

## Original Article

# Frailty as Predictor for Early Functional Outcomes After Radical Prostatectomy

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## Abstract

**Objectives:** While chronological aging does not necessarily impair oncological outcomes after radical prostatectomy, the role of frailty remains less clear. This study aimed to evaluate whether frailty significantly affects early continence rates following radical prostatectomy and to explore the potential association between frailty and postoperative complications. **Methods:** A retrospective cohort study of 212 patients undergoing radical prostatectomy was conducted. Preoperative frailty assessment employed a multimodal evaluation encompassing cardiovascular, respiratory, neurological, and urinary systems, supplemented by conventional risk measures such as physical performance status and biochemical markers. The primary endpoint was early continence recovery, while secondary outcomes included 30-day postoperative complications. **Results:** Comparative analysis revealed no statistically significant differences in baseline characteristics, oncological outcomes, or complication rates between the open and robotic-assisted surgical cohorts. However, frailty was strongly associated with reduced early continence recovery, irrespective of surgical technique ( $p < 0.001$ ). No significant association was detected between frailty and 30-day postoperative complications ( $p = 0.36$ ). **Conclusions:** This study highlights frailty as a pivotal predictor of early continence outcomes. The lack of association between frailty and postoperative complications suggests that comprehensive frailty assessment may be more relevant for anticipating functional recovery than predicting immediate surgical risks. These findings support integrating frailty evaluation into preoperative decision-making frameworks.

**Keywords:** Frailty, Functional outcomes, Radical prostatectomy

## Introduction

Frailty is a multidimensional and dynamic condition characterized by a decline in the body's physiological reserves, leading to reduced resilience and adaptive capacity<sup>1</sup>. This condition increases individuals' vulnerability to diverse stressors and has gained growing recognition as a significant factor influencing health outcomes, especially in the field of major oncologic surgical procedures.

Given that, the prevalence of surgical interventions in adult and geriatric populations has witnessed a notable increase in recent decades<sup>2,3</sup>, the question arises whether advanced age alone is sufficient to serve as a prognostic factor for postoperative complications. Subsequent research has shown that advanced age alone is not a reliable prognostic indicator, not only for postoperative complications but also for the length of hospital stay in older adults undergoing surgery. Instead, frailty phenotype

emerges as a significant risk factor<sup>4</sup>.

Although comprehensive geriatric assessment (CGA) has been implemented to improve surgical outcomes in older patients and evaluated in perioperative trials, the 2018 Cochrane review found that most studies were either retrospective or focused on hip fracture patients in randomized trials, indicating limited evidence of CGA's

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effectiveness beyond hip fracture<sup>5</sup>.

Despite the diverse methods of defining and quantifying frailty, the primary objective remains to assess its predictive value in relation to peri- and post-operative outcomes. The main objectives of this research were to assess the impact of frailty on early continence outcomes following radical prostatectomy and to investigate the potential relationship between frailty and post-surgical complications.

## Materials and Methods

In this retrospective, monocentric study we analysed 212 patients who underwent radical prostatectomy at the Department of Urology at Salem Hospital, Heidelberg, performed by two experienced surgeons, each being an expert in the respective surgical approach. The data were obtained from the routine hospital information system digital data management software (CGM Clinical).

The patients were stratified according to operation technique into open radical prostatectomy (ORP, n=103) and robot-assisted radical prostatectomy (RARP, n=109) group. The preoperative multimodal frailty assessment included patient admission status divided in four symptom groups: cardiovascular (presence of coronary heart disease, stroke, peripheral arterial disease or aortic disease), respiratory (asthma, chronic obstructive pulmonary disease (COPD)), neurological (epilepsy, Alzheimer's disease and other dementias, multiple sclerosis (MS), Parkinson's disease) and urinary (overactive bladder (OAB), incontinence preoperatively).

