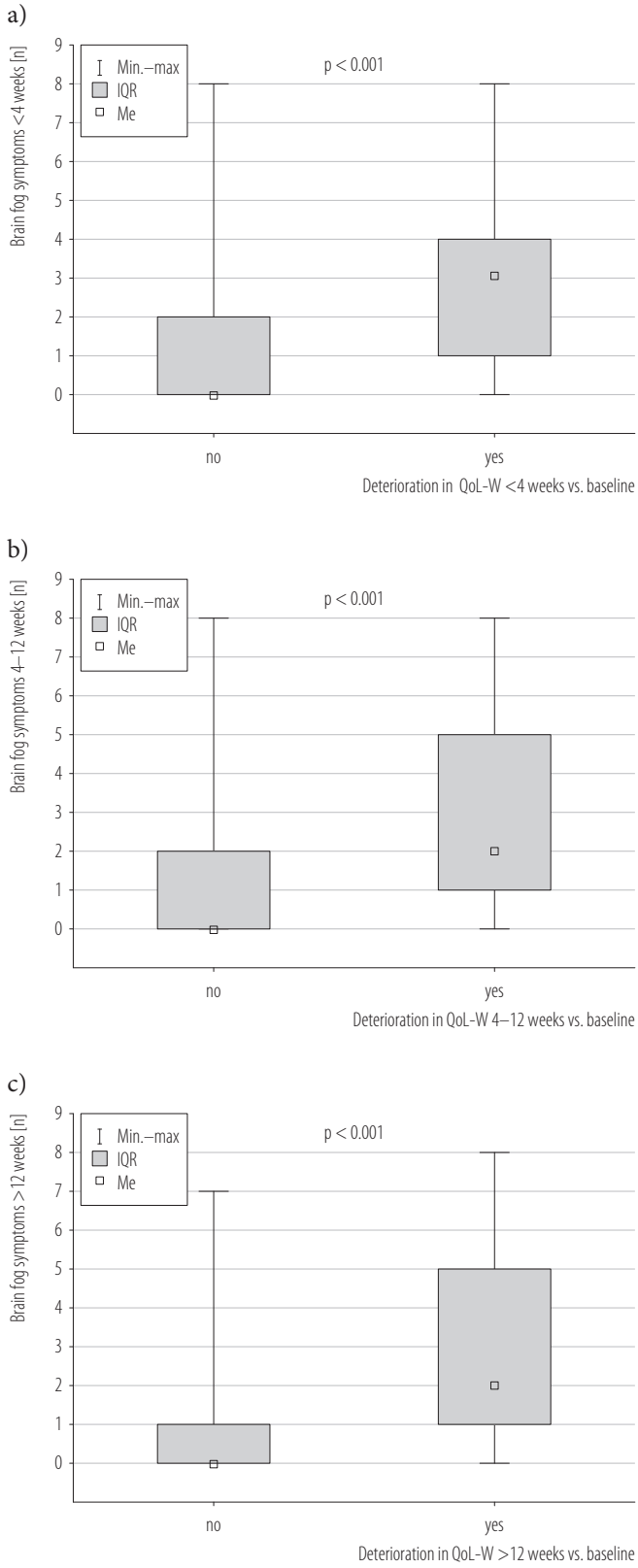
This research indicates that among Polish subjects with a low risk of mortality, who were admitted to hospital during the initial and most severe 2 waves of the pandemic:

- cognitive impairment (referred to as brain fog) is common and exerts the most substantial prolonged effect (lasting >12 weeks) on work-related quality of life;
- symptoms of brain fog surpass demographic factors, as well as the majority of underlying health conditions, admission status, and laboratory findings, in terms of their significance in contributing to the decline in QoL-W within >3 months after COVID-19 onset;
- specific components of brain fog that notably diminished the QoL-W were identified; these components, namely 'being able to respond coherently' and

