



저작자표시-비영리-변경금지 2.0 대한민국

이용자는 아래의 조건을 따르는 경우에 한하여 자유롭게

- 이 저작물을 복제, 배포, 전송, 전시, 공연 및 방송할 수 있습니다.

다음과 같은 조건을 따라야 합니다:



저작자표시. 귀하는 원저작자를 표시하여야 합니다.



비영리. 귀하는 이 저작물을 영리 목적으로 이용할 수 없습니다.



변경금지. 귀하는 이 저작물을 개작, 변형 또는 가공할 수 없습니다.

- 귀하는, 이 저작물의 재이용이나 배포의 경우, 이 저작물에 적용된 이용허락조건을 명확하게 나타내어야 합니다.
- 저작권자로부터 별도의 허가를 받으면 이러한 조건들은 적용되지 않습니다.

저작권법에 따른 이용자의 권리는 위의 내용에 의하여 영향을 받지 않습니다.

이것은 [이용허락규약\(Legal Code\)](#)을 이해하기 쉽게 요약한 것입니다.

[Disclaimer](#)

의학석사 학위논문

근치적 방광절제술에서 의료기록 기반 노쇠지수가
수술 후 1년 사망률에 미치는 영향

Impact of Chart-Derived Frailty Index on 1-Year Mortality after
Radical Cystectomy in 1,004 Patients with Bladder Cancer

울산대학교 대학원

의학과

이지웅

근치적 방광절제술에서 의료기록 기반 노쇠지수가
수술 후 1년 사망률에 미치는 영향

지도교수 김영국

이 논문을 의학석사 학위논문으로 제출함

2024년 02월

울산대학교 대학원

의학과

이지웅

이지웅의 의학석사 학위논문을 인준함

| | | |
|------|-------|---|
| 심사위원 | 박 준 영 | 인 |
| 심사위원 | 김 영 국 | 인 |
| 심사위원 | 서 영 주 | 인 |

울 산 대 학 교 대 학 원

2024년 2월

ABSTRACT

Background

Radical cystectomy is a major urologic procedure with high morbidity and mortality rates. The chart-derived frailty index (CFI) is an evaluation tool that could be calculated using demographic and routine laboratory variables without requiring additional cost and effort. Therefore, the author assessed the impact of CFI on 1-year mortality rates after radical cystectomy.

Methods

This retrospective study included patients with bladder cancer who underwent radical cystectomy in 2007–2021. CFI was the sum of the following five parameters: age >70 years, body mass index <18.5 kg/m², hematocrit <35%, albumin <3.4 g/dL, or creatinine >2.0 mg/dL. Patients were divided into those with a low (0–2) versus high (3–5) CFI. The 1-year all-cause and cancer-specific mortality rates after radical cystectomy were evaluated.

Results

Of 1,004 patients, 914 (91.0%) had a low CFI and 90 (9.0%) had a high CFI. The 1-year all-cause mortality rates of patients with a low versus high CFI were 12.0% and 27.8%, respectively ($P < 0.001$). Multivariate Cox regression analysis revealed that high CFI ($P < 0.001$), tumor stage ($P = 0.003$), and red blood cell transfusion amount ($P < 0.001$) were significantly associated with 1-year all-cause mortality after radical cystectomy. Kaplan–Meier analysis demonstrated significantly different 1-year all-cause and cancer-specific mortality rates after radical cystectomy between patients with a high CFI and those with a low CFI (log-rank test, both $P < 0.001$).

Conclusion

A high CFI is associated with higher 1-year mortality rates after radical cystectomy, suggesting that CFI can predict effectively postoperative outcomes in radical cystectomy.

TABLE OF CONTENTS

| | |
|----------------------------|-----|
| ABSTRACT..... | i |
| LIST OF FIGURES | iii |
| LIST OF TABLES..... | iv |
| | |
| INTRODUCTION..... | 1 |
| MATERIALS AND METHODS..... | 2 |
| RESULTS..... | 5 |
| DISCUSSION..... | 6 |
| CONCLUSION | 9 |
| REFERENCE | 17 |
| ABSTRACT IN KOREAN..... | 19 |

LIST OF FIGURES

| | |
|----------------|----|
| Figure 1 | 10 |
| Figure 2 | 11 |
| Figure 3 | 12 |
| Figure 4 | 13 |

LIST OF TABLES

| | |
|---------------|----|
| Table 1 | 14 |
| Table 2 | 15 |
| Table 3 | 16 |

INTRODUCTION

Although radical cystectomy is the preferred treatment for muscle-invasive bladder cancer, it is a urologic procedure with high morbidity and mortality rates.¹ Bladder cancer is prevalent among elderly individuals, featuring the highest median age among all cancers.^{2,3} Moreover, perioperative complication risks are amplified in elderly patients, who have lower physiological reserve and poor functional status.⁴ Therefore, preoperative risk stratification, which could be easily and effectively evaluated in the clinical setting, is required for elderly patients with bladder cancer.

Frailty is a multi-system deterioration in function characterized by a loss of physiologic reserve.⁵ Frailty could be discriminated from aging or disability alone.⁶ Recently, the concept of frailty has been adopted to predict oncological survival, disease progression, and postoperative outcomes.^{7,8} Particularly, in patients with cancer, frailty is positively correlated with postoperative mortality and morbidity.⁹ Therefore, evaluations of the preoperative frailty of patients with cancer are crucial. The chart-derived frailty index (CFI) is an evaluation tool that could be calculated using demographic (including age and body mass index [BMI]) and routine laboratory variables (including hematocrit, albumin, and creatinine) without requiring additional cost and effort. However, to the best of author's knowledge, no studies have evaluated the association between CFI and 1-year mortality rates in patients with bladder cancer who underwent radical cystectomy.

The author hypothesized that CFI as a useful index of frailty could predict the postoperative outcomes of radical cystectomy. Therefore, the author assessed the impact of preoperative CFI on postoperative 1-year mortality rates in patients with bladder cancer who underwent radical cystectomy.

