

Frailty Matters: The Success of the Modified Frailty Index-5 Score in Predicting Postoperative Outcomes in Radical Prostatectomy

Frailty Önemlidir: Modified Frailty Index-5 Skorunun Radikal Prostatektomide Postoperatif Sonuçları Öngörmede Başarısı

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ABSTRACT

Objective: Patients undergoing radical prostatectomy generally belong to an older population; therefore, in addition to chronological age, frailty has a substantial impact on clinical outcomes. This study aimed to evaluate the predictive value of the modified frailty index (mFI-5) for post-operative complications and functional outcomes in patients undergoing radical prostatectomy.

Materials and Methods: A retrospective analysis was conducted on 200 individuals who underwent radical prostatectomy between January 2016 and January 2024 in a high-volume tertiary center. Data collection included demographic characteristics, comorbidity profiles, histopathological findings, perioperative variables, postoperative complications and follow-up outcomes. Patients were stratified as having either high risk (≥ 2) or low risk (< 2) according to pre-operative mFI-5 scores. Postoperative complications constituted the primary endpoint, whereas functional outcomes were assessed as secondary endpoints.

Results: The study included 200 male patients, with a mean age of 64.7 ± 6.03 years. Fifty-four out of 200 patients (27%) were in the high-risk group (mFI-5 ≥ 2) while 146 patients (73%) were in low-risk group (mFI-5 < 2). While the rate of major complications (Clavien-Dindo ≥ 3) was significantly higher in high-risk group, the overall complication rate was similar between the groups. Readmission and reoperation rates were increased in the high-risk group; however, the difference did not reach statistical significance. Regarding functional outcomes, erectile dysfunction and urinary incontinence rates were similar between the groups.

Conclusion: This study highlights an association between higher mFI-5 scores and an increased risk of major postoperative complications after radical prostatectomy. Although mFI-5 should not be used as a stand-alone criterion for treatment selection, it may serve as a simple, rapid, and cost-effective adjunctive tool for preoperative risk stratification and individualized surgical decision-making.

Keywords: prostate cancer, radical prostatectomy, modified frailty index-5, complication, functional outcomes

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ÖZET

Amaç: Radikal prostatektomi uygulanan hastalar genellikle ileri yaş popülasyonuna aittir; bu nedenle kronolojik yaşa ek olarak, frailty (kırılganlık) klinik sonuçlar üzerinde önemli bir etkiye sahiptir. Bu çalışmanın amacı, radikal prostatektomi uygulanan hastalarda modifiye frailty indeksinin (mFI-5) postoperatif komplikasyonlar ve fonksiyonel sonuçlarını öngörmedeki başarısını değerlendirmektir.

Gereç ve Yöntemler: Ocak 2016 ile Ocak 2024 tarihleri arasında yüksek hacimli bir üçüncü basamak merkezde radikal prostatektomi uygulanan 200 hastanın verileri retrospektif olarak analiz edilmiştir. Demografik özellikler, komorbidite profilleri, histopatolojik bulgular, perioperatif değişkenler, postoperatif komplikasyonlar ve takip sonuçları değerlendirilmiştir. Hastalar, preoperatif mFI-5 skorlarına göre yüksek risk (≥ 2) ve düşük risk (< 2) olarak sınıflandırılmıştır. Postoperatif komplikasyonlar birincil sonlanım noktası olarak belirlenirken, fonksiyonel sonuçlar ikincil sonlanım noktaları olarak değerlendirilmiştir.

Bulgular: Çalışmaya 200 erkek hasta dahil edilmiş olup, ortalama yaş $64,7 \pm 6,03$ yıl olarak bulunmuştur. 200 hastanın 54'ü (%27) yüksek risk grubunda ($mFI-5 \geq 2$), 146'sı (%73) ise düşük risk grubunda ($mFI-5 < 2$) yer almıştır. Majör komplikasyon oranı (Clavien-Dindo ≥ 3) yüksek risk grubunda anlamlı derecede daha yüksek bulunurken, toplam komplikasyon oranı gruplar arasında benzer saptanmıştır. Tekrar başvuru ve re-operasyon oranları yüksek risk grubunda daha yüksek bulunmuş, ancak bu fark istatistiksel anlamlılığa ulaşmamıştır. Fonksiyonel sonuçlar açısından, erektil disfonksiyon ve üriner inkontinans oranlarının gruplar arasında benzer olduğu görülmüştür.