## Measures

### Frailty Assessment

To ensure a comprehensive evaluation, patients were assessed using a multimodal frailty scoring system, Clinical Frailty Scale (CFS) from the Canadian Study of Health and Aging<sup>6,15</sup>, along with clinical characteristics, functional capacity measures, and biochemical parameters<sup>7-9</sup>. This approach ensured a holistic assessment of patient frailty, enabling a detailed evaluation of its association with early continence recovery and postoperative complications, and aligns with established guidelines recommending the use of multiple assessment components over individual measures whenever feasible<sup>10</sup>.

### Functional Capacity Measures

To prevent underestimation of self-reported functional capacity, informant-based assessments were conducted using validated scoring systems:

**Basic Activities of Daily Living (BADL):** An informant-based evaluation of functional capacity using a simplified version of the BADL scale<sup>11</sup>.

**American Society of Anesthesiologists (ASA) Physical Status Classification:** Patients were classified into grades I through V, based on overall health and surgical risk, where I indicates a healthy patient and V represents a severely ill,

life-threatening condition<sup>12</sup>.

**New York Heart Association (NYHA) Functional Classification:** This system evaluated heart failure severity, grading patients from Class I (no symptoms or limitations) to Class IV (severe symptoms, even at rest)<sup>13</sup>.

**Barthel Index:** Functional disability was assessed based on ten activities of daily living, scored from 0 (completely dependent) to 100 (fully independent)<sup>14</sup>. The cut-off scores of 90 points were used in order to focus on patients that had just slight dependency.

These functional assessments provided critical insights into patients' baseline health status, aiding in frailty score calculation.

### Covariates

These preoperative clinical conditions were included based on their potential impact on surgical outcomes and frailty assessment:

**Cardiovascular:** Presence of coronary heart disease, stroke, peripheral arterial disease, or aortic disease.

**Respiratory:** History of asthma or chronic obstructive pulmonary disease (COPD).

**Neurological:** Diagnoses of epilepsy, Alzheimer's disease and other dementias, multiple sclerosis (MS), or Parkinson's disease.

**Urinary:** Preoperative urinary incontinence or overactive bladder (OAB).

These variables were treated as covariates in the statistical analysis due to their established association with frailty and postoperative outcomes.

### Biochemical Parameters

Laboratory tests were conducted to evaluate physiological reserves and systemic health. Inflammation markers included leukocyte count and C-reactive protein (CRP) levels, while hemoglobin concentration was assessed as a marker of anemia. Renal function was evaluated using serum creatinine levels.

