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ORIGINAL REPORT

Impact of Psychotherapeutic Support for Patients With Gastrointestinal Cancer Undergoing Surgery: 10-Year Survival Results of a Randomized Trial

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ABSTRACT

Purpose
The impact of psychotherapeutic support on survival for patients with gastrointestinal cancer undergoing surgery was studied.

Patients and Methods
A randomized controlled trial was conducted in cooperation with the Departments of General Surgery and Medical Psychology, University Hospital of Hamburg, Germany, from January 1991 to January 1993. Consenting patients (N = 271) with a preliminary diagnosis of cancer of the esophagus, stomach, liver/gallbladder, pancreas, or colon/rectum were stratified by sex and randomly assigned to a control group that received standard care as provided on the surgical wards, or to an experimental group that received formal psychotherapeutic support in addition to routine care during the hospital stay. From June 2003 to December 2003, the 10-year follow-up was conducted. Survival status for all patients was determined from our own records and from three external sources: the Hamburg cancer registry, family doctors, and the general citizen registration offices.

Results
Kaplan-Meier survival curves demonstrated better survival for the experimental group than the control group. The unadjusted significance level for group differences was $P = .0006$ for survival to 10 years. Cox regression models that took TNM staging or the residual tumor classification and tumor site into account also found significant differences at 10 years. Secondary analyses found that differences in favor of the experimental group occurred in patients with stomach, pancreatic, primary liver, or colorectal cancer.

Conclusion
The results of this study indicate that patients with gastrointestinal cancer, who undergo surgery for stomach, pancreatic, primary liver, or colorectal cancer, benefit from a formal program of psychotherapeutic support during the inpatient hospital stay in terms of long-term survival.

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INTRODUCTION

Psycho-oncology is currently a target of behavioral research in medicine. The effects of psychosocial interventions, although perceived by the lay community to be of benefit, remain controversial.[1,2] Moreover, there is still professional debate on the most appropriate timing of the intervention (before, during, or after medical treatment), which approaches are efficacious (standardized or individualized programs: individual, family, or group treatment), and whether or not psychosocial interventions influence survival.[3,4]

A recent review, covering the period from 1954 to 1999, included 329 psychosocial intervention trials, but only four of those focusing on survival showed at least fair methodology.[5] From these studies, with follow-up ranging from 1 to 6 years and sample sizes ranging from 66 to 121 patients, no conclusions or recommendations for psychosocial interventions could be made. In the same year, Spiegel in *Nature Reviews Cancer*,[4] identified five studies with potential benefit for cancer patients' survival, as well as five studies with neutral results and provided a salient review of these trials. Although the methods differed, both reviews concluded that, despite the growing body of knowledge in this area, further research was necessary. Since 2002, there has been one additional trial.[6] While no differences in survival were found, psychological outcomes were positive. In addition, Fawzy et al[15] presented the results of their 10-year follow-up and

concluded that the intervention effect was still significant for survival, but the relative risk (RR) for those who participated in the intervention (compared with those who did not) decreased compared to the original study (from RR = 6.89 to RR = 2.87).

In 1991, we undertook a randomized trial in the surgical department of the University Hospital of Hamburg-Eppendorf (Germany) to determine if an individualized program of psychotherapeutic support, provided during the inpatient hospital period to patients with gastrointestinal cancer and scheduled for surgery, would promote better quality of life than that perceived by patients not receiving this intervention. Because survivorship status is inherent in quality of life analyses, we first examined if and to what extent the psychotherapeutic support influenced survival. The results were published in 1999[7] and can be summarized as follows: during the first 2-year follow-up period, 69 of 136 patients in the experimental group and 45 of those 135 in the control group survived. The Kaplan-Meier survival curves found an unadjusted significance level for group differences of $P = .002$ (log-rank $\chi^2 = 9.47$). Cox regression models including TNM staging or the residual tumor classification (RTC) also found significant differences between the groups, in favor of the experimental patients.[7] This article presents survival results of the 10-year follow-up.

Objectives

In the original study, the experimental group receiving psychotherapeutic support demonstrated significantly better survival at 2 years than the group not receiving such support. The primary objective of this study was, thus, to examine survival at 10 years to determine if the survival advantage was maintained. A secondary objective was to determine if survival differences remained apparent by site of tumor.