Sonuçlar: Bu çalışma, radikal prostatektomi uygulanan hastalarda daha yüksek mFI-5 skorları ile daha yüksek majör komplikasyon oranları arasındaki ilişkiyi ortaya koymaktadır. Frailte değerlendirmesinde basit ve maliyet etkin bir ölçüt olan mFI-5, bu hasta grubunda preoperatif risk sınıflandırması ve hasta seçimi açısından önemli bir rol oynayabilir.

Anahtar Kelimeler: prostat kanseri, radikal prostatektomi, modifiye kırılganlık indeks-5, komplikasyon, fonksiyonel sonuçlar

INTRODUCTION

Prostate cancer is one of the most commonly diagnosed malignancies in men, and its incidence increases progressively with age (1). In these patients, radical prostatectomy (RP) is a curative treatment option and according to guidelines, it is recommended for patients with a life expectancy over 10 years (2). Although radical prostatectomy is a potentially curative treatment, prostate cancer primarily affects older men, who often have a higher burden of comorbidities and an increased risk of postoperative complications (1,3). Therefore, when deciding on RP, it is critically important to minimize risks and complications and to ensure appropriate patient selection for surgery. Several tools have been developed to aid in patient selection for RP, with reported sensitivity rates ranging from 65% to 84% (1,4–7).

In addition to traditional tools such as the American Society of Anesthesiologists classification (ASA) and the Charlson Comorbidity Index (CCI), frailty-based tools have increasingly been used to predict postoperative complications and functional outcomes (8,9). With the progressive aging of populations, frailty has emerged as an increasingly important determinant and has been demonstrated to influence the clinical course and outcomes of a wide range of diseases, including those requiring surgical intervention. Frailty refers to a state of reduced physiological resilience across multiple organ systems and can be evaluated either through phenotypic measures—such as muscle strength, walking speed, and recent falls—or through a deficit accumulation approach that considers existing comorbidities, functional capacity in daily activities, and observable physical impairments (10). Following the development of the 11-item modified frailty index (mFI-11) to enhance clinical practicality (8,9), a shorter version—the 5-item modified frailty index (mFI-5)—was subsequently introduced, with studies demonstrating that it produces outcomes comparable to the original index despite relying on fewer variables. (11). The mFI-5 consists of five variables—congestive heart failure, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, and functional health status—each contributing one point to the total score. Therefore, the present study aimed to evaluate the prognostic value of

the mFI-5 for postoperative complications and functional outcomes in patients undergoing radical retropubic prostatectomy (RRP) and extended lymph node dissection (eLND).

MATERIALS AND METHODS

Ethical Committee, the study was conducted in accordance with the ethical principles of the Declaration of Helsinki (193/2013 revision) and was approved by the Ethics Committee of Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye (Decision No: 2022/514/230/10; Approval Date: 27 July 2022).

In this study, data from patients who had undergone RRP and eLND for prostate cancer at a tertiary referral center between January 2016 and January 2024 were retrospectively evaluated. Exclusion criteria included incomplete data, radical prostatectomy performed for non-prostate adenocarcinoma indications, receipt of neoadjuvant hormonal therapy or radiotherapy, and the presence of metastatic disease.

All surgical procedures were performed by three experienced surgeons. All patients received cefazolin as antibiotic prophylaxis. Standard postoperative care included intravenous fluid replacement, analgesic therapy, and early mobilization within the first 12 hours after surgery. Low-molecular-weight heparin was administered starting on postoperative day 1 and continued for 30 days.

Data collection included demographic characteristics, comorbidity profiles (with Charlson Comorbidity Index scores), histopathological findings, intraoperative variables—namely operative time and transfusion requirement—and follow-up outcomes. Postoperative recovery parameters included time until first bowel movement, prolonged drain usage, and length of hospital stay.

