



University of
Zurich^{UZH}

Zurich Open Repository and
Archive

University of Zurich
Main Library
Strickhofstrasse 39
CH-8057 Zurich
www.zora.uzh.ch

Year: 2018

A Prospective Analysis of the Effects of Nerve-Sparing Radical Prostatectomy on Urinary Continence Based on Expanded Prostate Cancer Index Composite and International Index of Erectile Function Scoring Systems

Hefermehl, Lukas; Bossert, Karolin; Ramakrishnan, Venkat M; Seifert, Burkhardt; Lehmann, Kurt

Abstract: **PURPOSE** This study aims to objectively characterize the effect of successful nerve sparing (NS) during radical prostatectomy (RP) on postoperative urinary continence (UC) using International Index of Erectile Function (IIEF)-scores and a previously described Expanded Prostate Cancer Index Composite (EPIC) score cutoff value (COV) for UC. Several notable studies on this topic present conflicting outcomes. This is largely due to a lack of clear definitions and consensus regarding preserved erectile function (EF) and UC. **METHODS** This study is comprised of all patients who underwent RP at the Kantonsspital Baden, Switzerland, between 2004 and 2013. Patients completed self-assessment questionnaires for UC (EPIC) and EF (IIEF) pre- and postoperatively (3, 6, 9, 12, 18, and 24 months; yearly thereafter). We used a previously described EPIC subscore COV, with "satisfactory continence" signified by a score ≥ 85 . Statistical analysis was performed using Kaplan-Meier and Cox regression analyses for "surgeon-" and "IIEF-defined" NS definitions. **RESULTS** Of 236 men with a median age of 63 years (interquartile range [IQR], 59-66 years) and median follow-up time of 48 months (IQR, 30-78 months), 176 underwent unilateral (n=33) or bilateral (n=143) NS RP. Fifty-four underwent non-NS (NNS) RP. Kaplan-Meier analyses identified the following risk factors for UC: age, prostate volume, cancer risk group, and NS status. In surgeon-defined NS RP cases, multivariate analysis for regaining continence demonstrated no significant difference (hazard ratio [HR], 0.78; 95% confidence interval [CI], 0.48-1.25; $P=0.3$). With successful IIEF-defined NS RPs, regression analysis demonstrated no significant difference (HR, 0.89; 95% CI, 0.59-1.35; $P=0.58$). **Conclusions** In our population, analysis and comparison of surgeon- and IIEF-defined NS and NNS cohorts revealed that NS RP did not improve postoperative UC. The conservation of UC alone should not motivate surgeons or patients to pursue NS RP.

DOI: <https://doi.org/10.5213/inj.1836052.026>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-153340>

Journal Article

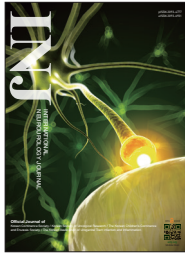
Published Version



The following work is licensed under a Creative Commons: Attribution 4.0 International (CC BY 4.0) License.

Originally published at:

Hefermehl, Lukas; Bossert, Karolin; Ramakrishnan, Venkat M; Seifert, Burkhardt; Lehmann, Kurt (2018). A Prospective Analysis of the Effects of Nerve-Sparing Radical Prostatectomy on Urinary Continence Based on Expanded Prostate Cancer Index Composite and International Index of Erectile Function Scoring Systems. *International Neurourology Journal*, 22(2):123-132.
DOI: <https://doi.org/10.5213/inj.1836052.026>



A Prospective Analysis of the Effects of Nerve-Sparing Radical Prostatectomy on Urinary Continence Based on Expanded Prostate Cancer Index Composite and International Index of Erectile Function Scoring Systems

Lukas Hefermehl^{1*}, Karolin Bossert^{1*}, Venkat M. Ramakrishnan¹, Burkhardt Seifert², Kurt Lehmann¹

¹Division of Urology, Department of Surgery, Kantonsspital Baden, Baden, Switzerland

²Department of Biostatistics, University of Zürich, The Epidemiology, Biostatistics and Prevention Institute, Zürich, Switzerland



Purpose: This study aims to objectively characterize the effect of successful nerve sparing (NS) during radical prostatectomy (RP) on postoperative urinary continence (UC) using International Index of Erectile Function (IIEF)-scores and a previously described Expanded Prostate Cancer Index Composite (EPIC) score cutoff value (COV) for UC. Several notable studies on this topic present conflicting outcomes. This is largely due to a lack of clear definitions and consensus regarding preserved erectile function (EF) and UC.

Methods: This study is comprised of all patients who underwent RP at the Kantonsspital Baden, Switzerland, between 2004 and 2013. Patients completed self-assessment questionnaires for UC (EPIC) and EF (IIEF) pre- and postoperatively (3, 6, 9, 12, 18, and 24 months; yearly thereafter). We used a previously described EPIC subscore COV, with “satisfactory continence” signified by a score > 85. Statistical analysis was performed using Kaplan-Meier and Cox regression analyses for “surgeon-” and “IIEF-defined” NS definitions.

Results: Of 236 men with a median age of 63 years (interquartile range [IQR], 59–66 years) and median follow-up time of 48 months (IQR, 30–78 months), 176 underwent unilateral (n = 33) or bilateral (n = 143) NS RP. Fifty-four underwent non-NS (NNS) RP. Kaplan-Meier analyses identified the following risk factors for UC: age, prostate volume, cancer risk group, and NS status. In surgeon-defined NS RP cases, multivariate analysis for regaining continence demonstrated no significant difference (hazard ratio [HR], 0.78; 95% confidence interval [CI], 0.48–1.25; P = 0.3). With successful IIEF-defined NS RPs, regression analysis demonstrated no significant difference (HR, 0.89; 95% CI, 0.59–1.35; P = 0.58).

