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Coping and survival in patients with leukemia undergoing allogeneic bone marrow transplantation—long-term follow-up of a prospective study

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Abstract

Objective: The exploratory study examined the relationship between coping and survival in patients undergoing bone marrow transplantation (BMT). **Methods:** Patients scheduled for BMT were recruited from 1990 until 1995 at the University Hospital of Ulm, Germany. They were interviewed before transplantation, and the corresponding records were checked in December 2002. Seventy-two audiotaped interviews could be analyzed for 34 coping strategies as defined in the Ulm Coping Manual (UCM). Main outcome measure was survival time post-BMT. **Results:** On average, the patients were 35 years old, 65% were male, and 56% diagnosed acute leukemia (AL). Four coping strategies were found to show a clear trend towards an association with survival time: *emotional support*, *acceptance*, *taking control*, and *compensation*. The last strategy was associated with shorter, the others with longer survival. **Conclusion:** We found further evidence for an association between coping and survival. Because of the possible wide-reaching consequences for clinical management, replication of the data is essential.

Keywords: Bone marrow transplantation; Cancer; Coping; Prospective study; Survival

Introduction

Hematopoietic stem cell transplantation has become a treatment for malignant hematological diseases, which before were incurable as in the case of chronic myeloid leukemia (CML). It has reached the state of a standard therapy for several malignancies and may be considered one of the real advances in medicine [1,2]. Numbers of performed transplants have risen over time. The International Bone Marrow Transplant Registry assessed that, worldwide, in 2002, 15,000 persons received an allogeneic, and 30,000 persons an autologous bone marrow transplantation (BMT; [3]). BMT requires high efforts on the part of both the patient and the staff of the transplant unit, and it still consumes considerable amounts of monetary and nonmonetary resources. BMT is performed in an intensive care setting, but the transplant associated mortality is high, with estimations of up to 36% [4]. The threat of a relapse or the development of a secondary malignancy persists for the surviving patients. Long-term survival (>5 years) can be assumed for approximately half of the patients with allogeneic BMT, varying with several factors such as diagnosis, stage of disease, age of the recipient, and human leukocyte antigen (HLA) compatibility [5–7].

The impact of psychosocial variables on the survival of cancer is under debate [8–12]. In their review regarding BMT, Hoodin and Weber [12] concluded that somatic factors do not necessarily outweigh any effect of psychosocial variables on survival. Identifying psychological variables before BMT that could enhance the outcome of the treatment has significant clinical implications. Such knowl-

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edge may help to identify patients at risk, to decide on the allocation of resources, such as psychotherapeutic support, and to increase the chances for both acceptable quality of life and long-term survival.

The first bone marrow transplant in Germany was performed at the University Hospital of Ulm in 1972. From the beginning, patients undergoing this life-threatening treatment received psychological attention. The psychosocial aspects of BMT have been studied systematically in our institution since 1985. After a retrospective study of patients' response to their disease [13,14], a descriptive, prospective study was initiated in 1989. The aim of the study was to gain insight into the coping process of patients undergoing BMT and their psychosocial rehabilitation.

A key study by Greer et al. [15,16] reported on prolonged survival of women with breast cancer, who exhibited the coping style called "Fighting Spirit". The study attracted our attention to associations between coping and survival time after BMT. Preliminary analyses on parts of the final sample [17–19] revealed correlations between coping and long-term survival [words in italics refer to labels of clusters of coping strategies as defined in the Ulm Coping Manual (UCM)]: *resignation/hopelessness* [20] and *distraction* [19] were associated with shorter, *fighting spirit* with longer survival [19].

The present paper is based on a sample of 72 patients and a significantly extended follow-up period (approximately 6 years longer than in the last analysis [19]). It presents findings with respect to coping and survival and subjects the previous analyses of data to a critical revision. A hypothesis-testing approach would be inappropriate because substantial parts of the data were already analyzed in the former publications. Hypotheses concerning survival would be post hoc hypotheses. Therefore, we consider this study as explorative.