MATERIALS AND METHODS

Study design and patients

This retrospective study was approved by the Institutional Review Board of Asan Medical Center, Seoul, Republic of Korea (approval no. 2022-0077). The author reviewed and analyzed the medical records of patients who underwent radical cystectomy due to bladder cancer at Asan Medical Center between January 2007 and April 2021. Patients for whom complete medical records were unavailable, those who underwent radical cystectomy combined with other surgery, and those who underwent radical cystectomy for other cancers were excluded.

Perioperative management

General anesthesia was induced with thiopental sodium or propofol and rocuronium and maintained with sevoflurane or desflurane. Arterial and central venous catheterizations were performed. The concentration of sevoflurane or desflurane was adjusted to maintain a bispectral index of 40–60. Mean arterial blood pressure was controlled to >65 mmHg using fluids and inotropic agents or vasopressors such as ephedrine, phenylephrine, or norepinephrine.

All procedures including radical cystectomy, pelvic lymphadenectomy, and urinary diversion were performed according to Asan Medical Center's standard protocol.¹⁰⁻¹² Urologic surgeons performed standard or extended pelvic lymph node dissections. A standard pelvic lymph node dissection included the external iliac, internal iliac, obturator, and perivesical lymph nodes. An extended lymph node dissection included the mentioned lymph nodes plus those at the level of the para-aorta, inferior vena cava, and common iliac artery. A urinary diversion with an ileal conduit or neobladder was performed at the surgeons' discretion.

Definition of CFI

CFI was defined according to the Amrock method.¹³ The CFI was represented by the sum of the five parameters: age >70 years, preoperative BMI <18.5 kg/m², hematocrit <35%, albumin <3.4 g/dL, or serum creatinine >2.0 mg/dL. Patients were divided into two groups: those with a high (3–5) or low (0–2) CFI.¹⁴

Data collection

The author collected the patients' demographic and preoperative variables including sex, age,

BMI, American Society of Anesthesiologist physical status, comorbidities (i.e., diabetes mellitus, hypertension, coronary artery disease, cerebrovascular disease, and chronic obstructive pulmonary disease), smoking history, tumor stage, tumor grade, neo-adjuvant chemotherapy, preoperative laboratory tests (i.e., hematocrit, platelets, albumin, creatinine, aspartate aminotransferase [AST], alanine aminotransferase [ALT], and uric acid levels), and CFI. Coronary artery disease included a history of myocardial infarction, angina, heart attack, interventional angioplasty, or coronary artery bypass graft surgery. Cerebrovascular disease included cerebrovascular accident, transient ischemic accident, stroke, or mini-stroke. Chronic obstructive pulmonary disease included chronic obstructive airway disease, emphysema, or chronic bronchitis. Tumor stage was evaluated by the 2010 American Joint Committee on Cancer tumor-node-metastasis staging system.¹⁵ Tumor grade was evaluated using the 2016 World Health Organization grading system.¹⁶ Neo-adjuvant chemotherapy was conducted with one of the following combinations: cisplatin and gemcitabine; cisplatin, sulfate, and doxorubicin; carboplatin and gemcitabine; or vinblastine and methotrexate.

The author collected intraoperative variables including operation time, hypotensive event, crystalloid and colloid amounts, red blood cell (RBC) transfusion rate and amount, and reversal agent of neuromuscular blockade in radical cystectomy. Intraoperative hypotension was defined as a mean arterial blood pressure <65 mmHg during more than 5 minutes. Crystalloids such as lactated Ringer's solution or PlasmaLyte and colloids such as 6% hydroxyethyl starch or 5% albumin were administered during the radical cystectomy. RBC transfusions were administered when serum hemoglobin concentration was <8 g/dL. A neostigmine-glycopyrrolate mixture or sugammadex was used to reverse neuromuscular blockade at the anesthesiologist's discretion.

The author collected postoperative outcomes including 1-year all-cause and cancer-specific mortalities.

Statistical analysis

Normality was tested using the Kolmogorov-Smirnov test. Continuous variables are expressed as median with interquartile range (Q1–Q3), while categorical variables are expressed as number (percent). Continuous variables were compared using the Mann–Whitney U-test and categorical variables were compared using the chi-square test or Fisher's exact test.

Univariate and multivariate cox regression analyses were performed to identify independent risk factors for postoperative 1-year all-cause mortality. All covariates with values of $P < 0.05$ in the univariate Cox regression analysis were included in the multivariate Cox regression analysis. Postoperative 1-year mortality rates between patients with a high versus low CFI were compared using the Kaplan–Meier analysis with log-rank test. The postoperative 1-year mortality rates were subgroup

analyzed based on both all-cause and cancer-specific mortality to investigate difference according to the causes of death. The variance inflation factor was examined to check for multicollinearity. Variables with a variance inflation factor >10 were considered highly multicollinear and excluded from the analyses. Values of P <0.05 were considered statistically significant. All statistical analyses were performed using MedCalc version 11.3.3.0 (MedCalc Software bvba, Mariakerke, Belgium) and SPSS® version 21.0 software (IBM, Armonk, NY, USA).

RESULTS

A total of 1,098 patients with bladder cancer underwent radical cystectomy between January 2007 and April 2021. Of them, 94 were excluded (seven due to incomplete medical records, 74 due to undergoing other surgical procedures combined with radical cystectomy, 13 due to undergoing radical cystectomy for other cancers). Thus, 1,004 patients were included in this study. A total of 914 (91.0%) patients had a low CFI, while 90 (9.0%) had a high CFI (Figure 1). The 1-year all-cause mortality rates after radical cystectomy of patients with a low versus high CFI were 12.0% and 27.8%, respectively (Figure 2).

