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ORIGINAL RESEARCH

Intrinsic Capacity Deficits and 6-Month Outcomes in Older Adults with Acute LRTIs: A Multi-Center Study

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Objective: Intrinsic capacity (IC), representing an individual's physical and mental abilities, is associated with adverse outcomes. Acute lower respiratory tract infections (LRTIs) contribute to poor long-term prognosis, yet effective assessment and intervention strategies remain limited. Given the critical role of IC in the aging population, understanding its prevalence and impact in older adults with LRTIs is crucial for improving management strategies. This study aims to characterize the domains and patterns of IC deficits and assess their influence on 6-month mortality and re-hospitalization in this population.

Methods: This was a multi-center prospective cohort study conducted in China. Patients aged over 65 years hospitalized for acute LRTIs were consecutively enrolled and underwent IC evaluations upon admission between April 15, 2021, and January 15, 2023. Outcomes included 6-month mortality and re-hospitalization. Latent class analysis identified patterns of IC deficits, and multivariable logistic regression models assessed associations between IC deficit domains/patterns and adverse outcomes.

Results: A total of 1,001 older patients were included, with a mean age of 76 years (IQR: 69–84). Most of (839, 83.8%) the patients had at least one IC domain deficit. The 6-month re-hospitalization and mortality rates were 20.7% (190/933) and 7.7% (70/914). More domains of IC deficits, particularly in cognition (OR 1.873) and vitality (OR 1.737) deficits were associated with increased 6-month re-hospitalization rates. Three distinct IC deficit patterns were identified: relatively robust (73.5%), limited vitality and locomotion (18.6%), and impaired cognition, vision, and hearing group (7.9%). Compared to the relatively robust group, the limited vitality and locomotion group had a significantly higher risk of re-hospitalization (OR 2.025, 95% CI 1.388–2.932).

Conclusion: IC deficits were prevalent and associated with increased re-hospitalization in older adults with LRTIs. Early detection and targeted interventions may reduce re-hospitalization rates and improve patient outcomes.

Keywords: ICOPE, intrinsic capacity, acute lower respiratory tract infections, older adults, long-term

Introduction

In 2017, WHO published the integrated care for older people (ICOPE) guidelines, which introduced a function-centered and person-centered approach to elderly care. The guidelines emphasize the significance of intrinsic capacity(IC), encompassing an individual's combined physical and mental abilities, providing a holistic overview of their health status.[1] The guidelines identified five domains of IC: locomotion, cognition, vitality, sensory, and psychological capacity. Specialists in geriatrics acknowledge that intrinsic capacity correlates with resilience, the patient's ability to recover from setbacks such as illness or injury.[2,3] However, this concept is predominantly applied at the community level and has not gained widespread adoption in non-geriatric fields. The role of IC in acute diseases is gaining traction in current research and has been found to be associated with short- and long-term outcomes, including hospitalization, functional decline,

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and mortality. However, conclusions have been inconsistent, and studies have been limited by small sample sizes, single-center designs, or retrospective methodologies.[4,5]

Acute lower respiratory tract infections (LRTIs) significantly contribute to mortality in older adults.[6] In 2019, there were approximately 6,318.64 cases of LRTIs per 100,000 people worldwide, resulting in 2.6 million deaths, with about half of these fatalities occurring among the elderly population.[6] Previous studies have shown that the older took high risk of long-term re-hospitalization and mortality following LTRIs.[7,8] For instance, elderly patients exhibit mortality rates as high as 30% within 1-year post-discharge, highlighting the severity and prolonged impact of these infections. Although acute anti-infective therapy remains essential, current clinical practices lack effective assessments and interventions tailored to improving long-term outcomes in elderly patients following an acute illness episode. If IC is associated with long-term adverse outcomes, it could provide a potential point for improving LRTIs management and addressing long-term prognostic challenges. However, evidences on the role of IC in the older with LRTIs remain limited.

Given these research gaps, we hypothesize that baseline impairment of intrinsic capacity in elderly patients with acute LRTIs is associated with adverse long-term prognoses. The study aimed to characterize intrinsic capacity impairment at the onset of acute infection and assess its impact on 6-month mortality and re-hospitalization.

Material and Methods

Study Design and Participants

This was a multi-center perspective cohort study, which was conducted in 12 hospitals, including tertiary, secondary and community hospitals across 6 provinces and cities in China. Patients were consecutively enrolled between April 15, 2021, and January 15, 2023. Patients who aged more than 65 years and hospitalized for acute LRTIs were enrolled. The diagnosis of LTRIs is made when one of the following two conditions is met: 1. The patient has a cough, thick sputum and wet rhonchi in the lungs with any of the following:(1) Fever. (2) Elevated total white blood cell and/or neutrophil count. (3) X-ray or Computed tomography shows inflammatory infiltrative lesions in the lungs. 2. Patients with chronic respiratory diseases in a stable phase (chronic bronchitis with or without obstructive emphysema, asthma, bronchiectasis), following an acute infection with pathogenetic changes or chest radiographs showing significant changes or new lesions compared with admission. The exclusion criteria were patients with completely dependent functional status, deafness, severe cognitive impairment, advanced malignant tumors, expected survival of less than 1 year.

