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Original Study

The Impact of Delirium on Recovery in Geriatric Rehabilitation after Acute Infection

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ABSTRACT

Objectives: Delirium is common during acute infection in older patients and is associated with functional decline. Geriatric rehabilitation (GR) can help older patients to return to their premorbid functional level. It is unknown whether delirium affects GR outcomes in patients with acute infection. We evaluated whether delirium affects trajectories of activities of daily living (ADL) and quality of life (QoL) recovery in GR after COVID-19 infection.

Design: This study was part of the EU-COGER study, a multicenter cohort study conducted between October 2020 and October 2021.

Setting and Participants: Participants were recruited after COVID-19 infection from 59 GR centers in 10 European countries.

Methods: Data were collected at GR admission, discharge, and at the 6-week and 6-month follow-ups. Trajectories of ADL [using the Barthel index (BI)] and QoL [using the EuroQol—5 Dimensions—5 Level (EQ-5D-5L)] recovery were examined using linear mixed models.

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[1] Membership of the EU-COGER consortium and COOP consortium is provided in, respectively, Supplementary Tables 1 and 2.

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Results: Of the 723 patients included (mean age 75.5 ± 9.9 years; 52.4% male), 28.9% had delirium before or during GR admission. Participants with delirium recovered in ADL at approximately the same rate as those without (linear slope effect = −0.13, SE 0.16, $P = .427$) up to an estimated BI score of 16.1 at 6 months. Similarly, participants with delirium recovered in QoL at approximately the same rate as those without (linear slope effect = −0.017, SE 0.015, $P = .248$), up to an estimated EQ-5D-5L score of 0.8 at 6 months.

Conclusions and Implications: Presence of delirium during the acute phase of infection or subsequent GR did not influence the recovery trajectory of ADL functioning and QoL.

Delirium is a common complication of acute infection in older adults, with an estimated prevalence of 33% in hospitalized patients aged ≥70 years.[1] Delirium can be triggered by known predisposing (eg, age and cognitive impairments) and precipitating (eg, hypoxemia and electrolyte abnormalities) risk factors. Preventative measures implemented in care settings during the COVID-19 pandemic (eg, social distancing and use of personal protective equipment) could have provoked or worsened delirium.[2-4] Short-term outcomes of delirium during hospitalization include decline in quality of life (QoL) and physical functioning, which may be persistent.[1]

After acute infection, geriatric rehabilitation (GR) can enable older adults to improve physical function and regain independence.[5] GR is defined as "a multidimensional approach of diagnostic and therapeutic interventions, the purpose of which is to optimize functional capacity, promote activity and preserve functional reserve and social participation" in older patients.[6] GR can be provided in an inpatient or outpatient setting by a multidisciplinary team specialized in rehabilitation of patients with multimorbidity and geriatric syndromes.[6,7]

The effect of delirium on GR outcomes in patients following acute infection remains unclear. A Scottish study, including hip fracture patients aged ≥50 years admitted to a trauma center during the COVID-19 pandemic, found that patients with delirium required post-acute inpatient rehabilitation significantly more often compared to patients without delirium.[8] Although this study reflects that delirium has a significant impact on prognosis, it remains to be investigated whether delirium affects long-term physical recovery of patients after acute infection. Knowledge about the impact of delirium patients' recovery in GR postinfection could help with the design of GR pathways and allocation of resources in the event of future pandemics. With this in mind, we evaluated whether delirium is associated with trajectories for activities of daily living (ADL) and QoL after COVID-19 infection in a multicenter cohort of patients undergoing GR and up to 6 months after discharge.

Methods

Study Design and Participants

The EU-COGER study was a multicenter observational cohort study that recruited participants from 59 centers in 10 countries (Czech Republic, Germany, Ireland, Israel, Italy, Malta, Russia, Spain, the Netherlands, and the United Kingdom) between October 2020 and October 2021. Consortium members contributing to the study are listed in Supplementary Tables 1 and 2. The rationale and design of the EU-COGER study has been described in detail elsewhere.[9] In short, patients were enrolled in GR centers by a local health care practitioner who was appointed as local study coordinator in each participating center. The local coordinator was responsible for identifying patients for inclusion and communication about the study to all those involved within their center.[10] Patients were eligible for inclusion if they were receiving multidisciplinary rehabilitation care, either institution based or at home, to support recovery from COVID-19 infection. The COVID-19 infection was confirmed with polymerase chain reaction (PCR) for viral RNA. Potential participants with severe cognitive impairment, which led to insufficient decisional capacities to participate in the study, were excluded. The institutional review committee of the Leiden University Medical Center approved the study (protocol number CoCo 2020-040). In all other countries, the local ethical regulations were followed, and approval from local ethics committee was sought if required by local regulations.

Data Collection

Demographics and clinical parameters were collected by local coordinators from electronic medical records at admission (T1) and discharge (T2) from GR. Data regarding premorbid health status and routine medical care data (T0) were collected retrospectively through referral letters from the hospital or general practitioner. Follow-up data were prospectively collected by phone at 6 weeks (T3) and 6 months (T4) after discharge from GR. A complete overview of all measures collected is described in the protocol paper.[9] Data were collected using Castor Electronic Data Capture.[11]

The primary outcome measure was ADL functioning, evaluated with the Barthel index (BI) at all time points (T0-T4).[12] The BI is a 10-item instrument, which can generate total scores ranging from 0 to 20, where a score of 20 represents complete independence for the ADL included. In centers where the ADL score was assessed using a different but comparable measure, for example, the Utrecht Scale for the Evaluation of Rehabilitation (USER) or the Functional Independence Measure (FIM), these were converted to the BI using standardized approaches.[13,14] The secondary outcome measure was QoL evaluated with the EuroQol–5 Dimensions–5 Level (EQ-5D-5L) QoL questionnaire from GR admission onward (T1-T4).[15] The EQ-5D-5L questionnaire is available in more than 200 languages and consists of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) that each have 5 response levels. The responses were converted into an index value with a maximum of 1 for optimal QoL, using available country tariffs.[16-22] For the Czech Republic and Russia, there were no country tariffs available and we used the country tariff of Poland as it is geographically the closest.