Patients' demographic, preoperative, and intraoperative variables were divided according to 1-year all-cause mortality rate after radical cystectomy in Tables 1 and 2. A high CFI, age, BMI, American Society of Anesthesiologists physical status, tumor stage, hematocrit, albumin, creatinine, AST, ALT, crystalloid amount, RBC transfusion rate, and RBC transfusion amount were all significantly different between patients with mortality and those with non-mortality.

Univariate Cox regression analysis revealed that high CFI, American Society of Anesthesiologists physical status, tumor stage, crystalloid amount, and RBC transfusion amount were significantly associated with 1-year all-cause mortality after radical cystectomy. The multivariate Cox regression analysis revealed that high CFI (odds ratio [OR], 2.312; 95% confidence interval [CI], 1.480–3.611; $P < 0.001$), tumor stage (OR, 1.674; 95% CI, 1.185–2.365; $P = 0.003$), and RBC transfusion amount (OR, 1.285; 95% CI, 1.211–1.363; $P < 0.001$) were significantly associated with 1-year all-cause mortality after radical cystectomy in patients with bladder cancer (Table 3). The 1-year all-cause mortality rates of patients with a CFI of 0, 1, 2, 3, and 4 were 7.1%, 11.9%, 21.9%, 26.3%, and 40.0%, respectively (Figure 3). The Kaplan-Meier analysis demonstrated similar trends in 1-year all cause and cancer-specific mortality rates after radical cystectomy in bladder cancer patients. In the Kaplan-Meier analysis, significant differences were observed in the 1-year all-cause and cancer-specific mortality rates after radical cystectomy between patients with high versus low CFI (log-rank test, both $P < 0.001$; Figures 4A, 4B).

DISCUSSION

The present study evaluated the association between preoperative frailty calculated by the CFI scoring system and postoperative 1-year mortality in 1,004 patients with bladder cancer who underwent radical cystectomy. A high CFI (score ≥ 3) was 9.0% (90/1,004). Postoperative 1-year all-cause mortality rates of patients with a low versus high CFI were 12.0% and 27.8%, respectively. This study revealed that a high CFI was associated with 1-year all-cause mortality after radical cystectomy in patients with bladder cancer. These findings suggest that CFI as an indicator of frailty is an easy and effective method of preoperatively identifying frail cohorts using demographic and routine laboratory variables in clinical practice.

Radical cystectomy, among the most complex urological surgery for bladder cancer, features high postoperative morbidity and mortality rates despite providing good long-term oncological prognosis.^{1,2} Bladder cancer occurs predominantly in elderly individuals with comorbidities, who are at considerable risk for postoperative complications and mortality.² As society continues to age, surgeons should perform radical cystectomy in elderly patients. Therefore, preoperative risk stratification for radical cystectomy candidates is increasingly important for improving the postoperative outcomes of these patients.

Frailty is not a synonymous with comorbidity but rather a multidimensional physiologic decline condition characterized by loss of physiologic reserve and decreased resistance to stressors.⁵ Patients with frailty have dysregulated immune and inflammatory responses and are vulnerable to intrinsic and extrinsic stressors.¹⁷ Frailty is increasingly common in patients with bladder cancer undergoing radical cystectomy and is considered an important risk factor for adverse outcomes and mortality.¹⁸⁻²⁰ Taken together, frailty evaluations have attracted attention to predict postoperative adverse outcomes such as prolonged hospitalization, morbidity, and mortality in radical cystectomy. However, methods used to assess frailty vary widely, as do the obtained results.

The author evaluated preoperative frailty using the CFI scoring system. This is first study to evaluate the association of CFI and postoperative mortality in radical cystectomy. The CFI was simply calculated using demographic variables (including age and BMI) and routine laboratory variables (including preoperative serum hematocrit, albumin, and creatinine levels).¹³ Amrock et al. demonstrated that the CFI effectively measures frailty compared to the Robinson score and 11-factor modified frailty index.¹³ Among various frailty evaluation tools, the Fried frailty index, a frailty assessment tool requiring prospective evaluation of functional capacity, includes unintentional weight loss, weakness, self-reported exhaustion, slow walking speed, and low physical activity.⁵ Another frailty assessment

tool, the 5-item modified frailty index score, requires careful medical history taking and is assessed by the number of comorbid conditions (including diabetes mellitus, hypertension, chronic obstructive pulmonary disease, and congestive heart failure) and functional health status.^{21,22} Compared with these other frailty tools, the CFI in this study seems to have clear advantages for assessing the preoperative frailty status. After preoperative frailty assessment by CFI as an objective tool, physicians can have an opportunity to improve postoperative outcomes in frail patients by the modification of frailty factors such as anemia and hypoalbuminemia in the preoperative period. Therefore, preoperative frailty status can be evaluated simply and effectively by the CFI scoring system in patients with bladder cancer who are undergoing radical cystectomy.

The present study found that 90 (9.0%) patients had a high CFI on three or more of the five frailty domains. The 1-year all-cause mortality rate after radical cystectomy was higher in patients with a high versus low CFI (27.8% vs. 12.0%, respectively). Moreover, the author found that a high preoperative CFI was an independent risk factor for 1-year mortality after radical cystectomy in patients with bladder cancer. In line with the present study's result, several previous studies revealed that frailty was significantly associated with postoperative complications and mortality in patients with bladder cancer who underwent radical cystectomy.^{21,23} In previous studies, frailty was evaluated by various frailty evaluation tools.^{21,23} Chappidi et al. reported that frailty was associated with adverse outcomes including Clavien grade 4 or 5 complications and overall mortality rate within 30 days after radical cystectomy.^{21,23} They evaluated frailty using the modified frailty index, which was defined based on comorbidities and activities of daily living.^{21,23} Likewise, Yamashita et al. reported that a high preoperative 5-item modified frailty index score could be a significant independent risk factor of a poor prognosis after radical cystectomy.²¹ Based on these considerations, the impact of preoperative frailty status on postoperative outcomes could not be ignored, and a preoperative frailty evaluation is needed to predict postoperative mortality in patients with bladder cancer who undergoing radical cystectomy.

