High Detection Rate and Risk Factors of Melanosis Coli in End-Stage Renal Disease Patients Awaiting Kidney Transplantation: A Single-Center Retrospective Study in China

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Abstract

Background. Rhubarb-containing Traditional Chinese Medicine (TCM) is widely used to manage chronic renal failure in China. Studies show that anthranoids contained in rhubarb are related to the occurrence of melanosis coli (MC). However, no study on the detection rate of MC in end-stage renal disease (ESRD) patients in China has been reported.

Methods. We conducted a retrospective study on 99 ESRD patients who received a colonoscopy as part of pre-transplant work-up between Jan 1, 2017 and July 1, 2020 in a single center in Beijing, China. 200 age- and gender-matched subjects with normal renal function and received a colonoscopy for health screening in the same period were randomly selected as control group. The detection rate of MC in ESRD patients and control subjects was calculated and compared. Univariate analysis and multivariate logistic regression were performed in succession to determine the association between ESRD and MC, and also probe the independent MC risk factors in ESRD patients.

Results. Among the 99 ESRD patients, MC was detected in 19, with a detection rate of 19.2% (95% confidence interval [CI]: 11.3%, 27.1%). In contrast, among 200 control subjects with normal renal function, MC was only detected in 1 subject, with an detection rate of 0.5% (95%CI: 0.5%, 1.5%) (ESRD vs. control: odds ratio [OR] = 47.263, 95% CI: 6.222, 358.981; $p = 0.000$). After adjustment of age, body mass index(BMI), albumin, hemoglobin and Charlson comorbidity index, being ESRD was still associated with the presence of MC (Odds ratio[95%CI]: 36.251[3.435, 382.559], $p = 0.003$). In ESRD patients, both univariate analysis (OR = 4.358, 95% CI: 1.329, 14.286; $p = 0.012$) and multivariate logistic regression (OR = 4.916, 95% CI: 1.462, 16.525, $p = 0.010$) found that past use of Rhubarb-containing TCM was the only independent risk factor of MC.

Conclusion. The prevalence of MC in this cohort of ESRD patients was 19.2%, which was significantly higher than that of control with normal renal function. Past use of Rhubarb-containing traditional Chinese herbs was the only independent risk factor for the detection of MC in these ESRD patients. Our work highlights firstly that when prescribing Rhubarb-containing TCM to ESRD patients, the risk of MC development should be alerted, and also there is a need for arranging high quality, well-designed studies to examine the prevalence, etiology, impact, management and prognosis of MC in ESRD patients, especially those awaiting kidney transplantation.

Introduction

Chronic kidney disease (CKD) has a high prevalence worldwide, and its prognosis is far from optimal, with renal failure as a frequent outcome, thus shapes a global healthcare challenge. In China, CKD has an overall prevalence of 10.8%, and the prevalence of stages 3 and above CKD is 1.7% ^[1]. Increasing loss of renal function is commonly unavoidable in moderate-to-severe CKD, when the estimated glomerular filtration rate (eGFR) is within $15-59 \text{ ml} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$. The management measure of CKD in this stage, including diet restriction plus keto acid supplementation ^[2], angiotensin-converting enzyme inhibitor

(ACEI) and angiotensin II receptor blocker (ARB) ^[3] etc., is usually somewhat useful but cannot reverse the final fate of CKD. The patients routinely advance into end-stage renal disease (ESRD) and need maintaining replacement therapy though great efforts have been made.

The incurable nature of middle and advanced-stage CKD leaves a place for Traditional Chinese Medicine (TCM) in China. The concept of CKD treatment (≥ 3 stage) in TCM includes supplementing qi, nourishing and activating blood, removing dampness and turbid toxin, clear the triple energizer and so on ^[4]. Hundreds of TCM herbs and numerous patent TCM medicines are widely used to treat chronic renal failure ^[5]. Rhubarb (in Chinese, Dahuang), prepared from the root of the *Rheum palmatum L* plant, is one of the most commonly prescribed herbs, and also is one of the main ingredients in majority of these patent TCM medicines ^[5]. In the concept of TCM, rhubarb has the effect of purgation, anti-stasis, astringent and so on ^[6]. Over 20 kinds of anthraquinones exist in rhubarb, including emodin, rhein, and aloe-emodin etc., which have been explored extensively in China ^[11]. In plenty of clinical studies, Rhubarb was found effective in slowing the progression of CKD, abating uremic symptoms, decreasing serum creatinine, raising hemoglobin levels, and adjusting lipid metabolism ^[5, 8, 9].

