Prostate cancer in kidney transplant recipients – a nationwide register study

Ola Bratt*†, Linda Drevin‡, Karl-Göran Prütz§, Stefan Carlsson††, Lars Wennberg** and Pär Stattin†††

*Department of Urology, Institute of Clinical Science, Sahlgrenska Academy, Gothenburg University, †Department of Urology, Sahlgrenska University Hospital, Gothenburg, ‡Regional Cancer Centre, Uppsala-Örebro, Uppsala, §Swedish Renal Registry, Ryhov Hospital, Jönköping, ¶Section of Urology, Department of Molecular Medicine and Surgery, Karolinska Institute, * **Department of Transplantation Surgery, Karolinska University Hospital, Stockholm, and †††Department of Surgical Sciences, Uppsala University, Uppsala, Sweden

Objective
To investigate whether post-transplantation immunosuppression negatively affects prostate cancer outcomes in male kidney transplant recipients.

Patients and Methods
We used the Swedish Renal Register and the National Prostate Cancer Register to identify all kidney transplantation recipients diagnosed with prostate cancer in Sweden 1998–2016. After linking these registers with Prostate Cancer Database Sweden (PCBaSe), a case-control study was designed to compare time period and risk category-specific probabilities of a prostate cancer diagnosis amongst kidney transplantation recipients versus the male general population. The registers did not include information about the specific immunosuppression agent used in all transplantation recipients. Data from PCBaSe were used to compare prostate cancer characteristics at diagnosis and survival for patients with prostate cancer with versus without a kidney transplant. Propensity score matching, Cox regression analysis and Fisher’s exact test were used and 95% confidence intervals (CIs) calculated.

Results
Almost half of the 133 kidney transplantation recipients were transplanted before the mid-1990s, when PSA testing became common. The transplant recipients were not more likely than age-matched control men to be diagnosed with any (odds ratio [OR] 0.84, 95% CI 0.70–0.99) or high-risk or metastatic prostate cancer (OR 0.84, 95% CI 0.62–1.13). None of the ORs for the different categories of prostate cancer increased with time since transplantation. Cancer characteristics at the time of diagnosis and cancer-specific survival were similar amongst transplant recipients and the control group of 665 men diagnosed with prostate cancer without a kidney transplant.

Conclusions
This Swedish nationwide, register-based study gave no indication that immunosuppression after kidney transplantation increases the risk of prostate cancer or adversely affects prostate cancer outcomes. The study suggests that men with untreated low-grade prostate cancer can be accepted for transplantation.

Keywords
incidence, prognosis, outcome, renal transplantation, immunosuppression, #ProstateCancer, #PCSM, #KidneyTransplant

Introduction
Active cancer has traditionally been considered a contraindication for organ transplantation because of concerns that the subsequent immunosuppressive therapy might facilitate cancer progression, and register studies have indeed shown increased incidence of and mortality from some cancer forms in transplant recipients [1,2]. Many transplant centres routinely screen men for prostate cancer with serum PSA tests before considering them for a kidney transplant [3,4]. For those men that are diagnosed with localised prostate cancer, transplantation is typically postponed until the cancer has been treated and the patient has been recurrence-free for 2–5 years, even if the cancer is of low-grade and would otherwise be managed with active surveillance (AS) [5,6].
A growing body of evidence suggests that low-grade prostate cancer, graded according to modern criteria [7,8], is indolent and lacks metastatic potential [9–11]. The practice of subjecting men with low-grade prostate cancer to a radical prostatectomy and prolonged subsequent follow-up before they can be accepted for an organ transplantation, can therefore be questioned, not least as longer time on dialysis is associated with worse outcomes after kidney transplantation [12,13]. Subclinical prostate cancer is highly prevalent in middle-aged and older men [14], even in those with a normal serum PSA level and a clinically benign prostate [15]. It is therefore reasonable to assume that, despite routine pre-transplantation investigations to exclude prostate cancer, many male kidney transplant recipients actually had an undetected prostate cancer at the time of the transplantation. If post-transplantation immunosuppression adversely affects prostate cancer outcomes, the incidence of advanced and poorly differentiated prostate cancer would thus be raised and the prostate cancer-specific survival poor in kidney transplant recipients.