Informed consent was obtained from all participants or their family members prior to the survey. The study was approved by the Beijing Hospital Ethics Committee (ClinicalTrials.gov ID, ChiCTR2400085045).

Measurements

Before starting the research, we held three training sessions for the assessors, who were doctors or nurses from the departments. In the final session, an examination was administered, and only those who passed were qualified to perform assessments, ensuring reliability and standardization. All participants were evaluated by these trained nurses at the time of enrollment. Each participant underwent the following assessments by the same assessors.

Intrinsic Capacity Domains

According to the WHO ICOPE guidelines, six conditions associated with IC, including: cognition, vitality, locomotion, psychological well-being, hearing capacity and visual capacity.[9] The locomotion domain was assessed once the infectious disease had stabilized, typically at clinical stability before discharge. While other IC domains were evaluated at admission. This timing ensured a more accurate measure of physical functional recovery, as locomotion may be temporarily impaired during the acute illness phase.

Cognition was screened by Mini Mental State Examination (MMSE, scores: 0–30, with lower scores indicative of worse cognitive impairment) (Permission for MMSE usage was obtained from PAR Inc).[10]

Vitality was assessed using body mass index (BMI, kg/m²) and a self-reported question regarding weight loss: "Have you unintentionally lost more than 5 kg over the past year?" A BMI < 18.5 kg/m² or an affirmative response to the weight loss question indicated limited vitality.

Locomotion was evaluated using the Short Physical Performance Battery (SPPB), which includes assessments of standing balance, a 4-meter walk test, and five repetitive chair stands (score range: 0–12). A SPPB score < 10 or a gait speed ≤ 0.8 m/s were used as thresholds indicating poor locomotion capacity.

Psychological well-being was assessed by Patient Health Questionnaire (PHQ-2), with a cutoff score of ≥3 indicating a potential presence of depression.[11]

Hearing capacity was assessed through self-report of "hearing problems" impacting daily activities or identification as functionally deaf during the interview.

Visual capacity was evaluated based on self-reported "eyesight problems" affecting daily activities or identification as functionally blind during the interview.

Outcomes and Follow-up

Study outcomes were defined as 6-month all-cause mortality and re-hospitalization. The medical staff in the study contacted the patients or their family members by phone at 1, 3, and 6 months after discharge to collect their survival status. Patients were considered lost to follow-up if they had no in-hospital assessments, no medical records and no response after three consecutive phone call attempts during the follow-up period.

Covariates

Covariates included in the analysis were potential confounders affecting the relationship between patient characteristics and adverse outcomes. These encompassed socio-demographic (age, sex, marital status), socioeconomic status (education, income perception, support from offspring), lifestyle (smoking and alcohol consumption), co-morbidity (Charlson Comorbidity Index, CCI) and severity of LRTIs, which was assessed by modalities of oxygen support: mild (no oxygen), moderate (nasal oxygen), and severe (high-flow or noninvasive ventilation, or mechanical ventilation). Laboratory test results at admission were also recorded.

Sample Size

Since no existing studies have examined the relationship between IC and LRTIs, the sample size was estimated based on previous research.[5] An odds ratio of 0.48 was reported for the association between IC score and mortality. The IC score ranged from 2 to 4, with a standard deviation of 0.5. Assuming a statistical power of 80% and a two-sided significance level of 0.05, and given a 6-month mortality rate of 7.7% for LRTIs, the estimated required sample size was approximately 819. Given the higher incidence of rehospitalization, this sample size is also sufficient to ensure adequate statistical power.

Statistical Analysis

Patients without completely IC dimension assessments were excluded from analyses and those lost to follow-up were excluded from the outcome analysis. Continuous variables were assessed for normality using the Shapiro–Wilk test and found not to follow a normal distribution. Hence, group comparisons for continuous variables were conducted using the Kruskal–Wallis test, followed by the Nemenyi post-hoc test. Categorical variables were compared using the Chi-square test or Fisher's exact test, followed by the Bonferrnoi post-hoc test.

Latent Class Analysis (LCA) is a type of finite mixture modeling that fits a series of models to data under the assumption that the observed multivariate distribution arises from a mixture of distributions.[12] This approach identifies subgroups by simultaneously considering multiple variables without focusing on outcomes, thus allowing to identify the clustering pattern of different pattern of IC deficit pattern. We explored models to identify 2 to 5 classes and compared them using the adjusted Bayesian Information Criterion (aBIC), Akaike's Information Criterion (AIC), Lo-Mendell-Rubin (LMR), Bootstrapped Likelihood Ratio Test (BLRT). The analysis was conducted by Mplus 8.7.

To evaluate the association of IC with the outcomes, we conducted multivariable logistic regression analysis adjusted for age, gender, severity of LRTIs, education level, marriage, attitude towards income, being able to obtain support from offspring or not, feeling of loneliness, CCI, and hemoglobin, neutrophil count, lymphocyte count and albumin, which were confirmed to have no collinearity through assessment of variance inflation factors. A two-tailed p-value of <0.05

was considered statistically significant, which was performed using R version 4.2.2. (R Foundation for Statistical Computing, Beijing, China).

