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ORIGINAL RESEARCH

# Preserving Neurovascular Bundles Preserves the Mind: Cognitive, Functional, and Quality-of-Life Outcomes of Nerve-Sparing Radical Prostatectomy

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**Introduction:** Radical prostatectomy (RP) is a standard curative treatment for localized Prostate cancer (PCa), but may negatively affect health-related quality of life (HRQoL) through urinary incontinence, erectile dysfunction, psychological distress, cognitive decline. Neurovascular bundle (NVB)–sparing techniques aim to preserve functional outcomes; however, their effects on neurocognitive performance remain unclear.

**Purpose:** This study evaluated the impact of bilateral NVB-sparing RP on cognitive function, psychological status, HRQoL, and biochemical recurrence in patients with PCa.

**Methods:** This retrospective study included 100 Caucasian patients who underwent laparoscopic RP between 2017 and 2022, either with bilateral intrafascial NVB preservation or without NVB sparing, according to European Association of Urology criteria. All surgeries were performed by high-volume surgeons with experience exceeding 250 RPs each. Cognitive function was assessed using a standardized computer-based test. Psychological and functional status was evaluated with the HADS Scale, ICIQ-UI SF and IIEF5 scale. HRQoL was measured with the EORTC QLQ-C30 and PR25 questionnaires. Serum prostate-specific antigen (PSA) and testosterone levels were analyzed.

**Results:** Patients undergoing NVB-sparing RP demonstrated faster reaction times and better visual working memory compared with the non–NVB-sparing group. Postoperative erectile function, urinary continence, and testosterone levels were significantly superior following NVB preservation. HRQoL outcomes favored NVB-sparing RP, including higher global health status, physical, emotional, and cognitive functioning, and reduced fatigue. Anxiety and depression scores were lower but did not reach statistical significance. Lower postoperative PSA and absence of biochemical recurrence were associated with better verbal memory and executive functioning. No significant differences in BCR rates were observed between groups.

**Conclusion:** Bilateral NVB-sparing RP preserves urinary and sexual function while supporting cognitive performance and psychosocial well-being, resulting in improved HRQoL without increasing the risk of BCR. These findings confirm the oncological safety of NVB-sparing RP and support the inclusion of neurocognitive and quality-of-life outcomes in surgical decision-making for patients with prostate cancer.

**Keywords:** prostate cancer, cognition, anxiety, depression, sexual dysfunction, nerve sparing prostatectomy

## Introduction

Prostate cancer (PCa) is one of the most common malignancies in men and remains a major public health concern due to its high incidence and treatment-related complications.[1] Despite advances in diagnostics and therapy, many patients

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experience long-term sequelae that substantially affect their quality of life. In addition to the well-documented complications such as urinary incontinence and erectile dysfunction, increasing attention has been directed toward cognitive impairment, which may occur both prior to treatment and as a consequence of oncological interventions.[2] Neurocognitive deficits, including deterioration in memory, attention, reaction speed, and executive functions, can significantly hinder daily functioning, worsen psychological well-being, and increase patient dependency.[3]

Radical prostatectomy (RP), one of the standard treatment options alongside radiotherapy for localized and locally advanced prostate cancer, is associated with the risk of compromising key domains of quality of life. The introduction of neurovascular bundle (NVB)–sparing techniques, subsequently refined in modern surgical practice, was originally aimed at minimizing postoperative erectile dysfunction and urinary incontinence. However, accumulating evidence suggests that the benefits of NVB preservation may extend beyond purely functional outcomes. Long-term data from the multiregional PROCAS study demonstrated superior health-related quality of life and better physical and emotional functioning in patients undergoing nerve-sparing RP compared with non–nerve-sparing techniques.[4] Given the close interplay between emotional well-being, functional recovery, and cognitive performance, NVB preservation may indirectly support postoperative cognitive outcomes through psychosocial mechanisms. In addition, cognitive impairment has been shown to be prevalent even before prostate cancer treatment, indicating pre-existing neurocognitive vulnerability that may interact with treatment-related factors.[3] Together, these observations provide a rationale for investigating the association between NVB-sparing RP and cognitive function in prostate cancer patients.