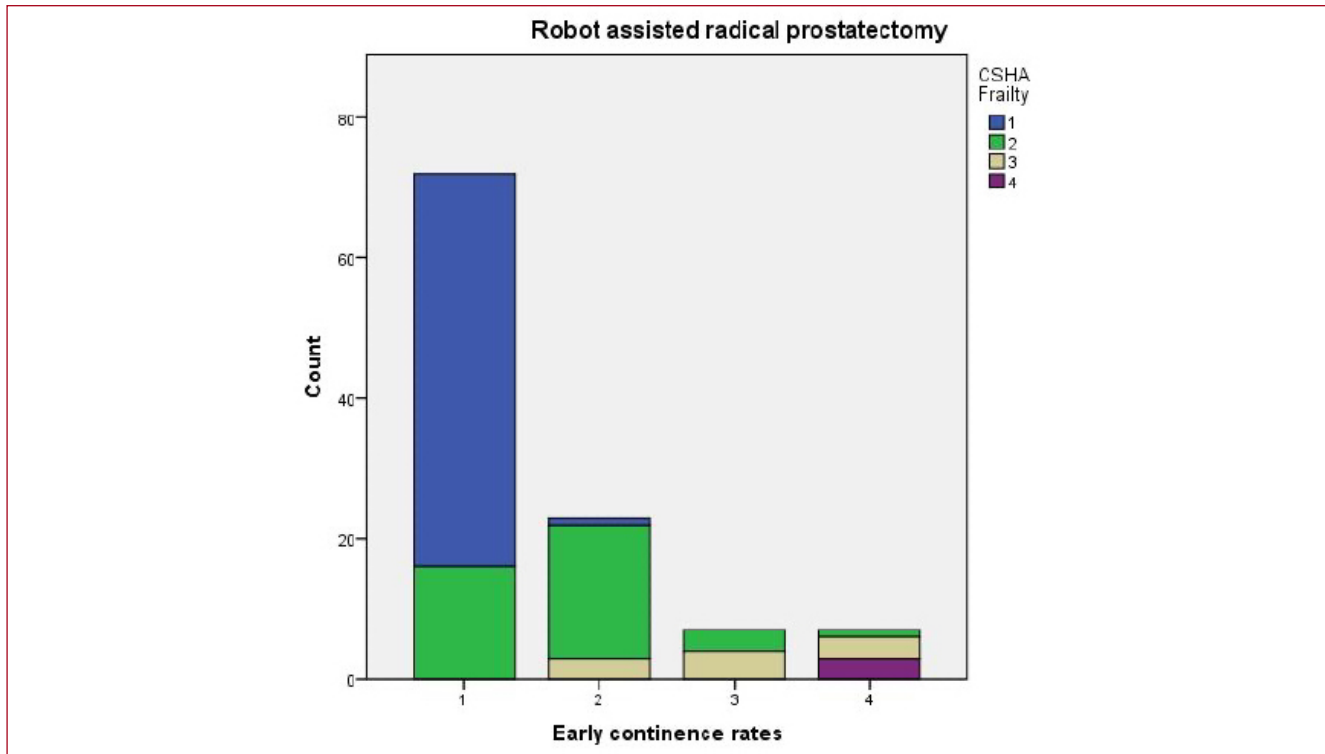
### Primary outcome

The primary outcome assessed was early continence rate using a standardized pad test. This test measures the amount of involuntary urine loss while performing predefined physical activities such as bending, coughing, climbing stairs and jumping with a full bladder (at least 150 ml) within 1 hour. Full continence was defined as Grade I as well as urine loss of 0 to 10g and number of urine pads per day (one). Mild urinary incontinence grade II and grade III were defined as urine loss of 10 to 25g and 25 to 50g respectively. Urine loss of exceeding 50g represented severe early incontinence, grade IV. To facilitate multivariate logistic regression analysis, early continence outcomes were categorized into two groups: "good outcome" (Grades I and II) and "poor outcome" (Grades III and IV), based on the standardized 1-hour pad test.

Variable	RARP, n	ORP, n	p-value
Age (median, years)	69.4	71.4	0.71
>65	82	83	
≤65	27	20	
Prostate size (median, ml)	44.2	45.0	0.61
iPSA (median, ng/ml)	7.4	7.7	0.55
ASA scale			0.68
1	4	11	
2	83	67	
3	22	25	
NYHA classification			0.29
1	93	83	
2	16	19	
3	n.a.	1	
Barthel Index			0.32
>90	49	42	
Comorbidity			0.81
cardiovascular	36	39	
respiratory	7	8	
neurological	9	7	
CSHA Frailty score			0.18
1	61	47	
2	37	42	
3	9	14	
4	2	n.a.	
Continence rates			0.71
1	74	74	
2	24	20	
3	7	7	
4	4	2	
T stage			0.45
T2	69	73	
T3a	26	18	
T3b	14	12	
Positive margins	24	26	0.89
Nerve-sparing	44	38	0.72
Gleason Score			0.45
≤7	89	81	
≥8	20	22	
Clavien Dindo			0.73
n.a.	99	86	
1	4	6	
2	5	5	
3a	1	3	
3b	n.a.	2	
4	n.a.	1	

RARP – robot assisted radical prostatectomy, ORP – open radical prostatectomy, iPSA – initial prostate specific antigen, ASA - American Society of Anesthesiologists, CSHA – Canadian Study of Health and Aging, n.a. – not applicable.

**Table 1.** Patient characteristics.



**Figure 1.** Correlation between frailty score and early continence rates in patients who underwent RARP ( $p < 0.001$ ).