PATIENTS AND METHODS

Original Trial: Design and Treatment Regimens

The original design, a two-arm randomized trial of standard care as provided in the surgical wards of the University Hospital of Hamburg-Eppendorf (Germany) in the early 1990s, or this standard care plus formal psychotherapeutic support, has been extensively described in a previous article.[7] In brief, from January 1991 to January 1993, 271 consenting patients who met defined inclusion criteria, including a preliminary diagnosis of cancer of the esophagus (n = 31), stomach (n = 40), pancreas (n = 40), liver/gallbladder (n = 108), or colon/rectum (n = 52), and who were scheduled for surgery, were stratified by sex, and allocated via a stratified, blocked, randomized design with randomly ordered block sizes to either routine care and services as delivered on the four surgical wards by ward personnel, or to similar care and services but with the addition of an assigned psychotherapist who provided treatment to the patient during both the pre- and postoperative inpatient hospital stay. This individual (one of two such therapists who had received specialized training for the study) provided educational information, a supportive relationship, and ongoing psychotherapeutic counseling to the patients at the bedside. Specifically, the therapist gave individualized care based on findings from the psychotherapeutic intake interview. In general, the therapists provided ongoing emotional and cognitive support to foster "fighting spirit" and to diminish "hope and helplessness."[8] Emphasis was placed on assisting the patient in forming questions for the other caregivers. While maintaining appropriate confidentiality, the patient's overall well-being was routinely discussed with the surgical team. More than 95% of inpatient interventions took place on the ward, and the remainder at other places within the hospital. The therapist also encouraged family and social support. Before discharge, the therapist explored the patient's emotional and cognitive interpretation of the surgery, and assisted the patient in planning for the future. Figure 1 provides a flow chart showing the overall study design including patient accrual; Table 1 shows reasons for nonparticipation of screened patients.

Instrumentation and Data Collection

Data on patients' sociodemographic and clinical characteristics, the process of care, and patient outcomes related to survival and quality of life were collected. Before random assignment and surgery, and at 10 to 14 days, and 3, 6, 12, and 24 months after surgery, patients completed European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire C30,[9] as well as the disease-specific module for each patient's cancer site. Baseline measurements of characteristics related to the surgical care process were made using defined criteria or established protocols, and were verified by the treating surgeons and/or the pathologists. Details can be found in the previous article.[7]

10-Year Follow-Up Study

For the 10-year follow-up study, three sources of information were used to obtain survival data. The Hamburg Cancer Registry *(Hamburger Krebs Register*), established in 1990, was the primary source. When its records were found to be incomplete, family doctors of persons enrolled on the original study were contacted by mail and asked to supply survival information from their records of individual patients. Each request contained information about the original study and copies of the ethical permission forms from the two agencies (*die Ärztekammer Hamburg* and *der Hamburgische Datenschutzbeauftragte*) that approved this study. If there was no response to the written request, a telephone call was made by the principal investigator to the physician or, in some cases, to his or her successor to determine survivor status of a particular patient. As a third source of information, the national registry of citizens (*das Einwohnermeldeamt*) that tracts individuals who change addresses within Germany was used.

Statistical Analysis

Analysis was based on the intent-to-treat model. This approach was taken despite the fact that for ethical reasons (the right for equality of treatment) patients were permitted to cross to the alternate group if they requested a change. The baseline characteristics of the patients in the experimental and control groups were compared to ensure that the composition of the groups was similar; differences were examined with χ^2 and t tests. As a crucial outcome, the difference in survival was first examined via Kaplan-Meier survival curves, log-rank test, and the generalized Wilcoxon statistic. To ensure that results were not influenced by group variations in key prognostic variables (tumor site, RTC, TNM stage, additional therapies, age), we controlled for them through Cox proportional hazards models. Using stepwise backward selection ($\alpha < .05$ for inclusion and $\alpha > .10$ for exclusion), the best fitting prognostic models were determined.

