

# **Complications and side effects of Robot Assisted Radical Prostatectomy with focus on anastomotic stenosis and urinary incontinence.**

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*To my family*



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## **ABSTRACT**

This thesis quantifies the risk of two postoperative complications: symptomatic anastomotic stenosis and post-prostatectomy incontinence (PPI), following radical prostatectomy. We aim to identify and explore the risk factors and predictive markers for these complications using data from multiple studies.

The **first paper** analyses data from over 4,000 patients in the Laparoscopic Prostatectomy Robot Open study to assess the incidence of symptomatic anastomotic stenosis after open and robot-assisted radical prostatectomy and its potential influence on urinary incontinence. The **second paper** utilizes patient data from the National Prostate Cancer Registry, collected between January 2017 and December 2021, to identify patient- and procedure-related risk factors for PPI. A prospective study, detailed in the **third paper**, the IPA-study, involves magnetic resonance imaging (MRI), urodynamic evaluations, and dynamic ultrasound of the pelvic floor to investigate the anatomical and functional causes of PPI. The **fourth paper** focuses on the correlation between membranous urethral length (MUL) as measured by MRI and the sphincteric functional urethral length (sFUL) from urethral pressure profiles. Anastomotic stenosis rates were low overall but were twice as prevalent following open radical prostatectomy compared to robot-assisted procedures. Increased suture numbers showed a protective trend. Strong association for PPI were found with factors such as older age, larger prostate volume, lesser degree of nerve sparing, and earlier urinary incontinence, as reported on electronic Patient-Reported Outcome Measures. Despite previous suggestions, no correlation was found between MUL and sFUL in our analysis.

The findings highlight significant differences in complication rates between surgical techniques and underscore the importance of various anatomical and functional factors in predicting postoperative outcomes. Our ongoing research, which will expand to a multi-center study in spring 2024, continues to build on these insights, aiming to refine predictive models for postoperative complications in prostate cancer surgery.

**Keywords:** anastomotic stenosis, urinary incontinence, prostate cancer, radical prostatectomy

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# SAMMANFATTNING PÅ SVENSKA

Prostatacancer är den vanligaste cancer hos svenska män med drygt 10 000 nya fall per år. De senaste decennierna har antalet fall ökat dels till följd av tidigare diagnostik, dels för att svenska män lever längre. När cancer diagnostiseras på ett tidigt stadium kan man ibland avvakta och bara följa tumörens utveckling, men om botande behandling behövs innebär det antingen operation eller strålbehandling. All botande behandling är förenad med risk för biverkningar eller komplikationer. Denna avhandling grundar sig på fyra arbeten som undersöker några av de komplikationer som kan förekomma efter operation. Dessa är anastomosstenos- d v s förträngning inom området där blåsan sytts ihop med urinröret efter att prostatan tagits bort och urininkontinens. För att undersöka förekomsten av anastomosstenos använde vi i delarbete I, data från LAPPRO-studien, en stor prospektiv svensk studie: LAPPRO med över fyra tusen patienter som opererades med öppen eller robotassisterad radikal prostatektomi. Vi fann att även om anastomosstenos var en relativt sällsynt komplikation så var den dubbelt så vanlig efter öppen än efter robotassisterad operation. I delarbete II använde vi data ur en stor svensk forskningsdatabas PCBaSe, för att undersöka riskfaktorer för postoperativ urininkontinens. Vi fann att högre ålder, större prostata och en operation som inte var nervsparande och större påverkan på urinrörstumpen ökade risken för läckage. I delarbete III beskriver vi en prospektiv multicenterstudie som har syfte att djupare undersöka patient- och operationsspecifika riskfaktorer för urinläckage, IPA-studien. I studien utförs undersökningar med magnetkamera, ultraljud och urodynamik både före och 3 månader robotassisterad operation för prostatacancer. Studien, som är multicenterstudie initierad vid Sahlgrenska Universitetssjukhuset, har hittills inkluderat ca 230 av de totalt 1000 planerade patienterna. I delarbete IV har vi, inom IPA-studien, undersökt hur membranös uretra på magnetkameraundersökning korrelerar med den verkliga funktionella externa slutmuskeln, uppmätt med hjälp av urodynamik. Vi fann inte något samband mellan dessa men området är dåligt beforskat och ytterligare studier i området är av stor vikt. Fynden belyser signifikanta skillnader i komplikationsfrekvens mellan kirurgiska tekniker och understryker vikten av olika anatomiska och funktionella faktorer för att förutsäga postoperativa resultat. Vår pågående forskning, som kommer att utökas till multicenterstudie under våren 2024, fortsätter att bygga på dessa insikter med målet att på sikt leda till bättre operationer, bättre information till patienterna och grund inför val av behandling.



# LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

- I. Koss Modig K, Arnsrud Godtman R, Bjartell A, Carlsson S, Haglind E, Hugosson J, Månsson M, Steineck G, Thorsteinsdottir T, Tyrizis S, Wallerstedt Lantz A, Wiklund P, Stranne J.**

**Vesicourethral Anastomotic Stenosis After Open or Robot-assisted Laparoscopic Retropubic Prostatectomy-Results from the Laparoscopic Prostatectomy Robot Open Trial. *Eur Urol Focus.* 2021 Mar;7(2):317-324**

- II. Koss Modig K, Arnsrud Godtman R, Månsson M, Stranne J.**

**Patient- and procedure specific risk-factors for urinary incontinence after Robot Assisted Radical Prostatectomy. A Nationwide, population-based study (*in manuscript*).**

- III. Koss Modig K, Arnsrud Godtman R, Langkilde F, Månsson M, Wallström J, Stranne J.**

**Incontinence Post Robot-Assisted Radical Prostatectomy: Anatomical and Functional Causes (IPA)- A Prospective, Observational, Clinical Trial (*submitted*).**

- IV. Koss Modig K, Månsson M, Arnsrud Godtman R, Langkilde F, Stranne J.**

**The correlation between membranous urethral length on MRI and sphincteric urethra length on urethral pressure profile prior to radical prostatectomy (*in manuscript*).**

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# ABBREVIATIONS

DRE	Digital Rectal Examination
FUL	Functional Urethral Length
IPA	Incontinence Post Robot Assisted Radical Prostatectomy, Anatomical and Functional Causes
ISUP	International Society of Urological Pathology
IPSS	International Prostate Symptom Score
LAPPRO	Laparoscopic Prostatectomy Robot Open Study
MRI	Magnetic Resonance Imaging
MUL	Membranous urethral length
NPCR	National Prostate Cancer Register
PCa	Prostate Cancer
PCBaSe	Prostate Cancer data Base Sweden
PIRADS	Prostate Imaging-Reporting and Data System
PPI	Post prostatectomy incontinence
PROM	Patient Reported Outcome Measures
PSA	Prostate specific antigen
RALP	Robot-Assisted Radical Prostatectomy
RP	Radical Prostatectomy
RRP	Retropubic Radical Prostatectomy
TRUS	Trans-rectal ultrasound



# 1 INTRODUCTION

Prostate cancer has become the most prevalent form of cancer in men during the last few decades. The increased detection rates have, in its turn, led to an increasing number of men undergoing curative treatment. However, this treatment can result in a long-term reduction in quality of life due to associated complications and side effects. When adhering to the Hippocratic ethical oath (“First, do not harm”), it is crucial to clearly understand these complications, side effects, and risk factors when discussing treatment options, performing surgery, and providing rehabilitation. While current research highlights some specific patient- and procedure-related risk factors, more clarity is needed.

The main goal of this thesis is to contribute to future knowledge on complications that can arise from surgical curative treatment for prostate cancer. This thesis also focuses on anastomotic stenosis and incontinence to achieve its main goal.

## 1.1 PROSTATE CANCER

The first case of prostate cancer (PCa) that was discovered during a histological examination was described in 1853 by a surgeon at the London Hospital Sir J. Adams (1). By then, it was seen as a “rare disease”. Today the situation is completely different as prostate cancer is the most frequently diagnosed malignancy in men in countries with a Western lifestyle(2, 3).

### 1.1.1 EPIDEMIOLOGY

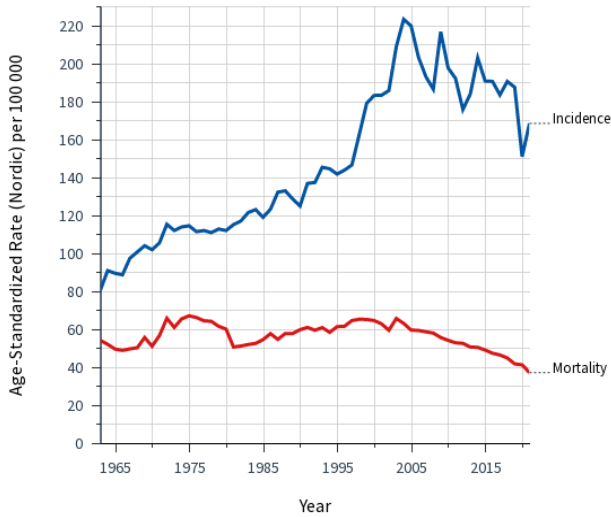
With over 10,000 new cases per year, PCa is the most common cancer among Swedish men (4). In 2022, 12,004 men were diagnosed after case numbers experienced a slight drop to 9,000 cases in 2019-2020, which was mainly due to the COVID-19 pandemic (4). The incidence doubled during 1990-2004, mainly due to more active diagnostics being performed, which included the introduction and common use of PSA testing and systematic biopsies.

Sweden, together with the rest of Western Europe, the Caribbean, Australia/New Zealand, North and South America and Southern Africa, have the highest age-standardized incidence rates, which suggests that lifestyle factors and heredity/genetical factors may play a role in the development of PCa (5). As Black men are 1.7 times more likely to be diagnosed with PCa in comparison to white men and are 2.1 times more likely to die of the disease, even socioeconomic factors may be of importance(6).

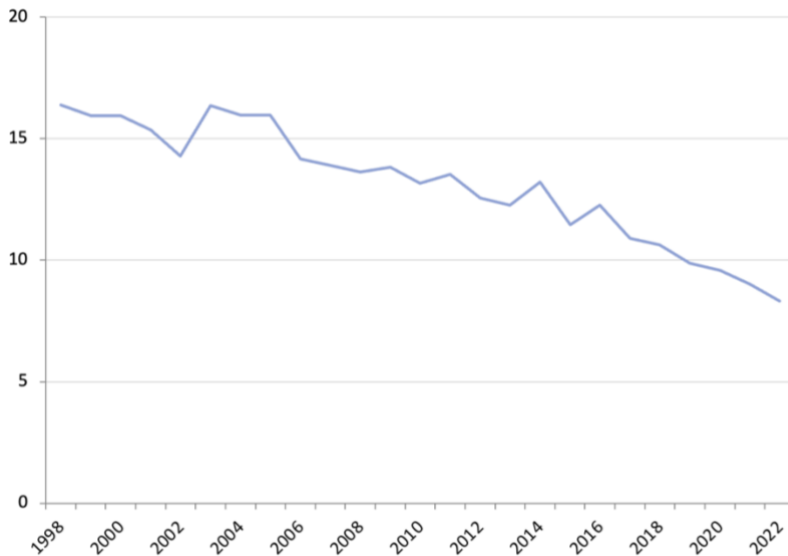
As prostate cancer is rarely seen among men younger than 50 years , the aging population is another factor behind the rise in incidence. Autopsy studies have demonstrated that PCa may be found in 36 % of Caucasian men and 51% of African Americans in the age range of 70-79, which suggest that the difference in incidence in the population is affected by more than screening(7).

PCa is a leading cause of cancer deaths in 48 of 185 countries and the highest age-standardized mortality rates are found in the less economically privileged parts of the world. These include the Caribbean, parts of South America and sub-Saharan Africa.

Globally, the differences in incidence and mortality can be attributed to differences in screening and access to and health infrastructure, but even lifestyle factors and germline genetic factors may contribute these differences (6, 8). Interestingly, when Black and white Americans are diagnosed with a similar clinical stage of PCa and are offered equal treatment, they have an equivalent outcome (9, 10). However, Black men are often diagnosed with more aggressive form of PCa. The cancer-specific 5-year survival of men with localized diseases is 97% in comparison to 30% when PCa is primarily metastasized (6).



**Figure 1.** Age standardized incidence (dark blue line) and mortality rate (red line) of PCa in Sweden between 1965 and 2020. The numbers represent cases and deaths per 100,000 patients. Adapted from Nordcan.



**Figure 2.** Prostate cancer mortality rates among men under 75yy from 1998 to 2022. Adapted from The National Board of Health and Welfare in Sweden.

## 1.1.2 DIAGNOSIS

The first Swedish textbook in urology, which was first published in 1898 and was written by Ali Krogius, mentions prostate cancer as a rare disease that may be diagnosed by performing a digital rectal examination (DRE) (11). The description of the findings is equal to what we today would describe as a locally advanced disease. Since the PSA testing has been established, even insignificant cancers can be diagnosed, which has become a challenge. Today's diagnostic pathway includes PSA testing and other diagnostic tests, magnetic resonance imaging (MRI), DRE, transrectal ultrasound (TRUS), and systematic or selected transrectal or perineal needle-core biopsies (12).

### 1.1.2.1 PSA

The Prostate-specific antigen (PSA) is a glycoprotein enzyme that is encoded by the KLK3 gene and secreted by the epithelial cells of the prostate to liquefy semen, which allows sperm to swim freely(13). PSA is crucial for the procreation but is mainly recognized today for its use in the early detection of PCa. A small portion of PSA leaks into systematic blood circulation while the remaining part binds to larger proteins. Increased leakage of PSA is seen when the cell architecture becomes disrupted by cancer.

Even if PSA is organ-specific, it is not cancer-specific and may also be elevated due to benign prostatic hypertrophy (BPH), prostatitis, and other non-malignant conditions (14). Other causes, such as urinary retention and physical manipulation during trans-urethral interventions, may also lead to increased values. To increase the specificity of the PSA test in older men and its sensitivity in younger men, an age-dependent cut of value is used (15). Sensitivity relates to a test's capacity to accurately detect individuals with the disease, whereas specificity relates to a test's ability to accurately identify those without the disease. *The Swedish National PCa Guidelines* recommend following age- dependent PSA cut-off values (16).

Age, years	PSA- cut off for future evaluation, ng/ml
<70	$\geq 3$
70-80	$\geq 5$
>80	$\geq 7$

**Table 1.** PSA cut-offs for future evaluations of different age groups according to The Swedish National Prostate Cancer Guidelines((16).

As mentioned previously, elevated PSA levels may be caused by other factors. In clinical practice, such factors must always be considered (17, 18). In general, a PSA value should never be evaluated alone. Higher PSA values are seen in patients who have larger prostates. A larger prostate is made up of more cells, which causes the release of more PSA. PSA density can be calculated by dividing the PSA value by the volume of the prostate and can be used as a guide in decision-making as it is known that values  $< 0.1\text{ng/l/cm}^3$  indicate prostate hyperplasia, whereas values  $>0.2$  indicate a high probability of PCa (19). A higher PSA density indicates a higher probability of clinically significant PCa (19).

Since its approval in 1986 by the U.S. Food and Drug Administration (FDA), PSA testing has become a common form of testing for prostate cancer and resulted in an initial increase in the number of new cases by 20% per year until 1992, when it reached a peak (20).

### 1.1.2.2 DIGITAL RECTAL EXAMINATION

A DRE should always be part of the clinical evaluation of a patient with elevated PSA levels or lower urinary tract symptoms (LUTS) to identify palpable tumours in the prostatic gland and rule out other abnormalities such as rectal malignancy. The Tumour-Node-Metastasis (TNM) classification system is based on clinical stage evaluation that involves DRE (21). However, DRE may not be possible in some cases due to anal stricture or anal/rectal amputation. Abnormal DRE in combination with elevated PSA value has been found to be associated with an increased risk of clinically significant tumours (22). As DRE enables the evaluation of the posterior part of the prostate, tumours that are located ventrally and small tumour masses may not be palpable. Even if other modalities that are used in modern diagnostic pathways seem to have more attention, it is important to emphasize the importance of using DRE for clinical stage (cT) evaluation and PCa staging. The clinical staging is crucial to making treatment choices and acts as a strong predictor of advanced PCa (23).

### 1.1.2.3 BIOMARKERS

There are several biomarker tests available, and some are under evaluation, aiming to offer guidance in deciding whether to biopsy in cases of elevated PSA levels or positive DRE (24). Among those tests is the Prostate Health Index (PHI) test, combining free and total PSA levels and the (-2) pro PSA isoform. The four-kallikrein (4K) score test measuring free, intact, and total PSA and kallikrein-like peptidase 2 (hK2) in addition to age, DRE, and prior biopsy status. Both tests have facilitated the improved prediction of clinically significant PCa in men with PSA levels between 2-10 ng/ml, which has reduced biopsies by 30 % but missed 10% of high-grade cancers (25). The Stockholm 3 test is a third test which, on the other hand combines plasma protein biomarkers, genetic markers, and clinical data (age, family history and previous prostate biopsy) to generate a score that indicates the risk of PCa and reduces unnecessary biopsies by about 30 % (26). Although these tests have improved the detection rate of clinically significant PCa and have reduce unnecessary biopsies, they require future evaluation of their value in combination with imaging and are therefore not recommended in the *Swedish Guidelines (16)*.

#### 1.1.2.4 TRANSRECTAL ULTRASOUND

The TRUS was previously referred to as “the prolonged finger of the urologist”. As an imaging modality for the evaluation of the prostate, TRUS has played a central role in revolutionizing the imaging and diagnosis of PCa since it was introduced in 1968 (27). The gray-scale TRUS is the most common imaging modality in urologic outpatient clinics as it enables volume calculations, the assessment of anatomical variations, the detection of hypoechoic lesions that indicate possible PCa, and guidance for biopsies (28, 29). Before serum PSA testing and technical improvements were made to TRUS, clinicians relied on DRE to detect PCa and digitally directed biopsies of suspected lesions. Hodge et al. introduced the TRUS- guided systematic sextant biopsy protocol in 1989 (30). Since then, many different protocols have been used to maximize the detection rate. Before the MRI was incorporated into the diagnostic pathway, 12-core biopsies were recommended as minimum (31). After the MRI was incorporated into the diagnostic pathway, targeted biopsies were recommended in the *EAU Guidelines* and *Swedish National Guidelines* (16). This was done to improve the detection of International Society of Urological Pathology (ISUP) grade >2 cancers, compared to systematic biopsies (32).