A large USA population-based study showed a similar incidence of prostate cancer in solid organ transplant recipients as in the general population [1]. Three other population-based studies have been published: one from Australia and New Zealand showing similar results as the USA study [16], and one from Ireland and another from Switzerland, reporting a substantially increased prostate cancer incidence in male kidney transplant recipients [17,18]. None of these studies differentiated between localised, low-grade prostate cancer (that is most often detected after PSA testing) and advanced or high-grade cancer (that is more likely to be lethal). Nor did they account for time on immunosuppression treatment.

We used nationwide, population-based Swedish registers to design a study that allowed for investigation of the association between time on immunosuppression and the probability of being diagnosed with any or advanced prostate cancer. We also compared cancer-specific survival in patients with prostate cancer with vs without a kidney transplant.

### Patients and Methods

The study used several nationwide population-based registers. The Swedish Renal Register (SNR) has collected data for all kidney transplantations in Sweden since 1966 [19]. The National Prostate Cancer Register of Sweden (NPCR) includes the clinical characteristics at the time of diagnosis and information about the primary treatment for all Swedish men diagnosed with prostate cancer since 1998. The Prostate Cancer database Sweden (PCBaSe) version 4, includes data up until the end of 2016 from the NPCR and several other nationwide registers with nearly complete capture rates [20,21], not only for men diagnosed with prostate cancer and registered in the NPCR but also for five control men per prostate cancer case. The control men were not diagnosed with prostate cancer on the day that their corresponding NPCR case was diagnosed with prostate cancer. They were randomly selected from the Swedish Register of the Total Population among men that were born in the same year and were residents in the same county as the NPCR case. A Charlson Comorbidity Index (CCI) was determined for each man by using the International Classification of Diseases (ICD) discharge diagnosis codes in the In-Patient Register [22].

We did three separate analyses:

1. A case-control study was designed to investigate the probability of being diagnosed with prostate cancer in male kidney transplant recipients vs men without a kidney transplant. Cases were all men in the NPCR that were diagnosed with prostate cancer between January 1998 and December 2016. The control group consisted of these cases’ five matched control men without prostate cancer in the PCBaSe. The exposure was kidney transplantation. To minimise bias from PSA testing of asymptomatic men, which specifically raises the incidence of low-risk and of low-volume intermediate-risk cancers, three separate analyses were done: one using all cases diagnosed with prostate cancer, another using cases diagnosed with non-low-risk cancer (T3–4 and/or N1 and/or M1 and/or Gleason Grade Group (GGG) 2–5, and/or PSA level ≥ 10 ng/mL), and a third using cases diagnosed with high-risk non-metastatic or metastatic disease only (T3–4 and/or N1 and/or M1 and/or GGG 4–5, and/or PSA level ≥ 20 ng/mL). A time period analysis was done to investigate whether the odds ratios (ORs) increased over time after transplantation, which would be expected if immunosuppression facilitates progression of prostate cancer [23].

2. The distributions of prostate cancer grade and stage at the time of diagnosis were compared for patients with prostate cancer with vs without a kidney transplant. For each kidney transplant recipient diagnosed with prostate cancer, five men were selected from the NPCR that were diagnosed the same calendar year in the same county at the same age and had a similar duration of education (≤ 9, 10–12 or ≥ 12 years), but who did not have any kidney transplantation before or after their prostate cancer diagnosis.

3. The overall and prostate cancer-specific survival of kidney transplant recipients diagnosed with prostate cancer were compared with the survival of the same matched control group of patients with prostate cancer as above.

The study was approved by the Ethics Review Board at Uppsala University.

### Statistics

In the case-control study that was done to assess the risk of prostate cancer in kidney transplant recipients, bivariate ORs with 95% CIs were calculated for the exposure (kidney transplantation) and the outcomes, the incidence of advanced and poorly differentiated prostate cancer, grade, and stage at the time of diagnosis were compared for patients with prostate cancer with vs without a kidney transplant. For each kidney transplant recipient diagnosed with prostate cancer, five men were selected from the NPCR that were diagnosed the same calendar year in the same county at the same age and had a similar duration of education (≤ 9, 10–12 or ≥ 12 years), but who did not have any kidney transplantation before or after their prostate cancer diagnosis. The study was approved by the Ethics Review Board at Uppsala University.
transplantation) among cases (men with prostate cancer) vs controls (matched men without prostate cancer).