RESULTS

Original Study Group Comparisons

Sociodemographic characteristics showed no significant differences by treatment group.[7] Similarly, clinical characteristics such as site of tumor, TNM staging, RTC, as well as postoperative treatment regimes at the time of the original study demonstrated no significant differences between experimental and control groups.[7] Postoperatively, our surgical investigator reviewed the preoperative information on sites of tumor and reclassified the liver/gallbladder patients using histopathologic information which had become available (Table 2). Again, there were no statistically significant differences between groups, although the experimental group had five patients with extrahepatic metastases from a primary gastrointestinal cancer, compared with one in the control group.

Descriptive Results of the Psychosocial Intervention

In addition to the semistructured intake interview, the experimental patients had a median of six contacts (mean 6.91; range, two to

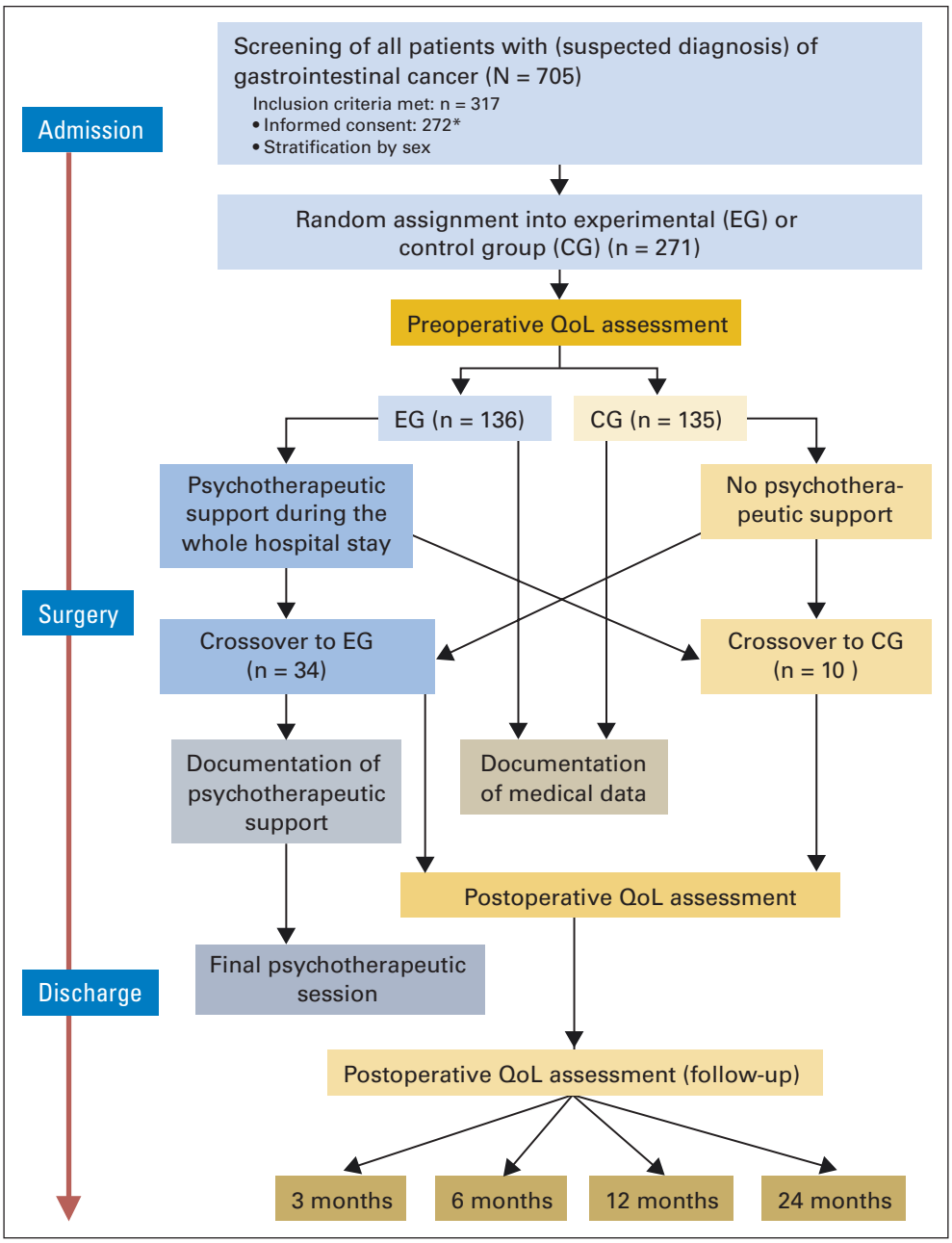

Fig 1. Study design and patient accrual. *One patient from the control group (CG) withdrew consent postoperatively. QoL, quality of life.