However, anthranoids contained in rhubarb have been linked to colonic toxicity, including the induction of melanosis coli (MC) ^[10, 11]. First described by Cruveilhier, in 1829, and named by Virchow in 1857, MC is a so called benign colonic condition featured by non-specific light to dark brown lipofuscin-like pigments in macrophages of colon's lamina propria ^[12, 13]. Lysosomes use apoptotic cells ingested by macrophages and then transported into the lamina propria to generate lipofuscin pigment, is thought to be MC's formation mechanism ^[14, 15]. In recent decades, the detection rate of MC has been progressively increased together with the aging of the people, the increasing popularity of constipation and advances in colonoscopic diagnosis ^[12, 16]. Factors associated with MC include female, elder, constipation and use of anthranoid laxatives ^[16, 17]. The detection rate of MC in China is believed lower than that in Western nations ^[16]. Investigations showed that MC may not be harmless, but a mark of chronic damage of colonic and intestinal mucosa ^[12]. MC is associated with an increased detection rate of adenoma, although the oncogenic effect of MC is still a subject of debate ^[12, 18]. A few studies have reported a link between colorectal cancer and MC ^[19, 20], however, other studies have shown no association ^[21, 22].

To our knowledge, no study concerning the detection rate and risk factors of MC in ESRD patients in China has been published till now, though rhubarb or rhubarb-containing TCM is widely used during the treatment of renal failure. During Jan 1, 2017 to July 1, 2020, we performed screening colonoscopy for some ESRD patients awaiting kidney transplantation. This study examined the detection rate of EC in these patients, compared it with that of a group of age- and gender-matched subjects without renal failure, and examined the risk factors of the development of EC in these patients.

Materials And Methods

Study participants

We performed a retrospective study of 99 ESRD patients who underwent colonoscopy as part of pre-transplant work-up in the eighth medical center of PLA General Hospital, Beijing, China, between Jan 1, 2017 and July 1, 2020. These patients came from different places of China, including Beijing (16 patients), Inner Mongolia (15), Hebei (11), Shanxi (11), Heinan (7), Heilongjiang (6), Tibet (4), Anhui (4), Liaoning (3), and other 13 provinces (22). The inclusion criteria were as follows: predialysis or postdialysis ESRD patients who sought kidney transplantation and underwent screening colonoscopy as part of pre-transplant work-up. The exclusion criteria were as follows: incomplete colonoscopy occurred in the patients, defined as failed to reach the ileocecal junction, due to the inadequate preparation, intolerant pain, tortuosity, stricture, and intro-operative complications. 200 age- and gender-matched subjects with normal renal function and received a colonoscopy for health screening or other minor indications in the same period were randomly selected as control. The following variables were collected from their medical records: age, sex, body mass index (BMI), cause of ESRD, time from serum creatinine elevation to dialysis or colonoscopy, dialysis modality, time on dialysis, blood urea nitrogen, serum creatinine, albumin, hemoglobin, serum parathyroid hormone, serum calcium, serum phosphorus, Charlson comorbidity index, past use of rhubarb-containing TCM, detection of MC. The study was reviewed and approved by the ethics committee of the PLA General Hospital. The requirement for informed consent was waived due to the retrospective design of this study.

Definitions

MC was defined as a gross appearance of brown or black discoloration of the colonic mucosa during colonoscopy^[18]. Pathological evaluation was performed in the cases with other benign and malignant diseases accompanied on colonoscopy.

Statistical analysis

Descriptive statistics were given for all demographic and clinical variables. All available variables were compared between ESRD and control groups, and also compared in ESRD group between patients with and without melanosis coli. After each comparison, all variables with p value of <0.500 were included in a multivariable logistic regression analysis with dichotomized being EC as outcome, for adjusting confounding factors between groups, and for discerning of factors associated with EC in ESRD group respectively. The statistical significance level was set to 0.05. All analyses were performed using Statistical Package for Social Sciences (SPSS) software version 21.