Conclusions: In our population, analysis and comparison of surgeon- and IIEF-defined NS and NNS cohorts revealed that NS RP did not improve postoperative UC. The conservation of UC alone should not motivate surgeons or patients to pursue NS RP.

Keywords: Prostate; Prostatectomy; Urinary incontinence; Self-assessment

- **Research Ethics:** This study was approved by the Research Ethics Committee of Ethikkommission Nordwest- und Zentralschweiz (EKNZ) (BASEC 2016-00323). Written informed consent was obtained from all subjects.
- **Conflict of Interest:** No potential conflict of interest relevant to this article was reported.

Corresponding author: Lukas Hefermehl  <https://orcid.org/0000-0002-8467-5333>
Division of Urology, Department of Surgery, Kantonsspital Baden, Im Ergel 1,
Baden, Switzerland

E-mail: lukas.hefermehl@gmail.com / Tel: +41-56-486-30-92 / Fax: +41-56-486-11-11

*Lukas Hefermehl and Karolin Bossert contributed equally to this study as co-first authors.

Submitted: February 17, 2018 / **Accepted after revision:** April 30, 2018



This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

While achieving the “trifecta” —being cancer-free, continent and potent— is the commonly anticipated goal of many radical prostatectomy (RP) patients, issues such as urinary incontinence (UI) and erectile dysfunction (ED) are often realities that considerably impact their quality of life (QoL) [1]. The nerve-sparing (NS) RP, pioneered by Walsh et al. [1] in the 1980s, sought to reduce rates of UI and ED through careful dissection of the neurovascular bundles away from the prostate during prostatectomy. Initial reports comparing Walsh's approach to its predecessor were promising and demonstrated improved urinary continence (UC). However, subsequent papers have painted a mosaic of results with variable rates of continence dictated by numerous potential confounders [2-9]. Such observations led us to question if NS RP was a clinically significant approach in our own patient population. With the exception of perineural invasion due to significant tumor burden, aggression, or extension, the NS RP is typically championed by urologic surgeons and educated patients [10].

Even if it is successfully performed, the positive effect of NS on postoperative UC is controversial. Some studies from the past decade have emphasized that NS approaches (1) should be performed whenever possible and within clinical reason [8], (2) reduce the time to regained continence [4], and (3) do not adversely affect pathologic outcomes [6]. To contrast, we and others have suggested that there is no significant difference between NS and non-NS procedures regarding long-term continence [5,7,11]. Tzou et al. [5] indicated that the similar outcomes of NNS and NS procedures might be attributable to large differences in data acquisition. Moreover, the heterogeneity of the definitions for continence, and especially for successful NS, further complicates this issue [12].

There is a discrepancy between the “intention to perform” NS and NS that is both successful and effective. Thus, from this, there are 2 possible ways to define NS. One definition is derived from the surgeon's operative note (surgeon-defined), which is a subjective definition that does not necessarily prove that the essential nerves were successfully spared. A second definition is based on functional outcomes such as preservation of penile erections, which is only possible if the neurovascular bundles (NVB) were themselves preserved. This is an objective way of indicating a successful NS surgery [13,14].

We surmised that if NS did indeed have an effect on continence, then there must be a correlation between potency and

continence. Therefore, we hypothesized that the most comprehensive definition of effective NS would be seen in the postoperative recovery of erectile function per the patient International Index of Erectile Function (IIEF)-scores (IIEF-defined). In consideration of the given endpoint of the study, we performed calculations for both surgeon-defined and IIEF-defined NS modalities. Here, we present the results of a prospective investigation on a cohort of patients who underwent RP at our institution over a 9-year period.

MATERIALS AND METHODS

Patient Collective/Cohort

All patients who underwent open RP between January 2004 and January 2013 at the Kantonsspital Baden, Switzerland, were enrolled in the study. During this period, all operations were performed in the same fashion by 5 surgeons; the same senior surgeon was present for all of the operations to provide consistent oversight. Furthermore, the NS step was performed by the senior surgeon in all cases.

Data Acquisition

Functional data was prospectively acquired using self-assessment questionnaires (described below). We also documented clinical and oncological data. Any missing data in the database was later obtained via the patients' medical records. The database was built using Access and Excel (Microsoft Corp., Redmond, WA, USA).

Self-Assessment Questionnaires

All patients were given a self-assessment questionnaire preoperatively, 3, 9, 12, 18, and 24 months postoperatively, and yearly thereafter. The questionnaire was comprised of 3 sections: (1) the urinary domain of the “Expanded Prostate Cancer Index Composite” (EPIC; discussed below); (2) the IIEF (discussed below); and (3) our institutional Likert system-based questionnaire (also discussed below; used since 1999) to globally assess QoL (Appendix 1).

Expanded Prostate Cancer Index Composite

The EPIC is a well-established and widely used instrument and is comprised of urinary, bowel, and sexual domains [15]. We used the EPIC urinary domain, which consists of 12 questions with 4 to 5 possible answers (symptoms related to obstruction, irritation, and incontinence etc.). Each question was scored on

a scale from 0 to 100. Subscores were summed and averaged to determine a total score for the whole assessment, with higher scores indicating better urinary function [15].

