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Intrinsic capacity with COVID-19 infection and late complications in the older adult population

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Abstract

Background: Intrinsic capacity (IC) decline, infection susceptibility, and post-COVID sequelae in older adults, intensified by the pandemic, demand probing IC domains' infection/outcome links and population-level strategies for sustaining functional health.

Methods: This cross-sectional study enrolled 600 older adults. IC was assessed using the World Health Organization's ICOPE framework. Post-COVID-19 condition was defined according to Centers for Disease Control and Prevention criteria, and late complications were evaluated via the culturally adapted and validated Persian C19-YRS questionnaire. COVID-19 infection status was confirmed through polymerase chain reaction testing of nasopharyngeal swabs or serological antibody assays. Statistical analyses were conducted using SPSS Version 22, including independent t-tests, analysis of variance, and regression models.

Results: Overall, most participants demonstrated relatively preserved IC across domains, although greater variability was observed in the psychological domain. In multivariable analysis, higher scores in the psychological IC domain were independently associated with COVID-19 infection (OR = 1.04, 95% CI: 1.00–1.08). Lower cognitive and sensory IC scores were significantly associated with poorer functional ability (B = −0.35, 95% CI: −0.66 to −0.04; and B = −0.50, 95% CI: −0.90 to −0.10, respectively), while higher sensory IC scores were associated with better general health among participants with post-COVID-19 complications (B = 0.24, 95% CI: 0.01–0.47).

Conclusion: These findings indicate meaningful associations between IC and both COVID-19 infection status and post-infectious health outcomes in older adults. Monitoring and supporting IC may be relevant for maintaining functional independence and quality of life in ageing populations during and after widespread infectious disease outbreaks.

Keywords: COVID-19, Intrinsic Capacity, Aging, Post-COVID Conditions.

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The foundation of healthy aging is an individual's intrinsic capacity (IC), which is the sum of their physical and mental abilities. IC represents the cumulative impact on environmental factors, lifestyle choices, and genetic predispositions (1). In contrast to temporary conditions brought on by acute diseases or trauma, IC is a lifelong process marked by the retention, deterioration, or preservation of functional abilities in a variety of domains. For older adults, IC provides the flexibility and resiliency required to deal with the aging challenges and maintain overall wellbeing (2). In later life, IC becomes critically important, directly shaping health outcomes and quality of life. Preserving IC is essential for maintaining independence, autonomy, and functional status (3). Declines in mobility, cognition, sensory function, or psychological health can severely limit daily activities, raising the risk of disability, dependency, and adverse health events in the elderly (4).

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The COVID-19 pandemic has highlighted how elderly populations are more susceptible to serious illnesses and unfavorable consequences. Advanced age is a well-established risk factor for severe complications, leading to disproportionately high rates of infection, hospitalization, and mortality among seniors (5). Moreover, the impact of COVID-19 extends far beyond the acute phase. There is growing recognition of its long-term effects, particularly in older adults. Persistent respiratory issues, cognitive deficits, cardiovascular sequelae, and psychological distress, collectively referred to as post-COVID-19 Condition (PCC), underscore the virus's lasting threat to IC and overall health in this group (6, 7).

Emerging research has begun exploring links between IC and COVID-19, including its late consequences (7-9). Studies have examined how pre-infection functional status influences COVID-19 outcomes (10), the role of frailty in disease severity (11), and recovery trajectories post-infection (12). However, significant knowledge gaps persist regarding the specific pathways through which COVID-19 affects the various domains of IC in the elderly. Furthermore, while existing studies often focus on hospitalized or severely ill patients, there is a notable lack of population-based data examining these associations in community-dwelling older adults with varying COVID-19 histories, including those with milder initial infections.

This study addresses these gaps by investigating the relationship between COVID-19 infection history and IC in a representative, population-based sample of community-dwelling elderly. Our approach is innovative in two key aspects: First, we employ a comprehensive, multidomain assessment of IC, moving beyond single metrics like frailty to capture a holistic view of capacity. Second, we specifically target a non-hospitalized, community-based cohort, including individuals across the spectrum of COVID-19 severity, which provides novel insights into the pandemic's broader impact on healthy aging. Therefore, the primary objective of this study is to determine the association between a history of COVID-19 infection and overall IC, as well as its specific domains (mobility, cognition, vitality, sensory, and psychological), among community-dwelling older adults, and to examine the relationship between the number of impaired IC domains and post-COVID-19 outcome domains. By clarifying these relationships, our findings aimed to inform targeted interventions and public health strategies designed to protect and enhance the well-being of older adults in the wake of the pandemic.