Complications developing within 90 days postoperatively were prospectively recorded and categorized based on the modified Clavien-Dindo Classification (CDC). In accordance with the CDC, grades 3–5 were defined as major complications, and grades 0–2 as minor or no complications. Outpatient medical records were also reviewed to identify any delayed complications.

Five predefined variables were used to retrospectively derive the mFI-5 score. Based on previous literature, an mFI-5 threshold of 2 was used to classify patients into low-risk (< 2) and high-risk (≥ 2) cohorts (12). The groups were compared regarding baseline characteristics, histopathological results, complications and postoperative outcomes.

Statistical Analysis

Given the retrospective nature of the study, data distribution was evaluated using the Kolmogorov-Smirnov test, which demonstrated non-normal distribution of the variables. Descriptive statistics were expressed as mean $\pm$ standard deviation, median with interquartile range (IQR), and frequencies, as appropriate. The Mann-Whitney U test was used to compare continuous variables between groups, while categorical data were evaluated using the Chi-square test or Fisher's exact test when indicated. Analyses were conducted using IBM SPSS version 25.0 (IBM Corp., Armonk, NY, USA). 2-tailed p -values less than 0.05 were deemed statistically significant. A priori sample size estimation was performed using simple random sampling to ensure adequate statistical power. Assuming a significance level of $\alpha = 0.05$, a 95% confidence level, an expected proportion of 0.5, and a margin of error of ± 0.05 , the minimum required sample size was calculated. Based on a total population of 372 patients who underwent radical prostatectomy at a high-volume tertiary referral center between January 2016 and January 2024, the estimated minimum sample size was 189 patients.

RESULTS

The research involved 200 male participants whose ages ranged from 48 to 79 years. The average age was 64.7 ± 6.03 years (median 65). The initial demographic and clinical features of the patients are detailed in Table 1.

A statistically significant difference was observed between the mFI-5 groups with respect to CDC ($p = 0.035$; $p < 0.05$). The incidence of major complications was significantly higher in patients with an mFI-5 score ≥ 2 (14.8%) compared with those with an mFI-5 score < 2 (5.5%). However, no statistically significant difference was found between the mFI-5 groups regarding overall complication rates based on the CDC ($p > 0.05$). Complications occurred in 27.4% of patients with an mFI-5 score < 2 and in 25.9% of patients with an mFI-5 score ≥ 2 . There was no statistically significant difference between the mFI-5 groups in terms of overall postoperative complications ($p > 0.05$).

Table 1. Demographic, clinical, perioperative, and pathological characteristics of cohort

		Mean $\pm$ SD	Median (IQR)
Age		64.7 $\pm$ 6.03	65 (61-68.75)
Length of Stay (day)		7.18 $\pm$ 4.4	6 (5-7)
PSA (ng/mL)		11.11 $\pm$ 10.68	7.95 (5.9-13)
Intensive care unit length of stay (day)		0.7 $\pm$ 1.36	0 (0-1)
Duration of drain (day)		4.41 $\pm$ 1.95	4 (3-5)
		N	%
Charlson comorbidity index	2	3	1.5
	3	25	12.5
	4	82	41
	5	62	31
	6	18	9
	7	8	4
	8	1	0.5
	9	1	0.5
Complications	Gastrointestinal tract	3	1.5
	Infection	17	8.5
	Genitourinary tract	6	3
	Cardiac	2	1
	Wound infection	10	5
	Pulmonary	5	2.5
	Others	2	1
T stage			
	T2	98	49
	T3	99	49.5
	T4	3	1.5

Although readmission and reoperation rates were numerically higher in patients with an mFI-5 score ≥ 2 compared with those with an mFI-5 score < 2 (readmission: 20.4% vs. 11.0%; reoperation: 13.0% vs. 9.6%), the differences between the groups were not statistically significant ($p > 0.05$). No statistically significant differences were observed between the mFI-5 groups with respect to operative time or length of hospital stay ($p > 0.05$).

Erectile dysfunction and urinary incontinence rates were comparable between patients with an mFI-5 score < 2 and those with an mFI-5 score ≥ 2 (erectile dysfunction: 26.7% vs. 16.7%; urinary incontinence: 55.5% vs. 46.3%), with no statistically significant differences observed between the groups ($p > 0.05$).

