A Retrospective Survey of Patients Undergoing Maintenance Hemodialysis vis-à-vis Cancer Prevalence

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Abstract: The present study investigated the cancer prevalence and anticancer treatment patients undergoing hemodialysis at Nagoya Memorial Hospital. We retrospectively analyzed 663 patients undergoing hemodialysis between September 2014 and August 2019, including patient characteristics such as age, sex, and underlying diseases, cancer type, and cancer treatment. Seventy-eight patients (11.9%) of the dialysis population were diagnosed with cancer. Cancer type was then compared between registered cancer patients undergoing maintenance dialysis (N = 78) and non-dialysis controls (N = 3279) during the same period.

Colorectal carcinoma is the most common malignancy diagnosed in our hospital, accounting for approximately 15% of all types of cancers. The data of anticancer treatment for this disease were compared between dialysis patients (N = 15) and controls (N = 563), whose clinical stages were defined according to the Japanese Classification of Colorectal, Appendiceal, and Anal Carcinoma. Since the need to administer chemotherapeutic agents to dialysis patients with colorectal carcinoma will increase, oncologists should collaborate with nephrologists to cautiously manage anticancer treatment to avoid severe toxicities.

Keywords: Hemodialysis, cancer incidence, colorectal carcinoma, anticancer treatment.

INTRODUCTION

In Japan malignancy has been the leading cause of death since 1980, and colorectal carcinoma is the most common type of cancer [1]. The incidence of colorectal carcinoma worldwide is predicted to increase from 1.3 million in 2012 [2] to 2.5 million new cases in 2035 [3]. The link between cancer and chronic kidney disease (CKD) can be explained by several mechanisms such as impaired immunity and release of cytokines [4]. Previous reports suggested that the risk of cancer development increased in patients with CKD and those undergoing maintenance dialysis [4, 5]. Several observational studies have supported the idea that the incidence of cancers in chronic dialysis patients is elevated compared with the general population [6-10]. expectancies of patients undergoing hemodialysis are recently increasing, and cancer is being recognized as a major cause of morbidity in the dialysis population [11]. Recent progress chemotherapy has prolonged the survival of cancer patients, and the need to administer chemotherapeutic agents to cancer patients undergoing dialysis will increase shortly [12, 13]. Clinicians caring for patients with this combination of diseases must develop expertise and become competent "onco-nephrologists"

To evaluate the risk of cancer in patients undergoing hemodialysis, we first determined the prevalence of various carcinomas at Nagoya Memorial Hospital during the past 5 years. We then compared the cancer sites between the dialysis population and non-dialysis controls. Lastly, we examined the anticancer treatment, especially in patients with colorectal carcinoma, which is one of the most common malignancies.

METHODS

Medical records were retrospectively reviewed to analyze patients undergoing hemodialysis during September 2014 and August 2019, including patient characteristics such as age, sex, and underlying diseases, cancer type, and cancer treatment. The chart review was approved by the ethics committee of our hospital (No 201606). Data on registered cancer patients were used to identify and enroll in non-dialysis controls. Cancers were defined using the International Statistical Classification of Disease and Related Health Problems, Tenth Revision (ICD -10), and patients diagnosed with cancer before the initiation of dialysis and who died within 28 days from the start of dialysis were excluded from analysis. The stage of colorectal carcinoma was classified according to the Japanese

^{[14],} because the appropriate dosing of anticancer agents is critical for preventing serious side effects while maintaining the therapeutic efficacy [15].

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Classification of Colorectal, Appendiceal, and Anal Carcinoma Third English Edition [16].