Results

Baseline Characteristics

After excluding participants under 65 years old (n=19) and those with incomplete IC domain assessments (n=35), a total of 1,001 patients were included in the analysis. The mean age was 76 years (IQR: 69 to 84 years) and 59.1% were male. The mean CCI was 4.0 (IQR: 3.0 to 6.0). Most patients were married (752, 75.1%), while 183 (18.3%) were widowed. A large majority (896, 89.5%) reported receiving support from their children when needed, and 119 (11.9%) reported feeling lonely. Regarding lifestyle, 30.0% were current smokers and 14.5% were current drinkers. Most patients had mild LRTIs (62.0%), followed by moderate (33.3%) and severe cases (4.7%). Additionally, 2.8% of patients required ICU admission. The median hemoglobin level was 124.0 g/L (IQR: 110.0 to 137.0), neutrophil count was 4.8×10^9/L (IQR: 3.2 to 7.2), lymphocyte count was 1.2×10^9/L (IQR: 0.8 to 1.7) and albumin was 36.6 g/L (IQR: 33.0 to 40.0) (Table 1).

Table 1 Baseline Characteristics of Older Patients With LRTIs Stratified by Intrinsic Capacity Deficit Status

	Total(n=1001)	Without IC Deficit	IC Deficit	P value
Age (median [IQR]), years	76.0 [69.0, 84.0]	76.0[69.0, 85.0]	76.0 [69.5, 84.0]	0.684
Gender (%)				0.153
Male	592 (59.1)	104 (64.20)	488 (58.16)	
Female	409 (40.9)	58 (35.80)	351 (41.84)	
Education level (n, %)				0.485
Illiteracy	56 (5.6)	7 (4.3)	49 (5.8)	
Primary school	172 (17.2)	33 (20.4)	139 (16.6)	
Secondary or high school	405 (40.5)	60 (37.0)	345 (41.1)	
College or higher	286 (28.6)	49 (30.3)	237 (28.3)	
Missing	82 (8.2)	13 (8.0)	69 (8.2)	
Marry status (n, %)				0.160
Unmarried	1(0.1)	1 (0.6)	0 (0.0)	
Married	752 (75.1)	125 (77.2)	627 (74.7)	
Divorced	16 (1.6)	1 (0.6)	15 (1.8)	
Widowed	183 (18.3)	26 (16.1)	157 (18.7)	
Missing	49 (4.9)	9 (5.6)	40 (4.8)	
Attitude towards income (n, %)				0.523
No income	80 (8.0)	12 (7.4)	68 (8.1)	
Highly satisfied	659 (65.8)	109 (67.3)	550 (65.6)	
Moderately satisfied	205 (20.5)	37 (22.8)	168 (20.0)	
Unsatisfied	44 (4.4)	4 (2.5)	40 (4.8)	
Missing	13 (1.3)	0 (0.0)	13 (1.6)	
Able to get support from offspring (n,%)	896 (89.5)	135 (83.3)	761 (90.7)	**0.005**
Feeling lonely (n, %)	126 (12.59)	22 (13.6)	104 (12.4)	
Smoking status (n, %)				0.733
Non-smoker	602 (60.1)	96 (59.3)	506 (60.3)	
Current smoker	99 (9.9)	14 (8.6)	85 (10.1)	
Former Smoker	300 (30.0)	52 (32.1)	248 (29.6)	
Alcohol Intake (n, %)				0.936
Non-drinker	705 (70.4)	115 (71.9)	590 (70.3)	
Current drinker	151 (15.1)	25 (15.4)	126 (15.0)	
Former drinker	145 (14.5)	22 (13.6)	123 (14.7)	

(*Continued*)

Table 1 (Continued).

	Total(n=1001)	Without IC Deficit	IC Deficit	P value
Severity of LRTIs(n, %)				**0.001**
Mild	621 (62.0)	121 (74.7)	500 (59.6)	
Moderate	333 (33.3)	41 (25.3)	292 (34.8)	
Severe	47 (4.7)	0 (0.0)	47 (5.6)	
ICU admission	27 (2.8)	4 (2.5)	23 (2.9)	0.980
CCI, (median [IQR])	4.0 [3.0, 6.0]	4.00 (3.0, 5.0)	4.00 (3.0, 6.0)	0.016
Hemoglobin (median [IQR]), g/L	124.0 [110.0, 137.0]	131.00 [119.0, 144.8]	122.00 [108.0, 134.8]	**<0.001**
Neutrophil count (median [IQR]),10^9/L	4.8 [3.2, 7.2]	4.09 [3.2, 6.1]	4.86 [3.2, 7.3]	**0.040**
Lymphocyte count (median [IQR]), 10^9/L	1.2 [0.8, 1.7]	1.45 [1.1, 1.8]	1.17 [0.8, 1.7]	**<0.001**
Albumin (median [IQR]), g/L	36.6 [33.0, 40.0]	38.0 [36.0, 42.0]	36.0 [32.6, 39.7]	**<0.001**

Notes: Severity of LRTIs was defined according to oxygen support: mild (no oxygen therapy), moderate (nasal oxygen), and severe (high-flow or noninvasive ventilation, or higher); P-values in bold indicate statistical significance ($p < 0.05$).
Abbreviations: LRTIs, lower respiratory tract infections; IC, Intrinsic capacity.