The independent variable of interest was delirium during the acute phase of infection or during the consecutive recovery trajectory (before or during GR). The presence of delirium was assessed through medical record review. Because these data were collected from routine clinical care records, the methods used for diagnosing delirium were heterogeneous across countries, with methods including clinical judgment, the Delirium Observation Screening Scale (DOSS), the 4 A's Test (4AT), or the Single Question in Delirium (SQiD). A DOSS score >3, 4AT score >3, or SQiD score >0 was used to define delirium.

Additional data were collected about intensive care unit (ICU) admission (yes/no), frailty, and comorbidities (eg, myocardial infarction, heart failure, dementia, stroke, and diabetes). The number of comorbidities was determined using the Functional Comorbidity

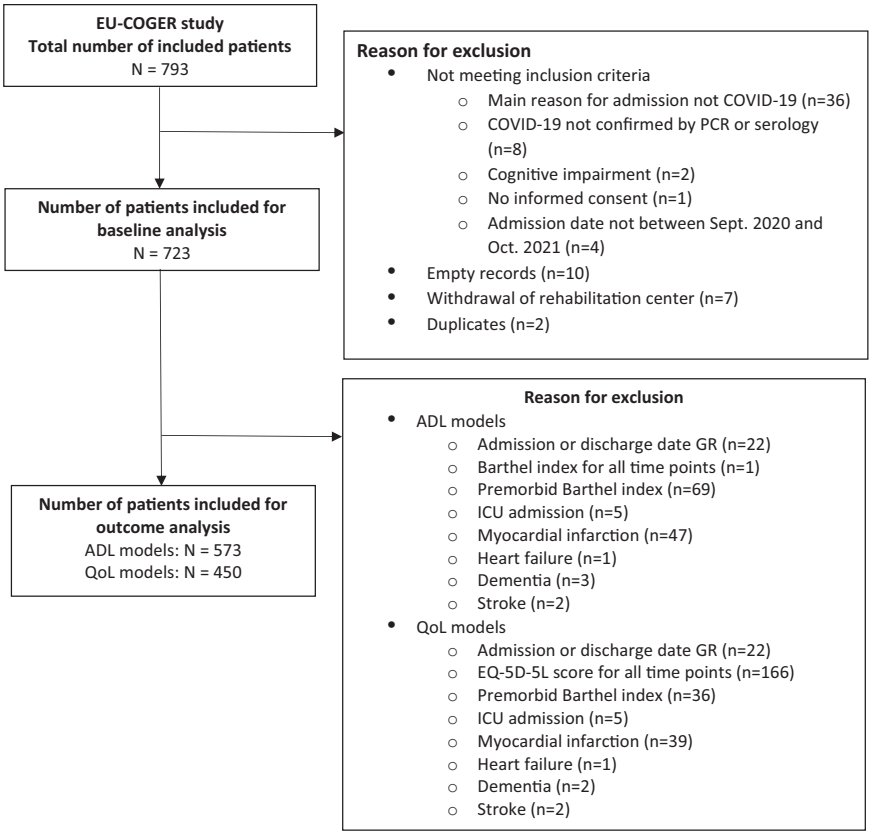

Fig. 1. Flowchart patient inclusions.

Index (FCI).[23] This index is the sum of 18 diagnoses associated with physical function. Frailty was measured using the Clinical Frailty Scale (CFS) and was categorized into 3 groups: fit (CFS score 1-3), prefrail (CFS score 4-5), and frail (CFS score 6-9).[24,25]

Statistical Analyses

Characteristics of study participants were summarized using descriptive statistics. Continuous data were presented as mean and SD or median and interquartile range, depending on the distribution of the data. Categorical data were presented as number (n) and percentage (%).

The trajectories of ADL and QoL recovery during and after GR were examined using linear mixed models, in which time was defined as months since GR admission. Three models were built for each outcome measure: an unconditional growth model, a univariable model in which delirium was added, and a fully adjusted model that included delirium and was adjusted for age, sex, premorbid BI, ICU admission, myocardial infarction, heart failure, dementia, stroke, and diabetes. A sensitivity analysis was performed using delirium starting before GR (during the acute phases of the COVID-19 infection) as an independent variable instead of delirium before or during GR. For this sensitivity analysis, 3 models were built in the same way as described above.

To identify the best-fitting unconditional models for ADL and QoL, we first checked whether the fixed slopes should be linear or quadratic. Second, we tested whether estimating random intercepts for variance between persons and between countries (3-level model) improved the model fit. Third, we tested whether estimating random linear and quadratic slopes for variance between persons and between countries improved the model fit. In every step, we fitted models using the default optimizer in the lmer R function nloptwrap, and optimizer Neldermead.[26] The model with the highest loglikelihood value (for nested models) was chosen as the best-fitting model. The models were built with unstructured variance-covariance matrices. Because premorbid data were collected for ADL (T0), these models were fitted with 2 splines. All records with missing values in 1 or more of the covariates were excluded from the analyses, and all covariates were mean-centered to present the change in ADL and QoL for a mean participant. We tested whether participants with missing values in the independent variables, who had to be excluded from complete case analysis, had similar recovery trajectories as the included participants. Outcomes were presented as parameter estimates (SE) for the fixed and random effects of the models. All models were build using R version 4.2.2 and R package lme4.

Results

A total of 793 records were initially created in the database. We excluded 70 records because the inclusion criteria were not met (n = 51), records were empty (n = 10), the GR center withdrew from the study (n = 7), or because they were duplicates (n = 2). This resulted in 723 participants available for baseline analysis. Additionally, participants were excluded from linear mixed model analyses when GR admission or discharge dates were missing, or all time points in ADL or QoL were missing, or participants had missing values in any of the covariates added to the models. This resulted in a total of 573 participants available for the analysis of ADL models and 450 participants available for the QoL models (Figure 1). No clinically relevant differences were observed for patients included and excluded in the final ADL and QoL models.