Methods

Study design and participants: The study was designed to explore IC and late post-COVID complications in older adults. This population-based cross-sectional study was conducted between September 2022 and February 2023 at comprehensive urban health service centers in Babol, a city in northern Iran with a population of 250, 217. The study targeted individuals aged 60 to 84 years. Eligible participants had no history of severe cognitive impairment, visual, hearing, or language impairments, or severe acute illness in the preceding three months. Additionally, participants included individuals who had experienced a confirmed COVID-19 infection (by positive PCR test) between 4 weeks and 12 months prior to the study, consistent with the CDC definition of post-COVID-19 Condition (PCC) (13). For all eligible individuals, the COVID-19 diagnosis was verified through electronic records to ensure consistency across data sources.

Sampling and data collection procedure: The initial list of potential participants with COVID-19 history was generated from the Health Vice-Chancellor portal system at Babol University of Medical Sciences, which registers confirmed PCR-positive cases in the region, where reporting of all positive PCR results in Babol is mandatory. As the entire target population has electronic health records within the national Integrated Health System (SIB), this initial list was cross-referenced and merged with the SIB database. Using SIB, two separate sampling frames were created: one for individuals aged 60–84 with a documented PCR-confirmed COVID-19 history, and another for those in the same age group without such a history. The same sampling strategy was applied to both frames to maintain comparability. Babol’s municipal districts served as the primary sampling frame, divided into two geographic strata. From each stratum, two comprehensive urban health centers were randomly selected. Eligible individuals from the two SIB-derived lists were then sampled proportionally from each of the four selected center using a stratified random method. All selected individuals were contacted by telephone, informed about the study’s objectives and procedures, and screened again for eligibility. Those who provided verbal agreement and met the eligibility criteria were scheduled for a visit at their respective health center. At the visit, written informed consent was obtained. A trained researcher then conducted face-to-face interviews to administer all questionnaires and complete the measurements (figure 1).