Results

Demographic and clinical characteristics of study population

Demographic and clinical characteristics of study population are shown in Table 1. There were no statistically significant difference in age (43.3 ± 11.0 vs. 44.6 ± 10.9 , $p = 0.339$) and distribution of sex (male 77[77.8%] vs. 155[77.5%], $p = 0.957$) between the two groups. The BMI of ESRD group was significantly lower than that of control group (22.7 ± 3.7 vs. 24.7 ± 3.8 , $p = 0.000$). In ESRD group, the

cause of ESRD was glomerulonephritis in 71 cases (71.7%), diabetic nephropathy in 16 cases (16.2%), hypertensive nephropathy in 7 cases (7.1%), polycystic kidney disease in 2 cases (2.0%), and unspecified in 3 cases (3.0%). The median time elapsed from serum creatinine elevation to dialysis or colonoscopy was 36 (IQR 12-72) months. Sixty-three ESRD patients (63.6%) were undergoing hemodialysis, 9 (9.1%) were undergoing peritoneal dialysis, and 27 (27.3%) were receiving predialysis care. Their median time on dialysis was 2.4 (IQR 0.0-10.8) months. Blood urea nitrogen (25.4 ± 9.8 vs. 4.9 ± 1.4 mmol/L, $p = 0.000$) and serum creatinine (909.6 ± 282.8 vs. 71.8 ± 13.7 μ mol/L, $p = 0.000$) was significantly higher, while albumin (36.9 ± 5.5 vs. 42.0 ± 8.2 g/L, $p = 0.000$) and hemoglobin (99.9 ± 19.5 vs. 143.1 ± 15.7 g/L, $p = 0.000$) was significantly lower in ESRD group vs. control group. The serum parathyroid hormone, calcium and phosphorus was 200.9 (IQR 104.1–330.0) pg/ml, 2.15 ± 0.21 mmol/L and 2.05 ± 0.55 mmol/L respectively in ESRD group. Charlson comorbidity index was low in both group, but significantly higher in ESRD group (1 [0–2] vs. 0 [0–1], $p = 0.007$), while the number of patients with ≥ 1 comorbidity was similar between the two groups (37 [37.4%] vs. 81 [40.5%], $p = 0.603$).

Table 1

Demographic, clinical characteristics and prevalence of melanosis coli in ESRD patients vs. control.

	ESRD group(n = 99)	Control group(n = 200)	Odds ratio(95%CI)	P- value
Age (years)	43.3 ± 11.0	44.6 ± 10.9	N.A.	0.339
Male, n(%)	77(77.8%)	155(77.5%)	1.016(0.570, 1.812)	0.957
Body mass index (kg/m ²)	22.7 ± 3.7	24.7 ± 3.8	N.A.	0.000
Cause of ESRD, n(%)				
Glomerulonephritis	71(71.7%)	N.A.	N.A.	N.A.
Others	28(28.3%)	N.A.	N.A.	N.A.
Diabetes	16(16.2%)	N.A.	N.A.	N.A.
Hypertension	7(7.1%)	N.A.	N.A.	N.A.
Polycystic kidney disease	2(2.0%)	N.A.	N.A.	N.A.
Unspecified	3(3.0%)	N.A.	N.A.	N.A.
Time from serum creatinine elevation to dialysis or colonoscopy (months)	36(12–72)	N.A.	N.A.	N.A.
Dialysis modality, n(%)				
Pre-dialysis	27(27.3%)	N.A.	N.A.	N.A.
Post-dialysis	71(71.7%)	N.A.	N.A.	N.A.
Hemodialysis	63(63.6%)	N.A.	N.A.	N.A.
Peritoneal dialysis	9(9.1%)	N.A.	N.A.	N.A.
Time on dialysis (months)	2.4(0.0– 10.8)	N.A.	N.A.	N.A.
Blood urea nitrogen (mmol/L)	25.4 ± 9.8	4.9 ± 1.4	N.A.	0.000
Serum creatinine (μmol/L)	909.6 ± 282.8	71.8 ± 13.7	N.A.	0.000
Albumin (g/L)	36.9 ± 5.5	42.0 ± 8.2	N.A.	0.000
Hemoglobin (g/L)	99.9 ± 19.5	143.1 ± 15.7	N.A.	0.000

Note: data are presented as mean ± standard deviation (SD), median (25–75% IQR[interquartile range]) or n(%) as appropriate.

Abbreviations: CI, confidence interval; ESRD, end-stage renal disease; n, number; N.A., not applicable; N.D., no data; TCM, Traditional Chinese Medicine.