International Index of Erectile Function

The IIEF-EF domain is an abbreviated version of the IIEF-15 that pertains specifically to erectile function as well as patient confidence in having and maintaining erections [16]. Specifically, the questionnaire is comprised of items 1, 2, 3, 4, 5, and 15 and is scored out of 30 points; each question is worth 5 points. Scores of 1–10 indicate severe ED, 11–16 indicate moderate ED, 17–21 indicate mild to moderate ED, 22–25 signify mild ED, and 26–30 represent no ED. For the purposes of this study, we state that scores <11 are ‘not potent’ and scores \geq 11 are ‘potent’.

Quality of Life

We asked questions concerning different aspects of QoL in the form of an internally developed 7-stepped Likert scale (0–6 points), which conforms to those aspects comprising International Prostate Symptom Score/quality of life questionnaires (Appendix 1).

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics ver. 23.0 (IBM Co., Armonk, NY, USA). To determine differences between groups for interval scaled and ordinal variables, we utilized the Mann-Whitney U-test. Categorical variables were appropriately compared using chi-square or Fisher exact tests. For continuous values, the means (with \pm standard deviation) or medians (with interquartile range) are given. Kaplan-Meier analysis for the recovery of continence within the follow-up time as well as multivariate Cox regression analyses for the 2 NS definitions (surgeon-defined and IIEF-defined [IIEF-EF \geq 11]) were used. Hazard ratios were presented with 95% confidence intervals.

Urinary Continence

A subgroup of the EPIC score, termed the “EPIC urinary incontinence” (EPIC-UI), is thought to be the most precise means of describing UI [17]. In an earlier publication, we determined that the optimal COV for “satisfactory continence” was >85 [12].

IIEF-Defined NS

We divided our analysis of IIEF-defined NS outcomes into 2 subgroups: (1) successful NS (henceforth: “NS [EF]”) are all pa-

tients who attained an IIEF-EF score of at least 11 during their follow-up, and (2) a group of patients who postoperatively never reached an IIEF of 11 (NNS [EF]). Men with preoperative erectile dysfunction (IIEF-EF < 11) were excluded from further analysis.

RESULTS

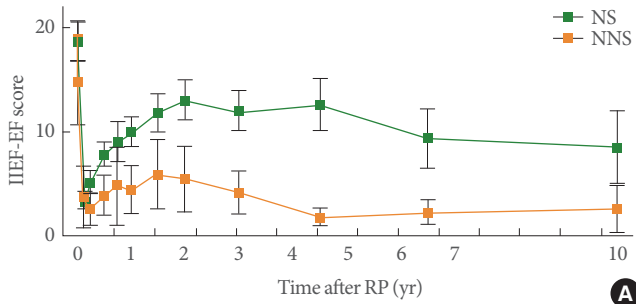
Between January 2004 and October 2013, 253 men underwent RP at our institution. Seventeen men did not complete preoperative questionnaires and were consequently excluded from the study. All clinical data from the remaining 236 patients were collected and compared. Applying our previously described quantifiable definition of continence (EPIC-UI > 85), a Kaplan-Meier analysis demonstrated a cumulative continence rate of 76% for the entire cohort. At 1 year postoperatively, 53% recovered satisfactory continence; at 2 years, 61%; and at 3 years, 65%.

Qualitative (Surgeon-Defined) vs. Quantitative (Postoperative IIEF-Defined) Definitions of NS

Surgeon-defined NS RP

Supplementary Tables 1–3 demonstrate an overview of the patient data concerning oncologic and functional data regarding surgeon-defined NS. Six patients were excluded from the analysis due to a lack of documentation regarding their NS status. Compared to those who underwent NS RP, patients who underwent NNS RP were significantly older (median age: 65 years [62–69 years] vs. 63 years [58–66 years], $P=0.0015$) and typically had prostate disease of higher stage (proportion of pT3 tumors: 44% [24 of 54] vs. 20% [34 of 174], $P<0.0001$) and grade (proportion of Gleason scores > 7: 46% [25 of 54] vs. 3% [5 of 175], $P<0.0001$). These patients also expressed a higher median prostate-specific antigen (PSA) at baseline (6.85 ng/mL [5.5–10.22 ng/mL] vs. 5.44 ng/mL [4.21–7 ng/mL], $P=0.0003$) as well as increased median PSA density (0.19 [0.14–0.32] vs. 0.17 [0.12–0.24], $P=0.023$). Macroscopic positive margins as well as positive lymph nodes were also more likely to occur in NNS RP patients versus those who underwent NS RP (R2: 15% [8 of 54] vs. 3% [6 of 176], $P=0.005$; pN1: 15% [8 of 54] vs. 3% [5 of 176], $P=0.002$).

Assessment of the surgeon-defined NS status on erectile function revealed a significant difference in the mean IIEF-EF scores between the surgeon-defined-NS and -NNS groups at 1 year postoperatively (10 ± 8.6 vs. 4.5 ± 6.8 , $P<0.0001$) (Fig. 1) as well as in the Kaplan-Meier estimates for the recovery of poten-



Time	NS	NNS	P-value
Preoperative	19 ± 10.5	15 ± 11.6	0.053
1.5 Months	3 ± 3.2	4 ± 7.2	0.079
3 Months	5 ± 6.1	3 ± 4.6	<0.0001
6 Months	8 ± 7	4 ± 5	<0.0001
9 Months	9 ± 8.4	5 ± 7.1	0.01
1 Year	10 ± 8.6	4 ± 6.8	<0.0001
1.5 Years	12 ± 9.7	6 ± 8.2	<0.0001
2 Years	13 ± 9.7	6 ± 7.2	<0.0001
3 Years	12 ± 9.8	4 ± 5.4	<0.0001
4.5 Years	13 ± 9.9	2 ± 1.6	<0.0001
6.5 Years	9 ± 9.1	2 ± 1.9	0.01
10 Years	9 ± 9	3 ± 1.6	0.22

Fig. 1. Mean IIEF-EF scores over time with surgeon-defined nerve-sparing (NS) status. Graphical (A) and table (B) overview of mean IIEF-EF scores and 95% confidence intervals with respect to surgeon-defined NS. IIEF-EF, International Index of Erectile Function (erectile function domain); RP, radical prostatectomy; NNS, non-NS. P-values were measured using the Mann-Whitney U-test. Values are presented as mean ± standard deviation.

cy (defined as an IIEF-EF > 10; 60% vs. 16%, P < 0.0001) (Fig. 2).

