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作成者（著者）	Kikuchi, Yoshinori / Yamaguchi, Kazuhisa / Funahashi, Kimihiko / Arita, Yoshiki / Shimojo, Nami / Watanabe, Kazumi / Koshikawa, Issei / Wakabayashi, Munehiro / Izawa, Atsuko / Kagami, Satoru / Kaneko, Tomoaki / Ushigome, Mitsunori / Shimada, Hideaki
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Original Article

Management of Postoperative Patients with Colorectal Cancer Using Information and Communication Technology: A Pilot Study

Yoshinori Kikuchi[1)*] Kazuhisa Yamaguchi[2)] Kimihiko Funahashi[3)]
Yoshiki Arita[4)] Nami Shimojo[5)] Kazumi Watanabe[4)]
Issei Koshikawa[4)] Munehiro Wakabayashi[2)] Atsuko Izawa[5)]
Satoru Kagami[3)] Tomoaki Kaneko[3)] Mitsunori Ushigome[3)]
and Hideaki Shimada[1, 3)]

[1)]Department of Clinical Oncology, Faculty of Medicine, Toho University, Tokyo, Japan
[2)]Division of Gastroenterology and Hepatology, Department of Internal Medicine (Omori), Toho University, Tokyo, Japan
[3)]Division of General and Gastroenterological Surgery, Department of Surgery (Omori), Toho University, Tokyo, Japan
[4)]Department of Pharmacy, Toho University Omori Medical Center, Tokyo, Japan
[5)]Department of Nursing, Toho University Omori Medical Center, Tokyo, Japan

ABSTRACT

Introduction: Outpatient chemotherapy patients have a lot of anxiety about treatment-related adverse events. There have been several reports suggesting that a telephone support system could reduce hand-foot syndrome with XELOX therapy. In this study, we investigated whether information and communication technology (ICT) tools could reduce patients' anxiety and adverse events.

Methods: Twenty patients with postoperative stage III colorectal cancer who were eligible for XELOX therapy were divided into two groups: 10 patients in the symptom-monitoring group using the ICT tool and 10 patients in the control group. The treatment completion rate, relative dose intensity, psychological distress and adjustment, and adverse events in each group were assessed. The study protocol was approved by the Ethics Committee of Toho University Omori Medical Center (M18124). This clinical trial is registered in the University Hospital Medical Information Network (UMIN) registry system (UMIN ID: 000035475) (https://center6.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000040380).

Results: There was no significant difference in the treatment completion rate, treatment duration, and relative dose intensity between the two groups, and there was a trend toward less anxiety in the symptom-monitoring group compared to that in the control group. Moreover, the symptom-monitoring group showed a trend toward lower diarrhea and peripheral neuropathy compared to that in the control group.

Conclusions: Our findings indicate that symptom-monitoring using ICT tools for outpatient chemotherapy could relieve patient anxiety and reduce adverse events.

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*Corresponding Author: Yoshinori Kikuchi, 6-11-1 Omori-nishi, Ota-ku, Tokyo, 143-8541, Japan, tel: +81–3–3762–4151
e-mail: y-kikuchi@med.toho-u.ac.jp
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KEYWORDS: adjuvant chemotherapy for colon cancer, HAD score, ICT tool, MAC score, XELOX therapy

Introduction

Thirty-six percent of patients with cancer have adjustment disorders, 6% have depression, and 4% have diagnostic criteria for delirium.[1] The reasons include anxiety about metastasis and recurrence, financial problems, and decreased quality of life (QOL) due to treatment. Capecitabine and Oxaliplatin are pharmaceutical drugs that cause hand-foot syndrome and peculiar peripheral neuropathy and decrease the patient's QOL.[2,3]

The standard adjuvant chemotherapy for stage III colorectal cancer is eight courses of XELOX (capecitabine and oxaliplatin) therapy or FOLFOX therapy (oxaliplatin/5-Fluorouracil/leucovorin).[4,5] Completing eight courses without adverse effects is suggested to improve the patients' QOL and resolve their psychological problems. Therefore, there have been several reports of telephone support systems improving hand-foot syndrome.[6–11] However, in the telephone support systems, there are some problems, namely, the patient cannot be contacted at a fixed time, and the adverse event cannot be confirmed by the medical staff due to the patient's self-report.

