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Outcome of Multimodality Therapy for Elderly Colorectal Cancer Patients

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Abstract

The aim of this study was to analyze patterns of multimodality therapy in elderly patients with advanced colorectal cancer. We enrolled 272 patients with colorectal cancer. All patients received chemotherapy and some patients received secondary cytoreductive surgery and/or radiofrequency ablation. We compared differences between elderly patients (age ≥75 years) and non-elderly patients (age <75 years), especially in relation to multimodality therapy. There were no significant differences in cancer-specific survival between elderly (n = 37) and non-elderly patients (n = 235).Twenty-seven percent of elderly and 35% of non-elderly patients received multimodality therapy, which resulted in prolonged survival. Although the main chemotherapy regimen was the same in both groups who received multimodality therapy, elderly patients who received chemotherapy alone seemed to be under-treated. For elderly patients, prognostic factors were host-related, such as comorbidities, whereas for non-elderly patients prognostic factors were tumor-related. Comorbidities and modified Glasgow Prognostic Score may be prognostic indicators in elderly patients receiving multimodality therapy. In conclusion, chronological age alone should not contraindicate multimodality therapy of colorectal cancer in elderly patients. Appropriate selection criteria for multimodality therapy in elderly patients should include not only tumor characteristics, but also host- and treatment-related factors.

Keywords: colorectal cancer, elderly patient, multimodality therapy

1. Introduction

Colorectal cancer (CRC), the commonest malignancy worldwide, mainly affects the elderly. The mean age at diagnosis is under 72 years, 40% of cases occurring in patients aged over 75 years (Köhne et al., 2008; Yang et al., 2004; Boyle et al., 2005; Christensen et al., 2009). The geriatric CRC population is a very heterogeneous group that includes patients with excellent health status and those with comorbid conditions, functional dependency, and limited life expectancy (Sanoff et al., 2007), all of which may considerably influence the outcome of CRC treatments.

The mainstay of CRC treatment is surgery, however, the role of chemotherapy has expanded considerably over the past 10 years. Modern chemotherapy, including molecular-targeted agents, has increased the survival time of patients with metastatic CRC to more than 2 years (Hurwitz et al., 2004; van Cutsem et al., 2009; Fuchs et al., 2007; Douillard et al., 2013). In addition, cytoreductive surgery for liver, lung, and other metastases has been widely used to achieve cure; however, metastasectomy is appropriate for only a few patients. Multimodality approaches, including surgery, radiotherapy, and chemotherapy, alone or in combination, have been proposed to further prolong survival of patients with recurrent or metastatic CRC. There have been efforts to increase the small proportion of patients receiving multimodality therapy by expanding the indications for it. Many studies have confirmed that chemotherapy can render some originally inoperable liver metastases resectable (Kusunoki et al., 1997; Kopetz et al., 2009; Kozloff et al., 2009; Folprecht et al., 2010; Wong et al., 2011). However, the indications for multimodality therapy in elderly patients with CRC have not been well defined. Elderly patients are more likely to have comorbidities and age-specific deteriorating organ function, which can reduce their tolerance of multimodality therapy, including surgery and modern chemotherapy. Published results for surgical morbidity and mortality rates are conflicting. Some studies show a correlation between age and postoperative

complications (Colorectal Cancer Collaborative Group, 2000; van Leeuwen et al., 2008; Lee et al., 2007; Grosso et al., 2012), whereas others do not (Schiffmann et al., 2008; She et al., 2013). Whether elderly patients can tolerate multimodality cancer treatment and benefit from it in the same way as younger patients is controversial. The aim of this study was to describe patterns of multimodality therapy in patients with CRC aged ≥75 years, and to compare the outcomes of elderly (≥75 years) and non-elderly (<75 years) groups.

2. Material and Methods

This was a retrospective study of all patients (n = 272) who received therapeutic chemotherapy for advanced or recurrent CRC in our Department of Gastrointestinal Surgery, from March 2000 to December 2012. This study included patients with histologically proven unresectable primary CRC, synchronous metastatic CRC, and metachronous metastatic or recurrent CRC. Patients who underwent initial simultaneous primary tumor resection and metastasectomy (e.g., lung and liver) were excluded. Exclusion criteria were any serious major organ dysfunction, a survival expectation of less than 3 months, and any other contraindication to enrollment in the study in the view of the patient's physician.