	ESRD group(n = 99)	Control group(n = 200)	Odds ratio(95%CI)	P-value
Serum parathyroid hormone (pg/ml)	200.9(104.1–330.0)	N.D.	N.A.	N.D.
Serum calcium(mmol/L)	2.15 ± 0.21	N.D.	N.A.	N.D.
Serum phosphorus (mmol/L)	2.05 ± 0.55	N.D.	N.A.	N.D.
Charlson comorbidity index	1(0–2)	0(0–1)	N.A.	0.007
≥ 1 comorbidity, n(%)	37(37.4%)	81(40.5%)	0.877(0.534, 1.439)	0.603
Past use of Rhubarb-containing TCM herbs, n(%)	52(52.5%)	N.D.	N.D.	N.D.
Presence of melanosis coli, n(%)	19(19.2%)	1(0.5%)	47.263(6.222, 358.981)	0.000
Note: data are presented as mean ± standard deviation (SD), median (25–75% IQR[interquartile range]) or n(%) as appropriate.				
Abbreviations: CI, confidence interval; ESRD, end-stage renal disease; n, number; N.A., not applicable; N.D., no data; TCM, Traditional Chinese Medicine.				

Detection rate of EC in the ESRD patients vs. control

Prevalence of EC in the two groups is also shown in Table 1. Among 99 ESRD patients, MC was detected in 19, with a prevalence of 19.2% (95% confidence interval[CI]: 11.3%, 27.1%). In contrast, among 200 control subjects, MC was detected in only 1, with an prevalence of 0.5% (95%CI: 0.5%, 1.5%) (ESRD vs. control: odds ratio[OR] = 47.263, 95% CI: 6.222, 358.981; p = 0.000). Logistic regression analysis of variables associated with melanosis coli is shown in Table 2. As shown, after adjustment of age, BMI, albumin, hemoglobin and Charlson comorbidity index, being ESRD was still associated with the suffer from MC (Odds ratio[95%CI]: 36.251[3.435, 382.559], p = 0.003).

Table 2

Logistic regression analysis of variables associated with melanosis coli in the whole population.

Variable	Crude		Adjusted	
	Odds ratio (95%CI)	P-Value	Odds ratio (95%CI)	P-Value
Age	0.972(0.934, 1.012)	0.173	0.973(0.922, 1.026)	0.315
Body mass index	0.889(0.783, 1.010)	0.071	0.992(0.857, 1.147)	0.909
Albumin	0.901(0.829, 0.979)	0.014	1.004(0.917, 1.100)	0.928
Hemoglobin	0.961(0.943, 0.978)	0.000	0.995(0.968, 1.022)	0.700
Charlson comorbidity index	1.247(0.800, 1.945)	0.329	1.078(0.645, 1.800)	0.775
ESRD	47.263(6.222, 358.981)	0.000	36.251(3.435, 382.559)	0.003
Abbreviations: CI, confidence interval; ESRD, end-stage renal disease.				

Factors associated with detection of EC in ESRD patients

In ESRD patients, both univariate analysis (OR = 4.358, 95% CI: 1.329, 14.286; $p = 0.012$; as shown in Table 3) and multivariate logistic regression (OR = 4.916, 95% CI: 1.462, 16.525; $p = 0.010$; as shown in Table 4) found that past use of Rhubarb-containing TCM herbs was the only independent risk factor of MC.

Table 3
Demographic and clinical variables in ESRD patients with vs. without melanosis coli.

	MC(n = 19)	Non-MC(n = 80)	Odds ratio(95%CI)	P-value
Age (years)	40.2 ± 12.1	44.1 ± 10.6	N.A.	0.162
Male, n(%)	13(68.4%)	64(80%)	0.542(0.178, 1.646)	0.275
Body mass index (kg/m ²)	22.5 ± 3.4	22.8 ± 3.8	N.A.	0.705
Cause of ESRD - Glomerulonephritis, n(%)	14(73.7%)	57(71.3%)	1.130(0.365, 3.498)	0.832
Time from serum creatinine elevation to dialysis or colonoscopy (months)	36(12–96)	36(24, 72)	N.A.	0.517
Post-dialysis, n(%)	12(63.2%)	60(75.0%)	0.571(0.198, 1.650)	0.297
Time on dialysis(months)	1.2(0–6)	2.4(0.15, 10.8)	N.A.	0.229
Blood urea nitrogen(mmol/L)	25.3 ± 9.1	25.5 ± 10.0	N.A.	0.942
Serum creatinine(μmol/L)	852.2 ± 242.5	923.3 ± 291.3	N.A.	0.327
Albumin (g/L)	37.2 ± 4.7	36.9 ± 5.6	N.A.	0.788
Hemoglobin (g/L)	99.6 ± 16.0	100.0 ± 20.3	N.A.	0.937
Serum parathyroid hormone(pg/ml)	204.8(158.6–300.0)	200.5(91.7, 379.8)	N.A.	0.628
Serum calcium(mmol/L)	2.12 ± 0.19	2.15 ± 0.21	N.A.	0.535
Serum phosphorus(mmol/L)	2.06 ± 0.38	2.05 ± 0.59	N.A.	0.903
Charlson comorbidity index	1(0–1)	1(0, 2)	N.A.	0.507
≥ 1 comorbidity, n(%)	8(42.1%)	29(36.3%)	1.279(0.462, 3.541)	0.635
Past use of Rhubarb-containing TCM herbs, n(%)	15(78.9%)	37(46.3%)	4.358(1.329, 14.286)	0.010
Note: data are presented as mean ± standard deviation (SD), median (25–75% IQR[interquartile range]) or n(%) as appropriate.				
Abbreviations: CI, confidence interval; ESRD, end-stage renal disease; MC, melanosis coli; n, number; N.A., not applicable; TCM, Traditional Chinese Medicine.				