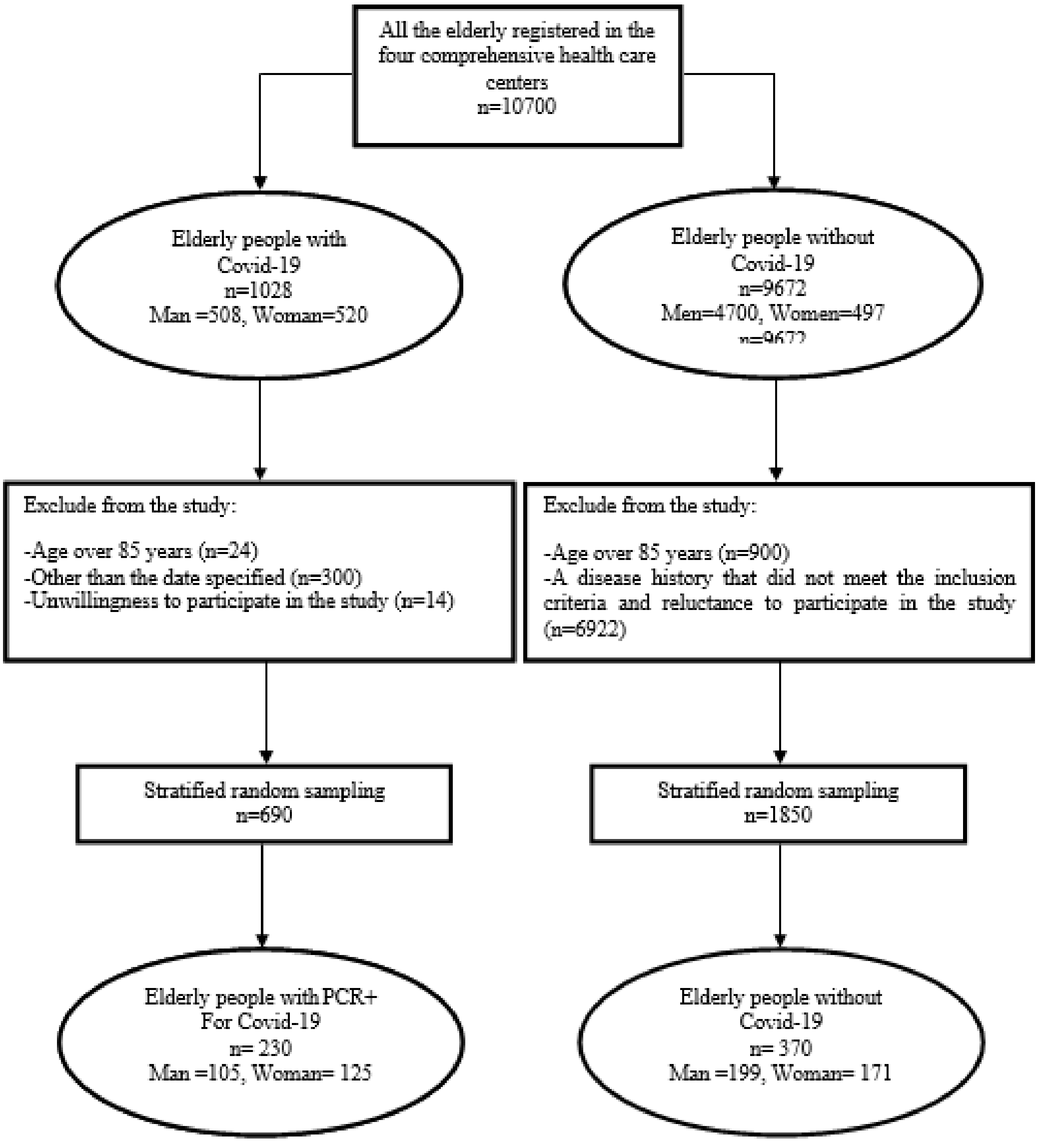

Figure 1. Flow diagram for recruitment of the participants

A brief record of the number of contacted individuals, non-responders, and final participants was maintained to document the flow. The same contact and invitation process was applied to both sampling frames, and reasons for non-participation (e.g., no response, refusal, or inability to attend) were logged to ensure transparency of the participant flow.

Sample size: The sample size was calculated using G*Power software Version 3.1. Based on previous studies (14, 15), a minimum five percent reduction in the IC of elderly individuals with COVID-19 was considered as the primary outcome. To detect this difference with a confidence level of 95% and a study power of 95%, and assuming a two-sided hypothesis, the software estimated a required sample size of 562 participants. Accounting for potential dropouts, the total sample size was adjusted to 600 individuals.

Data collection instruments: The measured variables encompassed individual characteristics, questionnaires on IC, as well as the C19-YRS questionnaire for late complications of Covid-19. The collected individual characteristics included age, gender, occupation, education level, economic status as perceived by the individual, retirement status, marital status, living arrangements (alone, with spouse, with spouse and children, or other arrangements), smoking status, polypharmacy (use of five or more medications), comorbidity (at least one additional medical conditions), hospitalization within the past year, physical activity (≥ half an hour per day for at least three times per week), and self-perceived health compared to peers.

Intrinsic capacity measurement (as independent variable): The assessment of IC domains was conducted in accordance with the WHO ICOPE guidelines (16).

Locomotion: The test known as the Short Physical Performance Battery (SPPB) was used to assess this domain. In this test, three tasks are timed including Balance test, Gait speed test, and Chair stand test. The results are scored out of four, with 0 representing the lowest performance and 12 representing the highest. The total of the scores from the three previously mentioned tests determines the final SPPB score.

Vitality: This domain was evaluated using the Full Mini Nutritional Assessment (MNA) questionnaire. People who score 24 or more are considered well-nourished, people who score between 23.5 and 17 are at risk of malnutrition, and people who score less than 17 are considered malnourished.

Cognition: The domain was evaluated using the Mini-Cog questionnaire. It consists of two sections: a clock drawing test (CDT) and a three-item memory recall test. The CDT produces a score of either 0 or 2, whereas the recall test is scored on a scale of 0 to 3. A total score of 0-2 suggests cognitive impairment, while 3-5 indicates lower likelihood, though further assessment is recommended if a score of 3 accompanies an abnormal clock.