2.1 Multimodality Therapy

According to our institutional policy for the treatment of metastatic CRC with an unresectable primary tumor, all patients enrolled in the study received 4–5 months of initial chemotherapy. All patients were informed about the possibility of secondary multimodality therapy using cytoreductive surgery and/or radiofrequency ablation (RFA) before their initial chemotherapy. Cytoreductive therapy was defined as surgery and/or RFA aimed at reducing tumor volume. Whether to proceed with multimodality therapy was determined by the response to chemotherapy. Cytoreductive surgery and/or RFA were considered for patients with partial responses or stable disease after systemic chemotherapy. Multidisciplinary discussions during chemotherapy determined the nature and timing of cytoreductive therapy for each patient. Our institutional Ethics Committee approved the study, and written informed consent was obtained from all patients who entered the study.

2.2 Chemotherapy

Approval for drugs takes much longer in Japan than in the west. Because Japanese national insurance did not allow treatment of CRC with oxaliplatin between 2000 and 2005, first-line chemotherapy for advanced CRC was 5-FU with or without irinotecan in the first five years of the study. For the remaining seven years, the study patients received the then first-line chemotherapy for advanced or recurrent CRC triple-drug chemotherapy, namely 5-fluorouracil (5-FU), folinic acid and oxaliplatin or irinotecan (FOLFOX or FOLFIRI), with or without bevacizumab or cetuximab. The molecular-targeted agents bevacizumab, cetuximab, and panitumumab were approved for use in 2007, 2008, and 2010, respectively. From 2007, bevacizumab with FOLFOX or FOLFIRI was used as first-line chemotherapy for advanced or recurrent CRC. From 2008, cetuximab with or without irinotecan was used as second- or third-line chemotherapy. From 2010, cetuximab or panitumumab with FOLFIRI or FOLFOX have been available in Japan as first-line chemotherapy in patients with wild-type *KRAS*. In patients with incomplete cytoreduction, chemotherapy was reintroduced depending on their performance status (PS). Patients with complete secondary cytoreduction received 5-FU-based adjuvant chemotherapy. Those with no extrahepatic metastases but with unresectable hepatic metastases underwent hepatic arterial infusion chemotherapy with 5-FU followed by secondary surgery (Kusunoki et al., 1997). Radiotherapy with concurrent 5-FU-based chemotherapy was used to improve the resectability of locally inoperable rectal cancer.

2.3 Study Variables

Patients were categorized into two groups based on age: an elderly group, aged ≥ 75 years and a non-elderly group aged <75 years. The age of 75 years was selected to divide the sample because approximately 40% of cases occurring in CRC patients aged over 75 years and the incidence increases with advancing age (Köhne et al., 2008; Yang et al., 2004; Boyle et al., 2005; Christensen et al., 2009). The comorbidity status was assessed by the Charlson index (Birim et al., 2003), which is a partially modified score including neither cancer nor age (Charlson et al., 1987). No patients had clinical evidence of infection or inflammatory conditions such as obstructive colitis or obstructive jaundice at that time. Routine laboratory tests, including serum C-reactive protein (CRP) and albumin concentrations and tumor markers such as carcinoembryonic antigen (CEA) (cut-off value, 6 ng/mL) were performed on the day of the first medical examination. Serum CRP serum concentrations were measured by turbidimetric immunoassay using an N-Assay TIA CRP-S kit (Nittobo Medical, Tokyo, Japan). Because this CRP assay has a lower detection limit than assays used in other studies (0.2 mg/dL vs >0.5 mg/dL) (McMillan et al., 2003, Crozier et al., 2006), the cut-off value for abnormal serum CRP was set at 0.5 mg/dL. As previously described, the original Glasgow Prognostic Score (GPS) (Forrest et al., 2003) was modified by the present authors according to the best predictive values calculated by receiver operating characteristic analysis to

create the instrument used in this study: the mGPS (Toiyama et al., 2011, Inoue et al., 2013). Briefly, patients with high CRP concentrations (>0.5 mg/dL) plus hypoalbuminemia (<3.5g/dL) were allocated a score of 2, patients with only one of these factors a score of 1, and patients with neither of these factors a score of 0.