### Secondary outcome

The secondary outcome was postoperative complication rate within 30 days of surgery using the Clavien-Dindo Classification<sup>16</sup>. Similarly to above mentioned logistic regression analysis, postoperative complications were classified using the Clavien-Dindo system, with Grades 0-2 considered a “good outcome” and Grades 3-5 representing a “poor outcome.” This classification enabled a more robust statistical evaluation of factors influencing continence recovery and postoperative morbidity.

### Statistical analysis

Kendall's tau\_b correlation coefficient, two-tailed test of significance and multivariate logistic regression analyses were used. The statistics were performed using SPSS© v23 and MedCalc© v20.1 software. The significance level was set at 0.05.

### Results

Our analysis revealed similarity between the RARP and ORP groups across various clinical and pathological parameters (Table 1). Age, a foundational demographic factor and often pivotal in frailty studies, displayed no significant difference between the groups ( $p = 0.91$ ). Most

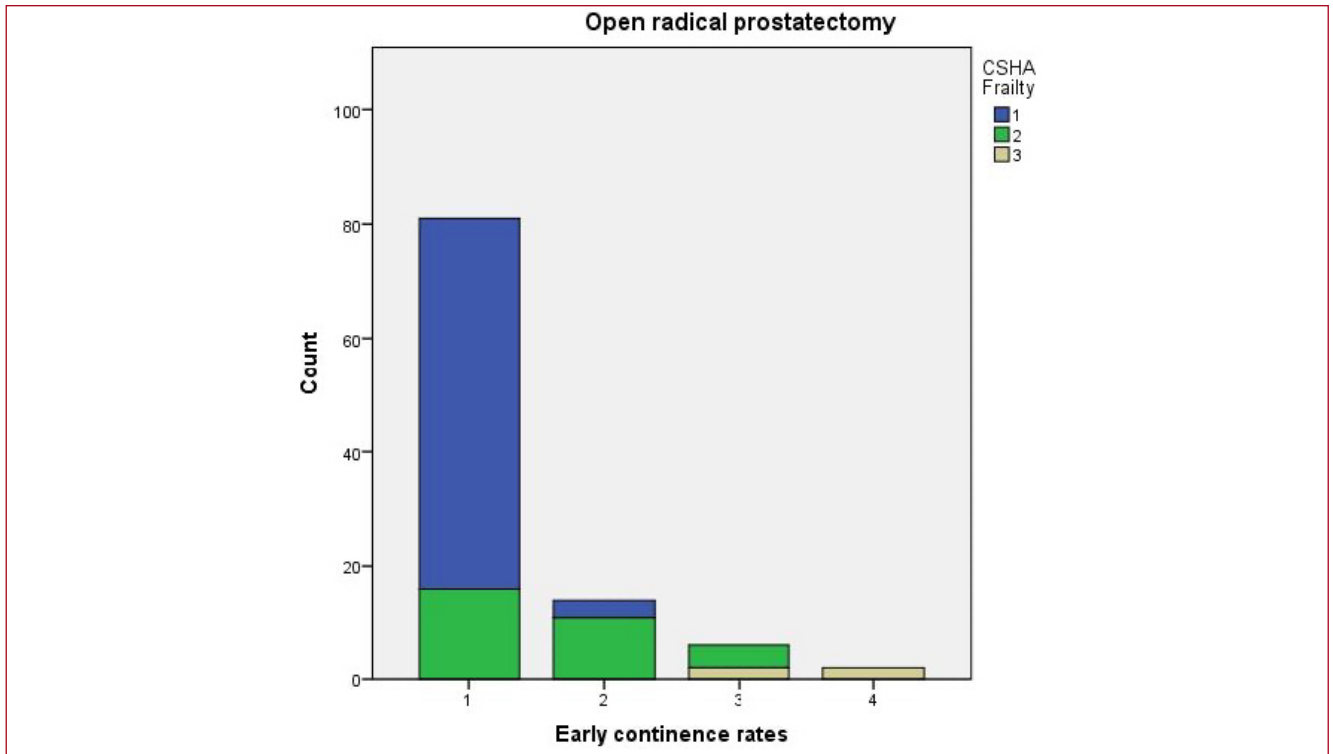
of the patients were older than 65 years (79% and 81% for RARP and ORP group respectively) and the distribution of comorbidities such as cardiovascular, respiratory, and neurological conditions were comparable between the two groups ( $p = 0.81$ ).