Psychology: A 15-item version of the Geriatric Depression Scale (GDS) was used to evaluate this domain. The range of scores is 0 to 15. A score of 0–5 denotes a normal mood; scores of 6–9 hints at the possibility of depression; and scores higher than 10 denote depression.

Sensory: This domain comprises two parts: hearing and vision assessment.

a. The whisper self-test was utilized to evaluate hearing.

b. The WHO Simple Eye Chart (Tumbling E eye chart) was employed for vision assessment.

To calculate intrinsic capacity, a standardized z score was first computed for each domain. Specifically, for each participant, the raw domain score was centered by subtracting the sample mean and then divided by the corresponding standard deviation. The total intrinsic capacity score was subsequently obtained by summing the domain-specific z scores. Higher total scores indicate better overall intrinsic capacity.

C19-YRS questionnaire (as dependent variable): The questionnaire aimed at evaluating PCC. The C19-YRS developed and psychometrically tested by O'Connor et al. to assess the symptoms and functional capacity of individuals following COVID-19 infection (17). The last version of this questionnaire comprises four sections, covering symptoms severity (10 questions), functional ability (5 questions), other symptoms (25 questions), and overall health (1 question). Tamadoni et al. psychometrically evaluated the Persian version of the questionnaire (18).

COVID-19 assessment (as dependent variable): The participants underwent COVID-19 testing using established diagnostic methods, which included polymerase chain reaction (PCR) testing of nasopharyngeal swabs or serological testing for antibodies. Alongside laboratory confirmation, clinical criteria such as symptomatology and exposure history were utilized to identify COVID-19 cases.

Statistical analysis: The independent samples t-test was utilized to examine the desired outcomes between groups, while One-Way ANOVA test was employed to compare variable mean across more than two categories of qualitative variables. Additionally, to assess relationships between qualitative variables, the chi-square test was applied. Logistic regression analysis was conducted to examine both the crude and adjusted effects of the study variables and elucidate their interrelationships. The effect size in the model was expressed using odds ratio (OR) and 95% confidence interval (CI). Sensitivity analyses were performed to assess the stability of results under different assumptions and conditions, thereby providing further insight into the reliability and validity of the study outcomes. All analyses were performed using SPSS Version 22 software, with a significance level set at $p<0.05$.

Results

The participants' characteristics: Overall, the mean scores of the IC domains suggested that most participants remained relatively preserved functional reserves across domains. Analysis of impaired IC domains showed that 60.8% (n = 365) of participants demonstrated preserved functioning across domains (table S1). Among the remaining participants, 52.8% had impairment in one domain and 31.3% had impairment in two domains (table S2). Nevertheless, noticeable inter-individual variation was observed, particularly in the psychological domain. Scores related to the severity and range of post-COVID-19 symptoms were generally low, indicating predominantly mild late manifestations. In contrast, functional ability and general health scores were lower among older adults who experienced late complications, reflecting less favorable health status in this subgroup (table 2).

IC domains and COVID-19 infection: Pearson's correlation analysis demonstrated moderate and statistically significant correlations among IC domains ($p < 0.001$; fig. 2). In univariate regression models, higher vitality domain scores were associated with lower odds of COVID-19 infection (OR = 0.90, 95% CI: 0.83–0.98). Conversely, higher scores in the psychological domain were associated with higher odds of infection (OR = 1.05, 95% CI: 1.02–1.09) (table 3). After adjustment for relevant covariates in multiple regression analysis, only the psychological domain remained statistically significant (OR = 1.04, 95% CI: 1.00–1.08). This finding indicates that the association between psychological IC and COVID-19 status may be complex and influenced by contextual or behavioral factors.

IC domains and post COVID-19 complications domains: The associations between IC domains and post-COVID-19 outcomes are presented in tables 4 and 5. Lower scores in the cognitive and sensory IC domains were independently associated with poorer functional ability (B = −0.35, 95% CI: −0.66 to −0.04; and B = −0.50, 95% CI: −0.90 to −0.10, respectively). Furthermore, higher sensory IC scores were significantly associated with better general health scores in older adults with late COVID-19 complications (B = 0.24, 95% CI: 0.01–0.47), both before and after adjustment. No statistically significant associations were observed between IC domains and the severity of post-COVID-19 symptoms.