25 contacts) with their psychotherapist. This translates into a mean duration of 222 contact minutes (range, 40 to 1,090 minutes; reassuring contacts of 10 minutes or fewer were not counted) with a median of 22 days in hospital (range, 3 to 144 days). A similar amount of time was spent by the therapist with the doctors and nurses discussing and exchanging patient-related information. For ethical reasons, 34 patients crossed from the control to the experimental group and 10 changed from the experimental to the control group. The patients who crossed to the experimental group received the same amount of treatment, but had no formal intake interview and received more contacts during the postoperative phase. Patients in the experimental group received different types of intervention: supportive therapy (81%), crisis intervention (12.3%), relaxation training (5.8%), and short psychotherapy (0.9%). Almost one third (31.5%) of all psychological interventions focused on information about diagnostic procedures, treatment, and rehabilitation, while the more psychosocial aspects such as life balance/existential matters, future expectations, relationships, and emotional coping were equally distributed with 10% to 15% each. The topics death and dying, silence/nonverbal communication, and small talk each accounted for approximately 5% of the overall treatment time.

Survival at 10 Years

Using the Hamburg Cancer Registry, 57 (50%) of 114 patients alive at the 2-year follow-up could be found. Information from the patient's physician provided data on an additional 46 (40%), and the national registry of citizens confirmed the status of the remaining 11 (10%). Survival status of all 271 patients was, thus, established.

Table 1. Reasons for Nonparticipation of Screened Patients

No. of Patients	Reason for Nonparticipation
705	Were identified and screened
107	Were too old
22	Had other operations or severe unrelated illness within the past 3 months
21	Did not speak sufficient German
5	Had a history of psychiatric illness requiring treatment
53	Were not scheduled for operation
13	Were too ill to participate
129	There was insufficient time for pre-operative assessment
13	Diagnostic testing immediately confirmed no tumor
13	Received care on nonsurgical wards
12	Were not included for various other reasons
317	Were approached for informed consent
45	Refused to participate in the trial
272	Were randomly assigned*
1	Patients withdrew consent postoperatively

*Two hundred seventy-two patients provided informed consent preoperatively, but one of the patients in the control group withdrew postoperatively. Therefore, 271 patients were included in the study.

Table 2. Information About Tumor Sites, Classifications, and Postoperative Treatments by Treatment Group (N = 271)

Characteristic	Experimental (n = 136) No.	Experimental (n = 136) %	Control (n = 135) No.	Control (n = 135) %
Suspected preoperative sites of tumor				
Esophagus	15	11.0	16	11.9
Stomach	19	14.0	21	15.6
Pancreas	18	13.2	22	16.3
Liver/gallbladder	54	36.8	54	40.0
Colon/rectum	30	22.1	22	16.3
Postoperative reclassification of patients with liver/gallbladder tumors				
No. of patients	54		54	
Liver/gallbladder (primary tumor)				
Liver metastases (primary/colorectal cancer)	22	40.7		
Liver metastases (other tumors)	21	38.9	23	42.6
Extrahepatic metastases (primary GI cancer)	6	11.1	23	42.6
	5	9.3	7	12.9
			1	1.9
Postoperative TNM staging				
No tumor/benign	11	8.1	11	8.1
Local	23	16.9	15	11.1
Locoregional	39	28.7	41	30.4
Metastatic	62	45.6	66	48.9
Missing	1	0.7	2	1.5
Residual tumor classification				
Benign tumor	11	8.1	11	8.1
R0	44	32.4	29	21.5
R1	21	15.4	16	11.9
R2	41	30.1	47	34.8
Inoperable				
Preoperative decision	9	6.6	19	14.1
Intraoperative decision	6	4.4	4	3.0
Unknown	4	2.9	9	6.7
Postoperative treatment*				
No further treatment	36	26.5	25	18.6
Reoperation	2	1.5	3	2.2
Chemotherapy	20	14.7	11	8.2
Radiotherapy	5	3.7	1	0.7
Alternative treatment†	18	13.2	6	4.4
Combination of two treatments	12	8.8	22	16.3
Combination of three treatments	4	2.9	1	0.7
Unknown	39	28.7	66	48.9

*These data are based mainly on patient reports.
†This treatment was most often the use of mistletoe in various forms of application.