None of the critical parameters when assessing the nature and progression of prostate cancer, such as prostate size, tumour stage, Gleason score and positive surgical margins showed a statistically significant difference between the groups. The median prostate size was 44.5ml and 45.0ml for RARP and ORP group respectively ( $p = 0.61$ ). When the disease spread is analysed, localized prostate cancer was found in 63% and 71% of patients in RARP and ORP group respectively. Positive surgical margins were also comparable ( $p = 0.89$ ).

The main measurements of patients' physical health status and cardiac function, ASA Scale and NYHA classification respectively, also showed no significant differences between the groups, with the vast majority of patients being classified into ASA 2 ( $p = 0.68$ ) and NYHA 1 ( $p = 0.29$ ) risk groups preoperatively.

Both groups had a near-even distribution between Barthel indexes indicating no significant difference in early postoperative functionality ( $p = 0.32$ ).

Patients with higher scores on the CSHA Clinical Frailty



**Figure 2.** Correlation between frailty score and early continence rates in patients who underwent ORP ( $p < 0.001$ ).

Scale tended to be of advanced age and exhibited a greater likelihood of cognitive impairment, diminished mobility, functional limitations and an increased incidence of comorbid conditions. Nevertheless, there was no statistical difference in early continence rates between the RARP and ORP groups ( $p = 0.71$ ).

However, there was a significant correlation between frailty score and early continence rates regardless of the surgical technique applied. After adjusting for variables such as patient admission status, ASA and NYHA classification, Barthel index, biochemical measurements for inflammation, anaemia and renal function parameter, multivariate linear model analysis found a strong correlation between frailty and early continence rates for RARP (Figure 1,  $p < 0.001$ ) and for ORP (Figure 2,  $p < 0.001$ ).

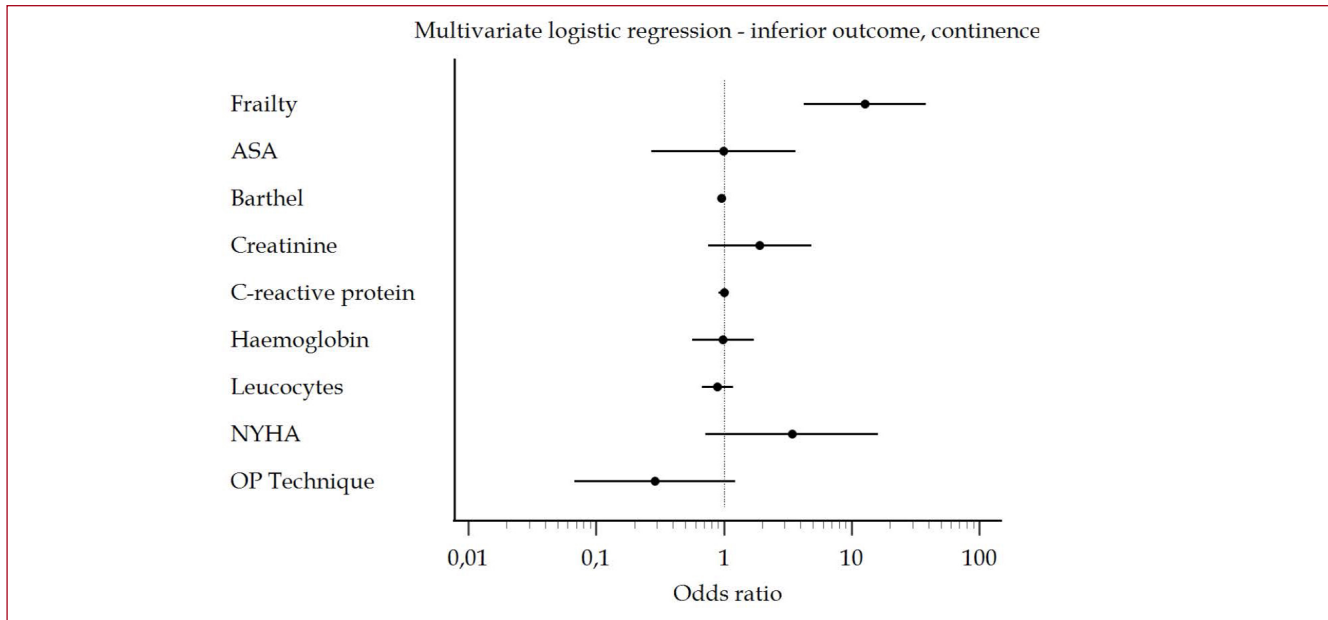
Furthermore, we categorized early continence rates of grade I and II as a “good outcome” and grades III and IV as a “poor outcome” in order to perform the multivariate logistic regression analysis. The same principle was applied to complication rates, where Clavien-Dindo complications of grade 2 or lower were defined as a “good outcome” and complications of grade 3 or higher as a “poor outcome”.