Prostate cancer grade and stage distributions at the time of diagnosis were compared for kidney transplant recipients’ vs patients with prostate cancer without a kidney transplant. The latter were selected from the PCBaSe using propensity score matching with Caliper 0.1 on age, calendar year of diagnosis, county of residence, and duration of education.

P values were calculated with Fisher’s exact test. Monte Carlo simulation was used for calculation of the P values for differences in the distribution of serum PSA levels at the time of diagnosis. P values were calculated both with and without Bonferroni correction for multiple testing.

Survival curves were constructed with the Kaplan–Meier method and differences in survival analysed with the log-rank test. The comparison group of men with prostate cancer but no kidney transplant was matched for age, calendar year of prostate cancer diagnosis, county of residence, and duration of education. Multivariable Cox proportional hazards models included GGG, T category, M category, and PSA level at the time of diagnosis, and curative treatment planned within 6 months from the time of diagnosis. Five imputation sets were pooled according to Rubin’s rule using R’s Mice package (R Foundation for Statistical Computing, Vienna, Austria). Hazard ratios (HRs) with 95% CIs were calculated.

R version 3.5.1 was used for statistical analysis, matching and imputation.

### Results

Among 185 579 men with prostate cancer in the NPCR, 133 (0.07%) had a kidney transplant before the date of their prostate cancer diagnosis. Their median (interquartile range [IQR]) age when they received the kidney transplant was 56 (48–62) years. The median (range, IQR) time from the kidney transplantation to the prostate cancer diagnosis was 10 (0–41, 6–18) years. The clinical characteristics of the 133 kidney transplant recipients and of the comparison group of 665 matched men with prostate cancer but no kidney transplant are shown in Table 1. Transplantation related data for the 133 kidney transplant recipients are shown in Table 2.

Amongst the control group of 923 221 prostate cancer-free men in the PCBaSe, 895 (0.1%) had a kidney transplantation a median of 10 years before the date when they were included in the PCBaSe (range 0–46, IQR 5–17 years). These proportions yielded an OR of 0.84 (95% CI 0.70–0.99), which means that the transplant recipients were 16% less likely to be diagnosed with prostate cancer than the matched control men. The ORs calculated for men with non-low-risk cancer and for men with high-risk cancer were similar (Table 3). The ORs did not increase with longer observation time after the transplantation (Table 4).

The 133 transplant recipients that were diagnosed with prostate cancer had more comorbidities than 665 matched men with prostate cancer but no kidney transplant, but their cancer characteristics at the time of diagnosis were similar (Table 1). Slightly smaller proportions of the transplant recipients had a PSA level of 3–9.9 ng/mL at diagnosis (41% vs 53%) and had radical local treatment (37% vs 49%). These differences were of borderline statistical significance (P = 0.03 and P = 0.02), but after Bonferroni correction for multiple testing they were no longer statistically significant (P > 0.1).

Of the 133 kidney transplant recipients with prostate cancer, 12 died from prostate cancer during follow-up (median 9 years). Five of them had localised and seven locally advanced or metastatic disease at the time of diagnosis. The 15-year prostate cancer-specific survival was similar for the transplant recipients and the 665 men with prostate cancer but no kidney transplants (Fig. 1). A multivariable Cox regression analysis, adjusting for differences in cancer characteristics, also showed no difference in survival between patients with prostate cancer with vs without a kidney transplant (HR for prostate cancer death 0.87, 95% CI 0.47–1.62). However, overall survival was 3.7 years shorter for the transplant recipients than for the comparison group of men with prostate cancer but no kidney transplant (8.7 vs 12.5 years, P = 0.003; Fig. 1).