**Table 4.** Change in quality of life at work in low-risk hospitalized patients within weeks following the onset of COVID-19 compared to pre-COVID interval

| Change | Participants [n (%)] (N = 539) | | | p |
|---|---|---|---|---|
| | 0–4 weeks after the COVID-19 onset (N = 181) | 4–12 weeks after the COVID-19 onset (N = 180) | >12 weeks after the COVID-19 onset (N = 178) | |
| None | 116 (64.09) | 119 (65.75) | 132 (72.93) | <0.001[a] |
| Deterioration | | | | |
| mild | 29 (16.02) | 29 (16.02) | 25 (13.81) | |
| moderate | 20 (11.05) | 18 (9.95) | 17 (9.40) | |
| severe | 16 (8.34) | 6 (3.32) | 1 (0.55) | |
| Improvement | | | | |
| mild | 0 (0.00) | 7 (3.87) | 2 (1.11) | |
| moderate | 0 (0.00) | 0 (0.00) | 1 (0.55) | |
| severe | 0 (0.00) | 1 (0.55) | 0 (0.00) | |

Data were evaluated with a Friedman ANOVA and Dunn's *post hoc* test.
[a] For all groups.




Data were compared with Mann-Withney U test.

**Figure 3.** The association between the quantity of brain fog symptoms and the decline in the quality of life at work (QoL-W) during different phases after COVID-19: a) acute phase (<4 weeks), b) subacute phase (4–12 weeks), and c) chronic phase (>12 weeks)

"recollection of recent information," exhibited a pronounced impact, with their presence increasing the likelihood of significantly lower QoL-W up to tenfold;

- certain biochemical measures, such as the first in-hospital highly sensitive cardiac troponin I levels measurement, could forecast the likelihood of experiencing brain fog; additionally, these measures had an indirect impact on decreasing QoL-W; specifically, when comparing the fourth quartile of highly sensitive cardiac troponin I levels to the first quartile, there was a more than threefold increased risk of developing brain fog symptoms after recovering from COVID-19.

This study is among the first to show that first troponin levels, measured during hospitalization due to COVID-19, are independent predictors of brain fog and its severity, and therefore indirectly QoL-W. So far, only few studies confirmed a prognostic role of cardiac biomarkers in developing post-COVID sequelae. For example, the highest troponin I levels during the acute phase of the SARS-CoV-2 infection correlated with the presence of fatigue 3 months after discharge from one of the hospitals in Wuhan, China [22]. In contrast to current research where between 1/4 and 1/3 of survivors reported decreased quality of life in all the time periods since the onset of infection, most of Chinese individuals came back to their pre-COVID work since they reported only mild functional impairment [22]. Notwithstanding, patients from Wuhan cohort were on average 15 years younger compared to present sample and, additionally, were less severely affected with comorbidities, such as diabetes mellitus, hypertension, and other cardiovascular diseases [22].

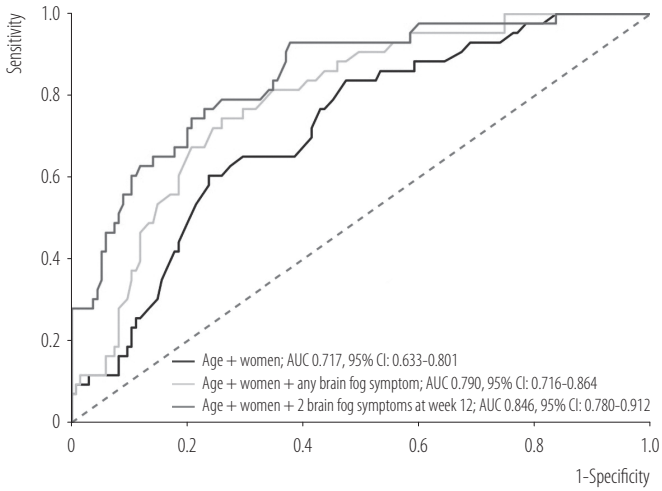
A recent Brazilian study of 480 subjects who presented with similar to ours demographic data showed instead that elevated troponin I levels in the acute phase of illness independently increased the risk of post-COVID cardiopulmonary symptoms, tiredness and fatigue within 90 days since hospital discharge [23]. Moreover, as shown in a large Maltese cohort of more than 2600 COVID-19 patients, significantly higher troponin T levels were found among cases previously hospitalized compared to those treated as outpatients during 5 month follow-up that might reflect ongoing inflammation in participants with initially more severe disease [24]. Similar conclusions came from an observation of 128 patients previously hospitalized at the University Medical Center in Texas where 77% of individuals had elevated troponin T levels of those being tested at follow-up [25].