Potential mechanisms underlying these associations may include shared vascular determinants of erectile and cerebral circulation, the neuroprotective role of testosterone, and the relevance of oncological markers such as prostate-specific antigen (PSA), which have been shown to correlate with neurocognitive outcomes.[5] Thus, consideration of neuropsychological aspects has become an essential component of comprehensive care for patients with PCa.

The aim of this study was to evaluate the impact of NVB-sparing techniques during RP on cognitive functioning, psychological well-being, and quality of life in the context of oncological and clinical outcomes.

# Materials and Methods

## Participants

A cohort of 100 Caucasian patients diagnosed with prostate cancer (PCa) was recruited for this study. All participants provided written informed consent prior to enrollment. The study population was sourced from an outpatient clinic specializing in urological treatments. Key demographic data, including age, education level, and physical activity, were collected from each participant (see Table 1 for detailed demographics).

To ensure the integrity of the study, a comprehensive medical history was obtained from all subjects. Relevant assessments were also conducted for common comorbidities known to affect cognitive function, such as diabetes and hypertension. Individuals with psychiatric disorders defined according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV), neurological abnormalities, or any history of substance abuse (including illicit drugs and alcohol) were excluded from participation.

All patients underwent radical prostatectomy (RP), performed either with or without preservation of the neurovascular bundles (NVBs). Qualification for NVB-sparing surgery was based on clinical characteristics and tumor localization, in accordance with the European Association of Urology (EAU) guidelines. NVB preservation was defined as bilateral intrafascial sparing of both neurovascular bundles; patients who underwent unilateral NVB preservation were excluded from the analysis. Patients who received neoadjuvant or adjuvant radiotherapy, chemotherapy, or androgen deprivation therapy prior to neuropsychological assessment were excluded from the study. This criterion has now been explicitly stated to minimize potential confounding effects on cognitive and psychological outcomes. NVB-sparing was offered to patients with low-risk disease and a low likelihood of extraprostatic extension on preoperative magnetic resonance imaging. All surgical procedures were performed laparoscopically by three high-volume surgeons, each with an experience of more than 250 RPs. General anesthesia was administered to all patients, either with propofol and sufentanil or with sevoflurane and sufentanil for anesthesia maintenance.

**Table 1** Demographic and Clinical Data of Study Subgroups

| Parameter | | Nerve Sparing (n=39) | Non-Nerve Sparing (n=61) | P |
|---|---|---|---|---|
| **Age (y)** | | 65.0 (59.0–70.0) | 67.0 (62.0–70.0) | 0.60 |
| **BMI (kg/m$^2$)** | | 26.4 (23.9–28.3) | 27.4 (25.8–30.2) | 0.042 |
| **Diabetes (n, %)** | | 5 (13%) | 8 (13%) | 0.98 |
| **Hypertension (n, %)** | | 20 (51%) | 36 (59%) | 0.51 |
| **MI (n, %)** | | 4 (10%) | 5 (8%) | 0.86 |
| **Stroke (n, %)** | | 3 (8%) | 4 (6.5%) | 0.91 |
| **Education** | **Basic (n, %)** | 0 | 5 (8%) | 0.11 |
| | **Vocational (n, %)** | 10 (25%) | 18 (29.5%) | |
| | **Secondary (n, %)** | 13 (33%) | 21 (34.5%) | |
| | **Higher (n, %)** | 16 (41%) | 17 (28%) | |
| **Physical activity** | **None (n, %)** | 9 (23%) | 24 (39%) | 0.034 |
| | **< 1x/week (n, %)** | 15 (38%) | 15 (24.5%) | |
| | **<3x/week** | 15 (38%) | 13 (21%) | |
| **Nicotinism (n, %)** | | 19 (49%) | 28 (46%) | 0.81 |
| **Time from surgery [m]** | | 22.0 (17.0–42.0) | 16.0 (10.0–29.0) | 0.017 |
| **ISUP Grade Group** | **1 (n,%)** | 29 (74%) | 29 (47.5%) | 0.005 |
| | **2 (n,%)** | 9 (23%) | 23 (37.5%) | |
| | **3 (n,%)** | 0 (0%) | 4 (6.5%) | |
| | **4 (n,%)** | 0 (0%) | 3 (5%) | |
| | **5 (n,%)** | 1 (2.5%) | 2 (3%) | |