This study also found other risk factors associated with 1-year mortality after radical cystectomy. High CFI, tumor stage, and RBC transfusion amount were associated with increased mortality in patients undergoing radical cystectomy for bladder cancer. In a prior study, tumor stage and volume of RBC transfusion were identified as factors contributing to increased morbidity and mortality. Tumor stage was found to be associated with surgical complexity, tumor progression and recurrence.²⁴ RBC transfusion amount was related to infection, tissue ischemia, and tumor recurrence due to immune modulation.²⁵ Meticulous patient blood management (PBM) should be encouraged to improve postoperative outcomes.

Relevant study limitations should be acknowledged. First, this study had a retrospective design; therefore, it was limited in size and subject to selection bias. However, the author included almost all

covariate factors related to mortality in patients with bladder cancer who underwent radical cystectomy. As another important limitation, this study's results might not be readily applicable in other types of facilities because all treatment was performed by highly specialized team at a large single center. Therefore, this study's results must be generalized cautiously.

CONCLUSION

This study demonstrated that preoperative frailty assessed via the CFI could be an independent significant predictor of postoperative outcomes including 1-year all-cause mortality after radical cystectomy in patients with bladder cancer. As the mean age of patients undergoing radical cystectomy continues to increase, preoperative assessments of frailty will become increasingly important in stratifying risk and optimizing outcomes. The CFI can be easily and simply calculated using preoperative demographic and laboratory variables, allowing the effective prediction of morbidity and mortality after radical cystectomy.

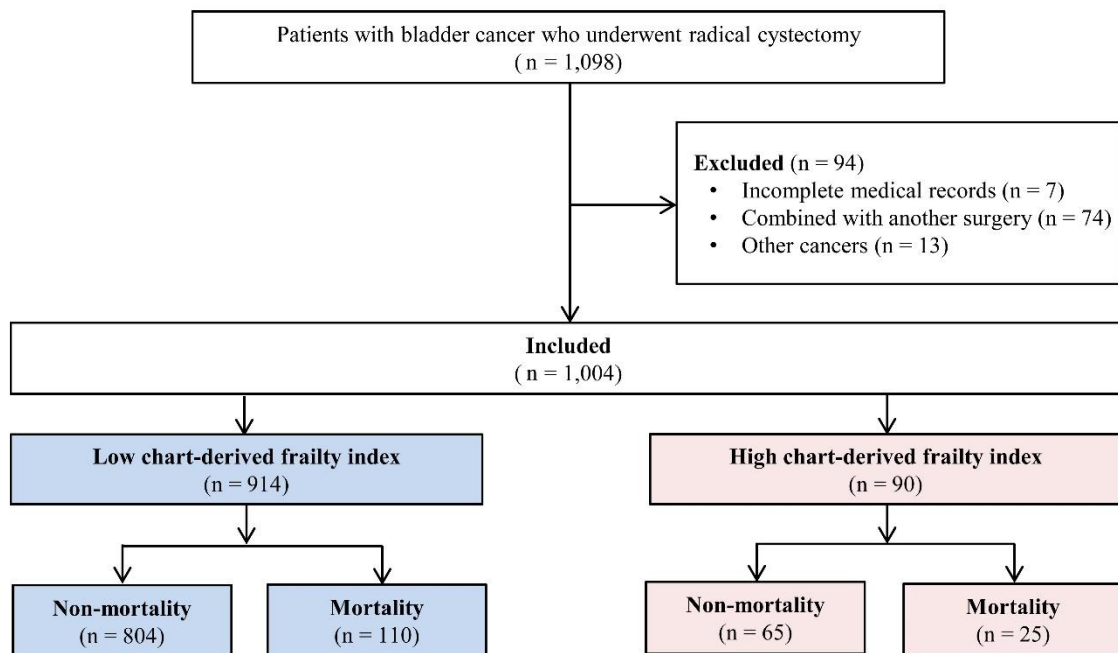


Figure 1. Flowchart of the study patients. The CFI was the sum of the following five parameters: age >70 years, body mass index <18.5 kg/m², hematocrit <35%, albumin <3.4 g/dL, or creatinine >2.0 mg/dL. A low CFI was defined as a score of 0–2, while a high CFI was defined as a score of 3–5. CFI, chart-derived frailty index.