**Table 5.** Independent predictors of the deterioration of quality of life at work in low-risk patients hospitalized due to COVID-19

| Predictor | OR (95% CI) | p |
|---|---|---|
| Model A | | |
| univariable model | | |
| age (per year) | 0.95 (0.93–0.98) | 0.001 |
| female sex | 2.32 (1.15–4.67) | 0.019 |
| obesity | 1.97 (0.98–3.97) | 0.056 |
| asthma | 2.83 (0.82–9.78) | 0.100 |
| brain fog symptom | 6.65 (2.47–17.93) | <0.001 |
| hs-cTnI >11.90 ng/l | 1.88 (0.74–4.80) | 0.188 |
| platelets (per $1 \times 10^9$/l) | 1.00 (1.00–1.01) | 0.025 |
| multivariable | | |
| age (per year) | 0.93 (0.89–0.97) | 0.003 |
| female sex | 4.31 (1.37–13.66) | 0.013 |
| brain fog symptom | 10.57 (2.19–51.07) | 0.003 |
| AUC | 0.790 (0.716–0.864) | |
| Hosmer-Lemeshow test | | 0.921 |
| Model B | | |
| univariable | | |
| age (per year) | 0.95 (0.93–0.98) | 0.001 |
| female sex | 2.32 (1.15–4.67) | 0.019 |
| "yes" answer to the question about the problems related to | | |
| 1. Writing, reading, and counting | 3.20 (1.15–8.90) | 0.003 |
| 2. Answering in an understandable way | 11.27 (3.73–34.02) | <0.001 |
| 3. Thoughts communication | 6.04 (2.51–14.55) | 0.001 |
| 4. Performing tasks simultaneously | 7.98 (3.63–17.52) | <0.001 |
| 5. Recalling new information | 6.19 (2.91–12.86) | <0.001 |
| 6. Remembering information from the past | 1.85 (0.86–3.95) | 0.115 |
| 7. Determining the current date | 3.63 (1.27–10.36) | 0.016 |
| 8. Finding the right way | 5.06 (1.51–16.88) | 0.008 |
| multivariable | | |
| age (per year) | 0.94 (0.90-0.97) | <0.001 |
| female sex | 3.67 (1.51-8.90) | 0.004 |
| "yes" answer to the question about the problems related to | | |
| 2. Answering in an understandable way | 9.91 (2.51-39.11) | 0.001 |
| 5. Recalling new information | 5.66 (2.37-13.54) | <0.001 |
| AUC | 0.846 (0.780–0.912) | |
| Hosmer-Lemeshow test | | 0.331 |

AUC – the area under the curve, hs-cTnI – high-sensitivity cardiac troponin I.

On the other hand, a recent meta-analysis of 24 biomarkers suggested that troponin was not associated with a risk of long COVID [26]. Notably, even the presence of concomitant heart abnormalities, appreciated on cardiac magnetic resonance imaging and estimated at a rate of 20% among long COVID patients




Models that included the presence of one or more brain fog symptoms had a higher area under the ROC curves than models that relied solely on age and sex as predictors. The detrioration in QoL-W was defined as a decrease of at least one level on a 4-point Likert scale compared to the pre-COVID-19 value.

**Figure 4.** Receiver operating characteristic (ROC) curves of models utilized to predict the deterioration of quality of life at work (QoL-W) during the chronic phase, after COVID-19

at 6-month follow-up, was also not predicted by troponin levels [27]. Therefore, whether increased troponin levels are a marker of neuropsychological post-COVID dysfunction, reflect residual post-infectious cardiac injury accompanying brain fog, or mirror the severity of the initial infection, needs to be addressed during future research.

In the current study, the authors were able to show that among subjects hospitalized due to mild COVID-19 during the first 2 waves of the pandemic in Poland, brain fog was very common and also the principal determinant of the QoL-W. Especially, inabilities to answer questions in understandable manner and to recall new information, were associated with nearly 10 and 6 times higher risk of deterioration in the QoL-W, respectively. Notably, brain fog symptoms were more important in predicting decrease in the QoL-W than demographics, concomitant diseases, pre-hospital treatment, severity of illness as measured with the MEWS scale on admission, and results of the laboratory tests. Authors' results stayed in line with an observation coming from a large UK cohort of 3754 patients diagnosed with post-COVID syndrome in 31 clinics, among whom 20% reported inability to work at all that was associated with increased brain fog intensity as perceived by patients when filling out questionnaire evaluating cognitive functions [28]. Similarly, among patients hospitalized in the University Hospital of Wurzburg during the first 2 waves of pandemic in Germany who did not require admission to an intensive care unit, only half of them returned to work and 1/5 still reported being fatigued [29]. Detailed neuropsychological interviews in small samples of German and American patients with long COVID suggested that brain fog was the principal factor affecting employment status of these individuals, resulting in perception of yet easily done tasks as new challenges [30], and not infrequently generating sick leave, even for several months [31].