2.4 Statistical Analysis

JMP version 7 software (SAS Institute, Cary, NC, USA) was used to perform statistical analyses. Data are presented as the mean ± standard deviation. Contingency tables were analyzed using Fisher's exact test or the χ^2 test with Yates' correction. Correlations between continuous and categorical variables were evaluated by the Mann-Whitney U test. Survival curves were constructed according to the Kaplan-Meier method and differences analyzed using the log-rank test. Each significant predictor identified was assessed by multivariate analysis using Cox's proportional hazards model. A P value of < 0.05 was considered significant.

3. Results

3.1 Relevant Patient Variables and Comorbidities

We performed a retrospective review of 272 patients treated in our department for unresectable primary, synchronous metastatic, and metachronous metastatic or recurrent CRC. There were 163 men (60%) and 109 women (40%), with a mean age of 64 years (range 29–85 years). Of these, we analyzed 37 elderly (age ≥75 years: 79 ± 3 years; range 75–85 years) and 235 non-elderly (age <75 years: 60 ± 10 years; range, 29–74 years) patients over the 12 years of the study. Table 1 summarizes the background characteristics of the 272 patients by age group. We found no differences between groups in tumor characteristics such as extent or tumor. However, there were significant correlations between age and PS (P = 0.0122) and comorbidity (P = 0.0003). To assess comorbid condition, we also measured the Charlson comorbidity index (CCI). Although this index was not significantly different for elderly (mean 0.270) than for non-elderly patients (mean 0.149), hypertension (P =0.0077) and cardiovascular disease (P = 0.0324) were present significantly more frequently in elderly than in non-elderly patients.

Table 1. Patient characteristics

Variables	**Total** (n=272)	**elderly (≥75)** (n=37)	**non-elderly (<75)** (n=235)	**p-value**
Gender				0.6721
Female	109	16	93	
Male	163	21	142	
PS				**0.0122**
0	112	8	104	
1	113	21	92	
2	31	8	23	
3	14	0	14	
4	2	0	2	
Comorbidities				
All comorbidities	83	20(54%)	63(27%)	**0.0008**
Diabetes mellitus	17	2(5%)	15(6%)	0.8194
Cardiovascular disease	4	2(5%)	2(1%)	**0.0324**
Hypertension	52	13(35%)	39(17%)	**0.0077**
Plumonary disease	13	3(8%)	10(4%)	0.3072
Charlson index				0.1553
0	133	28	205	
1	33	8	25	
2	6	1	5	
modified GPS				0.9201
0	157	22	135	
1	81	10	71	
2	34	5	29	

Variables	**Total** (n=272)	**elderly (≥75)** (n=37)	**non-elderly (<75)** (n=235)	**p-value**
Tumor state				0.8215
synchronous	159	21	138	
metachronous	113	16	97	
Tumor site				0.7905
Liver	78	12	66	
Lung	44	5	39	
Liver and lung	18	4	14	
Local recurrence	28	3	25	
Unresectable primary	22	3	19	
Lymphnode	13	2	11	
Dissemination	66	7	59	
Others	2	1	1	
Pathology				0.9748
Differentiated	243	33	210	
Non differentiated	29	4	25	
CEA				0.6373
<12ng/ml	120	15	105	
≥12ng/ml	152	22	130	
Chemotherapy				**0.0335**
5FU-based	38	7(19%)	31(13%)	
Irinotecan-based	95	8(22%)	87(37%)	
Oxaliplatin-based	72	16(43%)	56(24%)	
Molecular agents	67	6(16%)	61(26%)	
Response Rate (measurable)				0.7349
CR	6	0	6	
PR	90	10	80	
SD	129	21	108	
PD	33	5	28	
Radiotherapy				0.2629
yes	47	4	43	
no	225	33	192	
Secondary surgery and/or RFA				0.3472
yes	92	10(27%)	82(35%)	
no	180	27	153	

CEA, carcinoembryonic antigen; CR, complete response; mGPS, modified Glasgow Prognostic Score; PD, progressive disease; PR, partial response; PS, performance status; RFA, radiofrequency ablation; SD, stable disease.