Patients and methods

The study was approved by the ethics committee of the University of Ulm. At the time of setting up our study (late 1980s), there was great concern on the side of the reviewers that participating in our study would put additional stress on the patients. Therefore, data collection had to be restricted to a minimum. After admission for their scheduled BMT, the patients were preselected for the study by the transplanting physician. Physicians' major reasons to exclude patients were difficulties in understanding German, a poor general condition, and logistical reasons (direct referral to the Ulm BMT unit from external institutions without sufficient time to perform the interview prior to transplant). Then, they informed the patients about the study, assuring them that participation in the study was voluntary and that non-participation would have no influence on the treatment in the unit. We had no control on the physicians' selection process. Patients who showed willingness to participate were met by the research interviewers, and written informed consent was obtained.

One hundred seventy-four patients diagnosed with an acute myeloid, an acute lypmphoblastic, or a CML were scheduled for allogeneic BMT during the recruiting period from May 1990 to July 1995 at the transplantation unit of the University Hospital of Ulm. Finally, 81 patients were preselected, and 79 participated in our study. Two patients refused to be recorded, five tapes were found to have technical faults. The final 72 interviews lasted, on average, 33.9 min (S.D.=14.8, range=14–93 min). Patients' files were checked in December 2002 with respect to survival.

Coping was assessed using the UCM [20]. The UCM defines 34 coping strategies. For each strategy, the manual describes its function, gives advice on differentiating a certain strategy from related strategies, and several examples of patients' statements representative of the strategy. The basis for ratings are tape recorded semistructured interviews. They were conducted after informed consent and before the conditioning regimen and focused on disease-related themes such as the course of disease, prior treatment, and changes in private and working life as formerly described [17,19]. The trained raters (psychologists) had to listen to the tapes and decide if coping occurred. Then, they had to code the appropriate one of the 34 strategies. The rater and the interviewer were different persons. Raters were blind towards the further course of the patient's disease. Tschuschke, the main author of the UCM, and colleagues evaluated the interrater reliability as good [kappa ranging between .68 and .97 (mean .86) as formerly reported [17,21].

Statistical procedures

Statistical evaluation was performed using the SPSS for Windows software program [22]. Nonparametric evaluations of differences in the means between two independent groups were done using the Mann–Whitney U test, and the χ^2 test was used for fourfold tables (calculating exact instead of approximate test statistics). Survival analyses [23] were performed either according to Kaplan–Meier or using Cox regression. The dependent variable was survival time post-BMT until death or, in the case of censored data, time until last visit to the transplant centre as documented in the patients' files. Comparisons of probabilities were performed using the log-rank (Kaplan–Meier) or Wald statistic (Cox). Multiple variables (with dummy coding where required) were evaluated simultaneously in Cox regression models. The calculation of the internal consistency of scale values was done using Cronbach's alpha. A P value $<.05$ was considered statistically significant.

Results

Ninety three out of 174 patients died during follow-up. Their survival time ranges between 12 days and approx-

Table 1
Characteristics of all patients with leukemia treated with BMT between May 1990 and June 1995 at the University Hospital of Ulm, comparing participants and nonparticipants

		Nonparticipants (n=95)		Interviewed patients (n=79)		Final sample (n=72)		Group total (n=174)		
		Count	%	Count	%	Count	%	Count	%	χ^{2a} (P)
Age at BMT[b]	Younger	47	49.5	40	50.6	36	50.0	87	50.0	.005
	Older	48	50.5	39	49.4	36	50.0	87	50.0	(.999)
Stage of disease	Early[c]	57	60.0	57	72.2	51	70.8	114	65.5	2.10
	Not early	38	40.0	22	27.8	21	29.2	60	34.5	(.19)
HLA-identical	No	29	30.5	14	17.7	13	18.1	43	24.7	3.38
sibling	Yes	66	69.5	65	82.3	59	81.9	131	75.3	(.07)
Female donor to	No	68	71.6	60	75.9	55	76.4	128	73.6	.49
male recipient	Yes	27	28.4	19	24.1	17	23.6	46	26.4	(.60)
Gender	Female	37	38.9	28	35.4	25	34.7	65	37.4	.31
	Male	58	61.1	51	64.6	47	65.3	109	62.6	(.63)
Diagnosis	AL	66	69.5	46	58.2	40	55.6	112	64.4	3.42
	CML	29	30.5	33	41.8	32	44.4	62	35.6	(.08)
Total body	No	7	7.4	9	11.4	9	12.5	16	9.2	1.25
irradiation	Yes	88	92.6	70	88.6	63	87.5	158	90.8	(.30)
T-cell depletion	No	71	74.7	56	70.9	54	75.0	127	73.0	.002
	Yes	24	25.3	23	29.1	18	25.0	47	27.0	(.999)
CMV status	Negative	32	33.7	40	50.6	36	50.0	72	41.4	4.52
(patient)	Positive	63	66.3	39	49.4	36	50.0	102	58.6	(.04)