Transrectal biopsies are associated with a significant risk of infection, which, with increasing antibiotic resistance, presents a challenge to health system (33). Therefore, transperineal prostate biopsies were introduced as they do not involve the passage of the rectal wall and have been found to reduce the risk of infection (34). However, even though they lower the risk of infection, transperineal biopsies are more time- and resource-consuming for the health system and often cause more discomfort for the patient. Still, the *EAU Guidelines* recommend the use of transperineal approach to lower the risk of infectious complications (35). The transperineal approach is also used for patients when there is no access to the rectum due to surgical extirpation or anomalies.

The transperineal ultrasound is seldom used in ordinary urological practice but is more commonly used by physiotherapist to evaluate the pelvic floor muscles and pelvic floor mobility prior to and after radical prostatectomy (36).

### 1.1.2.5 MAGNETIC RESONANCE IMAGING (MRI)

The MRI is an imaging technique that offers a non-invasive, evaluation of the prostate, its shape, and surrounding structures. The technique is based on a physical phenomenon in which atomic nuclei are disturbed by electromagnetic waves known as nuclear magnetic resonance (NMR). The prostate MRI has undergone significant advancements in recent years: it transitioned from being a simple morphologic assessment that used T1- and T2- weighted pulse sequences to a multiparametric imaging techniques that combines anatomic imaging with functional and physiologic evaluations (37). These advancements have greatly improved the diagnostic capabilities of the prostate MRI and the detection and characterization of prostate cancer. Furthermore, the incorporation of functional evaluation with techniques such as diffusion-weighted imaging and perfusion imaging has helped distinguish between benign and malignant lesions. These advancements have revolutionized the clinical applications of the prostate MRI and enabled it to be used for image-guided biopsies, focal therapy, and radiation therapy.

For the multiparametric MRI (mpMRI), a five-point scale has been developed: the Prostate Imaging-Reporting and Data System (PI-RADS), which has been continuously studied and improved since it was first published in 2012. This five-point scale is based on the probability that a combination of the different mpMRI findings correlates with the presence of clinically significant PCa. Defining clinically significant PCa as Gleason score  $\geq 7$ , and/or volume  $\geq 0.5$ cc and/or an extra prostatic extension (EPE). The PI-RADS assessment categories are illustrated in Table 2.

1	Very low (clinically significant cancer is highly unlikely to be present)
2	Low (clinically significant cancer is unlikely to be present)
3	Intermediate (the presence of clinically significant cancer is equivocal)
4	High (clinically significant cancer is likely to be present)
5	Very high (clinically significant cancer is highly likely to be present)

**Table 2.** PI-RADS v 2.1 assessment categories for each lesion in the prostate.  
Adapted from PI-RADS v2.1(38)

The mpMRI's testing ability (sensitivity) to detect significant prostate cancer, as defined by the International Society of Urological Pathology as (ISUP)-grade  $\geq 2$  cancers, has been found to be strong (39). Even a comparison between the MRI and template biopsies (more than 20 cores) has demonstrated strong sensitivity for the detection of ISUP-grade  $>2$  cancers (32). The sensitivity for ISUP-grade  $>3$  cancers is very good (95%). The specificity is much lower for ISUP-grade  $<3$  cancers (0.35, 95%, CI: 0.26-0.46). The MRI is good at detection of ISUP-grade 2 or more cancers but identifies less than 30% of ISUP-grade 1 cancers especially if they are smaller than 5 mm in comparison to RP (39).

The MRI is a tool for the multiparametric assessment of the prostate to detect PCa and the evaluation of its shape and volume. Lesions that have been classified according to PI-RADS categories are described and evaluated for the eventual risk of extra-prostatic extension (EPE). The infiltrations of either the bladder neck or the external sphincter are also described. The evaluation process may result in a description of inflammatory changes as well as show atrophy of the gland and benign prostatic hyperplasia. Besides that, the MRI can be used to evaluate the form of the prostate, its apical form, and the presence of a median lobe, as well as the structures surrounding the gland(40, 41). The MRI also facilitates the evaluation of the membranous urethra and measurements of membranous urethral length (MUL)(42). Those measurements have been proposed to be done on high resolution sagittal T2-weighted images. In addition to measuring the MUL, the MRI can be used to

assess the form of prostatic apex and other structures surrounding the prostatic area, such as the thickness of the musculus levator ani, and detect signs of fibrosis within the external sphincter (43, 44). These measurements can be performed prior to a radical prostatectomy to predict the risk of incontinence or post-surgery and evaluate the eventual causes behind it (45, 46).

In summarizing the diagnostic tools used for PCa diagnosis and evaluation, one may note that transrectal ultrasound has been the main imaging method used for identifying and determining the extent of prostate cancer for many years. However, new techniques such as the mpMRI integrate both structural and functional imaging to furnish comprehensive details about the prostate gland and adjacent tissues, thus facilitating the improved visualization of suspicious areas.

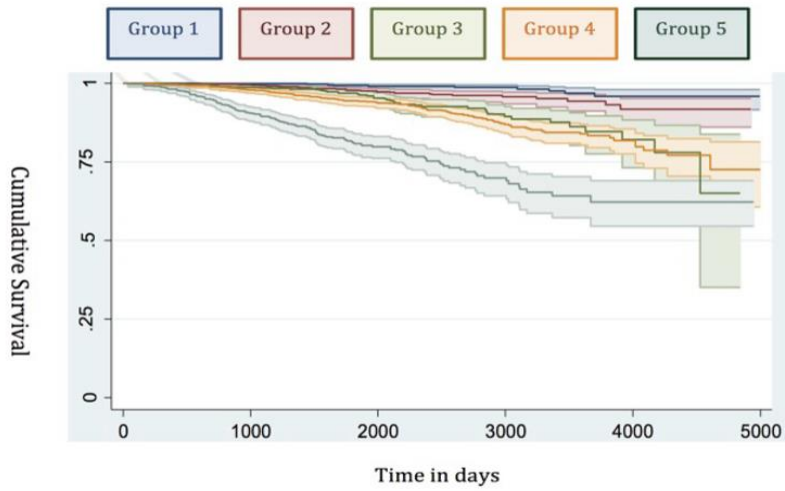
## 1.1.3 GRADING, STAGING AND RISK GROUPS

Grading and staging are crucial for determining appropriate treatment strategies and predicting patient outcomes.

### 1.1.3.1 GRADING

Grading refers to the evaluation of the appearance of tumor cells during microscopic examination, which helps physicians determine how aggressively the cancer may grow and spread.

Prostate cancer grading is done using the histologic Gleason score system that was originally described by Donald F. Gleason in 1966. This system is a five grade system that is based on histologic tumour architecture that reflects tissue abnormality (47). The higher the Gleason grade is, the more aberrant the cell architecture is. The system has been modified twice. The first modification involved eliminating the Gleason grade 1 and 2 (2005). In 2014, the ISUP grouped the Gleason scores into five categories to reflect the prognostic properties more precisely. Today, pathologists use both systems worldwide (48). The ISUP-grading system is a prognosis-based pathological classification that has been evaluated by Gnanapragasam et al. and has proven to be more effective in distinguishing patient groups with varying prognoses regarding mortality caused by PCa (49). The ISUP risk stratification is illustrated in Figure 3.



*Figure 3. ISUP risk stratification and prognosis, Gnanapragasam et al.(49)*

ISUP Grade	Gleason score
1	6 (3 + 3)
2	7 (3 + 4)
3	7 (4 + 3)
4	8 (4 + 4 or 3 + 5 or 5 + 3)
5	9-10 (4 + 5 or 5 + 4 or 5 + 5)

*Table 3. Comparison of ISUP-grades and Gleason scores.*

### 1.1.3.2 STAGING

Staging involves determining the extent of the cancer's spread beyond the prostate. The clinical stage of the primary tumour should be assessed using DRE, as it is included in the D'Amico risk group classification and recommended in the *EAU Guidelines* (35). As part of staging, the evaluation of regional lymph nodes is usually performed in connection with a diagnostic mpMRI, but if this is not deemed necessary, then a CT scan of the abdomen or Prostate-specific membrane antigen- position emission tomography (PSMA-PET-CT) is performed(50, 51). The presence of distant metastasis can be investigated with a bone scan, MRI, or PET-CT. The staging of prostate cancer is a crucial aspect of determining the extent and spread of the disease. It helps to choose the most appropriate treatment plan and determine a patient's prognosis. The most commonly used staging system for prostate cancer is the TNM system, which accounts for the size of a tumor (T), whether the cancer has spread to nearby lymph nodes (N), and whether it has metastasized to other parts of the body (M). There are also different grades of PCa, which range from low-grade (slow growing) to high-grade (fast-growing).

This information is important for determining the best course of action, which may involve surgery, radiation therapy, hormone therapy or a combination of these treatments. The TNM system provides a comprehensive framework for assessing the spread of the cancer, but it is also vital to consider the individual's quality of life, personal goals, and values when determining the most suitable treatment plan.

<b>Clinical (TNM) classification of PCa</b>	
<b>T - Primary Tumour (stage exclusively based on DRE)</b>	
<b>TX</b>	Primary tumour cannot be assessed
<b>T0</b>	No evidence of primary tumour
<b>T1</b>	Clinically inapparent tumour that is not palpable
T1a	Tumour incidental histological finding in 5% or less of tissue resected
T1b	Tumour incidental histological finding in more than 5% of tissue resected
T1c	Tumour identified with needle biopsy (e.g., because of elevated PSA)
<b>T2</b>	Tumour that is palpable and confined within the prostate
T2a	Tumour involves one half of one lobe or less
T2b	Tumour involves more than half of one lobe, but not both lobes
T2c	Tumour involves both lobes
<b>T3</b>	Tumour that extends palpably through the prostatic capsule
T3a	Extracapsular extension (unilateral or bilateral)
T3b	Tumour invades seminal vesicle(s)
<b>T4</b>	Tumour that is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall
<b>N - Regional (pelvic) Lymph Nodes<sup>1</sup></b>	
<b>NX</b>	Regional lymph nodes cannot be assessed
<b>N0</b>	No regional lymph node metastasis
<b>N1</b>	Regional lymph node metastasis
<b>M - Distant Metastasis<sup>2</sup></b>	
<b>M0</b>	No distant metastasis
<b>M1</b>	Distant metastasis
M1a	non-regional lymph node(s)
M1b	Bone(s)
M1c	Other site(s)

*Table 4. TNM classification according to EAU guidelines (35).*

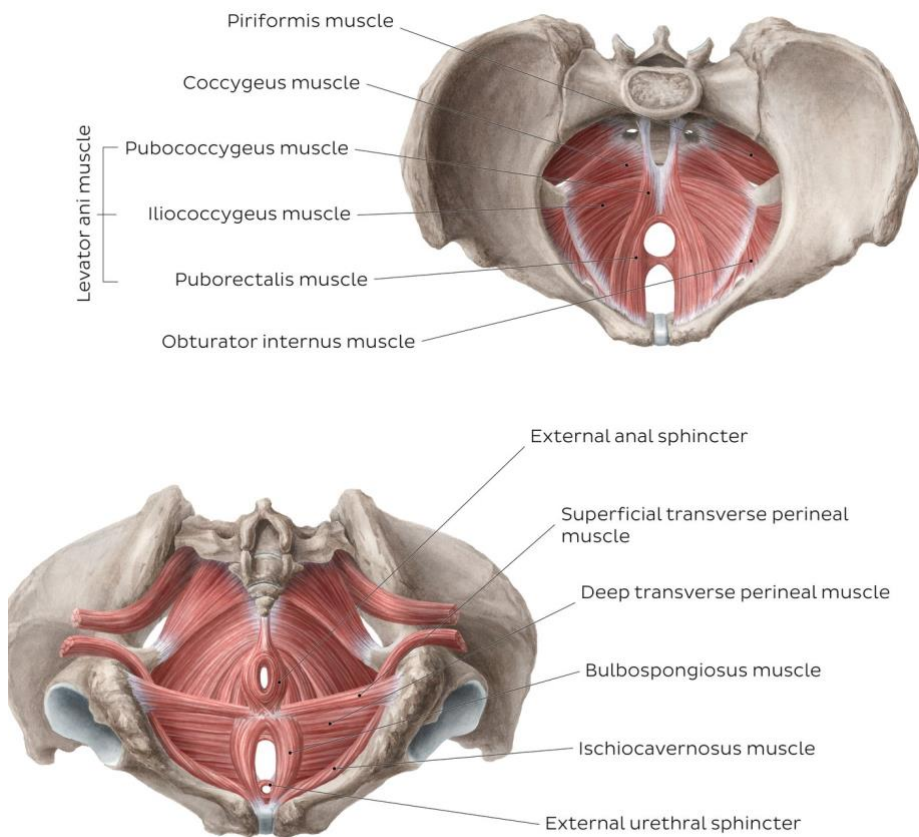
In 1998, Amico et al published the results of a study that investigates the biochemical recurrence after a radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy and proposed a risk classification system (52). The system provided a more clinically useful prediction of PSA relapse after a radical prostatectomy and radiation therapy in comparison to previously used methods (53). In general, the risk indicates the probability that a patient will die of PCa. For untreated PCa that lacks signs of metastasis, the risk classification is based on PSA values, clinical T-staging on DRE, and Gleason scores on systematic biopsies. *The Swedish National Guidelines* for PCa suggest a modified classification to aid management decisions and predict biochemical recurrence (Table 5).

<b>Risk</b>	<b>PSA level (ng/mL)</b>	<b>cT-stage</b>	<b>ISUP / GS</b>	<b>Other criteria</b>
<b>Very low</b>	< 10	cT1c	ISUP 1/GS 6	PSAD <0.15 ng/mL and <=8 mm ca in < 4 cores out of 8-12
<b>Low</b>	< 10	cT1-cT2a	ISUP 1/GS 6	And do not meet criteria for very low risk
<b>Favorable intermediate risk</b>	10-19	cT2b-cT2c	ISUP 2/ GS 7(3+4)	
<b>Unfavorable intermediate risk</b>	10-19		ISUP3/ GS 7(4+3)	Or GS 7(4+3)/(ISUP 3) or GS 7(3+4)/(ISUP 2) in more than 50% of biopsies
<b>High risk</b>	20-39	cT3a	ISUP 4/ GS 8	Or (EPE/SVI 5 on MRI)
<b>Very high risk</b>	>= 40	cT3b-cT4	ISUP 5/ GS 9-10	Or 2-3 of high-risk factors

*Table 5. Risk group classifications for PCa, adapted from the Swedish National Guidelines for PCa 2023.*

## 1.2 THE MALE PELVIS

As a patient's anatomy changes due to the removal of the prostate during a radical prostatectomy following presentation, is restricted to the structures surrounding the prostate. The male pelvic floor, which is also referred to as the pelvic diaphragm, is a complex structure formed of muscles, ligaments, and fascia. It offers support to pelvic organs and is crucial for urinary and fecal continence.

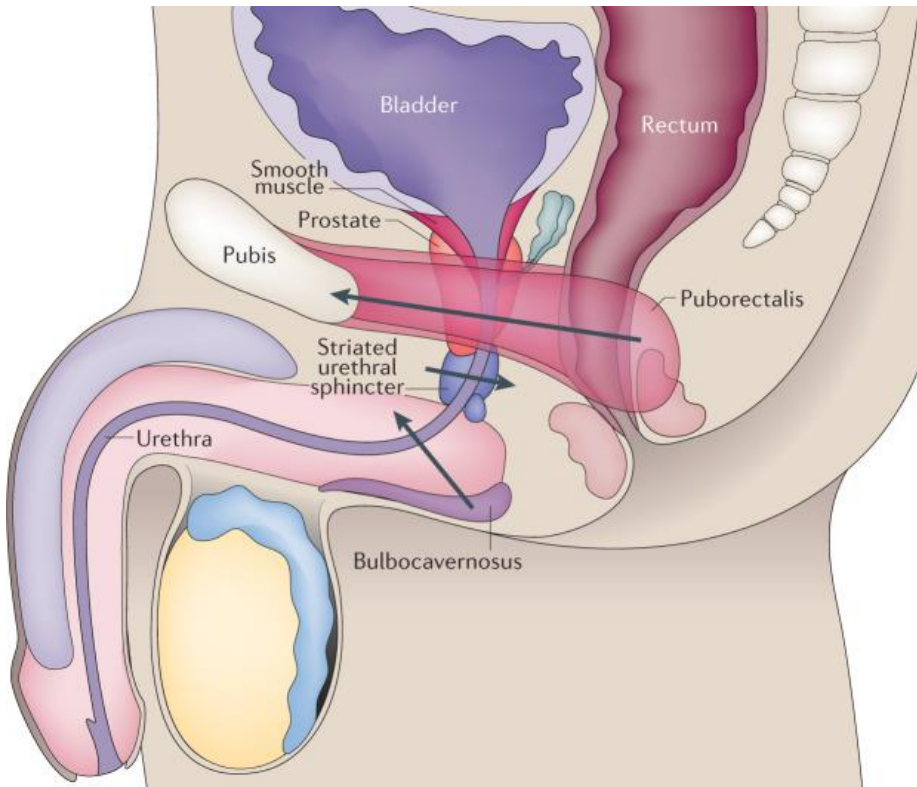


**Figure 4.** Male pelvic floor. Illustration from Kenhub.com

The pelvic floor is an arrangement of muscles that is suspended between the bony structures to form a hammock-like structure; its main function is to support the inner organs by contracting when the abdominal pressure rises. These contractions prevent urinary and faecal leakage. It also separates the pelvic cavity above from the perineum below and consists of the pelvic diaphragm, which in turn consists of the levator ani muscle. The levator ani is composed of three sets of fibres. Anteriorly, there is the pubococcygeus; some of its fibres even forming a loop around the prostate in males (the levator prostate), and some form the puboperinealis (54).