**Notes**: Data are shown as the median (25th to 75th quartile) or number (%). Inter-group differences were assessed using the Mann–Whitney *U*-test. Significant p-values shown in bold.

**Abbreviations**: BMI, body mass index; MI, myocardial infarction; y, years; m, months; ISUP, International Society of Urological Pathology.

Participants were fully informed about the objectives of the study and provided written informed consent prior to enrollment. The median age of the participants was 66 years, with a range spanning from 50 to 77 years. Ethical approval for the study was granted by the Bioethical Commission of Nicolaus Copernicus University, Collegium Medicum in Bydgoszcz (Approval No. 476/2017).

## Clinical Assessments and Biochemical Measures

Three measurements of Prostate-Specific Antigen (PSA) levels were conducted: prior to surgery, six weeks post-surgery, and during the current assessment. Total testosterone levels were measured during follow-up after radical treatment as part of supplementary care.

## International Index of Erectile Function (IIEF-5) Questionnaire

The IIEF-5 is a condensed version of the International Index of Erectile Function. It is known for its high sensitivity and reliability in assessing erectile dysfunction, regardless of its etiology. The questionnaire consists of five questions, with four addressing the prevalence and severity of erectile dysfunction, and one focused on sexual intercourse satisfaction.

## Subjective Assessment of Erection Quality

Patients rated their ability to achieve erections before and after surgery on a Likert's scale from 1 to 5, where a score of 1 indicated no erection, and a score of 5 indicated no problems with erections.

## International Consultation on Incontinence Questionnaire—Urinary Incontinence (ICIQ-UI)

The ICIQ-UI SF is a brief questionnaire designed to evaluate the severity of urinary incontinence and its impact on quality of life. It consists of four questions regarding the frequency of incontinence episodes, the volume of leakage, the overall impact of incontinence, and a self-diagnostic item. Respondents select the severity of their symptoms from a multi-level scale, with scores ranging from 0 to 21 points.

## Psychological Assessment

Emotional symptoms of depression and anxiety, along with their severity, were assessed using the Hospital Anxiety and Depression Scale (HADS). This self-assessment tool is effective for measuring atypical depressive and anxiety disorders in somatically ill patients. The HADS comprises two sections—one for anxiety and one for depression—each containing seven questions. Patients choose from four response options ranked by symptom severity. Scores for each part are summed individually, with higher scores indicating greater severity of anxiety and/or depressive disorders.

## Neuropsychological Assessment

The neuropsychological tests used in this study were selected to comprehensively assess key cognitive domains that may be affected following radical prostatectomy, including attention, processing speed, executive function, and memory. All assessments were performed using the Neurotest computerized battery, a standardized and validated tool widely applied in clinical and research settings for objective cognitive evaluation.

## Simple Reaction Time (SRT)

In the SRT task, participants respond to a stimulus presented on the computer screen by pressing a key whenever a green circle appears. The task starts with a practice round of five stimuli. The number of correct reactions and the average reaction time (in milliseconds) are recorded, measuring reaction time, general alertness, and motor speed.

## Go/No-Go Test

The Go/No-Go test comprises two components, denoted as "Go" and "NoGo". The "Go" component requires participants to press a key when a green square appears on the screen, whereas the "NoGo" component involves withholding a response when a blue square appears. Stimuli are presented randomly (75 green and 25 blue squares). This test evaluates response times, cognitive control, and inhibitory control by analyzing the number and percentage of correct and incorrect responses as well as the reaction times for correct "Go" responses.