During the 10-year follow-up period, 29 of 136 experimental patients and 13 of 135 control patients survived. Table 3 presents information on the survival status by TNM staging, RTC, and sex. A review of our 10-year data shows, that among those with metastases at the time of the original operation, only three of 62 patients in the experimental group and three of 66 patients in the control group were still alive. The results were different for those with local or regional involvement. Of the original patients with local disease, 13 (57%) of 23 patients in the experimental group and three (21%) of 15 in the control group were alive. Similarly, in those with regional involvement five (13%) of 39 patients in the experimental group compared with one (2%) of 41 in the control group were alive. In the group with benign tumors (11 of 11), eight subjects in the experimental group and six control group subjects were alive after 10 years; in those with missing TNM staging data (one of two), no patients were alive.

The cumulative proportions of all patients surviving in these groups are plotted in Figure 2. A visual comparison suggests a clinically important difference, and the test for the equality of survival curves supports a statistically significant difference in survival between patients receiving the experimental intervention and those in the control group (log-rank $\chi^2 = 11.73$; $P = .006$). Respecting the intent-to-treat approach, all patients, even those with no or a benign tumor (11 patients in each group), were included in the survival analysis. However, it should be noted that the exclusion of these patients did not affect the results at 10 years. (log-rank $\chi^2 = 10.43$; $P = .001$).

Despite the fact that there were no differences in the composition of the experimental and control groups with respect to site of tumor, TNM staging, or RTC,[7] adjusted analyses using Cox proportional hazards models were undertaken. The results are presented in Table 4. As presented, neither the hazard ratios nor the *P* values changed very much with the adjustment for each indicator of disease. In a stepwise regression, other factors like age, sex, and surgical experience were excluded from the model. Because data on additional therapies are based mainly on patient's report, thus being less valid than data from the charts, we decided not to include them in the statistical analysis. It should be noted, however, that the inclusion of the variable additional therapies (Table 2) did not affect the results of uni- or multivariate survival analyses (experimental group > control group) substantially. There are no significant survival differences between patients with or without additional therapy (log-rank $\chi^2 = 0.807$; $P = .369$). This result holds true for patients with and without chemotherapy alone (log-rank $\chi^2 = 0.212$; $P = .645$).

DISCUSSION

The focus in the psycho-oncology literature, as initiated by Spiegel et al,[10] has been on studies of women with metastatic breast disease. Of the five available randomized trials,[6,10,11-13] only that by Spiegel et al[10]

Table 3. Survival Status (No. of patients alive) at 2- and 10-Year Follow-Up for TNM Staging, Residual Tumor Classification, and Sex by Treatment Group

Characteristic	2-Year Follow-Up				10-Year Follow-Up			
	EG		CG		EG		CG	
	No.	%	No.	%	No.	%	No.	%
TNM staging								
Benign	11	100	8	88.9	8	72.7	6	66.7
Local	21	91.3	7	50.0	13	56.5	3	21.4
Regional	13	33.3	11	26.2	5	12.8	1	2.4
Metastatic	23	37.1	17	25.8	3	4.8	3	4.5
Unclear	1	100	2	50.0	0	0	0	0
Residual tumor classification								
Benign	11	100	6	85.7	8	72.7	5	71.4
R0	31	72.1	23	71.9	17	39.5	6	18.8
R1	15	71.4	5	27.8	3	14.3	0	0
R2	5	7.2	5	11.1	0	0	0	0
Inoperable	9	15.5	10	13.2	1	1.7	1	1.3
Missing	3	100	1	50.0	0	0	1	50.0
Tumor site								
Esophagus	5	7.2	4	8.9	0	0	0	0
Stomach	9	13.0	4	8.9	6	20.7	2	15.4
Pancreas	9	13.0	5	11.1	3	10.3	2	15.4
Colon/rectum	18	26.1	8	17.8	10	34.5	2	15.4
L/G primary	12	17.4	8	17.8	9	31.0	3	23.1
L/G colon met	14	20.3	13	28.9	1	3.4	3	23.1
L/G other met	2	2.9	3	6.7	0	0	1	7.7
L/G extrahep	0	0	0	0	0	0	0	0
Sex								
Male	34	41.0	25	29.8	13	15.7	5	6.0
Female	35	66.0	20	39.2	16	30.2	8	15.7
Total	69	50.7	45	33.3	29	21.3	13	9.6

