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Multiple domain resilience components and frailty, postoperative complications, and one year quality of life deterioration after pancreatectomy in older patients

Jung-Yeon Choi[1,2], Yoo-Seok Yoon[3,4], Kwang-il Kim[1,2]✉ & Cheol-Ho Kim[1]

The number of older adults is growing rapidly worldwide, and many surgical diseases are prevalent in this population. Resilience, the ability to adapt positively to adversity, remains a multisystemic process with no standardized objective measurement methods. The aim of this study was to identify the association between resilience components and frailty, postoperative complications, and quality of life changes after pancreatectomy in older patients. This study evaluated older patients (aged ≥ 65) scheduled for pancreatectomy between August 2020 and December 2023. Patients who underwent a Comprehensive Geriatric Assessment and signed informed consent were included. Frailty was determined by multidimensional frailty score more than 5. Neurohumoral resilience was measured using the ACTH stimulation test, cardiovascular autonomic function using orthostatic blood pressure measurement, and cognitive-motor function using dual-task gait tests. The primary outcome was postoperative complications, and the secondary outcome was the deterioration in quality of life one year after pancreatectomy. A total of 57 patients were included in the analysis. Among them, 17 (29.8%) were classified as frail, 10 patients (17.5%) experienced postoperative complications, and 12 patients (24.5%) had worsened quality of life after one year. Low blood pressure and slow usual gait speed was associated with frailty. Diminished cortisol responsiveness correlated with frailty and postoperative complications. Quality of life deterioration was associated with differences between dual-task (serial 7) gait speed and fast gait speed. This study highlights the potential association between multidomain resilience components, frailty, and clinical outcomes in older patients undergoing pancreatectomy. Future research should focus on developing robust, objective, and reliable resilience metrics for clinical use.

Keywords Frailty, Resilience, Postoperative complications, Quality of life, Pancreatectomy

The number of older people is rapidly increasing worldwide, making them the fastest-growing age group in the population. In Korea, the proportion of people aged 65 years or older reached 19.5%, exceeding 10 million, in July 2024. By 2050, this proportion is expected to increase to as high as 44%[1]. Gastrointestinal cancers, including pancreatic cancer, have the greatest incidence in the older population. Recently, pancreatic surgery has become safe and feasible, with reported mortality rates of less than 2% and acceptable morbidity rates[2]. Therefore, many older patients are now candidates for undergoing a pancreatectomy.

Frailty is defined as clinical state of increased vulnerability resulting from aging-associated decline in reserve and function across multiple physiologic systems such that the ability to cope with acute stressors is compromised[3]. Previous meta-analysis identified frailty prevalence in pancreatic cancer is common and showed

[1]Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea. [2]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea. [3]Department of Surgery, Seoul National University Bundang Hospital, Seongnam, Republic of Korea. [4]Department of Surgery, Seoul National University College of Medicine, Seoul, Republic of Korea. ✉email: kikim907@snu.ac.kr

increased relative risk of mortality[4]. Frailty has been operationally defined by counting the number of deficits accumulated over time. The Multidimensional Frailty Score (MFS) has been developed and validated as a frailty index for older surgical candidates[5,6].

Resilience originates from the Latin 'resilire' (to leap back). Resilience is described as the capacity to thrive or "bounce back" and adapt positively regardless of adverse events[7]. Resilience can be considered a multisystemic process where psychological, biological, social, and ecological systems interact to regain, sustain, and improve an individual's mental health after adversity[8]. However, there is no standardized method for measuring resilience and defining its state. While some subjective questionnaires can be used to assess resilience, no objective measurement method has been developed[9,10].

To identify resilience components of multiple domains, we measured the neurohormonal component (cortisol level under the ACTH stimulation test), the autonomic cardiovascular component (orthostatic blood pressure measurement test), and the dual task walking test (naming animal cards and serial sevens, where a patient counts down from one hundred by sevens). In this study, the association between resilience components and frailty, postoperative complications, and one-year quality of life deterioration after pancreatectomy in older patients was analyzed.

Methods

Study population

Older patients (aged ≥ 65) who were expected to undergo pancreatectomy at a single 1,300-bed teaching tertiary hospital were evaluated between August 2020 and December 2023. Patients referred to a geriatric team for the pre-surgical CGA and who signed informed consent were included in the study. Patients who did not complete the CGA or with missing CGA data were excluded. Additionally, participants whose operations were canceled due to metastasis or other reasons, and for whom no pancreatectomy was performed were excluded. Patients whose resilience and CGA could not performed before surgery were also excluded. Baseline demographic, anthropometric, and American Society of Anesthesiologists (ASA) classification data were retrieved from electronic medical records.