In recent years, cancer research using the symptom-monitoring system as an information and communication technology (ICT) tool has been reported to improve the patient's QOL and prolong survival.[12,13] However, there is no psychological analysis of patients, completion rate, and adverse events. Thus, in this study, the aim was to analyze patients who received adjuvant chemotherapy for colorectal cancer with and without the use of the symptom-monitoring system.

Methods

Patients and treatment

Between March 2019 and September 2020, 20 patients with colonic cancer were enrolled. Patients were eligible if XELOX therapy (capecitabine [1,000 mg/m^2, twice a day, on days 1-14, every three weeks] plus oxaliplatin [100/m, on days 1, every three weeks]) could be selected as postoperative adjuvant chemotherapy after stage III colorectal cancer surgery. Ten patients were assigned to the control group, and 10 patients were in the symptom-monitoring group using the permuted block method (4-2-4). All patients provided written informed consent.

Each group conducted two questionnaires: Hospital Anxiety and Depression (HAD) and Mental Adjustment to Cancer (MAC) during the pre- and post-treatment. The HAD scale is a 14 item self-assessment scale to measure psychological distress and has two factors: anxiety (seven items) and depression (seven items).[14] The patients were assessed by a scale of anxiety and depression: scores of 0-7 were non-cases, 8-10 were doubtful cases, and 11-21 were definite cases.

The MAC scale is a self-reported 40-item questionnaire that measures the psychological adjustment of patients who have cancer. Question items are further categorized into five subscales: Fighting Spirit (16 items, score range 16-64), Helplessness/Hopelessness (six items, score range 6-24), Anxious Preoccupation (nine items, score range 9-36), Fatalism (eight items, score range 8-32), and Avoidance (one item, score range 1-4).[15]

In the control group, two patients with adverse events (peripheral neuropathy and headache) were excluded, specifically, one patient had surgery for a stoma hernia, and one patient had an incomplete questionnaire. In the symptom-monitoring group, one patient with an allergy against capecitabine was excluded. Finally, six patients and nine patients in the control group and symptom-monitoring group, respectively, were evaluated (Fig. 1).

ICT tools

The medical care station system used in the ICT program was provided by Japan Embrace Inc., and information (administration method and side effects) of the drugs used in the system was provided by Chugai Pharmaceutical Co., Ltd. This ICT program can be used for personal and mobile computers. The ICT program requires a membership and can allow sharing of secure information. The system allows patients to report medication status, physical condition, and adverse event sites (head, digestive system, limbs) daily and allows medical staff to advise patients. The doctors, nurses, and pharmacists reviewed the patients monitored with the ICT program once per day in the symptom-monitoring group (Fig. 2).

Evaluation of the patient's psyche and statistical analysis

The modified Mann-Whitney U-test was used to com-

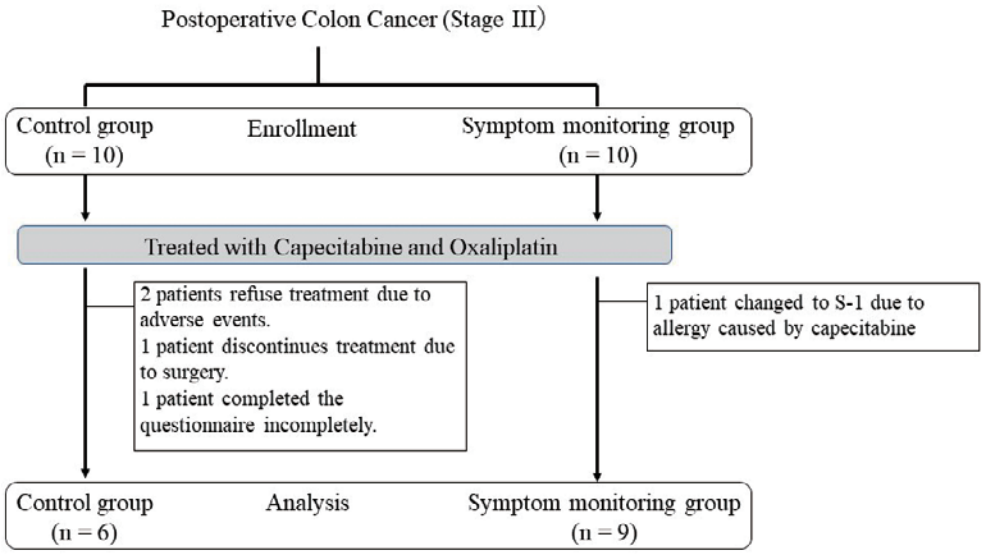

Fig. 1 CONSORT flow diagram.