Most patients (839, 83.8%) exhibited deficits in at least one IC domain. The most commonly impaired dimension was locomotion (803, 80.2%), followed by cognition (206, 20.6%), vitality (142, 14.2%), hearing (70, 7.0%), psychological well-being (68, 6.8%), and vision (63, 6.3%). Additionally, 248 patients had impairments in two dimensions, most commonly in cognition and locomotion (109, 10.9%), followed by vitality and cognition (77, 7.7%). There were 91 patients with impairments in three dimensions, most commonly in locomotion, vitality and cognition (24, 2.4%) (Figure 1).

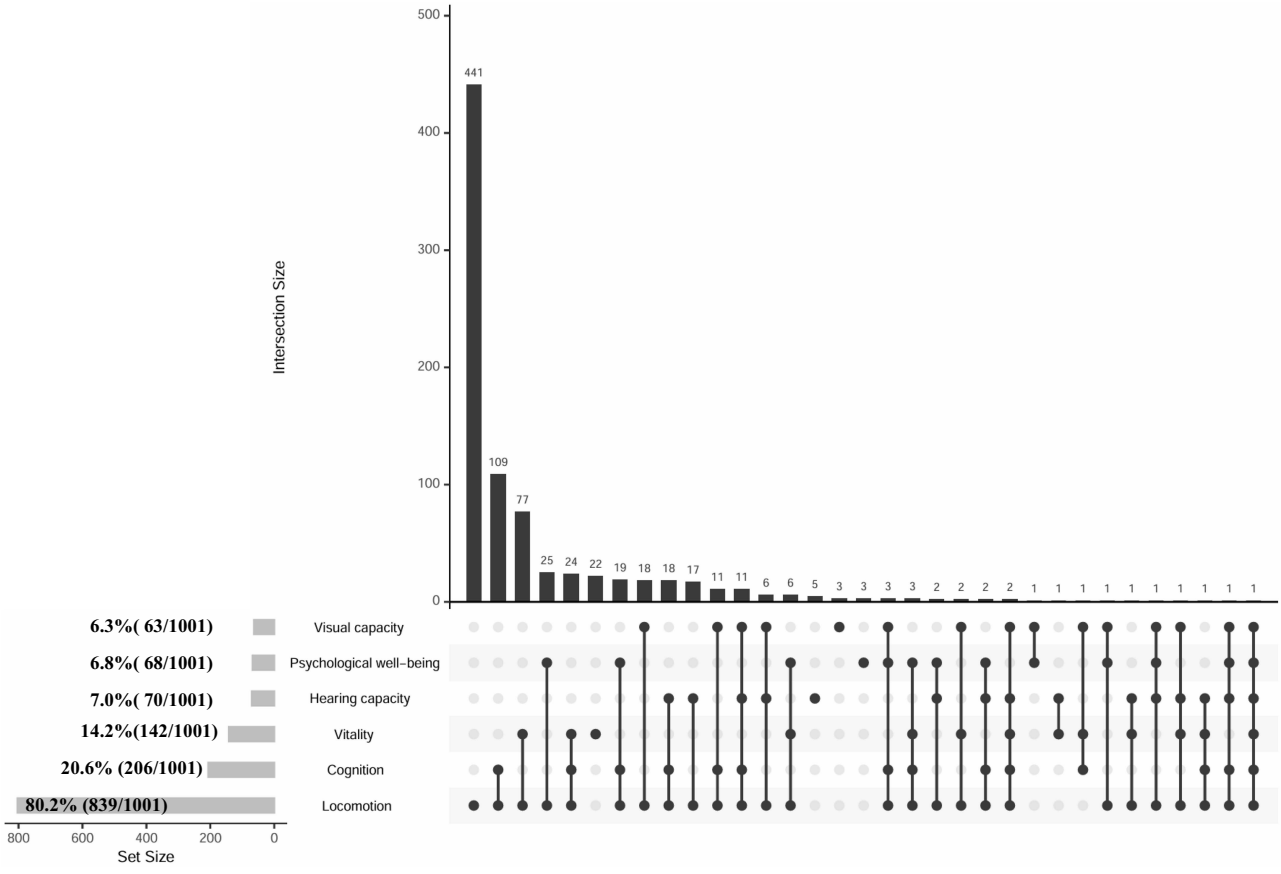

Figure 1 The deficits of intrinsic capacity in the older with LRTIs. The plot illustrates the prevalence and pattern of intrinsic capacity deficits. Left panel (horizontal bars): The total number and percentage of individuals with deficits in each intrinsic capacity domain. Top panel (vertical bars): The intersection size, representing the number of individuals with specific combinations of IC deficits. Bottom panel (dot matrix): The presence of specific IC deficits within each combination, with black dots indicating inclusion.