## Verbal Memory and Delayed Verbal Memory Tests (VMT and VMDT)

This assessment consists of five stages. The researcher reads a list of ten words five times, asking the participant to recall the words after each repetition. The words used remain constant throughout the test. The researcher records the number of correctly recalled words, intrusions (words not in the list), and perseverations (repetitions). After a 20-minute interval, the participant is asked to recall the words without assistance. This test assesses immediate auditory memory, learning progression across repetitions, and delayed memory retention.

## Visual Working Memory Test (VWMT)

In this test, seven covered playing cards are sequentially revealed and then covered again (each card is displayed for 2 seconds). The participant must memorize the layout. Subsequently, one card is shown, and the participant indicates its previous location. This process assesses spatial memory by tallying the number of correctly and incorrectly identified locations.

## Statistical Analysis

The Shapiro–Wilk test was employed initially to assess the normality of the distribution of study variables. Due to non-normal distribution, nonparametric tests were utilized in further analyses. The statistical significance of differences was evaluated using the Mann–Whitney *U*-test, while the Spearman correlation coefficient was employed to assess correlations. A p-value of less than 0.05 was considered statistically significant. Additionally, Cohen's d was calculated to facilitate comparisons across results. The statistical analysis were performed using Statistica software (Statistica Release 14.3).

# Results

Initial analyses were performed to examine demographic and clinical differences between the nerve-sparing and non-nerve-sparing surgery subgroups (Table 1). The nerve-sparing subgroup exhibited a significantly lower body mass index (BMI) at the time of the study and reported higher levels of physical activity. Additionally, this group had a significantly longer interval since the surgical procedure. Baseline disease progression, as assessed by the GRADE scale, was significantly less advanced in the nerve-sparing subgroup.

Subsequent analyses evaluated psychological outcomes, including the severity of depressive and anxiety symptoms, as well as cognitive functioning (Table 2). Although patients in the nerve-sparing group reported lower levels of depressive symptoms, the difference did not reach statistical significance. A similar, non-significant trend was observed for anxiety symptoms. In terms of neuropsychological performance, the nerve-sparing subgroup demonstrated significantly faster reaction times on the simple reaction time test and superior performance on the visual working memory task. No significant differences were observed between the groups across other cognitive measures.

**Table 2** Depressive, Anxiety and Cognitive Test Results for the Prostate Cancer Therapy Subgroups

| Parameter | Nerve Sparing (n=39) | Non-Nerve Sparing (n=61) | P |
|---|---|---|---|
| **HADS_A** | 3.0 (1.0–5.0) | 5.0 (2.0–7.0) | 0.076 |
| **HADS_D** | 2.0 (1.0–4.0) | 3.0 (1.0–7.0) | 0.19 |
| **SRT_C** | 25.0 (25.0–25.0) | 25.0 (25.0–25.0) | 0.21 |
| **SRT_RT [ms]** | 261.4 (226.2–302.0) | 290.9 (250.6–332.3) | 0.008 |
| **VM_1** | 6.0 (5.0–7.0) | 5.0 (4.0–7.0) | 0.52 |
| **VM_2** | 7.0 (6.0–8.0) | 7.0 (7.0–8.0) | 0.28 |
| **VM_3** | 8.0 (7.0–9.0) | 7.0 (6.0–8.0) | 0.23 |
| **VM_4** | 8.0 (7.0–10.0) | 8.0 (7.0–9.0) | 0.20 |
| **VM_5** | 8.0 (7.0–10.0) | 8.0 (7.0–9.0) | 0.22 |
| **VMDT** | 6.0 (5.0–7.0) | 5.0 (5.0–7.0) | 0.14 |
| **GoNoGo_C** | 74.0 (73.0–75.0) | 74.0 (73.0–75.0) | 0.42 |
| **GoNoGo_RT [ms]** | 350.6 (316.4–412.6) | 377.0 (339.4–416.5) | 0.21 |
| **GoNoGo incGO** | 1.0 (0.0–2.0) | 1.0 (0.0–2.0) | 0.41 |
| **GoNoGo incNoGo** | 5.0 (3.0–7.0) | 5.0 (2.0–8.0) | 0.79 |
| **VWMT_C** | 6.0 (4.0–7.0) | 5.0 (3.0–6.0) | 0.03 |
| **VWMT_CRT [ms]** | 3133 (2328–4110) | 3156 (2651–4586) | 0.42 |

**Notes**: Data are presented as median (25th–75th percentile). Intergroup differences were assessed using the Mann–Whitney *U*-test.

