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MAINTAINING QUALITY OF LIFE AFTER PROSTATE CANCER DIAGNOSIS

Doctoral Thesis

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Maintaining quality of life after prostate cancer diagnosis.

Front cover: *“Walking on the moon” – A safe path through barren landscape.* From Krýsuvík Geothermal Area, Iceland.

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To Ásgeir, Tómas Jökull, Ingibjörg and Svanbjörn Orri
– Thinking of you makes me happy –

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LIST OF MANUSCRIPTS

- I. Thorsteinsdottir T, Stranne J, Carlsson S, Anderberg B, Björholt I, Damber JE, Hugosson J, Wilderäng U, Wiklund P, Steineck G, Haglind E. LAPPRO: A prospective multi-centre comparative study of robot-assisted laparoscopic and retropubic radical prostatectomy for prostate cancer. *Scand J Urol Nephrol*. 2011; 45(2);102-12.
- II. Thorsteinsdottir T, Hedelin M, Stranne J, Valdimarsdóttir H, Wilderäng U, Haglind E, Steineck G. Intrusive thoughts and quality of life among men with prostate cancer before and three months after surgery – Data from the prospective LAPPRO trial. *Submitted manuscript*.
- III. Thorsteinsdottir T, Valdimarsdóttir H, Stranne J, Wilderäng U, Haglind E, Steineck G. Care-related predictors for negative intrusive thoughts after prostate cancer diagnosis – Data from the prospective LAPPRO Trial. *Submitted manuscript*.
- IV. Thorsteinsdottir T, Valdimarsdóttir H, Stranne J, Wilderäng U, Haglind E, Steineck G. Thoughts about one's own death when diagnosed with clinically localized prostate cancer. *Manuscript*.

ABSTRACT

Knowledge of real-life factors that are associated with men's self-assessed quality of life after prostate-cancer diagnosis could improve the support from health-care professionals in maintaining the men's quality of life.

Sudden, unwelcome and repetitive thoughts about a traumatic event – intrusive thoughts – constitute one factor of post-traumatic stress disorder. Recurrent thoughts of death, not just fear of dying, are one indicator for depressive disorder. Prior research suggests that psychological interventions targeting intrusive thoughts could facilitate coping with a traumatic event such as the diagnosis of prostate cancer. In this thesis the focus was on exploring and describing men's thoughts after prostate cancer diagnosis. The aim was to find suitable targets for interventions that can help men in maintaining their quality of life after radical prostatectomy as well as to identify those individuals who might need them most.

Methods

Following a one-year preparatory-phase including in-depth interviews, observations, questionnaire development, face-to-face validation and a pilot-study, the LAPPRO trial started inclusion on September 1 2008. Men planned for open or robot-assisted laparoscopic radical prostatectomy at 13 urological centers in Sweden were prospectively registered. During the first inclusion year, 971 men were enrolled, of which 833 (86%) answered two questionnaires, before and three months after surgery. These included questions on quality of life, intrusive thoughts, thoughts about death and care-related factors, among others.

Results

Before surgery, 603 men (73%) reported having negative intrusive thoughts about their prostate cancer at some time, as did 493 (59%) three months after surgery. Comparing those reporting negative intrusive thoughts at least weekly before surgery with those not reporting this, the prevalence ratio (PR) for waking up with anxiety after surgery was 3.9, for depressed mood 1.8 and for impaired self-assessed quality of life 1.3.

Men uncertain of cure by the planned surgery (PR 1.9), not prepared for urinary (PR 1.3) or sexual bother (PR 1.3) had more occurrence of negative intrusive thoughts before surgery. Reporting negative intrusive thoughts before surgery predicted reporting such thoughts three months after surgery (Adjusted Odds Ratio (OR) 3.6). Multivariate analysis revealed that younger age (OR 1.8), living alone (OR 1.7), and non-active health-care seeking (OR 0.5) predicted the occurrence of negative intrusive thoughts three months after surgery.

Twenty-five percent of the participants reported thoughts about their own death at least once a week during the previous month, before surgery and 18 percent three months after surgery. Men living in urban environment (OR 2.3) and those reporting having low control in their lives (OR 2.2), being uncertain of the future (OR 3.3) or crying (OR 2.0) before surgery, more often had thoughts about their own death three months after surgery.

Findings

A number of men diagnosed with clinically localized prostate cancer planned for surgery experienced intrusive thoughts with negative content as well as thoughts about their own death both before and three months after surgery. These thoughts were associated with various symptoms of psychological distress such as crying, feeling lack of control, uncertainty and not being prepared. Certain individuals seemed to be more vulnerable than others.

Conclusion

Despite the availability of treatments that can cure, the diagnosis of cancer is still frightening. The upcoming surgery for prostate cancer seems to lead to the accumulation of psychological reactions among men. Screening for and recognizing distressing thoughts could be valuable in supporting men shortly after prostate cancer diagnosis to maintain their quality of life. Intervention studies aiming at neutralizing negative intrusive thoughts, such as by expressive writing, could be designed based on our findings.

INTRODUCTION

One could say that the aim of science is the search for truth. The truth most certainly exists, but anyone practicing science would not necessarily have to look for the truth. Scientific methods can be applied to examine the appearances of reality and describe what is seen. Every step in such an examination involves a subjective factor: the essence of the studied objectives, the chosen and applied observations, the environment and disturbing moments, interpretation of what is seen and found, the presentation of those findings, and lastly how the findings are understood by the recipients. Instead of simply espousing a pessimistic view of science and thus decide not to engage in research on the grounds that there is no chance of finding the truth, most scientists decide to make the best of the situation. They search for the reality behind the appearances, attempting to come as close to the truth as possible. In this way, the scientific process is applied as a method, adapted to each and every research field. The first step in this process is to state a hypothesis declaring the possible reality, and then design the best study for testing that hypothesis. The particular reality found in the study, hopefully makes the world more understandable and maybe a better place to live in. Another essential aspect of science is that, there is always a reason to continue. There is always a reason to penetrate further into the essence of objects, to further explore and define a situation that has become a part of our knowledge thanks to research. There have been many scientific breakthroughs since the origin of mankind. The earth was found to be round; gravity made apples fall down, and so on. A century or two ago, cancer was not a well-known concept. Among the public it was called to die of gripes or bleed to death, among scientists the cause of the disease, on a cellular or genetic level, was not known. Today, dozens of analytical methods, used to define and describe the disease in the tiniest of details, are applied and various treatment options are available. The frightening, incomprehensible disease, cancer, has possibilities of cure. That is why it has become of interest to look at the person behind the disease.

When I started my professional carrier as a clinical nurse at a surgical ward, I took care of people recently diagnosed with cancer. After a few years of gradually acquiring the skills and techniques of the clinical routines, I had developed an interest in further studies. During my masters studies I discovered the rather limited empirical knowledge about cancer patients' emotional experiences at the time of surgery. Therefore, the opportunity to participate in the preparation of a study on outcomes after radical prostatectomy was appealing. I have been able to explore the situation of men diagnosed with prostate cancer, as well as to define and operationalize this experience through questionnaires. In this thesis, some aspects of the reality facing men with prostate cancer undergoing surgery will be elucidated. All in the hope of improving their situation in future health-care.

BACKGROUND

THE PROSTATE

The prostate (Figure 1) is typically a walnut to kiwi-sized gland located below the urine bladder and above the penis, just in front of the rectum. The urethra runs through the center of the prostate, from the bladder to the penis, leading urine out of the body. The gland together with the seminal vesicles and the bulbourethral glands produce approximately 95% of the seminal fluid that is secreted to nourish and protect the sperm coming from the testicles along with approximately 5% of the seminal fluid. The seminal vesicles and the spermatic duct open into the prostate, and during ejaculation, the seminal fluid is squeezed into the urethra, from where it is expelled.

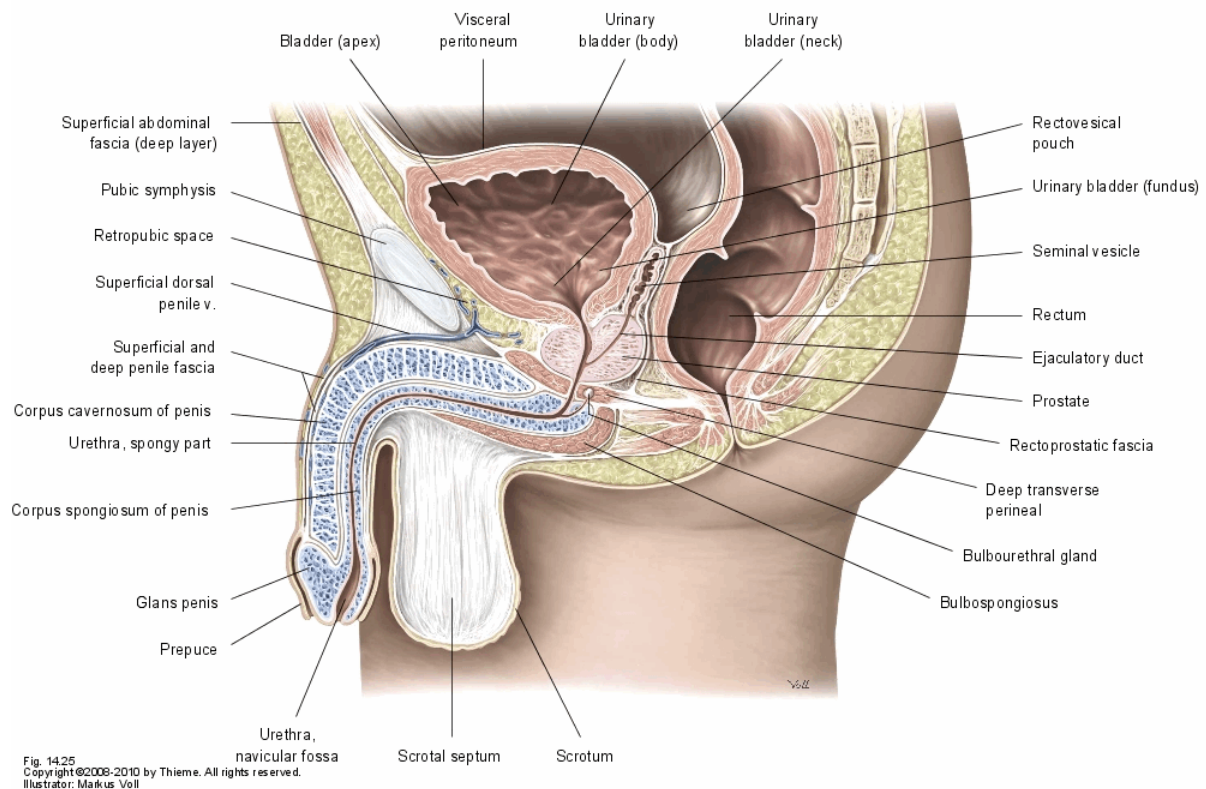


Figure 1. A schematic figure showing a side-view (sagittal section) of the prostate gland and its surroundings in the lower abdomen and pelvic cavity. The prostate lies just below the urinary bladder and surrounds the urethra. Imminent nerves and blood vessels lead to the penis as well as to the rectum and the anus.

(Gilroy et al., *Atlas of Anatomy*. All rights reserved. © Thieme 2008, www.thieme.com)

<http://www.thiemeteachingassistant.com.ezproxy.ub.gu.se/imageEditorXAML.aspx?imgid=15131>

PROSTATE CANCER

Epidemiology

Cancer in the prostate is the most commonly diagnosed malignancy in men in the United States. It is the second or third most common cause of male cancer-death in most “developed” countries (1, 2) after lung cancer and sometimes colorectal cancer. In Sweden, a population of 9 millions, prostate cancer was the most common cancer type in 2007, irrespective gender, constituting 34.2% of all cancers among men or 8,870 cases (3). Around the world about 258,000 men died from prostate cancer in the year 2008. Mortality rates are generally high in populations that are predominantly Afro-American (Caribbean and sub-Saharan Africa), but very low in Asia (4). According to registration in the Surveillance Epidemiology and End Results Database (SEER) in the United States, the age-adjusted incidence rate was 156.0 per 100,000 men per year based on cases diagnosed in 2004-2008 (5). In the year 2005 there were 34,302 new cases of prostate cancer in the United Kingdom, or age-adjusted incidence of 94.6 per 100,00 men, while 301,500 new cases were diagnosed in the European Union in 2006 (6). The age-adjusted death rate in the United States was 24.7 per 100,000 men per year (5) and 24.8 per 100,000 men in the United Kingdom (6). In Sweden, 2,398 men died of prostate cancer in 2010, a European age-standardized death rate of 61.6 per 100,000 men (7).