3.2 Therapeutic Approach

All patients received initial therapeutic chemotherapy; 92/272 (34%) also received chemotherapy as part of multimodality therapy following secondary cytoreductive surgery and/or RFA. A greater proportion of non-elderly patients than elderly patients received multimodality therapy, (82/235 [35%] and 10/37 [27%]), respectively; this difference was not significant. We also assessed the proportion of patients receiving each of four main chemotherapy regimens, the categories being 5-FU- based, irinotecan-based, oxaliplatin-based, and combinations including molecular agents. The main regimens of patients who received chemotherapy alone were significantly different: non-elderly patients most commonly received irinotecan-based or combinations including molecular agents, whereas elderly patients most often received oxaliplatin- based or 5-FU-based chemotherapy. As to the main initial regimen received by patients who subsequently underwent multimodality therapy, there

were no significant differences between the two groups.

3.3 Cancer-specific Survival

We assessed cancer-related mortality by Kaplan-Meier survival analysis. After a median follow up of 21 months, there were no significant differences in median survival time (MST) between elderly (32 months, 95% CI 24–39 months) and non-elderly patients (27 months, 95% CI 23–31 months). Multimodality therapy was associated with significantly better survival than chemotherapy alone in both elderly (P =0.0423) and non-elderly patients ($P < 0.0001$) (Fig. 1). Multimodality therapy resulted in longer overall survival than did chemotherapy alone for both elderly (median 53 months [95% CI 20–85 months] and 30 months [95% CI 20–40 months], respectively), and non-elderly patients (median 44 months [95% CI 32–55 months] and 20 months [95% CI 17–23 months, respectively). Cox univariate regression analyses identified different factors affecting cancer-specific survival in elderly than in non-elderly patients. In non-elderly patients, timing of metastasis (synchronous vs. metachronous), pathology (undifferentiated vs. differentiated), CEA concentration (≥ 12 vs. < 12 ng/mL), extent of dissemination, mGPS, PS, rate of response to chemotherapy, and multimodality therapy correlated significantly with cancer-specific survival (Table 2a). Conversely, in elderly patients there were no correlations between tumor characteristics and cancer-specific survival; however, patient characteristics, including comorbidity and therapeutic factors such as response rate, did correlate significantly with cancer-specific survival (Table 2b). Multivariate analysis using these characteristics showed that pathology (undifferentiated vs. differentiated), CEA concentration (> 12 vs. < 12 ng/mL), PS, response rate of chemotherapy, and multimodality therapy all had significant independent correlations with cancer specific survival time in non-elderly patients, whereas response rate was the only significant independent prognostic factor in elderly patients (Table 3).