### Discussion

The present nationwide, population-based study investigated the probability of being diagnosed with any or advanced prostate cancer in male kidney transplant recipients compared with the general male population. The present study also compared cancer characteristics and survival of male kidney transplant recipients diagnosed with prostate cancer vs patients with prostate cancer without a kidney transplant. The results gave no indication of that immunosuppression after kidney transplantation increases the risk of prostate cancer or negatively affects prostate cancer outcomes in transplant recipients.

Prostate cancer was slightly less commonly diagnosed in kidney transplant recipients than in control men. The most likely reason is that pre-transplantation investigations excluded some men with prevalent prostate cancer, thereby making the transplanted men a selected group with lower-than-average probability of a prostate cancer diagnosis over the next few years. The present study result that most strongly refutes a prostate cancer-promoting effect of immunosuppression is the absence of any indication of a more rapidly rising incidence of high-risk prostate cancer over time amongst transplant recipients than amongst control men, not even after > 9 years of follow-up. In the Gothenburg screening study, prostate cancer incidence and mortality were both reduced from the end of screening up until 9 years thereafter [24]. It is thus highly
unlikely that the selection bias introduced by pre-
transplantation investigations in our present study would affect
the probability of being diagnosed with a high-risk or
metastatic prostate cancer > 9 years after transplantation.

Some 20–40% of men in their fifties and sixties have a
subclinical prostate cancer [14], which often is missed by
investigations such as DRE, PSA tests and prostate biopsies
[15,25]. One can therefore assume that a substantial
proportion of the transplant recipients in our present study
had an undetected prostate cancer when they started
immunosuppression, despite pre-transplantation investigations
to exclude prostate cancer. Notably, half of the transplant
recipients were transplanted before the mid-1990s, when PSA
testing became common practice in Sweden [26]. Thus, the
transplant recipients in our present study with the longest

Table 1 Clinical characteristics of all 133 Swedish men who between 1998 and 2016 were diagnosed with prostate cancer after kidney transplantation, and for a comparison group of men with prostate cancer without a kidney transplant, matched for age, year of prostate cancer diagnosis, educational duration, and county of residence.

| Clinical characteristics at diagnosis and treatment planned within 6 months from diagnosis | Kidney transplant recipients diagnosed with prostate cancer (n = 133) | Matched men with prostate cancer but no kidney transplant (n = 665) | P* |
|---|---|---|---|
| Age at prostate cancer diagnosis, years | | | |
| Median (IQR) | 65 (61–71) | 66 (61–72) | | |
| <49, n (%) | 0 (0) | 13 (2) | | |
| 50–69, n (%) | 91 (68) | 420 (63) | | |
| ≥70, n (%) | 42 (32) | 232 (35) | | |
| CCI at the time of prostate cancer diagnosis | | | |
| Median (IQR) | 2 (2–3) | 0 (0–0) | | |
| 0, n (%) | 16 (12) | 529 (80) | <0.001 |
| 1, n (%) | 1 (1) | 75 (11) | | |
| 2, n (%) | 59 (44) | 37 (6) | | |
| 3, n (%) | 26 (20) | 17 (3) | | |
| ≥4, n (%) | 31 (23) | 7 (1) | | |
| Risk category, n (%) | | | |
| Low risk | 44 (33) | 208 (31) | | |
| Intermediate risk | 37 (28) | 201 (30) | 0.61 |
| High-risk non-metastatic | 29 (22) | 158 (24) | | |
| Distant metastasis | 13 (10) | 67 (10) | | |
| Missing | 10 (8) | 31 (5) | | |
| GGG, n (%) | | | |
| GGG 1 | 67 (50) | 307 (46) | | |
| GGG 2 or 3 | 46 (35) | 244 (37) | 0.49 |
| GGG 4 or 5 | 17 (13) | 106 (16) | | |
| Missing | 3 (2) | 8 (1) | | |
| PSA level, n (%) | | | |
| <3 ng/mL | 10 (8) | 26 (4) | | |
| 3–9.9 ng/mL | 54 (41) | 351 (53) | 0.03 |
| 10–19.9 ng/mL | 29 (22) | 115 (17) | | |
| 20–99 ng/mL | 26 (20) | 108 (16) | | |
| ≥100 ng/mL | 8 (6) | 52 (8) | | |
| Missing | 6 (5) | 13 (2) | | |
| Local T stage, n (%) | | | |
| T1 | 73 (55) | 360 (54) | | |
| T2 | 39 (29) | 182 (27) | 0.08 |
| T3 | 11 (8) | 93 (14) | | |
| T4 | 3 (2) | 18 (3) | | |
| Missing | 7 (5) | 12 (2) | | |
| M stage, n (%) | | | |
| M0 | 66 (50) | 367 (55) | | |
| MX | 57 (43) | 248 (37) | 0.54 |
| M1 | 10 (8) | 45 (7) | | |
| Missing | 0 (0) | 5 (1) | | |
| Primary treatment, n (%) | | | |
| AS or watchful waiting | 51 (38) | 175 (26) | | |
| Radical prostatectomy | 14 (11) | 206 (31) | 0.02 |
| Radiotherapy | 35 (26) | 119 (18) | | |
| Androgen-deprivation therapy | 28 (21) | 147 (22) | | |
| Other/missing | 5 (4) | 18 (3) | | |