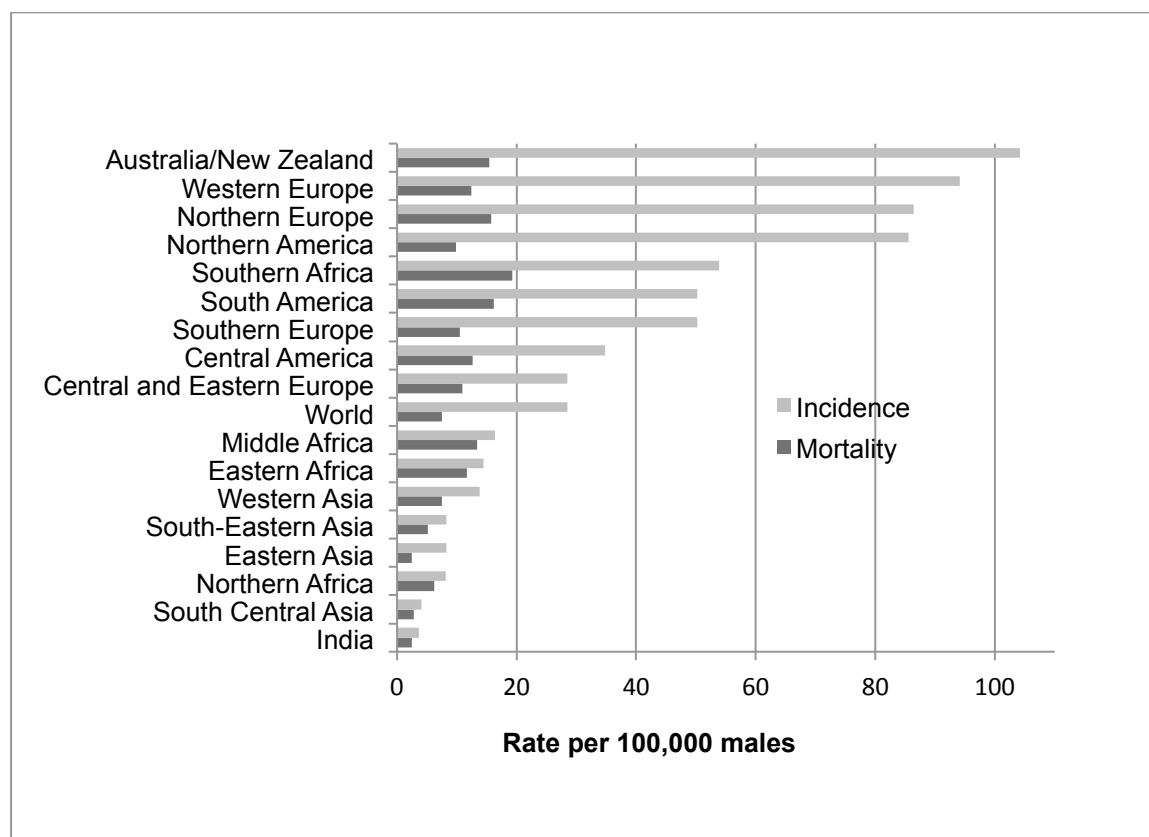


Figure 2. Estimates of age-standardized incidence and mortality rates for prostate cancer by world regions in the year of 2008 (6).

The lifetime risk of men born today in the United States to be diagnosed with prostate cancer is 16% or one out of every six men. The median age at diagnosis for cancer of the prostate was about 67 years during the last decade in the USA (5). The risk for prostate cancer rises steeply with age and cases in men under 50 years of age are rare. No one registered in the SEER database was diagnosed with prostate cancer under the age of 34 years between 2004 and 2008. During the same period 0.6% of men diagnosed with prostate cancer were between 35 and 44 years of age; 9.1% 45 to 54 years; 30.7% 55 to 64 years; 35.3% 65 to 74 years; 19.9% 75 to 84 years; and 4.4% older than 85 years of age (5). Figure 3 shows the age distribution in Sweden. In populations with increasing proportions of older people and because of more widespread prostate cancer antigen (PSA) screening, there will probably be a trend towards higher incidence of diagnosed prostate cancer. The incidence among younger men seems to be increasing, probably as a result of more screening.

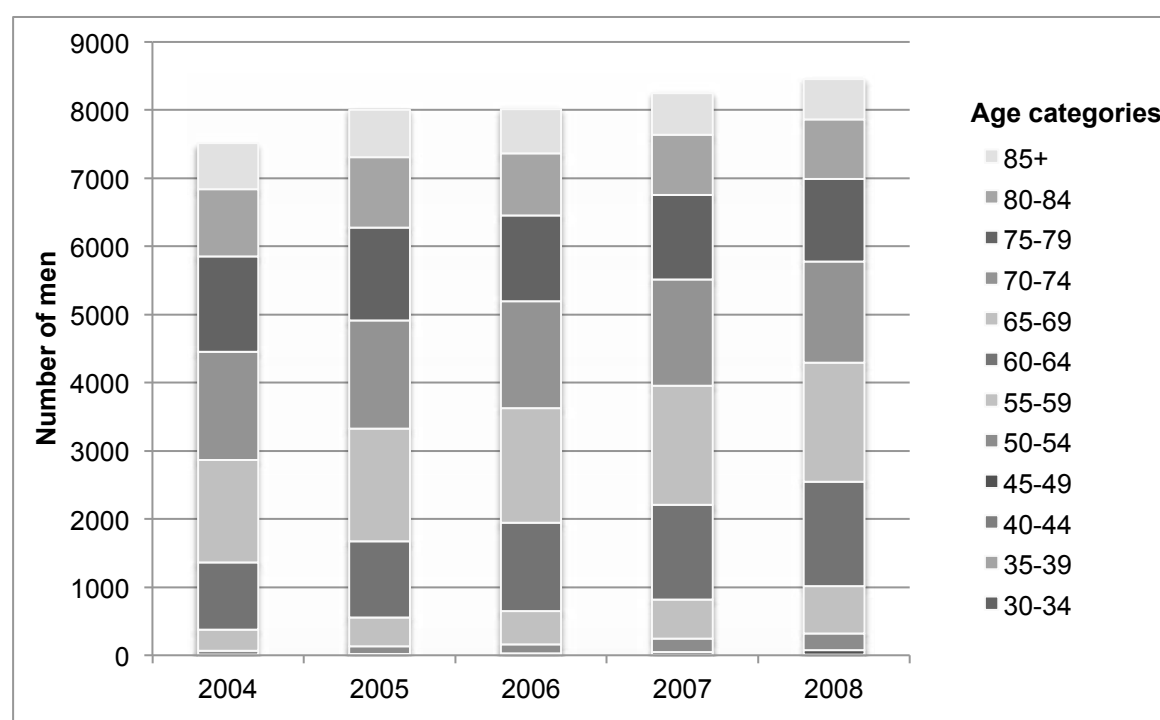


Figure 3. The yearly prevalence of prostate cancer in Sweden 2004-2008 divided into 5-year age categories. The prevalence among men under 60 years of age has increased during this period (*Graphic illustration T. Thorsteinsdottir and U. Wilderäng. Courtesy of the Swedish National Board of Health and Welfare (8)*).

Etiology and pathogenesis

Multiple factors have been associated with the risk for prostate cancer although the actual cause of the cancer is unknown. Studies have revealed that family history, older age, and African ethnicity enhance the overall risk as well as the malignancy's biological aggression (2, 6). In 9% of prostate cancers there seems to be an important familial disposition, and inheritance may also play a role in the remaining 91% of the affected men. In this way genetic factors could be

associated with the apparent higher prevalence and death rates in men of African ethnicity as well as age at disease onset (2). No certain modifiable risk factors for prostate cancer have been identified but certain kinds of diet may affect the risk. A calcium rich diet, high fat and low fiber diet may enhance the risk of prostate cancer, while lycopene, especially found in tomatoes, and selenium may reduce the risk (2, 6).

Prostate cancer can be divided into two extreme categories of aggressiveness; thereof the clinically latent tumors seem to become more prevalent with higher age. Tumors that are clinically aggressive have a higher potential for local invasion and metastasis than the more latent tumor types (2). Pathological staging and grading of the tumor are clinically relevant since these indicate firstly the biological aggressiveness, and secondly, the extent of local invasion or distant metastasis. The staging and grading of the tumor determine what treatment options are available. The Gleason grade-system has shown high correlation with the aggressiveness of prostate cancer and is commonly used for grading. The pathologist determines the grade by analyzing specimens from the prostate. First a grade is assigned to the most common tumor pattern in the specimens, then the grade of the second most common pattern is added. According to the TNM classification of malignant tumors from the year 2010, biopsy specimens are categorized into low Gleason grades (i.e. 2 to 4) that indicate well-differentiated tumors having little potential for metastases and moderately differentiated tumors with Gleason grades from 5 to 6. Tumors defined as Gleason grade from 7 to 10 have poor cellular differentiation and carry a high risk for metastasis (2, 9). The TNM system is recommended for staging the cancer. In the system clinical prostate cancer stage is divided into localized tumors that are contained within the prostate capsule (T1, T2) and advanced tumors that have extended beyond the capsule and/or into the seminal vesicles (T3) or invaded surrounding structures (T4). At stage T4 the tumor can have invaded the bladder neck, the external urethral sphincter, the rectum, the pelvic floor muscles and/or the pelvic wall. Prostate cancer primarily metastasizes to regional lymph nodes (N1), further to non-regional lymph nodes (M1a), bones (M1b) or distant organs (M1c) (2, 9).

Diagnosis and clinical signs

Prostate cancer can be detected by digital rectal examination but is more frequently detected by measurement of the prostate-specific antigen (PSA) in blood-samples. If cancer is suspected, the diagnosis is to be confirmed by trans-rectal biopsy. An abnormal digital rectal examination has a high prediction for the diagnosis of prostate cancer although a negative examination (normal palpation) results are not always to count on (10). Therefore, an abnormal digital rectal examination alone cannot confirm the diagnosis of prostate cancer. A serum PSA value less

than 3 or 4 ng/ml, dependent of guidelines, is regarded of as normal (10, 11), although in combination with an abnormal digital examination it could represent a malignancy (10). Abnormal PSA values up to 10 ng/ml are regarded as moderately suspicious, but if the values exceed 10 ng/ml the suspicion of prostate cancer is regarded as high (2). The definite diagnosis relies on trans-rectal ultrasound guided biopsy, where a probe is inserted into the rectum in order to image the prostate gland. Tissue samples are obtained by a biopsy-needle delivery system. The biopsies are then pathologically examined and graded. At each urological department there are clinical directives for the further examinations of patients in order to complete tumor staging. Bone scans or magnetic resonance imaging (MRI) can be recommended to exclude bone metastasis. Computed tomography (CT) or MRI of the abdomen and pelvis are performed if the tumor seems to be high risk, that is bulky or if there is suspicion of local tumor invasion or metastasis in lymph nodes or abdomen (2). In some cases, lymph node dissection and staging is performed if radiation therapy is planned.