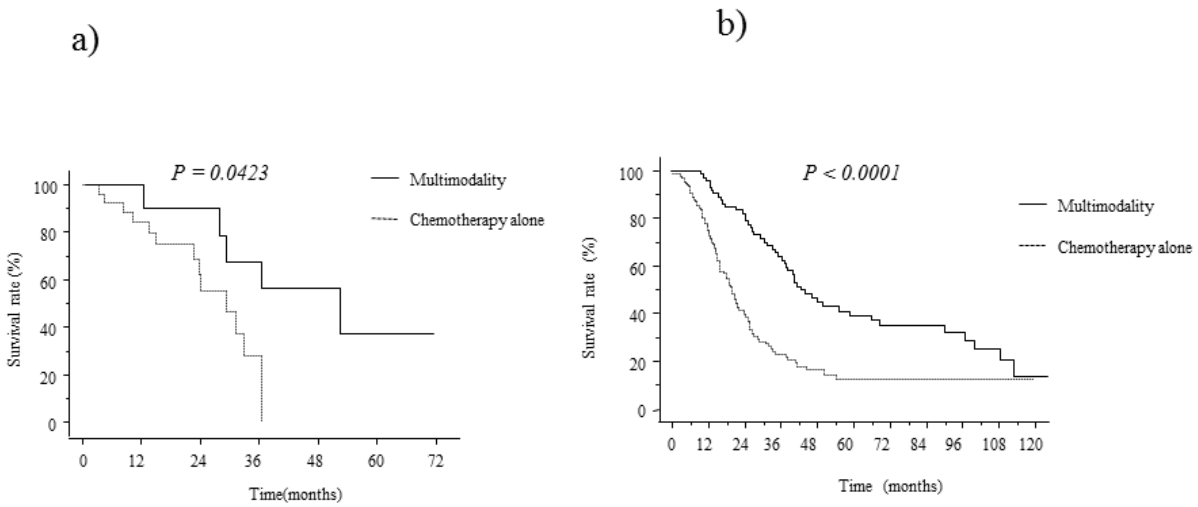

Figure 1. Multimodality therapy resulted in significantly better survival than did chemotherapy alone in both elderly (a) and non-elderly patients (b)

Table 2a. Univariate analysis in relation to cancer-specific mortality in non-elderly patients

Variables	p-value	Odds Ratio	95%CI
Gender (male vs. female)	0.1442	0.7825	0.563-1.087
PS (2-4 vs. 0-1)	**0.0005**	1.9685	1.342-2.890
Comorbidity (yes vs. no)	0.5496	1.119	0.775-1.613
Timing of metastasis (synchronous vs. metachronous)	**0.0038**	1.632	1.171-2.272
Pathology (undifferentiated vs. differentiated)	**0.0017**	2.173	1.337-3.533
Metastatic site (dissemination vs. others)	**0.0008**	1.845	1.289-2.646
CEA (≥12 vs. <12ng/ml)	**<0.0001**	2.086	1.492-2.916
mGPS (1-2 vs.0)	**0.0002**	1.861	1.347-2.572
Response rate (others vs. CR, PR)	**0.0015**	1.736	1.235-2.445
Secondary surgery and/or RFA	**<0.0001**	2.5641	1.786-3.676

PS, performance status; CEA, carcinoembryonic antigen; mGPS, modified Glasgow Prognostic Score

Table 2b. Multivariate analysis in relation to cancer-specific mortality in non-elderly patients

Variables	p-value	Odds Ratio	95%CI
PS (2-4 vs. 0-1)	0.1291	1.328	0.867-2.033
Timing of metastasis (synchronous vs. metachronous)	0.6411	1.092	0.755-1.577
Pathology (undifferentiated vs. differentiated)	**0.0077**	2.005	1.202-3.347
Metastatic site (dissemination vs. others)	**0.0323**	1.502	1.035-2.179
CEA (≥12 vs. <12ng/ml)	**0.0005**	1.862	1.311-2.644
mGPS (1-2 vs.0)	**0.0003**	1.982	1.367-2.874
Response rate (others vs. CR, PR)	**0.0041**	1.727	1.189-2.513
Secondary surgery and/or RFA	**<0.0001**	2.247	1.516-3.333

Table 3a. Univariate analysis in relation to cancer-specific mortality in elderly patients

Variables	p-value	Odds Ratio	95%CI
Gender (male vs. female)	0.744	1.179	0.439-3.175
PS (2-4 vs. 0-1)	0.521	0.709	0.248-2.024
Comorbidity (yes vs. no)	0.06	2.747	0.959-7.874
Hypertension (yes vs. no)	**0.023**	3.663	1.196-11.236
Timing of metastasis (synchronous vs. metachronous)	0.8676	0.924	0.363-2.350
Pathology (undifferentiated vs. differentiated)	0.7243	0.689	0.097-5.456
Metastatic site (dissemination vs. others)	0.539	0.629	0.143-2.672
CEA (≥12 vs. <12ng/ml)	0.3232	1.658	0.608-4.522
mGPS (1-2 vs.0)	0.1315	2.197	0.790-6.114
Response rate (others vs. CR, PR)	**0.0228**	4.545	1.235-16.666
Secondary surgery and/or RFA	0.051	3.322	0.995-11.111

