

Prediction of Emergency Hospitalization of Outpatients Receiving Cancer Chemotherapy

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Abstract. The purpose of this study was to establish criteria to predict the need for emergency hospitalization of patients receiving chemotherapy, based on information at presentation. 158 consecutive patients treated for cancer at the Cancer Chemotherapy Center in the University of Occupational and Environmental Health were examined. The number of emergency hospitalization cases for outpatients undergoing cancer chemotherapy was 14 (8.9%) and including seven lung carcinomas, six hematological carcinomas, and one mediastinal tumor. The reason for emergency hospitalization in twelve (85.7%) of the cases was infection. No significant difference was observed between the cases with and without emergency hospitalization regarding age, gender, cancer type, previous treatment, objective of the chemotherapy, or line of chemotherapy. A significantly higher number of the emergency cases were associated with performance status 2, severe adverse events and comorbidity than with a performance status 0-1 where there were no or only mild adverse events and no comorbidity. Multiple logistic regression models indicated that severe adverse events and comorbidities were independent predictive factors for patients with emergency hospitalization. By combining selected clinical information for outpatients receiving cancer chemotherapy, the need for emergency hospitalization could be predicted.

The outpatient management of cancer patients is becoming an increasingly used practice because of the improvement in quality of life, the discovery of new drugs without severe adverse effects, the use-effectiveness of hospital beds and medical cost-effectiveness (1-4). The risks and benefits of such a policy have not, however, been systematically

investigated and, to our knowledge, few data have so far been published (5). Emergency oncology is an important issue comprised of two categories: one encompasses acute reactions, such as drug extravasation and hypersensitivity reactions related to the chemotherapeutic agents, and occurs mainly at the cancer chemotherapy center (6); the second covers cases of emergency hospitalization for chronic adverse events, complications arising from the treatment effects, the induction of comorbidity and the exacerbation of cancer. It is therefore important to be able to predict emergency hospitalization in order to determine the appropriate selection criteria for outpatient chemotherapy. There are few reports of oncology emergencies in the literature, except for one case report (7, 8).

The aim of the present study was to evaluate the emergency hospitalization of outpatients receiving cancer chemotherapy and also to analyze the relationship between emergency hospitalization and clinical factors.

Patients and Methods

Patients. A retrospective cohort of 158 consecutive patients treated for cancer, between April 2005 and March 2006, at the cancer chemotherapy center in the University of Occupational and Environmental Health were examined. The clinical data were obtained based on chart review. The subjects in this series included 91 men and 67 women, with a mean age of 60.1 years (range, 16 to 90). The cancer types included 50 lung carcinomas, 57 hematological carcinomas, 19 breast carcinomas, 15 gynecological carcinomas, 7 gastrointestinal carcinomas, and 10 others. One hundred and eight patients had been previously treated including 47 with surgery, 13 with surgery+chemotherapy, 9 with surgery+chemotherapy+radiation, 4 with surgery+radiation, 19 with chemotherapy, 9 with chemotherapy+radiation, 2 with radiation, and 1 with bone marrow transplantation. The objectives of the chemotherapy were 44 adjuvant and 114 intensive therapies including 80 first line and 34 second or subsequent. The number of patients with severe adverse events and comorbidity were 30 and 47, respectively.

For the follow-up, patients were examined every week during chemotherapy and supportive care. The evaluations included a physical examination, chest roentgenography, an analysis of blood chemistry and measurements of tumor markers. If any symptoms or signs of clinical complications, the induction of comorbidity, or

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Table I. Patient characteristics with emergency admissions.