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Patterns of IC domain deficits were identified using LCA, with the three-class model selected as the best fit based on several indices (Table 2). This model exhibited the lowest AIC and aBIC values, alongside statistically significant p-values for LMR-LRT and BLRT. While the two-class model also showed significant p-values for LMR-LRT and BLRT, the three-class model demonstrated superior overall fit due to its lower AIC and aBIC values. The four- and five-class models did not replicate the optimal LMR-LRT and BLRT values and therefore were not considered further (Table S1).

Table 2 The Characteristic Between Different IC Deficit Patterns

	Group 1 "Relatively Robust" (N= 736)	**Group 2 "Impaired Cognition, Visual and Hearing" (N=79)**	**Group 3 "Limited Vitality and Locomotion" Group (N= 186)**	**Overall *P* value**	**Group 2 vs Group 1 *P* value**	**Group 3 vs Group 1 *P* value**
Age (median [IQR]), years	80.0[71.0,85.0]	81.0 [71.0, 86.0]	77.0 [71.0, 84.0]	**0.014**	**<0.001**	**<0.001**
Gender (n, %)				0.025	0.565	0.135
Male	442 (60.1)	54 (68.4)	96 (51.6)			
Female	294 (39.9)	25 (31.6)	90 (48.4)			
Education level (n, %)				0.575	–	–
Illiteracy	40 (5.4)	5 (6.3)	11 (5.9)			
Primary school	128 (17.4)	15 (19.0)	29 (15.6)			
Secondary or high school	297 (40.4)	26 (32.9)	82 (44.1)			
College or higher	216 (29.3)	22 (27.8)	48 (25.8)			
Missing	55 (7.5)	11 (13.9)	16 (8.6)			
Marry status (n, %)				0.797	–	–
Unmarried	0 (0.0)	1 (0.1)	0 (0.0)			
Married	53 (67.1)	555 (75.4)	144 (77.4)			
Divorced	1 (1.3)	13 (1.8)	2 (1.1)			
Widowed	19 (24.1)	132 (17.9)	32 (17.2)			
Missing	6 (7.6)	35 (4.8)	8 (4.3)			
Attitude towards income (n, %)				0.339	–	–
No income	64 (8.7)	3 (3.8)	13 (7.0)			
Highly satisfied	487 (66.2)	51 (64.6)	121 (65.1)			
Moderately satisfied	145 (19.7)	20 (25.3)	40 (21.5)			
Unsatisfied	33 (4.5)	2 (2.5)	9 (4.8)			
Missing	7 (1.0)	3 (3.8)	3 (1.6)			
Able to get support from offspring (n, %)	643 (87.4)	77 (97.5)	176 (94.6)	**0.001**	**0.040**	**0.022**
Feeling lonely (n, %)	90 (12.2)	12 (15.2)	24 (12.9)	0.745	–	–
Smoking status (n, %)				0.736	**–**	**–**
Non-smoker	444 (60.3)	47 (59.5)	111 (59.7)			
Current smoker	76 (10.3)	9 (11.4)	14 (7.5)			
Former Smoker	216 (29.3)	23 (29.1)	61 (32.8)			
Alcohol Intake (n, %)				0.494	-	-
Never-drinker	514 (69.8)	56 (70.9)	135 (72.6)			
Current drinker	116 (15.8)	14 (17.7)	21 (11.3)			
Former drinker	106 (14.4)	9 (11.4)	30 (16.1)			
Severity of LRTIs (n, %)				**<0.001**	**< 0.001**	**< 0.001**
Mild	492 (66.8)	38 (48.1)	91 (48.9)			
Moderate	238 (32.3)	34 (43.0)	61 (32.8)			
Severe	6 (0.8)	7 (8.9)	34 (18.3)			
CCI, (median [IQR])	4.0 [2.0, 5.0]	5.0 [3.0, 7.5]	5.0[4.0, 7.0]	**<0.001**	**<0.001**	**<0.001**
Hemoglobin (median [IQR]),g/L	126.0[113.0,138.0]	115.0 [103.8, 129.0]	117.5 [103.0, 129.0]	**<0.001**	**<0.001**	**<0.001**
Neutrophil count (median [IQR]), 10^9/L	4.6 [3.1, 7.0]	5.7 [3.7, 8.0]	4.9 [3.4, 7.5]	**0.034**	**0.043**	0.385
Lymphocyte count (median [IQR]), 10^9/L	1.3 [0.9, 1.7]	1.1 [0.7, 1.5]	1.1 [0.7, 1.5]	**0.002**	0.054	**0.004**
Albumin(median[IQR]), g/L	37.0 [34.0, 40.0]	35.00 [31.00, 39.10]	34.50 [30.90, 39.00]	**<0.001**	**0.008**	**<0.001**
Outcomes						
Death	51 (6.9)	7 (8.9)	12 (6.5)	0.774	-	-
Re-hospitalization	121 (16.4)	16 (20.3)	53 (28.5)	**0.001**	1.000	**<0.001**

Notes: Severity of diseases was defined according to oxygen support: mild (no oxygen therapy), moderate (nasal oxygen), and severe (high-flow or noninvasive ventilation, or higher). P-values in bold indicate statistical significance ($p < 0.05$).
Abbreviations: CCI, Charlson Comorbidity Index; IC: Intrinsic capacity.