Preoperative erectile function appeared to be an important parameter for further analysis. One hundred seventeen patients out of those who underwent surgeon-defined NS RP demonstrated preoperative IIEF-EF scores > 10. Kaplan-Meier analysis revealed that 27% of these patients ultimately did not reach IIEF-EF scores > 10 postoperatively (Fig. 3). Of those who underwent surgeon-defined NNS RP without preoperative ED (i.e., they were considered potent, with IIEF-EF scores > 10), 20% (11 of 55) achieved postoperative IIEF-EF scores > 10.

Collectively, these findings demonstrate a generalized failure rate in the surgeon's declaration of NS status, giving sufficient

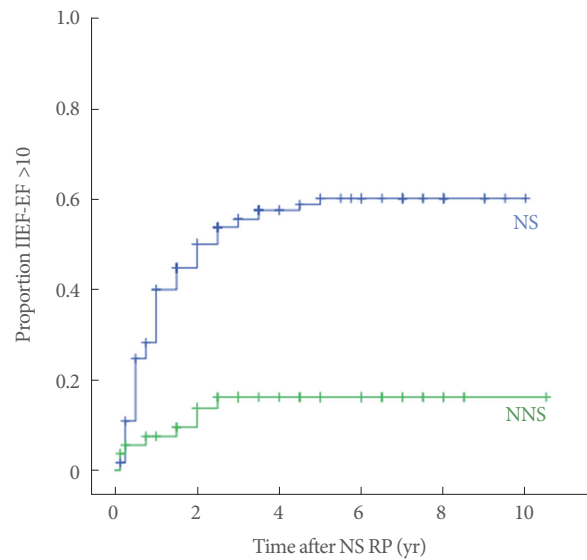


Fig. 2. Erectile function recovery (surgeon-defined NS). Kaplan-Meier curve outlining the recovery of erectile function (IIEF-EF score > 10) with respect to surgeon-defined NS. +/+ indicates censor. NS, nerve-sparing; NNS, non-NS; RP, radical prostatectomy; IIEF-EF, International Index of Erectile Function (erectile function domain).

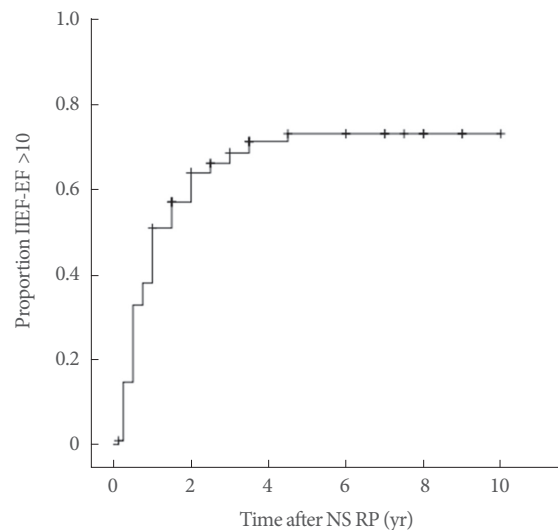


Fig. 3. Erectile function in patients without pre-existing erectile dysfunction (ED). Kaplan-Meier curve outlining the recovery of erectile function (International Index of Erectile Function [erectile function domain] score [IIEF-EF] > 10) in patients without preoperative total ED (IIEF-EF score ≤ 10). NS, nerve-sparing; RP, radical prostatectomy. + indicates censor.

reason to attempt a second approach to define NS status utilizing postoperative IIEF scores.