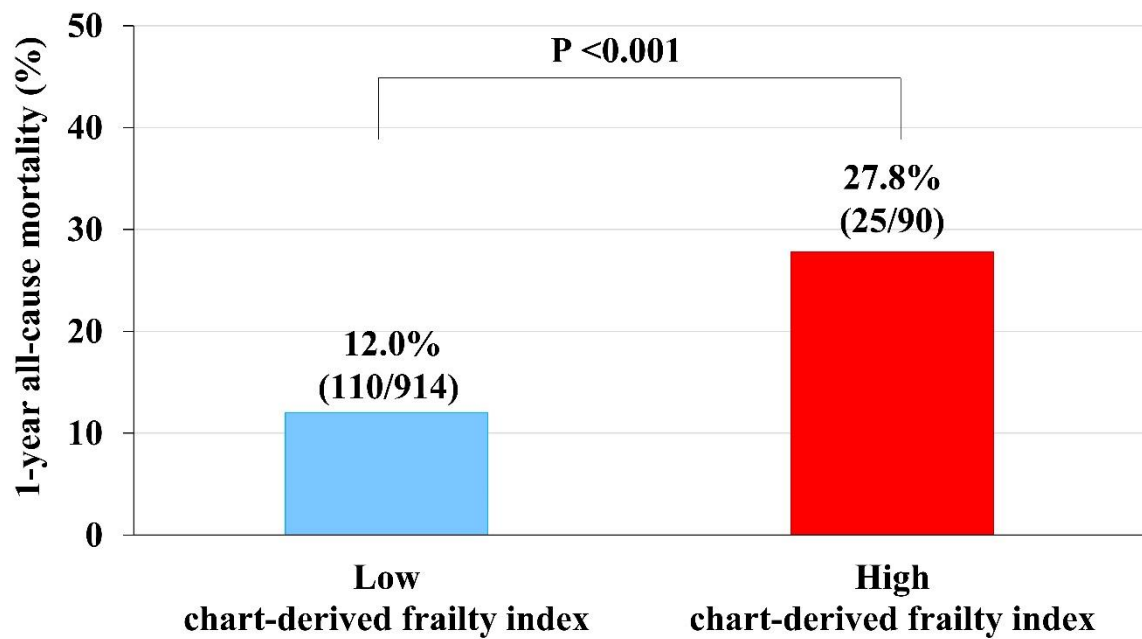


Figure 2. Comparison of 1-year all-cause mortality rates after radical cystectomy between patients with low versus high CFI. CFI was represented by the sum of the following five parameters: age >70 years, body mass index <18.5 kg/m², hematocrit <35%, albumin <3.4 g/dL, or creatinine >2.0 mg/dL. A low CFI was defined as a score of 0–2, while a high CFI was defined as a score of 3–5. CFI, chart-derived frailty index.

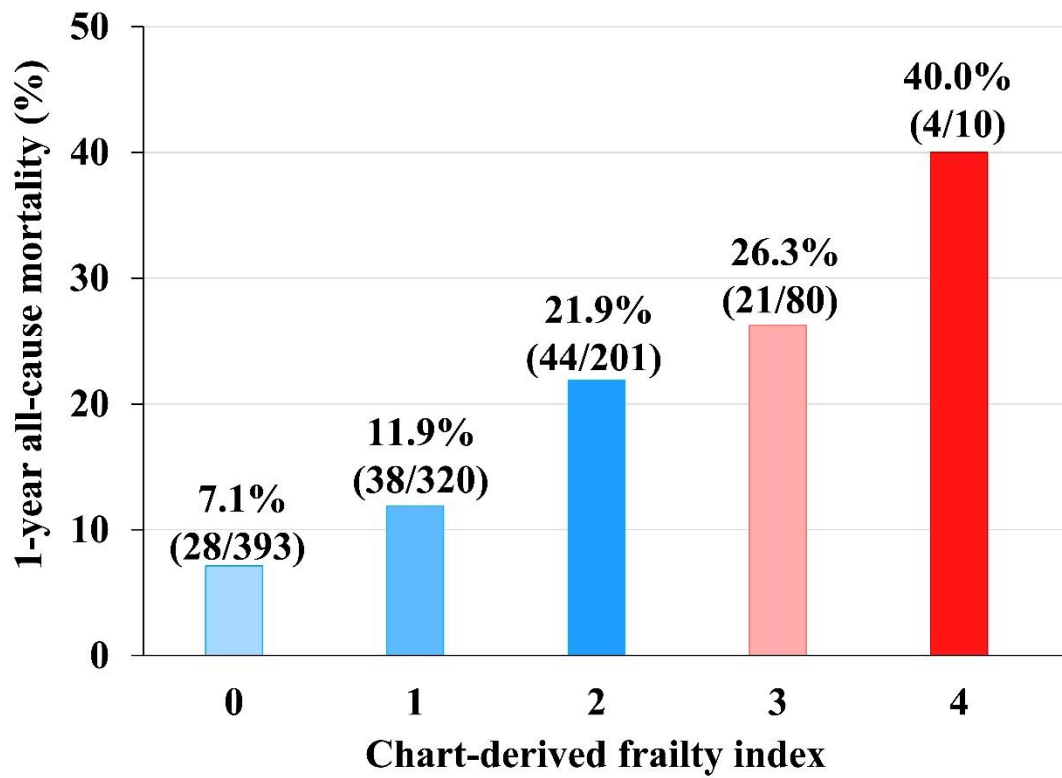


Figure 3. Comparison of 1-year all-cause mortality rates after radical cystectomy by CFI of 0, 1, 2, 3, 4, and 5. CFI of 5 was excluded as there was no patient meeting the criteria. The CFI was the sum of the following five parameters: age >70 years, body mass index <18.5 kg/m², hematocrit <35%, albumin <3.4 g/dL, or creatinine >2.0 mg/dL. CFI, chart-derived frailty index.