The χ^2 tests were performed for the fourfold tables combining dichotomous variables with nonparticipants/final sample.
[a] df=1.
[b] Median split at 35.3 years; mean age (standard deviation) for nonparticipants, interviewed patients, and final sample was 35.7 (10.8), 34.9 (9.6), and 35.0 (9.7) years, respectively.
[c] First chronic phase (CML)/first complete remission (AL).

imately 9 years (median=221 days) post-BMT. The 81 censored cases (=event had not occurred at day of follow-up) were observed between 3 and 12 years (median=3288 days). For our study sample of 72 patients, we registered 40 events (between 20 days and approximately 9 years, median=256.5 days) and 32 censored cases (approximately 6 to 12 years, median=3233 days).

Participants and nonparticipants

At the time of BMT, our study sample of 72 patients was, on average, 35 years old (range=16–55). Forty-seven patients were male and 40 patients were diagnosed with an acute leukemia (AL). Table 1 compares the 79 interviewed patients, the final sample of 72 patients, and the 95 nonparticipants in the study for several medical variables. There seems to be a trend towards an overrepresentation of the diagnosis CML, early stage of disease, and the availability of an HLA-identical sibling donor, and a significant overrepresentation of negative cytomegalovirus (CMV) status in the participating group. But this trend by which study participants, compared with nonparticipants, have more favorable conditions pretransplant does not result in prolonged survival post-BMT [median (mean) survival time 2316 (2338) days for nonparticipants (n=95), and 1990 (2340) days for the final sample (n=72); Kaplan–Meier survival analysis, log rank=.04, df=1, P=.84].

Additional information on marital status and education (usually not systematically documented in the medical records) is available only for 62 patients of our study sample of 72 due to missing data: 74% of these patients were married, and 32% had higher education (school >11 years). Comparing these 62 patients and the 10 patients with missing data, with respect to the variables mentioned in Table 1, we found no significant differences (χ^2 tests, all P values >.16). Therefore, we performed analyses involving these two variables with 62 cases.

Prognostic medical factors and survival time (total sample)

When examining the relationships between coping and survival, we need to statistically control for the influence of the prognostic medical factors. For this purpose, we consider four well-established hematological factors for risk assessment of patients before allogeneic BMT: recipient's age, stage of disease at time of transplantation, histocompatibility, and sex of donor and recipient [24]. Better outcome was associated with younger age, early stage of disease, an HLA-identical sibling donor, and no female donor in the case of a male recipient. We did not take into account the time from diagnosis to transplant because the suggested cut-off of 1 year (higher risk if >12 months) applies to CML, but not to AL. According to Bull and Spiegelhalter ([25], p. 1061), at least 10 events are needed for each predictive variable (covariates) in a Cox-regression model. With four medical and at least one coping variable as covariates and 40 events in the final sample, this rule could not be followed. Therefore, the four medical predictors were entered into a Cox-regression model (see Table 2), and a prognostic score for the total sample was computed as the sum of the variables weighted by the

Table 2
Cox regression model entering age, stage of disease at time of transplantation, histocompatibility, and sex of donor and recipient as covariates

Variables	*B*	S.E.	Wald	*df*	Sig.	Exp(*B*)
Age at BMT (years)	.020	0.011	3.602	1	.058	1.021
Stage of disease[a]	−.476	0.215	4.905	1	.027	0.621
HLA-identical sibling[a]	−.447	0.239	3.491	1	.062	0.640
Female donor to male recipient[a]	−.323	0.261	1.532	1	.216	0.724

B=beta weight; S.E.=standard error; Wald=Wald statistic; *df*=degrees of freedom; Sig.=significance; Exp(*B*)=e^B.
Exp(*B*) expresses the increase of risk for an increase of one unit in the corresponding variable keeping all other variables constant. For dummy-coded variables, Exp(*B*) represents the relative risk of the group with dummy coding=1 compared with the reference group coded=0.
[a] Dummy coded: 1, if early stage of disease, HLA-identical sibling donor, or female donor and male recipient respectively; 0, in all other cases.

