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## Implications of intrinsic capacity subtypes for post-PCI patients older than 45

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We aim to explore the contributing factors to intrinsic capacity (IC) in middle-aged and older patients after percutaneous coronary intervention (PCI). Intrinsic capacity comprises six core domains: cognition, locomotion, vitality, psychology, vision, and hearing. Each domain was assessed in detail using different scales, based on which the composite IC score was calculated. The study employed latent class analysis (LCA) to identify the various IC subtypes. Logistic regression analyses were used to determine the effect variables of IC subtypes. 318 middle-aged and older post-PCI patients filled out the assessments. Three distinct IC subtypes were found: 47.8% poor audition-vision group (class 1), 38% high cognition-psychology group (class 2), and 14.2% low locomotion-vitality group (class 3). The IC subtype classification may be impacted by factors such as cTnI, NT proBNP, cardiac function, exercise frequency, and comorbidities. Examining IC subtypes may be helpful for focused intervention, and further empirical research is still needed to determine their drivers.

Keywords Intrinsic capacity, PCI, Latent class analysis

Coronary heart disease (CHD) is the primary cause of death in cardiovascular disease (CVD), which has been a priority disease for prevention and control globally. The overall death rate from CHD among Chinese citizens, both urban and rural, was 283.27/100,000, according to the most recent China Health Statistics Yearbook. This rate rose sharply with age, with almost 74.3% of the population over 45. Percutaneous coronary intervention (PCI) is currently one of the primary treatments for CHD, and the statistics indicate that its growth rate is 26.4%. More attention must be given to the patient's general health after PCI in these cases.

Patients in the senior age group ( $\geq 75$ ) are more likely to get cautious or inadequate treatment, and becoming older is a proven indicator of a poor result following PCI<sup>1,2</sup>. Patients in this group who need to undergo PCI will again face the challenge of choosing the surgical methods and frequency<sup>3</sup>. The comorbidity, multiple medications, the number and severity of vascular lesions, and the number of stent implants may all affect the prognosis of patients undergoing PCI. Currently, the short-term functional recovery and long-term prognostic effects of drugs on patients after PCI are still unclear<sup>4</sup>. This prompts us to consider comprehensively from the perspectives of treatment, organization, and economy, while also paying attention to factors related to PCI and those that may affect the functional recovery of patients after PCI.

According to the most recent healthy ageing framework proposed by WHO, intrinsic capacity (IC) is considered the core of functional ability, which is defined as the sum of an individual's physiological and psychological abilities at any given time<sup>5</sup>. IC represents the amount of resources available to an individual's lifetime and requires a variety of health characteristics to fully reflect his or her overall state. The six interrelated domains of locomotion, cognition, vitality, psychology, vision, and hearing comprise the WHO's conceptualization of IC<sup>6,7</sup>. Intrinsic capacity declines since mid-adulthood. Studies have shown that 39.9–93.4% of middle-aged and older adults experience IC decline<sup>5,8–13</sup>, with individual characteristics (including biological indicators), lifestyles, treatments, and environments as the main influences on IC heterogeneity<sup>14–18</sup>.

Consistent with the WHO concept of interactions between IC and environments, studies have shown that 75% of the diversity in IC is driven by the cumulative effects of individual behavior and environmental exposures, which are controllable, while hereditary variables determine 25% of the diversity in IC. A recent review reached similar conclusions that social determinants (including socioeconomic status, lifestyles, psychosocial factors, material circumstances, and healthcare systems) significantly impact IC<sup>19</sup>. Understanding the socio-

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#### Methods

#### **Design and participants**

We conducted a cross-sectional study, and patients after PCI were chosen from a tertiary hospital in Zhejiang province through convenience sampling. The inclusion criteria were as follows: (1) age  $\geq$  45 years old; (2) emergency or elective PCI patients; (3) conscious, can communicate normally and cooperate in completing the assessments; (4) signed the informed consent, willing to accept the follow-up assessments. Patients with severe physical or mental illnesses, end-stage patients, pregnant women, and disabled individuals were excluded. Sociodemographic and clinical characteristics, individual behavior, environmental factors, and IC were collected through in-person interviews.