Approval for human experiments

The study protocol was reviewed and approved by an Institutional Review Board of Seoul National University Bundang Hospital [B-2007-622-301]. The study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. We confirm that informed consent was obtained from all participants. To avoid including vulnerable participants, those diagnosed with dementia or scoring 15 or lower on the Mini-Mental State Examination during the comprehensive geriatric assessment were excluded from this study. All recruited participants fully understood the study and voluntarily signed the informed consent form.

Comprehensive geriatric assessment

The MFS was calculated from the CGA and laboratory test data as previously described and validated[5,6]. The CGA was used to evaluate comorbidity, problems associated with medication, physical and psychosocial function, nutritional status, and risk of postoperative delirium. Comorbidity was evaluated using the Charlson Comorbidity Index. Physical function was assessed based on patients' activities of daily living (ADLs) and instrumental ADLs (IADLs) using the modified Barthel Index and Lawton & Brody Index, respectively. Psychosocial function was determined by evaluating the patients' cognitive function and mood status using the Korean version of the Mini-Mental State Examination (MMSE-KC) and the Korean Geriatric Depression Scale. Nutritional status was assessed using the Mini Nutritional Assessment (MNA), and the risk of postoperative delirium was analyzed using the Nursing Delirium Screening Scale. A practical assessment and calculation score has been described previously, and the cutoff value for identifying high-risk, frail individuals was defined as MFS > 5[5].

Multi-organ resilience measurement

To identify resilience objectively, we assessed neurohormonal function, cardiovascular autonomic function, and dual-task walking ability. Neurohumoral resilience was measured using the ACTH stimulation test, which evaluates how well the adrenal glands respond to adrenocorticotropic hormone (ACTH). Before ACTH injection, blood was drawn to measure basal cortisol levels. Blood was then drawn again at 30 and 60 min after ACTH injection to assess cortisol levels. To evaluate cardiovascular autonomic function, we measured baseline blood pressure after 5 min of rest in the supine position. After the patients stood up, blood pressure was measured at one, two-, and three-minutes post-standing. To measure the dual-tasking ability of the participants, we assessed usual gait speed, fast gait speed, gait speed while naming animals, and gait speed while performing the serial sevens task (counting down from one hundred by sevens). We recorded the maximum and minimum values for each assessment and calculated delta values by determining the differences between maximum and minimum values, or between dual-task gait speed and fast gait speed. Ratio values were also calculated by dividing minimum values by maximum values or dual-task gait speed by fast gait speed.

Outcome

The primary outcome was postoperative complications after pancreatectomy. Postoperative complications were retrospectively evaluated from the operation date to the discharge date. These complications were defined as composite outcomes of pneumonia, urinary tract infection, delirium, pulmonary thromboembolism, and unplanned ICU admission after surgery. Delirium was assessed by psychiatric consultation or retrospective chart review by one geriatrician (JY Choi) based on the Diagnostic and Statistical Manual of Mental Disorders, 5th edition criteria[11]. Pneumonia, urinary tract infection, and pulmonary thromboembolism were assessed and

diagnosed according to the standard National Surgical Quality Improvement Program definitions[12]. Unplanned ICU admission was defined as a transfer to an ICU within the hospitalization period after surgery.

The secondary outcome was worsening quality of life one year after pancreatectomy, which was defined as a decline in the EQ-5D-5 L score compared to the preoperative value[13].

Statistical analysis

Continuous variables are expressed as mean (standard deviation [SD]) or median (interquartile range [IQR]) and compared using the t-test. Categorical variables are presented as numbers or proportions, and the chi-square or Fisher's exact test was performed. We explored the association between resilience components, MFS, postoperative complications, and worsening quality of life using the t-test. All statistical analyses were performed using SPSS (version 25.0; IBM Corp., Armonk, NY, USA).

