

Increased risk of deficient mismatch repair colorectal cancer and its immediate precursor lesions after kidney transplantation

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Background

Kidney transplant recipients have an increased colorectal cancer (CRC) risk. We hypothesize that impaired immunosurveillance allows progression of sessile serrated lesions (SSL), leading to a higher incidence of immunogenic mismatch repair deficient (dMMR), but not mismatch repair proficient (pMMR) CRC.

Methods

The Dutch pathology registry (PALGA) was linked with the national transplant and cancer registry by probabilistic matching. If mismatch repair (MMR) status was unknown, the tissue was collected centrally, and the MMR status was determined with immunohistochemistry. Combined with data from Statistics Netherlands (CBS), standardized incidence ratios (SIR) were calculated with adjustment for age, sex, and incidence year.

Within the Dutch CRC screening program, kidney transplant patients were 1:4 matched to controls based on age, sex, and year of screening to assess premalignant lesions.

Results

20,181 kidney transplant patients were identified between 2000-2021. 218 CRCs were observed, resulting in an overall SIR of 1.11 (95%CI: 0.96-1.26). dMMR CRC occurred in 27% of kidney transplant patients with CRC (49/181) compared to 13% in the general CRC population (5,640/42,982). This resulted in a relative risk of 2.1 (95%CI:1.6-2.6) which remained significant when stratified for stage. The dMMR SIR was 3.05 (95%CI:2.18-4.25) and pMMR SIR 0.97 (95%CI:0.78-1.22).

1,336 polyps were identified in 488 kidney transplant patients that participated in the Dutch CRC screening program. SSL with dysplasia occurred more often in the transplantation cohort compared to the matched cohort, relative risk 2.3 (95%CI:1.3-3.9).

Conclusion

This nationwide study linked four different registries to retrieve high-quality pathology and clinical data of all kidney transplant patients in the Netherlands over several decades. We show an increased risk to develop dMMR CRC after kidney transplantation but not pMMR CRC in this matched analysis. This is supported by the increased detection of SSL with dysplasia (the immediate precursor of dMMR CRC) in kidney transplant patients at population screening. This would imply the need for adaptations in CRC screening for this patient group.