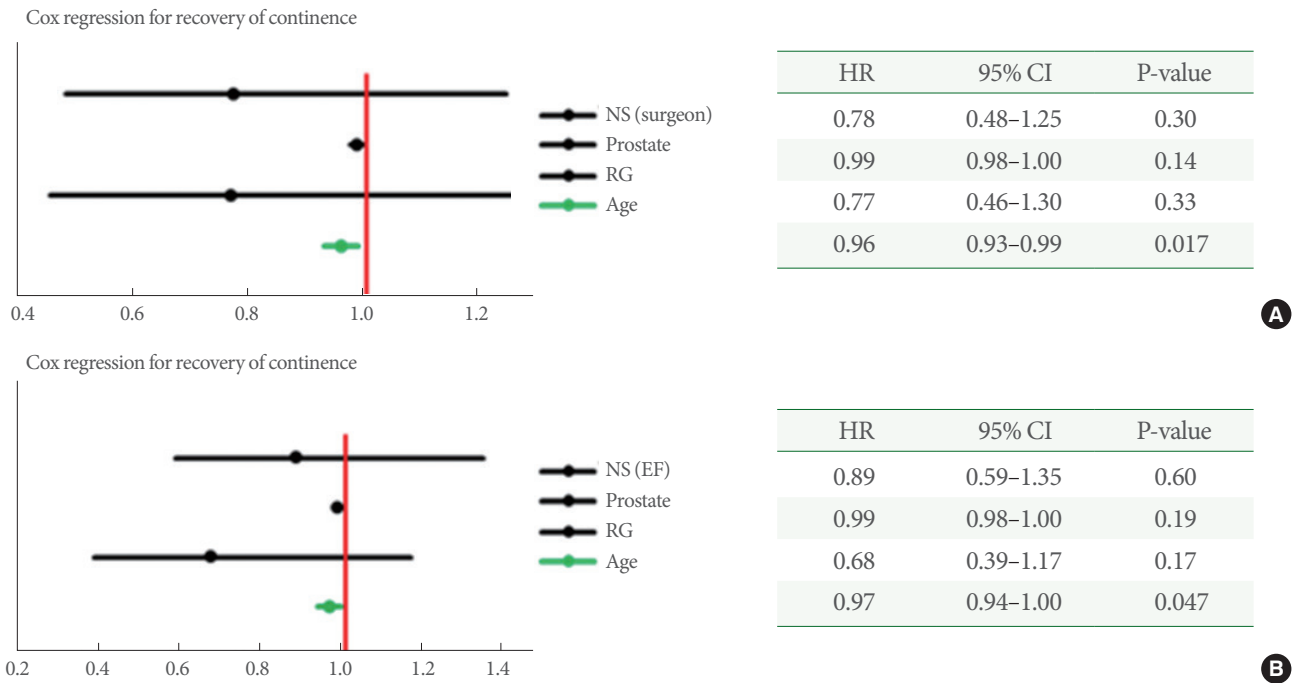


Fig. 4. Plots of urinary continence recovery. Hazard ratio (HR) plot of Cox regressions for the recovery of urinary continence (UI-85) as a function of surgeon-defined nerve-sparing (NS) status (A), and IIEF-defined NS status (B), with age (years), prostate volume (mL), European Association of Urology risk groups (RGs) 1 & 2, and a table overview of the results shown for each of the graphs. CI, confidence interval; IIEF, International Index of Erectile Function.

Postoperative IIEF-defined NS RP

Fifty-one men were excluded from our analyses due to preoperative ED (characterized by IIEF-EF scores <11). Still, we wished to determine if these exclusions would have yielded any significant findings; no significant differences in the EPIC-UI scores were observed at any time point between the excluded and remaining populations (Mann-Whitney U-test, P >0.05). As expected, the mean IIEF-EF scores in the excluded group were significantly lower preoperatively as well as during postoperative follow-up (Mann-Whitney U-test, P <0.05).

Supplementary Tables 4–6 depict the data at baseline as well as oncologic and functional data during follow-up for postoperative IIEF-defined NS. Patients with NNS (EF) were older (65 years [61–67 years] vs. 62 years [56–65 years], P = 0.0007), had a greater tumor stage (pT3: 34% [26 of 77] vs. 19% [22 of 115], P = 0.022) and had a higher grade (Gleason score >7: 31% [24 of 78] vs. 3% [4 of 115], P <0.0001) as well as higher PSA (6.7 ng/mL [5.43–9.63 ng/mL] vs. 5.4 ng/mL [4.27–6.73 ng/mL], P <0.0001) at baseline than patients who underwent successful IIEF-defined NS. NNS patients also exhibited a higher rate of macroscopic positive margins (pR2: 10% [8 of 78] vs. 3% [3 of

116], P = 0.024) and positive lymph nodes (pN1: 13% [10 of 78] vs. 2% [2 of 116], P = 0.002) than those who underwent successful IIEF-defined NS.

Influential Factors

Through Kaplan-Meier analyses, the following factors were found to negatively influence UC recovery and the postoperative timepoint at which UC was achieved: higher age (≥63 years, which is the median value of the respective Kaplan-Meier curve), positive lymph nodes, higher prostate volume (≥33 g, which is also the median value of the respective Kaplan-Meier curve), clinical high-risk group (RG3 as defined by D’Amico/European Association of Urology & American Urological Association guidelines), and NNS (surgeon) and NNS (EF) statuses (Supplementary Fig. 1) [18].

The following factors were not found to significantly influence the postoperative continence: senior surgeon performing the entire RP, uni- vs. bilateral NS, bilateral NS vs. unilateral NNS, preoperative IIEF-EF scores (>10, >18, and >21), preoperative continence (EPIC-UI >85), preoperative PSA values (<4, ≥4, <10, and ≥10), prior history of TURP or active sur-

veillance, biochemical recurrence, recurrence-free survival (2 or 5 years), use of androgen deprivation therapy, use of adjuvant radiotherapy, Gleason score (6, 7, and ≥ 8), tumor stage (pathological or clinical), positive margins, and metastasis.

Multivariate Regression Analyses

To test the prognosis regarding “recovery of continence” for the complete timeframe, parameters such as NS status, age, prostate volume, and cancer risk group were assessed using the Cox regression in a consolidated model [18]. Lymph node status was excluded due to a congruent representation with the risk group parameter as well as the low number of men with positive status ($n = 13$). Cox regression analyses with surgeon-defined NS (Fig. 4A) as well as IIEF-defined NS (Fig. 4B) revealed a significant negative influence on postoperative UC for higher age (≥ 63 years) only, but not for NS status.

To achieve maximum comparability, a Cox regression was performed for the binary “no pad” definition of UC as well, with an emphasis on the following factors: age, prostate volume, risk group, and NS (surgeon- and IIEF-defined) status. Neither surgeon- nor IIEF-defined NS statuses demonstrated significant influences on the recurrence of postoperative UC defined by a lack of pad usage (Appendix 2).