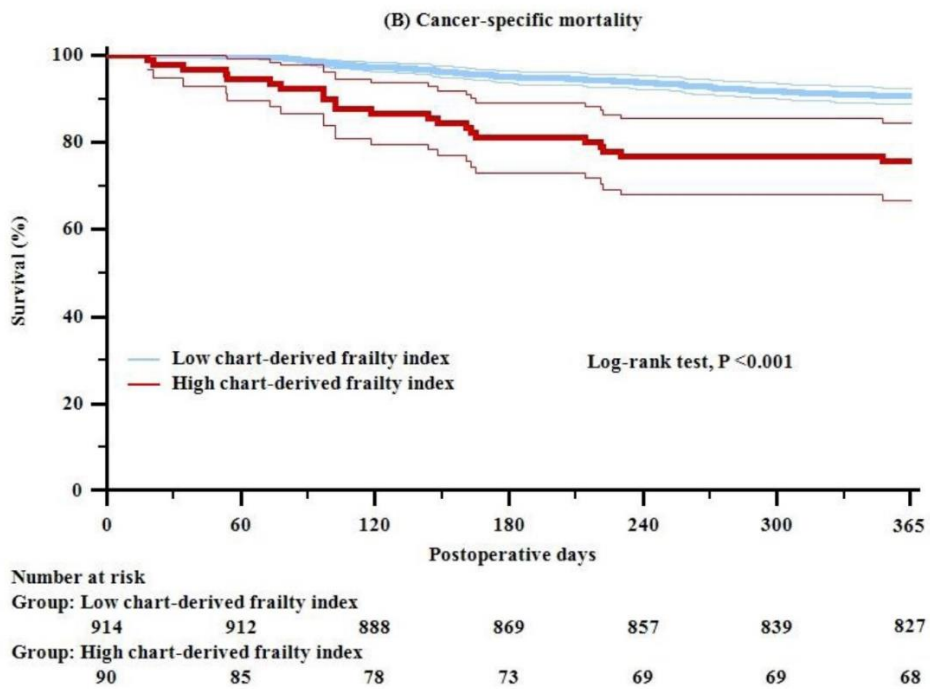
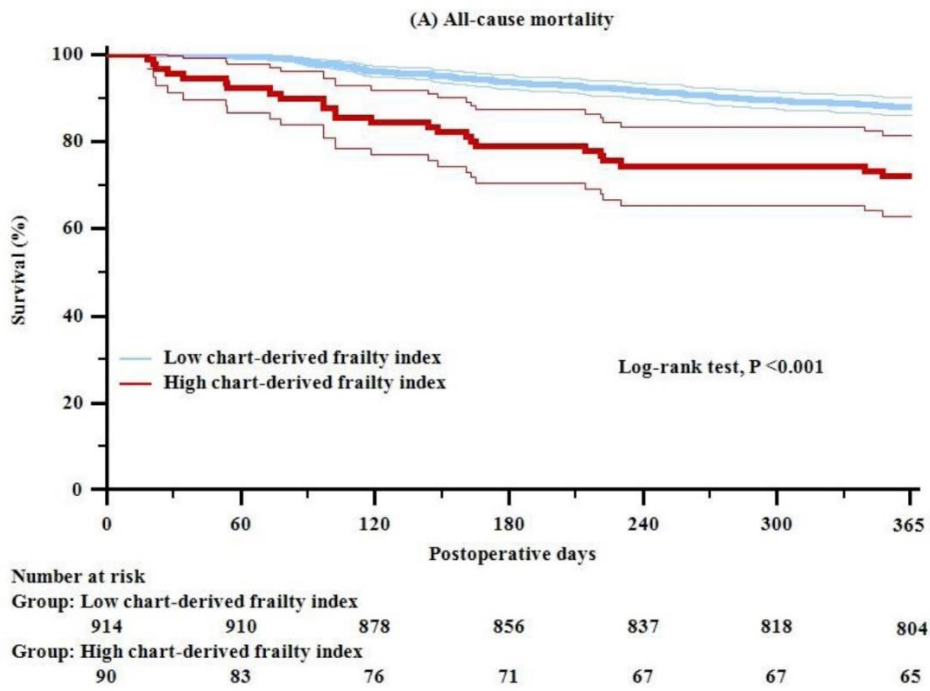


Figure 4. Kaplan–Meier curves of 1-year all-cause mortality (A) and 1-year cancer-specific mortality (B) including 95% confidence intervals. The two thin lines show the 95% confidence intervals.

Table 1. Patients' demographics and preoperative variables

| Variables | Non-mortality (n = 869) | Mortality (n = 135) | P |
|------------------------------------|----------------------------|------------------------|--------|
| Sex, male | 732 (84.2) | 112 (83.0) | 0.801 |
| Age, years | 65 (58–72) | 70 (62–75) | <0.001 |
| Body mass index, kg/m ² | 24.4 (22.0–26.5) | 24.0 (21.0–25.0) | <0.001 |
| ASA physical status | | | 0.011 |
| ≤2 | 757 (87.1) | 106 (78.5) | |
| ≥3 | 112 (12.9) | 29 (21.5) | |
| Diabetes mellitus | 177 (20.4) | 32 (23.7) | 0.425 |
| Hypertension | 367 (42.2) | 55 (40.7) | 0.779 |
| Coronary artery disease | 44 (5.1) | 11 (8.1) | 0.154 |
| Cerebrovascular disease | 36 (4.1) | 9 (6.7) | 0.260 |
| COPD | 39 (4.5) | 7 (5.2) | 0.824 |
| Smoking history | | | 0.519 |
| Current smoker | 94 (10.8) | 15 (11.1) | |
| Non-smoker | 370 (42.6) | 64 (47.4) | |
| Ex-smoker | 405 (46.6) | 56 (41.5) | |
| Tumor stage | | | 0.005 |
| ≤T2 | 615 (70.8) | 79 (58.5) | |
| ≥T3 | 254 (29.2) | 56 (41.5) | |
| Tumor grade | | | 0.272 |
| 2 | 53 (6.1) | 4 (3.0) | |
| 3 | 816 (93.9) | 131 (97.0) | |
| Neo-adjuvant chemotherapy | 240 (27.6) | 42 (31.1) | 0.411 |
| Preoperative laboratory tests | | | |
| Hematocrit (%) | 37.0 (32.9–40.8) | 34.5 (30.2–37.7) | <0.001 |
| Platelets (10 ³ /μL) | 231.0 (190.0–282.0) | 231.0 (200.0–287.0) | 0.781 |
| Albumin (g/dL) | 3.8 (3.5–4.0) | 3.5 (3.2–3.7) | <0.001 |
| Creatinine (mg/dL) | 0.93 (0.80–1.12) | 1.05 (0.81–1.24) | 0.005 |
| AST (IU/L) | 20.0 (17.0–25.0) | 19.0 (15.0–25.0) | 0.003 |
| ALT (IU/L) | 17.0 (12.0–24.0) | 13.0 (10.0–19.0) | <0.001 |
| Uric acid (mg/dL) | 5.2 (4.2–6.3) | 4.9 (3.9–6.3) | 0.507 |
| High CFI* | 65 (7.5) | 25 (18.5) | <0.001 |

Continuous variables are presented as the median (interquartile range), while categorical variables are shown as number (percentage). *CFI was calculated by summing the following five parameters: age >70 years, body mass index <18.5 kg/m², hematocrit <35%, albumin <3.4 g/dL, or serum creatinine >2.0 mg/dL. *A high CFI was defined as a score of 3–5.