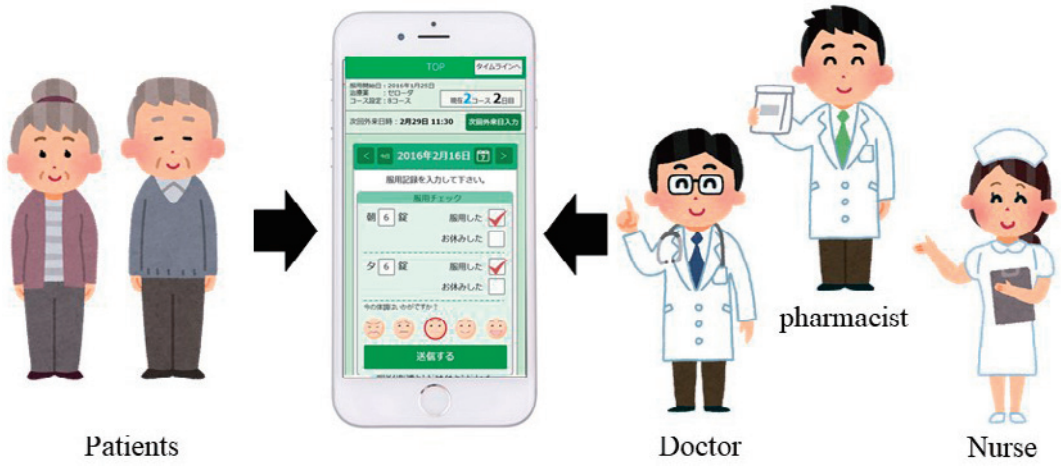

Fig. 2 Information and communication technology (ICT) program.
The medical staff checked the patient's symptoms once every 24 h using the ICT program.

pare the median age, median treatment period, relative dose intensity, and adverse events. Fisher's exact test was used to compare categorical data such as gender and treatment completion rate. The modified Wilcoxon signed-rank test was used to analyze the HAD and MAC scale.

All p-values were calculated using two-sided testing, and p-values<0.050 were considered statistically significant. All statistical analyses were performed with StatMate V for Win&Mac Hybrid (ATMS Co., Ltd., Tokyo, Japan) software.

Results

Patients' characteristics

Fifteen people (six in the control group and nine in the symptom-monitoring group), who were able to complete the questionnaire survey, were evaluated. The median age was 72 years (range 52-81) and 60 years (range 35-74) in control group and symptom-monitoring group, respectively. The symptom-monitoring group tended to have younger patients than that of the control group (p = 0.099). There was no significant difference in the male-to-female ratio between the two groups (p = 1.000). The completion rate of the eight courses of XELOX therapy was 60% in the control group and 90% in the symptom-monitoring group, showing no significant difference between the two groups (p = 0.303). The median treatment period was 192.5 d and 168 d in the control group and symptom-monitoring group, respectively. There was no significant difference in

Table 1

Factors	Control group (n = 6)	Symptom monitoring group (n = 9)	P value
median age (range)	72 y.o. (52-81)	60 y.o. (35-74)	0.099[a)]
gender (male/female)	3/3	4/5	1.000[b)]
Completion rate	60% (6/10)	90% (9/10)	0.303[b)]
Median treatment period	192.5 days (168-238)	168 days (168-217)	0.290[a)]
Median relative dose intensity (Capecitabine)	84.2% (61.8-100)	79.2% (62.5-100)	0.768[a)]
Median relative dose intensity (Oxaliplatin)	86.2% (70.4-100)	94.3% (59.4-100)	0.857[a)]