The intermediate portion comprises the puborectalis, where the fibres form a puborectal sling around the anorectal junction which forms a kink in the colon. Those intermediate fibers of the levator ani maintain an anorectal angle of 90 degrees, which prevents anal incontinence. The posterior fibers of the levator ani are known as the iliococcygeus muscle. The levator ani muscle can be consciously controlled due to somatic innervation and can be exercised using the Kegel maneuver.

Below the pelvic diaphragm/levator ani, there are four perineal muscles: the deep and superficial transversus perinei, the ischiocavernosus, and the bulbocavernosus. When the ischiocavernosus contracts, it squeezes and pushes blood towards the distal part of the genitals, which helps to maintain erection. Of those four muscles, the Bulbocavernosus is involved in maintaining continence.

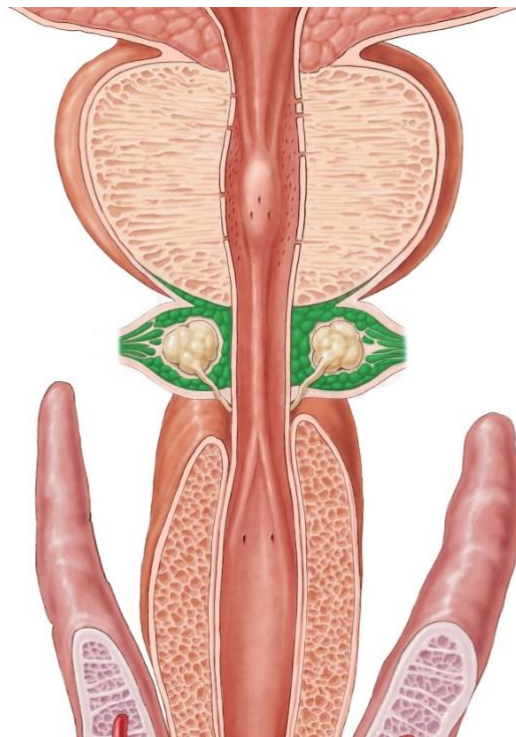


**Figure 5.** A sagittal view of the male pelvis. The black arrows indicate the direction of action during pelvic floor contraction. This figure does not include the pubourethralis. Reprinted with permission from Nature.com (36)

## 1.2.1 SPHINCTERS

A set of internal and external sphincter controls the urethra and anal canal. The internal urethral sphincter is located at the level of the bladder neck, and the external one is located right below the prostate at the base of the penis and at the level of the membranous urethra. Those sphincters are not attached to any bony structures.

The internal sphincters consist of smooth muscles that operate under involuntary control and are rich in mitochondria; they facilitate long contractions without causing fatigue. The external sphincters around the anus and urethra, on the other hand, consist of skeletal muscle and are controlled voluntarily. They are used to consciously hold urine and faecal back(55).



**Figure 6.** Coronal view of the proximal male urethra. The external urethral sphincter marked in green. Illustration by Kenhub.com.

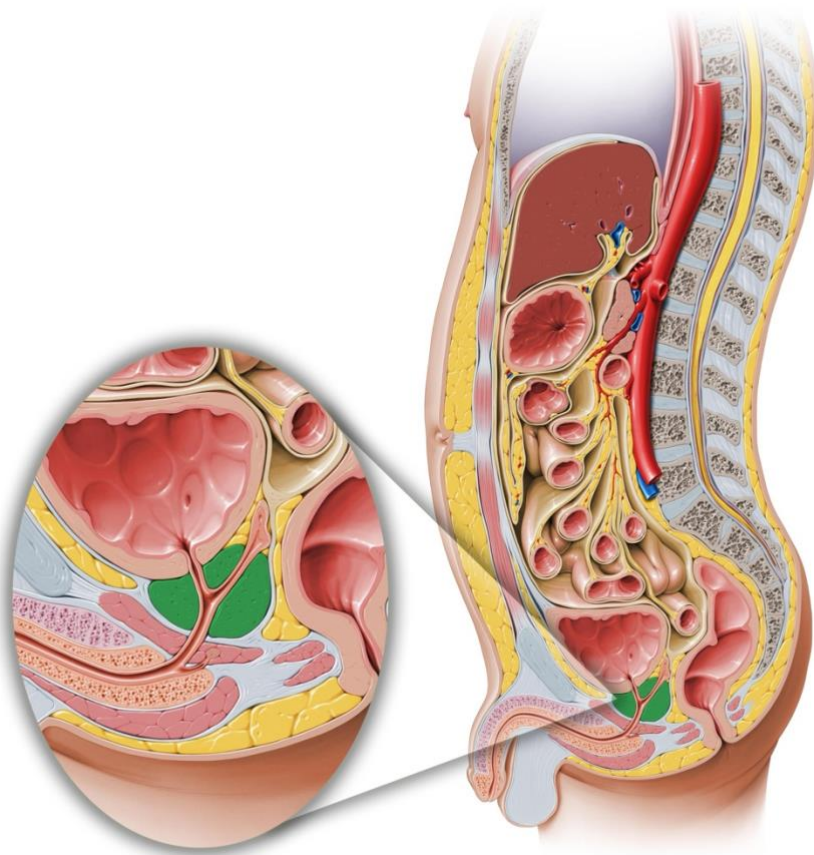
The external urethral sphincter is an omega-shaped muscle and is also called the rhabdosphincter. It is constructed of striated muscle fibers. It encloses the urethra ventrally and is anchored to the strong connective tissue of the perineal body. The muscle fibers are a mix of Type I and Type II fibres, which enables both fast and prolonged contraction (56).

Although the external urethral sphincter was previously thought to be solely controlled by somatic mechanisms, new anatomical findings indicate the involvement of autonomic innervation. This discovery raises questions concerning the conventional understanding of how the external urethral sphincter is innervated and provides opportunities for achieving advancements in comprehending and managing urinary incontinence. Preserving neurovascular bundles during radical prostatectomy allows for the preservation of the autonomic fibers that are found in the external sphincter. This is important as they contribute to continence recovery. The mechanism behind this is maintains the reflex activity within the external sphincter (57). Michl et al. found that the type of resection of structures around the prostatic apex and urethra, which they referred to as the nerve sparing surgery technique rather than the nerve sparing surgery itself, affects continence (58). The work of Steineck et al. showed that the grade of nerve sparing affects continence, which may support Michl et al.'s idea that the dissection around the prostatic apex rather than nerve sparing itself may be responsible for preserving continence (59). There is most probably a correlation between several factors that lead to preserved continence, which requires future evaluation.

Following radical prostatectomy, the role of the external sphincter becomes even more important as it compensates for the loss of internal sphincter functions due to the surgical removal of the prostate and part of the bladder neck. Innervated by the pudendal nerve, this muscle, which is voluntarily controlled, allows individuals to consciously prevent urine leakage during activities such as coughing or lifting heavy objects. Additionally, it collaborates with the pelvic floor muscles to support bladder functions and maintain continence. Preoperative exercises are used to improve the strength and function of the pelvic floor and optimize postoperative continence(36).

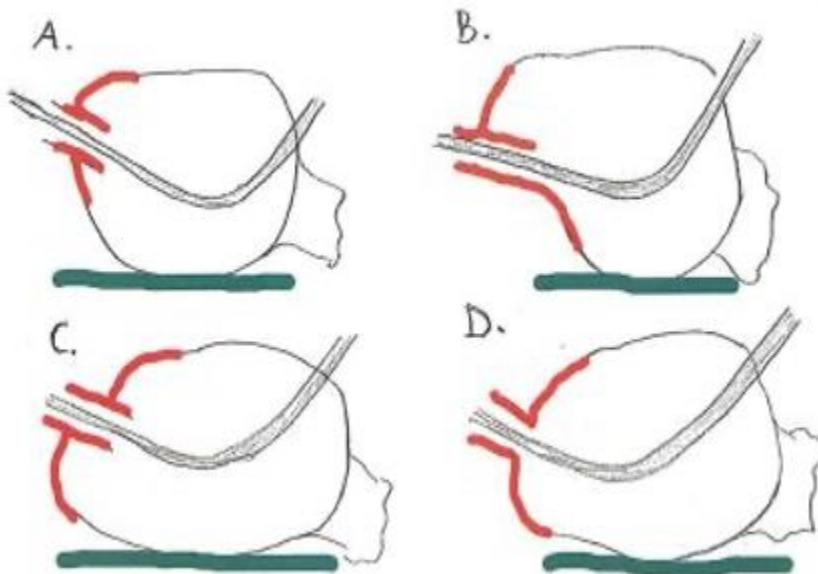
## 1.3 PROSTATE

In a 20-year-old male the prostate is about 20 cc or ml and is often compared to a walnut due to its size and shape, and as part of natural history, it usually enlarges. Senior collages usually have seen glands larger than 300 ml which younger urologists seldom see nowadays. Far from all prostates enlarge independent of the age of the patient.



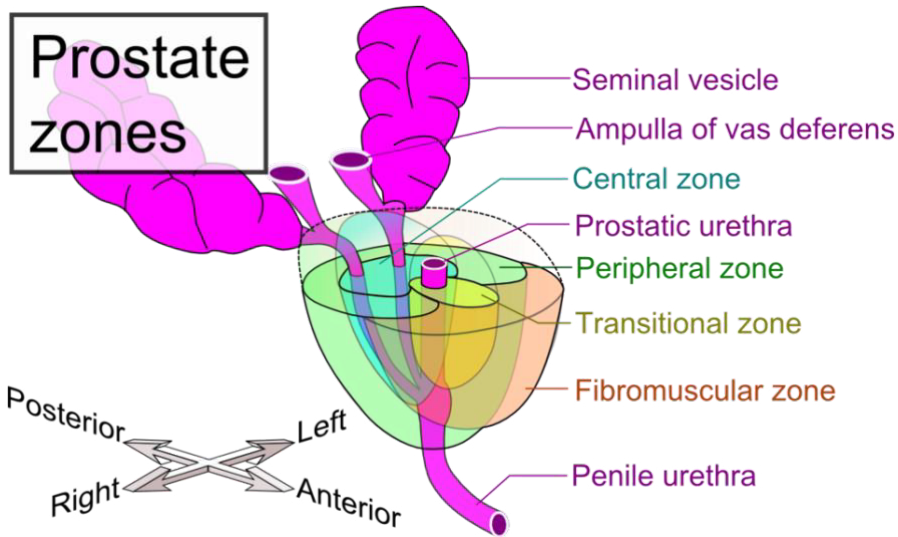
**Figure 7.** Male pelvic anatomy with the prostate marked in green. Image provided by Kenhub.com.

The prostate is located between the bladder and the pelvic diaphragm, with the rectum close behind it. It forms walls of the prostatic urethra and plays a crucial role in male fertility and sexual function. It is described anatomically as comprising five lobes. These include the anterior, posterior, right and left and a median lobe. The median lobe may, through its ingrowth into the bladder, disrupt the form of the bladder neck. When describing the anatomy of the prostate, it is important to pay attention to its apical part. It has been suggested that the form of the apical part may influence the risk of incontinence. Lee et al. presented in his work from 2006 division into four types of prostatic apex. These types do affect the risk of incontinence, and it can be understood that a type of apex with overlap affects the external sphincter (41, 60). An overlap by prostatic tissue over the membranous urethra (MUL), as illustrated by Apex types B and C, can affect surgical technique and decreasing the grade of the preservation of the urethral stump. As illustrated by Apex type D, without an overlap, a longer and thicker urethra stump can be preserved. The sphincter may also become ingrown into the prostatic apex, as illustrated by Type A, which in cases where the PCa is not located apically, can allow resection with maximal urethra length. When there is PCa in the apical part of the prostate and only a resection of the urethra with margin is possible, the intraprostatic MUL needs to be resected to secure the cure.



**Figure 8.** Types of prostatic apices according to Lee et. al. (41).

The gland is also micro-anatomically divided into zones, including the central zone, the transitional zone, the peripheral zone, and the anterior fibromuscular stroma. The peripheral zone, which is located posteriorly, is where 70-80% of PCa originates. This is followed by the central zone, where 20% of PCa originates. The transitional zone, which is located close to the proximal prostatic urethra, has a strong ability to grow and is most often the cause of hyperplasia rather than the location of cancer.



**Figure 9.** Zones of the prostate by Mikael. Häggström MD. Use with permission; the Public Domain Dedication is per Creative Commons Zero.

The prostate's function is dual as it produces prostatic fluid that through its alkaline characteristics, prolongs the lifespan of sperm and functions as part of a switch between urination and ejaculation. The switch between urination and ejaculation is facilitated by two longitudinal muscle systems in the prostatic urethra: the anteriorly located musculus dilatator urethrae and posteriorly located musculus ejaculatorius.

## 1.4 TREATMENT

As PCa has become the second most common cancer in the male population and the PSA testing is being widely used, there has been an increase in the detection rate of clinically insignificant cancers, which reflects the trend of overdiagnosis and the risk of subsequent over-treatment (61). The prognosis of PCa depends mainly on the age of the patient, their PSA values, their clinical stage, their Gleason score/ISUP grade, their TNM classification and the treatment modalities available. In general, PCa may be a subject of observation (deferred treatment), treated with curative or without curative intention.

Curative treatment may be offered in the forms of radical prostatectomy, radiotherapy, or as focal therapy. The ProtecT study group presented 2023, 15 years follow up outcomes showing low PCa mortality regardless of treatment assigned (62).

### 1.4.1 DEFERRED TREATMENT

Deferred treatment involves active surveillance and watchful waiting. Indolent prostate cancers represent a significant subset of cases and are referred to as clinically insignificant cancer as slow-growing tumour may not necessarily cause harm during a patient's lifetime. Active surveillance is a strategy for the management of slow-growing prostate cancer. It involves closely monitoring the cancer through regular check-ups, imaging, and biopsies and does not involve immediate treatment unless there are signs of advancement. This approach aims to prevent unnecessary treatment and its related side effects while ensuring that intervention is an option if the cancer exhibits increased aggressiveness.

Active surveillance (AS) was introduced in the 1990s to reduce the overtreatment of early detected and indolent PCa following the introduction of PSA testing (61). As the 10-year risk of disease progression is low in patients who have at least 10 years of life expectancy and low or favorable intermediate risk, AS is the recommended treatment option for patients whose PCa was detected early or is indolent (63). That allows monitoring of PCa with the intention of treating it while avoiding overtreatment. The percentage of

patients who undergo AS in Sweden and who are between 50-80 is high but varies between regions, which indicates differences in detection and follow up. Palmsted et al. presented 25-year results from the Gothenburg 1 trial at EAU2024; their findings demonstrate that death among patients undergoing AS is uncommon, but a large proportion of patients still require treatment (64). Similar results were presented by the ProtecT study group in 2023 (62) Postponing treatment gives patients time without the side effects that curative treatment can have. Conversely, watchful waiting (WW) involves conservative management for patients unsuitable for curative treatment due to age or comorbidity. As part of WW, palliative treatment is offered to address symptoms and to maintain a patient's quality of life. Such patients are usually offered non-curative hormonal treatments aimed at the disease.

## 1.4.2 FOCAL THERAPY

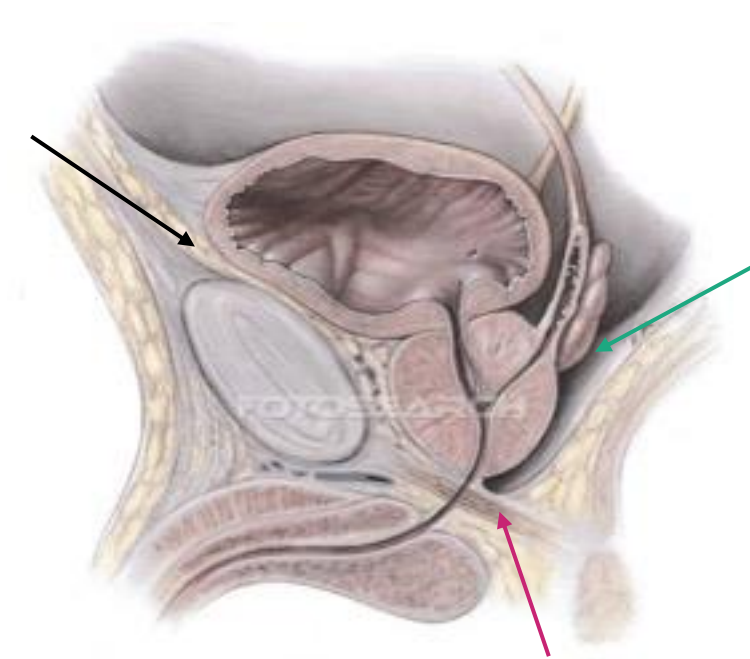
A curative treatment for PCa without any side effects would be a perfect option, but it does not exist as an established alternative. The principle of focal therapy involves treating well-defined tumours with the right properties and localization by using high intensity focus ultrasound (HIFU) or cryotherapy to minimize the side effects of PCa treatment. As focal therapy only targets the areas affected by PCa, it avoids causing damage to surrounding structures such as the rectum, urinary bladder, neurovascular bundles, and muscles. Focal therapy can, as therapeutic option, be compared to active surveillance as often small cancers seen as insignificant are treated and patients need to be followed up similar to AS. We still do not know if it fully treats or only lowers the risk of cancer progression; thus, this type of treatment requires future studies. However, there are 8 years oncological follow up data that are comparable to RP and radiation, but 17 % of patients needed a second focal therapy (65) The current *European* and *Swedish guidelines* recommend using focal therapy only within study settings as this treatment options needs to be evaluated further (35). This treatment is offered within a study setting at two centers in Sweden (56).