Case	Age (yr)	Gender	Cancer type	PS	Previous treatment	Objective of chemotherapy	Line	Regimen	Severe AE (Grade 3 or 4)	Comorbidity	Reason for admission
1	76	F	Lung cancer	2	C+R	Intensive	1	CBDCA+PTX	None	Hypertension, Diabetes mellitus	LOC
2	69	M	Lung cancer	1	None	Intensive	1	CBDCA+ PTX	None	None	Pneumonia
3	72	M	Lung cancer	1	S	Adjuvant	-	CBDCA +GEM	Neutropenia	Gastric ulcer	Pneumonia
4	48	M	Lung cancer	1	S+C+R	Intensive	3	gefitinib	None	None	Pneumonia
5	57	M	Lung cancer	1	S+R	Intensive	1	CBDCA+ PTX	None	Emphysema	Ileus
6	71	F	Lung cancer	1	S+C	Intensive	3	gefitinib	None	Gastric ulcer, Bronchial asthma	Pneumonia
7	71	F	Lung cancer	1	S	Adjuvant	-	CBDCA+ PTX	None	Hypertension, Diabetes mellitus	Pneumonia
8	56	M	Mediastinal tumor	1	S+R	Intensive	1	CBDCA+ PTX	None	Diabetes mellitus	Radiation pneumonitis, malignant pleural effusion
9	46	M	MDS	2	BMT	Intensive	1	PSL+CyA	Acute GVHD	Chronic GVHD	VZV infection
10	61	M	T cell lymphoma	0	None	Intensive	1	VP-16+CyA +PSL	Hypogamma globulinemia	Psoriasis vulgaris	CMV infection
11	65	F	NHL	2	None	Intensive	1	R-CHOP	Hypogamma globulinemia	None	Pneumonia
12	65	F	NHL	0	C	Intensive	2	R-CHOP	Neutropenia	Hypertension, Chronic Hepatitis	Febrile neutropenia
13	54	M	NHL	2	None	Intensive	1	R-CHOP	Hypogamma globulinemia	Liver Cirrhosis	Colitis, Ileus
14	59	M	CML	1	None	Intensive	1	imatinib	Fever, Allergic reaction	Hypertension	Allergic reaction

PS: performance status; S: surgery; C: chemotherapy; R: radiation therapy; BMT: bone marrow transplantation; MDS: myelodysplastic syndrome; NHL: non-hodgkin lymphoma; CML: chronic myelogenous leukemia; CBDCA: carboplatin; PTX: paclitaxel; GEM: gemcitabine; PSL: prednisolone; CyA: cyclosporin; R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine sulfate; AE: adverse event; LOC: loss of consciousness; VZV: varicella zoster virus; CMV: cytomegalovirus; GVHD: graft versus host disease.

exacerbation of the cancer appeared from these follow-up studies, then additional examinations were performed. A follow-up report was available for all patients. Toxicity was assessed using the National Cancer Institute-Common Toxicity Criteria. Informed consent was obtained either from all patients or from the patient's legal guardians.

Statistical analysis. The Fisher's exact test was used. Multivariate logistic regression was used to evaluate the independent associations. The Odds ratio and a 95% confidence interval (CI) were calculated for each variable. The statistical difference was considered to be significant if the *p*-value was less than 0.05. All data were analyzed with the use of Survival Tools for StatView (Abacus Concepts, Inc., Berkeley, California, USA).

Results

The number of emergency hospitalization cases was 14 (8.9%), including seven lung carcinomas, six hematological carcinomas, and one mediastinal tumor. Eleven, nine and

seven cases had comorbid disease, previous treatment and/or severe adverse events, respectively. The reason for emergency hospitalization in twelve (85.7%) cases was infection (Table I). The positive ratio was significantly higher in the emergency cases with performance status 2 severe adverse events, and comorbidities than in those with performance status 0-1, with no or only mild adverse events and without comorbidities, respectively. On the other hand, no significant difference was observed between the cases with and without emergency hospitalization regarding age, gender, cancer type, previous treatment, objective of chemotherapy and line of chemotherapy (Table II). Multiple logistic regression models indicated that severe adverse events and comorbidities were independent predictive factors for patients with emergency hospitalization (Table III). At 97.3% specificity, the positive and negative predictive values were 75.0% and 94.7%, respectively.

Table II. Relationships between patients with or without emergency admissions and the clinical characteristics in 158 outpatients receiving cancer chemotherapy.