Baseline characteristics of the 723 included participants are presented for those with and without delirium (before or during GR)

Table 1
Patient Characteristics for the Total Study Population and Compared Between Patients With and Without Delirium

	No. Available (%)	Total Study Population (N = 723)	Patients With Delirium (n = 209; 28.9%)	Patients Without Delirium (n = 514; 71.1%)
Patient characteristics				
Age at GR admission, mean (SD)	719 (99.4)	75.5 (9.9)	75.5 (10.1)	75.5 (9.8)
Male, n (%)	723 (100)	379 (52.4)	128 (61.2)	251 (48.8)
BMI at GR admission, mean (SD)	655 (90.6)	27.0 (5.6)	25.8 (5.0)	27.5 (5.7)
Living situation before GR admission, n (%)	720 (99.6)			
Own home		675 (93.8)	202 (97.1)	473 (92.4)
Nursing home		29 (4.0)	2 (1.0)	27 (5.3)
Assisted living		13 (1.8)	3 (1.4)	10 (2.0)
Other		3 (0.4)	1 (0.5)	2 (0.4)
FCI score, mean (SD)	634 (87.7)	3.2 (2.1)	3.0 (1.8)	3.3 (2.2)
Myocardial infarction, n (%)	662 (91.6)	88 (13.3)	26 (13.7)	62 (13.1)
Heart failure, n (%)	662 (91.6)	224 (33.8)	54 (28.4)	170 (36.0)
Dementia, n (%)	659 (91.1)	70 (10.6)	36 (18.9)	34 (7.2)
Stroke, n (%)	662 (91.6)	105 (15.9)	27 (14.1)	78 (16.6)
Diabetes, n (%)	665 (92)	219 (32.9)	65 (34.0)	154 (32.5)
Frailty (CFS score) at admission, n (%)	493 (68.2)			
CFS 1-3		51 (10.3)	5 (3.4)	46 (13.3)
CFS 4-5		129 (26.2)	35 (24.0)	94 (27.1)
CFS 6-9		313 (63.5)	106 (72.6)	207 (59.7)
In-hospital outcomes				
Hospital stay before GR admission, n (%)	720 (99.6)	653 (90.7)	204 (97.6)	449 (87.7)
Hospital length of stay, d, median (IQR)	645 (98.8)	23 (13-46.5)	34 (18-59)	21 (12-40)
ICU admission before GR admission, n (%)	711 (98.3)	240 (33.8)	102 (49.0)	138 (27.4)
Length of stay in ICU, d, median (IQR)	232 (96.7)	23 (11-43)	28 (16-49)	19 (7-41)
GR outcomes				
Length of stay in GR, d, median (IQR)	691 (95.6)	26 (16-40)	28 (20-44)	25 (15-38)
Discharge destination, n (%)	703 (97.2)			
Own home		544 (77.4)	152 (75.2)	392 (78.2)
Nursing home		83 (11.4)	29 (14.4)	54 (10.8)
Assisted living		20 (2.8)	5 (2.5)	15 (3.0)
Hospital		30 (4.3)	9 (4.5)	21 (4.2)
Deceased during GR		11 (1.6)	3 (1.5)	8 (1.6)
Other		15 (2.1)	4 (2.0)	11 (2.2)

FCI, Functional Comorbidity Index; IQR, interquartile range.

in Table 1. These participants were recruited from 59 GR sites in 10 European countries: Czech Republic (n = 53), Germany (n = 50), Ireland (n = 50), Israel (n = 32), Italy (n = 30), Malta (n = 17), Russia (n = 50), Spain (n = 96), the Netherlands (n = 293), and United Kingdom (n = 51). Overall, 209 (28.9%) patients had delirium. The majority of participants received inpatient rehabilitation. Of these, delirium started before GR admission in 189 patients (90.4%). For the patients with delirium commencing before GR, it had ended before GR admission in 119 patients (56.9%), whereas for the remaining 70 patients (33.5%) delirium was also reported during GR. Presence of delirium stratified by country is presented in Supplementary Table 3. Patients with delirium were more often male compared to those without (61.2% vs 48.8%). Additionally, participants with delirium were more often frail (CFS score ≥6) at GR admission than those without (72.6 vs 59.7%) and had longer stays in GR (median 27.5 vs 25 days). The patient characteristics of the subgroups of the ADL and QoL sample are presented in Supplementary Table 4. The patient characteristics and outcomes of both subgroups were found to be similar.

ADL Functioning Over Time

The BI scores of all participants over time were presented in Supplementary Table 5.

The best-fitting unconditional growth model for ADL recovery is a 3-level quadratic growth model with a linear random slope for both patient and country level. The unadjusted model showed a significant recovery in BI from 11.17 at GR admission up to 16.81 at 6 months postdischarge (Table 2). During and after GR admission, BI first increased steeply (linear slope $\beta = 2.56$, SE = 0.16, $P < .001$) and thereafter stabilized (quadratic slope $\beta = -0.27$, SE 0.01, $P < .001$). After adjustment for covariates in model 3, BI at GR admission was nearly similar for patients with and without delirium, estimated as 0.28 (SE = 0.20, $P = .163$) points lower for patients with delirium. During and after GR admission, patients with delirium recovered at approximately the same rate as patients without delirium (linear slope $\beta = -0.13$, SE = 0.16, $P = .427$; quadratic slope $\beta = -0.002$, SE = 0.02, $P = .914$) (Figure 2).

The sensitivity analysis including only patients for whom delirium started before GR admission is shown in Supplementary Table 6 and Supplementary Figure 1. It found that patients with delirium starting before GR admission (in the acute COVID-19 phase) had similar rates of ADL recovery as those without delirium.

QoL Over Time

The EQ-5D-5L scores of all participants over time are presented in Supplementary Table 5.