*Without correction for multiple testing.
clinical cancer characteristics at diagnosis. Furthermore, our present results support the subsequent transplantation and, indeed, shortens survival reduces quality of life but also impairs the outcome of a radical prostatectomy before transplantation. The latter is cancer in need of a kidney transplant do not need to undergo We therefore argue that men on AS for a low-grade prostate cancer when they started on immunosuppression. follow-up were particularly likely to have a subclinical prostate cancer when they started on immunosuppression. We therefore argue that men on AS for a low-grade prostate cancer in need of a kidney transplant do not need to undergo a radical prostatectomy before transplantation. The latter is particularly important, as longer time on dialysis not only reduces quality of life but also impairs the outcome of a subsequent transplantation and, indeed, shortens survival [11,12]. Furthermore, our present results support the conclusion from a recent systematic review that kidney transplant recipients with localised prostate cancer should be managed according to standard clinical guidelines [27]. Our present results, based on 133 prostate cancer cases, agree well with the by far largest study of cancer incidence amongst solid transplant recipients (1039 prostate cancer cases) [1], with a meta-analysis of six studies published before 2015 [28], and with a recent study from Australia and New Zealand (41 prostate cancer cases) [16]. At odds with these and with our present study are two smaller studies: one Irish (34 prostate cancer cases) and one Swiss (18 prostate cancer cases), which reported a seven-fold and a four-fold higher prostate cancer incidence in kidney transplant recipients compared with the male population [17,18]. One explanation for the raised incidence amongst Irish kidney transplant recipients is that they, in contrast with Irish men in general, were routinely offered PSA screening [17]. Neither the Irish nor the Swiss study described the method for comparing the prostate cancer incidence in kidney transplant recipients and in the general male population, e.g., whether the analysis was adjusted for differences in age, time period, or duration of follow-up, which makes their results difficult to interpret. In a recent report from the USA National Cancer Institute’s Transplant Cancer Match study, solid organ transplant recipients with localised prostate cancer had an adjusted HR of 1.6 (95% CI 1.1–2.3) for prostate cancer death after radical treatment [29]. Our present study included too few (five) kidney transplant recipients who died from a prostate cancer that was localised at the time of diagnosis to allow for a subgroup analysis similar to the one in the USA study. In the USA study, mortality from all cancer forms was analysed and a very large number of subgroup analyses were done without correction for multiple testing, so some of their statistically significant results may be random chance findings. Of note, is that prostate cancer mortality was not increased in men who had non-curative treatment in the USA study. A nationwide Irish study showed similar clinical outcomes for the 34 men diagnosed with prostate cancer after kidney transplantation as in the male Irish population [17]. However, even if transplant recipients with radically treated localised prostate cancer do have a 60% higher relative risk of dying from prostate cancer, this would translate to a mere 1% absolute increase after 10 years [30]. Considering that over half of the men in our present study died from other causes than prostate cancer within 10 years, a 1% absolute risk increase of prostate cancer death is of little clinical significance and does not outweigh the negative effects of a longer time on dialysis if transplantation is postponed. According to the SNR, the annual overall mortality is 19% in patients on chronic dialysis but only 3% in kidney transplant recipients [31]. A somewhat smaller proportion of men diagnosed with prostate cancer after kidney transplantation had a PSA level in the range 3–9.9 ng/mL at the time of diagnosis. The kidney