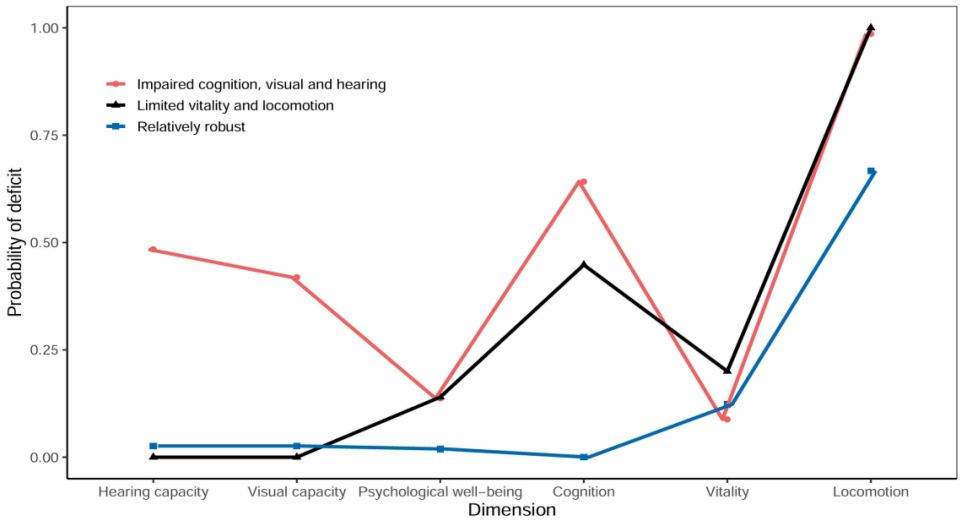

Figure 2 Three-class pattern of intrinsic capacity deficits in older adults with LRTIs identified by the best-fitting latent class analysis. The figure presents the results of a latent class analysis (LCA) used to identify subgroups of older adults with LRTIs based on their intrinsic capacity deficits. Three distinct classes were identified, represented by different lines: (1) Relatively robust group (blue line, n=736, 73.5%), (2) Limited vitality and locomotion group (red line, n=186, 18.6%), and (3) Impaired cognition, visual, and hearing group (black line, n=79, 7.9%). The y-axis represents the probability of deficits in each IC domain, and the x-axis lists the IC domains assessed.
Abbreviation: LRTIs, lower respiratory tract infections.

The results of the analysis were depicted in Figure 2, illustrating three distinct patterns: a "relatively robust" group (73.5%), a "limited vitality and locomotion" group (18.6%), and an "impaired cognition, visual, and hearing" group (7.9%). Compared to the "relatively robust" group, both the "limited vitality and locomotion" and "impaired cognition, visual, and hearing" groups exhibited lower levels of hemoglobin and albumin, a higher prevalence of severe infectious diseases, and a greater Charlson Comorbidity Index (CCI). Moreover, the "impaired cognition, visual, and hearing" group exhibited a higher average age compared to the "relatively robust" group. Additionally, the "limited vitality and locomotion" group showed a lower lymphocyte count, while the "impaired cognition, visual, and hearing" group exhibited a higher neutrophil count (Table 2) were and 7.7%.

During follow-up, 87 patients were lost, however, rehospitalization information was available for 19 of these patients (Figure S1). The 6-month re-hospitalization and mortality rates were 20.7% (190/933) and (70/914), respectively. After adjusted for demographic socioeconomic status, health information, severity of infectious disease and hemoglobin, levels of neutrophil count, lymphocyte count and albumin, the number of IC deficits [OR 1.299, 95% CI 1.041–1.621], cognition deficit [OR 1.873, 95% CI 1.191–2.922], and vitality deficit [OR 1.737, 95% CI 1.003–2.942] were associated with re-hospitalization. Comparing to "relatively robust" group, "limited vitality and locomotion" group [OR 2.025, 95% CI 1.388–2.932] was associated with re-hospitalization (Table 3). However, none of these factors was significantly associated with 6-month mortality.

Discussion

To the best of our knowledge, this was the first prospective study to analyze IC domain deficits in the older hospitalized with LRTIs, employing a data-driven approach to explore patterns of IC deficits and their associations with 6-month adverse outcomes. In our study, most of the participants exhibited at least one IC domain impairment, with locomotion being the most common dimension. Co-occurring impairments were also common, with "locomotion and cognition" being the most frequent combination. The number of IC domain deficits, as well as individual cognition and vitality deficits, were associated with 6-month re-hospitalization. Using an LCA model to identify distinct deficit patterns, three patterns emerged, with the "limited vitality and locomotion" pattern significantly associated with 6-month re-hospitalization.