Before the study began and throughout its duration, all patients were made aware of its goal. Before the patient's evaluation, informed consent was acquired. The hospital's ethical committee approved the study (No. 20240459) on April 16, 2024, and it was carried out in compliance with the Declaration of Helsinki.

#### Measures

#### Intrinsic capacity

According to previous literature and WHO's ICOPE guidelines, the measurement tools used to evaluate IC in this study are as follows: The mini-mental state examination (MMSE) was used to assess cognition and a score of  $\leq$  17 (illiteracy), 20 (primary school), 22 (middle school), or 23 (college) indicates cognitive impairment<sup>22,23</sup>. The short physical performance battery test (SPPB) was used to assess locomotion, with a score of  $\leq$  9 indicating a decline in physical function<sup>24</sup>. The patient health questionnaire-9 (PHQ-9) was used to assess psychology, and a score of  $\geq$  10 indicates depression<sup>25</sup>. Vitality was assessed using the mini-nutritional assessment short form (MNA-SF), with a score of  $\leq$  11 indicating nutritional deficiency<sup>26</sup>. Simple questions were used for the visual and auditory assessments. A decline in any IC domain was scored as a zero. The total IC score is 0–6 points, the higher the score, the better the IC one's own.

#### Other variables

Some variables were assessed through interviews, such as age, sex, religion, ethnicity, education, marital status, occupation, family income, living areas, medical insurance, smoking, drinking, daily dietary and exercise habits, chronic disease resource utilization (through Chronic Illness Resource Survey, CIRS<sup>27</sup>, higher scores on this scale represent the better, with a mean score  $\geq$  3 considered high). The Charlson comorbidity index<sup>28</sup> (CCI, reflecting the severity of comorbidities), the number of medications, cardiac function (NYHA GEADE), and the number of stent implantations were collected from the hospital's medical record system. We obtained information on multiple coronary artery lesions through medical imaging reports. During hospitalization, N-terminal pro-B-type (NT proBNP), cardiac troponin I (cTnI), creatine kinase (CK), creatine kinase isoenzymes (CK-MB), and hypersensitive C-reactive protein (hs-CRP) were documented for several times. We selected the records tested on patients' admission for analysis. We also referred to the hospital system's definition of the normal range for blood indicators.

#### Data analysis

Descriptive statistics were used for the assessed variables. Latent Class Analysis (LCA) was performed using Mplus 8.3 to explore the heterogeneous IC subtypes of middle-aged and older patients after PCI. For the present study, four latent class models were fitted to determine the optimal number of latent classes. The optimal number of classes was chosen based on a series of model fit statistics and the interpretability of the clusters. The model fit statistics included the Akaike information criterion (AIC), Schwarz's Bayesian information criterion (BIC), the sample-size-adjusted BIC (aBIC), and the lower information criterion indicating a better model fit. Lo–Mendell–Rubin likelihood ratio test (LMR), bootstrap likelihood ratio test (BLRT), and entropy were also selected as model fit statistics. Significant LMR and BLRT could help evaluate whether a k-class model is better than a k-1 class model. The entropy presents classification accuracy, and an entropy value closer to 1 indicates better accuracy. After identifying the best-fitting profile solution, each participant was assigned to a most likely heterogeneous subtype based on their posterior class probability (no less than 5% of the total number of individuals in each class). Factors assessed were compared between groups using Chi-square tests or nonparametric tests using SPSS version 25.0. Significant variables (P < 0.1) were included in multinomial logistic regression to explore the influencing factors of IC subtypes.

#### Results

#### Decline in IC and its domains

The total sample size collected was 318, and the rate of IC decline was 80.2% (composite IC  $\leq$ 5). The mean composite IC score in middle-aged and older post-PCI patients was 4.22 (1.39), while the proportion of the decline in each IC domain varies, with 5% of the patients having cognitive impairment, 27.7% having physical function decline, 41.5% having nutritional deficiency, 14.5% having depression, 43.7% having decreased vision, and 45.3% having decreased hearing (Table 1).