Linear regression analysis suggested a gradual pattern whereby a higher number of impaired domains was accompanied by slightly higher symptom severity scores and lower functional ability and general health scores; however, these trends did not reach statistical significance. With each additional impaired domain, the mean symptom severity score increased by 0.06 points, while functional ability and general health scores decreased by 0.24 and 0.09 points, respectively (tables S3–S5).

Table 1. Individual and clinical characteristics of the participants (N=600).

Variables	Frequency	Percent	Variables	Frequency	Percentage
Gender			**Polypharmacy**		
Female	296	50.7	No	299	49.8
Male	304	49.3	Yes	301	50.2
Education			**Comorbidity**		
Illiterate	108	18	No	345	57.5
Elementary/Guidance	200	33.3	Yes	255	42.5
Diploma	186	31	**Hospitalization history in the past year**		
University	106	17.7	No	516	86
Marital Status			Yes	84	14
Single	121	20.2	**Exercise**		
Married	479	79.8	No	218	36.3
Coexistence			Yes	382	63.7
Single	91	15.2	**Smoking**		
Spouse	299	49.8	No	556	92.7
Spouse/ Unmarried Child	180	30	Yes	44	7.3
Married Child	30	5	**Hookah**		
Occupation			No	584	98.3
Homemaker/Unemployed	231	38.5	Yes	16	1.7
Employed	85	14.2	**Perception Socio-economic situation**		
Retired Unemployed	209	34.8	Poor	177	29.5
Retired Working	75	12.5	Moderate	286	47.7
Receive pension			Good	137	22.8
No	215	35.8	**Health perception**		
Yes	385	64.2	Better than others	469	78.2
			Same/worse	131	21.8

Table 2. Intrinsic capacity domains and late complications of COVID-19

Variables	Mean (SD)	Min-Max points achievable	Min-Max points attainable	Median (interquartile range)
domainsIntrinsic capacity				
Locomotion	9.91 (2.19)	0-12	0-12	10 (9-12)
Vitality	28.10 (2.04)	18-30	0-30	29 (27-29)
Cognition	4.49 (0.97)	1-5	0-5	5 (5-5)
Psychology	2.81 (4.66)	0-15	0-15	0 (0-6)
Sensory	1.40 (0.73)	0-2	0-2	2 (1-2)
Total Intrinsic capacity	46.71 (4.94)	30-61	0-64	47 (44-49)
Late complications of Covid-19 domains				
Symptom severity	6.32 (5.00)	0-19	0-30	6 (2-10)
Functional ability	1.75 (2.20)	0-10	0-15	1 (0-3)
Other symptoms	1.75 (2.20)	0-10	0-15	1 (0-3)
Overall health	3.80 (2.84)	0-14	0-10	3 (2-6)

Table 3. Prediction of COVID-19 infection based on intrinsic capacity domains in regression analysis

Intrinsic capacity domains	Crude effect					Adjusted effect[1]				
	B (SE)	OR	Confidence Interval (95%) Lower	Upper	P-value	B (SE)	OR	Confidence Interval (95%) Lower	Upper	P-value
Locomotion	-0.007 (0.03)	0.99	0.92	1.07	0.846	-0.003(0.04)	1.00	0.91	1.09	0.951
Vitality	-0.10 (0.04)	0.90	0.83	0.98	0.014	-0.03(0.04)	0.96	0.87	1.06	0.453
Cognition	0.07 (0.08)	1.07	0.90	1.27	0.404	0.06(0.09)	1.06	0.87	1.29	0.536
Psychology	0.05 (0.01)	1.05	1.02	1.09	0.001	0.04(0.01)	1.04	1.00	1.08	0.019
Sensory	0.06 (0.11)	1.07	0.85	1.34	0.548	0.01(0.12)	1.01	0.79	1.31	0.889

[1] Adjusted for age, sex, occupation, polypharmacy, health perception status, hospitalization history in the past year, BMI, waist circumference, leg circumference.

