

Social Relationship Factors, Preoperative Depression, and Hospital Length of Stay in Surgical Patients

Henning Krampe¹ · Anke Barth-Zoubairi¹ · Tatjana Schnell^{2,3} · Anna-Lena Salz¹ · Léonie F. Kerper^{1,4} · Claudia D. Spies¹

Published online: 13 August 2018 © International Society of Behavioral Medicine 2018

Abstract

Purpose The interrelated associations of social relationship factors, depression, and outcomes of surgical patients are yet unexplored. The purpose of this study was to investigate whether depression mediates effects of general social support, loneliness, and living alone on hospital length of stay (LOS) of 2487 patients from diverse surgical fields.

Method Social relationship factors and depression were assessed prior to surgery. The PROCESS macro for SPSS was used to conduct three simple mediation models that tested the indirect effects of social relationship factors on LOS mediated through depression. The models were adjusted for age, gender, preoperative physical health, surgical field, severity of medical comorbidity, and extent of surgical procedure.

Results Social support and loneliness had significant indirect effects on LOS that were statistically mediated by preoperative depression. Lower social support and the feeling of loneliness were considerably related to higher depression which predicted longer LOS. While social support and loneliness had no direct effects on LOS, there was a small significant direct association of living alone with shorter LOS.

Conclusion Data suggest that social support and loneliness are indirectly related with surgical outcomes by an association with depression which in turn is related to worse outcomes.

Trial Registration NCT01357694

Keywords Depression · Length of hospital stay · Mediation analysis · Preoperative · Social support · Surgical

Introduction

There is considerable evidence that factors indicating the quality and quantity of social relationships are associated with both mental and physical health outcomes [1-12]. Among these factors, the strongest effects have been documented for perceived social support which can be described as the perceived

Henning Krampe henning.krampe@charite.de

- ¹ Department of Anesthesiology and Operative Intensive Care Medicine (CCM, CVK), Charité - Universitätsmedizin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Charitéplatz 1, 10117 Berlin, Germany
- ² Psychology of Personality and Individual Differences, Institute of Psychology, Leopold-Franzens-University, Innsbruck, Austria
- ³ MF Norwegian School of Theology, Oslo, Norway
- ⁴ Department of Anaesthesiology, Intensive Care, Emergency and Pain Medicine, Hospital Wolfenbuettel gGmbH, Wolfenbuettel, Germany

availability of social resources that improve an individual's coping with stress [1, 3, 11]. Higher levels of perceived social support are related to lower rates of morbidity and mortality in a wide range of conditions [1-3, 13-15].

During the last four decades, several theoretical models were developed to explain how social support might influence physical health [1, 9-11]. In a comprehensive review article, Uchino et al. state that a common feature of these models is that they suggest psychological mechanisms mediating stress-buffering and health-promoting effects of social support: "Importantly, major models of social support and health have postulated psychological mechanisms such as perceived stress, depression, and positive affect as important pathways

... In fact, we are not aware of a major theoretical model linking social support to health that does not postulate psychological mechanisms as potential pathways" [11, page 950]. Among the suggested mediators, depression is of particular interest because numerous studies demonstrated that worse social relationships are related to increased depression [7, 16]. Depression, in turn, has a major negative influence on the etiology, development, and course of a variety of medical diseases through diverse neurobiological mechanisms [17, 18]. Interestingly, recent research found that increased preoperative depression is also associated with worse outcomes in surgical patients [19–23]. Concerning the causality of the relationship between social support and depression, there are several longitudinal studies showing that higher levels of social support lead to a decrease of depressive symptoms; however, in some studies, the association between social support and depression also affecting the experience of social support [7, 16, 24].