**Abbreviations**: HADS_A, Hospital Anxiety and Depression Scale—anxiety subscale; HADS_D, Hospital Anxiety and Depression Scale—depression subscale; SRT_C, simple reaction time test (number of correct responses); SRT_RT, simple reaction time test (mean reaction time, ms); VM_1–VM_5, verbal memory test (number of words recalled in each of five trials); VMDT, verbal delayed memory test (number of words recalled); GoNoGo_C, Go/No-Go test (number of correct responses); GoNoGo incGO, number of incorrect Go responses; GoNoGo incNoGo, number of incorrect No-Go responses; VWMT_C, visual working memory test (number of correct responses); VWMT_CRT, visual working memory test (mean reaction time for correct responses, ms).

Biochemical parameters, specifically prostate-specific antigen (PSA) and testosterone levels, were then analyzed (Table 3). PSA levels did not differ significantly between the groups; however, testosterone concentrations were significantly higher in the nerve-sparing subgroup.

Postoperative complications were also assessed, beginning with erectile function (Table 4). Preoperatively, no significant differences were observed in subjective reports of erectile function. In contrast, postoperative assessments revealed significantly better erectile function among patients in the nerve-sparing group, as evidenced by both subjective evaluation and significantly higher scores on the International Index of Erectile Function (IIEF-5).

Urinary incontinence outcomes were assessed using the International Consultation on Incontinence Questionnaire (ICIQ) (Table 5). While overall ICIQ scores did not differ significantly between groups, stratified analysis indicated that lower ICIQ scores (1–4) were significantly more prevalent in the nerve-sparing group, suggesting better continence outcomes. A similar trend was observed for scores in the 5–8 range, though this did not reach statistical significance.

Quality of life (QoL) outcomes demonstrated multiple significant differences in favor of the nerve-sparing subgroup (Table 6). This group reported significantly higher global health status (p = 0.0009) and achieved superior outcomes across several domains of the EORTC QLQ-C30, including physical, role, emotional, and cognitive functioning. Additionally, they reported significantly lower levels of fatigue and fewer financial difficulties. On the prostate cancer–specific EORTC QLQ-PR25 subscale, the nerve-sparing group reported significantly better sexual functioning and significantly lower symptom burden related to urinary problems and hormonal

**Table 3** Biochemical Parameters in Trial Subgroups

| Parameter | Nerve Sparing (n=39) | Non-Nerve Sparing (n=61) | p |
|---|---|---|---|
| **PSA_pre operative [ng/mL]** | 7.3 (5.4–9.1) | 7.99 (5.4–12.2) | 0.22 |
| **PSA_ 6 weeks after operation [ng/mL]** | 0.008 (0.003–0.021) | 0.006 (0.003–0.034) | 0.65 |
| **PSA_ current [ng/mL]** | 0.003 (0.003–0.035) | 0.003 (0.003–0.028) | 0.87 |
| **Total testosterone [ng/mL]** | 5.6 (3.67–7.21) | 3.85 (3.1–5.76) | 0.034 |

**Notes**: Data are shown as the median (25th to 75th quartile). Inter-group differences were assessed using the Mann–Whitney *U*-test. Significant p-values shown in bold.
**Abbreviation**: PSA, prostate specific antigen.