| Variable | Kidney transplant recipients diagnosed with prostate cancer (n = 133) |
|----------|---------------------------------------------------------------------|
| Calendar year at transplantation, n (%) |
| 1969–1984 | 22 (17) |
| 1985–1994 | 36 (27) |
| 1995–2004 | 49 (37) |
| 2005–2014 | 26 (20) |
| Age at transplantation, years |
| Median (IQR) | 56 (47–63) |
| <30, n (%) | 6 (5) |
| 30–49, n (%) | 38 (29) |
| 50–69, n (%) | 82 (62) |
| ≥70, n (%) | 7 (5) |
| Time from transplantation to prostate cancer diagnosis, years |
| Median (IQR) | 10 (6–18) |
| <3, n (%) | 16 (12) |
| 3–6, n (%) | 28 (21) |
| 7–9, n (%) | 15 (11) |
| 9–12, n (%) | 18 (14) |
| ≥12, n (%) | 56 (42) |

The ORs were calculated in a case-control study including 185 579 men with prostate cancer and 923 221 matched prostate cancer-free men in the PCBaSe.

| Prostate cancer risk category | OR (95% CI) |
|-----------------------------|-------------|
| Any                         | 0.84 (0.70–0.99) |
| Not low risk                | 0.81 (0.65–1.01) |
| High risk, including N1 and M1 | 0.84 (0.62–1.13) |

| Years after transplantation | OR for a prostate cancer diagnosis (95% CI) |
|-----------------------------|------------------------------------------|
| <3                          | 0.63 (0.39–1.01) |
| 3–6                         | 0.71 (0.45–1.14) |
| 6–9                         | 0.93 (0.62–1.39) |
| 9–12                        | 0.74 (0.46–1.20) |
| ≥12                         | 0.97 (0.74–1.27) |

Table 2 Transplantation related data for all 133 Swedish men who were diagnosed with prostate cancer after kidney transplantation between 1998 and 2016.

Table 3 ORs for a prostate cancer diagnosis up to 47 years after transplantation in Swedish male kidney transplant recipients, stratified by clinical cancer characteristics at diagnosis.

Table 4 ORs for a prostate cancer diagnosis in Swedish male kidney transplant recipients compared with matched control men from the general population, stratified by follow-up time after the transplantation.
transplant recipients were also somewhat less likely to receive radical treatment than recently diagnosed patients with prostate cancer without a transplant. These differences probably reflect that kidney transplant recipients have a shorter life-expectancy as a consequence of higher comorbidity burden, more rapid progression of cardiovascular disease [32,33], and deleterious side-effects of long-term immunosuppression [34]. Strengths of our present study include that it covers the entire population of a whole country, the accuracy of the Swedish registries (which rely on unique personal identification numbers), the long-term follow-up, and the risk category-specific analysis that minimised detection bias from selective PSA testing.

Limitations include lack of exact information about the proportion of kidney transplant recipients that were screened for prostate cancer before transplantation, but since the mid-1990s most Swedish transplantation centres recommend PSA testing as part of the pre-transplant evaluation. Another limitation is that we had no information about recurrence, cancer progression or secondary treatment. The lack of detailed information about the type of immunosuppressing agents used means that we cannot rule out that long-term treatment with some specific agents facilitates progression of prostate cancer.

Conclusions

In the present nationwide study, the diagnosis of any and of advanced prostate cancer, clinical prostate cancer characteristics and prostate cancer-specific mortality were similar amongst male kidney transplant recipients compared with matched control men without a kidney transplant. The probability of an advanced or poorly differentiated prostate cancer did not increase more over time in transplant recipients than in control men. Almost half of the transplant recipients were transplanted before PSA testing became part of the routine pre-transplantation evaluation and more than half had been on immunosuppression for >9 years. Immunosuppression after kidney transplantation is thus unlikely to adversely affect prostate cancer initiation or progression. This suggests that men on AS for a low-grade prostate cancer can be accepted for transplantation without first having to undergo radical treatment for their cancer.