Table 2
Linear Mixed Model for Change in ADL Functioning (n = 573)

	Model 1: Unconditional Model		Model 2: Univariable Model for Delirium at Any Time Point		Model 3: Multivariable Model for Delirium at Any Time Point*	
Fixed effects	Estimate (SE)	*P* Value	Estimate (SE)	*P* Value	Estimate (SE)	*P* Value
Intercept at GR admission						
ADL functioning	11.17 (1.04)	<.001	11.12 (1.03)	<.001	11.25 (0.93)	<.001
Delirium	N/A		−0.01 (0.31)	.99	−0.28 (0.20)	.16
Change after admission, per month						
Linear slope	2.56 (0.16)	<.001	2.57 (0.16)	<.001	2.73 (0.14)	<.001
Delirium: linear slope	N/A		−0.27 (0.18)	.13	−0.13 (0.16)	.43
Quadratic slope	−0.27 (0.01)	<.001	−0.27 (0.01)	<.001	−0.29 (0.01)	<.001
Delirium: quadratic slope	N/A		0.02 (0.02)	.38	−0.002 (0.02)	.91
Random effects	Variance (SD)		Variance (SD)		Variance (SD)	
At admission (intercept)						
Between-persons variance	13.18 (3.63)		13.17 (3.63)		12.93 (3.60)	
Between-countries variance	10.36 (3.22)		10.19 (3.19)		8.27 (2.88)	
After admission (slope of change)						
Between-persons variance	0.20 (0.45)		0.21 (0.45)		0.26 (0.51)	
Between-countries variance	0.15 (0.39)		0.15 (0.39)		0.12 (0.35)	
Residual	8.56 (2.93)		8.53 (2.92)		5.77 (2.40)	

*Model 3 is adjusted for age, sex, premorbid ADL, ICU admission, myocardial infarction, heart failure, dementia, stroke, and diabetes mellitus.

The best-fitting unconditional growth model for QoL was a 3-level quadratic growth model with a random intercept on both the patient and country level, and a linear random slope only on patient level. The model was fitted using the Nelder_Mead optimizer. The unadjusted model showed a significant recovery in EQ-5D-5L from 0.562 at GR admission up to 0.802 at 6 months post discharge (Table 3). During and after GR admission, EQ-5D-5L first increased steeply (linear slope $\beta = 0.118$, SE = 0.007, $P < .001$) and thereafter stabilized (quadratic slope $\beta = -0.013$, SE = 0.001, $P < .001$). After adjustment for covariates in model 3, EQ-5D-5L at GR admission was nearly similar for patients with and without delirium, estimated as 0.005 (SE = 0.028, $P = .869$) points higher for patients with delirium. During and after GR admission, patients with delirium recovered at approximately the same rate as patients without delirium (linear slope $\beta = -0.017$, SE = 0.015, $P = .248$; quadratic slope $\beta = 0.002$, SE 0.002, $P = .319$) (Figure 3).

The sensitivity analysis in which the trajectory of QoL recovery for patients in whom delirium started before GR was analyzed is shown in Supplementary Table 7 and Supplementary Figure 2. It found that patients for whom delirium started before GR (in the acute COVID-19 phase) had similar rates of QoL recovery compared to patients without delirium.

Discussion

The aim of this study was to investigate the impact of delirium on recovery of ADL and QoL in COVID-19 patients in Europe, during GR and up to 6 months after discharge. This study had 3 main findings. First, 28.9% of the patients had delirium during the acute phase of infection or subsequent recovery. Second, the rates of recovery in ADL and QoL were comparable between patients with and without

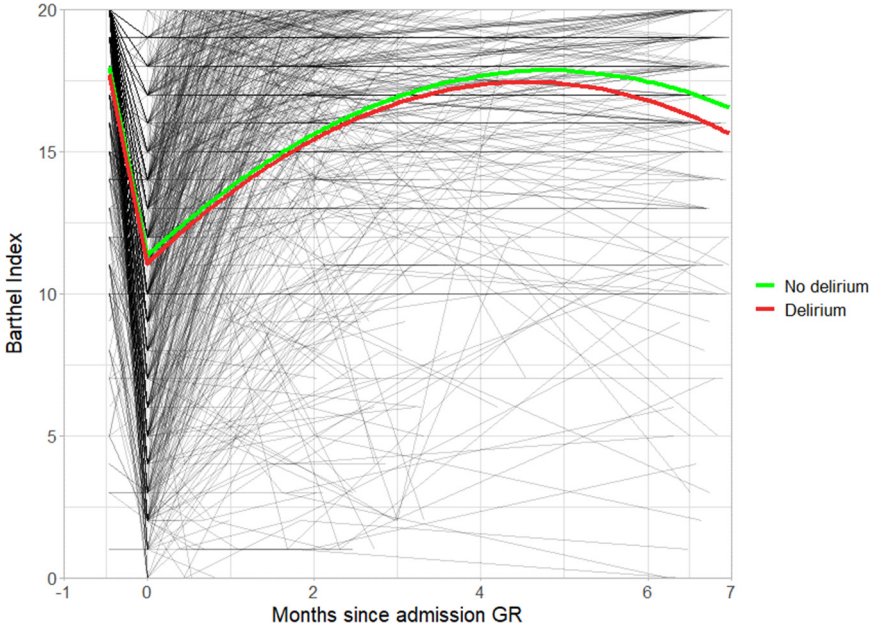

Fig. 2. Trajectory of ADL functioning for patients with and without a delirium (n = 573).