Today, most men with localized prostate cancer are diagnosed based on PSA screening, without prior physical symptoms. Occasionally, men have symptoms from the lower urinary tract that appear to be caused by the enlarged prostate and a localized tumor. These symptoms could be episodes of nocturia, i.e. the need to get up in the night to urinate; frequent daytime voiding; blood in the urine; or a weak urinary stream. Advanced prostate cancer is more likely to present with symptoms from the lower urinary tract, bone pain in the pelvis or lower back, pathological fractures, or general symptoms such as fatigue, blood in the urine, nausea, vomiting, and weight loss (2, 6).

Prognosis and treatment

Patients with localized prostate tumors have a favorable prognosis, even without initial treatment. Relative survival is a measure of net survival calculated by comparing observed (overall) survival with expected survival from a comparable set of people that do not have the disease. In this manner the excess mortality that is associated with a cancer diagnosis is measured as well as the survival of the cancer patients in comparison to the general population thereby estimating the effect of cancer (5). In Sweden, the 5-year relative survival, was found to be 87.3% and the 10-year relative survival was 68.5% (3). The prostate cancer-specific survival rate was found to be 85.0% for men with initially untreated localized prostate cancer in a Swedish cohort (12). In USA, Afro-American men had lower 5-year survival rates, compared to white men (5). The more common PSA testing in USA has not only resulted in higher prostate cancer incidence but also a much higher proportion of early stage cases being diagnosed compared to populations where testing is less common. This has lead to lower

mortality rates relative to incidence in USA (13). For instance, 60-70% of the prostate cancers diagnosed in Japanese men have extended beyond the prostate versus only 11% in US white men (6, 14).

As reflected in the survival statistics, most diagnosed men have prostate cancer at an early stage and the available treatment modalities aiming to cure are rather aggressive. Unfortunately, because of the anatomical position of the prostate gland, this also means that during treatment there is a risk of injuring the nerves and vessels in close proximity to the prostate gland, which in turn can lead to malfunction in the adjacent structures or organs following treatment (15-17). The available options for care of localized prostate cancer vary between different hospitals, but include active surveillance, external beam radiotherapy, interstitial radiotherapy (brachytherapy), adjuvant hormonal therapy, radical prostatectomy among others.

Active surveillance

Active surveillance is based on the increased recognition that clinically latent tumors may not need any treatment. Many men are diagnosed with tumors that will not progress to a clinically noticeable stage during their lifetime. This is especially applicable if the men's life expectancy is less than 10 years (18-20) or if they have a low-risk disease. In a Swedish cohort, the 10-year prostate cancer-specific mortality for men with low-risk disease was found to be 2.4% (16). Active surveillance may therefore be a suitable treatment option for men with low-risk tumors and short life expectancy. The aim of active surveillance is to follow men with early diagnosed, small volume low-grade disease who have not undergone immediate therapy. The men are monitored by PSA-testing every three to 12 months, digital rectal-examination, and in most programs prostate biopsies at regular intervals. The men are further observed for bothersome symptoms from the lower urinary tract, acute urinary retention, systemic signs or symptoms possibly indicating metastasis. Curative treatment is initiated at the first sign of progression and if cure is still possible (2, 19).

External beam radiation therapy

Curative radiation therapy can either be external or interstitial, meaning that the radiation source is either outside or inside the body (2). External beam radiation therapy has shown a well acceptable disease-free survival compared to other treatments among low-risk patients in shorter follow-ups (21, 22), and to decrease prostate cancer-specific mortality at 10-years follow-up compared to surveillance (20). The 3-dimensional planning techniques, developed during the 1990's, allow for high-dose radiation to be administered safely and have reduced the risk of toxicities that were ensued by the older techniques. Computer software is applied to

integrate computerized tomographic (CT) imaging of the patients' organs with the aim of conforming the radiation dose-volume more precisely to the prostate. Thereby, the risk of excessive radiation to the adjacent structures, such as the bladder and rectum, is minimized. Presently, the state-of-the-art technique is this intensity-modulated radiation therapy (2, 21).

Adjuvant androgen deprivation therapy

Using androgen deprivation (hormonal) therapy as a primary or a single treatment for clinically localized prostate cancer is generally not recommended by clinical guidelines (21). Androgen deprivation therapy usually consists of either medical or surgical castration, or a combination of castration and anti-androgens. It is not recommended before radical prostatectomy, but can prolong survival in selected patients before, during and/or after radiation therapy. Combined to external radiation therapy, androgen deprivation therapy has been found to have a 10% 10-years survival benefit for patients with locally advanced cancer, and it can be beneficial if other treatments have missed the extension of tumor beyond the prostate margins (21, 23).

Brachytherapy

Interstitial radiotherapy or brachytherapy involves placing low- or high-energy radioactive sources inside the prostate gland under ultrasonic or computerized-tomographic guidance. Permanent implant seeds that gradually lose their radioactivity are sometimes used. The radiation sources emit relatively low levels of localized irradiation to the cancer cells, and therefore cause minimal damage to the adjacent tissues and structures, such as the bladder and rectum. Brachytherapy to the prostate is sometimes used in combination with external radiation and has become more widely used, especially for men with early, clinically localized prostate cancer (2, 21).

Radical prostatectomy

Surgery is the most common treatment for localized prostate cancer. The number of radical prostatectomies in Sweden was 2,247 in 2008 (24), that is 26% of all diagnosed cases that year. During the year 2007, estimated 156,000 men underwent radical prostatectomy in the United States (25). Surgery for early prostate cancer has been found to have a 15-years survival benefit of 5% compared to a control group of non-treated prostate cancer patients, also among men with low risk tumors (26). Radical prostatectomy involves removing the entire prostate and the seminal vesicles. In selected cases the lymph nodes in the pelvis and/or lower abdomen are removed. The procedure can be performed by an open approach, laparoscopic, and robot-assisted laparoscopic surgery (2).



Figure 4. Radical prostatectomy. On the left, a photo from open radical prostatectomy showing the abdominal wound, the scrubbed-in urological surgeon wearing magnifying glasses and his assistant exploring the pelvic cavity with their hands; their vision is limited. On the right, an ongoing robot-assisted laparoscopic procedure where the urological surgeon is sitting at the robot-console, looking at a screen with three-dimensional view of the surgical area and controlling the surgical instruments (robot-arms) with anti-shaking, interactive control sticks. (Figure on the left from: <http://www.windsorurology.co.uk>; figure on the right from: <http://www.intuitivesurgical.com/>)

Radical prostatectomy has been the main surgical technique for over two decades and remains the standard treatment for localized disease. In the past few years, robot-assisted laparoscopic prostatectomy has gained popularity as a minimally invasive alternative that to a large extent accounts for the increased incidence of radical prostatectomies, at least in the USA (27). In the open procedure the pelvic cavity is entered through an incision in the midline of the lower abdomen, between the umbilicus and the top of the pubic bone (2, 28). In laparoscopic and robot-assisted procedures three to six small incisions are made through the umbilicus and abdomen to enter the surgical instruments to be used. The abdominal cavity is insufflated with carbon dioxide to enhance the vision of organs and structures (2). Regardless of technique, the pelvic cavity will be explored and the structures identified, such as the urinary bladder, prostate, urethra, blood vessels, and nerves. The prostate is released from the surrounding fascia, the vessels (dorsal vein complex), the vertebral pedicles and the neurovascular bundle, and separated from the urethra and the bladder. The prostate and the seminal vesicles are removed and the urethra and bladder are reconnected. Depending on the extent of tumor invasion, one or both of the neurovascular bundles are preserved (nerve-sparing) as well as the bladder-neck in order to avoid erectile dysfunction and urinary incontinence (2, 28). Pelvic lymph nodes are resected if there is a suspicion of metastasis, usually including removal of all node-bearing tissue from the larger part of the pelvic cavity. Radical prostatectomy is, according to general guidelines, the appropriate therapy for men with clinically localized prostate cancer wanting curative therapy, where a complete surgical excision is possible and with a life expectancy of ten years or more and no comorbid conditions contraindicating

surgery (21). Further, there are indications that the procedure should be performed by experienced, high-volume surgeons at high-volume clinical centers since this probably provides better outcomes (29).

Advantages and disadvantages of care options

The advantages of active surveillance include avoiding possible side effects of definitive therapy, fewer long-term physical symptoms, and reducing the risk of unnecessary treatment for small, latent tumors. The possible disadvantages, on the other hand, include missing the opportunity to cure, risk for progression, subsequent treatment may be more complex, more difficult to perform nerve-sparing surgery because the tumor may have grown, increased anxiety, as well as frequent medical exams and biopsies. Further, it remains uncertain how the natural progression of prostate cancer is in the long-term (21). The possible advantages of external-beam radiation therapy include avoiding surgery- and anesthesia-related complications such as bleeding, disturbed fluid-electrolyte balance, and cardio-vascular problems. Further the incidence of urinary incontinence and urethral strictures seems to be low, and erectile function may possibly be preserved. Disadvantages of external-beam radiation therapy include a long treatment course (two months), temporary and long-term bladder, bowel, and sphincter symptoms, such as fecal leakage and bleeding as well as the increased risk for future erectile dysfunction (21, 30). Adding androgen deprivation therapy to local therapies seems to be associated with erectile dysfunction, fatigue, emotional distress and low quality of life (21, 31, 32). The possible advantages of brachytherapy include the short treatment time (one day), good cancer control rates for low-risk tumors, low risk for incontinence, and possibilities of preserving the erectile function, at least in short-term (2, 21). The possible disadvantages include the need for general anesthesia, the risk of acute urinary retention, as well as long-lasting voiding symptoms (21). The disadvantages of radical prostatectomy; i.e. blood loss, urinary incontinence, and erectile dysfunction, could be reduced by careful surgical technique including controlling vessels, preservation of urethral length, bladder neck and nerves, as well as avoiding damage to the sphincter mechanisms (21, 33), although further studies are needed to confirm this. The advantage of a robot-assisted laparoscopic approach over open surgery could be the avoidance of a midline incision, minimizing blood loss, possibly reducing postoperative recovery time and surgical pain. A disadvantage of the robot-assisted technique is the lack of haptic feedback from tissues as well as possible concerns about the anatomical orientation as compared to the open procedure. This is possibly compensated for in the robotic procedure by a clear three-dimensional view, sharper light, precision in instrument movements, and better ergonomics for the surgeon (2, 33). The question if oncological outcomes are improved by the robot-assisted technique remains unanswered by current evidence. The

economical costs could also be higher because of expensive and disposable equipment (34). Irrespective of technique, surgeons aim to minimize the long-lasting physical side effects of surgery, primarily immediate erectile dysfunction and urinary incontinence (16, 17).

QUALITY OF LIFE

Definitions

The concept of quality of life generally stands for goodness of life, however in relation to health it is about how good life is in terms of health. Quality of life is by now a well-established concept within medical research although there is no consensus on a single definition. Most researchers agree that the concept is complex, subjective and multi-dimensional including both positive and negative sides of life (35, 36). The World Health Organization (WHO) has defined health-related quality of life as the “individual’s perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards and concerns” (37). This has further been operationalized in a measurement scale including 100 variables with the aim of evaluating health-related quality of life in population-based studies (38). Through the years, many different measurement scales, each defining quality of life in its own way have been developed and applied in clinical research. There are, however, ongoing discussions whether it is reasonable to study quality of life as a multi-dimensional concept, i.e. including many questions on various symptoms. The application of a single question valuing the individual’s own assessment of quality of life has been proposed. The idea is grounded on that quality of life is what the individual defines it to be and the measured level is the assessment of his own definition (39-41). In this way, the studied individuals’ quality of life is not constituted in a definition that researchers have decided upon and possibly includes various aspects of life and health. On the contrary, self-assessed quality of life is a phenomenon experienced by the individual that can relate to or be affected by other aspects of life or health. In health-care studies we can therefore in general see two ways of operationalizing or studying quality of life. These are shown in Figure 5.