In summary, the multivariate logistic regression analysis demonstrated frailty as independent variable, significantly influencing the likelihood of an outcome (Figure 3). The chi-

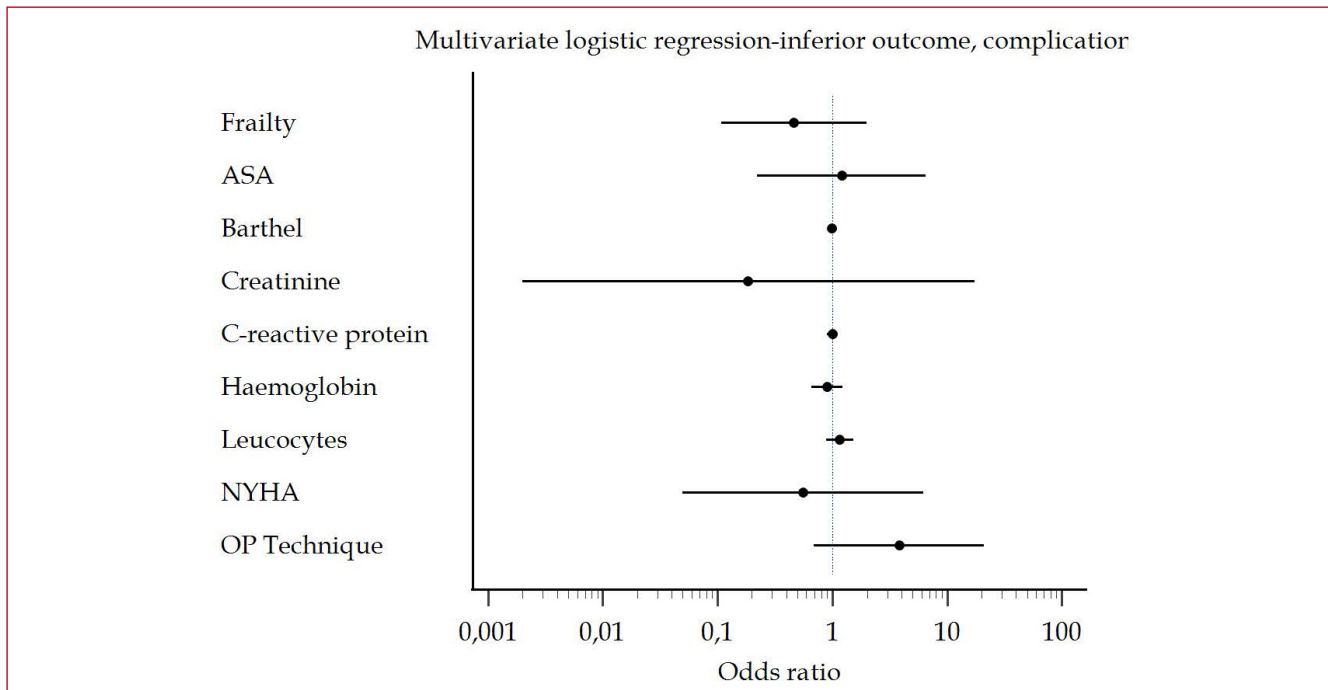
squared test for model fit showed a significant difference between the null model and the full model (chi-squared = 75.375,  $df = 9$ ,  $p < 0.001$ ), indicating that the model is a good fit for the data. The Nagelkerke  $R^2$  value (0.629) suggests that the model explains a substantial portion of the variance in the dependent variable. Notably, the “frail” variable had a coefficient of 2.542 and an odds ratio of 12.708 (95% CI), suggesting a strong predictive role. In addition, when categorized based on Clavien-Dindo classification, the comprehensive analysis consistently points toward the absence of a noteworthy impact of frailty on complication rates within the studied dataset (Figure 4). The coefficient for the “frail” variable was -0.763, and the corresponding odds ratio was 0.467 (95% CI). These values suggest that frailty was not significantly associated with an increased likelihood of complications (Nagelkerke  $R^2 = 0.102$ ).