In surgical patients, the association of social support and outcomes has been less often studied, and this might also be due to some uncertainty of which outcome variables might be comparable for different surgical fields [14, 15, 19]. Hospital length of stay (LOS) is an established indicator of recovery time that can be used as a valid and robust outcome measure across diverse surgical fields and procedures, as well as medical diseases [25]. However, there are only five studies that have investigated the relations between social support and LOS in surgical patients, four from cardiovascular surgery [26–29], and one from maxillofacial surgery [30]. Three of these investigations showed small but statistically significant relationships between lower social support and longer LOS [26, 28, 30], and two showed no significant associations of social support and LOS [27, 29].

In a recent study of the authors' research group including 2624 surgical patients, it was found that LOS of patients with clinically significant depression was longer than LOS of patients without depression [21]. Importantly, the association of depression and prolonged LOS was independent of the impact of age, gender, and essential somatic factors. So far, there are no prospective studies that investigate the associations of social relationship factors, depression, and LOS in large samples of patients from diverse surgical fields. The study at hand, which is based on a new data set, aims to investigate how perceived social support and two social relationship factors indicating facets of objective and subjective social isolation, living alone and feeling of loneliness, are related to preoperative depression and LOS in patients from diverse surgical fields. Living alone and feelings of loneliness are moderately negatively related to social support; however, these three social relationship factors have shown to be discrete constructs associated with both mental and physical health [3–5, 7, 8, 12, 31-35]. Thus, it is worthwhile to investigate to what extent the three social relationship factors contribute independently from each other to the prediction of preoperative depression and LOS. Considering the strong evidence of poor social relationships as risk factors for depression, and given that major theoretical models suggest depression as a psychological pathway through which social support affects physical health, the question arises as to what extent mediation processes may play a role within the associations between social relations, depression, and LOS. The hypotheses of this study were that

the social relationship factors would show indirect effects on longer LOS that would be statistically mediated by preoperative depression, as well as additional direct effects that would be independent from the effects of depression and the demographic and somatic covariates. Concerning the direction of the associations, it was expected that (1) higher perceived social support would be associated with lower depression and shorter LOS, (2) living alone and feeling of loneliness would be associated with higher depression and longer LOS, and (3) higher depression would be associated with longer LOS.

Methods

Setting, Study Design, and Patient Sample

This prospective observational study is a part of a research project investigating Bridging Intervention in Anesthesiology (BRIA) which was approved by the Ethics Committee of Charité University Medicine Berlin [EA1/014/11] and registered with ClinicalTrials.gov. [Identifier: NCT01357694]. The study was conducted according to the principles expressed in the Declaration of Helsinki. Data were collected from November 2011 to June 2012, and participants provided written informed consent for all procedures. The full details of the setting and assessment instruments are available elsewhere [36, 37].

Preoperative data were collected within a computerassisted psychosocial self-assessment including questionnaires of depression and perceived social support. This assessment was performed before the anesthesiological examination in the preoperative assessment clinics of the Charité -Universitätsmedizin Berlin, Campus Charité Mitte and Campus Virchow Klinikum, Berlin, Germany. Recruitment of participants was carried out from Monday to Friday between 9.00 am and 5.00 pm in order to cover the complete opening hours of the assessment clinics. Six months after the preoperative assessment, medical data were obtained from the electronic patient management system of the hospital.

Eligibility criteria were defined as follows. Inclusion criteria: written informed consent to participate after having been properly instructed; patient of the preoperative anesthesiological assessment clinic; age ≥ 18 years. Exclusion criteria: surgery with an emergency or urgent indication; inability to attend the preoperative assessment clinic (bedside visit); insufficient knowledge of German language; members of the hospital staff; admitted in police custody; accommodation in an institution by official or court order; being under guardianship; psychiatric, neurological, or other conditions associated with limited legal capability, or limited capability of being properly instructed or giving informed consent. The eligibility criteria were listed in

the written patient information, and they were assessed by psychologists via open questions and additional double-checking of patient files.

Of the 7236 patients assessed for eligibility, 3541 were not eligible according to inclusion/exclusion criteria, 991 refused to participate, and data from 217 patients were not available for data analyses. As a result, data of 2487 patients were analyzed in this study. Figure 1 shows the details of the inclusion process.