DISCUSSION

Though the pathogenesis of UI after RP for most patients is based on the presumed intraoperative destruction of the NVB as well as the innervated accompanying muscle tissue, the influence of NS RP on UC preservation remains controversial [3,9,19,20]. Initial reports comparing Walsh’s approach to its predecessor were promising, respectively demonstrating rates of continence as high as 85% versus 16% [21]. Yet, the analysis of over 3 decades’ worth of international NS prostatectomies has yielded a notable mix of results. Flynn and Webster [22] reported a high heterogeneity of outcomes, with post-RP UI spanning the low single-digits up to 74%. To that end, Sanda et al. [2] pointed to age, high PSA scores, and race as factors that affected post-RP UI rates. Reeves and colleagues suggested that NS RP ultimately resulted in earlier recovery of UC but at the 1- and 2-year follow-ups, there was no difference in the rates of continence between those who underwent NS RP versus those who underwent NNS RP [7]. In totality, such studies are highly variable with respect to their data analysis and interpretation [9].

Oftentimes, the available data assessing UI or NS are ac-

quired in different descriptive manners and, at the same time, UI and NS often lack consistent definitions. UI for example, is often defined as being reliant on one or no pads, while NS is usually defined by the surgeon or pathology reports [3-9,12]. However, our study is based on self-reporting questionnaires; here, successful NS is defined by a satisfactory functional outcome regarding erectile function, which proves that the cavernous nerves were maintained and are functional. In another regard, strongly influencing variables such as age have not been recognized in many studies [23]. Lastly, the impact of modern surgical advances (such as laparoscopic- and robotic-assisted techniques) lack widespread systematic assessment with respect to UI. To this end, a recent publication demonstrated similar functional outcomes between open and robotic-assisted RPs [24].

Kundu et al. [20] assessed the impacts of NS and demonstrated similar results to ours. A positive association was seen between young age and preservation of continence, but none was seen between NS and the prevention of UI [20]. To contrast, Park et al. [6] analyzed a cohort of 360 patients, revealing significantly better UC rates with NS. However, they defined continence as requiring “no pad.” Slight differences from this definition, such as subjectively good continence despite the use of security pads during physical activity, were otherwise classified as “incontinent.” Furthermore, the study utilized only surgeon-defined NS statuses; histologic assessment of functional nerve preservation was not performed, and postoperative potency outcome was not reported. This methodology is congruent to several other studies but not all [3,8,25]. Other studies have defined NS in more unique ways. For example, in addition to using surgeon-defined NS statuses, Tzou et al. [5] performed a subgroup analysis with “successful NS” defined as one that ultimately yielded an erection “firm enough for intercourse.” Of note, this study did not demonstrate any influence of NS on UI. Taking all of this into account, we believe that the controversy surrounding the efficacy of NS RP on UC essentially lies with the definition of continence and the definition of NS. In an attempt to address this, we were the first to use the EPIC scoring system to quantitatively define continence [12]. EPIC allowed us to describe continence in a more nuanced fashion, versus simply relying on the binary definition of “pad” vs. “no pad.” In this study, we expanded upon our quantitative definition of UI by also quantifying the functional outcomes of NS RP using the IIEF scoring system.

A point of distinction between the NNS and NS cohorts is that the NNS group was significantly older and their tumor

burden significantly larger (Supplementary Tables 2, 5). Traditional wisdom might indicate that an older group with higher tumor burden (receiving NNS surgery) would have impaired continence compared to a younger group with less tumor burden (receiving NS surgery). However, we found no such differences.

To establish a degree of homology with prior work, we also performed a subanalysis using surgeon-defined NS. Here, too, we found no difference in UI rates between either definition of NS and NNS surgery. We also performed a subanalysis using the term “successful NS,” but strayed away from defining success based on penile tumescence for intercourse [5]. Instead, we relied upon another clear, widely accepted scoring system — IIEF — to assess potency. In all of these subanalyses, NS did not influence the return or preservation of UC.

Such results are surprising because there is a preponderance of data supporting the NS approach. However, our study demonstrates a different approach to defining “NS,” which ultimately impacted how we assessed postoperative outcomes. Additionally, there is a growing body of work that questions the role of the NVB in explicitly innervating the urinary sphincters versus its more clear-cut role in innervating the penis and contributing to potency [26–29]. This is still an area of debate, as a recent publication suggested that the NS technique (and not NVB preservation) was paramount to UC preservation [30].

Strengths of this study include: long follow-up (up to 9 years), largely unchanged, single institution, and single senior surgeon.

On the other hand a corresponding criticism to our single-center status and geographic location would undoubtedly be having a small cohort size. However, the number of patients in our study is comparable in size to several studies [7]. Furthermore, even if significant differences in the postoperative UC of NS and NNS surgeries were seen with higher patient volumes, the clinical relevance of NS surgery would still be called into question.

In conclusion, in this study, we used the IIEF-EF scoring system to objectively measure the postoperative success of NS RP and found that NS RP did not improve postoperative UC. NS surgery conducted with the intent of improving postoperative UC is not necessarily evidence-based. Conservation of UC should not be the primary motivating factor in whether or not a patient and surgeon decide to pursue NS RP and should be highly questioned in the presence of preoperative ED.

SUPPLEMENTARY MATERIALS

Supplementary Tables and Figure can be found via <https://doi.org/10.5213/inj.1836052.026>.

[org/10.5213/inj.1836052.026](https://doi.org/10.5213/inj.1836052.026).