corresponding beta-weight from the Cox-regression model. This score serves to divide the patients into two prognostic groups by a median split. We will refer to this new prognostic dichotomous variable as *somatic prognosis*. Both groups differed significantly (log rank=17.7, *df*=1, $P<.0005$), with a mean survival time of 2953 days for favorable prognosis (median could not be calculated due to more than 50% censored cases) and 1719 (median 563) days post-BMT for unfavorable prognosis. The final sample and the nonparticipants do not differ with respect to somatic prognosis ($\chi^2=.93$, *df*=1, $P=.35$).

Revision of data analysis

Following theoretical considerations, the 34 UCM coping strategies were grouped into the six clusters *cognitive structuring*, *compliance*, *distraction*, *fighting spirit*, *passive reception*/*resignation*, and *social contacts*.

Table 3
Percentage of patients who mentioned the particular coping strategy (%), results for Kaplan–Meier survival analyses for coping strategies: log rank-statistics and *P* values for unadjusted (P_{unadj}) and adjusted for somatic prognosis (P_{adj})

Number	Coping strategy	%	Log rank[a]	P_{unadj}	Log rank[a]	P_{adj}
01	Diverting activity	32	<0.005	.98	0.12	.73
02	Hesitation	43	0.03	.86	0.10	.75
03	Active compliance	74	0.01	.92	0.38	.54
04	Active avoidance	13	0.04	.85	0.01	.90
05	**Accepting**	57	5.47	**.019**	9.18	**.002**
06	Altruism	50	0.85	.36	0.35	.56
07	Anticipation	64	<0.005	.96	0.19	.66
08	Attribution	28	0.78	.38	0.23	.63
09	Rebelling	62	0.12	.73	0.42	.52
10	Taking the initiative	57	0.01	.91	1.25	.26
11	**Emotional support**	89	8.10	**.004**	6.19	**.013**
12	Rumination	54	2.77	.096	0.47	.49
13	Humor	32	5.60	.018	3.01	.083
14	Information seeking	61	2.22	.14	0.62	.43
15	Cognitive distraction	19	1.26	.26	0.97	.32
16	**Compensation**	6	6.15	**.013**	5.79	**.016**
17	Model learning	42	0.90	.34	0.97	.33
18	Optimism / hope	81	0.92	.34	0.29	.59
19	Passive compliance	53	0.05	.83	0.13	.72
20	Positive fantasies	33	0.45	.50	1.19	.28
21	Positive reframing	32	0.06	.80	0.02	.88
22	Problem analysis	82	1.34	.25	1.56	.21
23	Stimulus control	60	0.74	.39	0.13	.72
24	Relativizing	54	0.01	.94	0.09	.77
25	Resignation/hopelessness	40	4.03	.045	2.63	.10
26	Self valorization	51	1.26	.26	0.51	.48
27	**Taking control**	68	5.28	**.022**	5.69	**.017**
28	Giving meaning	31	0.08	.77	0.13	.72
29	Social distraction	17	2.13	.14	3.17	.075
30	Social retreat	31	1.33	.25	5.14	.023
31	Stoicism	53	1.27	.26	1.00	.32
32	Wishful thinking	38	2.76	.096	0.91	.34
33	Wish fulfillment	15	0.27	.60	0.82	.37
34	Fatalism	18	2.94	.086	1.96	.16

Bold = strategies with $P < .05$ for both log rank-tests.
[a] *df*=1 for all log rank tests.