Abbreviations: EG, experimental group; CG, control group; L/G, liver/gallbladder; met, metastases; extrahep, extrahepatic.

reported a significant difference in survival for women receiving a psychosocial intervention. In the literature it appears that psychotherapeutic treatment has a more positive impact on patients with leukemia,[14] melanoma,[15] Hodgkin's disease, non-Hodgkin's lymphoma,[16] and (endstage) cancer of different tumor sites.[17,18]

The original results of this study in terms of survival benefits for the experimental patients were somewhat surprising and had not been hypothesized. Thus, it seems useful to compare our protocol with those of the trials mentioned above to determine which aspects of our approach might be of special importance.

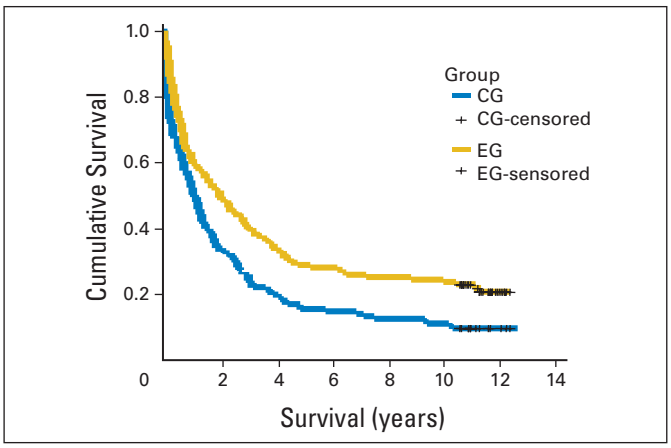

Fig 2. Cumulative proportions of patients surviving in the experimental group (EG; n = 136) and the control group (CG; n = 135).

Different from several trials,[6,10-13] we started our interventions preoperatively, during the diagnostic phase. Clinical experience suggests that this is the time of the greatest anxiety/uncertainty. The therapists were involved preoperatively, to deal with specific anxieties related to surgery. They helped during the first postoperative week when patients have to face two different stressors: physical impairment due to extensive surgery and psychological distress due to uncertainty about the prognosis. The therapists also assisted the patients in coping with predictable stressful events, such as communication of the histopathologic findings or the necessity of adjuvant treatment. Given the low physical and mental state, this often cumulates not just in a significant decrease of hope and confidence, but in a real personal crisis (eg, What will happen with me and my life, to my family?). Based on clinical experience, being present when things happen might be more effective than talking about such events weeks later.

Similar to the trial by Fawzy et al,[15] we focused not just on active coping but on information about all aspects of surgery and oncological treatment.

The discharge interview—when the patients reviewed their time in the hospital—targeted emotional integration of the whole event. It included elements of cognitive-existential therapy as in the trials by Spiegel et al or Kissane et al.[6,10]

The reason why only some studies of patients receiving psychotherapeutic support do better than some that do not may be related to the timing of the intervention. Perhaps expecting positive effects from

Table 4. Cox Proportional Hazards Models for Survival by Group: Covariates Include TNM Staging, Tumor Sites, and Residual Tumor Classification