### **1.4.3 RADIOTHERAPY**

As a curative treatment radiotherapy, (RT) and RP have similar oncological outcomes (66). For patients who have cT3 disease, radiotherapy is the first recommended option outside clinical trials (35). For patients who have inflammatory bowel disease or were previously given radiation within the prostatic area, radiation should be avoided due to the risk of developing severe complications, such as fistula formation. The treatment can be given in the form of external beam radiation (EBRT) alone, in combination with brachytherapy, as brachytherapy, or, since a few years ago, as hypo-fractionated treatment. Radiotherapy, in combination, with neoadjuvant or adjuvant hormone therapy, has been found to be superior to RT alone and is offered to patients with high-risk tumours (67). Thanks to the dynamic development of radiation technology and treatment protocols, radiation therapy is an excellent treatment option for some patients, but like surgery, it involves side effects that could affect a patient's quality of life. Among the common side effects of EBRT are diarrhea, dysuria, urinary frequency, and proctitis, as well as fatigue (68). Those side effects are mainly caused by the damage to tissues surrounding the prostate. In an attempt to minimize those complications, volumetric modulated arc therapy (VMAT) and intensity modulated RT in combination with gold markers have been developed (69). According to the *Swedish Guidelines*, radiation therapy is recommended as a treatment option for patients with cT3 disease because of the risk of positive margins (16).

## 1.4.4 RADICAL PROSTATECTOMY

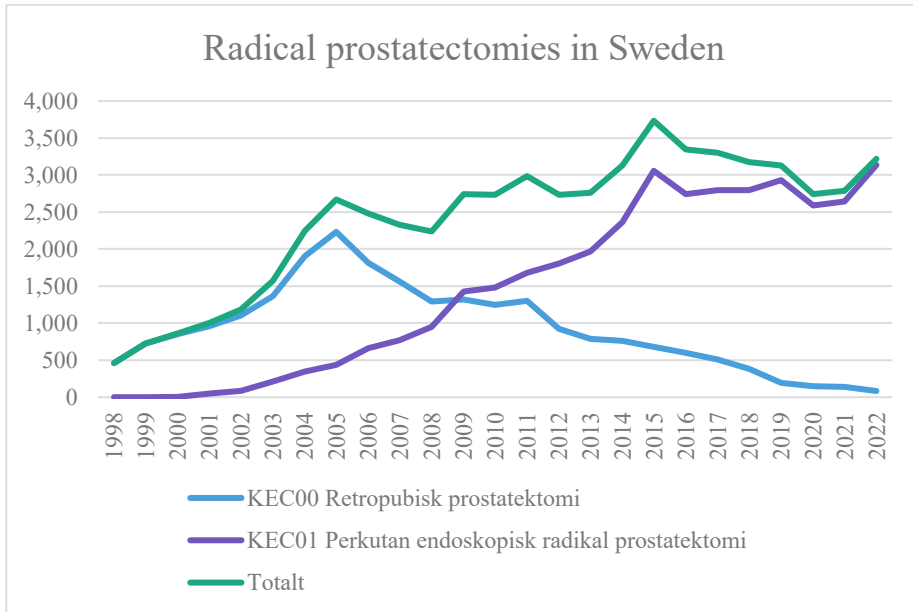
Radical prostatectomy involves the removal of the entire prostate and seminal vesicles (SV), which is followed by the restoration of urinary tract continuity via vesico-urethral anastomosis. As the prostate is located between the urinary bladder and pelvic diaphragm, the access to it, is challenging and different approaches have been used over time.



**Figure 10.** Different ways to approach the prostate, the black arrow shows the retropubic way, green arrow the retziussparing and red arrow perineal approach. Image adapted from Photoserch.

The first report of a total prostatectomy that was performed on a cadaver was made by Kuchler in 1866 and was followed by the first prostatectomy in human by Billroth in 1869, as well as first perineal prostatectomy, which was performed by Young in 1905 (70-72). In 1945 the first perineal prostatectomy series with long-term results were, presented by Young and Millin, who

described a “simple prostatectomy” by retropubic approach the same year (73, 74). In 1959, Campbell described a radical retropubic prostatectomy, but it was not until 1983 that a radical prostatectomy with the preservation of the neurovascular bundles was described by Walsh (75, 76). Twenty years later the first report of a laparoscopic prostatectomy was presented by Schuessler, and in 1998 the first series of laparoscopic RP was presented (77). The most commonly used technique today is the robot-assisted radical prostatectomy (RALP), which was first described in 2001. The robotic approach will continue to be a mainstay in the treatment of PCa as it is a minimally invasive surgical management technique (78). The choice of technique: RRP or RALP in different countries depends mostly on access to the daVinci Robotic system, which is governed by economic conditions. Both techniques produce similar oncological results, but the RALP involves shorter hospital admissions, less blood loss, shorter catheter time, and less postoperative pain. The Laparoscopic Prostatectomy Robot Open (LAPPRO) study, which compares RALP and retropubic radical prostatectomy (RRP) presented 8 years results showing significantly lower prostate cancer specific mortality in RALP group compared to RRP (RR 0.56, 95 CI 0.34-0.93) most prominent for patients with high-risk tumours. There was no significant difference in incontinence 8 years after surgery but better erectile function in favour for RALP (79). Several other studies presented an advantage of RALP in terms of erectile function (56). The retzius-sparing robot assisted approach has been evaluated and offers preservation of the anterior structures responsible for continence and shows promising results at centers where it is used (80, 81).



**Figure 11.** Radical prostatectomies in Sweden between 1998 and 2022. Open retropubic prostatectomies are represented by the blue line, and the RALPs are represented by the purple line; the total is represented by the green line. Adapted from *The Swedish National Board of Health and Welfare*.

Even though the modern radical prostatectomy nowadays is a routine procedure that is frequently performed with minimally invasive techniques such as the RALP, it still decreases patients' quality of life by affecting continence and erectile function, despite the improvements that have been made to the surgical technique. The retzius-sparing robot assisted approach offers preservation of the anterior structures responsible for continence and shows promising results at centers where it is used (80, 81).

## 1.5 COMPLICATIONS AND SIDE EFFECTS

While discussing the treatment of PCa, side effects must always be considered, as well as the risk of complications. What is a complication, and what is a side effect? The definition of a complication, according to *Oxford Concise Colour Medical Dictionary* (82) is: “ a disease or condition arising during the course of or as a consequence of another disease”. In general, “complications refer to other diseases or symptoms that occur in relation to a given disease while side effects to undesirable effects that occur concomitantly with the originally intended outcome”.

If an otherwise healthy athletic 55-year-old male undergoes a bilateral nerve sparing procedure without any per operative complications and is incontinent a year after surgery, then the incontinence may be considered a complication rather than a side effect of surgery. But if a 75-year-old male with diabetes who has an inactive lifestyle undergoes a partial nerve sparing surgery and experiences incontinence after 12 months, then the incontinence may be considered a side effect.

Does having risk factors that could lead to urinary leakage makes incontinence a side effect and not having any risk factors makes it a complication? Is the use of one pad per day in a patient who has several risk factors that could lead to the development of urinary incontinence a complication or side effect ? As a urologic surgeon performing radical prostatectomies, I would prefer to call heavy incontinence in any patient and incontinence that occurs independent of grade in a patient who lacks risk factors a complication. While “light” incontinence in a patient who has several risk factors is more of a side effect from a surgical point of view. In patients who have anastomotic stenosis, some researchers have hypothesized that the tendency to develop wide scars or excessive scar tissue after surgery may indicate a higher risk of developing anastomotic stenosis. In such cases, anastomotic stenosis may be seen as a side effect rather than a complication, but this requires future research (83). Anastomotic stenosis that occurs after a radical prostatectomy may be seen as complication as long as strong patient-related risk factors are absent.

### 1.5.1.1 ERECTILE DYSFUNCTION

Erectile dysfunction is the most common side effect of the radical prostatectomy and affects 70% of patients a year after radical prostatectomy, according to Ficcaro et al.(84). When compared to the open technique, the surgical cautery-free technique and the RALP were found to favour postoperative erectile function. Among the patient- related risk factors, some factors that can negatively affect postoperative erectile function are higher age and the preoperative erectile dysfunction (85).

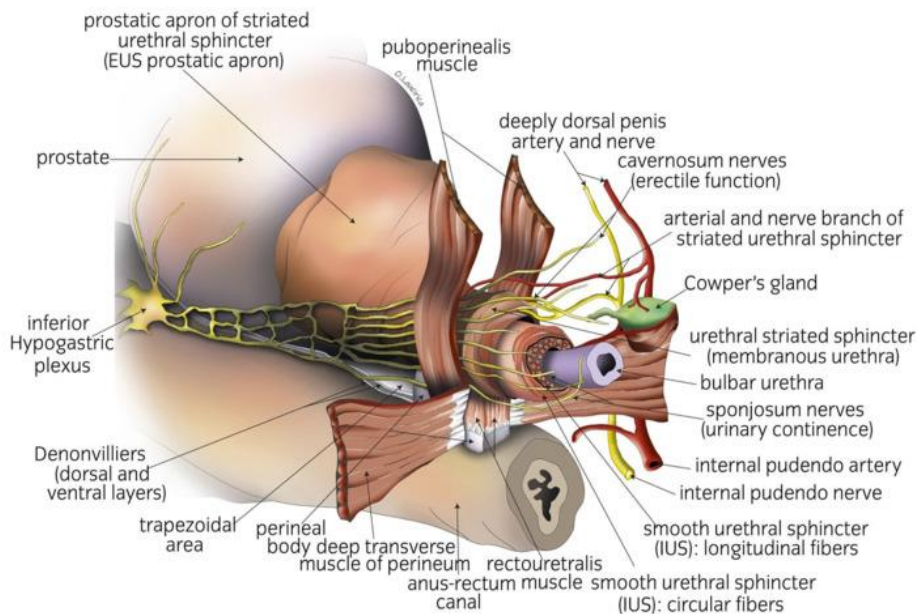
### 1.5.2 ANASTOMOTIC STENOSIS

The major reconstructive step during radical prostatectomy that occurs after the prostate has been removed is the creation of continuity in the urinary passage via an anastomosis. During an open radical prostatectomy, this step is usually performed using single sutures, whereas when an RALP is being performed, the anastomosis is sewn with a continuous suture. Two studies compared incidence of anastomotic stenosis after open radical prostatectomy and RALP and found it more common after open surgery (86, 87).

The anastomosis is usually located just above the external sphincter. The healing process may sometimes become exaggerated, causing excessive fibrotic tissue formation. Sometimes normal healing can be disturbed by anastomotic leakage or infection, which causes the consequent excessive formation of scar tissue. When this happens at the level of the anastomosis, it is called anastomotic stenosis, but if there is a narrowing in the urethra in a part of urethra surrounded by corpus spongiosum, it is called anastomotic stricture. In the literature, use of those definitions varies and is sometimes incorrect. Anastomotic stenosis should be defined as narrowing at the lever of the anastomosis between the bladder and urethra. This narrowing may cause slow urinary flow and sometimes total obliteration and can be managed with dilatation or incision, but these treatments involve the risk of urinary leakage. Is anastomotic stenosis a complication or a side effect? In my opinion, it is a complication rather than a side effect. Urinary leakage that is caused by surgical intervention that is performed to treat anastomotic stenosis may result in incontinence, which, in turn, may be seen as a side effect.

### 1.5.3 INCONTINENCE

Urinary incontinence (UI) can affect humans of all ages and genders. Regardless of who is affected, it causes both a reduction in an individual's quality of life for the individual (88, 89), costs for both the individual and society, and an environmental impact. The subject received a special attention from the European Association of Urology (EAU) and EU in 2023 due to its the high economic impact on society. The focus of this following part is on urinary incontinence in male patients who have undergone a radical prostatectomy, which is also referred to as post-prostatectomy incontinence (PPI).



**Figure 12.** Illustration of the anatomical landmarks that relate to early continence according to Katsimperis et al. *Front Surg.*(90) with permission.

Ficcara et al. found that urinary incontinence after radical prostatectomy, defined as the use of any pad, affects 16% of patients. They also discussed the significant advantage of undergoing an RALP in comparison to undergoing

open surgery (91). Over time, different modifications have been made to the surgical technique to improve the outcomes of urinary continence. In the LAPPRO cohort, Steineck et al. found that patients who underwent surgery with a higher grade of nerve sparing experienced improved continence a year after surgery (92). Preservation of the bladder neck was found to improve short-term continence according to a study by Freire et al. (93). Operative technique aiming to preserve the length of the membranous urethra and external sphincter with subapical urethral dissection have been found to favorably affect the recovery of continence (90, 94).

The complicating factors in assessing incontinence are the facts that it can be defined in many different ways and that patients with the same grade of incontinence may experience different grades of discomfort (88). Wallerstedt et al., who evaluated a Swedish cohort of 1,179 men, reported that patients with only occasional leakage reported significant bother. Authors found that among patients who used less than one pad, 31% reported significant or moderate bother, while only 6% reported similar bother in O pad group (88).

Not much is known about urinary incontinence in the general population. One might assume that it affects older men, but few studies discuss the prevalence of unintentional urinary leakage among all age groups. The prevalence of UI among men as well as women increases with age, and it is suggested that 11-34 % of older men are affected and 2-11% on daily basis (95). However, in 1997, Malmsten et al. evaluated 7,763 Swedish men aged 45-99 and found an overall prevalence of urinary incontinence of 9.2 % (96). Of those men, 4,072 were still available for analysis, and the results demonstrated that the number of participants who experienced incontinence had doubled 11 years later (97). Those studies show that among men at the age of 45, the prevalence of urinary incontinence is 3.6 % and was increasing gradually with age.

Before radical prostatectomy, urinary leakage is prevented using four main mechanisms: the stable detrusor function, the urinary sphincter, urethral pressure within the prostatic urethra, and the external urinary sphincter (rhabdosphincter)/pelvic floor. After RP the mechanisms that remind to prevent leakage are the external sphincter/pelvic floor muscles and often stable detrusor muscle. That means that the remaining mechanisms have to respond for greater part to prevent urinary leakage.

The most common type of incontinence that is experienced after a radical prostatectomy is stress incontinence (98). Stress incontinence is thought to be

caused by sphincter insufficiency after an RP, which results in lower closure pressure and tone (99). External sphincter insufficiency is thought to be present in almost 90 % of patients with PPI and is visualized as a reduction in maximal urethral closure pressure (MUCP)(100). The sphincter may be affected in different ways. Direct damage to the muscle fibers may occur during apical dissection, and innervation may be affected due to damage to the somatic nerve fibers from the pudendal nerve as well as autonomic nerve fibers, such as the pudendal and autonomic nerve fibers. Fibrosis may also develop in the area of anastomosis, which may cause a decrease in the elasticity of the sphincteric urethra. Stress incontinence is a condition that leads to involuntary urine loss as an effect of the vesical pressure exceeding the maximal urethral pressure in the absence of detrusor activity (101).

Urge incontinence involves detrusor overactivity and is more often seen among patients who have undergone radiation therapy. It causes involuntary leakage that is accompanied by compelling desire to urinate. It has previously been found that passage of fluid through the urethra may increase the afferent nerve activity of the proximal urethra and may induce involuntary detrusor contractions (102). Stress incontinence may therefore be a factor behind urge incontinence in patients who experienced mixed forms of incontinence after undergoing radical prostatectomy. A combination of stress and urge incontinence may also be present in patients who undergo RP and is considered a form of mixed incontinence.

The International Continence Society (ICS) recommends using the pad weight test to evaluate incontinence as it allows one to evaluate “exact“ urine loss, but it is resource-intensive for the patient and health system (103). Therefore, validated self-reported questionnaires are more widely used to obtain patient measurements. Among these questionnaires are the International Consultation on Incontinence Questionnaire (ICIQ), the Expanded Prostate Cancer Index Composite (EPIC)(104), and the Swedish ePROM. These questionnaires include questions on the use of pads to define a patient’s incontinence and its severity. Among different definitions used are “complete continence” (defined as use of 0 pads per day) and “social continence” (defined as the use of one security pad per day (105, 106). As incontinence may be defined in different ways, evaluating the number of patients who are affected is challenging. Arnsrud et al. assessed PPI a year after surgery by studying 4668 patients with 12 months continence data. PPI was investigated by use of three different questions resulting in three different values ( 14%, 27 % and 32 %) (107).

When discussing incontinence, it is therefore crucial to understand which definition a researcher is using and how they have collected their information.

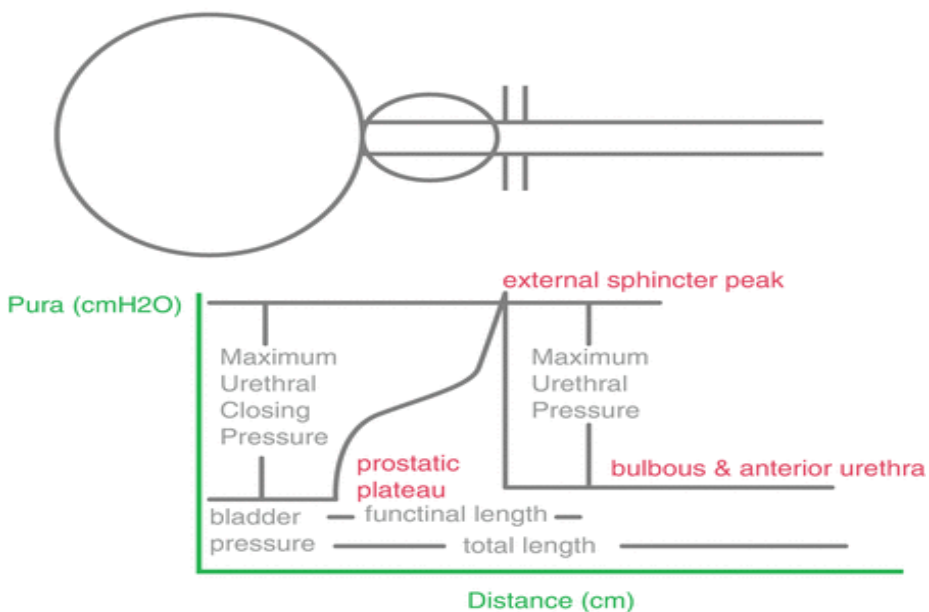
## 1.5.4 URODYNAMICS

Urodynamic and urethral pressure profiles are important diagnostic tools that are used to evaluate the lower urinary tract in male patients. These procedures are used specifically to gather valuable information about bladder function, detrusor contraction strength, and urethral pressure dynamics.