Quality-of-life research

Different measurement instruments have been developed to study quality of life in different populations, for different reasons and in various situations. Thus, quality of life has been studied among people having various diseases, from an economical or social aspect, in sickness and in health. In relation to disease, most of the research focuses on health-related quality of life. This outcome has by and by become as well acknowledged as survival in studies on the effect of various medical treatments (35, 36). The concept of health-related quality of life as an outcome was first introduced within medical research in oncology during the 1960’s. At that

time, it was uncommon to use the patients' experiences in the evaluation of medical treatment, as opposed to relying solely on medical data, assessed by the health-care professionals or biomarker values (42). The patients' quality of life became an independent aim of treatment. Not only to add years to life but to add life to years.

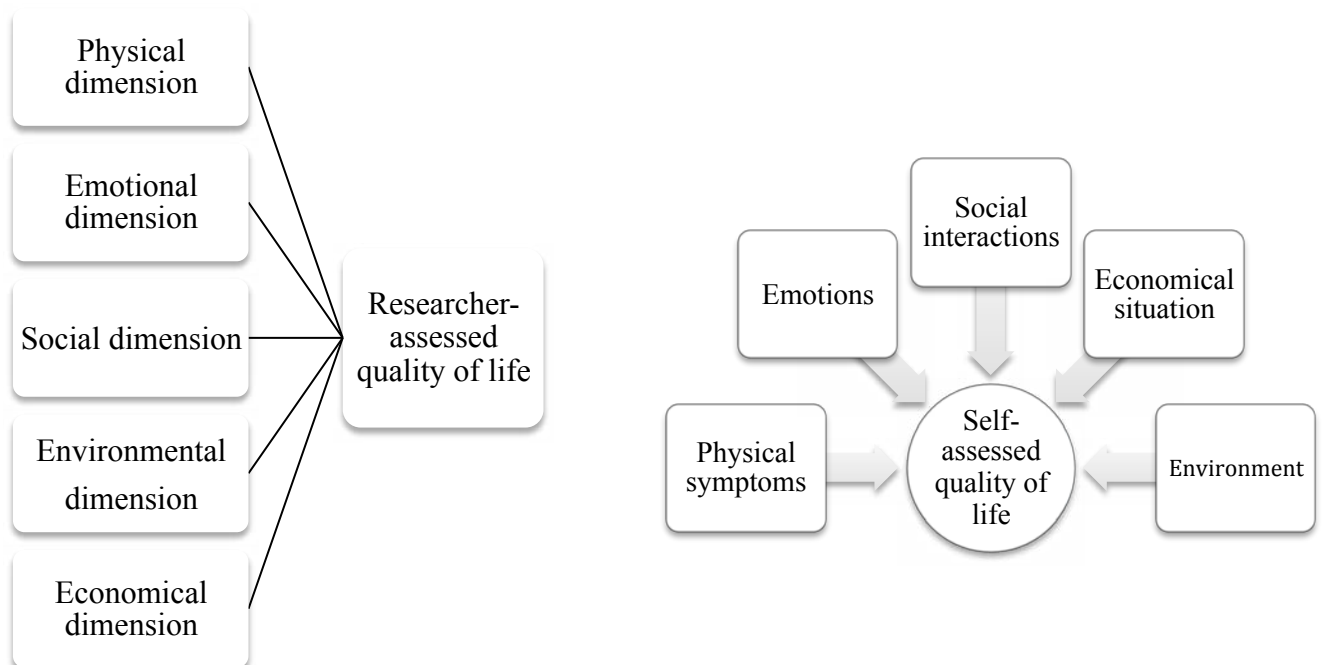


Figure 5. A schematic figure showing two views of how to look at and study quality of life. On the left is researcher-assessed quality of life, a multi-dimensional construct, here constituted of five different dimensions that often are included in the measurement instruments. On the right is self-assessed quality of life; a specific phenomenon defined and assessed by the individual himself that can be affected by various factors in his life, some of which are shown.

Quality of life after prostate cancer treatment

As mentioned above, different treatment strategies for localized prostate cancer have different advantages and disadvantages for the patient in question. Some are related to the direct effect of the treatment, such as tissue damage and other side effects, while others are related to how procedures influence the patients' daily life, such as time duration and frequency of controls. Presumably, both of these aspects affect how the men experience and assess their daily life; that is their quality of life in general.

The side-effect profiles of different treatments are not totally clear. All treatment modalities for localized prostate cancer seem to have a significant impact on health-related quality of life. In a longitudinal study of 247 men, interstitial radiation therapy and external radiation therapy provided worse and more long-lasting bowel problems than radical prostatectomy (43). When combining three treatment modalities for localized prostate cancer, urinary incontinence among

patients having had radiation appeared to get worse by time up to four years after treatment, while disease-specific symptoms after radical prostatectomy were relatively stable between 2.6 and 6.2 years post-treatment (44). A cohort-study of 144 men with locally advanced disease, revealed that androgen deprivation therapy combined with local therapy (radiation or surgery) enhanced the risk for emotional distress and fatigue (32). Further, only 24% of men not undergoing curative treatment initially but eventually having androgen deprivation therapy, reported high self-assessed quality of life as did 60% of the men who had undergone radical prostatectomy four years earlier (45). Based on longitudinal data, the technique used during surgery can affect the resolution of urinary incontinence after prostatectomy (46, 47), but if continued, urinary leakage will increase with normal aging. It is more common with persisting erectile and sexual difficulties up to 12 years after surgery, at least to some degree (46). Urinary and sexual function seem to be less affected by surgery among younger men, under 55 years of age, than in older men (48).

Prostate cancer has not only been found to be associated with treatment-induced physical problems but also with psychological distress. Not only the treatment can be distressful but also the diagnosis itself. Especially younger men seem to experience anxiety and post-traumatic symptoms in relation to prostate cancer diagnosis (49). Receiving prostate cancer diagnosis has been related to higher suicide risk (50) as well as its treatment appears to lower marriage quality (51). Prospective studies have indicated that depressive symptoms among men treated for prostate cancer can predict quality of life (52, 53). Further, the findings of an Australian study revealed that symptoms of anxiety and depression before treatment predicted such symptoms one year after treatment (54).

Recently published, studies have addressed the relation between an experience of physical symptoms after treatment and emotional aspects often in form of bother of symptoms. In a Japanese study, men experiencing urinary and bowel symptoms after radical prostatectomy or external beam radiotherapy tended to suffer from moderate to high distress compared to men reporting no or few symptoms (55). One year after retro-pubic radical prostatectomy at a German hospital 75% of the 236 participating men had returned to their baseline physical health, 73% to baseline mental health level, 75% to baseline urinary continence and 26% to baseline level of potency. Mental health recovered more slowly than physical health as measured at the three follow-up assessments during this year (47). In a cross-sectional survey performed 2.5 months to 4 years after surgery, 408 patients (68% of 600 eligible participants) with prostate cancer who had undergone robot-assisted radical prostatectomy at one hospital,

the interference between overall incontinence bother scores and general quality of life were quite low. Patients reported that most incontinence occurred during physical activity but 35% reported interference with sleep. Of the patients 31% experienced some anxiety due to urinary difficulties and 51% had to occasionally change clothes due to leakage. Patients did not report much interference with traveling, visiting friends or family and family life. The most bothersome aspects of incontinence were its effects on partner relationship, sexual life and energy levels. It appears, that despite patient concerns of incontinence after prostatectomy they report little interference with quality of life (56). The prior lack of empirical data on the emotional distress related to physical symptoms can mostly be explained by the nature of the data (i.e. cross-sectional, heterogeneity of the population, low generalizability) or the insensitivity of the applied quality-of-life instruments. Emotional factors may play a larger role in men's assessment of quality of life after radical prostatectomy, than previously reflected in studies, independent of the occurrence of physical symptoms.

Quality of life and psychological adaptation

A person's adjustment to stressful or life-changing events is often referred to as coping. As defined by theorists, coping includes the specific thoughts and behaviors of a person in his or hers efforts to adjust (57). According to the theoretical model of coping, by Lazarus and Folkman, two processes are included. Firstly, there is appraisal, defined as the individual evaluation of the event's significance as well as evaluating his resources to face the event (trauma). A person's appraisal of any given trauma can have effect on the person's emotions and the resulting coping process. Secondly, the coping process, which includes the resources in form of thoughts and behaviors used in order to regulate the trauma, manage it and maintain well-being. The outcome of the appraisal and coping will eventually be reflected in the person's daily life (58). Individual coping skills can vary, but three types of strategies have been identified. Appraisal-focused coping includes modifying how one thinks about the trauma that is cognitive adaption. Problem-focused coping strategy includes attempts to deal with the cause of the trauma, to take actions to manage it. Emotion-focused coping strategies include the release of suppressed emotions, to manage the emotions arising from the perception of the trauma (36).

The diagnosis of illness can be seen as a trauma leading to a personal crisis in which coping is vital to maintain homeostasis in life. Coping in general, psychological adaptation to the diagnosis of cancer in particular, can be described as an on-going process in which the individual tries to manage the emotional distress, to solve the specific cancer-related problems, and gain control over the cancer-related stress. Adaptation to a cancer diagnosis is not a

unitary, single event, but rather a series of on-going coping responses to the multiple tasks associated with living with cancer. Patients face multiple challenges during the clinical course of the disease. Specific periods of crisis or significant challenge can include receiving the diagnosis, the treatment choice, end of treatment and remission, recurrence and palliative care, and survivorship. Each of these events has certain coping tasks, including existential questions, emotional responses, and specific problems such as treatment-related symptoms (36).

When diagnosed with prostate cancer coping seems to be an important mediator in maintaining quality of life (59) but in studies men have appeared to react differently to receiving the diagnosis and to use different approaches to adapt (52). Men who reported distress in relation to receiving the diagnosis, in form of harm or loss, reported worse physical and mental health. If the diagnosis was perceived as a challenge, men were more likely to use problem-focused coping, if it was related to loss, emotion-focused coping was more common (60). The reaction to the diagnosis is most certainly based on many factors. Factors such as age, previous health, socio-economic status including marital status and education as well as care-related factors such as local hospital directives, information given, and prior experience of the health-care system could relate to how men react to the prostate cancer diagnosis. Consequently this could affect men's choice of treatment and how they will fare in years after treatment. Studies have revealed differences between men choosing different treatment modalities. In USA, studies have found that men choosing radical prostatectomy are younger, Caucasian, employed, have higher income, and have a child living at home, as compared to men choosing other treatment modalities (52, 61), but this could be reflected differently in countries with other types of health-care systems. An "innovative" treatment modality such as robot-assisted laparoscopic prostatectomy could cause high expectations of treatment outcome, which in turn can lead to more regrets about the treatment choice if physical symptoms appear after surgery (62).

Since prostate cancer today is more frequently diagnosed at an early stage, more men have surgery and consequently live with long-term symptoms. The short hospital-care after surgery that has been implemented during the last two decades, results in less contact between patient and health-care professionals. The treatment methods are evolving towards minimizing physical symptoms, but still, men have to cope with the diagnosis of cancer. Therefore, more studies the emotional reactions after diagnosis are needed. Interventions and care aiming at maintaining pre-treatment quality of life may be of importance.

Interventions for maintaining quality of life

Several psychological interventions have been tried out and studied in aspects of improving men's quality of life after prostate cancer diagnosis, and several studies are ongoing. However, results on any positive effect of the interventions are limited (63). Such interventions do not necessarily need to be complicated or vary much from clinical routines. A study found an effect when health-care professionals made an extra assessment of the patient's physical function before treatment for localized prostate cancer. This appeared to be associated with better health-related quality of life after treatment than the participants had expected (64). The simple and modifiable process of extra care appeared to serve as a potential target to improve quality of care for patients with prostate cancer.