**Table 4** Erectile Function in Study Subgroups

| Parameter | Nerve Sparing (n=39) | Non-Nerve Sparing (n=61) | p |
|---|---|---|---|
| **Erectile dysfunction before surgery (Likert 1–5)** | 4.0 (3.0–5.0) | 4.0 (3.0–5.0) | 0.55 |
| **Erectile dysfunction after surgery (Likert 1–5)** | 3.0 (1.0–4.0) | 1.0 (1.0–1.0) | 0.000006 |
| **IIEF-5** | 7.0 (0.0–18.0) | 0.0 (0.0–2.0) | 0.000014 |

**Notes**: Data are shown as the median (25th to 75th quartile). Inter-group differences were assessed using the Mann–Whitney *U*-test. Significant p-values shown in bold.
**Abbreviation**: IIEF-5, International Index of Erectile Function.

**Table 5** ICIQ Scale Results in Study Subgroups

| Parameter | Nerve Sparing (n=39) | Non-Nerve Sparing (n=61) | p |
|---|---|---|---|
| **ICIQ 1–4** | 1.0 (1.0–1.0) | 1.0 (1.0–2.0) | 0.012 |
| **ICIQ 5–8** | 1.0 (1.0–5.0) | 3.0 (1.0–5.0) | 0.23 |
| **ICIQ total** | 1.0 (1.0–7.0) | 4.0 (0.0–10.0) | 0.18 |

**Notes**: Data are shown as the median (25th to 75th quartile). Inter-group differences were assessed using the Mann–Whitney *U*-test. Significant p-values shown in bold.
**Abbreviation**: ICIQ, International Consultation on Incontinence Modular Questionnaire.

**Table 6** Quality of Life Dimensions in Study Subgroups

| Parameter | Nerve Sparing (n=39) | Non-Nerve Sparing (n=61) | p |
|---|---|---|---|
| **EORTC QLQ** | | | |
| **Global health status** | 12.0 (10.0–12.0) | 10.0 (8.0–11.0) | 0.0009 |
| **Physical functioning** | 5.0 (5.0–7.0) | 6.0 (5.0–8.0) | 0.015 |
| **Role functioning** | 2.0 (2.0–2.0) | 2.0 (2.0–3.0) | 0.014 |
| **Emotional functioning** | 4.0 (4.0–6.0) | 6.0 (4.0–7.0) | 0.017 |
| **Cognitive functioning** | 2.0 (2.0–3.0) | 3.0 (2.0–4.0) | 0.004 |
| **Social functioning** | 2.0 (2.0–2.0) | 2.0 (2.0–4.0) | 0.016 |
| **Fatigue** | 3.0 (3.0–4.0) | 4.0 (3.0–6.0) | 0.004 |
| **Nausea and vomiting** | 2.0 (2.0–2.0) | 2.0 (2.0–2.0) | 0.79 |
| **Pain** | 2.0 (2.0–3.0) | 2.0 (2.0–3.0) | 0.057 |
| **Dyspnoe** | 1.0 (1.0–1.0) | 1.0 (1.0–1.0) | 0.11 |
| **Insomnia** | 1.0 (1.0–2.0) | 1.0 (1.0–2.0) | 0.72 |
| **Appetite loss** | 1.0 (1.0–1.0) | 1.0 (1.0–1.0) | 0.079 |
| **Constipation** | 1.0 (1.0–1.0) | 1.0 (1.0–1.0) | 0.53 |
| **Diarrhoea** | 1.0 (1.0–1.0) | 1.0 (1.0–1.0) | 0.20 |
| **Financial difficulties** | 1.0 (1.0–1.0) | 1.0 (1.0–2.0) | 0.017 |
| **EORTC PR25** | | | |
| **Sexual activity** | 2.0 (2.0–2.0) | 2.0 (2.0–4.0) | 0.039 |
| **Sexual functioning** | 13.0 (3.0–17.0) | 3.0 (2.0–4.0) | 0.00004 |
| **Urinary symptoms** | 10.0 (8.0–13.0) | 11.0 (9.0–15.0) | 0.013 |
| **Bowel symptoms** | 4.0 (4.0–4.0) | 4.0 (4.0–5.0) | 0.20 |
| **Hormonal treatment-related symptoms** | 7.0 (6.0–8.0) | 8.0 (7.0–10.0) | 0.007 |
| **Incontinence aid** | 1.0 (0.0–2.0) | 0.0 (0.0–2.0) | 0.92 |

**Notes**: Data are shown as median (25th – 75th quartile). The significance of differences between groups was assessed using U Mann Whitney's test. Statistically significant values are marked in bold.
**Abbreviations**: EORTC QLQ, European Organization for Research and Treatment of Cancer questionnaire; EORTC PR25, prostate cancer-specific module of European Organization for Research and Treatment of Cancer questionnaire.