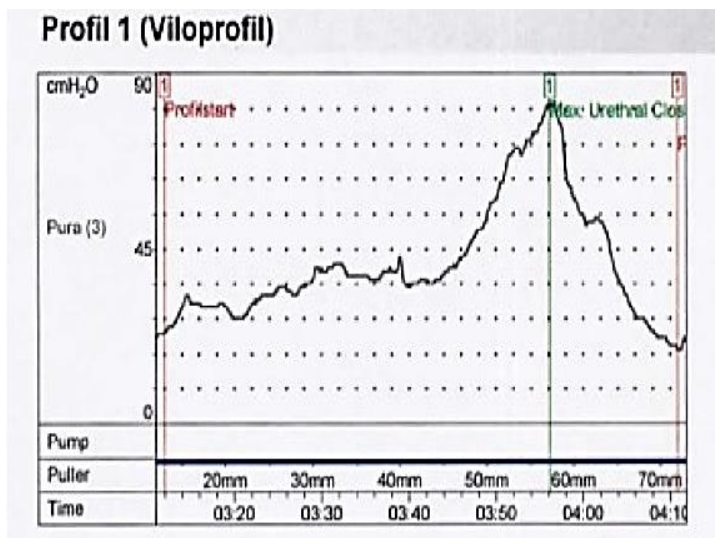
Furthermore, the evaluation of the lower urinary tract in male patients through urodynamic and the urethral pressure profile is a component of urodynamic testing that is used to measure the pressure along the length of the urethra. One of the key parameters that is measured during a UPP is the MUCP, which is the maximum difference between the urethral pressure and the intravesical (bladder) pressure during the filling phase of the bladder, while the patient is not voiding. The MUCP reflects the strength of the urethra's closure at rest and is important for maintaining continence. Low MUCP can indicate intrinsic sphincter deficiency, which is a condition where the urinary sphincter is unable to maintain a seal that prevents urine from leaking out. During UPP, a catheter is inserted into the bladder and pulled back through the urethra to measure the pressure at various points. The highest pressure recorded during this procedure is considered the MUCP. The functional urethral length refers to the length of the urethra over which a closure pressure can be maintained against the bladder pressure; it is essentially the part of the urethra that actively contributes to continence.

A shortened functional urethral length may be associated with stress urinary incontinence since it indicates that the mechanism that maintains continence has been compromised. UPP generates a curve that in male may be divided into a prostatic part seen as prostatic plateau and a sphincteric part reflecting the external sphincter(108).

**RESTING URETHRAL PRESSURE PROFILE IN MALE**



**Figure 13.** Urethral Profilometry by Giancarlo Vignoli, used with permission from Springer Nature (108).



**Figure 14.** A Urethral Pressure Profile (UPP) generated during urodynamics.

## 1.6 STATISTICAL METHODOLOGY

Epidemiological research is used to uncover the relationships between various factors in a population and the occurrence of diseases or health outcomes such as urinary incontinence. Understanding the distinction between causation and correlation is important in this type of research. Although correlation suggests a relationship between two variables, causation means that one variable directly influences another.

Confounding and mediation play central roles in understanding causal relationships between variables. Confounding occurs when a third variable affects both the independent and dependent variables, which leads to a mistaken association between the two. Conversely, mediation occurs when the relationship between the independent and dependent variables is influenced by a third variable(109).

Linear regression is used to examine the relationship between one or more independent and a continuous dependent variable. This method facilitates the determination of the strength and direction of the association between variables.

Additionally, a logistic regression is often applied when the dependent variable is dichotomous, such as the presence or absence of a complication such as urinary incontinence. This method is valuable for assessing the odds ratio of a particular outcome that occurs in relation to different exposures.

Multivariable regression offers the ability to control confounding by adjusting for confounding variables. In contrast to a linear regression, which assumes a continuous and normally distributed dependent variable.

Missing data is considered problematic to maintain the accuracy and reliability of the findings. Various methods, such as data imputation, complete case analysis, and likelihood-based approaches, can be used to address missing data.

MICE, which stands for Multiple Imputation by Chained Equations, is a method that is used to deal with missing data in a dataset. The MICE method is powerful because it accounts for uncertainty about the missing values by

creating several imputed datasets and combining the results based on each of them to provide a more accurate analysis (110).

Confidence intervals help to quantify the uncertainty surrounding an estimated effect. They indicate a range of values within which one can be reasonably confident that the true value lies. A narrower confidence interval suggests more precise estimates, whereas a wider interval reflects greater uncertainty.

Statistical significance is used to measure the likelihood that an observed effect has not been caused by chance. It is typically assessed using p-values, where a low p-value ( $<5\%$ ) indicates that the observed effect is unlikely to be purely coincidental.

When evaluating the effect of a risk factor, it is important to consider the relative risk and odds ratio. Relative risk is a measure that is used to assess the strength of association between an exposure and an outcome in a clinical trial. It is calculated by dividing the risk of the outcome in the exposed group by the risk of the outcome in the unexposed group. The odds ratio is calculated by comparing the odds of exposure among cases to the odds of exposure among controls. Like the relative risk, an odds ratio value that is greater than 1 indicates a positive association, while a value that is less than 1 signifies a negative association.

## 2 AIMS

The overall objective of this thesis is to quantify the risk of two known postoperative complications/side effects of the radical prostatectomy and to identify and explore the risk- and predictive factors behind them.

Objectives of each paper are as follows:

1. *To compare the risk of developing symptomatic anastomotic stenosis after open- and robot-assisted radical prostatectomies and to explore the risk factors that are associated with anastomotic stenosis development and its subsequent influence on the risk of PPI.*
2. *To identify patient- and surgery related factors behind PPI at 3 and 12 months after undergoing an RALP.*
3. *To describe the study design, procedures, and study population of the Incontinence Post robot assisted radical prostatectomy, Anatomical and functional causes (IPA) trial, a prospective observational trial further investigating the patient-, and procedure specific factors behind PPI and the changes in the pelvic floor and sphincter apparatus.*
4. *To evaluate how well MUL on MRI correlates to sFUL that is derived from UPP, and to assess if the shape of the prostate apex influences any such correlation.*

## 3 PATIENTS AND METHODS

The papers that are part of this thesis include various data sources and methodologies that are used to explore two well-known complications that occur after radical prostatectomy. The sources are the Laparoscopic Prostatectomy Robot Open (LAPPRO) trial (**Paper I**), the Prostate Cancer data Base Sweden (PCBASE) database (**Paper II**) and the Incontinence Post robot assisted radical prostatectomy, Anatomical and functional causes (IPA) study (**Paper III-IV**).

### 3.1 STUDY POPULATION AND DATA COLLECTION

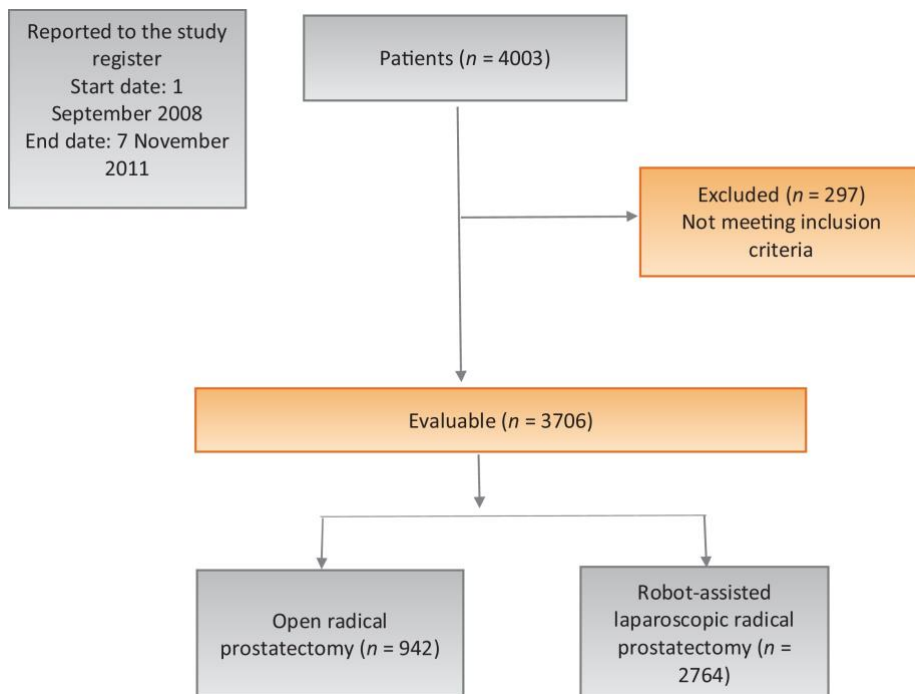
#### *Paper I*

The study population of **paper I** consisted of patients included in the LAPPRO study.

The LAPPRO trial is a non-randomized prospective study that aims to compare the well-established open RRP and the more novel RALP by examining continence 12 months after surgery, which was established as the primary endpoint for the trial. Between September 1, 2008, and November 7, 2011, at 14 urological departments, patients were prospectively included. Seven centers had performed RALP, and the remaining seven RRP. The choice of surgical approach depended on the geographical location rather than the size of the center: among these centers were academic, public, and private hospitals. All the participating centers had a well-established urology department, or very experienced urologist who specialized in prostate cancer and performed around 50 radical prostatectomies each year. The patients were not randomized for the LAPPRO study as the choice of surgery depended on which type of surgery was used at the participating center. The urologists who performed these surgeries had performed at least 100 procedures by the time the study took place. Patients younger than 75 who had PSA levels of <20 ng/ml and clinical stage of < T4 and did not have metastasis were offered inclusion. The clinical data was collected by healthcare personnel who used clinical record forms (CRFs) before surgery and then at intervals of 6-12 weeks and 3, 12 and 24 months after surgery. The validated patient questionnaires included questions about functional and oncological outcomes and were collected both

preoperatively and at 3, 12 and 24 months after surgery. The study was described in detail in the work by Thorsteinsdottir et al.(111). Since the end of inclusion in the LAPPRO study, functional results that have been gathered at 3, 12 , 24 months and 8 years after surgery have been published (79, 112-114).

Between September 2008 and November 2011, 4,003 men were enrolled in the trial, and 3,706 were deemed evaluable. The data on stenosis, risk factors, confounders, and incontinence were collected from patient' questionnaires and CRF.



**Figure 15.** Flow chart that illustrates the study population in Paper I with permission.

Anastomotic stenosis was identified using two criteria. First, a hospital admission with an ICD10-SE diagnosis code or a NOMESCO operative code for anastomotic stricture cleavage as recorded in the CRFs. Second, patient confirmation of undergoing cleavage or dilatation of an anastomotic stricture in post-operative questionnaires. Urinary incontinence in the LAPPRO study was assessed using the following question:

“How often do you change pad, diaper or sanitary aid during a typical day (24 h)?” with answering categories:

1. “Not applicable, I don’t use pads, diapers or any sanitary aids.”
2. “Less often than once every 24 hours.”
3. “About once every 24 hours.”
4. “About two to three times every 24 hours.”
5. “About four to five times every 24 hours.”
6. “About six times or more often every 24 hours.”

The definition of incontinence that is used in **Paper I** defines incontinence as requiring a patient to use at least one protective pad every 24 hours, which demonstrates the dichotomy between categories 2 and 3.

The study was approved by the Gothenburg regional ethical review board (number 277-07) and is registered in the Current Controlled Trials database (ISRCTN06393679).

## *Paper II*

The study population for **Paper II** consisted of patients who were registered in the National Prostate Cancer Register (NPCR) and were part of the Prostate Cancer data Base Sweden (PCBaSe) research database.

PCBaSe is a population-based, nationwide research database, based on men in NPCR and other nationwide registers through cross-linkages by use of the Swedish identity number. The NPCR of Sweden captures comprehensive data for 98 % of all incident cases of PCa. The registration of all cancer cases in the Swedish National Cancer Register is mandatory and mandated by law. One critical element of gathering data in prostate cancer registries is the incorporation of thorough demographic and clinical details. This includes information that relates to a patient's age at diagnosis, tumour stage, Gleason score, PSA levels, treatment methods, and follow-up results. The data in NPCR are collected through the use of diagnostic forms, primary treatment, and work-up forms, as well as two curative treatment forms. There are two curative treatment forms: one for radiotherapy and one for prostatectomy in Sweden (PiS) form. The PiS form has two versions: a shorter version with 60 variables and an extensive form that includes 83 variables. The variables in the PiS form include descriptions of aspects of the procedure being performed, such as the grade of nerve sparing, the volume of blood loss, cutting anastomotic suture and the level of urethral division. The practice of filling in the PiS form depends on the department's established practices and the urologic surgeon's preferences.

Electronic Patient-Reported Outcome Measures (ePROMs) are a valuable tool that can be used to assess a patient's health status before and after a radical prostatectomy. Baseline ePROM are collected prior to the surgical or radiological treatment, and postoperative ePROM are collected after 3 and 12 months during the follow-up period. ePROMs facilitate the evaluation of functional outcomes after radical treatment and, in particular after radical prostatectomies. ePROMs include questions on urinary function and enables the collection of data on urinary leakage.

For **Paper II**, urinary incontinence was assessed using a question from an ePROM:

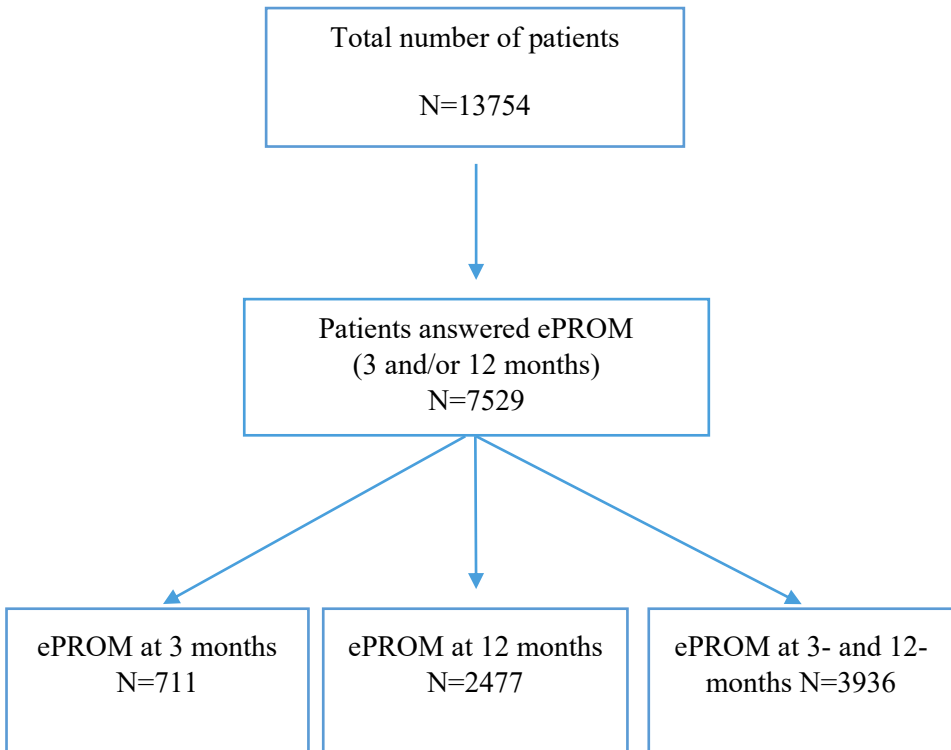
“How many pads do you use per 24 hours due to urinary leakage?” Several responses were provided:

1. “I do not use pads”.
2. “Less than 1 per 24 hours.”
3. “Approximately 1 per 24 hours.”
4. “Approximately 2 per 24hours.”
5. “Approximately 3-4 per 24 hours.”
6. “Approximately 5 or more per 24hours.”

For primary and secondary endpoints in **Paper II**, incontinence was defined as the use of more than one safety pad (i.e. alternatives 4-6) and the use of any pad (i.e. alternative 2-6), respectively.

To evaluate patient and surgery related risk factors data collected in diagnostic and curative treatment forms was used.

For **Paper II**, patients registered in NPCR between January 2017 and December 2021 and who had completed the ePROM at 3 and/or 12 months post-surgery were studied, and the Flow chart visualizes participation.



**Figure 16.** Flow chart of the study population in Paper II.

The PCBaSe was initially approved by the Umeå regional ethical review board (number 2013-153-31), and the following versions were approved by the Uppsala regional review board Dnr: 2016/239, 2019 2019/03196. The study was described in detail in the work by Van Hemelrijck et al.(115).

### ***Paper III-IV***

For **Papers III** and **IV**, the study population consisted of patients who were included in the IPA study.

The IPA study is a prospective multicenter clinical trial that incorporates MRI, urodynamics, TRUS, and recording surgery, to identify and evaluate various risk-factors for post-RALP incontinence. Patients who were scheduled to undergo RALP and lacked preoperative incontinence on a direct question were offered participation. After signing informed consent forms, the participants took part in a preoperative urodynamic evaluation, which included a UPP and TRUS was performed. Preoperative mpMRIs were also conducted to evaluate the participants anatomical structures. The surgeries were recorded for future evaluation. Three months after surgery, the urodynamic evaluation, UPP, TRUS and MRIs were performed. The data on continence was collected via ePROMs 3 and 12 months after surgery. Since the first patient was included in dec 2017 and by March 2023, 219 patients had been included. All of those 219 patients were patients at the department of Urology at Sahlgrenska University Hospital in Gothenburg. Beginning in the spring 2024, the study will also include participants from the urology department at Karolinska University Hospital in Stockholm and the urology department at Skaraborgs Hospital in Skövde. The collected data includes measurements of anatomical structures that were gained via mpMRIs, functional measurements from UPP profiles, and recordings of pelvic floor movements from TRUS for future measurements of pelvic floor movement, as well as recordings of surgeries to evaluate surgical technique. Incontinence in the IPA study is addressed with the following question:

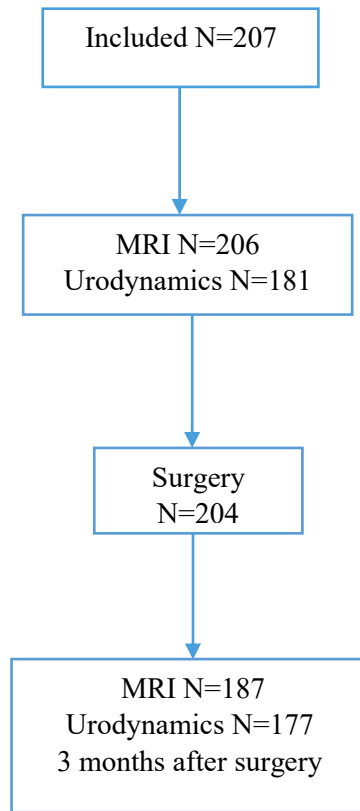
“How many pads do you use per 24 hours due to urinary leakage?” the participants could choose from several responses:

1. “I do not use pads.”
2. “Less than 1 per 24 hours.”
3. “Approximately 1 per 24 hours.”
4. “Approximately 2 per 24hours.”
5. “Approximately 3-4 per 24 hours.”
6. “Approximately 5 or more per 24hours.”