RESULTS

Overall 663 patients (460 males, 197 females) underwent hemodialysis at least once at the Nagoya Memorial Hospital during the past 5 years. Of these, 102 patients had cancer; however, after abiding by the exclusion criteria mentioned in the method section, there remained 78 hemodialysis patients suffering from cancer (11.9%). The age distribution of the 663 patients is shown in Table 1, which demonstrates that cancer incidence was high from the forties to the seventies. In the 78 patients undergoing maintenance dialysis, the most frequent cancer sites were the kidney (N = 16), colon/rectum (N = 15), stomach (N = 13), and lung/bronchus (N = 8) (Table 2). Cancer sites in dialysis patients were then compared with those in the non-dialysis controls (N = 3279). Colorectal carcinoma was the most common malignancy (N = 630) among all types of cancers diagnosed in our hospital. The clinical stages of 578 patients with this malignancy could be determined (dialysis: 15 and non-dialysis: 563) (Table 3). The rate of colorectal carcinoma among all types of cancers was similar between the patients undergoing maintenance dialysis (19.2%, 15/78) and non-dialysis patients (17.2%, 563/3279). In contrast, the rate of renal cell cancer was much higher in dialysis patients (20.5%, 16/78) than in the non-dialysis controls (1.2%, 39/3279).

We then examined antineoplastic treatment in dialysis patients; surgery was conducted in 14/16

Table 1: Age Distribution of Hemodialysis Patients

Age (Years)	30-39	40-49	50-59	60-69	70-79	80-89	90 <	Total
Dialysis patients	4	21	69	132	235	179	23	663
Male	4	15	54	94	166	118	9	460
Female	0	6	15	35	68	61	12	197
Cancer	0	3	11	19	28	16	1	78
Cancer incidence (%)	0	14.3	15.9	14.4	11.9	8.9	4.3	11.9

Table 2: Comparison of Cancer Site between Dialysis Patients and Non-Dialysis Controls

	Total	Dialysis	Non-dialysis
Colon/ rectum	630	15	615
Stomach	339	13	326
Lung	318	8	310
Prostate	282	4	278
Urinary tract	229	4	225
Breast	217	1	216
Uterus	197	0	197
Lymphoma	181	2	179
Leukemia	161	3	158
Pancreas	117	2	115
Liver	101	1	100
Soft tissue	91	3	88
Myeloma	60	3	57
Kidney	55	16	39
Biliary	55	2	53
Unknown origin	33	1	32
Total	3357	78	3279

Table 3: Stage Classification of Colorectal Cancer

	0	I	11	III	IV	Total
Total	136	112	111	111	108	578
Dialysis patients	3	6	4	0	2	15
Non-dialysis controls	133	106	107	111	106	563

The stage of colorectal cancer was classified according to the Japanese Classification of Colorectal, Appendiceal, and Anal Carcinoma, Third English Edition [16]. Among the 630 registered cancer cases in the Nagoya Memorial Hospital, 578 cases could be determined from the registered data, including patients on dialysis (N = 15) and non-dialysis controls (N = 563).

Table 4: Anticancer Treatment for Colorectal Cancer

	Dialysis patients	Non-dialysis controls	
Endoscopic treatment	6/15	163/563	
Surgery	8/15	312/563	
Chemotherapy	0/15	170/563	

patients with carcinoma of renal origin, 8/15 patients with colorectal carcinoma, 5/13 patients with gastric carcinoma, and 3/8 patients with lung carcinoma. Chemotherapy was administered to two patients with carcinoma of renal origin, and six patients with lung carcinoma received chemotherapeutic agents, whereas none of the patients with colorectal carcinoma received chemotherapeutic cycles. Among the patients with colorectal carcinoma patients, the rates of endoscopic and surgical treatment were comparable between patients undergoing maintenance dialysis (40.0%, 6/15 and 53.3%, 8/15) and those of the non-dialysis controls (28.9%, 163/563 and 55.4%, 312/563), while the rate of chemotherapy was incompatible between the two groups of patients (0%, 0/15 vs. 30.2%, 170/563) (Table 4).

DISCUSSION

Most patients with end-stage renal disease undergoing dialysis die of either cardiac disease or

infection [15], with malignancy being the third most common cause of death in Japan [8]. Recent studies have confirmed that the standardized incidence ratio (SIR) of malignancy should be high in dialysis patients (Table 5) [6-10]. The occurrence of common solid carcinomas such as colorectal, breast, lung, and stomach has not increased in the dialysis population, whereas the occurrence of carcinoma of renal origin has consistently increased. Our present study also demonstrated that the risk of carcinoma of renal origin was elevated in dialysis patients. One possible factor for this occurrence may be the fact that acquired cystic kidney disease observed in end-stage renal failure is associated with an increased occurrence of renal cell carcinoma.