[a)] modified Mann-Whitney U test
[b)] Fisher's exact test

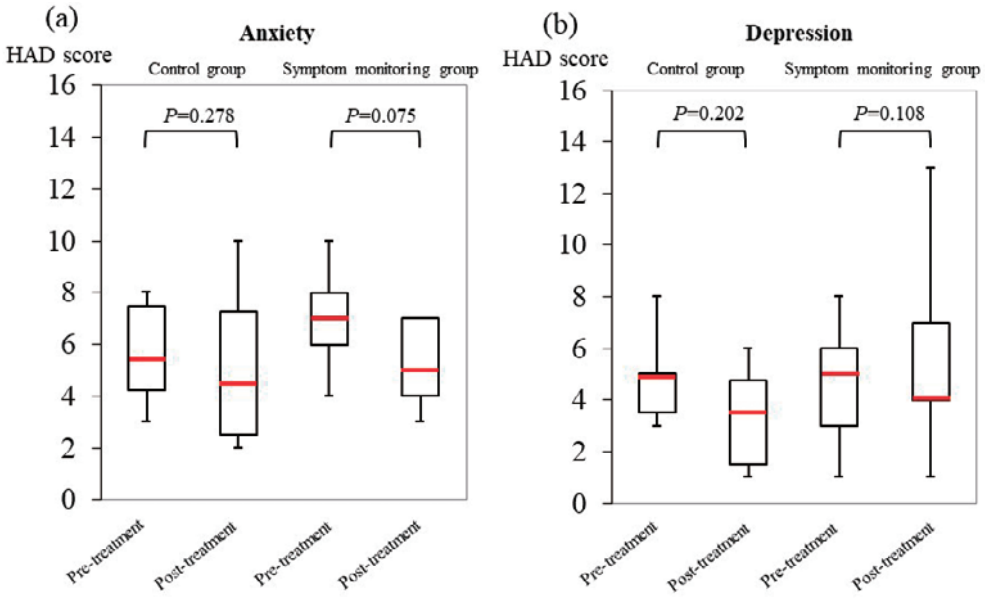

Fig. 3 Comparison of the Hospital Anxiety and Depression (HAD) scores before and after treatment in the control group (n = 6) and symptom-monitoring group (n = 9). The modified Wilcoxon signed-rank test was used for pre- and post-treatment comparisons.
(a) Anxiety; (b) Depression.

the treatment period between the two groups (p = 0.290). The relative dose intensity of Capecitabine and Oxaliplatin did not differ significantly between the control group and the symptom-monitoring group (p = 0.768 and 0.857) (Table 1).

HAD score and MAC score

The anxiety and depression of the patients in the control group and the symptom-monitoring group were evaluated by the HAD score before and after treatment. The results showed that anxiety tended to decrease in the symptom-monitoring group (p = 0.075) (Fig. 3a), but depression was not significantly different between the two groups (p = 0.202 and p = 0.108, respectively) (Fig. 3b). In contrast, between the control group and the symptom-monitoring group, five items were compared pre- and post- treatment by MAC score (Fig. 4): Fighting Spirit, Helpless/Hopeless, Anxious Preoccupation, Fatalism, and Avoidance. As a result, the symptom-monitoring group showed a significant decrease in post-treatment Avoidance (p = 0.042) (Fig. 4e).

Adverse events

The extent of myelosuppression, hepatotoxicity, hand-foot syndrome, and peripheral neuropathy between the control group and the symptom-monitoring group was assessed. The results showed that nausea tended to be higher in the symptom-monitoring group (p = 0.080), whereas diarrhea (p = 0.088) and peripheral neuropathy (p = 0.089) tended to be higher in the control group. There