CEA, carcinoembryonic antigen; mGPS, modified Glasgow Prognostic Score; PS, performance status

Table 3b. Multivariate analysis in relation to cancer-specific mortality in elderly patients

Variables	p-value	Odds Ratio	95%CI
Hypertension (yes vs. no)	0.9123	1.0235	0.673-1.558
Response rate (others vs. CR, PR)	**0.0016**	1.7631	1.231-2.445

3.4 Multimodality Therapy in Elderly Patients

Having confirmed that multimodality therapy prolonged survival in both non-elderly and elderly patients, we evaluated the correlation between comorbidities and the use of multimodality therapy. The CCI index correlated significantly with the use of multimodality therapy in the overall group of 272 patients (P = 0.0463). Of the patients who underwent multimodality therapy, 85/92 (92%) were in the category CCI 0, 7/92 (8%) CCI 1 and none in CCI 2. In contrast, of the patients who received chemotherapy alone, 148/180 (82%) were in the category CCI 0, 26/180 (14%) in CCI 1 and 6/180 (4%) in CCI 2. This trend differed between elderly and non-elderly patients. All comorbidities and the CCI category were significantly correlated with contraindication to multimodality therapy in non-elderly patients; however, this was not so in elderly patients (P = 0.0234, P = 0.0166, respectively). In the latter group, only hypertension tended toward correlating with contraindications to multimodality therapy (P = 0.0513).

To explorer useful predictors of indications for multimodality therapy in elderly patients, we also evaluated the prognostic significance of several clinical factors in 10 elderly patients who underwent multimodality therapy. In these elderly patients, the disease sites were initially unresectable primary, local recurrence, liver, bladder and peritoneal metastases. We performed reductive surgery in eight patients; three with liver metastases, two peritoneal metastases, one primary, one local recurrence, and one bladder involvement. We administered RFA for liver metastases to the other two patients. Kaplan-Meier survival analysis showed that patients with comorbidity (n = 4) had poorer survival than did those without comorbidity (n = 6) (3-year survival 83% vs. 25%, P = 0.0649) (Fig. 2). However, there were no significant differences in survival according to tumor characteristics such as timing of metastasis, pathology, and CEA concentration. Furthermore, we found no difference in survival between elderly and non-elderly patients who received chemotherapy alone. Interestingly, there were significant differences in survival according to mGPS (0 vs.1–2), with MST of 53 months (95% CI 20–85 months) for mGPS 0 (n = 8), and 12 months (95% CI 7–31 months) for mGPS1-2 (n = 2) (P = 0.0012) (Fig. 3). In contrast, there was no significant correlation between mGPS and survival in the elderly patients who received chemotherapy alone.