The prevalence of colorectal carcinoma, the second largest in our dialysis population, was similar to that in the non-dialysis controls, although individuals with CKD were found to have a significantly increased risk of colorectal carcinoma compared with the general

Table 5: The Risk of Cancer in Dialysis Patients

	SIR Overall malignancy	95%CI	SIR Kidney cancer	95% CI	SIR Colorectal cancer	95% CI	References
Taiwan	1.4	1.3-1.4	7.2	5.7-8.9	1.0	0.9-1.1	Lin HF (2012)
USA	1.42	1.41-1.43	4.03	3.88-4.19	1.27	1.23-1.30	Butler AM (2015)
Japan (Male)	1.07	1.00-1.14	3.59	2.77-4.51	0.93	0.74-1.15	Kaizu K (2015)
China	1.44	1.26-1.65	12.28	8.44-17.08	1.53	1.11-2.05	Cheung CY (2016)
Korea	1.71	1.61-1.81	6.75	4.85-9.60	1.36	1.20-1.53	Kwon SK (2019)

SIR= standardized incidence ratio. 95% CI= 95% confidence interval.

population in a previous review [17]. This discrepancy may have arisen due to the difference in the study population; our study dealt with dialysis patients only, whereas the systematic review analyzed patients with CKD, including renal transplant patients. The overall incidence of cancer was found to be markedly increased after transplantation (SIR, 3.27; 95% confidence interval [CI], 3.09 - 3.46), whereas during dialysis it was only slightly increased (SIR, 1.35; 95% CI, 1.27 - 1.45) [5].

The incidence of cancer may further increase with the progressive aging of the dialysis patients [8, 12]. However, physicians have indeed been reluctant to use anticancer drugs in cancer patients undergoing dialysis, because very little is known about the optimal timing and dosage adjustments depending on the dialysis session. Colorectal carcinoma, the most common type of malignancy in Japan [1], is a major threat to human health [2, 18]. Our hospital had no experience in administering chemotherapeutic agents to colorectal carcinoma patients undergoing dialysis, until 2019, as shown in Table 4; however, the need for anticancer treatment in patients with comorbidities is certain to be increased. At the time of writing up this study, a metastatic colonic cancer patient undergoing chronic dialysis was receiving FOLFIRI combined with panitumumab [19] followed by oxaliplatin-based chemotherapy. The dosage of chemotherapeutic agents used in such dialysis patients frequently requires dosage adjustment to avoid severe toxicities [15]. Oncologists should collaborate with nephrologists and cautiously manage anticancer treatment. The field of onco-nephrology, which includes anticancer treatment for dialysis patients, should be associated with the management of acute kidney injury, CKD, and various electrolyte imbalances in cancer patients as well as kidney-related toxicities caused by chemotherapeutic agents or immunotherapies [14, 20].

Our study bears several limitations for performing statistical analysis. First, only few cases could be gathered and the clinical data were derived from only one hospital. Second, it was a retrospective study and information on cancer risk including family history and smoking was absent from our data. Third, we could not categorize the reason for dialysis in terms of the etiology due to the lack of such information in some patients.

CONCLUSION

In conclusion, an increased risk of developing carcinomas of various organs has been observed in our patients undergoing chronic dialysis. Among this colon/rectum remains one of the most common cancer sites in both dialysis patients and non-dialysis controls. As, with the advancing technology, the life expectancy of the dialysis population is increasing along with an increased risk of a greater number of such patients developing colorectal carcinoma, it feels imperative to provide comprehensive and safe chemotherapy for this group of patients.

DECLARATIONS

Availability of data and material: Technical appendix and dataset are available from the corresponding author at kina@hospy.or.jp

COMPETING INTERESTS

The authors have no conflict of interest to declare.

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AUTHOR'S CONTRIBUTIONS:

K.I. and S.K. are responsible for manuscript publication. K.I. and Y.O. designed the study. K.I., Y.H., K.I., M.T., and M.S. collected data. K.I., M.K., and Y.O. wrote the manuscript.

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