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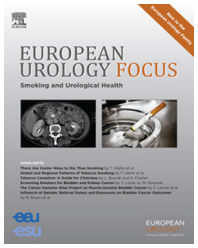

Review – Prostate Cancer

Management of Localised Prostate Cancer in Kidney Transplant Patients: A Systematic Review from the EAU Guidelines on Renal Transplantation Panel

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Abstract

Context: Cancer development after kidney transplant (KT) has become a major problem, and currently, it is one of the primary causes of death in this population. Urological cancers after KT such as prostate cancer (PCa) have also increased, partly due to the increasing age of recipients and prolonged survival. PCa is the second most commonly diagnosed cancer in men, accounting for 15% of all cancers. Managing localised PCa after KT remains challenging because of treating an immunosuppressed patient with a kidney graft in the pelvic cavity. Several papers reporting PCa treatment after KT have been published. Merging all the available data and summarising most important evidence could be useful for scientific community involved in this issue.
Objective: To systematically review all the available evidence in literature regarding the management of localised PCa after KT.
Evidence acquisition: Computerised bibliographic search of Medline, Embase, and Cochrane databases was performed for all studies reporting outcomes of localised PCa diagnosed in KT patients undergoing curative treatments, including surgery, external beam radiotherapy (EBR) and brachytherapy.
Evidence synthesis: In total, 41?studies included 319?patients with localised PCa after KT. Their mean age was 61.8 (range, 47–79) yr and mean time from KT to PCa was 122 (range, 2–336) mo. Mean prostate-specific antigen was 8.5 (range, 0.3–82), most frequent biopsy Gleason score was 3 + 3 (50.5%), 62.1% were cT1-cT2, and 56.1% belonged to low-intermediate D'Amico-risk groups. Surgery was performed in 82.1%. After mean follow-up of 33 (range, 1–240) mo, cancer-specific survival at 5?yr was 97.5%, 87.5%, and 94.4% after surgery, EBR, and brachytherapy, respectively.
Conclusions: Radical prostatectomy is the preferred treatment of localised PCa after KT. Overall oncological outcomes do not seem to be worse than general population when performed in referral centres. Other curative treatments such as EBR or brachytherapy were less frequently used; however, brachytherapy showed promising results in a small number of patients. Further better-quality studies should help to clarify the optimal method of managing localised PCa after KT.
Patient summary: Localised PCa after KT seems to have similar oncological outcomes after curative treatments than in general population, with surgery being the most common option for treatment.

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1. Introduction

Kidney transplant (KT) is the best treatment for patients with end-stage renal disease. Cancer development after KT has become a major concern as it is currently one of the main causes of death in this population. Urological cancers, such as prostate cancer (PCa), also have an increased incidence after KT, which is partly due to the increasing age of recipients and prolonged survival after transplantation. PCa remains the second most commonly diagnosed cancer in men, accounting for 15% of all cancers diagnosed, and the most frequent non-skin solid neoplasm in men who have undergone KT [1]. Majority of them are localised; therefore, they are suitable for undergoing curative treatments according to current clinical practice guidelines [2]. Given the progressive rise in the number of transplants performed and the higher life expectancy of recipients, urological surgeons involved in oncological and transplant surgery have to be familiar while dealing with this clinical situation.

Treatment of localised PCa after KT remains challenging, not only for treating urological cancer in an immunosuppressed patient but mainly due to the presence of the kidney graft in the pelvic cavity and very close to the prostate, which can play a negative role when treating the prostate with surgery or radiation, or even when subsequent kidney transplants need to be considered. In clinical studies, none of the immunosuppressant drugs have clearly demonstrated an increase or decrease in PCa risk; also, its incidence is not clearly increased in this particular population. Thus, several studies have reported a slightly increased incidence while others report a similar [3–5] but without the clear epidemiologic relation seen in other urological cancers such as renal cell carcinoma.

Several papers reporting PCa treatment have been published during last decades. Merging all the available data and summarising most important evidence found could help in providing some recommendations to urological and kidney transplant scientific community involved in treating these patients.

The aim of this study was to perform a systematic review (SR) to appraise all the available evidence regarding the management of localised PCa in renal transplant recipients.

2. Evidence acquisition

2.1. Data sources and searches

This SR was performed according to the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses*: the PRISMA Statement [6]. Databases searched were Embase, Medline, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials. No language or year restrictions were applied. The database search was also complemented by screening the reference lists of the included studies.

2.2. Study selection

Studies eligible for inclusion were those reporting the oncological outcomes of patients who, having a previous KT, were diagnosed and treated for localised PCa with even RP, external beam radiotherapy (EBR), or brachytherapy. There was no language or year restriction. All study designs were eligible for inclusion except for reviews, editorials, or studies published as a conference abstract only. All identified abstracts were placed in a bibliography management software program (EndNote X7) and sorted according to inclusion and exclusion folders by drag and drop. Titles and abstracts of all identified studies were independently reviewed by two authors (VH, RB) and discrepancies resolved by a third reviewer (ORF).

2.3. Data extraction and risk of bias assessment

Data from eligible reports were extracted independently. A data-abstraction sheet was created a priori including year of publication, study type and its level of evidence, number of patients, age, follow-up, time from KT to PCa diagnosis, baseline immunosuppression, prostate-specific antigen (PSA) at diagnosis, biopsy Gleason score, clinical staging (cT), and EAU/D'Amico risk groups. Surgical data included approach, estimated blood loss (EBL), surgical time, and lymph node dissection (LND), whereas radiation data included total dose in Gy, usage or not of androgen deprivation (AD) and its duration. Pathology data included specimen Gleason score, specimen staging (pT, pN), and surgical margins (SM). Outcomes assessed were PCa recurrence, cancer-specific survival (CSS), overall survival (OS), and graft survival (GS) at 1-, 3-, and 5-yr time-points. PSA during follow-up was also collected as well as early (< 3mo) and late (>3 mo) complications according to Clavien-Dindo classification.

2.4. Data synthesis

A narrative synthesis of the data was performed. Primary outcomes (oncological) were PCa recurrence, CSS, and OS. Secondary outcomes (non-oncological) were GS, PSA levels, and complications according to Clavien-Dindo classification system.

3. Evidence synthesis

3.1. Search results

The search retrieved 1042 articles whose abstracts were screened; of this, 991 were excluded. A total of 51 full text articles went on for eligibility assessment. Of these, 16 were excluded. After the hand search of the reference lists of the included full-text papers, another six studies were included. Thus, a total of 41 studies were included in this SR (Fig. 1).

3.2. Characteristics of studies, population, and interventions

The 41 studies included a total of 319 patients with localised PCa after KT treated with radical surgery, EBR, or brachytherapy (Table 1).

All the studies were non-randomised, retrospective, and comparative studies or retrospective case series/reports recruiting patients between 1977 and 2017, all of them with

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