There were a few researches analyzing intrinsic capacity in patients hospitalized for acute diseases.[4,5,13] Consistent with our findings, prior research reported high prevalence rates of IC impairments among older hospitalized patients. For

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Table 3 Logistic Analysis of the Number, Individual Domains, and Different Patterns of Intrinsic Capacity Deficits in Relation to 6-month Re-Hospitalization and Mortality

Variables	6-Month Re-Hospitalization (n=190)				6-Month Mortality (n=70)			
	Crude OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value	OR 95% CI	*P* value	aOR 95% CI	*P* value
Number of IC domain deficits	1.212(1.034–1.421)	**0.018**	1.299 (1.041–1.621)	**0.025**	1.109(0.863–1.409)	0.404	1.711(0.711–3.781)	0.351
IC domain deficit								
Cognition	1.721(1.200–2.470)	**0.003**	1.873(1.191–2.922)	**0.006**	1.056(0.565–1.864)	0.855	0.834(0.351–1.803)	0.660
Vitality	1.626(1.075–2.459)	**0.021**	1.737 (1.003–2.942)	**0.043**	1.417(0.725–2.585)	0.278	1.711(0.711–3.781)	0.203
Locomotion	0.944(0.638–1.398)	0.774	0.908(0.577–1.454)	0.682	1.206(0.657–2.400)	0.566	1.502(0.678–3.708)	0.343
Psychological well-being	1.212(1.034–1.421)	0.192	1.431(0.698–2.805)	0.309	0.385(0.062–1.267)	0.191	0.437(0.069–1.610)	0.285
Hearing capacity	1.072(0.584–1.970)	0.822	0.834 (0.333–1.870)	0.677	1.270(0.477–2.827)	0.592	1.816(0.565–4.889)	0.270
Visual capacity	1.005(0.525–1.924)	0.989	1.410 (0.641–2.901)	0.368	1.736(0.698–3.733)	0.191	1.613(0. 442–4.632)	0.415
Different IC deficits patterns								
Relatively robust	Ref		Ref		Ref			
Impaired cognition, visual and hearing	1.290(0.700–2.258)	0.390	1.280 (0.624–2.489)	0.360	1.305(0.545–2.809)	0.527	1.471(0.512–3.653)	0.435
Limited vitality and locomotion	2.025(1.388–2.932)	**<0.001**	1.706(1.206–2.621)	**0.016**	0.927(0.462–1.718)	0.818	0.852(0.390–1.734)	0.671

Notes: Adjusted for age, gender, education level, marriage, attitude towards income, able to get support from offspring, feeling lonely, Charlson Comorbidity Index, severity of diseases, level of hemoglobin, neutrophil count, lymphocyte count and albumin; P-values in bold indicate statistical significance ($p < 0.05$).

Abbreviation: IC, Intrinsic capacity.

instance, a study conducted with a modest sample size of hospitalized older adults reported that 95.6% participants exhibited impairment in at least one IC domain, with vitality being the most affected, followed by cognition, locomotion, psychological well-being, and sensory functions.[4] Another retrospective study[5] conducted in Zhejiang did not mention the prevalence of IC deficits but identified sensory deficit as the predominant issue, with locomotion coming in second. Echoing our findings, these studies did not uncover a direct link between individual IC domain deficit and mortality. Findings regarding the relationship between the IC composite score and long-term mortality remain inconsistent. Our results align with another study[13] that found no significant association between IC and 6-month mortality or rehospitalization. However, the IC composite score was linked to 1-year mortality in another research.[5] Additionally, a study conducted among nursing home residents indicated that a one-unit increase in locomotion performance and nutrition score decreased the probability of death by 12% (HR 0.88; 95% CI 0.78–0.99) and 4% (HR 0.96; 95% CI 0.93–0.99), respectively.[14] Possible explanations for these discrepancies include multifactorial determinants of mortality among acutely ill older adults, such as disease severity, comorbidities, and post-discharge care availability, which could overshadow the predictive ability of IC alone. Furthermore, the relatively short follow-up periods in both previous studies and the current investigation might have limited the ability to detect the long-term effects of IC impairments on mortality. Although our study did not directly associate IC deficits with mortality, we found that the "limited vitality and locomotion" pattern was linked to more severe infections, which are strongly associated with increased mortality, as confirmed by several studies.[15,16]

Previous studies conducted in acute diseases did not further analyze long-term hospitalization, whereas our study found a strong association between re-hospitalization and IC deficits. A study conducted in nursing homes found that declines in the vitality domain and the psychological domain were associated with hospitalizations for nursing home-acquired pneumonia.[17] Additionally, the IC cognitive domain deficit was associated with hospitalization.[18] Another study reported that a 1-point lower IC score (on a scale of 0–100) was associated with a 6% increase in the risk of nurse house stay.[19] Similarly, Yu et al found that cognitive decline and limited mobility significantly predicted emergency department visits during a one-year follow-up.[20] Although studies have reached different conclusions about the correlation between the extent and types of intrinsic capacity impairment and hospitalization,[21] they consistently show that IC deficits were linked to patient prognosis.