Expressive Writing is a brief intervention, which simply aims at encouraging individuals to write about their personal experiences of a traumatic or distressful event under a limited period of time and at a few time points during treatment. A growing number of studies have examined the effects of Expressive Writing among cancer patients, generally showing beneficial results for the participants (65-67). A pilot study by Rosenberg and colleagues found that prostate cancer patients (n=15) randomized to expressive writing intervention had fewer physical symptoms and health-care visits than a non-writing control group. The researchers found that the intervention was appreciated by the participants (67). Another study on patients having writing sessions at an outpatient cancer clinic revealed that half of the participants (n=71) reported that writing lead to changes in their thoughts about their illness immediately after the writing session. More than half of the participants reported changes in their thoughts three weeks later; those who reported changes in their thoughts about the illness immediately after the session had better quality of life at three weeks follow-up (66). Interventions such as Expressive Writing may therefore be a potential way of supporting coping among men with prostate cancer diagnosis although carefully planned and performed studies, based on scientific knowledge, are required before implementing into clinical practice.

AIMS

The overall aim of the thesis was to explore and describe aspects of men's quality of life after prostate cancer diagnosis in order to find suitable targets for interventions that can support men in maintaining their quality of life after radical prostatectomy.

The specific aims were as follows:

- To design, develop and describe a study design suitable for studying men's quality of life after prostate cancer diagnosis before and after surgery.
- To explore men's intrusive thoughts before and after prostate cancer diagnosis, study the prevalence and contents of such thoughts as well as their associations with selected quality-of-life measures.
- To determine if certain care-related factors or health background were associated with higher prevalence of negative intrusive thoughts.
- To study the prevalence of thoughts about one's own death among men planned for radical prostatectomy and to find out the characteristics of men for whom such thoughts are harmful.

METHODOLOGICAL STUDY (Paper I)

The LAPPRO trial is based on the primary hypothesis that compared to open surgery, robot-assisted laparoscopic radical prostatectomy results in fewer long-term complications, primarily urinary leakage, without affecting cancer outcome. LAPPRO is an acronym for LAParoscopic Prostatectomy Robot Open. To test this hypothesis, the study's steering committee designed a rigorous study including detailed registration of the confounding factors and modifiers possible to have effect on the association between surgical method and outcome. These include quality of life, symptoms, care-related aspects, economical factors and clinical procedures. The basic idea is to study the implementation of a new health-care technique in aspects of clinical outcomes as well as patient assessments. Earlier experience indicates that patients are positively affected by participating in similar studies (68, 69). The LAPPRO trial was approved by The Regional Ethical Review Board in Gothenburg (Dnr. 277-07) and registered in the Current Controlled Trials database (ISRCTN06393679).

According to clinical epidemiological methods based on the hierarchical step-model for causation of bias (70), the development of patient questionnaires started with a qualitative phase. The aim of this phase was to recognize the real-life factors that are important for men in the situation that the proposed study group would be in, and turning these into measurable variables in the study.

QUALITATIVE PHASE – QUESTIONNAIRE DEVELOPMENT

In-depth interviews

At first, a letter was sent to eight men having undergone surgery three to six months earlier, asking if they were willing to be interviewed about their experiences after prostate cancer surgery. The letter informed them that the information would be used to develop a questionnaire and that they would be contacted by telephone to find out if they were willing to participate. Two men could not be reached via telephone, but the remaining six all participated. Four interviews were performed in the men's home and two at the interviewer's office. The aim was to perform in-depth interviews allowing the interviewed persons to talk freely about their experiences after the prostate cancer diagnosis. When needed the interviewer, however, referred to the discussion topics as formulated for a semi-structured interview. These discussion topics included:

- How has the diagnosis affected your life?
- How has the surgery affected your life?

- Your view of what quality of life is?
- The most important persons for you during this time?
- Emotions you felt after the prostate cancer diagnosis?
- The present situation compared to the period around surgery?
- How did you handle the meaning of the cancer diagnosis and your emotions?
- Your experience of the health-care system?

The six interviews lasted from 30 minutes up to three hours, and the transcribed results were from nine to 16 printout pages. They were subsequently read and analyzed with a phenomenologic approach by coding and categorizing common phenomena in the text (71). The phenomena, their categories and the emerging themes are shown in Figure 6.

The first theme was preparedness. For example, the men described how they had believed it would be their turn next because they had known someone who had been diagnosed and treated for prostate cancer. They also mentioned their age or that someone close to them had been sick:

I expect that with age something will appear and then it is all about just taking care of that ... (Participant number 5)

Those who knew someone diagnosed with prostate cancer or had gathered information by other sources were prepared for surgery-induced symptoms.

Was almost most scared for the thing about incontinence – you hear from many that, like, it is never over. But it is ok. (1)

I had read rather much, both on the Internet and I had gotten a book on prostate cancer so I had prepared rather well there and thought it was just doing this surgery and then everything would be fine. So I didn't feel so worried there, directly, but it all went through rather well. (6)

~

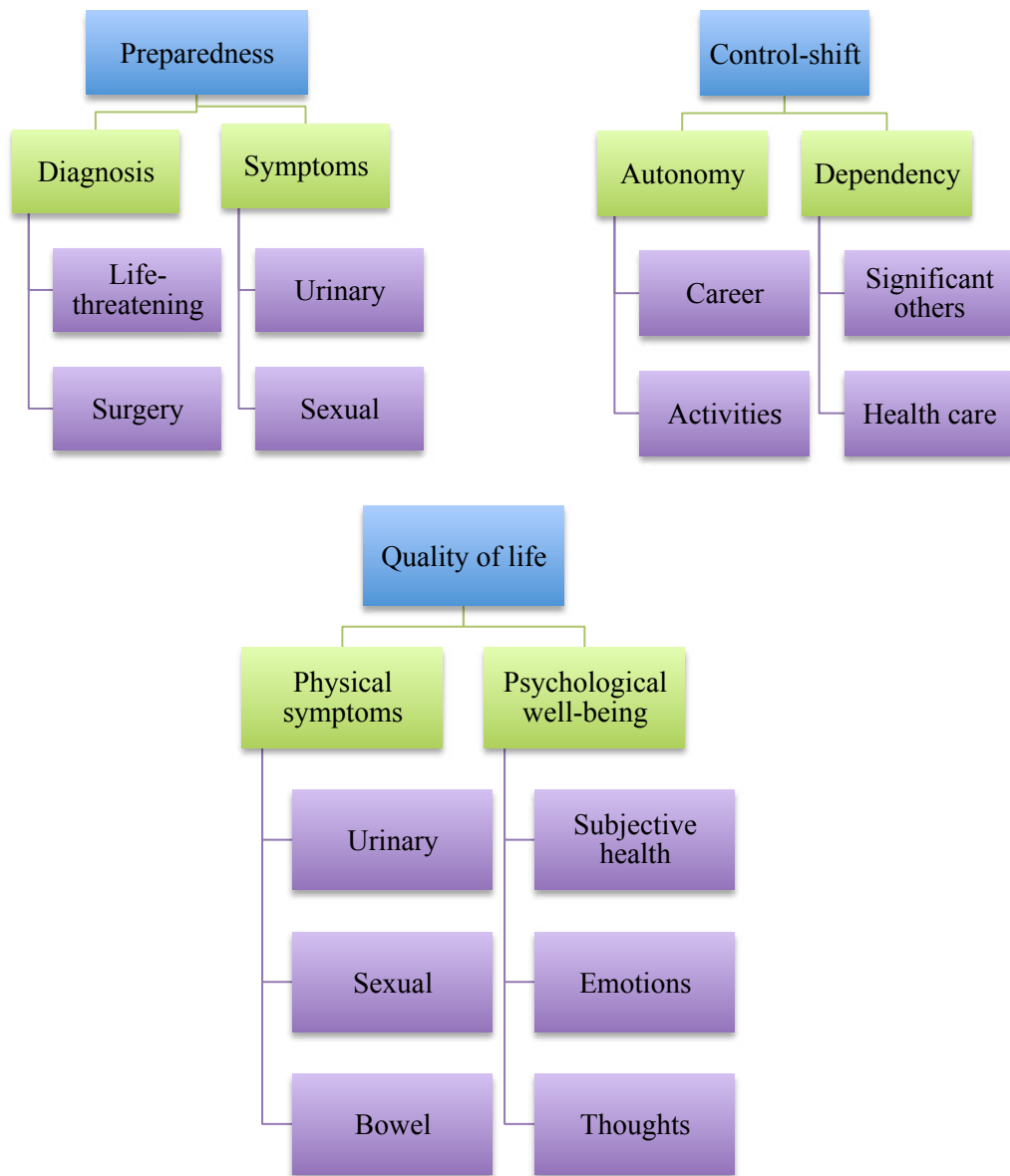


Figure 6. The results from the in-depth interviews with six men diagnosed with prostate cancer. The flow charts show the themes (blue), categories (green) and phenomena (purple) that were subsequently included as variables in the study questionnaires.

The second theme included, the men's description of a shift between autonomy, i.e. being in control over their own life, to dependency. They had been socially and physically active before but that had changed. They felt uncertain and could not control what happened to them. When choosing treatment they had relied on their doctor's recommendations and after surgery they were relying on the support of their wives.

... and because he thought that he could take it away, I believed it too (1)

... mostly my wife and it was luckily so that she just got retired so she has been able to help me with all the transport back and forth to the hospital (2)

The third theme, quality of life, revealed different description things that mattered for the interviewed men.

It is of course to be able to keep on going and to be clear headed. For me it is most important not to come in, lying like a parcel maybe, in a nursing home or something like that, that's how I see that you should manage as long as possible (3)

... it is perhaps that human relationships are worth so much more than gadgets, but especially this bit that you value persons who do not suck your energy (4).

And the emotional part was also there:

I sat here in the garden during nights and contemplated if I had six months left, what you should do if you just have six months left of your life? So, I don't want to say it was a near-death experience, but it was such a tough period, you are only able to manage by yourself. (...)
So, the summer was long. I damn didn't sleep much. It was just brooding you know. (5)

Study-specific questionnaires

The themes from the interviews were the basis for creating new questions to be included in the study questionnaires, especially on phenomena not previously studied in detail, such as thoughts about the cancer. Questions derived from questionnaires used in similar study groups at the Division of Clinical Cancer Epidemiology were also revised and included. When phrasing questions, we deliberately tried to use the wordings given by the interviewed men as exactly as possible, without compromising the conceptual entity. Response scales were developed to match each conceptual theme as carefully as possible. For example, in questions about frequency such as “How often during the past month have you had negative thoughts about your prostate cancer, suddenly and unintentionally?”, a person-incidence scale was used, with the following verbal categories: “Never”, “More seldom than once a week”, “At least once a week”, “At least three times a week”, “At least once a day”, “At least three times a day”, “At least seven times a day”. For questions such as “How stiff was your penis during sexual activity during the past month?” a person-prevalence scale was considered more appropriate: “My penis has never been stiff enough for intercourse”, “My penis has during half of the occasions been stiff enough ...”, “... during more than half of the occasions...”, “... always been ...”. Questions considered difficult to quantify were phrased in the following manner, “Some people easily talk about their health or bothers with others. How does that apply to you?”. The response scale was: “Do not agree at all”, “Agree to some extent”, “Agree to a large extent”

and “Agree completely”. The time frame for the questions was based on the nature of the respective question. Thereby, questions on quality of life, emotional well-being, sexual and urinary symptoms referred to the past month. Questions including post-operative recovery, emotional, and practical support referred to since the time after surgery. Questions on complications or disease recurrence referred to the time after the last follow-up, i.e. since the questionnaires at three and twelve months’ were answered.

The questionnaires were prepared and validity tested by specialists both group-wise and face-to-face. The specialists included urologists, surgeons, nurses, psychologists, clinical epidemiologists, oncologists, statisticians, as well as a linguist. After receiving comments and revisions, a primary version was tested for face-validity. Meetings with men were planned to take place either when they were preparing for prostate-cancer surgery or at a follow-up visit at a urological clinic. They were accompanied while they answered the questionnaires. If the man hesitated or showed signs of not understanding the questions or not having had any experience of the phenomenon in question, this was discussed and the message taken back to revise the questions. Successively, when no more participants suggested any changes, the final version for the pilot study was determined.