Furthermore, there was no difference in postoperative complication rates between the groups, as most of the patients did not experience any deviation from the postoperative course. No significant correlation between frailty and postoperative complications was documented ( $p = 0.61$ , ORP and  $p = 0.54$ , RARP).

Finally, the serum biochemical measurements for inflammation, anaemia and renal function were documented and were comparable between the groups (Table 2) and



**Figure 3.** Multivariate logistic regression, factors influencing the continence rates. ASA - American Society of Anesthesiologists Classification, NYHA - New York Heart Association Functional Classification.



**Figure 4.** Multivariate logistic regression, factors influencing the complication rates.

Variable	RARP	ORP	p-value
Leucocytes ≤10/nl >10/nl	95 14	81 22	0.61
C-reactive protein ≤5mg/l >5mg/l	95 15	90 13	0.84
Haemoglobin ≤13.5g/dl >13.5g/dl	23 86	15 88	0.50
Creatinine ≤1.2mg/dl >1.2mg/dl	91 18	89 14	0.54

RARP – robot assisted radical prostatectomy, ORP – open radical prostatectomy.

**Table 2.** Serum biochemical measurements with corresponding reference values.

showed no correlation to frailty ( $p=0.36$  for RARP and  $p=0.44$  for ORP).

## Discussion

Previous studies found that the majority of population undergoing abdominal surgery is pre-frail or frail<sup>17</sup>. Others reported that, on average, every seventh patient who undergoes radical prostatectomy is frail and that proportion is on the rise<sup>18</sup>. However, literature addressing frailty and ORP remains limited. On the other hand, there are reports that have highlighted the correlation and clinical implications of frailty in patients subjected to RARP, noting that after RARP, the pad-free continence rate was lower in the frail group, though the difference was not statistically significant<sup>19</sup>. Our results revealed a significant negative correlation between frailty scores and early continence, regardless of surgical approach ( $p<0.001$ ). Interestingly, some authors have indicated that nearly 10% of patients utilized one or more pads daily preceding RARP, irrespective of their frailty status<sup>20</sup>. Given that urinary incontinence is observed to be twice as common among frail elderly individuals compared to their non-frail counterparts<sup>21</sup>, it underscores the necessity to consider multiple factors for individual decision-making and preoperative patient assessment.