#### Latent class analysis

To identify the heterogenous subtypes of IC among 318 patients after PCI, an LCA was performed on the entire sample using six indicator variables (locomotion, cognition, psychology, vitality, vision, and hearing). The results of LCA (Table 2) indicated that BLRT was significant for the two- to four-class solutions. However, LMR suggested that the 2-class and the 3-class were better than the 4-class and 5-class, respectively. Models with 3-class showed lower AIC, BIC, and aBIC than models with 2-class. Moreover, entropy values in 3-class solutions were much higher than in 2-class solutions. Therefore, the 3-class solutions were chosen to be the best fit to the data based on a series of model fit statistics.

Figure 1 shows the mean scores of six domains of IC (locomotion, cognition, psychology, vitality, vision, and hearing). The y-axis represents the probability of domains, while the x-axis represents IC domains used

Variables	Frequency (%)				
Age					
45-74	247 (77.7)				
≥75	71 (22.3)				
Sex					
Male	241 (75.8)				
Female	77 (24.2)				
Religion					
None	297 (93.4)				
Buddhism, Christianity or Islam	21 (6.6)				
Ethnicity					
Han	316 (99.4)				
Others	2 (0.6)				
Marital status					
Married	301 (94.7)				
Single, widowed, or divorced	17 (5.3)				
Occupation					
Employed	87 (27.4)				
Retired or unemployed	231 (72.6)				
Education					
Illiteracy	35 (11)				
Primary school	98 (30.8)				
Middle school	135 (42.5)				
College	50 (15.7)				
Family income (yuan)					
< 8000	112 (35.2)				
≥8000	206 (64.8)				
Living areas					
Urban	188 (59.1)				
Rural	130 (40.9)				
Medical insurance					
Medically insured	307 (96.5)				
Uninsured	11 (3.5)				
Smoking					
Yes	72 (22.6)				
Have quit smoking or never	246 (77.4)				
Drinking					
Yes	85 (26.7)				
Have quit drinking or never	233 (73.3)				

 Table 1. Basic characteristics of the population.

Model	AIC	BIC	aBIC	Entropy	LMR	BLRT
2	5810.917	5871.109	5820.361	0.550	P=0.0392	P = 0.000
3	5774.160	5864.449	5788.327	0.796	P=0.0083	P = 0.000
4	5758.320	5878.687	5777.190	0.728	P=0.1055	P = 0.000
5	5753.524	5904.006	5777.135	0.787	P=0.3478	P=0.050

Table 2. Fitting indicators for latent class models of intrinsic capacity subtypes.

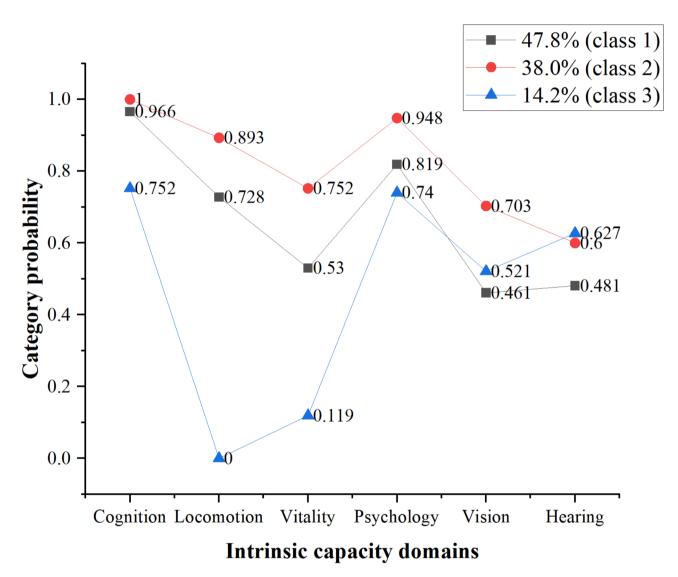


Fig. 1. Intrinsic capacity subtypes.

for the latent class analysis. The three lines showed different IC patterns for the three subtypes (Fig. 1). The first class (47.8%) was labeled as the "low audition-vision group" representing individuals with impairments predominantly in two IC domains (vision and hearing). The second class (38.0%) was labeled as the "high cognition-psychology group" representing individuals with almost no decline in two IC domains (cognition and psychology). The third class (14.2%) was labeled as the "low locomotion-vitality group" representing individuals with impairments mainly in two domains of IC (locomotion and vitality).