Results

During recruitment period, total 74 patients were signed voluntarily to informed consent. Three participants withdrew their consent, surgery of six patients were cancelled because of further evaluation found the metastasis, four patients could not undergo CGA because of tight surgery schedule and one patient excluded because couldn't complete the CGA. Three participants additionally excluded because pancreatectomy was excluded from the scope of the surgery. Consequently, the analysis was conducted on a total of 57 participants. Total 17 patients (29.8%) were classified to frail (MFS > 5). Ten patients (17.5%) experienced postoperative complications. Six patients unplanned admitted to intensive care unit, three patients suffered postoperative pneumonia and five patients experienced postoperative delirium. Among 49 patients who completed one-year assessment, 24.5% ($n = 12$) of participants worsened their quality of life compared to preoperative assessment.

Among the patients who underwent pancreatectomy, frail (MFS > 5) patients were tend to older, poor nutritional status (lower body mass index, mini nutritional assessment score and mid-arm circumference) and decreased cognitive function score (MMSE-KC) Resilience components according to frailty status reveals lower maximum and minimum systolic and diastolic blood pressure were associated with frailty. Lower differences between maximum cortisol level and minimum cortisol level (Delta Cortisol) were associated with frailty ($p = 0.038$). Slower usual gait speed also correlated with frailty. ($p = 0.045$) (Table 1).

For the primary outcome, patients who experienced postoperative complications tend to have higher minimum cortisol levels ($p = 0.038$) and lower cortisol ratios (minimum cortisol level / maximum cortisol level) ($p = 0.030$) Otherwise, maximum, minimum, delta or ratio systolic and diastolic blood pressure or gait speed and dual task gait speed were not correlated with postoperative complications after pancreatectomy in older patients. (Table 2) For the secondary outcome, patients whose quality of life was worsen than preoperative at one year after pancreatectomy associated with higher difference between fast gait speed and usual gait speed, higher ratio of gait speed (usual gait speed / fast gait speed). Among the dual task walking test, difference between fast gait speed and gait speed with serial 7 test ($p = 0.004$) and ratios between serial 7 dual task gait speed and fast gait speed ($p = 0.014$) was correlated with worsened quality of life. The result of dual task gait speed with naming were similar between the groups. (Table 3).

Discussion

This study aimed to examine the association between subjectively measured multi-organ derived resilience components and frailty status, postoperative complications and one-year quality of life deterioration in older patients undergoing pancreatectomy. Measuring resilience components by ACTH stimulation test, orthostatic hypotension test and dual task gait speed test were clinically affordable and most of the participants complete the assessment. Our findings revealed significant insights into how frailty and resilience interact and impact clinical outcomes after significant stressor, pancreatectomy.

Our study confirmed frail patients exhibited poor nutritional status and cognitive function, aligning with previous studies that have highlighted the multifaceted nature of frailty[5,6,14]. The lower maximum and minimum systolic and diastolic blood pressure observed in frail patients suggests similar implications to previous studies indicating that blood pressure declines over the ten years preceding death, with a steeper decline in those who are frail[15]. The result of diminished cortisol responsiveness also correlated with frailty is similar to the previous study of frailty was associated with blunted diurnal cortisol pattern[16]. Similar to the results of previous study, frail patients exhibited slower gait speed[17]. These results which suggest a compromised physiologic reserve, and this diminished reserve likely to contribute to the increased vulnerability to stressors and adverse events, reinforcing the need for multidimensional preoperative assessment and tailored perioperative intervention for older surgical populations.

The primary outcome of postoperative complications was significantly associated with higher minimum cortisol levels and lower cortisol ratios. This indicates that patients with an impaired stress response, as evidenced by a less dynamic cortisol profile, are at greater risk of postoperative complications. For the secondary outcome of quality-of-life deterioration one-year post-pancreatectomy was linked to differences in gait speed metrics, particularly those involving dual-task conditions. Patients with a greater disparity between fast gait speed and usual gait speed, as well as those with poorer performance on dual task walking tests, were more likely to experience a decline in quality of life. This highlights the role of cognitive-motor integration and the ability to maintain function under complex conditions as critical components of resilience.