Table 3
Linear Mixed Model for Change in QoL (n = 450)

	Model 1: Unconditional Model		Model 2: Univariable Model for Delirium at Any Time Point		Model 3: Multivariable Model for Delirium at Any Time Point*	
Fixed effects	Estimate (SE)	*P* Value	Estimate (SE)	*P* Value	Estimate (SE)	*P* Value
Intercept at GR admission						
QoL	0.562 (0.462)	<.001	0.561 (0.046)	<.001	0.574 (0.039)	<.001
Delirium	N/A		−0.011 (0.028)	.70	0.005 (0.028)	.87
Change after admission, per month						
Linear slope	0.118 (0.007)	<.001	0.119 (0.007)	<.001	0.120 (0.007)	<.001
Delirium: linear slope	N/A		−0.014 (0.014)	.31	−0.017 (0.015)	.25
Quadratic slope	−0.013 (0.001)	<.001	−0.013 (0.001)	<.001	−0.013 (0.001)	<.001
Delirium: quadratic slope	N/A		0.002 (0.002)	.19	0.002 (0.002)	.32
Random effects	Variance (SD)		Variance (SD)		Variance (SD)	
Intercept at GR admission						
Between-persons variance	0.038 (0.195)		0.038 (0.196)		0.031 (0.176)	
Between-countries variance	0.017 (0.132)		0.017 (0.131)		0.012 (0.111)	
Linear slope						
Between-persons variance	0.001 (0.031)		0.001 (0.031)		0.001 (0.026)	
Residual	0.030 (0.174)		0.030 (0.174)		0.030 (0.174)	

*Model 3 is adjusted for age, sex, premorbid ADL, ICU admission, myocardial infarction, heart failure, dementia, stroke, and diabetes mellitus.

delirium. Third, both patients with and without delirium seemed to recover back to premorbid ADL levels.

No studies have investigated the association between delirium and recovery trajectories in GR. There have, though, been studies considering the association between delirium and ADL and QoL recovery in other contexts such as after ICU admission due to COVID-19 or after hip fracture. A Chinese study, including 130 patients aged ≥65 years undergoing elective orthopedic surgery found that patients with delirium experienced greater decline in ADL (16 vs 9 points on the Chinese ADL index, which ranges from 14 to 56 points) compared to those without delirium 24-36 months postoperatively.[27] Meanwhile, a Portuguese study, including 124 COVID-19 patients (mean age 62 years, interquartile range 24-86) admitted to the ICU, found that patients with delirium had worse QoL (based on the EQ-5D-5L questionnaire) 1-2 months after hospital discharge than those without delirium.[28]

Our study found no such impact from delirium on recovery of physical function and quality of life. A possible explanation for our findings could be that our study sample is a selected group of patients. Patients who were expected not to benefit from GR may not have been referred to GR or accepted for rehabilitation and thus might have been excluded from our study. Referral criteria for GR might have been stricter than usual as the need for GR during the COVID-19 pandemic grew substantially while the capacity of hospitals and GR centers was severely constrained.[29] In addition, patients with delirium who died during hospitalization were not included in this study. Other studies with highly selected samples also did not find an impact of delirium on recovery. For instance, a Dutch study including 1292 ICU patients (median age 65 years, interquartile range 58-85) did not find an association between delirium and quality of life (assessed with the Short Form-36v1) in those who survived up to a median of 18 months after ICU discharge.[30] Similarly, a prospective Chinese study including

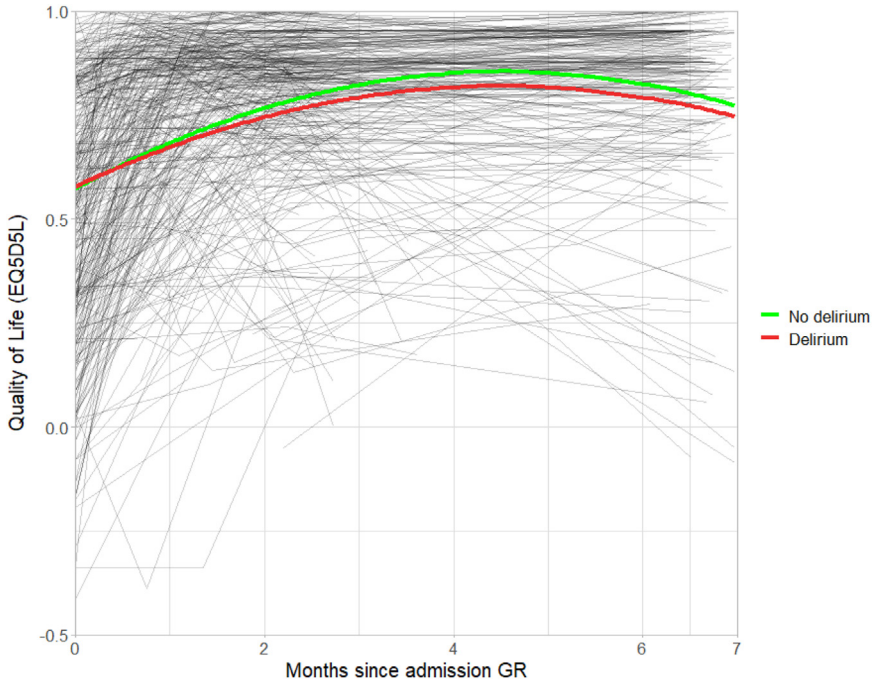

Fig. 3. Trajectory of QoL for patients with and without a delirium (n = 450).

127 participants aged ≥65 years found no difference in delirium and ADL function at a 24-month follow-up after a laryngectomy.[31] Moreover, a study including 341 COVID-19 patients aged ≥60 years in the United States did not find an association between delirium and increase in functional disability (defined as dependence in any of 15 functional activities (ADL, instrumental ADL, and mobility) 6 months after hospital discharge (OR 1.17, 95% CI 0.99-1.38).[32]

Our study has several limitations that need to be considered when interpreting the results. The BI is restricted to basic ADL and does not include more complex tasks (instrumental activities of daily living). This could have contributed to a ceiling effect. However, the BI is the most commonly used outcome measure in GR to capture basic ADL and it was expected to capture change in ADL among post−COVID-19 patients. The EQ-5D-5L questionnaire only captures broad categories and may miss smaller variations in quality of life. Patients with severe cognitive impairment were excluded in this study. Because delirium is highly correlated with neurodegenerative disorders like dementia, the true prevalence of delirium in COVID-19 patients in GR could be underestimated in this study. Further, the assessment method for delirium was heterogeneous across countries and we did not collect information on the duration and severity of delirium, which might have affected ADL and QoL trajectories. As we collected data on delirium retrospectively, it was not possible to assess these factors. Additionally, this study did not collect more detailed outcome measures such as instrumental ADL, because only routine clinical data were collected. Lastly, given that the majority of patients were provided inpatient rehabilitation, our findings primarily reflect the characteristics and outcomes associated with inpatient GR.