#### Influencing factors on IC subtypes

Univariate analysis results showed age, sex, occupation, education, drinking, exercise frequency, exercise duration, CCI, number of medications, heart function (NYHA GRADE), multiple coronary artery lesions ( $\geq 2$  large vessels and  $\geq 50\%$  stenosis), number of stent implants, NT proBNP, and cTnI were significantly different across the three IC subtypes.

The assignment of variables can be found in Table 3 (highest assigned value as reference). The results of multinomial logistic regression analysis showed that when comparing class 1 and class 3 (class 3 as reference), NYHA GRADE III–IV (OR=4.31, 95% CI [1.49–12.5]) and abnormal NT proBNP (OR=2.79, 95% CI [1.17–6.62]) were more likely to be categorized into class 3 (low locomotion-vitality group). When comparing class 2 and class 3 (class 3 as reference), exercise frequency  $\geq$  5 times per week (OR=3.12, 95% CI [1.08–8.98]), lower CCI points (OR=0.34, 95% CI [0.13–0.89]) were more likely to be categorized into class 2 (high cognition-psychology group). NYHA GRADE III–IV (OR=7.81, 95% CI [1.45–41.67]), abnormal cTnI (OR=4.90, 95% CI [1.81–13.33]) were more likely to be categorized into class 3 (low locomotion-vitality group) (Tables 4, 5).

#### Discussion

"Old age" has its own physiological definition, with 60 or 65 years of age often used as the threshold for entering old age in demographics. Most of the existing studies on IC have focused on community-dwelling older adults<sup>14,29,30</sup>, while only few studies included middle-aged adults or situated the context in a hospitalized setting. Middle-aged people, as a group entering old age, are more likely to be more resistant and resilient and have a higher marginal value for maintaining IC than patients already in old age. To our knowledge, this is the first study to explore the heterogeneous IC subtypes as well as investigate the influence factors of IC subtypes among both middle-aged and older patients after PCI. Although the widespread use of PCI in recent decades has greatly improved the prognosis of patients with CHD, patients still face major burdens from PCI-related unfavorable outcomes, and functional recovery of patients after discharge requires comprehensive attention. We found that the prevalence of IC decline in this population was 80.2%, which was higher than previous studies analyzing the IC decline of patients with CVD (64.1–68.3%)<sup>31–33</sup>. Possible reasons are the differences in regions, populations, and disease severity, or different tools have been used for assessing each domain of IC, despite the recommendations in ICOPE guidelines proposed by WHO. Future research could compare the features of the IC domain decline in post-PCI patients across different age groups and offer a detailed examination of the dose-response relationship between environmental or individual factors and the IC decline using standardized IC scoring.

In the context of precision medicine's ongoing development, better information is required to comprehend how different IC subtypes react to specific interventions. Stratifying middle-aged and older post-PCI patients by IC subtypes offers a workable path for identifying populations for whom interventions are most effective and may be more appropriate than categorizing them by age or comorbidity index. Our results revealed three distinct IC subtypes. Comorbidities, cardiac function, exercise frequency, NT proBNP, and cTnI were potential categorization-influencing factors. Highly specific and sensitive inflammatory indicators for identifying IC decline remain elusive. Tumor necrosis factor-alpha, C-reactive protein, and interleukin-6 may all be indicators of IC decline<sup>34</sup>, however, their outcomes with composite IC or each IC domain are not always consistent. A recent study found that soluble suppression of tumorigenicity 2 (sST2) was associated with microvascular occlusion after PCI in ST-segment elevation myocardial infarction (STEMI) patients<sup>35</sup>. Changes in sST2 may also affect IC in patients after PCI. Taking individual variability or the illness features of a comparable group into account, investigating the use of various analytes rather than depending on a single marker may be more advantageous and informative for tracking IC decline. Future studies can also explore the impact of more new markers on the prognosis of patients undergoing PCI.