Another study encompassing 547 patients evaluated through an online questionnaire nearly 300 days after the SARS-CoV-2 infection showed that >80% of people still reported lower quality of life, that was associated with pain, discomfort, or impairment of usual activities, and that was significantly more prevalent than in normative population [32]. Decreased quality of life compared to general population was also revealed among UK patients after 5 months since initial hospitalization due to COVID-19 and, interestingly, these individuals expressed higher fatigue rates with no significant accompanying differences during cognitive testing [33]. Finally, in authors' previous study related to non-hospitalized patients with COVID-19, some specific symptoms of brain fog were found to be associated with QoL-W impairment after 3 months since the onset of the SARS-CoV-2 infection [15]. Similarly to the current research, these symptoms included inability to answer questions in understandable way, and, additionally, difficulties with remote memory and multitasking, and were more important predictors of QoL-W than demographics, including age [15].

In an Irish study of 988 patients evaluated with an anonymous online questionnaire, it was shown that 38% and 30% of respondents felt severe and moderate impact of their post-COVID symptoms on working abilities, respectively, whereas 45% of individuals reported memory disturbances [34]. In a small UK cohort, deficits in episodic memory and attention were found during objective testing within 6–9 months after the SARS-CoV-2 infection, even in people not aware of residual post-COVID symptoms [35]; however, improvement with time was seen that resembled also observation coming from the current study. Nevertheless, still many individuals even months after an initial SARS-CoV-2 infection suffer from brain fog symptoms significantly affecting both working abilities and the quality of life that previous studies have tried to link with ongoing inflammation and neurotoxicity [36,37].

This study has several important limitations, including a small cohort size and retrospective design, as presented in authors' previous papers [15,19]. Moreover, research was based on outcomes given by participants once only and months after the acute phase of COVID-19, therefore, the authors were not able to confirm accuracy of responses, which might potentially lead to bias. Notwithstanding, presented multivariable models, especially regarding QoL-W, were simple and had satisfactory AUC values. Another limitation of the current study was the prolonged time from hospital admission to troponin level measurement, that in 90% of patients lasted <24 h, but in the rest of individuals could take up to few days. Nevertheless, only the first measurement of troponin level during hospitalization was took into account when performing statistical analyses. Unfortunately, data on troponin level change over time was also not gathered. Moreover, there was no information on type of the work performed by participants before the diagnosis of COVID-19, specifically related to mental or physical professional condition. Finally, the QoL-W was evaluated only with a 4-point Likert scale rather than with other specially designed questionnaires. However, previously validated BF-COVID questionnaire was used and other studies also relied on instruments utilizing a 4-point Likert scale in measurement of quality of life at work, e.g., *Leiden Quality of Work Life Questionnaire and Work Alienation* [15,17,38].

## CONCLUSIONS

In summary, nearly half of COVID-19 survivors hospitalized during the first 2 waves of pandemic in Poland experience lingering residual brain fog, a primary factor in reduced QoL-W, particularly impacting communication and memory recall. The presence of brain fog symptoms affects work-related quality of life with greater significance than demographic factors, concomitant diseases, pre-hospital treatment, initial severity of infection, and laboratory results. Notably, specific serum biomarkers measured during hospitalization, such as the first measurement of troponin levels, mostly within the first 24 h since admission, independently predict brain fog symptoms persisting >12 weeks post-SARS-CoV-2 infection onset. Occupational medicine practitioners should prioritize their attention on younger individuals and females, after recovering from COVID-19, who express challenges in answering questions in understandable way or recalling new information. This subgroup is at heightened risk of experiencing a decline in QoL-W.

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**Collecting material**: Żaneta Chatys-Bogacka, Iwona Mazurkiewicz
**Statistical analysis**: Leszek Drabik
**Interpretation of results**: Leszek Drabik, Marcin Wnuk
**References**: Marcin Wnuk

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