Variable	Hazard Ratio	95% CI	*P*
TNM			
Benign	1	—	0
Local	3.207	1.262 to 8.152	
Regional	9.889	4.140 to 23.620	
Distant metastases	19.679	8.220 to 47.110	
Diagnosis			
Colon/rectum	1	—	0
Liver/gallbladder other metastases	0.605	0.307 to 1.192	
Liver/gallbladder colon metastases	0.585	0.363 to 0.942	
Liver/gallbladder extrahepatic metastases	2.048	0.845 to 4.963	
Liver/gallbladder primary tumor	2.101	1.292 to 3.417	
Stomach	1.663	1.018 to 2.699	
Esophagus	2.129	0.997 to 2.776	
Pancreas	2.129	1.326 to 3.419	
Treatment			
Control group	1	—	.003
Experimental group	0.653	0.495 to 0.861	
Residual tumor classification			
Benign	1	—	0
Inoperable	15.807	7.198 to 34.709	
R0	3.151	1.471 to 6.753	
R1	5.603	2.588 to 12.130	
R2	17.713	8.196 to 38.277	
Diagnosis			
Colon/rectum	1	—	.002
Liver/gallbladder other metastases	0.837	0.431 to 1.624	
Liver/gallbladder colon metastases	1.051	0.674 to 1.639	
Liver/gallbladder extrahepatic metastases	1.751	0.720 to 4.259	
Liver/gallbladder primary tumor	1.940	1.164 to 3.231	
Stomach	1.445	0.900 to 2.319	
Esophagus	2.104	1.261 to 3.510	
Pancreas	1.758	1.096 to 2.819	
Treatment			
Control group	1	—	.013
Experimental group	0.693	0.519 to 0.924	

NOTE. Because of colinearity of TNM and R margin, no overall model could be calculated.

psychotherapeutic treatment in patients with metastatic disease is often too late in the course of the disease to have an impact. Stress reduction, if that is the causal mechanism, may have to occur earlier, both in terms of tumor stage and intervention, to achieve positive results. The recent study by Kissane et al[6]—that examined early-stage cancer with intervention that started after the medical treatment found, like most other studies of breast cancer, psychological benefits but no influence on survival—may support our suggestion.

The mechanism of early stress reduction seems to be important, since over the 2-year follow-up we found no indication that pre- and postoperative adjuvant therapies had a substantial impact on survival. The mechanisms of how this supportive approach influences better coping, more awareness toward health behaviors, and enhanced social support remain theoretical because these rather complex concepts were not measured distinctly.

Recent results of brain research have begun to identify the molecular basis of emotion, especially fear.[19] However, one can only speculate to which extent those results may contribute to explaining the survival results of this study.[20] If reduced, fear may influence the immune system to continue to function more efficiently,[21] and it may have facilitated better survival in the experimental group. This conjecture, of course, remains purely hypothetical.

Limitations and Weaknesses

The strengths of this trial, its closeness to daily clinical practice, and its focus on individual patient's needs, are at the same time its weaknesses. Accruing cancer patients preoperatively did not allow for stratification by tumor site because the diagnosis was preliminary at random assignment. This led to the inclusion of 22 patients with no or benign tumors (whose exclusion did not alter the results). The individualized approach, which certainly reflects the reality of daily, psycho-oncological cancer care, makes replication trials difficult. Another limitation is the fact that we could only compare those adjuvant therapies that took place within our hospital. For the follow-up we had to rely on patients' self-report. Nonetheless, neither the information from the charts nor that from the patients give any indication that there were meaningful differences between the groups concerning the additional treatments or that those small differences could account for the overall survival differences. However, the biggest limitation in extrapolating the results was the change in the health care system. Compared with the time of the original trial, preoperative inpatient hospital days have dropped to 1 or 2, thus reducing the opportunity for preoperative interventions, or perhaps necessitating new approaches to implementing psychosocial care preoperatively.[22]

Conclusion and Implications

We have conducted a randomized controlled trial of psychotherapeutic support to assess its value when used with gastrointestinal cancer patients undergoing surgery. At 10 years we controlled for the long-term effects of all variables known to be of prognostic importance in cancer treatment. Being a part of the intervention group that received psycho-oncological support during the surgical inpatient treatment period remains, like TNM stage, RTC, and tumor site, an independent prognostic factor for survival at 10 years. Therefore, we conclude that an individualized psycho-oncological approach delivered within an interdisciplinary surgical team that intervenes as early as possible preoperatively has a significant (both statistically and clinically) impact on long-term survival of patients with gastrointestinal cancer. In terms of costs and benefits, the provision of time-limited individual counseling, an average of 222 minutes of patient-therapist contact, and a similar amount of time with the patient's physicians (an investment of about 7 hours per patient), yields rather substantial benefits to survival.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