This study emphasized the complexity of resilience as a multi-systemic process involving psychological, biological, and functional domains. Since resilience questionnaires are known to related frailty status, the absence of standardized methods for measuring resilience remains a challenge, yet our approach utilizing neurohormonal, cardiovascular, and cognitive-motor assessments provide a comprehensive framework for future

	MFS ≤ 5 (*n* = 40)	MFS > 5 (*n* = 17)	*p* values
Demographic			
Age (year)	72.2 (4.4)	76.0 (4.9)	0.006
Sex (man)	23 (57.5%)	11 (64.7%)	0.612
Body mass index (kg/m^2)	24.2 (2.2)	22.3 (2.4)	0.006
ASA class (1/2/3)	0/27/13	1/9/7	0.850
Comprehensive geriatric assessment			
Charlson's comorbidity index	2.7 (1.1)	3.2 (1.2)	0.158
Number of Medications	5.0 (3.7)	5.4 (3.2)	0.699
ADL dependency (partial and full)	0 (0%)	0 (0%)	NA
IADL dependency	0 (0%)	0 (0%)	NA
MMSE-KC	26.8 (2.4)	25.1 (3.7)	0.044
SGDS-K	2.3 (2.4)	3.7 (3.8)	0.085
Timed up and go test	10.4 (1.9)	11.4 (2.6)	0.108
MNA	25.2 (2.8)	21.1 (4.6)	0.002
Mid-arm circumference (cm)	26.4 (1.9)	24.7 (2.0)	0.003
Low grip strength	9 (22.5%)	5 (29.4%)	0.579
Eq-5D	0.860 (0.053)	0.862 (0.065)	0.896
Resilience components			
Maximum SBP	133.7 (19.4)	122.7 (14.4)	0.040
Minimum SBP	119.5 (16.7)	110.0 (13.2)	0.043
Delta SBP	14.2 (9.9)	12.7 (6.5)	0.562
Ratio SBP	1.12 (0.09)	1.12 (0.06)	0.862
Maximum DBP	83.7 (9.8)	79.5 (9.0)	0.014
Minimum DBP	74.8 (7.2)	69.5 (7.6)	0.014
Delta DBP	8.7 (4.4)	7.0 (4.5)	0.196
Ratio DBP	1.11 (0.05)	1.10 (0.07)	0.442
Maximum Cortisol	30.3 (9.3)	26.1 (6.2)	0.096
Minimum Cortisol	11.3 (4.8)	11.2 (4.4)	0.938
Delta Cortisol	19.2 (6.6)	15.0 (6.5)	0.038
Ratio Cortisol	2.92 (0.93)	2.74 (1.69)	0.605
Fast gait	1.6 (0.3)	1.6 (0.3)	0.420
Usual gait	1.3 (0.2)	1.2 (0.2)	0.045
Delta gait	0.35 (0.15)	0.41 (0.29)	0.275
Ratio gait	1.28 (0.12)	1.42 (0.55)	0.288
Delta naming gait	0.16 (0.15)	0.18 (0.25)	0.700
Ratio naming gait	0.91 (0.08)	0.89 (0.14)	0.642
Delta serial7 gait	0.17 (0.12)	0.21 (0.24)	0.512
Ratio Serial7 gait	0.90 (0.06)	0.88 (0.13)	0.493

Table 1. Baseline characteristics of demographic, comprehensive geriatric assessment components and resilience components by Multidimensional Frailty score. Data are presented as mean (SD) or number (%). *ADL* activities of daily living, *ASA* American Society of Anesthesiologists, *IADL* instrumental activities of daily living, *MMSE-KC* Korean version of the Mini-Mental Status Examination, *SGDS-K* Short Form of the Korean Geriatric Depression Scale, *MNA* Mini Nutritional Assessment, *WBC* white blood cell. Significant values are in bold.

research[7,18]. The development of objective, reliable resilience metrics is essential for advancing personalized geriatric medicine, particularly for older adults undergoing major surgical procedures.

This study has some limitations. Since we conducted prospective cohort study, The number of recruited patients were insufficient. Therefore, it is possible that the significance of the resilience components was not adequately verified. Although there may be methodologies that involve applying greater stress or conducting repeated measurements to better capture the concept of resilience, such approaches might be impractical for clinical use. So, we attempted to measure the resilience of various organ systems with mini challenges using three methods (ACTH stimulation test, orthostatic hypotension test and dual task gait test) to investigate components that encompass the concept of resilience. However, the methodology used in this study may not have been sufficiently sensitive to detect actual resilience.