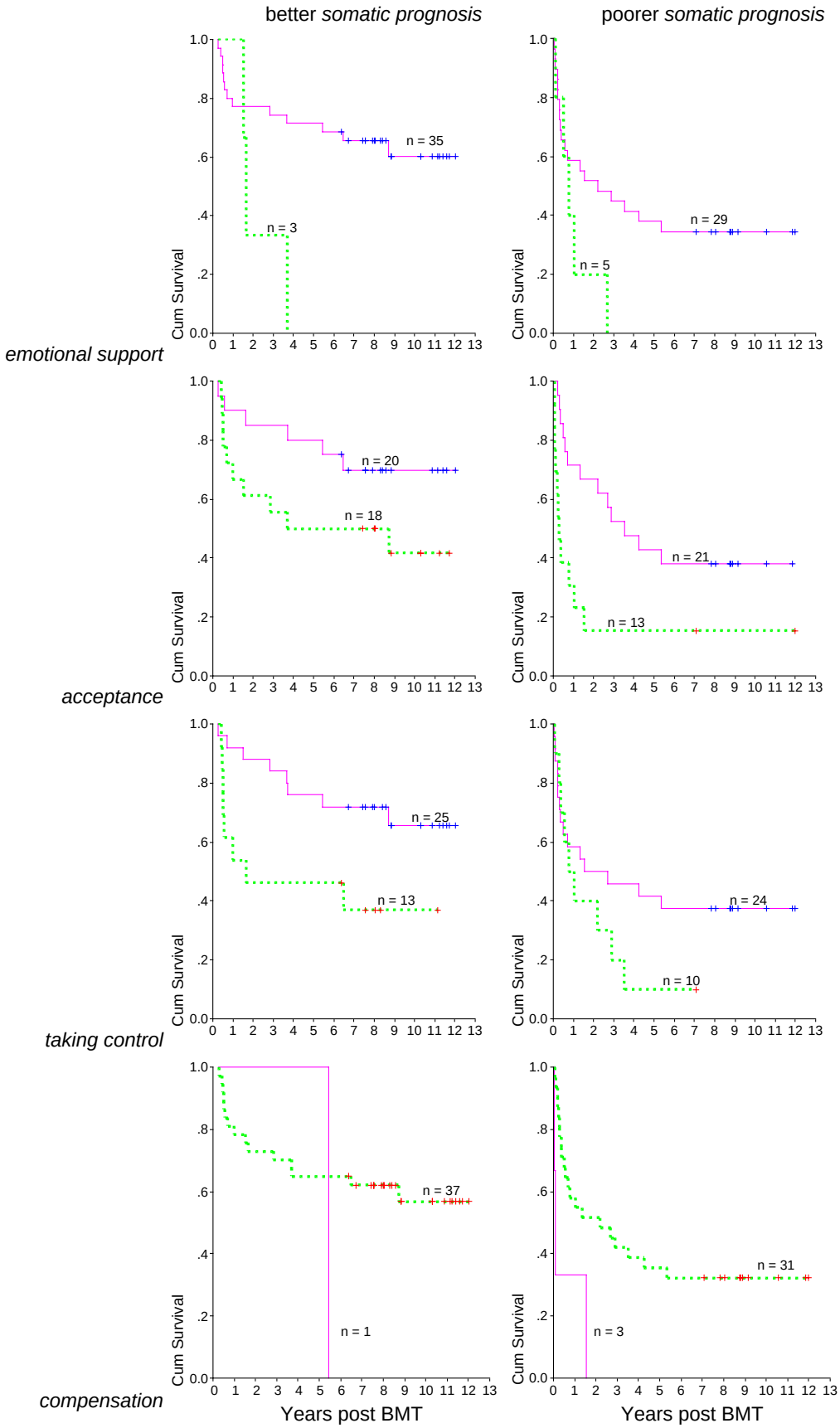

Fig. 1. Kaplan–Meier survival curves (years post-BMT) for the coping strategies emotional support, acceptance, taking control, and compensation comparing the presence (solid line) and absence (broken line) of each strategy opposing the groups with better and poorer somatic prognosis.

Table 4
Mean and median survival times (with 95% confidence interval) for poor, intermediate, and good coping patterns

Coping pattern	Patients	Censored cases	Mean (95% CI)	Median (95% CI)
Poor (coping score=2)	17	2	563 (141–986)	189 (48–330)
Intermediate (coping score=3)	30	12	2276 (1627–2925)	1354 (0–2772)
Good (coping score=4)	25	18	3342 (2668–4016)	Cannot be calculated

Scores for strategies were calculated as the frequency of occurrences of a strategy during an interview divided by interview length, and cluster scores as the mean strategy scores for strategies included in the cluster [19]. The formerly published results [17–19] are based on these scores for coping clusters. Since that time, we have come to interpret this grouping of individual strategies into coping clusters as problematic. Analyzing the internal consistencies of the six clusters in the final sample, we find that Cronbach's alpha ranges from −.02 (cluster compliance) to .41 (cluster distraction). All scales contain individual strategies that correlate negatively. Thus, grouping individual strategies in clusters receives no or only slight empirical support.

