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Short Communication Open Access

Profound Connection between Chronic Kidney Disease and Both Colorectal Cancer and Renal Cell Carcinoma

Ito C* and Nagata D

Division of Nephrology, Department of Medicine, Jichi Medical University, Japan

Abstract

Cancer risk in maintenance hemodialysis patients has been studied epidemiology, which might be influenced by various factors. On the contrary, investigation of cancer-bearing in non-dialysis chronic kidney disease patients has been rarely reported. Recently, we revealed relatively frequent past history of both colorectal cancer and renal cell carcinoma ahead of dialysis introduction and prevalence of colorectal cancer during the dialysis introduction period. In this article, we discuss the pathological relationship between chronic kidney disease and colorectal cancer and furthermore outline the susceptibility of chronic kidney disease after treatment of renal cell carcinoma.

Keywords: Colorectal cancer; Renal cell carcinoma; Chronic kidney disease; Hypovitaminosis D; Vitamin D receptor polymorphisms; Methylenetetrahydrofolate reductase polymorphisms; Radical nephrectomy

Short Communication

The incidence of malignant tumors in non-dialysis chronic kidney disease (CKD) and end-stage renal disease (ESRD) patients compared with the general population remains under debate [1–3]. Excess tumor burden in these populations is inconclusive, in part because study designs are not prospective, adequate size case-cohort studies. Most research on dialysis patients is conducted on the methodological ground that patient identification and selection processes are simpler than for non-dialysis CKD patients, and that cancer screening is carried out routinely in almost all dialysis centers. At any rate, most of nephrologists or dialysis clinicians realize a fact that it is not rare to encounter cancer-bearing patients when dialysis introduction. Recent study also showed that the most common diagnostic period in which malignant tumors are identified in dialysis patients is after a few of years of dialysis introduction [4].

Vamvakas et al. reported that the potential mechanisms for malignant transformation in ESRD are impaired function of the immune system, reduced antioxidant defense, and accumulation of carcinogenic compounds [5]. Unfortunately, each potential factor has not been verified clinically in ESRD patients since publication of the authors' research. As the mechanisms are either pleiotropic or other genetic or dialysis-related factors, such as exogenous viral infection, exposure to bisphenol A from the dialysis membrane [6] or the presence of diabetes mellitus [7], findings can be difficult to interpret. Individual tissue or organ tumorigenesis is thought to be affected by dialysis duration [8]. To reduce the possibility of these additional factors having an effect, it is desirable that the possible scope of tumorigenesis in CKD patients be limited to non-dialysis CKD or the introduction to dialysis period.

Recently, we reported the relatively-high incidence of colorectal carcinoma CRC before and during the dialysis introduction period [9]. A causal relationship between CKD and CRC have been assumed. Recent epidemiological and gene analysis data suggest that hypovitaminosis D or vitamin D receptor polymorphisms are associated with CRC [10,11]. The anti-tumoral actions of $1,25(OH)_2D_3$ towards CRC are known to be inhibition of proliferation, pro-apoptotic effects, induction of differentiation, inhibition of angiogenesis, and detoxification [12]. Whereas CKD is a well-known cause of hypovitaminosis D [13], the latest meta-analysis negates an association between vitamin D receptor polymorphisms and the development of ESRD [14]. The significance of hypovitaminosis D and vitamin D receptor polymorphisms in CKD patients with CRC is not entirely determined. At this stage, hypovitaminosis D is a promising link between CRC and CKD (Figure 1).

Folate and homocysteine metabolism abnormality is thought to be an independent risk factor for the development of CKD [15,16]; although, serum levels of folate and homocysteine in non-dialysis CKD or ESRD patients with CRC have not been clearly identified. Polymorphic associations in key folate-metabolizing genes, mainly methylenetetrahydrofolate reductase (MFHR), with susceptibility to CRC have been extensively studied. MFHR C677T polymorphism is a common genotype showing increased risk of CKD [17] and CRC [18] (Figure 1), and further studies examining commonality are expected.

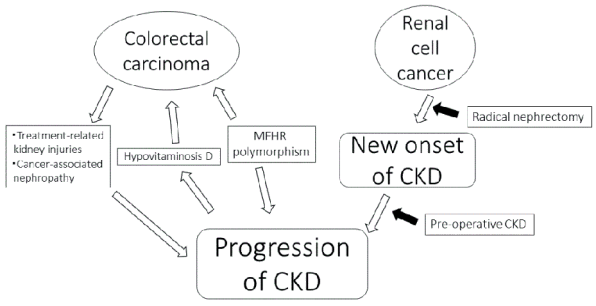

Figure 1: Connection between chronic kidney disease and both colorectal cancer and renal cell carcinoma.

***Corresponding author:** Chiharu Ito, Division of Nephrology, Department of Medicine, Jichi Medical University, Yakushiji 3311-1, Shimotsuke, Tochigi, Japan 329-0498, Tel: +81-285-58-7346; Fax: +81-285-44-4869; E-mail: ichiharu@jichi.ac.jp

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Treatment-related kidney injuries with oxaliplatin [19] and cancer-associated nephropathy are also suggested causes of CKD in CRC patients (Figure 1).

From our previous study, it appeared that a past history of renal cell carcinoma (RCC) was common to dialysis patients [9]. In this study, all patients who had RCC had received unilateral radical nephrectomy (RN). It is evident that patients undergoing RN have a high rate of new onset CKD [20], and that the presence of preoperative CKD is an independent risk factor for further progression of renal insufficiency after renal surgery [21] (Figure 1). A recent Taiwanese study reported that patients with RCC undergoing RN do not have a significantly higher risk of ESRD than those undergoing partial nephrectomy [22]. In that study, the median follow-up was 48 months, which is too short a time to draw any significant conclusions. Follow-up of residual renal function after RN may still be required to intervene before the development of ESRD.

From review and discussion of the above studies, it is suggested that the pathological conditions and treatments of CRC are linked with the development of CKD, and RN for RCC might lead to the development of ERSD. Further research is needed to determine any clinico-epidemiological linkage between these two carcinomas and non-dialysis-CKD or ESRD.

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