AUTHOR CONTRIBUTION STATEMENT

- Full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis: *Lukas Hefermehl, Karolin Bossert, Venkat M. Ramakrishnan, Burkhardt Seifert, Kurt Lehmann*
- Study concept and design: *Lukas Hefermehl, Kurt Lehmann*
- Acquisition of data: *Lukas Hefermehl, Karolin Bossert, Kurt Lehmann*
- Analysis and interpretation of data: *Lukas Hefermehl, Karolin Bossert, Venkat M. Ramakrishnan, Burkhardt Seifert, Kurt Lehmann*
- Drafting of the manuscript: *Lukas Hefermehl, Karolin Bossert, Venkat M. Ramakrishnan, Burkhardt Seifert, Kurt Lehmann*
- Critical revision of the manuscript for important intellectual content: *Venkat M. Ramakrishnan, Burkhardt Seifert*
- Statistical analysis: *Lukas Hefermehl, Karolin Bossert, Burkhardt Seifert*
- Study supervision: *Lukas Hefermehl, Kurt Lehmann*

REFERENCES

1. Walsh PC, Lepor H, Eggleston JC. Radical prostatectomy with preservation of sexual function: anatomical and pathological considerations. *Prostate* 1983;4:473–85.
2. Sanda MG, Dunn RL, Michalski J, Sandler HM, Northouse L, Hembroff L, et al. Quality of life and satisfaction with outcome among prostate-cancer survivors. *N Engl J Med* 2008;358:1250–61.
3. Suardi N, Moschini M, Gallina A, Gandaglia G, Abdollah F, Capitanio U, et al. Nerve-sparing approach during radical prostatectomy is strongly associated with the rate of postoperative urinary continence recovery. *BJU Int* 2013;111:717–22.
4. Nandipati KC, Raina R, Agarwal A, Zippe CD. Nerve-sparing surgery significantly affects long-term continence after radical prostatectomy. *Urology* 2007;70:1127–30.
5. Tzou DT, Dalkin BL, Christopher BA, Cui H. The failure of a nerve sparing template to improve urinary continence after radical prostatectomy: attention to study design. *Urol Oncol* 2009;27:358–62.
6. Park YH, Kwon OS, Hong SH, Kim SW, Hwang TK, Lee JY. Effect of nerve-sparing radical prostatectomy on urinary continence in patients with preoperative erectile dysfunction. *Int Neurourol J* 2016;20:69–74.
7. Reeves F, Preece P, Kapoor J, Everaerts W, Murphy DG, Corcoran

- NM, et al. Preservation of the neurovascular bundles is associated with improved time to continence after radical prostatectomy but not long-term continence rates: results of a systematic review and meta-analysis. *Eur Urol* 2015;68:692-704.
8. Burkhard FC, Kessler TM, Fleischmann A, Thalmann GN, Schumacher M, Studer UE. Nerve sparing open radical retropubic prostatectomy: does it have an impact on urinary continence? *J Urol* 2006;176:189-95.
 9. Nguyen LN, Head L, Witiuk K, Punjani N, Mallick R, Cnossen S, et al. The risks and benefits of cavernous neurovascular bundle sparing during radical prostatectomy: a systematic review and meta-analysis. *J Urol* 2017;198:760-9.
 10. Sidana A, Hernandez DJ, Feng Z, Partin AW, Trock BJ, Saha S, et al. Treatment decision-making for localized prostate cancer: what younger men choose and why. *Prostate* 2012;72:58-64.
 11. Lehmann K, Mazzola B, Beatrice J, Zahner M. Are functional cavernous nerves relevant for urinary continence after radical prostatectomy? *J Urol* 2009;181:(4 Suppl):719.
 12. Bossert K, Ramakrishnan VM, Seifert B, Lehmann K, Hefermehl LJ. Urinary incontinence-85: An Expanded Prostate Cancer Composite (EPIC) score cutoff value for urinary incontinence determined using long-term functional data by repeated prospective EPIC-score self-assessment after radical prostatectomy. *Int Neurourol J* 2017;21:302-8.
 13. da Silva GM, Zmora O, Börjesson L, Mizhari N, Daniel N, Khandwala F, et al. The efficacy of a nerve stimulator (CaverMap) to enhance autonomic nerve identification and confirm nerve preservation during total mesorectal excision. *Dis Colon Rectum* 2004;47:2032-8.
 14. Kim HL, Mhoon DA, Brendler CB. Does the CaverMap device help preserve potency? *Curr Urol Rep* 2001;2:214-7.
 15. Wei JT, Dunn RL, Litwin MS, Sandler HM, Sanda MG. Development and validation of the expanded prostate cancer index composite (EPIC) for comprehensive assessment of health-related quality of life in men with prostate cancer. *Urology* 2000;56:899-905.
 16. Rosen RC, Cappelleri JC, Gendrano N 3rd. The International Index of Erectile Function (IIEF): a state-of-the-science review. *Int J Impot Res* 2002;14:226-44.
 17. Wagner AA, Cheng PJ, Carneiro A, Dovirak O, Khosla A, Taylor KN, et al. Clinical use of expanded prostate cancer index composite for clinical practice to assess patient reported prostate cancer quality of life following robot-assisted radical prostatectomy. *J Urol* 2017;197:109-14.
 18. D'Amico AV, Whittington R, Malkowicz SB, Weinstein M, Tomaszewski JE, Schultz D, et al. Predicting prostate specific antigen outcome preoperatively in the prostate specific antigen era. *J Urol* 2001;166:2185-8.
 19. Pick DL, Osann K, Skarecky D, Narula N, Finley DS, Ahlering TE. The impact of cavernosal nerve preservation on continence after robotic radical prostatectomy. *BJU Int* 2011;108:1492-6.
 20. Kundu SD, Roehl KA, Eggener SE, Antenor JA, Han M, Catalona WJ. Potency, continence and complications in 3,477 consecutive radical retropubic prostatectomies. *J Urol* 2004;172(6 Pt 1):2227-31.
 21. Fowler JE Jr, Clayton M, Sharifi R, Mouli K, Ojeda L, Ray PS. Early experience with Walsh technique of radical retropubic prostatectomy. *Urology* 1987;29:242-6.
 22. Flynn BJ, Webster GD. Evaluation and surgical management of intrinsic sphincter deficiency after radical prostatectomy. *Rev Urol* 2004;6:180-6.
 23. Mandel P, Graefen M, Michl U, Huland H, Tilki D. The effect of age on functional outcomes after radical prostatectomy. *Urol Oncol* 2015;33:203.e11-8.
 24. Yaxley JW, Coughlin GD, Chambers SK, Occhipinti S, Samarantunga H, Zajdlewicz L, et al. Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: early outcomes from a randomised controlled phase 3 study. *Lancet* 2016;388:1057-66.
 25. Harris CR, Punnen S, Carroll PR. Men with low preoperative sexual function may benefit from nerve sparing radical prostatectomy. *J Urol* 2013;190:981-6.
 26. Walz J, Burnett AL, Costello AJ, Eastham JA, Graefen M, Guillonneau B, et al. A critical analysis of the current knowledge of surgical anatomy related to optimization of cancer control and preservation of continence and erection in candidates for radical prostatectomy. *Eur Urol* 2010;57:179-92.
 27. Murphy DG, Costello AJ. How can the autonomic nervous system contribute to urinary continence following radical prostatectomy? A "boson-like" conundrum. *Eur Urol* 2013;63:445-7.
 28. Walsh PC, Epstein JI, Lowe FC. Potency following radical prostatectomy with wide unilateral excision of the neurovascular bundle. *J Urol* 1987;138:823-7.
 29. Basal S, Wambi C, Acikel C, Gupta M, Badani K. Optimal strategy for penile rehabilitation after robot-assisted radical prostatectomy based on preoperative erectile function. *BJU Int* 2013;111:658-65.
 30. Michl U, Tennstedt P, Feldmeier L, Mandel P, Oh SJ, Ahyai S, et al. Nerve-sparing surgery technique, not the preservation of the neurovascular bundles, leads to improved long-term continence rates after radical prostatectomy. *Eur Urol* 2016;69:584-9.

