Risk of cancer in patients with polycystic kidney disease

Tung-Min Yu and colleagues report an increased susceptibility to colon, liver, and kidney cancer in patients with autosomal dominant polycystic kidney disease (ADPKD) before receiving renal replacement therapy, when compared with patients without the disease but with a similar (or no) degree of renal impairment. Large studies have shown an excess risk of cancer in patients with chronic kidney disease, end-stage renal disease, or those on renal replacement therapy. Available data for cancer incidence in patients with ADPKD on dialysis, or after transplantation, show an increased risk of neoplasms, mostly skin and kidney, when compared with the general population, but not to other patients on renal replacement therapy without ADPKD. However, a recent study found patients with ADPKD were at a slightly higher risk of having post-transplant malignancies, when compared with other patients with end-stage renal disease not related to ADPKD. The risk of cancer in patients with ADPKD before renal replacement therapy is still unclear, and the work of Yu and colleagues is undoubtedly welcome.

We would like to comment here on potential misclassification and detection biases that might have inflated cancer incidence in the study. Regarding misclassification, were all patients genetically assessed, or was diagnosis based on family history? 15% of patients with ADPKD have a negative family history, which could lead to misclassification. Although the definition of end-stage renal disease is unambiguous, it seems that the definition of chronic kidney disease is unclear. Which glomerular filtration rate cut-off values were used? How often were patients developing chronic kidney disease assessed? Were all patients with chronic kidney disease comparable in terms of glomerular filtration rate? Progression of chronic kidney disease in patients with cystic kidney disease is associated with kidney cancer, and uneven distribution of chronic kidney disease stages between groups could lead to substantial differences in the incidence of kidney cancer.

Regarding over-diagnosis, patients with ADPKD are at high risk for several comorbidities that might lead to various diagnostic procedures, with potential over-diagnosis of unanticipated findings with an unclear effect. Although the increased prevalence of diverticular disease in patients with ADPKD is debatable, a lower clinical threshold for colonoscopy might contribute to an over-diagnosis bias. An enhanced description of medical procedures (colonoscopy) is necessary. A systematic study showed an association of diverticular disease with colon adenoma, but not carcinoma. A detection bias could result from more colon adenomas than carcinomas being included in the ADPKD group. A better description of cancer type or staging and diagnostic procedures involved would be needed. The question of whether or not patients with ADPKD truly present with a higher risk for neoplasia should also be addressed in a population younger than 20 years. Such analysis would be of particular value in answering whether genetic versus environmental effects were involved in the results from this study, since several paediatric cancers have been associated with mTOR pathway upregulation.

Although Yu and colleagues’ study is well conducted, its limitations need to be considered. Overall, it seems premature for the authors to suggest the study of mTOR inhibitors, which come with their specific sets of undesirable long-term effects, for the prevention of neoplasia in patients with ADPKD.

We declare no competing interests.

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