## Discussion

The results of our study are consistent with the well-established importance of neurovascular bundle (NVB)–sparing techniques in radical prostatectomy (RP), not only in the context of preserving sexual function and urinary continence, but also, which is particularly relevant, in terms of cognitive functioning. Preservation of the NVBs, introduced into urological practice and subsequently refined in modern surgical techniques, currently represents the gold standard in the pursuit of maximizing quality of life after RP.[6] As demonstrated in our cohort analysis, patients in whom bilateral NVB preservation was achieved not only obtained better functional outcomes with respect to erectile function and continence. Moreover, our data indicate that NVB-sparing surgery positively correlates with improved neurocognitive functioning (simple reaction time SRT_RT, $p = 0.008$, and visual memory VWMT_C, $p = 0.03$), which may suggest shared neurophysiological mechanisms underlying these phenomena.[7] A potential marker of this relationship may be the preoperative self-reported quality of erections, which could reflect not only intact vascular function within the pelvic region, but also cerebrovascular and coronary circulation integrity, a finding well supported by previous research.[8–10]

The application of NVB-sparing techniques should not be regarded as an oncological compromise. Advances in imaging, particularly high-resolution magnetic resonance imaging (MRI), combined with modern minimally invasive techniques, have significantly improved the accuracy of local staging and patient selection, as well as facilitated precise NVB-sparing procedures.[11] With appropriate selection, based on D'Amico risk stratification and multiparametric MRI findings, NVB preservation does not increase the risk of positive surgical margins or biochemical recurrence.[12] In our study, consistent with previous reports, patient selection in line with European Association of Urology (EAU) guidelines

enabled the application of NVB-sparing without a significant impact on positive surgical margin rates or biochemical recurrence.[12,13]

Importantly, as we have demonstrated in our earlier work, lower PSA levels after radical prostatectomy correlated with superior performance in cognitive function tests. Preoperative PSA concentrations, however, did not show a significant association with neurocognitive parameters. Long-term postoperative follow-up revealed a clear relationship: patients with lower PSA values achieved better results in verbal memory and executive function tests, suggesting that oncological treatment efficacy may influence overall cognitive performance.[14] Previous studies have also suggested that PSA may serve as a marker of cognitive function. Sternberg et al reported a significant association between PSA levels and cognitive status in patients with Alzheimer's disease, mild cognitive impairment, and in control subjects.[15] Lin et al confirmed a correlation between elevated PSA levels and an increased risk of prostate cancer among patients with Alzheimer's disease.[16] The underlying mechanisms remain unclear. The presence of PSA in cerebrospinal fluid may affect brain function; however, its concentrations are usually very low, and higher values are most often attributable to central nervous system metastases.[5]

Postoperative PSA levels also appear to be an important factor in the context of anxiety and depressive symptoms as assessed by the HADS scale.[14] Furthermore, our study demonstrated that NVB-sparing was associated with lower severity of these symptoms. This may be partly related to better functional outcomes regarding erectile function (IIEF-5 scale) and urinary continence (ICIQ scale) observed in NVB-sparing patients. These findings highlight that both oncological outcomes (PSA levels) and functional aspects (NVB preservation) are important for the psychological well-being of patients after prostatectomy. In addition to worse cognitive functioning in patients with more advanced histopathological disease, the lack of NVB preservation itself may represent an additional factor negatively affecting neurocognitive performance.