Most past studies reported the correlation between frailty and continence rate at 12 months where the results are based solely on number of pads used, without quantifying the exact amount of urine loss. Therefore, our multimodal study provides unique perspective into how frailty and early continence are inescapably intertwined and additionally gives a direct comparison between two surgical techniques. The results of our study elucidate a striking similarity between the RARP and ORP groups across a myriad of clinical and pathological parameters. It is noteworthy

that a majority of patients across both groups were aged above 65, underscoring the geriatric nature of this population. Furthermore, the comorbidity profile, spanning cardiovascular, respiratory, and neurological comorbidities, was almost identically distributed between these surgical cohorts.

In the context of prostate cancer specifics, pivotal indicators like PSA, tumour stage and the Gleason score, highlighted a statistical parity between the RARP and ORP groups. This uniformity persisted even in the analysis of disease spread and surgical margins.

As certain studies have postulated, while advanced age might not compromise oncological outcomes post-RARP, elderly patients tend to exhibit a higher incidence of high-risk disease<sup>22</sup>. Such observations are congruent with our results.

A comprehensive review encompassing 23 studies explored the relationship between frailty and postoperative outcome, reporting a significant association between frailty and increased mortality and postoperative complications<sup>23</sup>. Another review found that frailty was associated with an increased postoperative complications rate, although there was no association between complications and classic prognostic factors such as ASA classification<sup>24</sup>. These results are not consistent with our findings. We reported no significant correlation between frailty and postoperative complications, as most of the patients did not experience any deviation from the postoperative course.

We did not utilize the ASA classification solely but in combination with NYHA classification, taking into account that frailty is an independent predictor of mortality in cardiovascular disease and is found in 15–74% of patients with heart failure<sup>25</sup>. This was epitomized in our data, wherein the majority of patients were preoperatively categorized into the ASA 2 and NYHA 1 risk categories, indicating a uniform

preoperative health status across both surgical modalities. Certain studies have recommended a 60-point threshold for the Barthel index, emphasizing that it should not be the sole predictor of outcomes<sup>26</sup>. Our threshold was higher on purpose, enabling us to identify patients with just slight dependency.

Our results highlight the significance of frailty as an independent variable in predicting the studied outcome. The chi-squared test and the substantial Nagelkerke R<sup>2</sup> value affirm the model's reliability in explaining the outcome variance. Notably, frailty emerges as a potent predictor, significantly increasing the likelihood of the outcome.

However, when the analysis is specifically focused on complications, the results shift. Categorized analysis based on Clavien-Dindo classification reveals that frailty is not a significant predictor of complications within the studied dataset. This nuanced finding suggests that while frailty is influential in predicting the broader outcome, it may not play a significant role in predicting complications specifically. Further research may be needed to explore this relationship in more detail and across different contexts.

Lastly, while some studies have shown associations between higher inflammatory parameters, anaemia, worse renal function, and frailty<sup>27,28</sup>, our findings remained devoid of any such correlations between the aforementioned parameters and frailty.

We acknowledge that this study has several potential limitations, its single-center character and relatively small sample size being some of them. In addition, we were not able to obtain the Body-Mass-Index and G8 scores due to lack of initial data.

Overall, our study reinforces the importance of frailty as a critical parameter in preoperative assessments, offering novel insights into its relationship with early postoperative outcomes. We found no significant correlation between frailty and postoperative complications, in contrast to the observed linkages in broader literature. Further research is essential to consolidate these findings and explore the underlying mechanisms that drive these observed correlations and discrepancies.

#### Ethics approval

*The project was approved by the national research ethics committee, Ethics Commission of the State Medical Chamber of Baden-Württemberg (F-2023-120).*

#### Authors' contributions

*Mladen Stankovic contributed to the study's conception, design, and data acquisition, drafted the initial manuscript, and approved the final version. Christian Weber and Martin Koser were involved in data interpretation and critically revised the manuscript for intellectual content, providing final approval. Norbert Weidner assisted with data acquisition, statistical analysis, manuscript drafting, and revisions. All authors reviewed, approved the final manuscript, and agreed to be accountable for the accuracy and integrity of the work.*

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