Conception and design: Thomas Küchler, Doris Henne-Bruns, Sharon Wood-Dauphinee
Provision of study materials or patients: Stefanie Rappat
Collection and assembly of data: Stefanie Rappat
Data analysis and interpretation: Thomas Küchler, Beate Bestmann, Stefanie Rappat, Doris Henne-Bruns, Sharon Wood-Dauphinee
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Other: Doris Henne-Bruns [principal surgical investigator]

REFERENCES

1. Ross L, Boesen EH, Dalton SO, et al: Mind and cancer: Does psychosocial intervention improve survival and psychological well-being? Eur J Cancer 38:1447-1457, 2002

2. Chow E, Tsao MN, Harth T: Does psychosocial intervention improve survival in cancer? A meta-analysis. Palliat Med 18:25-31, 2004

3. Spiegel D: Mind matters – group therapy and survival in breast cancer. N Engl J Med 345:1767-1768, 2001

4. Spiegel D: Effects of psychotherapy on cancer survival. Nat Rev Cancer 2:383-389, 2002

5. Newell SA, Sanson-Fisher RW, Savolainen NJ: Systematic review of psychological therapies for cancer patients: Overview and recommendations for future research. J Natl Cancer Inst 94:558-584, 2002

6. Kissane DW, Love A, Hatton A, et al: Effect of cognitive-existential group therapy on survival in early-stage breast cancer. J Clin Oncol 22:4255-4260, 2004

7. Kuechler T, Henne-Bruns D, Rappat S, et al: Impact of psychotherapeutic support on gastrointestinal patients undergoing surgery. Hepatogastroenterology 46:322-335, 1999

8. Greer S, Moorey S, Watson M: Patients adjustment to cancer: The Mental Adjustment to Cancer (MAC) scale vs. clinical ratings. J Psychosomat Res 33:373-377, 1989

9. Aaronson NK, Ahmedzai S, Bergman B, et al: The European Organisation for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 85:365-376, 1993

10. Spiegel D, Bloom JR, Kraemer HC, et al: Effect of psychosocial treatment on survival of patients with metastatic breast cancer. Lancet 2:888-891, 1989

11. Cunningham AJ, Edmonds CV, Jenkins GP, et al: A randomized controlled trial of the effects of group psychological therapy on survival in women with metastatic breast cancer. Psychooncology 7:508-517, 1998

12. Edelmann S, Lemon J, Bell DR, et al: Effects of group cognitive behaviour therapy on the survival time of patients with metastatic breast cancer. Psychooncology 8:474-481, 1999

13. Goodwin PJ, Leszcz M, Ennis M, et al: The effect of group psychosocial support on survival in metastatic breast cancer. N Engl J Med 345:1719-1726, 2001

14. Richardson JL, Shelton DR, Krailo M, et al: The effect of compliance with treatment on survival among patients with hematological malignancies. J Clin Oncol 8:356-364, 1990

15. Fawzy FI, Canada AL, Fawzy NW: Malignant melanoma: Effects of a brief, structured. Arch Gen Psychiatry 60:100-103, 2003

16. Ratcliffe MA, Dawson AA, Walker EG: Eysenck personality inventory L-scores in patients with Hodgkin's disease and non-Hodgkin's lymphoma. Psychooncology 4:39-45, 1995

17. Linn MW, Linn BS, Harris R: Effects of counseling for late stage cancer patients. Cancer 49: 1048-1055, 1982

18. Ilnyckyi A, Farber J, Cheang MC, et al: A randomized controlled trial of psychotherapeutic intervention in cancer patients. Ann R Coll Physicians Surg Can 27:93-96, 1994

19. Shumyatsky GP, Tsvetkov E, Malleret G, et al: Identification of a signaling network in lateral nucleus of amygdala important for inhibiting memory specifically related to learned fear. Cell 111:905-918, 2002

20. Dudai Y: Fear thou not. Nature. 421:325-327, 2003

21. Ader R, Felten D, Cohen N: Interaction between the brain and the immune system. Annu Rev Pharmacol Toxicol 30:561-602, 1990

22. Berend M, Teren K, Sagermann R, et al: The "Kiel model": A psychooncological support program following international standards. Psychooncology 15:172, 2006 (suppl)

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