Measure of Depression

Fig. 1 Flowchart of phases of the

clinical trial

The 7-item depression scale of the Hospital Anxiety and Depression Scale (HADS) was used to assess depressive symptoms. The HADS-D is an internationally widely used and validated self-report scale for depressive symptoms in general medical patients [38–40]. Items are rated on a 4-point Likert scale from 0 to 3, and the sum score ranges from 0 to 21. In the German test manual, a cutoff point \geq 9 is recommended to identify clinically significant depression [39]. According to a recent meta-analysis, this cutoff point has a sensitivity of 0.751 and a specificity of 0.798 for the criterion standard "major depressive disorder" [41]. In the present sample, the Cronbach alpha of the HADS-D was 0.82, indicating good reliability.

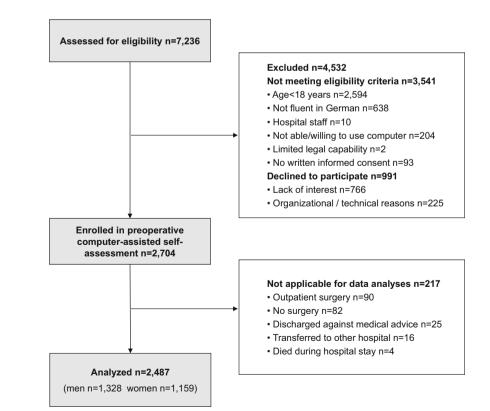
Measures of Social Relationship Factors

Social support was measured with an eight-item self-report subscale of the Berlin Social Support Scales (BSSS) [42]. This subscale assesses general emotional and instrumental perceived social support, and items are rated on a 4-point Likert scale from 1 to 4. In the present sample, the scale shows high reliability with a Cronbach alpha of 0.93.

Single-item questions of the preoperative psychosocial self-assessment measured the two other social relationship factors, living alone versus living together with at least 1 other person, and feeling of loneliness. Both items were binary-coded: not living alone = 0, living alone = 1; not feeling lonely = 0, feeling lonely = 1.

Medical Measures

As an overall indicator for the physical health status, the evaluation of patients' perioperative risk according to the ASA (American Society of Anesthesiologists) physical status classification system was used [43, 44]. This evaluation was performed by the anesthesiologists who did the preoperative assessment. The ASA categories comprise healthy patients (ASA I), patients with mild systemic disease and no functional limitations (ASA II), patients with severe systemic disease with definite functional limitation (ASA III), and patients with



severe systemic disease that is a constant threat to life (ASA IV). For the present analyses, the four ASA categories were dichotomized by collapsing ASA I and II, as well as ASA III and IV.

The surgical field comprises the categories (1) head, neck, and neurosurgery; (2) abdomino-thoracic surgery; and (3) peripheral surgery [20, 21, 45, 46].

The severity of medical comorbidity was assessed with the Charlson Comorbidity Index (CCI, [47]) which is a widely used weighted classification system of comorbidity to measure cumulative burden of disease in clinical outcome research. According to the coding algorithm of Quan et al. [48], data of the hospital's electronic patient management system were screened for ICD-10 codes indicating the 19 CCI comorbidities. The CCI was calculated taking both major and secondary diagnoses into account. For data analyses, raw scores were transformed to four comorbidity grades according to Charlson et al. [47]: (0) "none": 0 points; (1) "low": 1-2 points; (2) "moderate": 3-4 points; and (3) "high": ≥ 5 points.

To quantify the extent of the specific surgical procedures that patients underwent, the 4-point item "operative severity" of the POSSUM scoring system (Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity) was applied [49, 50]. Based on previously published classification schemes, the specific surgical procedures were assigned to one of the four severity grades (minor = 1; moderate = 2; major = 4; major+ = 8). For this classification, the standardized German codes of surgical procedures were used [51].

Outcome LOS was measured in days by subtracting the date of admission to hospital from the date of discharge from hospital.