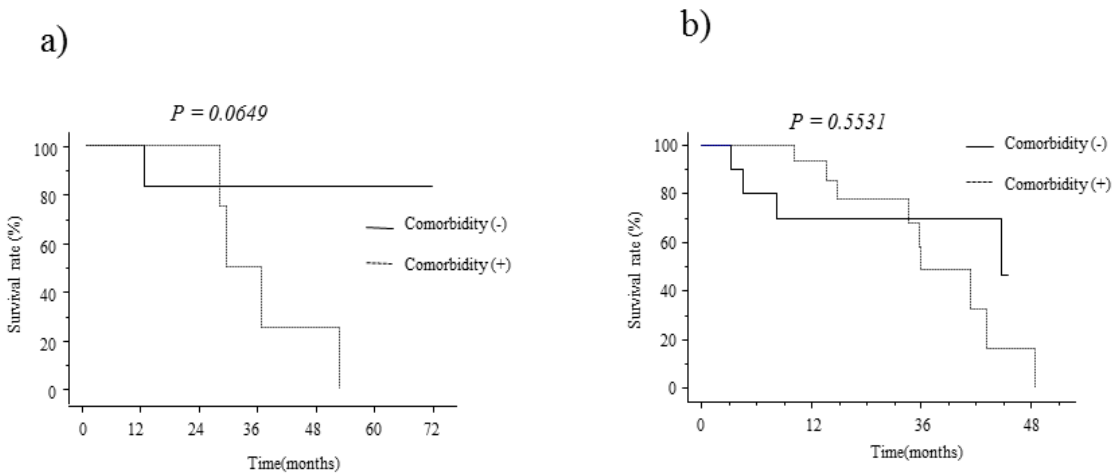

Figure 2. Kaplan-Meier survival curves of elderly patients receiving multimodality therapy showing that those with comorbidity had inferior survival to without comorbidity (a). For elderly patients who received chemotherapy alone, there was no comorbidity-related difference in survival (b)

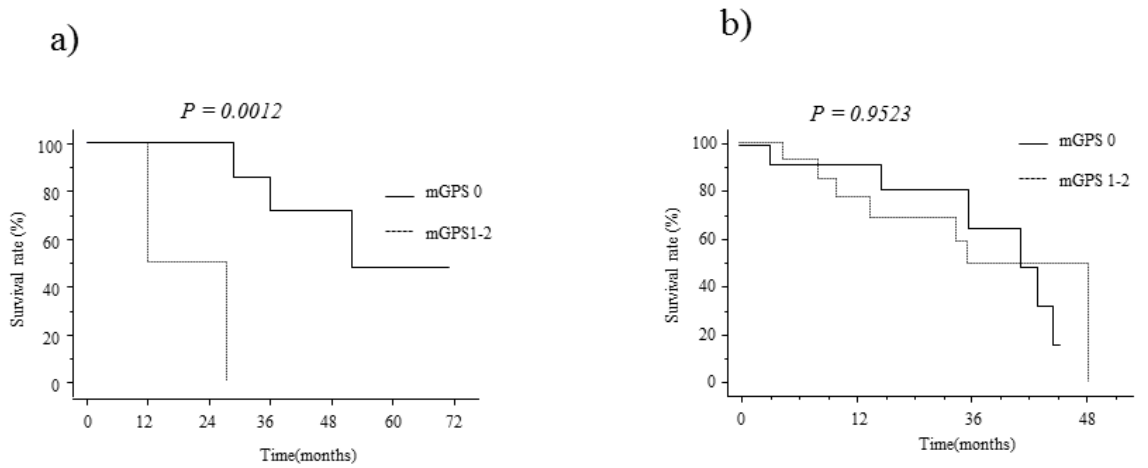

Figure 3. Relationship between mGPS (0, 1–2) and cancer-specific survival time in patients who received multimodality therapy (a) or chemotherapy alone (b)

4. Discussion

Colorectal cancer is a major cause of cancer deaths in developed countries. Because the populations of these nations, including Japan, are rapidly aging, clinicians will be faced with treating many patients with advanced cancer, including those with metastatic or recurrent CRC. Recent advances in CRC treatment have resulted in prolongation of survival even in patients with advanced stages of disease. However, clinical decision-making regarding modern multimodality therapy for advanced CRC in elderly patients is complex, because of the lack of data regarding optimal chemotherapy regimens, timing of cytoreductive therapy and the use of multimodality therapy in these patients. In a systematic review of surgery for CRC in 34,194 elderly patients, researchers found the incidence of postoperative morbidity and mortality increased progressively with advancing age. However, although overall survival was less in elderly than non-elderly patients, age-related differences in cancer-specific survival were much less pronounced (Colorectal Cancer Collaborative Group., 2000). Because most of the definitive clinical trials have excluded subjects of advanced age or with a poor PS, there is still uncertainly regarding the optimal use of systemic chemotherapy in elderly patients with CRC. Many of the clinical trials that have included elderly patients have documented similar survival rates and toxicity profiles for elderly and younger patients (Köhne et al., 2008). Most researchers agree that age alone should not be a contraindication to the use of standard chemotherapy and that fit elderly patients can receive similar aggressive chemotherapy as younger patients; however, identification of the elderly patients who are most likely to benefit from chemotherapy warrants further investigation (Colorectal Cancer Collaborative Group., 2000). Indications for modern chemotherapy followed by cytoreductive therapy in elderly patients remain largely unknown. In addition, because of the potential for worsening comorbidities to cause poorer outcomes, the utility of metastasectomy, including hepatectomy and pulmonary resection, in elderly patients is also controversial. There have been recent reports of decreased survival and higher postoperative morbidity associated with this procedure in the elderly (Adam et al., 2010; Nagano et al., 2005; Endoh et al., 2013).