Disease recurrence and mortality rates were elevated in patients with a mFI-5 score ≥ 2 compared to those with a mFI-5 score < 2 (recurrence: 24.1% vs. 14.4%; mortality: 11.1% vs. 5.5%); yet these differences were not statistically significant ($p > 0.05$).

Table 2. Comparison of postoperative outcomes between the groups

		mFI-5 < 2 (n=146)	mFI-5 ≥ 2 (n=54)	p
Clavien Dindo Classification	Overall complication	40 (%27.4)	14 (%25.9)	0.835
	Minor (< grade 3)	32 (%21.9)	6 (%11.1)	0.035*
	Major ($\geq$ grade 3)	8 (%5.5)	8 (%14.8)	
Complications	Gastrointestinal tract	3 (%2.1)	0 (%0)	0.565
	Infection	13 (%8.9)	4 (%7.4)	1.000
	Genitourinary	6 (%4.1)	0 (%0)	0.194
	Cardiac	1 (%0.7)	1 (%1.9)	0.468
	Wound infection	8 (%5.5)	2 (%3.7)	1.000
	Pulmonary	3 (%2.1)	2 (%3.7)	0.613
	Others	0 (%0)	2 (%3.7)	0.072
Surgical Margin Positivity		40 (%27.4)	21 (%38.9)	0.117
Re-admission		16 (%11)	11 (%20.4)	0.084
Re-operation		14 (%9.6)	7 (%13)	0.490
Erectile Dysfunction		39 (%26.7)	9 (%16.7)	0.140
Urinary Incontinence		81 (%55.5)	25 (%46.3)	0.248
Anastomosis Stricture		21 (%14.4)	10 (%18.5)	0.473
Recurrence		21 (%14.4)	13 (%24.1)	0.105
Overall Mortality		8 (%5.5)	6 (%11.1)	0.210
Operation Time mean$\pm$SD /Median (Q1-Q3)		201.91 $\pm$ 57.44/ 190 (160-230)	194,63 $\pm$ 65,62/ 180 (150-230)	0.204
Length of stay Median (Q1-Q3)		6 (5-8)	6 (5-7)	0.277

Categorical variables were compared using the Chi-square test or Fisher's Exact test where appropriate. Continuous variables were analyzed using the Mann-Whitney U test. Data are presented as n (%) for categorical variables and median (Q1–Q3) for continuous variables. A p value < 0.05 was considered statistically significant.

DISCUSSION

As significance of frailty and biological age in surgical patients has become increasingly recognized, novel scoring systems have been developed to improve the prediction of postoperative outcomes. Due to the limitations of traditional tools, the mFI-5 was introduced in 2017 as a novel frailty-based predictive model for postoperative outcomes in elderly patients (11). This study explored the association of mFI-5 with complications occurring after radical retropubic prostatectomy (RRP) and extended lymph node dissection (eLND). Our findings are concordant with existing evidence, demonstrating a higher incidence of CDC major complications in the high-risk mFI-5 group, while complication subtypes did not differ significantly between groups. The high-risk group demonstrated higher readmission and reoperation rates, but the differences did not achieve statistical significance. Unlike previous studies, we also examined the relationship between frailty and overall survival as well as disease recurrence, but no significant association with higher mFI-5 scores was identified. These findings suggest that the mFI-5 may be a useful adjunctive tool for preoperative risk stratification in patients considered for radical prostatectomy. Rather than serving as a stand-alone determinant of treatment selection, mFI-5 may help identify patients who require more detailed perioperative counseling, optimization of comorbidities, and individualized surgical planning.