For the primary endpoint in the **IPA** study, incontinence was defined as “the need to use any pad, at three months” and for the three secondary endpoints, “the need to use any pad at 12 months” , “the need to use more than safety pad at 3 and 12 months” respectively. Incontinence is defined as “the need to use any pad” (i.e., alternatives 2-6) and “the need to use more than safety pad” (i.e. alternative 4-6).

The study was approved by the Gothenburg regional ethical review board (number 131-16) and is registered in the Current Controlled Trials database (ISRCTN67297115).

IPA study is an ongoing study that involves continued inclusion. For **Paper III**, the first 207 patients who were included in the study until October 2023 were part of the evaluation. For **Paper IV**, the first 155 patients who were included in the study were included in the analysis. All 155 had undergone MRI, and 128 had a UPP curve of quality, which allowed to perform sFUL measurements.



**Figure 17.** Flow chart that illustrates the participation in IPA study until October 2023. A complete Flow chart may be found in Paper III.

The study was approved by the Gothenburg regional ethical review board (number 131-16) and is registered in the Current Controlled Trials database (ISRCTN67297115).

## 3.2 STATISTICAL METHODS

The various statistical methods that have been applied in Papers I, II, III, and IV of this thesis are summarized in the following paragraphs.

**Paper I.** As the LAPPRO study was not designed to explore the development of anastomotic stenosis, no power calculation was performed. The least absolute shrinkage and selection operator (LASSO) method was used for the selection of risk factors and confounders that were to be used in the adjusted and unadjusted regression analyses. The LASSO is a regression analysis method that is used to select variables and regularize them to avoid overfitting (116). The selection criterion for risk factors and confounders required the participants to have complete information.

To conduct multivariable modelling with binary outcomes, we used log-binominal regression models that resulted in adjusted and unadjusted relative risks (RR) and 95% confidence Intervals (CI) to investigate the effects of the type of operation on the occurrence of anastomotic stenosis. The RR were unadjusted and adjusted for a) patient-related risk factors, b) patient- and surgery-related risk factors, and c) the main surgeons experience.

The MICE method was used to handle missing data among potential risk factors. To address the influence of the number of sutures, an analysis was performed separately for each type of surgical technique. To explore the risk of co-variations of postoperative radiation therapy, a subgroup analysis was performed to compare patients who did and did not undergo radiation using a log-binominal regression model with anastomotic stenosis as a dependent and radiation as an independent variable.

**Paper II.** We explored the association between selected risk factors and postoperative urinary incontinence using both univariable and multivariable modified Poisson regression. The choice of regression method was dependent on the outcome variable, and as incontinence was a discrete outcome variable, we found the Poisson to be the most suitable choice. The results were presented as RR with a 95% CI.

To assess the problem of missing data for studied risk factors (but not for continence data), the MICE method for imputation was used (110, 117). We did not use the MICE method for imputation to gather continence data. Instead, we performed imputation of incontinence data according to the flow chart in Paper II; patients who had not answered the 3-months ePROM but were incontinent at 12-months were considered to be incontinent even at 3 months. Patients who were continent at 3 months and who had not answered the 12-months ePROM were considered to be continent at 12 months. To ensure that the imputation of missing data did not affect the final results, an additional sensitivity analysis was performed on complete cases.

**Paper III.** As Paper III describes the methodology of the IPA trial, a power calculation is presented. As power is the probability of the correct rejection of the null hypothesis and is affected by sample size and statistical significance, a power analysis was performed. The MUL is a well-established risk factor that relates to post-prostatectomy incontinence. It can be measured on MRI prior to surgery, and it was utilized in the power calculation.

To detect a 10 % increase in the risk of incontinence per mm of shortening of the MUL with 80 % power and a statistical significance level of 0.05, a sample size of 800 patients was calculated. As there is always some degree of drop-out and missing data, we estimated it at 10 %. To compensate for the missing data and be able to conduct an explorative analysis, we targeted a sample size of 1,000 patients. When enrolment is completed, an analysis of the primary and secondary endpoints will be possible, and multivariable regression analyses will be conducted to identify patient-and/or procedure-specific risk factors behind incontinence.

**Paper IV.** This paper represents a sub-study within the IPA study that was conducted on, why continence was not considered for analysis to not interfere with the results of the endpoints in the IPA study. To assess the relationship between MUL based on MRI and sFUL, from UPP linear regression was included in **Paper IV**. The coefficient of determination ( $R^2$ ) was used to indicate the proportion of variation in the sFUL as explained using the MUL. To evaluate the influence of the type of prostatic apex on the correlation between MUL and sFUL, the regression lines were fitted for each apex type separately. The measurements of the MUL were performed in consensus between urologist and radiologist.

## 4 RESULTS

The findings of the papers in this thesis are summarized in Table 6. More detailed results are provided in the included papers.

Paper	Research questions	Findings
I.	What is the risk of developing anastomotic stenosis (AS) after RALP and RRP respectively? Which factors rise the risk of developing AS? Does AS influence risk of urinary incontinence?	Symptomatic AS developed in 1.9%, 71 of 3706 men within 12 months after surgery. The risk of developing AS after RRP was 2.7 times higher than after RALP, RR 2.7 (95% CI, 1.70-4.27). The higher number of sutures/takes was associated with lower risk of stenosis which was significant in the RALP group. The risk of urinary incontinence 24 months after surgery was significantly higher among patients with symptomatic stenosis RR 2.01(95% CI, 1.43-2.64).
II.	Which patient- and surgery related risk factors increase the risk of urinary incontinence 3 and 12 months after surgery?	Higher age and larger prostate volume were the two strongest patient related risk factors for UI. Division of urethra with margin from apex and no nerve sparing procedure were the strongest surgery related risk factors for UI after RALP. Younger patients with smaller prostates and with nerve sparing procedure had almost 50% lower risk of UI after surgery. The incidence of UI after surgery depended on the definition used.
III.	To provide a detailed description of the design and procedures of the IPA study. To what extent do the included patients participate in planned procedures within the IPA study?	The study population amounted to 207 patients until October 2023 with an increasing rate of accrual. 187 of those had pre- and postoperative MRI and 177 pre- and post-operative urodynamics and UPP.
IV.	To investigate if MUL on MRI can be used as a proxy for sFUL reflecting the external sphincter?	The lack of correlation between MUL and sFUL (p-value = 0.34), $R^2 = <0.001$ , indicates that the MUL on MRI do not represent the actual functional sphincter length as measured by sFUL. The type of prostatic apex did not affect lack of correlation.

**Table 6.** Overview of the papers in this thesis. The findings of the papers are summarized. In this table anastomotic stenosis is referred to as AS.

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## 5 DISCUSSION

### 5.1 OVERALL SUMMARY

In this thesis, two complications of RALP are investigated: anastomotic stenosis and urinary incontinence. In the **first paper** we investigated the risk of anastomotic stenosis after RRP and RALP and how the anastomotic stenosis can influence the risk of incontinence. We found that anastomotic stenosis was more than twice as common in patients who underwent RRP (3.6%) in comparison to patients who underwent RALP (1.3%), and that incontinence was twice as common in patients with anastomotic stenosis (118).

In the context of incontinence, we used analysis of the PCBaSe cohort that is presented in **Paper II**, to identify several risk factors that rate to PPI. The strongest association with PPI was found for higher age, larger prostate, no nerve sparing procedures, and division of the urethra with a margin from the prostatic apex. Those findings underline the importance of including patient-centered information in shared decision-making regarding the choice of treatment. In **Paper III**, we present the methodology of the IPA study, which is a clinical observational trial that is being conducted to investigate both anatomical and functional causes of PPI and the current study population. In **Paper IV**, the association between the anatomical MRI measures of MUL and the functional sFUL reflecting external sphincter is evaluated. There was a lack of association between MUL and sFUL which emphasizes the need for future studies of the external sphincteric apparatus using UPP and MRI.

## 5.2 ANASTOMOTIC STENOSIS

Given that the number of previous studies that investigating anastomotic stenosis that occurs after radical prostatectomies is limited and their small sample sizes, there was a clear need to explore this complication with a large study population (83, 86, 87, 119, 120). The LAPPRO cohort offered such a study population and enabled evaluation of anastomotic stenosis after two of the most frequently used surgical methods for radical prostatectomy. The finding that anastomotic stenosis is twice as common among patients after open radical prostatectomy in comparison to RALP indicates that there may be surgery-related risk factors rather than only patient-related ones; these risk factors could have the strongest impact on anastomotic stenosis formation.

The incidence of anastomotic stenosis in the material was lower in comparison to previously presented data, and the fact that anastomotic stenosis is seen among patients after RALP indicates that even if the surgical technique becomes better, some complications will still arise. In the attempt to evaluate anastomotic stenosis, patients with the complication may be identified in different ways. To find all cases of anastomotic stenosis in a study population, would require participants to undergo cystoscopies, as some patients may not have any symptoms. In the study population in **Paper I**, patients with symptomatic anastomotic stenosis were identified using CRFs as other types of physical examination were not part of the LAPPRO study protocol (111). As anastomotic stenosis may require surgical intervention, certain patients would have to undergo surgery, while others would only require dilatation.

The doubled risk of developing anastomotic stenosis after open radical prostatectomy indicates that the surgical technique itself has a major impact on anastomotic stenosis formation. Except for the difference in approach: open versus minimally invasive, the major difference between those methods is the way anastomosis is created.

The results demonstrate that a cutting suture in the urethra or bladder neck raises the risk of patients developing anastomotic stenosis after RRP. The placement of sutures in the openly sutured anastomosis is more challenging, and if a suture cuts through the tissue, it may be difficult to simply replace it with another one. Damaged tissue may itself be a sign of a fragile tissue condition and could facilitate urinary leakage through anastomosis, which, in turn results in more inflammation and the excessive formation of scar tissue.

A cutting anastomotic suture while using the minimally invasive technique may be more easily discovered directly due to better vision, and another take may replace it, which could prevent disconnection within anastomosis.

The results also demonstrated that the number of takes by continuous suture lowered the incidence of stenosis in patients after RALP but not after an RRP. The number of single sutures in the open technique varies less than the number of takes in the continued suture, which could explain the difference seen between the methods. Typically, six single sutures are used as part of the RRP. The relatively smaller number of surgeries analyzed (887 RRP surgeries and 2,707 RALP surgeries) may explain why the protective trend of the number of takes or sutures was most clear under the RALP.

The results also highlight some additional risk factors that could affect the development of anastomotic stenosis beyond the type of operation being performed, such as diabetes, previous trans urethral resection of prostate (TUR-P), and the operating surgeon's experience. Diabetes may influence the healing process and indicate additional comorbidity. A TUR-P affects the anatomy at the bladder neck, which may be wider after resection and could make the anastomosis more challenging to perform. It can be speculated that more experienced surgeons perform more challenging surgeries and are prone to using fewer takes. As such, a sub-analysis was not conducted according to the statistical analysis plan.

Urinary incontinence among patients in the LAPPRO cohort with symptomatic anastomotic stenosis was twice as common as it was among patients without this complication. This was in line with other studies (98). We know that surgical intervention for anastomotic stenosis involves cutting of scar tissue, which may even involve causing damage to the surrounding tissue and, in particular, the external sphincter. The scar tissue itself may affect the sphincter by impairing its function and making it more inflexible. The studied cohort of patients did not allow for the evaluation of patients with anastomotic stenosis regarding other scar tissue present on the body i.e. hypertrophic scars which has been found to correlate with anastomotic stenosis in a study by Park et al.(83).

A question may arise regarding the time of anastomotic stenosis formation. For the analysis in **Paper I**, data collected up to 24 months after surgery was evaluated. However, this raises the following question: "What if there is a possibility of anastatic stenosis forming after that period?". Previous

publications indicate that most of strictures developed within a year after surgery, which is in line with our findings; Elliott et al. found the risk to be highest during the first 6 months and almost non-existent 24 months after radical prostatectomy (121). Despite the particularly low incidence of formation of anastomotic stenosis after an RALP, it is important to inform patients about this potential complication.

### 5.3 URINARY INCONTINENCE

As urinary incontinence that occurs after radical prostatectomy is affecting a considerable number of patients who are undergoing curative treatment, there is a need to evaluate patient- and surgery-related risk factors. For **Paper II**, we were able to evaluate a large study population from the PCBaSe, and we found that increased age, larger prostates, a lack of nerve sparing surgery, and the division of the urethra further from the apex were factors that raised the risk for PPI occurrence 3 and 12 months after surgery. Similar risk factors may also be found in other studies and were even presented in a metanalysis that was conducted by Lardas et.al (122).

For **Paper II**, we evaluated incontinence using a question that concerned pad use. As incontinence can be defined in many ways, two definitions were used: the primary definition focused on the use of more than one safety pad in a day, and the secondary definition focused on the use of any pad in a day. For the primary definition, the RR for PPI was higher than it was for the secondary definition, both at 3 and 12 months and with a wider CI. As CI indicates the accuracy of estimation, one could speculate that the results from the analysis that used the pad-free definition of continence exhibit more accurate results. Independent of the definition of incontinence, the RR and 95% CI were higher at 12 months in comparison to 3 months. Using the secondary/pad-free definition, we found that almost half of the patients who answered the PROM at 12 months post-surgery had PPI. An improvement in continence over time during the first year after surgery was seen, which is in line with other studies (123). We also observed that a patient younger than 65, with a prostate volume under 60 ml and a nerve sparing surgery had half of the risk of incontinence in comparison to a patient who had several of the previously mentioned risk

factors. This indicates the importance of discussing risk factors prior to surgery and the need for future studies that can explain and help prevent PPI.

The flow chart in **Paper II** indicates that only 7,529 patients of 13,754 answered ePROM 3 and /or 12 months after surgery. This demonstrates that half of the patients who underwent radical prostatectomies would not complete their ePROM; and we do not know the reason behind. For this study we found unsatisfactory levels of missing data on some of the surgical factors were present, which indicates that surgeons may choose the shorter version of PiS form. The low number of ePROMs being answered and the high levels of missing data concerning the analyzed surgery-related factors represent the major limitations of this study and one important limitations of research overall. Other limitation is the fact that incontinence at baseline was not addressed in this study. The reason behind was low number of ePROMs at baseline and previously reported low rate of incontinence at baseline in the PCBaSe data in the work by Arnsrud et al. (107).

## 5.4 HOW DO WE MOVE ON?

To address the complexity of PPI and to evaluate both anatomical and functional causes behind this side effect or complication, the IPA study was initiated. **Paper III** describes the methodology and shows the population that was included from the beginning of the study until October 2023. The willingness to participate in this clinical study was strong, and the inclusion rate was mostly affected by logistical obstacles. As the IPA study is being conducted to evaluate the anatomical and functional reasons behind PPI, it involves MRI and functional evaluation that incorporate urodynamics and TRUS.

All the included patients had undergone TRUS during their diagnostic pathways. The evaluation of the pelvic floor movement that uses TRUS is a new approach as earlier clinical research that aimed to investigate the MUL and movement patterns within this area used transperineal ultrasound. Transperineal ultrasound is used by physiotherapists, mainly in Australia, to evaluate pelvic floor exercises. The major advantage of using the transperineal ultrasound is its noninvasive nature, which allows for a more convenient examination of the patient as foreign body does not need to be inserted into the rectum. The TRUS, however, is a well-established examination method that is familiar to all urologists and captures pelvic mobility well. Within the IPA trial, TRUS were used to evaluate pelvic floor movement patterns, as well as among other things, pinch variations between patients and changes in connection to surgery. As TRUS has not been used for this purpose previously, the analysis of collected data will help us define measures and signs to look for during preoperative evaluation, which enable to assess the risk of postoperative dysfunction.

The mpMRI provides excellent images for measuring both the MUL, as mentioned previously, but even other structures can be assessed.

Levator ani thickness that was measured on MRI was found to affect the risk of developing PPI (43). The inclusion of this measure in the MRI evaluation is important to assess as there is only one published study that indicates its importance for understanding PPI (43). The shape of the prostatic apex has been found to affect the risk of PPI in the study by Lee et al., which highlights the need to evaluate its importance for PPI in a larger population (41).

While discussing the external sphincter and its importance in understanding PPI, it is crucial to evaluate how the shortening of MUL, apical dissection, or a drop in MUCP affects the risk of developing PPI. Therefore, both recorded surgeries, measurements using postoperative MRI and functional studies will provide data for evaluation. Urodynamics allow evaluation of the bladder function before and after surgery and will provide information on both detrusor underactivity and overactivity and how the radical prostatectomy itself affects changes in the function of detrusor. Some patients may find the idea of clinical examinations such as TRUS and urodynamics unpleasant and may choose to not to participate. In general, patients tend to more easily participate in less invasive parts of a study, and more of the participants had undergone MRI than urodynamics.

Since the start in November 2017 to March 2024, 219 patients have been included with 100 % having preoperative MRI and 188 urodynamics prior to surgery. Two hundred and seventeen had surgery and 191 had a follow-up MRI's, alongside and 181 had urodynamics 3 months after surgery.