The latent category analysis can initially reveal the characteristics of impaired capacities belonging to specific IC subtypes. However, we found that there is no difference in chronic disease resource utilization between the three IC subtypes, which may be due to monocentric environmental sampling bias or explained by the fact that IC has a certain degree of group similarity in a similar context. The feasibility of the classification of IC subtypes suggests that the cognitive, locomotor, psychological, visual, and auditory subdomains can be considered overt manifestations of capacity. On the other hand, this also reveals that the effect of severe impairment of a particular

Variables	Assignments
Age	$45 - 74 = 1, \ge 75 = 2$
Sex	Male = 1, Female = 2
Occupation	Employed = 1, Retired or unemployed = 2
Education	Illiteracy = 1, primary school = 2, middle school = 3, college = 4
Drinking	Yes = 1, Have quit drinking or never = 2
Exercise frequency (per week)	$< 5 \text{ times/week} = 1, \ge 5 \text{ times/week} = 2$
Exercise duration (per time)	$< 30 \text{ min/time} = 1, \ge 30 \text{ min/time} = 2$
CCI	$0-3p \text{ oints}=1, \ge 4 \text{ points}=2$
Number of medications	<5=1,≥5=2
NYHA	Grade I–II = 1, Grade III–IV = 2
Number of stent implants	$1 \sim 2 = 1, \ge 3 = 2$
Number of coronary lesions	1 large vessel or < 50% stenosis = 1, $\geq$ 2 large vessels and $\geq$ 50% stenosis = 2
NT proBNP (pg/mL)	≤ 300 (normal range) = 1, >3 00 = 2
cTnI (ng/L)	$\leq$ 54 (normal range) = 1, >5 4 = 2

#### Table 3. Variables assignments.

Variables	Class 1 N=152 (47.8%)	Class 2 N=121 (38%)	Class 3 N=45 (14.2%)	X <sup>2</sup>	Р
Age, n (%)				18.861	< 0.001
45-74	112	108	27		
≥75	40	13	18		
Sex, n (%)	-	1		10.544	< 0.001
Male	103	102	36		
Female	49	19	9		
Religion		1		0.301	0.908
None	141	113	43		
Buddhism, Christianity or Islam	11	8	2		
Ethnicity		1		0.627	1
Han	151	120	45		
Others	1	1	0		
Marital status		1		0.126	1
Married	144	114	43		
Single/widowed/divorced	8	7	2		
Occupational status				23.005	< 0.001
Incumbency	31	51	5		
Jobless or unemployed, retired	121	70	40		
Education	1			24.278	< 0.001
Primary school and below	85	33	15	21.270	
Middle school and above	67	88	30		
Monthly per capita household inco		00	50	1.166	0.558
< 8000	51	42	19	1.100	0.558
≥8000	101	79	26		
	101	/3	20	0.445	0.804
Living areas	07	74	27	0.445	0.804
Urban	87	74	27		
Rural	65	47	18		0.000
Type of medical expenses	1	1	1	2.612	0.276
Medically insured	144	119	43		
Uninsured	8	2	2		
Smoking		1	1	0.201	0.901
Yes	33	29	10		
Have quit smoking or never	119	92	35		
Drinking	-		1	10.295	0.006
Yes	28	42	15		
Have quit drinking or never	124	79	30		
Diet					
(1) Dietary preference				1.410	0.504
Heavy taste	86	60	23		
Insipid	66	61	22		
(2) Dietary frequency (per day)				3.812	0.127
3 times	140	118	43		
< or>3 times	12	3	2		
(3) Eating on time every day				1.625	0.432
Yes	135	109	43		
No	17	12	2		
Exercise		1	I	1	1
(1) Types				3.396	0.175
Light	134	103	43		
Moderate or heavy	18	18	2		
(2) Frequency (per week)				17.887	< 0.001
< 5 times	71	30	24		
≥5 times	81	91	24 21		
(3) Duration (each time)	01	71		9.957	< 0.001
< 30 min	61	30	21	2.75/	< 0.001
< 50 IIIII	01	30	41		