This study is strengthened by the large sample size of 723 patients coming from 59 health centers in 10 European countries. This increases the generalizability of our findings. Further, this study had a long follow-up period (up to 6 months after GR discharge) and regular follow-up intervals, maximizing sensitivity to change over time.

Although this study provides insight into the relationship between delirium and recovery trajectories of COVID-19 patients in GR, certain features remain unclear. For instance, qualitative studies might help to gain more knowledge into the psychological consequences of delirium in this specific patient group. Additionally, because delirium is highly correlated with cognition, more research is needed into the long-term impact of delirium on cognitive function.

Conclusions and Implications

To conclude, this study found that delirium did not affect ADL and QoL recovery after acute COVID-19 infection. These results can help inform triage for GR during periods of resource constraint and may be useful in widening participation in GR, by ensuring that patients with delirium are not unduly excluded.

Disclosure

The authors declare no conflicts of interest.

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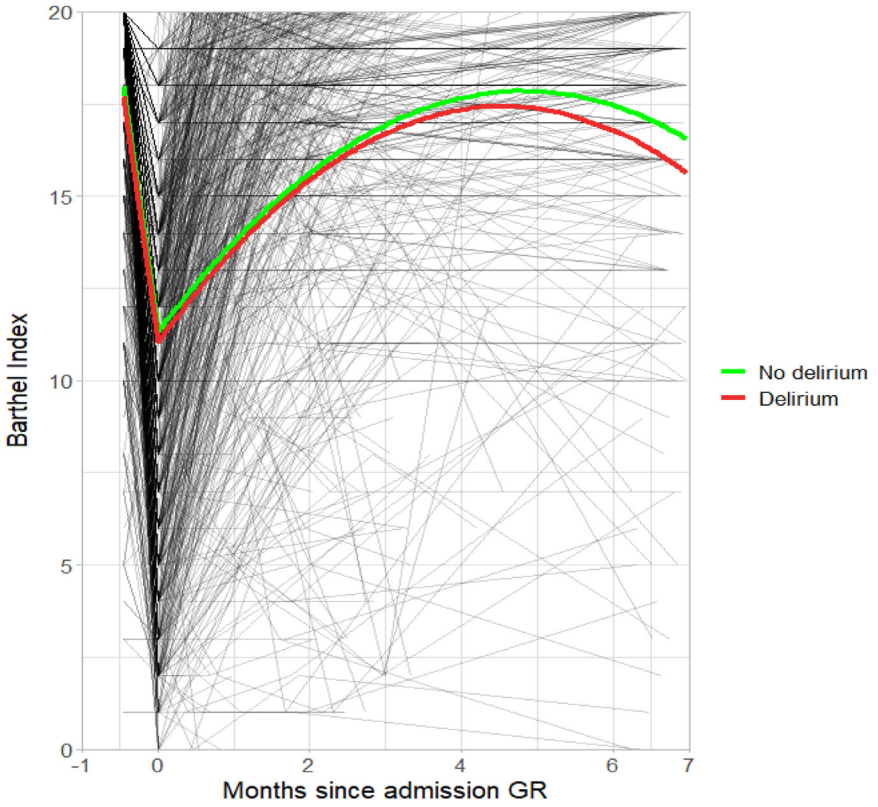
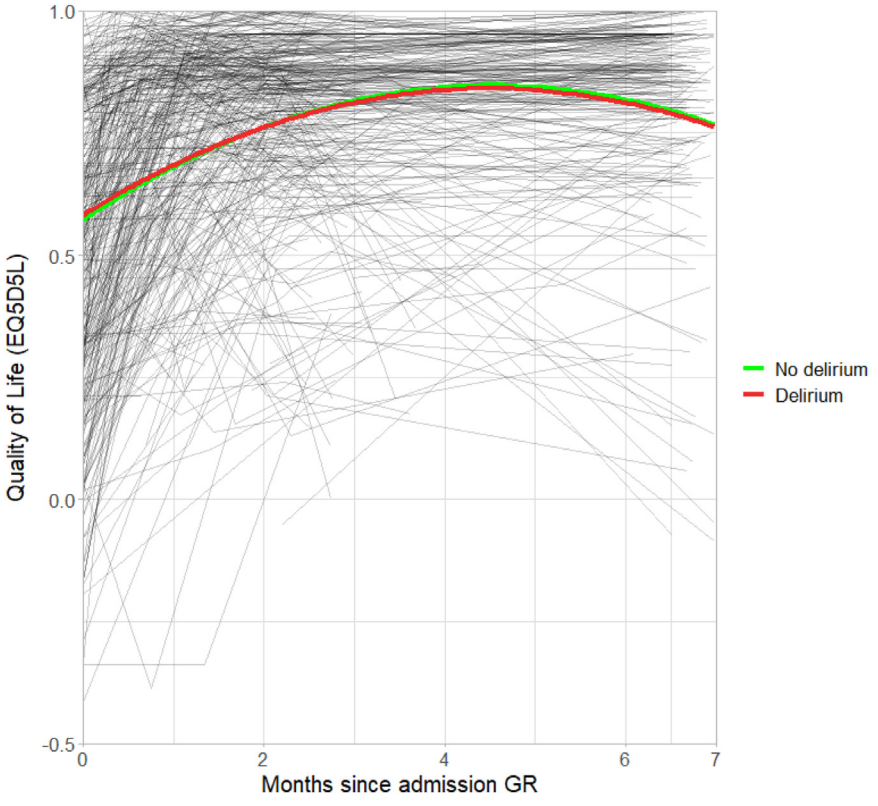


Supplementary Figure S1. Trajectory of ADL functioning for patients with and without delirium starting before GR.



Supplementary Figure S2. Trajectory of QoL for patients with and without delirium starting before GR.