Table 4
Logistic regression analysis of factors associated with melanosis coli in ESRD patients.

Variable	Crude	Adjusted		
	Odds ratio (95%CI)	P- Value	Odds ratio (95%CI)	P- Value
Age	0.968(0.924, 1.013)	0.164	0.960(0.912, 1.011)	0.118
Male	0.542(0.178, 1.646)	0.280	0.354(0.096, 1.307)	0.119
Post-dialysis	0.572(0.198, 1.650)	0.301	0.614(0.160, 2.354)	0.447
Time on dialysis	0.984(0.947, 1.023)	0.415	0.993(0.949, 1.038)	0.743
Serum creatinine	0.999(0.997, 1.001)	0.325	0.999(0.997, 1.001)	0.541
Past use of Rhubarb-containing TCM herbs	4.358(1.329 14.286)	0.015	5.748(1.549, 21.324)	0.009
Abbreviations: CI, confidence interval; ESRD, end-stage renal disease; TCM, Traditional Chinese Medicine.				

Discussion

As far as we know, this is by far the first article concerning the detection rate and risk factors of EC in ESRD patients. Our patients came from different places of China, which means that they have good representativeness. The major finding of our study is that the detection rate of EC in those ESRD patients reached as high as 19.2%, as compared to 0.5% in the control subjects with normal renal function. After adjusting confounding factors, the detection rate of EC in ESRD group was still higher than that in control. Furthermore, both univariate and multivariate analysis showed that past use of rhubarb-containing TCM medicine was the only risk factor for detection of EC in ESRD patients. AlAmeel T et al ^[23] published their screening colonoscopic results in 169 renal transplant candidates, but no MC was reported. Zheng Y et al ^[24] also reported no MC in 469 screening colonoscopies during kidney transplant evaluation. The difference between their results and ours maybe come from the different population, different treatment background and different focus of attention.

Different detection rates of EC in general population have been reported by different studies in the literature. In autopsy studies, the prevalence of EC is relatively high. In one study, MC was found in 119 of 200 consecutive autopsies, with a prevalence of 59.5% ^[25]. In another international multicentre study ^[26], MC was found in 34% of all autopsies. However, in endoscopic studies, the figure was much lower. Wittoesch JH et al ^[17] reported that 750 cases of MC was found in 91,472 colonoscopies from 1950 to 1954 at the Mayo Clinic, with a prevalence of 0.82%. In another series of patients, he found 137 cases of

MC in 12,131 routine proctoscopic examinations from March 1 to September 30, 1955, giving a prevalence of 1.13%^[17]. Wang S et al^[16] conducted a multicenter study in China, and detected 6,090 cases of MC in 342,922 colonoscopies between January 2006 and October 2016, obtaining a detection rate of 1.78%. Our study is an endoscopic study, so in control subjects with kidney function normal, we observed a detection rate in a similar level, which was 0.5%. Our detection rate is lower than that reported by Wang S et al^[16], possibly because our patients are much younger (mean 44.6 vs. 60 years old). Data showed that elder age was related to higher detection rate of EC. In age ≤ 44 years group of Wang S et al study^[16], the detection rate of MC was 0.85, which was much similar to our results.