The calculation of scores (frequency divided by interview length) for individual strategies as a measure of their intensity does not appear to be justified, neither on the basis of content in general nor in the literature or empirically in the present study. As Oakland and Ostell state ([26], p. 149): "the problem with simply correlating the frequency of use of a particular strategy with an outcome measure is that it assumes that using the strategy will have uniform effects regardless of other aspects of the situation and the person". Empirically, in our raw value matrix (72 cases by 34 strategies), more than half (54.8%) of the cells contain zeroes. Another 19.5% contain a "1". No individual strategy, with the exception of the strategies *emotional support*, *optimism/hope*, and *problem analysis*, was reported at least twice by more than half of the patients studied. We therefore concentrate our further evaluation on the binary information (presence or absence) of the individual coping strategies.

Coping and medical/sociodemographic variables

To explore possible relationships between coping and other variables, we performed significance tests between the 34 coping indicator variables on one hand and 12 medical and sociodemographic variables [i.e., the nine variables mentioned in Table 1, somatic prognosis, education (higher vs. lower), and marital state (single vs. married)] on the other hand. From these 408 (34 strategies×12 variables) χ^2 tests, 22 showed P values <.05, a number that would be expected by mere chance. But nine of these 22 significances are observed with somatic prognosis: *anticipation*, *rebelling*, *taking the initiative*, *rumination*, *humor*, *information seeking*, *stimulus control*, *social retreat*, and *wishful thinking*. Hence, there seems to be a relationship between medical status before BMT and coping, but no clear empirical support was found for any other associations with medical and sociodemographic variables.

Coping and survival

Each coping variable was subjected to Kaplan–Meier survival analyses as single predictor without and with stratification for somatic prognosis. Table 3 summarizes

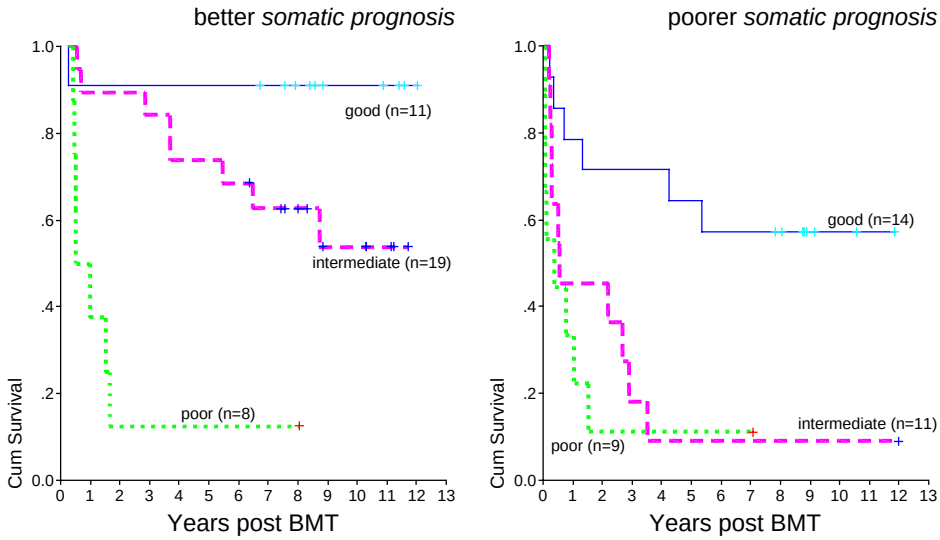

Fig. 2. Kaplan–Meier survival curves (years post-BMT) for the three groups with good, intermediate, and poor coping style by better and poorer somatic prognosis.

the *P* values for all log rank tests. Further attention will be directed to those strategies that passed the level of significance in both evaluations: *emotional support*, *acceptance*, *taking control*, and *compensation*. The latter strategy is associated with shorter, the other three with longer survival. These four strategies (one unfavorable strategy and three favorable strategies) are not associated with any of the abovementioned 12 medical and sociodemographic variables (all *P* values >.05). They are statistically independent from each other, too (all *P* values >.29).

Fig. 1 shows the Kaplan–Meier survival curves comparing the presence or absence of these coping strategies in patients with better and poorer somatic prognosis.