Acknowledgements

This project was made possible by the continuous work of the NPCR steering group: P Stattin (chairman), I. Franck Lissbrant (deputy chairman), K. Hellström (coordinator), F. Sandin, M. Nyberg, O. Bratt, C. Thellenberg Karlsson, Johan Styrke, M. Törnblom, S. Carlsson, M. Hjälm Eriksson, Stefan Carlsson, D. Robinson, M. Andén, J. Hugosson, Olof Ståhl, O. Akre, P. Fransson, E. Johansson and C. Waller (patient representative). The PCBaSe is supported by grants from The Swedish Cancer Society (2016-0700) and the Swedish Research Council (2017-00847). O. Bratt received grants from the Swedish Cancer Society (2016-464).
Conflicts of Interest

Neither Dr Bratt nor any of the other researchers/authors have anything to disclose.

References

1. Engels EA, Pfeiffer RM, Fraumeni JF Jr et al. Spectrum of cancer risk among US solid organ transplant recipients. JAMA 2011; 306: 1891–901
2. Au EH, Chapman JR, Craig JC et al. Overall and site-specific cancer mortality in patients on dialysis and after kidney transplant. J Am Soc Nephrol 2019; 30: 471–80
3. Gin GE, Pereira JF, Weinberg AD et al. Prostate-specific antigen screening and prostate cancer treatment in renal transplantation candidates: a survey of U.S. transplantation centers. Urol Oncol 2016; 34: e9–13
4. Tonkin-Crine S, Pruthi R, Taylor DM et al. Assessing consensus between UK renal clinicians on listing for kidney transplantation: a modified Delphi study. Transplant Direct 2018; 4: e43. DOI: 10.1097/TXD.0000000000000782
5. Nieto T, Inston N, Codynell P. Renal transplantation in adults. BMJ 2016; 355: i6158. DOI: 10.1136/bmj.i6158.
6. Aminsharifi A, Simon R, Polascik TJ et al. Evaluation and active treatment versus active surveillance of localized prostate cancer in renal transplant patients in the era of low and very low risk prostate cancer. J Urol 2019; 202: 469–74
7. Epstein JJ, Allsbrook WC Jr, Amin MB, Egevad LL, Committee IG. The 2005 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma. Am J Surg Pathol 2005; 29: 1228–42.
8. Epstein JJ, Egevad L, Amin MB et al. The 2014 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma: definition of grading patterns and proposal for a new grading system. Am J Surg Pathol 2016; 40: 244–52.
9. Anderson BB, Oberlin DT, Razmara AA et al. Extraprostatic extension is extremely rare for contemporary Gleason score 6 prostate cancer. Eur Urol 2017; 72: 455–60
10. Ross HM, Kryvenko ON, Cowan JE, Simko J, Wheeler TM, Epstein JJ. Do adenocarcinomas of the prostate with Gleason score (GS) 6 have the potential to metastasize to lymph nodes? Am J Surg Pathol 2012; 36: 1346–52
11. Wenger H, Weiner AB, Razmara A, Paner GP, Eggener SE. Risk of lymph node metastases in pathological Gleason score ≤6 prostate adenocarcinoma: Analysis of institutional and population-based databases. Urol Oncol 2017; 35: 31.e1–31.e6
12. Resende L, Guerra J, Santana A, Mil-Homens C, Abreu F, da Costa AG. Influence of dialysis duration and modality on kidney transplant outcomes. Transplant Proc 2009; 41: 837–9
13. Helanterä, Salmela K, KylönenL, Koskinen P, Grönhalgen-Riska C, Finne P. Pretransplant dialysis duration and risk of death after kidney transplantation in the current era. Transplantation 2014; 98: 458–64
14. Bell KJ, Del Mar C, Wright G, Dickinson J, Glasziou P. Prevalence of incidental prostate cancer: A systematic review of autopsy studies. Int J Cancer 2015; 137: 1749–57
15. Thompson IM, Pauker DK, Goodman PJ et al. Prevalence of prostate cancer among men with a prostate-specific antigen level ≤4.0 ng per millilitre. N Engl J Med 2004; 350: 2239–46