Table 4. The relationship between functional ability domain of late complications of COVID-19 and intrinsic capacity domains

Intrinsic capacity domains	Crude effect				Adjusted effect[1]			
	B (SE)	Confidence Interval (95%) Lower	Upper	P-value	B (SE)	Confidence Interval (95%) Lower	Upper	P-value
Locomotion	-0.11 (0.06)	-0.24	0.02	0.102	-0.09 (0.07)	-0.24	0.05	0.218
Vitality	-0.08 (0.06)	-0.22	0.04	0.191	-0.07 (0.07)	-0.22	0.06	0.289
Cognition	-0.35 (0.15)	-0.66	-0.04	0.026	-0.35 (0.16)	-0.67	-0.03	0.029
Psychology	0.03 (0.02)	-0.09	0.09	0.199	0.04 (0.03)	-0.10	0.01	0.144
Sensory	-0.50 (0.20)	-0.90	-0.10	0.014	-0.44 (0.21)	-0.86	-0.02	0.039

[1] Adjusted for age, sex, occupation, polypharmacy, health perception status, hospitalization history in the past year, BMI, waist circumference, leg circumference.

Table 5. The relationship between the general health domain of late complications of COVID-19 with the intrinsic capacity domains

Intrinsic capacity domains	Crude effect				Adjusted effect[1]			
	B (SE)	Confidence Interval (95%)		P-value	B (SE)	Confidence Interval (95%)		P-value
		Lower	Upper			Lower	Upper	
Locomotion	0.06 (0.03)	-0.01	0.14	0.096	0.05 (0.04)	-0.02	0.14	0.174
Vitality	0.01 (0.03)	-0.05	0.09	0.618	0.01 (0.04)	-0.06	0.09	0.724
Cognition	0.12 (0.09)	-0.05	0.30	0.171	0.14 (0.09)	-0.03	0.33	0.111
Psychology	-0.02 (0.17)	-0.05	0.01	0.233	-0.01 (0.01)	-0.05	-0.01	0.364
Sensory	0.24 (0.11)	0.01	0.47	0.041	0.25 (0.12)	0.01	0.49	0.036

[1] Adjusted for age, sex, occupation, polypharmacy, health perception status, hospitalization history in the past year, BMI, waist circumference, leg circumference.

Discussion

The objective of this study was to explore the connection between IC and the occurrence of COVID-19 infection, as well as its subsequent late complications, within community-dwelling older adults. Unlike much of the existing literature, which has predominantly examined hospitalized or frail individuals, our study adopted a population-based design and assessed intrinsic capacity across its core domains, offering a broader perspective on these relationships. We identified a noteworthy association between diminished IC in the psychological domain and having a documented history of PCR-confirmed COVID-19 infection in the elderly population, based on multiple regression analysis. Additionally, our findings highlighted a correlation between the cognitive and sensory domains of IC and the presence of late complications following COVID-19 infection, particularly affecting functional ability and overall health status. By identifying these distinct patterns in a representative community sample, our work clarifies the associations between varying levels of IC, documented COVID-19 status, and post-infection manifestations, representing, to our knowledge, the first population-based investigation of these associations and expanding the scope of IC research to emerging public health challenges.

Our study builds upon a robust foundation of prior research investigating IC and its intricate connections with various health-related concepts. Previous articles in the field have extensively explored IC's correlation with aging syndromes (4, 19, 20), elucidating its role as a key indicator for assessing the health status of older adults. These studies examined multifaceted dimensions of IC, ranging from physical functionality to psychological well-being, to unravel its interplay with aging. While some focused on specific IC domains linked to age-related decline (21), others addressed general health outcomes and quality of life (7). Moreover, IC has been shown to predict functional decline (22) and mortality risk (23). Recent evidence further supports these findings: Zhao et al. conducted a systematic review and meta-analysis highlighting adverse health outcomes such as disability, fall, hospital admission, frailty and mortality associated with IC decline across older populations (24); Guaraldi et al. reported that lower IC and frailty–resilience phenotypes in post-acute COVID-19 patients were linked to poorer quality of life and persistent symptoms (7); Hernandes et al. in population-based cohorts, demonstrated inverse associations between IC and functional decline or hospitalization (25); and and Tay et al. emphasized that declines in IC may precede clinically manifest frailty, thereby increasing the risk of adverse outcomes (26). By integrating these findings, our population-based study complements and extends prior evidence, showing that specific IC domains, particularly psychological, cognitive, and sensory capacities, are independently associated with documented COVID-19 infection and subsequent late complications among community-dwelling older adults.