Although the feasibility of NVB-sparing depends directly on the local stage of prostate cancer on MRI and clinical parameters, in many patients the intraoperative performance of this step—regardless of surgical approach—may be challenging.[17,18] Patients without NVB preservation were older, had higher BMI, and carried a greater burden of cardiovascular and metabolic comorbidities. In obese men, robotic prostatectomy has been associated with longer operative times, greater blood loss, higher rates of positive surgical margins, and increased risk of conversion to open surgery.[19] However, with the progressive refinement of NVB-sparing techniques, the impact of these factors has markedly decreased over time.[20,21]

In light of these findings, high BMI may no longer significantly limit the feasibility of NVB preservation, yet it remains an important risk factor for cognitive impairment. A recent cross-sectional study demonstrated a significant decline in cognitive function and reduced brain-derived neurotrophic factor (BDNF) levels with increasing BMI.[22] High BMI is also a risk factor for hypogonadotropic hypogonadism, which may contribute to cognitive decline in men.[23] Preoperative total testosterone concentrations above 300 ng/mL represent a predictive factor for postoperative erectile function after NVB-sparing surgery.[24] Higher testosterone levels in older men have been associated with healthier lifestyle behaviors, which may partly explain our observations.[25]

In our cohort, contrary to earlier reports suggesting no significant differences in most quality-of-life parameters between patients undergoing nerve-sparing and non-nerve-sparing prostatectomy, the results obtained here indicate a clear advantage of the NVB-sparing group.[4] These patients achieved significantly higher overall health status, better scores in physical, role, emotional, and cognitive functioning, and reported lower fatigue and fewer financial difficulties. These findings suggest that NVB preservation may provide long-term benefits not only in the sexual domain but also in the broader context of quality of life in prostate cancer survivors.

## Limitations

The main limitations of this study include its retrospective design and the use of laparoscopic technique, although all procedures were performed by highly experienced NVB-sparing surgeons. In addition, postoperative neuropsychological assessments were carried out at varying time intervals, which may have affected the comparability of results.

## Conclusion

Bilateral NVB-sparing radical prostatectomy was associated with significantly faster reaction times and better visual working memory compared with non–NVB-sparing surgery. Patients in the NVB-sparing group also demonstrated significantly better postoperative erectile function, higher testosterone levels, more favorable urinary continence profiles, and superior health-related quality of life, including higher global health status and improved physical, emotional, and cognitive functioning. No significant differences in PSA levels or biochemical recurrence rates were observed between groups, indicating comparable oncological outcomes.

## Abbreviations

BDNF, Brain-Derived Neurotrophic Factor; BMI, Body Mass Index; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders; Fourth Edition; EAU, European Association of Urology; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; Core 30; EORTC QLQ-PR25, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; Prostate Cancer–Specific Module; HADS, Hospital Anxiety and Depression Scale; HRQoL, Health-Related Quality of Life; ICIQ, International Consultation on Incontinence Questionnaire; ICIQ-UI SF, International Consultation on Incontinence Questionnaire, Urinary Incontinence Short Form; IIEF-5, International Index of Erectile Function; 5-item version; MoCA, Montreal Cognitive Assessment; MRI, Magnetic Resonance Imaging; NVB, Neurovascular Bundle; PCa, Prostate Cancer; PSA, Prostate-Specific Antigen; QoL, Quality of Life; RP, Radical Prostatectomy; SRT, Simple Reaction Time; VMDT, Verbal Memory Delayed Test; VMT, Verbal Memory Test; VWMT, Visual Working Memory Test.

## Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Bioethics Committee of Nicolaus Copernicus University, Collegium Medicum in Bydgoszcz (Approval No. KB 508/2017). Written informed consent was obtained from all participants prior to inclusion in the study.

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## Author Contributions

BB and AP conceived and designed the study. PJ, KG, WT, FM, and FD collected the data. AP and AB performed the neuropsychological assessments. MB conducted the statistical analysis. BB drafted the manuscript. All authors critically revised the manuscript and approved the final version.

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The author(s) report no conflicts of interest in this work.

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