Appendix 1. Quality of life questionnaire

1. How would you describe your overall quality of life?

Satisfied	Happy	Mostly happy	Indifferent	Mostly unhappy	Unhappy	Dissatisfied
0	1	2	3	4	5	6

2. How would you describe your quality of life regarding the changes due to your disease?

Satisfied	Happy	Mostly happy	Indifferent	Mostly unhappy	Unhappy	Dissatisfied
0	1	2	3	4	5	6

3. How content are you with your urinary continence?

Satisfied	Happy	Mostly happy	Indifferent	Mostly unhappy	Unhappy	Dissatisfied
0	1	2	3	4	5	6

4. How would you describe the quality of your sexuality?

Satisfied	Happy	Mostly happy	Indifferent	Mostly unhappy	Unhappy	Dissatisfied
0	1	2	3	4	5	6

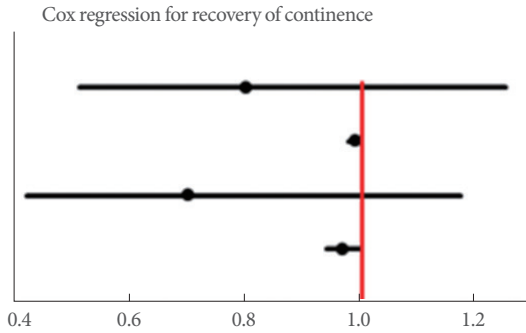
5. How would you describe the quality of your partnership?

Satisfied	Happy	Mostly happy	Indifferent	Mostly unhappy	Unhappy	Dissatisfied
0	1	2	3	4	5	6

6. How satisfied are you with your social life (for e.g., going out, friends, hobbies)?

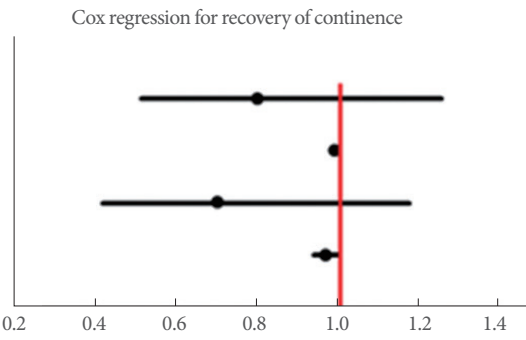
Satisfied	Happy	Mostly happy	Indifferent	Mostly unhappy	Unhappy	Dissatisfied
0	1	2	3	4	5	6

Appendix 2. Hazard ratio (HR) plots of the Cox regressions for the recovery of continence (no pad)



HR	95% CI	P-value
0.80	0.51–1.25	0.33
0.99	0.98–1.00	0.17
0.70	0.42–1.18	0.18
0.97	0.94–1.00	0.06

A



HR	95% CI	P-value
0.83	0.55–1.24	0.35
0.99	0.98–1.00	0.32
0.65	0.38–1.12	0.13
0.97	0.94–1.00	0.08

B

Hazard ratio (HR) plots of the Cox regressions for the recovery of continence (no pad) as a function of the following factors: (A) Surgeon- and (B) IIEF-defined nerve-sparing (NS), with both plots also showing age (years), prostate volume (mL), European Association of Urology risk groups (RGs) 1 & 2, and table overviews of the results. CI, confidence interval; IIEF, International Index of Erectile Function.