Numerous factors pertaining to nutritional, psychological, cognitive, and sensory aspects can shape how COVID-19 infections are experienced. Understanding and adhering to public health recommendations can be impacted by cognitive abilities such as memory, focus, and executive function (27). Additionally, nutritional deficiencies (28, 29) and psychological factors (30, 31) have been discussed in the literature as correlates of increased vulnerability to viral infections. Individuals experiencing sensory impairments, like those affecting vision or hearing, demonstrate increased vulnerability to COVID-19. This heightened risk may stem from challenges in interpreting environmental cues and healthcare instructions (32). Thus, in order to enhance IC and lessen inequality, accessible communication strategies, assistive technology, and tailored support services are required.

The differential associations observed between IC domains and late post-COVID-19 complications highlight the interdependent contributions of cognitive, sensory, psychological, and vitality capacities to overall vulnerability in older adults. These findings suggest that the cumulative burden of impairments across multiple IC domains may amplify functional decline and post-infection health deficits, emphasizing the importance of comprehensive, multidomain assessment. By considering multiple domains of IC rather than focusing on a single function, this perspective offers a conceptual framework to identify older adults at higher risk of adverse outcomes and to inform future research and interventions aimed at mitigating long-term consequences of COVID-19. Long-term COVID symptoms can be highly debilitating, underscoring the need for targeted rehabilitation and support to address the complex challenges faced by affected individuals (33).

This investigation's methodological rigor is anchored in a population-based, stratified random sampling design (n=600), which supports robust internal validity and generalizability. Core constructs were measured with precision: IC through the standardized ICOPE battery (SPPB, MNA, Mini-Cog, GDS) and post-COVID sequelae via a culturally adapted and validated Persian C19-YRS instrument, while SARS-CoV-2 infection status was objectively confirmed via PCR records. Analytical models were adjusted for major confounding variables, and the study protocol adhered to STROBE guidelines and ethical standards. These strengths are contextualized, however, by several limitations. The observational, cross-sectional nature of the data limits inferences regarding causality and the temporal sequence between IC and post-acute outcomes. Potential recall bias, survivor bias, and heterogeneity in post-infection timing, along with under-documentation of longer-term complications remain considerations inherent to the use of self-reported and administrative health data. Despite comprehensive ascertainment of PCR-positive cases through the local public health portal, misclassification of untested asymptomatic or mild infections cannot be entirely ruled out, which is a common limitation of population-based studies. Moreover, findings derived from this single geographical cohort may not be fully transferable to settings with differing healthcare infrastructures or demographic compositions. Consequently, future prospective longitudinal studies are warranted to corroborate these associations and explore their mechanistic pathways.

In conclusion, our study has unveiled significant associations between diminished psychological and vitality domains of IC and higher likelihood of COVID-19 infection among the older people. Furthermore, our findings have illuminated correlations between the cognitive and sensory domains of IC and the presence of late complications following COVID-19 infection, notably affecting functional ability and overall health status. These findings underscore the importance of IC as a factor associated with COVID-19 susceptibility and post-infection outcomes in older adults. For clinical practice, these results suggest that routine geriatric assessments should move beyond evaluating single domains or frailty alone. Instead, a multidimensional evaluation of IC, encompassing psychological, cognitive, sensory, and vitality components, could help identify older adults who may be more prone to specific COVID-19-related outcomes and long-term post-infection complications. Preventive strategies and rehabilitation programs can be tailored accordingly, focusing on integrated interventions that support psychological well-being, cognitive and sensory function, and overall vitality. Such an approach would not only build resilience against COVID-19 but also promote healthier aging more broadly.

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Ethics approval: The study protocol received approval from the National System of Ethics in Biomedical Research and the Research Ethics Committee of Babol University of Medical Sciences (Ethics ID: MUBABOL.HRI.REC.1401.134 IR). All procedures were conducted in accordance with the STROBE Statement (Supplementary Material). Measures were implemented to safeguard confidentiality, privacy, and ensure voluntary participation of participants throughout the study. Written informed consent was obtained from all the participants. All procedures adhered to the Declaration of Helsinki.

Conflict of interests: The authors declare no competing interests, financial or non-financial, and all have reviewed and approved the final manuscript.

Authors' contribution: Study concept and design were developed by Afsaneh Bakhtiari, Hossein-Ali Nikbakht, and Manoj Sivan. Data acquisition was performed by Negar Tamadoni and Maryam Ghorbanzadeh. Data analysis and interpretation were carried out by Hossein-Ali Nikbakht and Afsaneh Bakhtiari. The manuscript was drafted by Afsaneh Bakhtiari.

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