Characteristics	Total	Patients with emergency admissions	%	Patients without emergency admissions	p-value
All cases	158	14	8.9	144	
Age (yr)					
<60	66	6	9.1	60	
≥60	92	8	8.7	84	0.93
Gender					
Male	91	9	9.9	82	
Female	67	5	7.4	62	0.60
Cancer type					
Lung	50	7	14.0	43	
Hematological	57	6	10.5	51	
Breast	19	0	0	19	
Gynecological	15	0	0	15	
Gastrointestinal	7	0	0	7	
Others	10	1	10.0	9	0.58 ^a
Previous treatment					
Yes	108	9	8.3	99	
Surgery	47	2	4.3	45	
Surgery+ chemotherapy	13	1	7.7	12	
Surgery+ Chemotherapy+ radiation	9	1	11.1	8	
Surgery+ radiation	4	2	50.0	2	
Chemotherapy	19	1	5.3	18	
Chemotherapy+ radiation	9	1	11.1	8	
Radiation	2	0	0	2	
Bone marrow transplantation	1	1	100.0	0	
No	54	5	9.3	49	0.90 ^b
Performance status					
0-1	154	10	6.5	144	
2	4	4	100.0	0	<0.001
Objective of chemotherapy					
Adjuvant	44	2	4.5	42	
Intensive	114	12	10.5	102	0.24
Line					
First	80	9	11.3	71	
Second or subsequent	34	3	8.8	31	0.70
Severe AE (Grade 3 or 4)					
Yes	30	7	23.3	23	
No	128	7	5.5	121	0.002
Comorbidity					
Yes	47	12	25.5	35	
Pulmonary	2	1	50.0	1	
Cardiovascular	4	0	0	4	
Gastrointestinal	2	0	0	2	
Metabolic disease ^d	25	5	20.0	20	
Others	14	3	21.4	11	
No	111	3	2.7	108	<0.001 ^c

The p-value was calculated between: ^alung cancer and hematological cancer, ^bprevious treatment and no treatment, ^cpatients with and without comorbidity. ^dMetabolic disease included hyperlipidemia, hypertension and diabetes mellitus. AE: adverse event.

Discussion

Ninety percent of cancer patients are treated on an outpatient basis in the United States (4), in comparison to only 60% in Japan (9), although this figure has been increasing. In fact, our investigation by questionnaire revealed that a majority of patients wish to receive cancer chemotherapy on an outpatient basis, but also have serious reservations about the associated adverse events. It is therefore important to examine the occurrence of oncology emergencies in order to be prepared for emergency hospitalization of outpatients receiving cancer chemotherapy.

However, it is often difficult to predict oncology emergencies because patients with cancer often have complex medical problems (6, 10, 11). In this study, the number of emergency hospitalizations for outpatients undergoing cancer chemotherapy was 14 cases (8.9%) mainly due to infection. These results were consistent with previous findings (12). Comorbidity and severe adverse events were independent predictive factors for emergency hospitalization patients. Therefore, it is possible to predict emergency hospitalization and create a proper environment for the treatment of such patients by judging high-risk groups.

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Table III. Multivariate analysis of the clinical factors contributing to the emergency admission of outpatients receiving cancer chemotherapy.

Variable	Beta	Standard error	χ^2	Odds ratio	95% CI	p-value
Age (yr): ≥ 60	-0.633	0.695	0.829	0.531	0.136 to 2.075	0.3626
Gender: Male	-0.061	0.702	0.007	0.941	0.238 to 3.726	0.9310
Intensive therapy	0.634	0.906	0.489	1.884	0.319 to 11.123	0.4843
Previous treatment	1.957	1.131	2.992	7.076	0.771 to 64.982	0.0837
Severe AE	1.714	0.745	5.289	5.550	1.288 to 23.916	0.0215
Comorbidity	2.796	0.798	12.283	16.375	3.429 to 78.208	<0.001

AE: adverse event.

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