To best of our knowledge, except for our study, only one other study analyzed IC deficit patterns,[22] which was conducted in hospital outpatient settings and community public health centers in Taiwan. That study found that different deficit patterns were associated with excess polypharmacy, adverse drug reactions, and potentially inappropriate medications, but it did not mention hospitalization and mortality in the follow-up. The prevalence of different IC deficits in their study was lower than in our study, and the impairment patterns differed, likely due to the different study settings, as their population was more likely to be healthy and active older people. Our study revealed that besides locomotion, cognitive and vitality impairments often cluster together with impairments in other IC domains rather than forming independent categories, and were associated with prognosis. This may imply that different dimensions have varying prognostic value in terms of outcomes.[23]

Prior research has also shown that multi-domain interventions have the potential to improve mobility, cognition, nutritional status, depressive symptoms, and other factors[24,25]. According to the ICOPE guidelines, individuals with impaired locomotion are recommended to engage in multicomponent exercise programs, incorporating aerobic, resistance, balance, and flexibility training, along with increased protein intake and nutritional interventions. For patients with cognitive impairment, cognitive stimulation programs are advised to support cognitive function. Those with sensory deficits, such as vision or hearing impairment, may benefit from assistive devices. Additionally, for individuals experiencing depression, healthcare providers can implement short-term, structured interventions to improve mental well-being. These approaches collectively support the preventive and reversible nature of IC.[1] This perspective could also improve the care of elderly infectious patients, and suggest that alongside infection management, multidimensional assessment of intrinsic capacity impairment be undertaken. Since older patients often experience loss of functional capacities due to acute episodes, changes in living environments, and the interactions between these factors, it is crucial to assess IC domains for the older hospitalized with LRTIs as early as possible and to develop and optimize comprehensive health intervention and care plans. Although intrinsic capacity (IC) assessment and intervention hold

significant potential for improving patient outcomes in acute illness, several implementation barriers remain. For example, standardized IC assessments require specialized training, which may not be widely available, particularly in resource-limited healthcare settings. Therefore, developing simple yet effective IC assessment and intervention protocols is essential for broader clinical adoption. Future research should examine disease-specific IC deficits, longitudinally track IC trajectories, and evaluate multidimensional interventions to strengthen the evidence base and optimize clinical practice.

To sum up, this study has several notable strengths. It is the first, to our knowledge, to comprehensively evaluate IC in elderly patients hospitalized with LRTIs over a six-month follow-up period. The prospective, multicenter design across diverse healthcare settings significantly enhances the generalizability of our findings. Clinically, this study underscores the importance of early identification of IC impairments, providing clinicians with actionable insights to develop targeted interventions. Tailored strategies, including individualized rehabilitation, nutritional support, cognitive training, and medication management, can help mitigate IC deficits associated with higher re-hospitalization risks, ultimately improving patient outcomes.

Our study has some limitations. Firstly, it did not establish a definitive relationship between intrinsic capacity and mortality, the possible reason was that the follow-up period was limited to six months, resulting in an insufficient observation period to detect significant outcomes. Secondly, potential bias may arise from the choice of measurement instruments. While WHO suggests several assessment options,[26–28] consensus on suitable IC assessment tools for acute conditions is lacking, and the validity of available tools requires further investigation. Moreover, our assessment focused on post-infection IC status, while baseline IC prior to illness onset may better reflect patient resilience.[29] However, this is an inherent limitation of studies involving hospitalized patients and employing trajectory analyses or dynamic monitoring approaches in future studies could help better capture patients' true baseline IC.

Conclusions

IC domain deficits were highly prevalent in the older with LRTIs, the greater number and pattern of IC deficits, individual cognition and vitality domain deficits were associated with 6-month hospitalization. Early detection of IC deficits allows for timely interventions, potentially reducing re-hospitalization and improving overall health outcomes.

Abbreviations

LRTIs, lower respiratory tract infection; ICOPE, Integrated care for older people; IC, Intrinsic capacity; BADL, basic activity of daily living; BI, Barthel Index; GA, Geriatric assessment; PHQ-2, Patient Health Questionnaire-2; MMSE, Minimum Mental State Examination; CCI, Charlson Comorbidity Index.

Data Sharing Statement

Raw data are available upon reasonable request with the corresponding author.

Ethics Statement

The study was approved by the Ethics Committee. (ClinicalTrials.gov ID, ChiCTR2400085045). All participants provided written informed consent in accordance with the Declaration of Helsinki to participate in the study.

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An unauthorized version of the Chinese MMSE was used by the study team without permission, however this has now been rectified with PAR. The MMSE is a copyrighted instrument and may not be used or reproduced in whole or in part, in any form or language, or by any means without written permission of PAR (www.parinc.com).

Author Contributions

Bingxuan Weng and Jin Jin are first authors and contributed equally to this paper. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final

approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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