In conclusion, our study underscores the potential role of resilience in predicting the outcomes of older patients undergoing pancreatectomy. Minimal reaction of adrenal gland at ACTH stimulation associated with

	Complication (–) (n = 47)	Complication (+) (n = 10)	p values
Maximum SBP	130.0 (18.7)	132.1 (18.8)	0.749
Minimum SBP	116.4 (15.9)	117.8 (18.5)	0.807
Delta SBP	13.6 (9.4)	14.3 (6.8)	0.824
Ratio SBP	1.12 (0.08)	1.13 (0.07)	0.823
Maximum DBP	81.6 (10.2)	80.3 (9.8)	0.706
Minimum DBP	73.2 (7.8)	73.6 (7.3)	0.868
Delta DBP	8.5 (4.4)	6.7 (4.6)	0.251
Ratio DBP	1.12 (0.06)	1.09 (0.06)	0.205
Maximum Cortisol	29.2 (9.3)	28.5 (4.8)	0.828
Minimum Cortisol	10.7 (4.6)	14.0 (3.6)	0.038
Delta Cortisol	18.5 (7.0)	14.5 (4.6)	0.094
Ratio Cortisol	3.03 (1.24)	2.13 (0.51)	0.030
Fast gait	1.6 (0.3)	1.6 (0.3)	0.969
Usual gait	1.3 (0.2)	1.2 (0.3)	0.209
Delta gait	0.35 (0.15)	0.45 (0.36)	0.403
Ratio gait	1.28 (0.12)	1.50 (0.72)	0.349
Delta naming gait	0.15 (0.15)	0.23 (0.28)	0.203
Ratio naming gait	0.91 (0.09)	0.87 (0.14)	0.241
Delta serial7 gait	0.17 (0.13)	0.21 (0.26)	0.542
Ratio Serial7 gait	0.90 (0.08)	0.88 (0.14)	0.727

Table 2. Association between Baseline Resilience Components and postoperative complication. Significant values are in bold.

	Not worsen Eq-5D (n = 37)	Worsen Eq-5D (n = 12)	p values
Maximum SBP	130.4 (17.5)	124.8 (18.1)	0.340
Minimum SBP	117.2 (16.8)	112.3 (12.4)	0.356
Delta SBP	13.2 (9.2)	12.4 (7.2)	0.799
Ratio SBP	1.12 (0.88)	1.11 (0.05)	0.735
Maximum DBP	82.8 (10.8)	77.0 (9.1)	0.100
Minimum DBP	73.8 (8.6)	70.3 (5.4)	0.181
Delta DBP	9.0 (4.4)	6.8 (4.8)	0.144
Ratio DBP	1.12 (0.06)	1.09 (0.07)	0.156
Maximum Cortisol	29.3 (9.6)	28.0 (6.5)	0.665
Minimum Cortisol	10.8 (4.8)	11.4 (3.5)	0.665
Delta Cortisol	18.5 (7.0)	16.6 (6.2)	0.391
Ratio Cortisol	3.01 (1.27)	2.64 (1.06)	0.375
Fast gait	1.6 (0.3)	1.7 (0.3)	0.088
Usual gait	1.3 (0.2)	1.3 (0.2)	0.744
Delta gait	0.32 (0.14)	0.45 (0.13)	**0.005**
Ratio gait	1.26 (0.11)	1.36 (0.10)	**0.007**
Delta naming gait	0.13 (0.12)	0.19 (0.21)	0.238
Ratio naming gait	0.92 (0.08)	0.90 (0.10)	0.504
Delta serial7 gait	0.13 (0.11)	0.25 (0.12)	**0.004**
Ratio Serial7 gait	0.92 (0.07)	0.86 (0.05)	**0.014**

Table 3. Association between Baseline Resilience Components and worsening quality of life one year after surgery. Significant values are in bold.

frailty and postoperative outcome. Lower blood pressure is associated with frailty and impaired cognitive-motor integration associated with worsening quality of life after surgery. By advancing our understanding of the interplay between frailty, multidimensional resilience components, and surgical outcomes, we pave the way for more effective, individualized patient risk stratification and build the resilience that enhance both immediate and long-term health related outcomes and quality of life[19].

Data availability

Anonymized datasets can be made available on reasonable request after approval from the trial management committee and after signing a data access agreement. Proposals should be directed to the corresponding author.

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Author contributions

Conceptualization, data curation, formal analysis, investigation, methodology, visualization, funding acquisition, and writing of the original draft: J-Y C. Conceptualization, resources, validation, writing–review & editing: Y-S Y. Conceptualization, investigation, funding acquisition, writing–review, and editing: K-i K. Conceptualization, investigation, project administration, writing–review, and editing: C-H K.

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Additional information

Correspondence and requests for materials should be addressed to K.-i.K.