To illustrate the potential impact of the four identified strategies, a coping score was defined as "1+number of favorable strategies—1 if compensation was rated", ranging from 0 to 4. Table 4 shows the survival times for three groups with good (coping score=4), intermediate (coping score=3), or poor coping (coping score=2). The differences between the survival curves (see Fig. 2) are highly significant (not adjusted for somatic prognosis: log rank=24.5, *df*=2, *P*<.0005; adjusted for somatic prognosis: log rank=25.6, *df*=2, *P*<.0005). The three groups differ considerably with respect to mean survival: approximately 9, 6, and 2 years post-BMT, respectively.

Discussion

We prospectively investigated the relation between coping and survival post-BMT in 72 patients. In studies relating psychological variables to survival in cancer patients, small or heterogeneous samples and short follow-ups, as well as neglecting somatic variables, were often criticized. With respect to the homogeneity of the sample, we restricted our study to leukemia patients and allogeneic transplantation. Regarding psychosocial factors and survival in this circumscribed group of patients, no other prospectively designed study [27–36] includes a larger (sub-) sample or had a longer follow-up period. Furthermore, we paid special attention to the control for somatic variables by considering well-known hematological risk factors [24]. We reanalyzed formerly published data gathered in a prospectively designed study with an increased sample size and extended follow-up period, and subjected the original strategy of data analysis to a rigorous revision, eliminating several shortcomings of the previous analyses.

The use of objective assessments for measuring the role of psychosocial variables on the survival of a malignant disease seems to have advantages. In a review, Hürny [37] reported that most positive results were gained by studies using interviews and that psychometric methods failed to produce unequivocal findings. He assumed that the interviewer–patient interaction yields additional prognostic relevant information. This conclusion is supported by the observation in the present study that interviews with patients who had no emotional support were, on average, about 13 min shorter than in those who did (22 vs. 35 min; difference highly significant, *P*<.001). Concerning BMT, self-assessments by questionnaires yield conflicting results [27,31–33]. On the other hand, investigations with objective assessments based on less structured interviews report effects of psychosocial variables on survival [29,38]. Giving items by a questionnaire provokes different answers than open questions in an interview. We think that, with our interview, we are closer to the patient's internal cognitive representation of the coping process than is possible with stimulated recall by standardized questionnaires.

Besides somatic prognosis, only the four coping strategies, emotional support, acceptance, taking control, and compensation, were associated with survival. These strategies were not correlated with somatic prognosis. Therefore, we conclude that coping is an additional factor influencing survival and not just a surrogate parameter for the health status of the patients.

Emotional support means expressing one's own feelings and sorrows and looking for emotional support from others and is part of social support in general. Empirical evidence for the positive effect of social relationships on survival in cancer patients has been found in the reviews by Watson and Greer [11] and Fox [9]. Formal quantitative factors, such as patients' marital status or the size of their social network, do not appear to play as important a role as subjective, qualitative factors do, such as the feeling of belonging to a network or the experience of support [39]. In our study, all patients without emotional support died within 4 years after BMT. The experience of emotional support may be the crucial active ingredient in social support. Recent results from Bolwell et al. [40] are pointing in the same direction: The presence of a consistent caregiver during inpatient time is associated with improved survival during the first year post-BMT.

Acceptance of the disease as a strategy means that patients cope actively in the sense of an active, realistic cognitive and behavioral confrontation with their current situation. It is distinct from a passive, stoic acceptance of the situation as described by Molassiotis et al. [41] that we would label as *stoicism* or *fatalism*. Taking control consists of motivating one's self to face the challenge, to consciously direct one's own behavior, and to control one's own emotions. We suppose that these two strategies represent the active coping seen by many research groups as evidence of "good" coping [42–45]. Both strategies include fundamental aspects of a fighting attitude, as described by Greer ([46], p. 44): "These patients fully accept the diagnosis, adopt an optimistic attitude and may see their illness as a challenge. They express a determination to fight the cancer . . . ". In earlier studies, Greer et al. [15,16] reported on an association between fighting spirit and survival of breast cancer, but failed to replicate these findings in a recent study [47], where only helplessness/hopelessness was negatively predictive of survival. We assume that this coping factor is comparable to our strategy resignation, for which we found

only a weak tendency (see Table 4). This discrepancy between the earlier and later results of Greer's group may be related not only to differences in the number of cases (62 vs. 578 patients) but also in the sampling methods, because they originally used the clinical interview format [46].