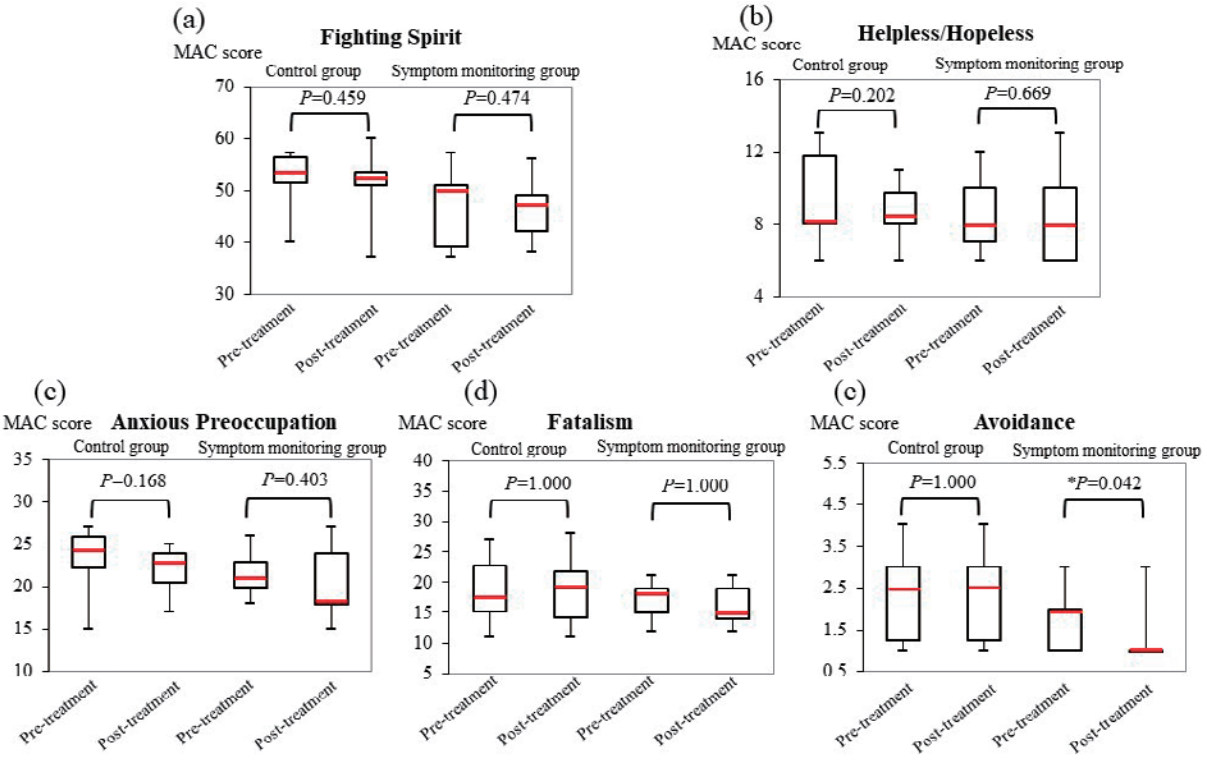

Fig. 4 Comparison of the Mental Adjustment to Cancer (MAC) scores before and after treatment in the control group (n = 6) and symptom-monitoring group (n = 9). The modified Wilcoxon signed-rank test was used for pre- and post-treatment comparisons.
(a) Fighting Spirit; (b) Helpless/Hopeless; (c) Anxious Preoccupation; (d) Fatalism; and (e) Avoidance.

Table 2

Adverse event	Control group (n = 6)					Symptom monitoring group (n = 9)					*P* value
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	
Leukopenia	5	1	0	0	0	4	1	3	1	0	0.108
Neutropenia	3	3	0	0	0	5	1	2	1	0	0.746
Anemia	0	5	1	0	0	1	7	1	0	0	0.554
Thrombocytopenia	1	4	1	0	0	1	7	0	1	0	1.000
Increased bilirubin	5	0	1	0	0	7	2	0	0	0	1.000
Increased AST	0	5	1	0	0	0	9	0	0	0	0.276
Increased ALT	3	3	0	0	0	4	5	0	0	0	0.891
Nausea	6	0	0	0	0	5	3	1	0	0	0.080
Diarrhea	2	3	1	0	0	7	2	0	0	0	0.088
Hand-foot syndrome	4	0	1	1	0	7	0	1	1	0	0.761
Neurosensory	0	4	2	0	0	0	9	0	0	0	0.089

modified Mann-Whitney U test

was no significant difference in hand-foot syndrome between the two groups ($p = 0.761$) (Table 2).