Supplementary Table 1
EU-COGER Consortium List

Name of Health Center	Country	Study Coordinator 1	Study Coordinator 2	Study Coordinator 3
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Geriatrische Rehabilitationsklinik Diakonissenkrankenhaus Mannheim	Germany	Diana Franke-Chowdhury		
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Beaumont Hospital	Ireland	Frances Dockery	Kara McLoughlin	
Fliman geriatric rehabilitation center	Israel	Bahaa Francis		
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Karin Grech Hospital	Malta	Mark Vassallo	Maria Bonnici	
Russian Clinical and Research Center of Gerontology	Russia	Olga Nikolaevna Tkacheva	Ksenia Eruslanova	
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Hospital Universitari Sant Joan de Reus	Spain	Esther Roquer Fanlo		
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BrabantZorg	The Netherlands	Liesbeth Sikken	Irma Baars	
Ijsselheem	The Netherlands	Nathalie Deden		
Topaz Revitel	The Netherlands	Gerda Nijgh	Sylvia van der Drift	
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TriviumMeulenbeltZorg Hengelo	The Netherlands	Laura de Vries		
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Careyn	The Netherlands	Laura Langendoen-Wigman		
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Argos Zorggroep	The Netherlands	Mathilde Meerkerk		
Meriant (Alliade)	The Netherlands	Lianne Willemstein	Krisztina Krasznai	
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Laurens Intermezzo Zuid	The Netherlands	Janette Tazmi		
de Wever	The Netherlands	Eveline Keustermans		
Icare − De Boshof	The Netherlands	Janetta de Vries	Sanne van Weers	
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Florence	The Netherlands	Patricia te Pas	Eva Lodewijks	
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Zorggroep Maas en Waal	The Netherlands	Carolien de Croon		
Attent	The Netherlands	Christa van Schieveen		
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Kennemerhart Schoterhof	The Netherlands	Patricia van Berlo		
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Harrogate District Hospital	United Kingdom	Sarah Chadwick	Rebecca Watts	
Imperial College Healthcare NHS Trust	United Kingdom	Melani Dani	Jackie McNicholas	
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Calderdale & Huddersfield	United Kingdom	Vincent Chau		
Derbyshire Community Health Services	United Kingdom	Andy Cole		

Supplementary Table 2
COOP Consortium List

Health Care Center	Country	Name
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Radboud University Medical Center, Nijmegen	The Netherlands	René Melis

Supplementary Table 3
Participants With and Without Delirium by Country

Country, n (%)	Total Study Population (N = 723)	Patients With Delirium (n = 209; 28.9%)	Patients Without Delirium (n = 514; 71.1%)
Czech Republic	53 (7.3)	21 (10.0)	32 (6.2)
Germany	50 (6.9)	11 (5.3)	39 (7.6)
Ireland	50 (6.9)	11 (5.3)	39 (7.6)
Israel	32 (4.4)	12 (5.7)	20 (3.9)
Italy	30 (4.1)	3 (1.4)	27 (5.3)
Malta	17 (2.4)	4 (1.9)	13 (2.5)
Russia	50 (6.9)	1 (0.5)	49 (9.5)
Spain	96 (13.3)	44 (21.1)	52 (10.1)
The Netherlands	293 (40.5)	76 (36.4)	217 (42.2)
United Kingdom	52 (7.2)	26 (12.4)	26 (5.1)

Supplementary Table 4
Patient Characteristics for the Total Study Population and Compared Between the ADL and QoL Sample

	No. Available (%)	Total Study Population (N = 723)	ADL Sample (n = 573; 79.3%)	QoL Sample (n = 450; 62.2%)
Patient characteristics				
Age at GR admission, mean (SD)	719 (99.4)	75.5 (9.9)	75.8 (9.8)	75.0 (9.6)
Male, n (%)	723 (100)	379 (52.4)	299 (52.2)	237 (52.7)
BMI at GR admission, mean (SD)	655 (90.6)	27.0 (5.6)	27.1 (5.7)	27.1 (5.7)
Living situation before GR admission, n (%)	720 (99.6)			
Own home		675 (93.8)	533 (93.2)	417 (92.7)
Nursing home		29 (4.0)	27 (4.7)	24 (5.3)
Assisted living		13 (1.8)	10 (1.7)	7 (1.6)
Other		3 (0.4)	2 (0.3)	2 (0.4)
Delirium, n (%)	723 (100)	209 (28.9)	173 (30.2)	125 (27.8)
FCI score, mean (SD)	634 (87.7)	3.2 (2.1)	3.3 (2.1)	3.3 (2.2)
Myocardial infarction, n (%)	662 (91.6)	88 (13.3)	78 (13.6)	56 (12.4)
Heart failure, n (%)	662 (91.6)	224 (33.8)	193 (33.7)	150 (33.3)
Dementia, n (%)	659 (91.1)	70 (10.6)	68 (11.9)	48 (10.7)
Stroke, n (%)	662 (91.6)	105 (15.9)	86 (15.0)	69 (15.3)
Diabetes, n (%)	665 (92)	219 (32.9)	191 (33.3)	149 (33.1)
Frailty (CFS score) at admission, n (%)	493 (68.2)			
CFS 1-3		51 (10.3)	45 (10.1)	44 (11.5)
CFS 4-5		129 (26.2)	116 (26.0)	109 (28.5)
CFS 6-9		313 (63.5)	285 (63.9)	229 (59.9)
In-hospital outcomes				
Hospital stay before GR admission, n (%)	720 (99.6)	653 (90.7)	523 (91.3)	407 (90.4)
Hospital length of stay, d, median (IQR)	645 (98.8)	23 (13-46.5)	24 (14-47)	26 (14-51)
ICU admission before GR admission, n (%)	711 (98.3)	240 (33.8)	187 (32.6)	158 (35.1)
Length of stay in ICU, d, median (IQR)	232 (96.7)	23 (11-43)	27 (12-45)	27 (12-45)
GR outcomes				
Length of stay in GR, d, median (IQR)	691 (95.6)	26 (16-40)	26 (16-40)	26 (15-38)
Discharge destination, n (%)	703 (97.2)			
Own home		544 (77.4)	427 (74.8)	348 (77.5)
Nursing home		83 (11.8)	77 (13.5)	59 (13.1)
Assisted living		20 (2.8)	19 (3.3)	12 (2.7)
Hospital		30 (4.3)	26 (4.6)	15 (3.3)
Deceased during GR		11 (1.6)	8 (1.4)	2 (0.4)
Other		15 (2.1)	14 (2.5)	13 (2.9)

ADL, activities of daily living; BMI, body mass index; CFS, Clinical Frailty Scale; FCI, Functional Comorbidity Index; GR, geriatric rehabilitation; ICU, intensive care unit; IQR, interquartile range.