Compensation, as defined in the UCM, means vicarious satisfaction or abreaction of several impulses. Behaviors such as excessive sleep, alcoholic abuse, overuse of tranquilizers, etc., belong to this category. In our sample, it is an unfavorable coping behavior. An understanding of compensation as a marker for unhealthy behavior seems to be self-evident, but due to the small number of only four patients who reported this behavior, its association to survival is susceptible to chance. Therefore, to discuss the impact of compensation on survival in more detail would require further research with more cases.

We were astonished about the magnitude of the effects seen in Figs. 1 and 2. Even if the effects were lower, the question arises as to how "good coping" translates into prolonged survival. Several pathways for the connection of diagnosis- and treatment-related stress on the course of the disease can be considered [48,49]. Coping can influence compliance and health behaviors that impact on morbidity and mortality many years after BMT. It may be that patients with an active coping style may better fit to the health care system and thereby raise their chances of receiving earlier diagnostics and treatments. In addition, the direct effects of coping efforts on the neuroendocrine and/or neuroimmunological systems may exist. Myeloablative conditioning regime is somehow like resetting the immune system to zero. During the recovery period, psychosocial variables eventually have more long-term influence on the further course of the disease than during other stages of the disease.

For illustrative purposes, we divided the patients into three different groups according to their coping score. Apparently, the patients with an unfavorable coping style (score =2) had a disadvantageous course of disease. If our results can be confirmed in another study, this assignment of patients to groups could be useful for a more differentiated clinical approach. We assessed coping with the disease for the whole time from the diagnosis to the time of the interview. If it is the case that coping during this pretransplant period is relevant for the posttransplant course of the disease, our results strongly argue for early psychological interventions. We do not know if unfavorable coping could be changed in this challenging situation of life threat. Nevertheless, as a next step, we should try to influence maladaptive coping patterns. Patients with unfavorable coping styles might benefit from preparatory psychotherapeutic treatment. In consequence, results of BMT may be ameliorated. Education, behavioral training, individual psychotherapy, and group interventions are beneficial ways of supporting cancer patients [50]. With our results, we offer some ideas as to what direction therapeutic methods should go. Probably, acceptance and taking control may be best addressed by confrontation and cognitive–behavioral methods. Compensation requires, at least, education and behavioral training, while emotional support may be fostered in the therapeutic alliance or through participation in support groups. Which intervention serves best is an empirical question.

Maybe, moderating or intervening variables (e.g., health behavior and compliance) exist that are correlated with both coping and survival. Therefore, further research should direct towards identifying such variables, too. Unfortunately, we were not able to collect more data on psychosocial variables in depth due to the concerns of the reviewers of our project. By now, we know that the participants were not unduly stressed by the interviews and would have been able and probably willing to answer to a package of questionnaires. In a further study, more information should be gathered, at least on psychological distress (e.g., depression, anxiety, and mood) and quality of life.

With respect to the fact that the interviews with patients who reported no emotional support were shorter than that of those with patients who did one could argue that the talkativeness of the patients would have been responsible for our results. The duration of the interview per se was not associated with survival time. A more complex view will stress the patient–interviewer interaction that allows the patient to talk about his situation and overtly express his feelings and emotions. In that view, it could be the case that not the coping strategy "emotional support" is associated with survival. It can well be the case that a patient receives emotional support but he does not talk about it in the interview setting. Then eventually this nonexpression may be responsible for the significances we have found. This thought reminds to the concept of "ambivalence over expressing emotion" that seems to be correlated with well-being [51]. It seems to be worth to study this variable in further studies in this field, too.

We are well aware that our findings have to be seen as results of an exploratory analysis. With respect to the recruiting process, our sample is quite selective and representing perhaps a special group. Nevertheless, we have found associations between coping and survival for this selective sample. Maybe, other strategies would have been predictive for other patients, other diseases, or other treatment categories but that needs empirical clarification. Besides all considerations, the fact of multiple testing and the possibility of chance findings remain. Because of their possible wide-ranging implications, however, the results must be replicated in a further prospective study, which we already have initiated [52].

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