Discussion

The findings demonstrate that the psychological aspects, completion rate, and adverse events of adjuvant chemotherapy patients after surgery for colorectal cancer using the Xeloda application utilizing the ICT tool. The results showed that anxiety tended to decrease, and avoidance of cancer significantly decreased in the symptom-monitoring group. Diarrhea and neuropathy tended to be less frequent in the symptom-monitoring group than in the

control group.

The completion rate of postoperative adjuvant chemotherapy for colorectal cancer has been reported to be approximately 70.2%-74.1% for FOLFOX therapy and 64%-68% for XELOX therapy. These results suggest that XELOX therapy tends to have a lower completion rate than that of FOLFOX therapy. Oxaliplatin causes peripheral neuropathy and decrease the QOL of patients. Therefore, the dose of Oxaliplatin for FOLFOX therapy should be 85 mg/m^2, and the dose for XELOX therapy should be as high as 130 mg/m^2. Matsuo et al. reported that the oxaliplatin group had significantly more drug withdrawal and dose reductions due to neutropenia, thrombocytopenia, and peripheral neuropathy.[16] In our previous telephone-supported study, the completion rate of XELOX therapy was 67.3%,[6] and the completion rate in the control group in this study was almost the same at 60%. In this study, one patient in the symptom-monitoring group who was DLST-positive for Capecitabine was excluded from the study. However, that patient completed eight courses using S-1. Hence, all patients in the symptom-monitoring group completed the treatment, but two patients in the control group discontinued the treatment due to adverse events. For these reasons, the control group did not reduce the dose appropriately for the patients due to the lack of patient's information. As a result, the completion rate decreased, and the treatment period was prolonged due to discontinuation or extension of treatment. On the other hand, in the symptom-monitoring group, medical staff (doctor, nurses, and pharmacists) checked the patient's status within 24 h, answered questions as appropriate, and checked images taken by the patient. Therefore, the symptom-monitoring group reduced the dose to an appropriate level at any time, which may have improved the completion rate and shortened the treatment period.

Evaluation of outpatients with chemotherapy using the HAD scale reported that 40% had mild depression, and 12% had moderate or severe depression and anxiety.[17] In the SMILE study with telephone support, there was no significant difference in the HAD scores.[8] However, in this study, the HAD score showed a decreasing trend for anxiety. For this reason, the ICT program always received comments from medical staff within 24 h, and it seemed that the patient's anxiety resolved. In addition, the MAC score showed a significant decrease in the symptom-monitoring group for avoidance of cancer. The question in the Avoidance section is "I don't really believe I had cancer." This result suggests that the symptom-monitoring group can relieve anxiety and forget about cancer by contacting medical staff every day. However, since the number of cases is small and the evaluation is based on only one item, it is insufficient.

In this study, the symptom-monitoring group tended to have lower diarrhea and peripheral neuropathy than the control group. The symptom-monitoring group, like the HAD score, is managed by medical staff 24 h a day; therefore, it is thought that this allows early countermeasures against side effects. It has been reported that the ICT program is effective in preventing side effects of cancer treatment.[18] However, the symptom-monitoring group showed a stronger trend toward nausea. It was suggested that the reason for this was that one patient in the symptom-monitoring group had grade 2 nausea, which statistically increased the trend, while the control group had less nausea due to the longer withdrawal period caused by postponement of treatment.

The limitation of this study is that it was a pilot study with a very limited number of patients, and some patients were not able to complete the study due to adverse events, so there was no statistically significant difference.

In conclusion, these results suggest that the symptom-monitoring system using ICT tools can provide patients with appropriate advice and treatment for adverse events of anticancer drugs within 24 h, increase the completion rate, and reduce patients' anxiety.

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Authors' contribution: YK and HS drafted the manuscript. YK, KY, KF, YA, NS, KW, IK, MW, AI, SK, TK, and MU were involved in study design and data interpretation. All authors read and approved the final manuscript.

Ethics statement: The study protocol was approved by the Ethics Committee of Toho University Omori Medical Center (M18124). This clinical trial is registered in the University Hospital Medical Information Network (UMIN) registry system (UMIN ID: 000035475).

Conflicts of interest: All the authors, except one, report that they have no conflict of interest to disclose. Dr. Funahashi received re-

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