Since the topics included in the questionnaires were adapted to the respective time-point of the trajectory, the four different questionnaires have different numbers of questions. The pre-operative questionnaire is the shortest one with 207 questions, 284 questions are included in the three-month questionnaire, 305 in the 12-month and 332 in the 24-month questionnaire. The questionnaires were provided in color-printed paperbacks, each with a different nature photograph on the front.

Pilot-study

A pilot study was performed to test the data-collection methods and to give an indication of the participation rate. The filled-out questionnaires were carefully read to see whether men had left certain questions unanswered or had given written comments. Four urological departments participated in the pilot-study including 100 patients, and all medical case-report forms and patient questionnaires were examined.

During this data-collection examination, a few minor issues arose. One was about the inclusion of patients to the study, i.e. at which time-point in the referral procedure the patient should be included, at the first-visit at the urological clinic or at admission to hospital for surgery. The adequate time-points for the patients to answer the pre-operative questionnaire had to be

determined and adapted at each urological department according to the local routines. The time-period between the decision about and time of surgery was in most cases short, therefore each department was allowed to choose the time-point and routine that best suited them. After the pilot-study, the questionnaires were also revised. For some questions, there was an apparent need of adding response categories at either end of the scale, or a “not applicable” category, since the participants wrote comments on the side, or left questions unanswered. As an example, at first, the highest incidence category for the question on negative intrusive thoughts was “Yes, at least once every day”. In the pilot study some participants wrote “all the time” on the side of the question. In the final version of the questionnaires, two response categories were added, i.e. “Yes, at least three times a day” and “Yes, at least seven times a day”. The collected experiences from the pilot-study procedures and testing were used for the main study logistics.

QUANTITATIVE PHASE – THE LAPPRO TRIAL

Data collection

The enrollment of participants in the LAPPRO trial started on September 1 2008 and had on August 31 2011 included 3660 men from 13 urological departments in Sweden. In the beginning, six departments participated, gradually growing in number to 12 during the first study year and a later addition of one department. As described in paper I, patients answer a questionnaire at the urological department at admission to surgery or at home if patient admission is done over the phone, as in the case of three of the participating departments. Participants answer the other three questionnaires at home, 3, 12 and 24 months after the date of surgery and send them back to the study secretariat in Gothenburg. A patient contact database was developed in the FileMakerPro software program to keep track of included participants, time-points for sending and receiving the questionnaires. The participants are informed about whom to contact if they have questions or considerations about the study on the whole or individual questions. Participants have called by phone, sent e-mails and photos, written postcards and letters to the assistants in the study secretary.

Data entry

Assistants entered the answers from the collected questionnaires in the EpiData software program, which was pre-programmed to identify possible false entries in form of inappropriate values, as an effort of minimizing bias. All doubtful answers, such as double-marked, written notes on the side or instead of marking a response, were decided upon by the doctoral student and in some cases referred to the principal investigators. These decisions were registered to enable later references as well as to ensure consistency of data-entries by different assistants, and over time. Randomly chosen questionnaires were controlled for reliability of data entering

at two time-points in the data-entry process. Answers to open-ended questions and all written comments were entered into a word processor, identified by question number, to be referred to or analyzed.

Statistical analysis

A specialized statistician did all statistical analyses using the statistical programs SAS and R (see manuscripts II-IV for details).

QUALITY-OF-LIFE STUDIES (II – IV)

STUDY POPULATION

The participants in the studies were men included in the LAPPRO trial between September 1, 2008 and August 31, 2009. These were men planned for surgery for prostate cancer at 12 urological departments in Sweden, shown in Figure 7. The criteria for inclusion in LAPPRO were: to be fit for surgery, to be able to read and write Swedish, and to sign an informed consent for participation. For statistical analysis of the primary end-point in LAPPRO, only men fulfilling stricter criteria will be included (72). For participants, the study procedures were by and large the same as the regular admittance and follow-up procedures at the respective departments. The differences included outlined guidelines for post-operative recovery before discharge, controlling the possibility of prolonged sick leave after two weeks postoperatively and then weekly, the patient questionnaires, and the detailed registration of medical data.

Sahlgrenska University Hospital, Gothenburg
Carlanderska Hospital, Gothenburg
Capio Lundby Hospital, Gothenburg
Karolinska University Hospital, Solna
Karolinska University Hospital, Huddinge
UroClinic, Stockholm
Capio St:Görans Hospital, Stockholm
Stockholm South General Hospital, Stockholm
Skåne University Hospital, Malmö
Alingsås General Hospital, Alingsås
Uddevalla Hospital, Uddevalla
Helsingborgs General Hospital, Helsingborg
Hallands Hospital, Kungsbacka-Varberg



Figure 7. The urological departments participating in the LAPPRO trial. The figure shows a schematic indication of the location of the 13 hospitals in Sweden.

The participants were men between 41 and 77 years of age, three individuals were under 45 years and three over 75 years. The mean age was 62.6 years (standard deviation 6.2). The educational level of the study population was similar to men in the respective age group in the general population in Sweden, 38% had finished college or university. Most of the men were married or living with a partner (84%), only 21 being widowers. Less than half of the participants (48%) lived in rural areas or in a smaller town. More than half of the men were employed (56%), 38 (5%) were on short or long-term sick leave and 298 (36%) were retired. Sixty-seven percent had intercurrent illnesses or symptoms before surgery, the most prevalent

illness was hypertension (n=264; 32%) followed by prostatitis (n=89; 11%). More than half of the men (54%) had tumors defined as clinical T1 tumor-stage according to rectal palpation before surgery, while 40% were defined as T2 or T3 tumors preoperatively.

PARTICIPATION RATE

The study population in this thesis was restricted to the men who had answered the study questionnaires before and three months after surgery. Questionnaires from some participants were not collected at the departments and some participants were enrolled to the secretariat too late for collection of the three months questionnaire. The reasons for non-participation after enrolment are shown in Table 1.

Table 1. The study population.	No.	%
Number of men included in the LAPPRO trial*	971	100
Not returning any questionnaire	46	4.7
Missed at urological department/late report to secretariat	7	0.7
Physical reasons	3	0.3
Psycho-social reasons	4	0.4
Other reasons (language, relocation etc.)	1	0.1
Agreed to participate but did not return questionnaires	31	3.2
Not returning questionnaire before surgery	72	7.4
Missed at urological department/late report to secretariat	56	5.8
Physical reasons	0	0
Psycho-social reasons	2	0.2
Other reasons (language, relocation etc.)	0	0
Agreed to participate but did not return questionnaires	14	1.4
Not returning questionnaire 3 months after surgery	20	2.1
Missed at urological department/late report to secretariat	0	0
Physical reasons	2	0.2
Psycho-social reasons	3	0.3
Other reasons (language, relocation etc.)	4	0.4
Agreed to participate but did not return questionnaires	11	1.1
Total non-replying	138	14.1
Participants returning two questionnaires	833	85.9

* Between September 1 2008 and August 31 2009.

RESULTS

PAPER II

The aim of paper II was in a way explorative, firstly to study the prevalence of intrusive thoughts as well as the participants' self-reported understanding of the phenomena by using qualitative methods. Secondly, the aim was to see if there were cross-sectional and longitudinal associations with selected quality-of-life measures.

The results revealed that before surgery, 603 men (73%) reported having negative intrusive thoughts about their prostate cancer at some time, whereas three months after surgery the corresponding number was 493 (59%) reported this. The prevalence difference was statistically significant ($p < 0.0001$) between the two time points. Before surgery, approximately 40% of the men compared with 54% three months later reported positive thoughts about prostate cancer at some time. Comparing those reporting with those not reporting negative intrusive thoughts at least once a week before surgery, the prevalence ratio (95% confidence interval) three months after surgery for waking up with anxiety at least once a week was 3.8 (2.7 to 5.4), for depressed mood 1.8 (1.5 to 2.1) and for impaired self-assessed quality of life 1.3 (1.2 to 1.5). There was a statistically significant trend between reporting more prevalence of negative thoughts before surgery and higher percentage of men having impaired quality of life after surgery ($p < 0.0001$).

PAPER III

In paper III, we wanted to go further and find out if there were any individual characteristics or modifiable care-related factors that predicted the occurrence of negative intrusive thoughts. The following health-background factors related to reporting negative intrusive thoughts before surgery: younger age (PR 1.26, CI 1.00 to 1.58), intercurrent illness (PR 1.23, CI 1.03 to 1.48), low-to-moderate self-assessed physical health (PR 1.50, CI 1.25 to 1.79), alcohol consumption (PR 1.36, CI 1.02 to 1.81), anti-depressive medication (PR 1.80, CI 1.38 to 2.34) and bodily pain (PR 1.46, CI 1.21 to 1.76). The modifiable care-related factors that were independently associated with higher prevalence of negative intrusive thoughts before surgery were: uncertainty of cure (PR 1.93, CI 1.59 to 2.35), not being prepared for urinary (PR 1.32, CI 1.09 to 1.61), or sexual bother (PR 1.32, CI 1.04 to 1.67). Multivariate analysis revealed that reporting negative intrusive thoughts before surgery was the strongest predictor for reporting such thoughts three months after surgery (adjusted odds ratio (OR) 3.59, CI 2.39 to 5.39) but younger age (OR 1.84, CI 1.08 to 3.15), living alone (OR 1.70, CI 1.04 to 2.80), and non-active

health-care seeking (OR 0.52, CI 0.35 to 0.77) also predicted the occurrence of negative intrusive thoughts three months after surgery.

PAPER IV

Recurrent thoughts of death, not just fear of dying, are one indicator out of nine for depressive disorder (73) and possibly a low severity level for thinking about suicide. In paper IV, the aim was to identify predictors for thinking about one's own death among prostate cancer patients shortly after receiving the diagnosis. The results revealed that twenty-five percent of the participants had thoughts about their own death at least once a week before surgery and 18 percent three months after surgery. Urban living (Adjusted Relative Risk (RR) 2.28, CI 1.17 to 4.45), low control (RR 2.15, CI 1.32 to 3.50), uncertainty about the future (RR 3.26, CI 1.09 to 3.26) and crying (RR 1.96, CI 1.29 to 2.97) before surgery predicted thoughts about one's own death after surgery.

DISCUSSION

METHODOLOGICAL CONSIDERATIONS - VALIDITY

The validity of a study can be seen as the extent to which the scientific conclusions correspond to the real life studied. All studies include errors, either a systematic error which can introduce bias, or a random error which can influence the precision of the study. Within our research group we utilize a tool called the hierarchical step-model for causation of bias to identify the possible sources of bias in a study (Figure 8). According to this model, each step of the research process may introduce deviations that turn out as an error or a correction of the adjusted effect measure. The model depicts how a real-life study (such as ours) deviates from “the perfect study” and proceeds in four steps towards a calculated, often adjusted, effect-parameter (70).

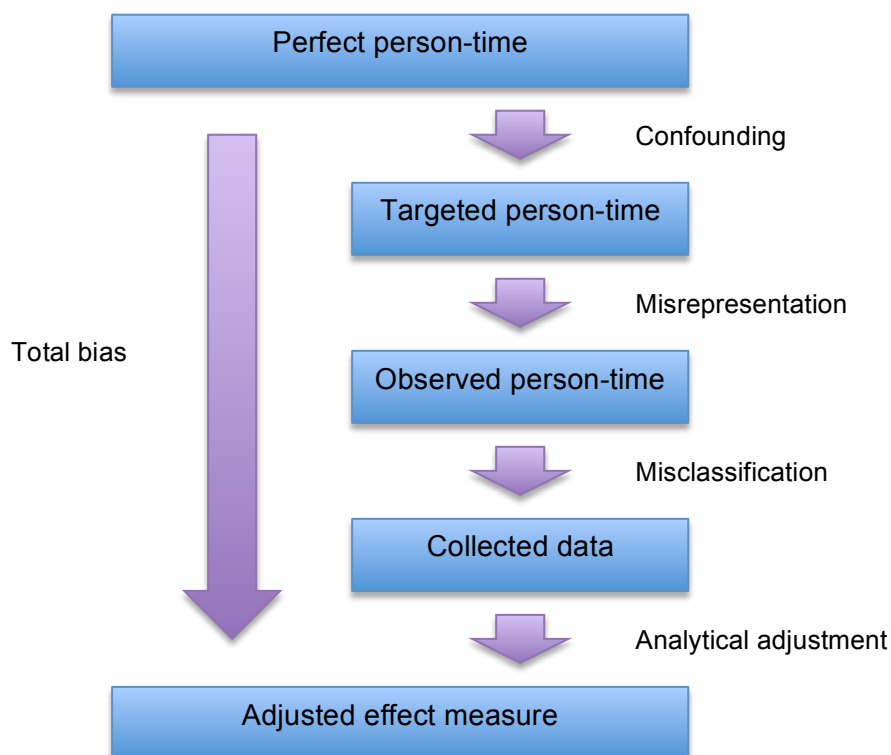


Figure 8. The different steps in the research process for a clinical study with the corresponding biasing factors (errors) – The hierarchical step-model for causation of bias in clinical epidemiological studies.