Statistical Analyses

The primary objective of this study was to examine to which extent preoperative depression mediated relations between the three social relationship factors and LOS. The PROCESS macro for SPSS [52, 53] was used to conduct three simple mediation analyses based on two multiple linear regression models. Categorical covariates with more than two categories were dummy coded before the inclusion into the regression model. The outcome variable "LOS (days)" measured the number of days of hospital stay. Because it was essentially positively skewed (skewness = 4.81), a transformed variable "LOS (days)" [54]. This transformed outcome variable "LOS (days)" [54]. This transformed outcome variable had a skewness of 0.48 which was acceptable for entering it as the dependent variable in the linear regression models.

The first step of the mediation analyses was based on a multiple linear regression model predicting depression as measured with the continuous HADS-D sum score. The model included simultaneously the three relationship factors social support, living alone, and feeling of loneliness. It was additionally adjusted for the covariates age, gender, preoperative physical health, surgical field, severity of medical comorbidity, and extent of surgical procedure, because these variables have been demonstrated to be important demographic and medical factors predicting LOS of surgical patients [20, 21]. In a next step, the HADS-D sum score was included in the predictor variables, and LOS was predicted within a second multiple linear regression model. Thus, the three mediation models were simultaneously adjusted for all of the three social relationship factors and the abovementioned demographic and medical covariates.

Figure 2 shows a graphical depiction of mediation analysis in form of a path diagram. The path c demonstrates a simple relationship between an independent variable X and a dependent variable Y. The paths a, b, and c' demonstrate the elements of a mediated relationship; they illustrate the different direct effects of the independent variable X and the mediator M. The coefficient a refers to the prediction of the mediator variable (*M*; here depression) by the independent variable (*X*; here perceived social support, living alone, feeling of loneliness), and the coefficient b refers to the prediction of the dependent variable (Y; here Ln LOS) by the mediator variable M. The coefficient c' refers to the prediction of the dependent variable Y by the independent variable X. Both coefficients b and c' are based on regression models that are adjusted for both the independent variable (X) and the mediator variable (M), whereas the coefficient c in the upper path of Fig. 1, called the total effect of X, refers to the prediction of Y by Xin a model that is not adjusted for the mediator variable. The indirect effects of each of the three social relationship factors on LOS were expressed as the products of the unstandardized

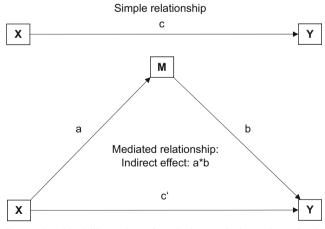


Fig. 2 Graphical illustration of mediation analysis. Path *c*: simple relationship between independent variable *X* and dependent variable *Y*. Path *a*: prediction of mediator variable (*M*) by independent variable (*X*). Path *b*: prediction of dependent variable (*Y*) by the mediator variable (*M*). Path *c*': prediction of dependent variable *Y* by the independent variable *X* and *X* and *X* and *X* and *X* and *Y* and

ordinary least square (OLS) regression coefficients $a \times b$. The indirect effects were tested with a bias-corrected bootstrapping approach based on 5000 bootstrap samples [52]. An indirect effect was considered statistically significant when the 95% bootstrap confidence intervals of the product $a \times b$ did not include 0. According to Hayes and Rockwood (2017), contemporary mediation analysis goes without the once applied criteria of former causal step models of mediation; in particular, it does not require the *a* path, *b* path, or *c* path (i.e., total effect) to be statistically significant [52, page 43]. Following a suggestion of Hayes [52, page 185f.], the effect sizes of $a \times b$ were estimated by the partially standardized effect ab_{ps} with 95% bootstrap confidence intervals. In models with one or more covariates, ab_{ps} expresses the indirect effect relative to the standard error of the estimate (SD_{v+}) of the dependent variable *Y*, with the definition $ab_{ps} = ab/SD_{y+}$ [55].

