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The Risk of Tumour Recurrence in Patients Undergoing Renal Transplantation for End-stage Renal Disease after Previous Treatment for a Urological Cancer: A Systematic Review

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Abstract

Context: Renal transplantation is the gold standard renal replacement therapy in end-stage renal disease owing to its superior survival and quality of life compared with dialysis. When the potential recipient has a history of cancer, the waiting period before radiotherapy is usually based on the Cincinnati Registry.
Objective: To systematically review all available evidence on the risk of cancer recurrence in end-stage renal disease patients with a history of urological cancer.
Evidence acquisition: Medline, Embase, and the Cochrane Library were searched up to March 2017 for all relevant publications reporting oncologic outcomes of urological cancer in patients who subsequently received a transplantation or remained on dialysis. The primary outcome was time to tumour recurrence. Secondary outcomes included cancer-specific and overall survival. Data were narratively synthesised in light of methodological and clinical heterogeneity. The risk of bias of each included study was assessed.
Evidence synthesis: Thirty-two retrospective studies enrolling 2519 patients (1733 dialysed, 786 radiotherapy) were included. For renal cell carcinomas, the risks of recurrence, cancer-specific, and overall survival were similar between transplantation and dialysis. For prostate cancer, most of the tumours had favourable prognoses consistent with nomograms. Studies dealing with urothelial carcinomas (UCs) mainly included upper urinary tract UC in the context of aristolochic acid nephropathy, for which the risks of synchronous bilateral tumour and recurrence were high. Data on testicular cancer were scarce.
Conclusions: Immunosuppression after renal transplantation does not affect the outcomes and natural history of low-risk renal cell carcinomas and prostate cancer. Therefore, the waiting time from successful treatment for these cancers to

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transplantation could be reduced. Except in the particular situation of aristolochic acid nephropathy, more studies are needed to standardise the waiting period after UC owing to the paucity of data.

Patient summary: Renal transplantation does not appear to increase the risk of recurrence of renal carcinoma or the recurrence of low-risk prostate cancer compared with dialysis. More reliable evidence is required to recommend a standard waiting period especially for urothelial and testicular carcinomas.

1. Introduction

Renal transplantation is the gold standard renal replacement therapy in end-stage renal disease (ESRD) owing to its superior survival and quality of life compared with other replacement therapies [1,2].

The standard procedure for transplantation candidates includes systematic screening for the presence of any active/latent cancer or a history of cancer [3]. In transplantation candidates with a previous history of urological cancer, it can be challenging to decide if patients are suitable for transplantation and if so how long the waiting period prior to transplantation should be. So far, the clinical decision has been mainly based on the Cincinnati Registry, which essentially considers the type of tumour and the time between its treatment and kidney transplantation [4]. The waiting period varies from less than 2 yr to at least 5 yr according to the Registry. However, the Cincinnati Registry has several deficiencies: (1) the treatment and the staging of the disease are not defined, (2) the epidemiology of tumours, (3) the diagnostic and therapeutic procedures/tests have changed, and (4) the prognostic tools have improved.

The objective of this systematic review was to appraise all available evidence on the risk of cancer recurrence in ESRD patients who underwent transplantation after having been successfully treated for a urological cancer. The primary objectives were to determine in patients with chronic kidney disease (CKD) 4/5 and a history of urological cancer, the risk of tumour recurrence after transplantation compared with renal replacement therapy (peritoneal and haemodialysis). The secondary objectives were to report on the overall and cancer-specific survival of transplanted and nontransplanted patients with a history of malignancy and to determine for each urological cancer the minimum tumour-free waiting period prior to transplantation.

2. Evidence acquisition

2.1. Data sources and searches

The systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses [5]. The systematic review protocol was registered with PROSPERO (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016046867). Studies (January 1, 1995, to March 1, 2016) were identified by highly sensitive searches of electronic databases (Medline, Embase, Cochrane library databases). The initial literature search was performed in February 2016 and an updated search performed in March 2017. The search was complimented by additional sources including the reference lists of included studies. The search strategy is described in detail in Supplementary data.

2.2. Study selection

There was no restriction on types of study design. All randomised control studies, nonrandomised comparative studies, and noncomparative studies (single-arm cohort studies, case reports), and meta-analyses published in the English language were included.

2.3. Types of participants

The study population was adults ($\geq$ 18 yr) with CKD 4/5 and previous urological cancer under renal replacement therapy or who subsequently underwent renal transplantation.

2.4. Data collection and data extraction

Following deduplication of abstracts, two reviewers (R.B. and V.H.) screened all abstracts and full-text articles independently. Disagreement was resolved by a third party (M.B.). References cited in all full-text articles were also assessed for additional relevant articles. A standardised data-extraction form was developed a priori to collect information on study design, patient characteristics (sex and age, type of urological cancer, baseline risk of tumour recurrence [based on stage, grade, histology, or risk stratification using nomograms or risk groups]), interventions (duration of dialysis before cancer treatment, type and duration of immunosuppressive regimens, duration of tumour-free period prior to transplantation), and outcome measures (cancer recurrence, cancer-specific, and overall survival).

2.5. Risk of bias assessment

Two reviewers (R.B. and V.H.) independently assessed the risk of bias (RoB) of each included study any discrepancies were revolved by a third reviewer (M.B.). The Cochrane RoB tool was used for RoB assessment. For nonrandomised studies, the tool was modified to include an additional domain to assess the risk of confounding bias. A list of five important potential confounders was developed a priori with clinical content experts (European Association of Urology Renal Transplantation Guidelines Panel) [6,7]. The confounders included were: (1) type of urological cancer, (2) baseline

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