Confounding

In the first step of the model, investigators identify the targeted person-time in epidemiological terms, meaning the population that the researcher attempts to study and during which period of time. During this step, the systematic errors presented as confounding factors, may be identified and in some cases controlled for, which is essential in epidemiological studies (74). To be

defined as a confounding factor, the variable must be associated with the exposure as well as a causal influence on the outcome. If the prevalence of risk factors for the outcome differ between the groups that are being compared, the observed association can be distorted (74). Therefore, questions were included in the questionnaires on many of the possible confounders identified in the preparation phase: age, education, employment status, marital status, religion/spirituality, previous psychological morbidity and many more.

The findings of paper II indicate a longitudinal causality between the studied variables. We believe that the associations revealed are unlikely to be explained by confounding factors. The possible confounder on the associations on which we have no information is low quality of life before the diagnosis of prostate cancer (before enrollment) that could have affected both the prevalence of negative intrusive thoughts before surgery as well as quality of life after surgery. We recognize the possibility of reverse association between the variables, that impaired quality of life, waking up in the night or feeling depressive could cause more negative intrusive thoughts, but do not think that this makes the results less interesting.

In paper III we reveal cross-sectional associations on which we hesitate to state causal direction. Alcohol consumption, anti-depressants, low self-assessed health, living alone, intercurrent illnesses, and bodily pain could as well be the result of frequent negative thinking about the cancer as vice versa. The possible confounders on the association between the care-related factors, uncertainty of becoming cured and low preparedness of symptoms, are on the other hand the received information from the health-care professionals before surgery as well as how the men decided upon their treatment. These factors were unfortunately not well operationalized in the questionnaires. However, existing national care directives, including the practices for patient education, should minimize this confounding effect, assuming that all the participants had access to the same kind of information.

Misrepresentation

In the second step of the hierarchical step-model, bias due to non-participation and selection-induced problems is introduced, since this reveals a difference between the targeted person-time and the observed person-time. In our study, all men undergoing radical prostatectomy at 13 hospitals in Sweden, accepting to participate were to be enrolled to the secretariat. To minimize the risk of non-participation and selection of participants, members of the study secretariat visited all departments before the start of the study to inform and motivate the personnel. However, it is possible that an unknown number of men have been missed due to factors in clinical routines, communication, or for other reasons. In the group of 971 men that

were enrolled during the first study year, 833 answered the two first questionnaires and therefore fulfilled the criteria to be included in the study cohort presented here. We have some information on the non-participants revealing no difference from the participants, regarding mean age, clinical tumor stage and the percentage of men reporting negative intrusive thoughts or thoughts about death more than once a week among those answering one questionnaire out of two. However, we cannot exclude the possibility that the effect measures revealed had been different among the non-participants, which in turn might represent the targeted person time wrongly.

Misclassification

A systematic error including a difference between the calculated effect measure of the observed person-time and the crude effect measure in the data may originate when there are errors in the measurements (70, 74). Therefore we systematically tried to minimize measurement errors during the preparatory phase of the study and by using self-assessed outcome measures. The questions stated were based on phenomena and wordings from in-depth interviews with men having the same experience as the targeted study population. By using one question for one phenomenon, we strive for a clear and mutual definition of the concepts studied, meaning that the researcher and the participant understand the questions in the same way. The questions were therefore validated face-to-face with men undergoing radical prostatectomy to assure this common understanding of the concepts. Open-ended questions were stated and analyzed to confirm this understanding. The self-administered questionnaires were collected by a third party to prevent interviewer-related problems, such as to propitiating, the respective doctor or hospital, or avenging them. None of the studies include comparison between groups so the risk of measurement errors regarding distribution differences is not relevant.

Analytical adjustment

If the systematic errors have been addressed, the random error remains. Random error is the variability in the data that cannot readily be explained. Here, the statistics enter the step-model. Their role is to estimate the effects after correcting for biases. In our studies, the point estimates, prevalence ratios, odds ratios and relative risks, are always presented with 95% confidence intervals as the measurement of precision. In paper IV, statistical tests by Bayesian Model Averaging were performed in an attempt to control for not selecting redundant variables as predictors. A strict selection criterion for significant association was applied to avoid a random selection of true predictors (75, 76). The design and inclusion criteria of the LAPPRO trial largely simplify the problem in the consequent studies. The trial population is restricted to one gender, to individuals choosing and being healthy enough for surgery and to the rather

homogenous group reading and writing Swedish, minimizing the variability effect of possible cultural differences in the Swedish population.

FINDINGS AND INTERPRETATIONS

The study design

The rigorous study design of the LAPPRO trial provides the opportunity to study the experiences of men undergoing surgery for clinically localized prostate cancer. When all data have been collected, information on pre-operative medical data, surgical elements, pathology, morbidity and mortality can be associated with various patient reported symptoms and demographics. Here, only a very small part of the extensive data that is going to be available has been analyzed and presented. In the coming years, a number of reports from the trial will reveal a detailed view of the experience of prostate cancer patients.

Maintaining quality of life

As shown in the schematic Figure 9, we have found that there is an association between negative intrusive thoughts and quality of life, and that negative intrusive thoughts associate with reporting thoughts about one's own death. There are several studies on men's quality of life after prostate cancer diagnosis and treatment. However, the emotional symptoms among men undergoing radical prostatectomy have not been extensively explored. Measuring self-assessed quality of life, based on the respondents' own definitions, provides a way to single out important symptoms, meaning those that influence, as well as those modifiable symptoms occurring in this situation

In the research for paper II we found, the variable of negative intrusive thoughts to be a valid and sensitive indicator of quality of life. We claim this because of the strong effect measures found in the association with the three outcome variables, and because of the supporting data on the association of intrusion of thoughts with the same variables. Reflecting upon the qualitative results, the participants seem to relate to the phenomenon and make the association with their quality of life themselves. The most important finding was the longitudinal association between negative intrusive thoughts before surgery and impaired quality of life three months after surgery. These results agree with indications from earlier studies showing that men who experienced more distress after the cancer diagnosis and those who applied emotion-focused coping reported worse health (52, 60). This could mean that an intervention provided already before surgery targeting the negative intrusive thoughts could be effective in the long-term. Psychological interventions have appeared to be effective in neutralizing

intrusive thoughts (66, 77, 78), and we therefore suggest that they constitute a suitable target among men with prostate cancer needing support.

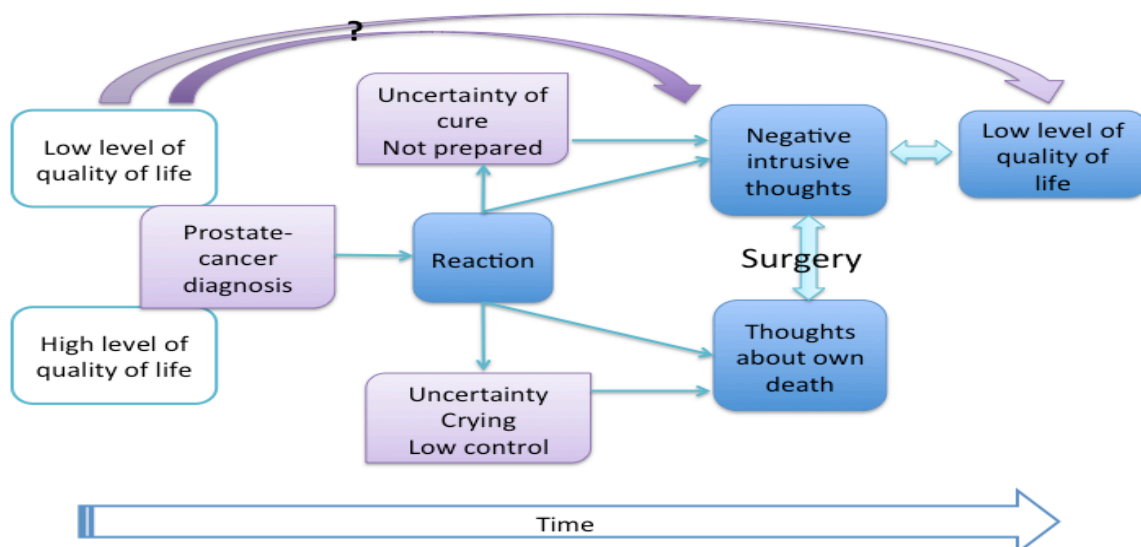


Figure 9. A schematic presentation of the main findings of the thesis. Approaching surgery for clinically localized prostate cancer men's reactions are signaled by negative intrusive thoughts about their cancer and thoughts about their own death. Men who are uncertain of becoming cured and those who are not prepared for possible treatment-induced symptoms before surgery experience consequent negative intrusive thoughts to a larger extent than men who are certain of becoming cured or are prepared for symptoms. Men who are uncertain about the future, who cry or lack control of life, report consequently more often thoughts about their own death. The level of quality of life before prostate cancer diagnosis could have an effect on men's experiences before and after surgery, and be a confounder in the reported associations.

The predictors for negative intrusive thoughts found and revealed in the results of paper III, indicate an interesting discrepancy in the treatment choice of a subgroup of the participants. It seems that a group of men who do not believe in becoming cured although they have chosen a curative and rather aggressive treatment modality, experience consequent distress. This reflects the apparent decision-related distress men go through when choosing treatment for localized prostate cancer as well as their high expectations (79-81). Unfortunately no general clinical guidelines can aid the decision of which treatment to choose on an individual bases. Our results further show that the distress can be persisting, the prevalence of negative intrusive thoughts three months after surgery is twofold among men who before surgery are not certain of becoming cured. Younger men, those living alone and those who actively seek care could possibly be considered a risk group for distress. These findings may have clinical relevance in future studies and interventions.

Paper IV was based on the recent registry-based, retrospective studies that revealed an increased risk of suicide among cancer patients in general (82, 83), as well as among prostate cancer patients in particular (84-86). The delicate subject-matter and the timing of the questions, that is shortly before and after surgery, resulted in deliberately choosing a guarded wording, maybe explaining the higher prevalence of thoughts about death as compared to the direct question on “being better off dead” (87). However, many other questions on psychological and emotional factors were stated and strengthened our findings. The results revealed an association of signs of social isolation and emotional disposition with persisting thoughts about death. The identification of vulnerable individuals for example by asking the right questions during the admission process before surgery, is to be highly recommended and could possibly prevent such symptoms from developing into psychiatric illness.