ALT, alanine aminotransferase; ASA, American Society of Anesthesiologists; AST, aspartate aminotransferase; CFI, chart-derived frailty index; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease

Table 2. Patients' intraoperative variables

| Variables | Non-mortality (n = 869) | Mortality (n = 135) | P |
|------------------------------|------------------------------------|--------------------------------|----------|
| Operation time, min | 400 (298–474) | 410 (311–487) | 0.500 |
| Hypotensive event | 148 (17.0) | 25 (18.5) | 0.713 |
| Crystalloid amount, mL/kg | 45.8 (33.6–60.0) | 49.2 (34.9–71.6) | 0.043 |
| Colloid amount, mL/kg | 10.0 (0.0–17.2) | 11.9 (4.1–16.7) | 0.337 |
| RBC transfusion rate | 440 (50.6) | 97 (71.9) | <0.001 |
| RBC transfusion amount, unit | 1 (0–2) | 2 (0–4) | <0.001 |
| Reversal agent of NMB | | | 0.091 |
| Neostigmine-glycopyrrolate | 722 (83.1) | 104 (77.0) | |
| Sugammadex | 147 (16.9) | 31 (23.0) | |

Data are shown as median (interquartile range) or number of patients (%) as appropriate.
NMB, neuromuscular blockade; RBC, red blood cells

Table 3. Univariate and multivariate Cox proportional hazard regression analyses of risk factors associated with 1-year all-cause mortality after radical cystectomy

| Variables | Univariate analysis | | Multivariate analysis | |
|---------------------------|----------------------|--------|-----------------------|--------|
| | HR (95% CI) | P | HR (95% CI) | P |
| Sex, male | 0.926 (0.591–1.450) | 0.736 | | |
| ASA physical status | | 0.007 | | |
| ≤2 | 1.000 | | | |
| ≥3 | 1.762 (1.168–2.657) | | | |
| Diabetes mellitus | 1.207 (0.812–1.794) | 0.353 | | |
| Hypertension | 0.948 (0.673–1.337) | 0.761 | | |
| Coronary artery disease | 1.609 (0.868–2.981) | 0.131 | | |
| Cerebrovascular disease | 1.591 (0.809–3.128) | 0.179 | | |
| COPD | 1.197 (0.559–2.562) | 0.643 | | |
| Tumor stage | 1.667 (1.184–2.348) | 0.003 | 1.674 (1.185–2.365) | 0.003 |
| Tumor grade | 2.064 (0.763– 5.581) | 0.153 | | |
| Neo-adjuvant chemotherapy | 1.189 (0.826– 1.712) | 0.352 | | |
| AST | 0.983 (0.961–1.005) | 0.132 | | |
| ALT | 0.986 (0.970–1.002) | 0.086 | | |
| Uric acid | 0.967 (0.866–1.079) | 0.550 | | |
| High CFI* | 2.661 (1.723–4.108) | <0.001 | 2.312 (1.480–3.611) | <0.001 |
| Operation time | 1.000 (0.999–1.002) | 0.799 | | |
| Hypotensive event | 1.116 (0.723–1.722) | 0.621 | | |
| Crystalloid amount | 1.009 (1.002–1.015) | 0.006 | | |
| Colloid amount | 1.003 (0.990–1.017) | 0.612 | | |
| RBC transfusion amount | 1.278 (1.208–1.353) | <0.001 | 1.285 (1.211–1.363) | <0.001 |
| Reversal agent of NMB | 1.444 (0.967–2.157) | 0.073 | | |

All covariates (i.e., ASA physical status, tumor stage, high CFI, crystalloid amount, and RBC transfusion amount) with values of P<0.05 on the univariate Cox proportional hazard regression analysis were included in the multivariate Cox proportional hazard regression analysis with the forward conditional method. *CFI was calculated as the sum of the following five parameters: age >70 years, preoperative body mass index <18.5 kg/m², hematocrit <35%, albumin <3.4 g/dL, or serum creatinine >2.0 mg/dL. *A high CFI was defined as a score of 3–5.

ALT, alanine aminotransferase; ASA, American Society of Anesthesiologists; AST, aspartate aminotransferase; CFI, chart-derived frailty index, CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; NMB, neuromuscular blockade; RBC, red blood cell

REFERENCES

1. Stein JP, Lieskovsky G, Cote R, et al. Radical cystectomy in the treatment of invasive bladder cancer: long-term results in 1,054 patients. *J Clin Oncol* 2001; **19**(3): 666-75.
2. Shabsigh A, Korets R, Vora KC, et al. Defining early morbidity of radical cystectomy for patients with bladder cancer using a standardized reporting methodology. *Eur Urol* 2009; **55**(1): 164-74.
3. Antoni S, Ferlay J, Soerjomataram I, Znaor A, Jemal A, Bray F. Bladder Cancer Incidence and Mortality: A Global Overview and Recent Trends. *Eur Urol* 2017; **71**(1): 96-108.
4. Goldspink DF. Ageing and activity: their effects on the functional reserve capacities of the heart and vascular smooth and skeletal muscles. *Ergonomics* 2005; **48**(11-14): 1334-51.
5. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; **56**(3): M146-56.
6. Hogan DB, MacKnight C, Bergman H, Steering Committee CIOF, Aging. Models, definitions, and criteria of frailty. *Aging Clin Exp Res* 2003; **15**(3 Suppl): 1-29.
7. Brummel NE, Bell SP, Girard TD, et al. Frailty and Subsequent Disability and Mortality among Patients with Critical Illness. *Am J Respir Crit Care Med* 2017; **196**(1): 64-72.
8. Bagshaw SM, Stelfox HT, Johnson JA, et al. Long-term association between frailty and health-related quality of life among survivors of critical illness: a prospective multicenter cohort study. *Crit Care Med* 2015; **43**(5): 973-82.
9. Okabe H, Ohsaki T, Ogawa K, et al. Frailty predicts severe postoperative complications after elective colorectal surgery. *Am J Surg* 2019; **217**(4): 677-81.
10. Yu J, Park JY, Ha S, Hwang JH, Kim YK. C-reactive Protein/Albumin Ratio and Acute Kidney Injury after Radical Cystectomy among Elderly Patients: A Propensity Score-Matched Analysis. *Dis Markers* 2020; **2020**: 8818445.
11. Yu J, Hong B, Park JY, et al. Comparison of a Significant Decline in the Glomerular Filtration Rate between Ileal Conduit and Ileal Neobladder Urinary Diversions after Radical Cystectomy: A Propensity Score-Matched Analysis. *J Clin Med* 2020; **9**(7).
12. Yu J, Hong B, Park JY, Hwang JH, Kim YK. Impact of Prognostic Nutritional Index on Postoperative Pulmonary Complications in Radical Cystectomy: A Propensity Score-Matched Analysis. *Ann Surg Oncol* 2021; **28**(3): 1859-69.
13. Amrock LG, Neuman MD, Lin HM, Deiner S. Can routine preoperative data predict adverse outcomes in the elderly? Development and validation of a simple risk model incorporating a chart-derived frailty score. *J Am Coll Surg* 2014; **219**(4): 684-94.
14. Zhao H, Wei P, Feng Y. Association Between Frailty and Clinical Outcomes and Quality of Life in