Currently, a large number of patients undergoing abdominal surgery are classified as pre-frail or frail (13). In a large-scale study evaluating approximately 92,000 patients who were treated with RP, nearly 1-seventh of the cohort was identified as frail. This study demonstrated that frailty was significantly linked to an elevated risk of postoperative complications and prolonged hospitalization in patients treated with RP (14). Likewise, the literature indicates that frailty remains a significant determinant of postoperative complications in patients treated with RP (15). In a cohort of patients who underwent robotic-assisted radical prostatectomy, the authors observed that higher mFI-5 values were associated with greater overall and high-grade complication rates within 90 days after surgery (16). Similarly, Demirci et al. (17) demonstrated that increasing frailty was correlated with a higher incidence of CDC grade ≥ 3 complications. In another cohort of patients undergoing radical prostatectomy in which the mFI-5 was evaluated, a higher mFI-5 score was identified as an independent predictor of early mortality and adverse postoperative outcomes (18). Additionally, Lascano et al. (15) reported that increasing mFI scores were associated with higher rates of CDC grade IV complications and hospital readmissions. Overall, the findings reported in the literature are consistent with the results of the present study.

Beyond postoperative complications, the relationship between frailty and functional outcomes in patients undergoing radical prostatectomy has also been investigated in the literature. Stankovic et al. (19) demonstrated that higher frailty scores were associated with a reduction in early postoperative continence rates, supporting the notion that frailty adversely affects functional recovery. In contrast, Togashi et al. (20) reported no significant association between frailty and 12-month pad-free continence rates. This discrepancy may be partly explained by differences in surgical approach, as their cohort consisted exclusively of patients undergoing robotic-assisted radical prostatectomy, whereas the present study included patients treated with open radical prostatectomy. In our analysis, postoperative erectile dysfunction and urinary incontinence rates at 12 months were comparable between the mFI-5 groups, aligning more closely with the findings of Togashi et al. (20). However, the absence of detailed baseline functional data, including preoperative erectile function and continence status, limits the interpretation of these outcomes. Therefore, the present findings should not be interpreted as definitive evidence that frailty has no effect on functional recovery after radical prostatectomy.

Frailty has been reported as a potential predictor of overall survival in various malignancies (17,21). In particular, Demirci et al. (17) observed an association between higher mFI-5 scores and poorer overall survival. Despite its predictive value for postoperative complications, the mFI-5 score showed no significant impact on overall survival in this patient population following radical prostatectomy. This lack of concordance with previous reports may be partially explained by methodological differences, including the small cohort and short follow-up period, potentially resulting in insufficient power to identify a meaningful association.

This study is subject to several limitations that warrant consideration in the interpretation of its findings. This study is primarily limited by its retrospective design. The single-center setting and relatively small cohort further constrain the external validity of the findings. Another important limitation is the lack of detailed preoperative functional status data, including baseline erectile function and urinary continence. Therefore, postoperative erectile dysfunction and urinary incontinence rates should be interpreted with caution, as it cannot be determined whether these outcomes developed after surgery or reflected pre-existing functional impairment. This limitation may have reduced the ability of the study to accurately assess the independent relationship between frailty and functional recovery after radical prostatectomy. Furthermore, the inclusion of patients operated on by different surgeons may have introduced potential bias related to variations in surgical technique and surgeon experience. Moreover, although overall survival and disease recurrence were evaluated, cancer-specific survival and data on adjuvant or salvage treatments were not analyzed, which may have affected survival-related outcomes.

Future studies with larger patient populations, multicenter designs, and prospective methodologies are warranted to better clarify the role of frailty in radical prostatectomy outcomes. In addition, investigations incorporating established composite outcome measures, such as trifecta outcomes (erectile function, urinary continence, and oncological control) and pentaecta outcomes (trifecta plus negative surgical margins and reduced perioperative complications), may provide more comprehensive insights and contribute further to the existing literature.

CONCLUSION

In conclusion, higher mFI-5 scores were associated with an increased risk of major postoperative complications after radical prostatectomy. Although mFI-5 should not be used as a stand-alone criterion for treatment selection, it may serve as a simple, rapid, and cost-free adjunctive tool for preoperative risk stratification, perioperative counseling, and individualized surgical planning. Further prospective and multicenter studies are needed to validate its role in predicting functional and oncological outcomes after radical prostatectomy.

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Author contributions:

Conceptualization and Methodology: OO, CC, ED ; Investigation: OMI, YKA, BHS ; Resources: YKA, BHS ; Writing - Original Draft; OMI, ED, CC; Writing - Review & Editing; OMI, AHS; Supervision: OO,CC.

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