On the other hand, in ESRD group, we found 19 cases of MC in 99 ESRD patients, with a detection rate of 19.2%, which was astonishingly higher than that of control group. After adjusting age, BMI, serum albumin, hemoglobin, charlson comorbidity index, the detection rate in ESRD group was still higher than control, which means that other factors related to ESRD were the cause. In the second part of the study, we examined the risk factors of MC in ESRD patients using univariate and multivariate analyses, and found that only past use of rhubarb-containing TCM medicine was associated with the detection of MC. Rhubarb has long been found as a risk factor of MC. The study results of Badiali D et al^[27] showed that MC was significantly associated with consumption of anthracene drugs. They found that the prevalence of MC in patients taking anthracene drugs was significantly higher (52.0%) than that without taking anthracene drugs (8.0%)^[27]. Wittoesch JH et al^[17] reported that in 750 MC patients, 718 were habitual users of laxatives, while in another series of 137 MC patients, laxatives were used regularly by 132 patients, in which 113 patients used cathartics containing emodin. In an animal study, Chen JY et al^[14] fed extract of crude rhubarb to guinea pigs for 60 days, and found that rhubarb successfully induced MC with a dosage dependent manner. In another animal study, Cheng Y et al^[15] fed rhubarb extract to Sprague-Dawley rats for 90 days, and saw MC formation in the rats' colon. They also found that rhein was the metabolite of rhubarb responsible for its toxicity^[15]. Our study showed that in 19 ESRD and with MC patients, 15 (78.9%) used rhubarb-containing TCM herbs in the past, while in 80 ESRD and without MC patients, 37 (46.3%) used such herbs, which means a significant difference. Our results indicate that in ESRD patients, consumption of rhubarb-containing TCM medicine carries the risk of MC development, just as in general population with normal renal function.

The relationship between EC and colorectal neoplasm has long been a concern. Liu ZH et al^[12] reported that MC is associated with a higher incidence of colonic non-adenoma polyps, low-grade adenomas, and distal ileal ulcers, which means that MC may not be a harmless pigmentation, but an indication of chronic colonic and intestinal injury. Blackett JW et al^[28] reported that the presence of MC was associated with increased adenoma detection. Siegers CP^[19] found in a prospective study of 1095 patients that the incidence of EC was 6.9% for patients with normal endoscopy, 9.8% for patients with adenomas and 18.6% for patients with colorectal carcinomas. A relative risk of 3.04 (1.18, 4.90; 95% confidence interval) was calculated for colorectal cancer as a result of MC from these data^[19]. Morgenstern L et al^[20] reported that 17% of MC was accompanied by invasive adenocarcinoma. The

data of Biernacka-Wawrzonek D et al ^[29] showed that colon cancer was found in 11.9% of MC patients. Given that ESRD patients undergoing kidney transplantation already have a significantly higher risk of colorectal cancer ^[30], the high prevalence of EC in ESRD patients may further raise this risk.

There exist a number of limitations in this study. Firstly, this is a retrospective study, so selection bias can't be avoided. Secondly, this is a single center study, the sample size is relatively small, and only Chinese population is included. Thirdly, because the data is derived from medical record review, sometimes there is the problem of incoherence, inconsistent in the information provided. For example, bowel habit such as constipation or diarrhea was not described in detail but marked as normal in most of the patients, possibly because it's not directly related to the condition for hospitalization, thus can't be analyzed as an risk factor. Therefore, future prospective, multicenter, multi-national, well-designed studies with large sample size are warranted to assess the detection rate and risk factors of MC in ESRD patients.

In conclusion, there is a significantly higher detection rate of EC in this cohort of ESRD patients than control subjects without renal failure. The detection of EC in ESRD patients is independently related to the past use of rhubarb-containing TCM herbs. We feel that use rhubarb-containing TCM herbs to treat renal failure is the main reason for the occurrence of EC, and therefore recommend take cautions when prescribing those kind of therapies in renal failure patients. Caution of the development of EC should also be placed in the package inserts of rhubarb-containing TCM medicine. Considering that EC is a sign of colonic and intestinal mucosa injury, and the possible association of MC with development of colorectal cancer, the clinical significance of the high detection rate of EC in ESRD patients, and its influence on the long-term prognosis of kidney transplantation, demands further study in the future.

Declarations

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Data Availability Statements

The data underlying this article will be shared on reasonable request to the corresponding author.

Authors' contributions

Zhang W conceived and designed the study and wrote the manuscript. Zhou W, Wang Y, Li Y and Huang W participated in data collection and analysis. All authors were involved in drafting and revising the manuscript, providing intellectual content of critical importance to the work described and approving the final version of the manuscript.

Conflict of interest statement

The authors declare that they have no conflict of interest to disclose. The results presented in this article have not been published previously in whole or part, except in abstract format.

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