The inclusion and exclusion criteria in the IPA trial may be seen as both the strengths and weaknesses of the study. The inclusion of patients who had no preoperative urinary leakage has enabled the future evaluation of a cohort of preoperatively continent men. We will not be able to evaluate preoperatively incontinent men. As all the participants filled out IPSS forms prior to surgery, patient-reported baseline data included in those forms will be complete. It is crucial for all patients who participate in a clinical trial to understand the study information and provide their informed consent. This means that some potential participants of various nationalities may not participate due to language barriers. It is widely acknowledged in the literature that conducting successful clinical trials is challenging. The IPA study like other studies, was affected by the Covid-19 pandemic, mainly by slowed inclusion rate, which has been seen even in many other studies and presented by Nomali et al.(124). Effective trial management necessitates meticulous planning, dedicated personnel involvement, the mainstance of patients safety and confidence, and the formulation of scientific hypotheses that offer the potential to generate new knowledge that is beneficial to both the patients and the healthcare system. The IPA study presents a promising opportunity to enhance the common understanding of PPI. With the upcoming multicenter inclusion, we anticipate that enrolment will accelerate and that we will be able to conduct an efficient data analysis with results generating new knowledge. The IPA study is unique in its design combining several diagnostic modalities aiming to evaluate causes

to incontinence, its major strength is beside that it evaluates important anatomical as well as functional variables not only prior to but even after surgery. Majority of previous studies have addressed potential risk factors only prior to surgery, which made more extensive evaluation not possible.

## 5.5 EXTERNAL SPHINCTER EVALUATION

Given the impact of MUL on preoperative MRI as a risk factor for PPI and its association with the external sphincter, we aimed to investigate the correlation between MUL and sFUL in the UPP profile in **Paper IV**.

There was a lack of significant correlation between MUL and sFUL which we interpreted as MUL not representing the sFUL. It is difficult to make any comparison to other studies as there are none that directly address the subject. Mayers (1998) suggested in his work defining the anatomy of radical prostatectomy by MRI that “Sphincteric urethra might be more appropriate than Membranous urethra” as name of what we relate to as MUL on MRI and sFUL on UPP (40). However, until Talavera’s proposal in 2022, there were no other studies that suggest a division of functional urethral length (FUL) into prostatic and sphincteric parts (125). **Paper IV** represents the first study in which a correlation between an anatomical structure (MUL) has been studied together with a functional part of the UPP.

The lack of correlation may have been caused by several factors, one of which is the variation of UPP curves. As the UPP is a dynamic, functional examination, the curves that are produced differ between patients, and there are no standard guidelines that can be applied for measurement because the subject has not been addressed before. The UPP curves require future study as they represent the sphincteric part of FUL that is considered to be crucial to maintaining continence. The results also indicate that MUL, even if it is considered to represent the external sphincter, may correlate more with other anatomical structures such as the thickness of pelvic diaphragm rather than the rhabdosphincter and it needs future evaluation.

## 6 CONCLUSIONS

Based on the results of the present thesis, the following conclusions could be made:

Anastomotic stenosis develops within the first year after surgery and its incidence is strongly affected by the type of surgery. The development of anastomotic stenosis doubles the risk of urinary incontinence two years after surgery.

The patient- and surgery related risk factors for PPI after surgery emphasize the need of information and shared decision making while choosing curative treatment. There is a need of future studies in order to find additional risk factors responsible for the PPI in patients.

The IPA study had progressed well regarding accrual and feasibility with acceptable participation rates and dropout rates. The upcoming results will help with identification and understanding of various risk factors for PPI and facilitate better decision making choosing appropriate treatment.

The investigated correlation between the anatomical structure MUL and functional part of UPP reflecting the external sphincter couldn't be confirmed. How sFUL and apex type affects the risk of UI remains to be investigated.

## 7 FUTURE PERSPECTIVES

During the work on this thesis, some ideas concerning areas that require future evaluation arose.

Complications such as anastomotic stenosis, even if they are less common, affect patients' quality of life, and we should be aware of that they exist. Even if only 1.3 % of patients are affected after RALP, one must consider that given the number of patients who undergo radical prostatectomies annually, the number of patients who have symptomatic stenosis is quite high. Those patients often undergo intervention, and half of them become incontinent.

Studies that address this group of patients and even the treatments that they are offered could provide new knowledge. The LAPPRO study included patients who underwent radical prostatectomy between 2007 and 2011. This study was conducted during the era of RALP being a new way to perform radical prostatectomy. Experienced surgeons were those with more than 100 surgeries performed. In 2024, an experienced surgeon is one with much more than 100 surgeries. How many men undergoing radical prostatectomies today are affected by this complication?

Incontinence is a more common complication. The population in **paper II** indicates that both patients and health workers do not find questionnaires about patient health necessary. How else can one explain the fact that only 3,936 participants out of 13,754 completed their ePROM both 3 and 12 months after surgery? This trend indicates that patients and departments require more information and that further studies should be conducted to evaluate why patients who are offered excellent treatment options and departments performing those, do not participate in the evaluation of their results. Missing values for some of the surgical variables indicate the potential for improvement. The main question concerns whether urologists can improve the reporting of what they do to elevate quality and enable future research? The question is if, and how AI could assist NPCR in collection of ePROMS and PiS forms?

The IPA study will provide new knowledge and, using different modalities such as MRI and TRUS, will hopefully even make those useful as future everyday evaluation tools of prognostic factors for PPI. The design with even postoperative anatomical and functional evaluation will enable to much more in-depth study changes due to radical prostatectomy and their influence on PPI.

The relationship between the thickness of the penile bulb and PPI, and the penile bulb and the thickness of Bulbocavernosus muscle, are factors that may require future research.

Why is age such a strong PPI risk factor and even in men not undergoing radical prostatectomy? Muscles do not get stronger without exercise, and it would be very interesting to study how biological age correlate to thickness of Levator ani muscle on MRI?

How does continence change over long time and is there a difference between men that carry on pelvic floor training and those that stop?

Paper IV involved measurements of MUL on mpMRI. After hours of measurements, it is at least obvious for me that a radiologist and urologist see things best together. Therefore, we should work together on, and for better guidance for urologists to be able to evaluate basic structures on mpMRI and use simple measures such as MUL while discussing treatment with patients. We should also discuss incorporation of MUL and prostatic apex type in ordinary MRI reports.

While discussing patients with PPI, it is important to focus on those men who have most severe leakage and need AMS 800 or a sling. Which risk factors do they have and how can we identify those patients in advance?

As pelvic floor training facilitates erectile function it is important to consider studies that investigate the influence pelvic floor training on erectile function in patients under active surveillance.

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## REFERENCES

1. Adams J. The case of scirrhus of the prostate gland with corresponding affliction of the lymphatic glands in the lumbar region and in the pelvis. *Lancet*. 1853;1:393.
2. Culp MB, Soerjomataram I, Efstathiou JA, Bray F, Jemal A. Recent Global Patterns in Prostate Cancer Incidence and Mortality Rates. *Eur Urol*. 2020;77(1):38-52.
3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021;71(3):209-49.
4. Engholm G, Ferlay J, Christensen N, Bray F, Gjerstorff ML, Klint A, et al. NordCAN--a Nordic tool for cancer information, planning, quality control and research. *Acta Oncol*. 2010;49(5):725-36.
5. Bergengren O, Pekala KR, Matsoukas K, Fainberg J, Mungovan SF, Bratt O, et al. 2022 Update on Prostate Cancer Epidemiology and Risk Factors-A Systematic Review. *Eur Urol*. 2023;84(2):191-206.
6. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. *CA Cancer J Clin*. 2022;72(1):7-33.
7. Jahn JL, Giovannucci EL, Stampfer MJ. The high prevalence of undiagnosed prostate cancer at autopsy: implications for epidemiology and treatment of prostate cancer in the Prostate-specific Antigen-era. *Int J Cancer*. 2015;137(12):2795-802.
8. Neupane S, Bray F, Auvinen A. National economic and development indicators and international variation in prostate cancer incidence and mortality: an ecological analysis. *World J Urol*. 2017;35(6):851-8.
9. Rude T, Walter D, Ciprut S, Kelly MD, Wang C, Fagerlin A, et al. Interaction between race and prostate cancer treatment benefit in the Veterans Health Administration. *Cancer*. 2021;127(21):3985-90.
10. McKay RR, Sarkar RR, Kumar A, Einck JP, Garraway IP, Lynch JA, et al. Outcomes of Black men with prostate cancer treated with radiation therapy in the Veterans Health Administration. *Cancer*. 2021;127(3):403-11.
11. B U. Urologi historia- Några droppar från ett stort flöde2020.
12. EAU Guidelines. Edn. presented at the EAU Annual Congress Paris 2024
13. Balk SP, Ko YJ, Bubley GJ. Biology of prostate-specific antigen. *J Clin Oncol*. 2003;21(2):383-91.

14. Stamey TA, Yang N, Hay AR, McNeal JE, Freiha FS, Redwine E. Prostate-specific antigen as a serum marker for adenocarcinoma of the prostate. *The New England journal of medicine*. 1987;317(15):909-16.
15. Vickers AJ, Till C, Tangen CM, Lilja H, Thompson IM. An empirical evaluation of guidelines on prostate-specific antigen velocity in prostate cancer detection. *J Natl Cancer Inst*. 2011;103(6):462-9.
16. Regionala cancercentrum i samverkan. Nationellt vårdprogram för prostatacancer; version 6.1. <https://kunskapsbanken.cancercentrum.se/diagnoser/prostatacancer/2021> (citerad 2021-08-19) [
17. De Nunzio C, Lombardo R, Nacchia A, Tema G, Tubaro A. Repeat prostate-specific antigen (PSA) test before prostate biopsy: a 20% decrease in PSA values is associated with a reduced risk of cancer and particularly of high-grade cancer. *BJU Int*. 2018;122(1):83-8.
18. Nordström T, Adolfsson J, Grönberg H, Eklund M. Repeat Prostate-Specific Antigen Tests Before Prostate Biopsy Decisions. *J Natl Cancer Inst*. 2016;108(12).
19. Nordström T, Akre O, Aly M, Grönberg H, Eklund M. Prostate-specific antigen (PSA) density in the diagnostic algorithm of prostate cancer. *Prostate Cancer Prostatic Dis*. 2018;21(1):57-63.
20. Kouriefs C, Sahoyl M, Grange P, Muir G. Prostate specific antigen through the years. *Arch Ital Urol Androl*. 2009;81(4):195-8.
21. Paner GP, Stadler WM, Hansel DE, Montironi R, Lin DW, Amin MB. Updates in the Eighth Edition of the Tumor-Node-Metastasis Staging Classification for Urologic Cancers. *Eur Urol*. 2018;73(4):560-9.
22. Gosselaar C, Roobol MJ, Roemeling S, Schröder FH. The role of the digital rectal examination in subsequent screening visits in the European randomized study of screening for prostate cancer (ERSPC), Rotterdam. *Eur Urol*. 2008;54(3):581-8.
23. Prebay ZJ, Medeiros R, Doolittle J, Langenstroer P, Jacobsohn K, See WA, et al. The prognostic value of digital rectal exam for the existence of advanced pathologic features after prostatectomy. *Prostate*. 2021;81(14):1064-70.
24. Kretschmer A, Tilki D. Biomarkers in prostate cancer - Current clinical utility and future perspectives. *Crit Rev Oncol Hematol*. 2017;120:180-93.
25. Nordström T, Vickers A, Assel M, Lilja H, Grönberg H, Eklund M. Comparison Between the Four-kallikrein Panel and Prostate Health Index for Predicting Prostate Cancer. *Eur Urol*. 2015;68(1):139-46.
26. Grönberg H, Adolfsson J, Aly M, Nordström T, Wiklund P, Brandberg Y, et al. Prostate cancer screening in men aged 50-69 years (STHLM3): a prospective population-based diagnostic study. *Lancet Oncol*. 2015;16(16):1667-76.

27. Cooner WH, Mosley BR, Rutherford CL, Jr., Beard JH, Pond HS, Bass RB, Jr., et al. Clinical application of transrectal ultrasonography and prostate specific antigen in the search for prostate cancer. *J Urol.* 1988;139(4):758-61.
28. Bates TS, Reynard JM, Peters TJ, Gingell JC. Determination of prostatic volume with transrectal ultrasound: A study of intra-observer and interobserver variation. *J Urol.* 1996;155(4):1299-300.
29. Mitterberger M, Horninger W, Aigner F, Pinggera GM, Steppan I, Rehder P, et al. Ultrasound of the prostate. *Cancer Imaging.* 2010;10(1):40-8.
30. Hodge KK, McNeal JE, Terris MK, Stamey TA. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. *J Urol.* 1989;142(1):71-4; discussion 4-5.
31. Eichler K, Hempel S, Wilby J, Myers L, Bachmann LM, Kleijnen J. Diagnostic value of systematic biopsy methods in the investigation of prostate cancer: a systematic review. *J Urol.* 2006;175(5):1605-12.
32. Drost FH, Osses DF, Nieboer D, Steyerberg EW, Bangma CH, Roobol MJ, et al. Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer. *Cochrane Database Syst Rev.* 2019;4(4):Cd012663.
33. Borghesi M, Ahmed H, Nam R, Schaeffer E, Schiavina R, Taneja S, et al. Complications After Systematic, Random, and Image-guided Prostate Biopsy. *Eur Urol.* 2017;71(3):353-65.
34. Werneburg GT, Adler A, Zhang A, Mukherjee SD, Haywood S, Miller AW, et al. Transperineal Prostate Biopsy is Associated With Lower Tissue Core Pathogen Burden Relative to Transrectal Biopsy: Mechanistic Underpinnings for Lower Infection Risk in the Transperineal Approach. *Urology.* 2022;165:1-8.
35. EAU Guidelines. Edn. presented at the EAU Annual Congress Paris 2024 [Internet]. 2024.
36. Mungovan SF, Carlsson SV, Gass GC, Graham PL, Sandhu JS, Akin O, et al. Preoperative exercise interventions to optimize continence outcomes following radical prostatectomy. *Nat Rev Urol.* 2021;18(5):259-81.
37. Yoo S, Kim JK, Jeong IG. Multiparametric magnetic resonance imaging for prostate cancer: A review and update for urologists. *Korean J Urol.* 2015;56(7):487-97.
38. Turkbey B, Rosenkrantz AB, Haider MA, Padhani AR, Villeirs G, Macura KJ, et al. Prostate Imaging Reporting and Data System Version 2.1: 2019 Update of Prostate Imaging Reporting and Data System Version 2. *Eur Urol.* 2019;76(3):340-51.
39. Bratan F, Niaf E, Melodelima C, Chesnais AL, Souchon R, Mège-Lechevallier F, et al. Influence of imaging and histological factors on

prostate cancer detection and localisation on multiparametric MRI: a prospective study. *Eur Radiol.* 2013;23(7):2019-29.

40. Myers RP, Cahill DR, Devine RM, King BF. Anatomy of radical prostatectomy as defined by magnetic resonance imaging. *J Urol.* 1998;159(6):2148-58.

41. Lee SE, Byun SS, Lee HJ, Song SH, Chang IH, Kim YJ, et al. Impact of variations in prostatic apex shape on early recovery of urinary continence after radical retropubic prostatectomy. *Urology.* 2006;68(1):137-41.

42. Mungovan SF, Sandhu JS, Akin O, Smart NA, Graham PL, Patel MI. Preoperative Membranous Urethral Length Measurement and Continence Recovery Following Radical Prostatectomy: A Systematic Review and Meta-analysis. *Eur Urol.* 2017;71(3):368-78.

43. Tutolo M, Rosiello G, Stabile G, Tasso G, Oreggia D, De Wever L, et al. The key role of levator ani thickness for early urinary continence recovery in patients undergoing robot-assisted radical prostatectomy: A multi-institutional study. *Neurourol Urodyn.* 2022;41(7):1563-72.

44. Paparel P, Akin O, Sandhu JS, Otero JR, Serio AM, Scardino PT, et al. Recovery of urinary continence after radical prostatectomy: association with urethral length and urethral fibrosis measured by preoperative and postoperative endorectal magnetic resonance imaging. *Eur Urol.* 2009;55(3):629-37.

45. Kim LHC, Patel A, Kinsella N, Sharabiani MTA, Ap Dafydd D, Cahill D. Association Between Preoperative Magnetic Resonance Imaging-based Urethral Parameters and Continence Recovery Following Robot-assisted Radical Prostatectomy. *Eur Urol Focus.* 2020;6(5):1013-20.

46. Boellaard TN, van Dijk-de Haan MC, Heijmink S, Tillier CN, Veerman H, Mertens LS, et al. Membranous urethral length measurement on preoperative MRI to predict incontinence after radical prostatectomy: a literature review towards a proposal for measurement standardization. *Eur Radiol.* 2024;34(4):2621-40.

47. Gleason DF. Classification of prostatic carcinomas. *Cancer Chemother Rep.* 1966;50(3):125-8.

48. Epstein JI, Zelefsky MJ, Sjoberg DD, Nelson JB, Egevad L, Magi-Galluzzi C, et al. A Contemporary Prostate Cancer Grading System: A Validated Alternative to the Gleason Score. *Eur Urol.* 2016;69(3):428-35.

49. Gnanapragasam VJ, Lophatananon A, Wright KA, Muir KR, Gavin A, Greenberg DC. Improving Clinical Risk Stratification at Diagnosis in Primary Prostate Cancer: A Prognostic Modelling Study. *PLoS Med.* 2016;13(8):e1002063.

50. Hofman MS, Lawrentschuk N, Francis RJ, Tang C, Vela I, Thomas P, et al. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy

(proPSMA): a prospective, randomised, multicentre study. *Lancet*. 2020;395(10231):1208-16.

51. Emmett L, Buteau J, Papa N, Moon D, Thompson J, Roberts MJ, et al. The Additive Diagnostic Value of Prostate-specific Membrane Antigen Positron Emission Tomography Computed Tomography to Multiparametric Magnetic Resonance Imaging Triage in the Diagnosis of Prostate Cancer (PRIMARY): A Prospective Multicentre Study. *Eur Urol*. 2021;80(6):682-9.

52. D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Blank K, Broderick GA, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. *Jama*. 1998;280(11):969-74.