- Older Adults Following Hip Fracture Surgery: A Retrospective Cohort Study. *Anesth Analg* 2022; **134**(5): 1035-42.
15. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol* 2010; **17**(6): 1471-4.
 16. Comperat EM, Burger M, Gontero P, et al. Grading of Urothelial Carcinoma and The New "World Health Organisation Classification of Tumours of the Urinary System and Male Genital Organs 2016". *Eur Urol Focus* 2019; **5**(3): 457-66.
 17. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci* 2004; **59**(3): 255-63.
 18. Hewitt J, Long S, Carter B, Bach S, McCarthy K, Clegg A. The prevalence of frailty and its association with clinical outcomes in general surgery: a systematic review and meta-analysis. *Age Ageing* 2018; **47**(6): 793-800.
 19. Parikh N, Sharma P. Frailty as a prognostic indicator in the radical cystectomy population: a review. *Int Urol Nephrol* 2019; **51**(8): 1281-90.
 20. De Nunzio C, Cicione A, Izquierdo L, et al. Multicenter Analysis of Postoperative Complications in Octogenarians After Radical Cystectomy and Ureterocutaneostomy: The Role of the Frailty Index. *Clin Genitourin Cancer* 2019; **17**(5): 402-7.
 21. Yamashita S, Mashima N, Higuchi M, et al. Modified 5-Item Frailty Index Score as Prognostic Marker After Radical Cystectomy in Bladder Cancer. *Clin Genitourin Cancer* 2021.
 22. Subramaniam S, Aalberg JJ, Soriano RP, Divino CM. The 5-Factor Modified Frailty Index in the Geriatric Surgical Population. *Am Surg* 2021; **87**(9): 1420-5.
 23. Chappidi MR, Kates M, Patel HD, et al. Frailty as a marker of adverse outcomes in patients with bladder cancer undergoing radical cystectomy. *Urol Oncol* 2016; **34**(6): 256 e1-6.
 24. May M, Helke C, Nitzke T, Vogler H, Hoschke B. Survival rates after radical cystectomy according to tumor stage of bladder carcinoma at first presentation. *Urol Int* 2004; **72**(2): 103-11.
 25. Morgan TM, Barocas DA, Chang SS, et al. The relationship between perioperative blood transfusion and overall mortality in patients undergoing radical cystectomy for bladder cancer. *Urol Oncol* 2013; **31**(6): 871-7.

ABSTRACT IN KOREAN

국문 초록

서론

근치적 방광절제술은 근치윤성 방광암의 표준치료로, 합병증과 사망률이 높은 비뇨기과 수술이다. 의료기록 기반 노쇠지수는 환자기본정보와 기본실험실검사를 통해 구할 수 있는 간편한 노쇠평가 도구이다. 따라서 본 연구는 의료기록 기반 노쇠지수가 근치적 방광절제술 후 1년 사망률에 미치는 영향을 평가하고자 한다.

연구방법

본 연구는 2007년부터 2021년까지 근치적 방광절제술을 시행 받은 환자를 대상으로 한 후향적 연구이다. 의료기록기반 노쇠지수는 다음 5가지 항목 중 해당하는 항목의 개수로 정의하였다: 나이 >70세, 체질량지수 <18.5kg/m², 헤마토크릿 <35%, 알부민 <3.4g/dL, 크레아티닌 >2.0mg/dL. 해당하는 항목이 2개 이하인 경우 낮은 노쇠지수군으로, 3개 이상인 경우 높은 노쇠지수군으로 정의하였다. 근치적 방광절제술 후 1년 사망률을 노쇠지수에 따라 평가하였다.

연구결과

1004명의 환자를 연구 대상으로 선정하였다. 노쇠지수가 낮은 군은 914명 (91.0%)이고, 노쇠지수가 높은 군은 90명 (9.0%)이었다. 1년 사망률은 노쇠지수가 낮은 군과 높은 군에서 각각 12.0% 그리고 27.8%였다 ($P < 0.001$). 다변량 회귀분석에서 근치적

방광절제술 후 사망의 위험인자는 높은 노쇠지수 ($P < 0.001$), 종양단계 ($P = 0.003$), 적혈구 수혈량 ($P < 0.001$)이었다. 카플란-마이어 생존분석에서 노쇠지수가 낮은 군에 비해 높은 군에서 1년 사망률이 유의하게 높았다 (로그순위법, $P < 0.001$).

결론

근치적 방광절제술에서 높은 노쇠지수는 1년 사망률 증가와 관련 있다. 따라서 의료기록기반 노쇠지수는 근치적 방광절제술 환자에서 수술 후 예후를 평가하는데 도움이 될 것이다.