Supplementary Table 5
Outcome Measures Over Time

	Available (Nonmissing) Values, n (%)	Total, Mean (SD) (N = 723)	Patients With Delirium, Mean (SD) (n = 209; 28.9%)	Patients Without Delirium, Mean (SD) (n = 514; 71.1%)
ADL functioning (Barthel index)				
Premorbid	641 (88.7)	17.9 (3.6)	18.1 (3.3)	17.9 (3.7)
GR admission	714 (98.8)	10.9 (5.4)	9.1 (5.4)	11.7 (5.2)
GR discharge	655 (90.6)	15.9 (4.7)	14.8 (5.6)	16.4 (4.2)
6 wk after discharge	515 (71.2)	16.8 (4.5)	15.8 (5.1)	17.2 (4.2)
6 mo after discharge	509 (70.4)	16.9 (4.4)	15.8 (5.2)	17.3 (4.0)
Quality of life (EQ-5D-5L)				
GR admission	471 (65.1)	0.52 (0.32)	0.47 (0.31)	0.54 (0.33)
GR discharge	413 (57.1)	0.77 (0.22)	0.73 (0.26)	0.79 (0.20)
6 wk after discharge	423 (58.5)	0.78 (0.20)	0.74 (0.22)	0.79 (0.20)
6 mo after discharge	425 (58.8)	0.77 (0.25)	0.74 (0.25)	0.77 (0.25)

ADL, activities of daily living; EQ-5D-5L, EuroQol−5 Dimensions−5 Level; GR, geriatric rehabilitation.

Supplementary Table 6
Linear Mixed Model for Change in ADL Functioning for Delirium Starting Before GR (n = 573)

	Model 1: Unconditional Model		Model 2: Univariable Model for Delirium Starting Before GR		Model 3: Multivariable Model for Delirium Starting Before GR*	
Fixed effects	Estimate (SE)	*P* Value	Estimate (SE)	*P* Value	Estimate (SE)	*P* Value
Intercept at GR admission						
ADL functioning	11.2 (1.0)	<.001	11.6 (1.0)	<.001	11.3 (0.9)	<.001
Delirium	N/A		0.07 (0.3)	.81	−0.3 (0.2)	.18
Change after admission, per month						
Linear slope	2.6 (0.2)	<.001	2.6 (0.2)	<.001	2.7 (0.1)	<.001
Delirium: linear slope	N/A	<.001	−0.09 (0.2)	.61	0.1 (0.2)	.55
Quadratic slope	−0.3 (0.01)		−0.3 (0.01)	<.001	−0.3 (0.01)	<.001
Delirium: quadratic slope	N/A		0.004 (0.02)	.86	−0.03 (0.02)	.21
Random effects	Variance (SD)		Variance (SD)		Variance (SD)	
Intercept at GR admission						
Between-persons variance	13.2 (3.6)		13.2 (3.6)		13.0 (3.6)	
Between-countries variance	10.2 (3.2)		10.2 (3.2)		8.3 (2.9)	
After admission (slope of change)						
Between-persons variance	0.2 (0.5)		0.2 (0.5)		0.3 (0.5)	
Between-countries variance	0.2 (0.4)		0.2 (0.4)		0.1 (0.3)	
Residual	8.6 (2.9)		8.5 (2.9)		5.8 (2.4)	

ADL, activities of daily living; GR, geriatric rehabilitation.
*Model 3 is adjusted for age, sex, premorbid ADL, ICU admission, myocardial infarction, heart failure, dementia, stroke, and diabetes mellitus.

Supplementary Table 7
Linear Mixed Model for Change in QoL (n = 450)

	Model 1: Unconditional Model		Model 2: Univariable Model for Delirium Starting Before GR		Model 3: Multivariable Model for Delirium Starting Before GR*	
Fixed effects	Estimate (SE)	*P* Value	Estimate (SE)	*P* Value	Estimate (SE)	*P* Value
Intercept at GR admission						
QoL	0.6 (0.05)	<.001	0.6 (0.05)	<.001	0.6 (0.04)	<.001
Delirium	N/A		−0.06 (0.03)	.84	0.001 (0.03)	.73
Change after admission, per month						
Linear slope	0.1 (0.007)	<.001	0.1 (0.007)	<.001	0.1 (0.007)	<.001
Delirium: linear slope	N/A		−0.004 (0.01)	.77	−0.006 (0.02)	.68
Quadratic slope	−0.01 (0.0008)	<.001	−0.01 (0.0008)	<.001	−0.01 (0.0009)	<.001
Delirium: quadratic slope	N/A		0.001 (0.002)	.45	0.0006 (0.002)	.75
Random effects	Variance (SD)		Variance (SD)		Variance (SD)	
Intercept at GR admission						
Between-persons variance	0.04 (0.2)		0.04 (0.2)		0.03 (0.2)	
Between-countries variance	0.02 (0.1)		0.02 (0.1)		0.01 (0.1)	
After admission (slope of change)						
Between-persons variance	0.001 (0.03)		0.001 (0.02)		0.0007 (0.03)	
Residual	0.03 (0.2)		0.03 (0.2)		0.03 (0.2)	

GR, geriatric rehabilitation; QoL, quality of life.
*Model 3 is adjusted for age, sex, premorbid ADL, ICU admission, myocardial infarction, heart failure, dementia, stroke and diabetes mellitus.