16. Vajdic CM, McDonald SP, McCredie MR et al. Cancer incidence before and after kidney transplantation. JAMA 2006; 296: 2823–31
17. Haroon UH, Davis NF, Mohan P et al. Incidence, management, and clinical outcomes of prostate cancer in kidney transplant recipients. Exp Clin Transplant 2019; 17: 298–303
18. Lengwiler E, Stampf S, Zippelius A et al. Solid cancer development in solid organ transplant recipients within the Swiss Transplant Cohort Study. Swiss Med Wkly 2019; 149: w20078. DOI: 10.4414/ smw.2019.20078.
19. Schön S, Ekberg H, Wikström B, Oden A, Ahlmen J. Renal replacement therapy in Sweden. Scand J Urol Nephrol 2004; 38: 332–9
20. Van Hemelrijck M, Wigertz A, Sandin F et al. Cohort profile: the national prostate cancer register of Sweden and prostate cancer data base Sweden 2.0. Int J Epidemiol 2013; 42: 956–67
21. Tomic K, Berglund A, Robinson D et al. Capture rate and representativity of the National Prostate Cancer Register of Sweden. Acta Oncol 2015; 54: 158–63
22. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghi I. WA. New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. J Clin Epidemiol 2004; 57: 1288–94
23. Smith JK, Lambert PC, Botha JL, Jones DR. Providing more up-to-date estimates of patient survival: a comparison of standard survival analysis with period analysis using life-table methods and proportional hazards models. J Clin Epidemiol 2004; 57: 14–20
24. Grenabo Bergdahl A, Holmberg E, Moss S, Hugosson J. Incidence of prostate cancer after termination of screening in a population-based randomised screening trial. Eur Urol 2013; 64: 703–9
25. Ahmed HU, El-Shater Bosaily A, Brown LC et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet 2017; 389: 815–22
26. Bratt O, Berglund A, Adolfsson J et al. Prostate cancer diagnosed after prostate-specific antigen testing of men without clinical signs of the disease: a population-based study from the National Prostate Cancer Register of Sweden. Scand J Urol Nephrol 2010; 44: 384–90
27. Hevia V, Boissier R, Rodríguez-Faba O et al. Management of localised prostate cancer in kidney transplant patients: a systematic review from the EAU Guidelines on Renal Transplantation Panel. Eur Urol Focus 2018; 4: 153–62
28. Shang W, Huang L, Li L et al. Cancer risk in patients receiving renal replacement therapy: a meta-analysis of cohort studies. Mol Clin Oncol 2016; 5: 315–25
29. D’Arcy ME, Coigill AE, Lynch CF et al. Survival after a cancer diagnosis among solid organ transplant recipients in the United States. Cancer 2019; 125: 933–42
30. Stattin P, Holmberg E, Johansson JE et al. Outcomes in localized prostate cancer: National Prostate Cancer Register of Sweden follow-up study. J Natl Cancer Inst 2010; 102: 950–8
31. (SNR) TSRR. Annual Report, 2018. Available at: https://www.medscinet. net/snr/rapporterdocs/Svenskt%20Njurregister%202018.pdf. Accessed August 2019
32. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. Am J Kidney Dis 1998; 32: S112–9
33. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004; 351: 1296–1305
34. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. Am J Transplant 2009; 9 (Suppl. 3): S1–155

Correspondence: Ola Bratt, Department of Urology, Sahlgrenska University Hospital, Bruna stråket 11B, SE-413 45 Gothenburg, Sweden.

e-mail: ola.bratt@vgregion.se

Abbreviations: AS, active surveillance; CCI, Charlson Comorbidity Index; GGG, Gleason Grade Group; HR, hazard ratio; IQR, interquartile range; NPCR, National Prostate Cancer Register of Sweden; OR, odds ratio; PCBAse, Prostate Cancer database Sweden; SNR, Swedish Renal Register.