Descriptive results were expressed as relative frequencies in percent, mean, and standard deviation, as well as median and range of the 25th to 75th percentiles (interquartile range [IQR]). Bivariate correlations were tested using Pearson's correlation analyses. The comparison of LOS of groups with and without clinically significant depression were performed with the Mann-Whitney U test. For all statistical tests except the bootstrapping method, a two-tailed p value ≤ 0.05 was considered statistically significant.

Results

Sample Characteristics and Bivariate Relationships Among the Variables Under Study

Demographic, medical, and psychological characteristics of the included 2487 study participants are summarized in Tables 1 and 2. Perceived social support, loneliness, and depression showed moderate bivariate inter-correlations, whereas the correlations between living alone and the other social relationship factors and depression, as well as between depression and the LOS variables were small; the social relationship factors and both the original and the transformed LOS variables were weakly correlated (Table 2). A comparison of patients with clinically significant depression (n = 359) and those without depression (n = 2128) showed that LOS was significantly longer in patients with depression (Md = 4, IQR = 2 to 6 versus Md = 3, IQR = 2 to 5; p < 0.001).

Simple Mediation Analyses

The results of the multiple linear regression models for the prediction of the mediator variable depression and the dependent variable LOS are demonstrated in Table 3. Figures 3, 4, and 5 show the results of three simple mediation models testing the indirect effects of the social relationship factors on

Table 1Sample characteristics (N = 2487)

	Number or mean	% or SD		
Age (Years)	47.53	15.82		
Male	1328	53.4		
Physical health (ASA Classification	l) ^a			
ASA I, II	2132	85.7		
ASA III, IV	355	14.3		
Surgical field				
Neuro-, head and neck surgery	668	26.9		
Abdomino-thoracic surgery	932	37.5		
Peripheral surgery	887	35.7		
Medical comorbidity (CCI) ^b				
0 "none"	1642	66.0		
1 "low"	519	20.9		
2 "moderate"	168	6.8		
3 "high"	158	6.4		
Extent of surgical procedure (POSS	UM operative severity	item) ^c		
1 "minor"	912	36.7		
2 "moderate"	837	33.7		
4 "major"	547	22.0		
8 "major+"	191	7.7		

^a ASA classification (American Society of Anesthesiologists); ASA I, II: healthy patients (ASA I), and patients with mild systemic disease, no functional limitations (ASA II); ASA III, IV: patients with severe systemic disease with definite functional limitation (ASA III) and patients with severe systemic disease that is a constant threat to life (ASA IV). ^b CCI (Charlson Comorbidity Index). ^c POSSUM (Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity), item operative severity

LOS mediated through depression. The direct effects are indicated by the unstandardized OLS regression coefficients a, b, and c'; the indirect effects are indicated by the product of $a \times b$.

Social support and loneliness had significant indirect effects on LOS. The indirect effect of social support resulted in a negative product of *ab* of -0.046 (SE = 0.012; CI₉₅ [-0.070, -0.023]; $ab_{ps} = -0.080$ CI₉₅ [-0.121, -0.040]) (Fig. 3). Patients with higher perceived social support had lower depression which was associated with shorter LOS. Feeling of loneliness exhibited a significant positive indirect effect *ab* of 0.044 (SE = 0.012; CI₉₅ [0.023, 0.070]; $ab_{ps} =$ 0.077; CI₉₅ [0.040, 0.120]) (Fig. 4). Patients who felt lonely had stronger depression which was associated with longer LOS. Finally, the indirect effect of living alone was not significant, with *ab* of -0.002 (SE = 0.002; CI₉₅ [-0.007, 0.002]; $ab_{ps} = -0.003$ CI₉₅ [-0.012, 0.004]) (Fig. 5).