In our study, although elderly patients were more likely to have a poor PS and comorbidities, there were no significant differences in cancer-specific survival time between elderly and non-elderly patients. Interestingly, factors affecting cancer-specific survival were different in the elderly and non-elderly groups. Treatment-related prognostic factors were common to both groups. However, elderly patients had various host-related prognostic factors such as comorbidities, whereas tumor-related prognostic factors were characteristic in the non-elderly group. Multivariate analysis revealed that various tumor-related (pathology, serum CEA concentration), host-related (PS) and treatment-related factors (response rate and multimodality therapy) all had significant independent correlations with survival in non-elderly patients, whereas only treatment-related factors (response rate) was an independent prognostic factor in elderly patients. Although multimodality therapy was an independent prognostic factor in only non-elderly patients, we found that the survival benefit of multimodality therapy in both elderly and non-elderly patients was comparable to that of chemotherapy alone. As a consequence of differences in the main chemotherapy regimen that each group received, elderly patients were less likely than non-elderly patients to receive multimodality therapy (27 vs. 35%).

It seems likely that elderly patients were under-treated compared with non-elderly patients, especially those who received chemotherapy alone. Of the patients who received chemotherapy alone, elderly patients were more likely to receive oxaliplatin-based or 5-FU-based chemotherapy, probably because these types of chemotherapy are less aggressive and more readily tolerated than modern first line chemotherapy that includes molecular agents. These findings imply that under-treatment occurred because of physician preferences; however, cancer-specific survival of elderly and non-elderly patients who received chemotherapy alone was not significantly different. Elderly and non-elderly groups who went on to undergo multimodality therapy did not differ significantly in the initial main chemotherapy regimen they received. In other words, elderly patients who were able to undergo the same aggressive chemotherapy as non-elderly patients were more likely to continue on to multimodality therapy. In elderly patients, therapeutic decisions concerning palliative chemotherapy versus conversion chemotherapy prior to multimodality therapy must be made on an individual basis, however, the factors that determine the optimal therapeutic approach in elderly patients are not well known. In this regard, one important consideration is overall survival time after secondary cytoreductive therapy. In the current study, the survival of elderly patients with comorbidity was inferior to that of those without comorbidity, even after multimodality therapy. Our findings suggest that both tumor-related factors such as treatment markers and host-related factors may be more reliable prognostic indicators in elderly patients undergoing multimodality therapy than they are in non-elderly patients. Because GPS is a well-known surrogate marker for response to treatment and can be used to predict tumor recurrence in a variety of cancers (McMillan et al., 2003; Crozier et al., 2006; Forrest et al., 2003; Proctor et al., 2011), and because we recently reported the usefulness of a modified GPS in patients undergoing multimodality therapy for advanced CRC (Toiyama et al., 2011; Inoue et al., 2013), we assessed its value in the current study. Our findings suggest that modified GPS is a potential prognostic marker for elderly patients receiving multimodality therapy.

Limitations of our study included the small number of patients with huge difference considering its dimension (37 versus 235) and that it was a single-site study; consequently, the findings may not be applicable to all elderly patients with CRC, and more patients should be involved to explore useful predictors of indications for multimodality therapy in elderly patients. However, we were able to identify patterns associated with multimodality therapy in patients aged >75 years with CRC and to compare the outcomes of elderly and non-elderly patients.

5. Conclusion

Chronological age alone should not be a contraindication to multimodality therapy of CRC in elderly patients. To improve survival in the elderly, selection of palliative chemotherapy versus or active multimodality therapy for patients is very important. Furthermore, appropriate selection criteria for multimodality therapy in elderly patients may include not only tumor characteristics but also host- or treatment-related factors such as comorbidities or surrogate markers, including modified GPS.

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