Variables	Class 1 N=152 (47.8%)	Class 2 N=121 (38%)	Class 3 N=45 (14.2%)	X2	P
≥30 min	91	91	24		
Chronic disease resource utilization				3.851	0.150
High (items≥3 points)	93	72	34		
Low (items < 3 points)	59	49	11		
CCI				32.012	< 0.001
0-3 points	77	94	16		
≥4 points	75	27	29		
Number of medications				12.619	0.002
< 5	73	72	13		
≥5 (polypharmacy)	79	49	32		
NYHA				35.084	< 0.001
Grade I –II	140	119	29		
Grade III–IV	12	2	16		
Number of stent implants				8.319	0.016
1-2	100	88	22		
≥3	52	33	23		
Number of coronary lesions				5.534	0.063
1 large vessel or < 50% stenosis	81	73	18		
$\geq 2$ large vessels and $\geq 50\%$ stenosis	71	48	27		
NT proBNP (pg/mL)				26.006	< 0.001
≤ 300	108	95	17		
> 300	44	26	28		
cTnI (ng/L)				14.744	0.001
cTnI≤54	116	107	28		
cTnI>54	36	14	17		
CK (U/L)		1		3.625	0.168
50-310	131	108	35		
< 50 or > 310	21	13	10		
CK-MB (IU/L)				3.346	0.186
≤24	130	107	43		
>24	22	14	2		
hs-CRP (mg/L)					0.112
≤6	135	108	35		
>6	17	13	10		
				1	1

#### Table 4. Differences between intrinsic capacity subtypes.

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	OR (95%CI)		
Variables	Class 1 vs. Class 3	Class 2 vs. Class 3	
NYHA	4.31 (1.49–12.5)	7.81 (1.45-41.67)	
NT proBNP	2.79 (1.17-6.62)	-	
Exercise frequency	-	3.12 (1.08-8.98)	
cTnI	-	4.90 (1.81-13.33)	
CCI	-	0.34 (0.13-0.89)	

Table 5. Results of multinominal regression analysis.

capacity on the composite IC may be covered in the short term, which would hinder the early identification of IC decline.

#### Limitations

This study has inherent bias because it is a single-center investigation. We anticipate further optimization techniques in the future to enhance this research. First, the IC subtypes we created for middle-aged and older adults after PCI may not be applicable to other populations or situations due to the degree of generalization, and the IC characteristics and correlations of other populations have not yet been studied. Second, the results'

generalizability might be constrained by the small sample size. In the future, multicenter research comparing differences in IC characteristics across different populations and their causes may be undertaken. Furthermore, the more microscopic perspective enables early detection of IC deterioration and precise intervention. Future studies could look more closely at the characteristics of impaired capacities under a certain IC subtype, including which capacities are commonly affected at the same time and whether restoring the bridge capacity improves the others. Finally, to further clarify the link between IC and the environment, dynamic monitoring to analyze longitudinal associations from a prospective standpoint is a problem worth exploring for future research.

#### Conclusion

Our findings reflect two main conclusions: From a macro viewpoint, the possible connection between a characteristic group's health and the multi-level environment, in its broadest sense, offers a helpful guide for enhancing the effectiveness of interventions. From a micro perspective, a quick decline in an individual's functioning might result from changes in one domain of IC, which can be easily disregarded in terms of their impact on composite IC. This highlights the significance of focusing on individual heterogeneity and monitoring dynamics.

#### Data availability

Data is provided within the supplementary information files.

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#### Competing interests

The authors declare no competing interests.

#### Additional information

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