THE FUTURE

Our findings raise further research questions and ideas for clinical implications:

- Analysis of the follow-up questionnaires of the study-cohort at 12 and 24 months after surgery, aiming at studying if the prevalence of psychological symptoms, self-assessed quality of life, decisional regret as well as incidence of psychiatric disorder change over time.
- Analysis of the follow-up questionnaires in aspects of experienced bother because of physical symptoms, to find out if low preparedness and more negative intrusive thoughts before surgery predict more bother from symptoms 12 and 24 months after surgery.
- Designing a prospective intervention study for men like those identified in Paper III and who are planned for radical prostatectomy. The intervention would be to modify the found predictors for negative intrusive thoughts by responsive communication. Health-care professionals could evaluate, respond to and enhance the men's preparedness for the possibly emerging physical symptoms after surgery as well as their apprehension of the disease prognosis in the actual situation.
- A prospective intervention study about the effects of Expressive Writing. Men experiencing constraints in talking about their cancer could experience more intrusive thoughts about the prostate cancer diagnosis. Expressive Writing provides the men with means that could help them to start talking about their cancer when they need to, and thereby disengage from the negative intrusive thoughts.
- Direct clinical implications of the results of this thesis in urological care could be to screen for harmful thoughts among men by successively asking "What are you thinking now?", "How do you think about your cancer?", "How are you sleeping at night?" and based on the responses: "Have you had feelings like lack of control, hopelessness or have you been crying?", and possibly end with "Have you thought about your own death recently?". Men describing negative thoughts or thoughts about their own death might need further support or psychological referral.

GENERAL CONCLUSIONS

By means of a rigorous study design and self-assessed measures, we have acquired more knowledge of the situation of men after receiving a prostate cancer diagnosis. This knowledge will hopefully contribute to the scientific literature and then in turn contribute to the implementation of better practice within the health-care system. If applied, it may help clinicians to plan for interventions aiming at enhancing the probability of maintaining quality of life.

This thesis as well as the prior research emphasizes that some men are vulnerable to psychological distress and, possibly, to develop psychiatric disorder after the diagnosis of clinically localized prostate cancer. This is indicated by the prevalence of negative intrusive thoughts about prostate cancer as well as men's thoughts about their own death before and after radical prostatectomy.

Despite advances in the medical sciences and the present ability to cure, the diagnosis of cancer is still frightening. Parallel to the technical development in cancer medical treatment, including new surgical techniques, there is need for providing more intense patient information and focused care because of the trauma that the cancer diagnosis causes. There is a risk that advanced medical and surgical strategies will shorten the time needed for the medical procedures. As a result of that, the health-care professionals may have a less time available to support patients in dealing with the emotional aspects of the disease. Our results have revealed indicators of vulnerability that need more attention. By using these indicators clinicians could detect and intervene with these vulnerable individuals and thereby hopefully restore their health after treatment for prostate cancer. For example, the upcoming surgery may result in the accumulation of psychological reactions among men more than the prostate cancer diagnosis itself. These reactions may predict the possibility of impaired quality of life following surgery. Therefore, screening for harmful thoughts before surgery could be a valuable tool to support men with prostate cancer in maintaining their quality of life.

SUMMARY IN SWEDISH – Svensk sammanfattning

För att kunna utveckla ett bättre stöd för män som har erhållit diagnosen prostatacancer och i förlängningen bevara deras livskvalitet behövs mer kunskap om vilka psykologiska faktorer som är relaterade till deras självskattade livskvalitet. Plötsligt påträngande tankar uppstår ofta efter en påfrestande händelse och utgör ett kriterium i posttraumatiskt stress syndrom. Psykologiska interventioner har visat sig kunna underlätta hur människor hanterar en cancerdiagnos samt minska effekten av påträngande tankar.

Syfte

Avhandlingen syftar till att studera och beskriva mäns tankar efter att de har erhållit diagnosen prostatacancer, samt studera huruvida dessa var relaterade till deras livskvalitet. Syftet var även att hitta vilka bakgrunds- och vårdrelaterade faktorer som är relaterade till förekomsten av skadliga tankar.

Metod

I djupintervjuer berättade män som opererats för cancer i prostatakörteln bland annat om återkommande tankar om cancer och behandlingen. Deras beskrivning av erfarenheten efter cancerdiagnosen gjordes om till frågor som inkluderades i fyra omfattande frågeformulär som används i den pågående LAPPRO-studien vid 13 urologkliniker i Sverige. Studiens huvudsyfte är att jämföra utfall efter öppen kirurgi och robotstyrd titthålskirurgi vid prostatacancer. Män som deltar i studien besvarar dessa frågeformulär före operationen och tre, tolv samt tjugofyra månader efter operationen. Under studiens första år, från 1 september 2008 till 31 augusti 2009, opererades 971 män. Av dessa besvarade 831 (86 %) de två första frågeformulären.

Resultat

Våra resultat visar att 73 % av männen någon gång haft plötsligt påträngande negativa tankar om sin cancer före och 59 % tre månader efter operationen. Att ha plötsligt påträngande negativa tankar åtminstone en gång i veckan under en månad var relaterat till att vakna mitt i natten med oro eller ångest minst en gång i veckan (förekomstkvot, PR 3,9), samt att någon gång känna sig nedstämd (PR 1,8) eller att värdera sin livskvalitet som nedsatt (PR 1,3).

Bland män under 55 år (oddskvot, OR 1,8) och ensamboende (OR 1,7) var plötsligt påträngande negativa tankar tre månader efter operationen mer vanliga, men mindre vanliga bland de som inte sökte vård aktivt för misstanke om prostatacancer (OR 0,5). Att vara osäker på att operationen botar cancer (PR 1,9), samt att inte vara förberedd på urinbesvär (PR 1,3) eller sexuella besvär (PR 1,3) var oberoende relaterat till plötsligt påträngande negativa tankar före operationen.

Före operationen tänkte en fjärdedel av männen på sin egen död åtminstone en gång i veckan eller oftare under den senaste månaden. Att vara stadsbo (OR 2,3), inte ha kontroll över sitt liv (OR 2,2), vara osäker på framtiden (OR 3,3) eller ha gråtit åtminstone en gång i veckan (OR 2,0) före operationen var relaterat till att ha tankar om sin egen död tre månader efter operationen.

Konklusion

Trots möjligheter till bot kan en cancerdiagnos vara skrämmande. Möjligtvis ackumulerar den förestående operationen psykologiska reaktioner hos män med prostatacancer.

Nytta

Att screena för och upptäcka skadliga tankar bland män som erhållit diagnosen prostatacancer kan vara ett viktigt steg i att ge dem stöd att bevara livskvaliteten efter operationen. Interventioner som syftar till att neutralisera negativa tankar eller minska deras påverkan på livskvaliteten kan vara värdefulla men kräver mer studier.

SUMMARY IN ICELANDIC – Samantekt á íslensku

Þekking á þeim tilfinningalegu þáttum sem tengjast skertum lífsgæðum karlmanna eftir að hafa greinst með blöðruhálskirtilskrabbamein er takmörkuð. Til að viðhalda lífsgæðum eftir meðferð blöðruhálskirtilskrabbameins gætu íhlutanir sem bæta tilfinningalega líðan skipt máli.

Þrálátar hugsanir eru einkenni sem er tengt við áfallaröskun, og koma oft fram eftir streituvaldandi atburði. Þrálátar hugsanir eru síendurteknaðar, óvelkomnaðar og koma án viðvörðunar. Hugsanir um eigin dauða, geta gefið til kynna depurð eða þunglyndisröskun. Rannsóknir á fólki sem greinst hefur með krabbamein gefa til kynna að íhlutanir sem beinast að því að draga úr þrálátum hugsunum gætu hjálpað fólki að takast á við þá streitu sem fylgir greiningunni.

Markmið doktorsritgerðarinnar var að finna tilfinningalega þætti sem mögulegar íhlutanir gætu beinst til að efla lífsgæði karlmanna eftir aðgerð við blöðruhálskirtilskrabbameini. Þrjár tilgátur voru settar fram: a) að aukið algengi þráláttra hugsana tengist skertum lífsgæðum fyrir og eftir skurðaðgerð; b) að bakgrunnur og umönnunartengdir þættir spái fyrir um algengi þráláttra hugsana; c) að bakgrunnur, heilbrigði og tilfinningaleg líðan spái fyrir um algengi hugsana um eigin dauða.

Aðferð: Spurningalistar voru byggðir á fyrri rannsóknarniðurstöðum og niðurstöðum djúpvíðtala við karlmenn með reynslu af blöðruhálskirtilskrabbameini. Eftir það voru þeir prófaðir með viðtölum (sýndarréttmæti) og í forrannsókn (n=100) á sjúklingum til að kanna réttmæti spurninga, gagnasöfnunarferlið og svarshlutfall.

Þann 1. september 2008 hófst LAPPRO, framsæ rannsókn sem ætlað er að bera saman niðurstöður eftir opnar aðgerðir við blöðruhálskirtilskrabbameini annars vegar, og kviðsjáraðgerðir með aðstoð vélmennis hins vegar. 31. ágúst 2011 voru 3660 þátttakendur frá 13 þvagfæraskurðeildum í Svíþjóð skráðir. Fyrsta árið gengust 971 karlmenn undir aðgerð. Af þeim svöruðu 833, 86%, tveimur fyrstu spurningalistunum, fyrir skurðaaðgerð og þremur mánuðum eftir aðgerð.

Niðurstöður: Fyrir skurðaðgerð höfðu 603 (73%) karlmenn, stöku sinnum haft neikvæðar þrálátar hugsanir um krabbameinið, þremur mánuðum eftir aðgerð 493 (59%). Samanborið við þá sem ekki höfðu slíkar hugsanir var algengihlutfallið (PR) hjá þeim sem höfðu neikvæðar þrálátar hugsanir að minnsta kosti einu sinni í viku: 3,8 fyrir að vakna á nóttunni með kvíða, 1,8

fyrir depurð og 1,3 fyrir skert lífsgæði. Fyrir skurðaðgerð reyndust óvissa um lækningu (PR 1,9), að ekki vera búinn óþægindi frá þvagfærum (PR 1,3) eða við kynlíf (PR 1,3) vera óháð tengd auknum neikvæðum þrálátum hugsunum. Samkvæmt fjölþáttagreiningu reyndist sterkasti spáþátturinn fyrir neikvæðum þrálátum hugsunum eftir aðgerð voru slíkar hugsanir fyrir aðgerð (OR 3,6). Yngri menn (OR 1,8) og þeir sem bjuggu einir (OR 1,7) reyndust hafa aukna tíðni neikvæðna þráláttra hugsana þremur mánuðum eftir skurðaðgerð en þeir sem höfðu verið óvirkir í leit til heilbrigðisþjónustunnar höfðu lægra algengi (OR 0,5).

Tuttugu og fimm prósent þátttakenda höfðu haft hugsanir um eigin dauða að minnsta kosti einu sinni í viku síðastliðinn mánuð, fyrir aðgerð, og 18% þremur mánuðum eftir aðgerð. Karlmennt sem bjuggu í þéttbýli (OR 2,3), töldu sig ekki hafa stjórn í lífi sínu (OR 2,2), voru óvissir um framtíðina (OR 3,3) eða höfðu grátið að minnsta kosti einu sinni í viku (OR 2,0) fyrir aðgerð hugsuðu oftar um sinn eigin dauða þremur mánuðum eftir skurðaðgerðina, heldur en aðrir.

Lærdómur: Krabbamein vekur upp ýmsar tilfinningar óháð möguleika á lækningu. Margir karlmenn greindir með klínískt staðbundið blöðruhálskirtilskrabbamein upplifðu neikvæðar þrálátar hugsanir um krabbameinið og/eða hugsanir um eigin dauða bæði fyrir og þremur mánuðum eftir skurðaðgerð. Hugsanirnar tengdust ýmsum sálrænum einkennum, líkt og gráti, stjórnleysi, óvissu, og því að vera óviðbúinn. Vissir einstaklingsbundnir þættir gætu skýrt aukið algengi.

Hagnýting: Til að efla lífsgæði karlmanna eftir skurðaðgerð við blöðruhálskirtilskrabbameini gæti verið gagnlegt að skima fyrir og bera kennsl á hugsanir sem hafa neikvæð áhrif á líðan þeirra. Nota mætti niðurstöðurnar til að hanna íhlutun sem gæti minnkað áhrif neikvæðra þráláttra hugsana á líðan karlmanna með blöðruhálskirtilskrabbamein, til dæmis með tjáningarskrifum.

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