53. D'Amico AV, Desjardin A, Chen MH, Paik S, Schultz D, Renshaw AA, et al. Analyzing outcome-based staging for clinically localized adenocarcinoma of the prostate. *Cancer*. 1998;83(10):2172-80.

54. Gowda SN, Bordoni B. Anatomy, Abdomen and Pelvis: Levator Ani Muscle. *StatPearls*. Treasure Island (FL): StatPearls Publishing

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55. Sam P, Jiang J, Leslie SW, LaGrange CA. Anatomy, Abdomen and Pelvis, Sphincter Urethrae. *StatPearls*. Treasure Island (FL): StatPearls Publishing

Copyright © 2024, StatPearls Publishing LLC.; 2024.

56. Tokunaka S, Okamura K, Fujii H, Yachiku S. The proportions of fiber types in human external urethral sphincter: electrophoretic analysis of myosin. *Urol Res*. 1990;18(5):341-4.

57. Nyangoh Timoh K, Moszkowicz D, Creze M, Zaitouna M, Felber M, Lebacle C, et al. The male external urethral sphincter is autonomically innervated. *Clin Anat*. 2021;34(2):263-71.

58. 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(4):584-9.

59. Steineck G, Bjartell A, Hugosson J, Axén E, Carlsson S, Stranne J, et al. Degree of preservation of the neurovascular bundles during radical prostatectomy and urinary continence 1 year after surgery. *Eur Urol*. 2015;67(3):559-68.

60. Wenzel M, Preisser F, Mueller M, Theissen LH, Welte MN, Hoeh B, et al. Effect of prostatic apex shape (Lee types) and urethral sphincter length in preoperative MRI on very early continence rates after radical prostatectomy. *Int Urol Nephrol*. 2021;53(7):1297-303.

61. Klotz L. Overdiagnosis in urologic cancer : For World Journal of Urology Symposium on active surveillance in prostate and renal cancer. *World J Urol.* 2022;40(1):1-8.
62. Hamdy FC, Donovan JL, Lane JA, Metcalfe C, Davis M, Turner EL, et al. Fifteen-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer. *The New England journal of medicine.* 2023;388(17):1547-58.
63. Carlsson S, Benfante N, Alvim R, Sjoberg DD, Vickers A, Reuter VE, et al. Risk of Metastasis in Men with Grade Group 2 Prostate Cancer Managed with Active Surveillance at a Tertiary Cancer Center. *J Urol.* 2020;203(6):1117-21.
64. Palmstedt E. MM, Hugosson J., Arnsrud Godtman R. 25-year outcomes for men on active surveillance after screen detected prostate cancer in the Göteborg-1 trial  
  
. 39th Annual EAU Congress; 2024; PARIS2024.
65. Shah TT, Reddy D, Peters M, Ball D, Kim NH, Gomez EG, et al. Focal therapy compared to radical prostatectomy for non-metastatic prostate cancer: a propensity score-matched study. *Prostate Cancer Prostatic Dis.* 2021;24(2):567-74.
66. Hamdy FC, Donovan JL, Lane JA, Mason M, Metcalfe C, Holding P, et al. 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer. *The New England journal of medicine.* 2016;375(15):1415-24.
67. D'Amico AV, Chen MH, Renshaw AA, Loffredo M, Kantoff PW. Androgen suppression and radiation vs radiation alone for prostate cancer: a randomized trial. *Jama.* 2008;299(3):289-95.
68. Matzinger O, Duclos F, van den Bergh A, Carrie C, Villà S, Kitsios P, et al. Acute toxicity of curative radiotherapy for intermediate- and high-risk localised prostate cancer in the EORTC trial 22991. *Eur J Cancer.* 2009;45(16):2825-34.
69. Yu T, Zhang Q, Zheng T, Shi H, Liu Y, Feng S, et al. The Effectiveness of Intensity Modulated Radiation Therapy versus Three-Dimensional Radiation Therapy in Prostate Cancer: A Meta-Analysis of the Literatures. *PLoS One.* 2016;11(5):e0154499.
70. Küchler H. Ueber Prostatavergrösserungen. *Dtsch Klin.* 1866;18:458-60.
71. Billroth T. Carcinoma der prostata. *Chir Erfahrungen, Zurich.* 1860.
72. Young HH. The early diagnosis and radical cure of carcinoma of the prostate. Being a study of 40 cases and presentation of a radical operation which was carried out in four cases. 1905. *J Urol.* 2002;167(2 Pt 2):939-46; discussion 47.

73. Young HH. The cure of cancer of the prostate by radical perineal prostatectomy (prostate- seminal vesiculectomy): history, literature and statistics of Young's operation. *The Journal of Urology*. 1945;53(1):188-252.
74. Millin T. Retropubic prostatectomy; a new extravesical technique; report of 20 cases. *Lancet*. 1945;2(6380):693-6.
75. Campbell EW. Total prostatectomy with preliminary ligation of the vascular pedicles. *J Urol*. 1959;81(3):464-7.
76. Walsh PC, Lepor H, Eggleston JC. Radical prostatectomy with preservation of sexual function: anatomical and pathological considerations. *Prostate*. 1983;4(5):473-85.
77. Schuessler WW, Schulam PG, Clayman RV, Kavoussi LR. Laparoscopic radical prostatectomy: initial short-term experience. *Urology*. 1997;50(6):854-7.
78. Binder J, Kramer W. Robotically-assisted laparoscopic radical prostatectomy. *BJU Int*. 2001;87(4):408-10.
79. Lantz A, Bock D, Akre O, Angenete E, Bjartell A, Carlsson S, et al. Functional and Oncological Outcomes After Open Versus Robot-assisted Laparoscopic Radical Prostatectomy for Localised Prostate Cancer: 8-Year Follow-up. *Eur Urol*. 2021;80(5):650-60.
80. Galfano A, Ascione A, Grimaldi S, Petralia G, Strada E, Bocciardi AM. A new anatomic approach for robot-assisted laparoscopic prostatectomy: a feasibility study for completely intrafascial surgery. *Eur Urol*. 2010;58(3):457-61.
81. Lee J, Kim HY, Goh HJ, Heo JE, Almujaalhem A, Alqahtani AA, et al. Retzius Sparing Robot-Assisted Radical Prostatectomy Conveys Early Regain of Continence over Conventional Robot-Assisted Radical Prostatectomy: A Propensity Score Matched Analysis of 1,863 Patients. *J Urol*. 2020;203(1):137-44.
82. Oxford concise Colour Medical Dictionary.
83. Park R, Martin S, Goldberg JD, Lepor H. Anastomotic strictures following radical prostatectomy: insights into incidence, effectiveness of intervention, effect on continence, and factors predisposing to occurrence. *Urology*. 2001;57(4):742-6.
84. Ficarra V, Novara G, Ahlering TE, Costello A, Eastham JA, Graefen M, et al. Systematic review and meta-analysis of studies reporting potency rates after robot-assisted radical prostatectomy. *Eur Urol*. 2012;62(3):418-30.
85. Shikanov S, Desai V, Razmaria A, Zagaja GP, Shalhav AL. Robotic radical prostatectomy for elderly patients: probability of achieving continence and potency 1 year after surgery. *J Urol*. 2010;183(5):1803-7.
86. Jacobsen A, Berg KD, Iversen P, Brasso K, Roder MA. Anastomotic complications after robot-assisted laparoscopic and open radical

- prostatectomy. *Scand J Urol.* 2016;50(4):274-9. doi: 10.3109/21681805.2016.1145735. Epub 2016 Mar 10.
87. Webb DR, Sethi K, Gee K. An analysis of the causes of bladder neck contracture after open and robot-assisted laparoscopic radical prostatectomy. *BJU Int.* 2009;103(7):957-63. doi: 10.1111/j.464-410X.2008.08278.x. Epub 2008 Dec 5.
88. Wallerstedt A, Carlsson S, Nilsson AE, Johansson E, Nyberg T, Steineck G, et al. Pad use and patient reported bother from urinary leakage after radical prostatectomy. *J Urol.* 2012;187(1):196-200.
89. Pizzol D, Demurtas J, Celotto S, Maggi S, Smith L, Angiolelli G, et al. Urinary incontinence and quality of life: a systematic review and meta-analysis. *Aging Clin Exp Res.* 2021;33(1):25-35.
90. Katsimperis S, Juliebø-Jones P, Ta A, Tandogdu Z, Al-Bermani O, Bellos T, et al. Surgical techniques to preserve continence after robot-assisted radical prostatectomy. *Front Surg.* 2023;10:1289765.
91. Ficarra V, Novara G, Rosen RC, Artibani W, Carroll PR, Costello A, et al. Systematic review and meta-analysis of studies reporting urinary continence recovery after robot-assisted radical prostatectomy. *Eur Urol.* 2012;62(3):405-17.
92. Steineck G, Bjartell A, Hugosson J, Axen E, Carlsson S, Stranne J, et al. Degree of preservation of the neurovascular bundles during radical prostatectomy and urinary continence 1 year after surgery. *Eur Urol.* 2015;67(3):559-68. doi: 10.1016/j.eururo.2014.10.011. Epub Oct 28.
93. Freire MP, Weinberg AC, Lei Y, Soukup JR, Lipsitz SR, Prasad SM, et al. Anatomic bladder neck preservation during robotic-assisted laparoscopic radical prostatectomy: description of technique and outcomes. *Eur Urol.* 2009;56(6):972-80.
94. Walz J, Epstein JI, Ganzer R, Graefen M, Guazzoni G, Kaouk J, et al. A Critical Analysis of the Current Knowledge of Surgical Anatomy of the Prostate Related to Optimisation of Cancer Control and Preservation of Continence and Erection in Candidates for Radical Prostatectomy: An Update. *Eur Urol.* 2016;70(2):301-11.
95. Buckley BS, Lapitan MC. Prevalence of urinary incontinence in men, women, and children--current evidence: findings of the Fourth International Consultation on Incontinence. *Urology.* 2010;76(2):265-70.
96. Malmsten UG, Milsom I, Molander U, Norlén LJ. Urinary incontinence and lower urinary tract symptoms: an epidemiological study of men aged 45 to 99 years. *J Urol.* 1997;158(5):1733-7.
97. Malmsten UG, Molander U, Peeker R, Irwin DE, Milsom I. Urinary incontinence, overactive bladder, and other lower urinary tract symptoms: a longitudinal population-based survey in men aged 45-103 years. *Eur Urol.* 2010;58(1):149-56.

98. Sacco E, Prayer-Galetti T, Pinto F, Fracalanza S, Betto G, Pagano F, et al. Urinary incontinence after radical prostatectomy: incidence by definition, risk factors and temporal trend in a large series with a long-term follow-up. *BJU Int.* 2006;97(6):1234-41. doi: 10.1111/j.464-410X.2006.06185.x.
99. Dubbelman YD, Groen J, Wildhagen MF, Rikken B, Bosch JL. Urodynamic quantification of decrease in sphincter function after radical prostatectomy: relation to postoperative continence status and the effect of intensive pelvic floor muscle exercises. *Neurourol Urodyn.* 2012;31(5):646-51.
100. Dubbelman YD, Bosch JL. Urethral sphincter function before and after radical prostatectomy: Systematic review of the prognostic value of various assessment techniques. *Neurourol Urodyn.* 2013;32(7):957-63.
101. Heesakkers JP, Gerretsen RR. Urinary incontinence: sphincter functioning from a urological perspective. *Digestion.* 2004;69(2):93-101.
102. Jung SY, Fraser MO, Ozawa H, Yokoyama O, Yoshiyama M, De Groat WC, et al. Urethral afferent nerve activity affects the micturition reflex; implication for the relationship between stress incontinence and detrusor instability. *J Urol.* 1999;162(1):204-12.
103. Abrams P, Andersson KE, Birder L, Brubaker L, Cardozo L, Chapple C, et al. Fourth International Consultation on Incontinence Recommendations of the International Scientific Committee: Evaluation and treatment of urinary incontinence, pelvic organ prolapse, and fecal incontinence. *Neurourol Urodyn.* 2010;29(1):213-40.
104. Martin NE, Massey L, Stowell C, Bangma C, Briganti A, Bill-Axelson A, et al. Defining a standard set of patient-centered outcomes for men with localized prostate cancer. *Eur Urol.* 2015;67(3):460-7.
105. Tienza A, Graham PL, Robles JE, Diez-Caballero F, Rosell D, Pascual JI, et al. Daily Pad Usage Versus the International Consultation on Incontinence Questionnaire Short Form for Continence Assessment Following Radical Prostatectomy. *Int Neurourol J.* 2020;24(2):156-62.
106. Kretschmer A, Hübner W, Sandhu JS, Bauer RM. Evaluation and Management of Postprostatectomy Incontinence: A Systematic Review of Current Literature. *Eur Urol Focus.* 2016;2(3):245-59.
107. Arnsrud Godtman R, Persson E, Bergengren O, Carlsson S, Johansson E, Robinsson D, et al. Surgeon volume and patient-reported urinary incontinence after radical prostatectomy. Population-based register study in Sweden. *Scand J Urol.* 2022;56(5-6):343-50.
108. Vignoli G. Urethral Profilometry. *Urodynamics: A Quick Pocket Guide.* Cham: Springer International Publishing; 2017. p. 143-54.
109. Vickers AJ, Steineck G. Prognosis, Effect Modification, and Mediation. *Eur Urol.* 2018;74(3):243-5.

110. Legendre B, Cerasuolo D, Dejardin O, Boyer A. [How to deal with missing data? Multiple imputation by chained equations: recommendations and explanations for clinical practice]. *Nephrol Ther.* 2023;19(3):171-9.
111. Thorsteinsdottir T, Stranne J, Carlsson S, Anderberg B, Bjorholt I, Damber JE, et al. LAPPRO: a prospective multicentre comparative study of robot-assisted laparoscopic and retropubic radical prostatectomy for prostate cancer. *Scand J Urol Nephrol.* 2011;45(2):102-12. doi: 10.3109/00365599.2010.532506. Epub 2010 Nov 29.
112. Nyberg M, Hugosson J, Wiklund P, Sjoberg D, Wilderäng U, Carlsson SV, et al. Functional and Oncologic Outcomes Between Open and Robotic Radical Prostatectomy at 24-month Follow-up in the Swedish LAPPRO Trial. *Eur Urol Oncol.* 2018;1(5):353-60.
113. Haglund E, Carlsson S, Stranne J, Wallerstedt A, Wilderäng U, Thorsteinsdottir T, et al. Urinary Incontinence and Erectile Dysfunction After Robotic Versus Open Radical Prostatectomy: A Prospective, Controlled, Nonrandomised Trial. *Eur Urol.* 2015;68(2):216-25.
114. Wallerstedt A, Tyritzis SI, Thorsteinsdottir T, Carlsson S, Stranne J, Gustafsson O, et al. Short-term results after robot-assisted laparoscopic radical prostatectomy compared to open radical prostatectomy. *Eur Urol.* 2015;67(4):660-70.
115. Van Hemelrijck M, Wigertz A, Sandin F, Garmo H, Hellstrom K, Fransson P, et al. Cohort Profile: the National Prostate Cancer Register of Sweden and Prostate Cancer data Base Sweden 2.0. *Int J Epidemiol.* 2013;42(4):956-67.
116. Steyerberg EW, Eijkemans MJ, Harrell FE, Jr., Habbema JD. Prognostic modelling with logistic regression analysis: a comparison of selection and estimation methods in small data sets. *Statistics in medicine.* 2000;19(8):1059-79.
117. Azur MJ, Stuart EA, Frangakis C, Leaf PJ. Multiple imputation by chained equations: what is it and how does it work? *Int J Methods Psychiatr Res.* 2011;20(1):40-9. doi: 10.1002/mpr.329.
118. Modig KK, Godtman RA, Bjartell A, Carlsson S, Haglund E, Hugosson J, et al. Vesicourethral Anastomotic Stenosis After Open or Robot-assisted Laparoscopic Retropubic Prostatectomy-Results from the Laparoscopic Prostatectomy Robot Open Trial. *Eur Urol Focus.* 2021;7(2):317-24.
119. Surya BV, Provet J, Johanson KE, Brown J. Anastomotic strictures following radical prostatectomy: risk factors and management. *J Urol.* 1990;143(4):755-8.
120. Msezane LP, Reynolds WS, Gofrit ON, Shalhav AL, Zagaja GP, Zorn KC. Bladder neck contracture after robot-assisted laparoscopic

radical prostatectomy: evaluation of incidence and risk factors and impact on urinary function. *J Endourol.* 2008;22(1):97-104.

121. Elliott SP, Meng MV, Elkin EP, McAninch JW, Duchane J, Carroll PR. Incidence of urethral stricture after primary treatment for prostate cancer: data From CaPSURE. *J Urol.* 2007;178(2):529-34; discussion 34. doi: 10.1016/j.juro.2007.03.126. Epub Jun 13.

122. Lardas M, Grivas N, Debray TPA, Zattoni F, Berridge C, Cumberbatch M, et al. Patient- and Tumour-related Prognostic Factors for Urinary Incontinence After Radical Prostatectomy for Nonmetastatic Prostate Cancer: A Systematic Review and Meta-analysis. *Eur Urol Focus.* 2022;8(3):674-89.

123. Greenberg SA, Cowan JE, Lonergan PE, Washington SL, 3rd, Nguyen HG, Zagoria RJ, et al. The effect of preoperative membranous urethral length on likelihood of postoperative urinary incontinence after robot-assisted radical prostatectomy. *Prostate Cancer Prostatic Dis.* 2022;25(2):344-50.

124. Nomali M, Mehrdad N, Heidari ME, Ayati A, Yadegar A, Payab M, et al. Challenges and solutions in clinical research during the COVID-19 pandemic: A narrative review. *Health Sci Rep.* 2023;6(8):e1482.

125. Talavera JR, Martínez BB, Perez MS, Pisaca MFR, Díaz DC. Prediction of Postradical Prostatectomy Urinary Incontinence Through the Combination of the Urethral Pressure Profile With Electromyography of the Urethral Sphincter. *Int Neurourol J.* 2022;26(Suppl 1):S68-75.