There were no significant independent direct effects (c') of social support and loneliness on LOS (Table 3). However, living alone had a small but significant independent direct effect with a negative direction indicating that patients who lived alone had shorter LOS (c' = -0.052; SE = 0.027; p = 0.050). The total effects of social support, loneliness, and

	Number or mean	% or SD	Perceived social support	Living alone	Loneliness	Depression	Clin. sign. depression	LOS, days
Perceived social support ^a	3.70	0.49						
Living alone ^b	658	26.5	-0.14***					
Loneliness ^c	232	9.3	-0.37***	0.17***				
Depression ^d	4.36	3.72	-0.49***	0.08***	0.38***			
Clinically sign. depression ^d	359	14.4	-0.42***	0.10***	0.33***	0.78***		
LOS, days	4.57	4.83	-0.04	-0.02	-0.02	0.10***	0.08***	
Ln LOS, days ^e	1.22	0.72	-0.01	-0.05*	-0.04*	0.11***	0.08***	0.83***

***p<0.001, **p<0.01, *p<0.05

^a BSSS (Berlin Social Support Scales), subscale perceived social support with higher scores indicating higher social support (range: 1–4). ^b Living alone (no = 0, yes = 1). ^c Loneliness (no = 0, yes = 1). ^d HADS-D (Hospital Anxiety and Depression Scale), subscale depression with higher scores indicating higher depression (range: 0–21); clinically significant depression according to HADS-D sum score cutoff \geq 9. ^e The transformed variable Ln LOS (days) was calculated by taking the natural logarithm of the original variable LOS (days)

living alone were c = -0.038 (SE = 0.026; p = 0.136), c = -0.009 (SE = 0.044; p = 0.845), and c = -0.054 (SE = 0.027; p = 0.043), respectively.

Discussion

In this study of patients from diverse surgical fields, perceived social support and feeling of loneliness showed significant indirect effects on LOS that were mediated by preoperative depression. In mediation models which were adjusted for the three investigated social relationship factors and for relevant demographic and medical covariates, lower social support, and the feeling of loneliness were significantly related to higher depression which predicted longer LOS. The indirect effect of living alone was not significant. While social support and feeling of loneliness had no direct effects on LOS, there was, contrary to the authors' hypotheses, a small direct association of living alone being related to shorter LOS.

Although there are no established rules of thumb to label the effect size ab_{ps} as small, medium, or high [52, page 184– 193], the indirect effects of social support and feeling of loneliness seem to be small. Interestingly, the bivariate intercorrelations of social support, depression, and LOS of this study are of similar and sometimes even greater magnitude compared with the corresponding correlations found in two landmark studies on social support, depression, and LOS of patients who underwent cardiovascular surgery [26, 27]. Indeed, a comprehensive systematic review of previous research suggests that associations of psychosocial factors and surgical outcome parameters do not have large effects but consist of manifold and multiply-determined relations of moderate and small effect size [19].

The results of the study at hand are consistent with previous studies that found substantial associations of social support and loneliness with depression and other indicators of mental distress [7, 8, 16, 31, 35]. Living alone had weak associations with the other social relationship factors and depression, as well as a small, but significant direct association with shorter LOS. These findings reflect previous findings suggesting that living alone is an equivocal indicator of social isolation [3, 4]. Living alone can indeed be both a risk factor and, under certain circumstances, also a protective factor for mental and physical health. Most importantly, some people living alone may have other resources of social connectedness with significant others, e.g., close and supportive relations with friends and family members without the need of living together. As a result, findings of associations of living alone and health outcomes are varying and less robust compared to the respective findings concerning subjective ratings of social support and loneliness [3, 4, 33].

To the authors' knowledge, there are no previous investigations of whether preoperative depression mediates indirect effects of social relationship factors on LOS of surgical patients. However, there are investigations of the direct effects of depression and social relationship factors on surgical outcomes. The current finding that preoperative depression predicts longer LOS can be regarded as a replication of recent findings in two different large samples of surgical patients [20, 21], and it is comparable to the results of previous investigations of small patient samples from specific surgical fields [e.g., 26, 27, 56–59]. Concerning the lack of a direct association between higher social support and lower LOS, data of the study at hand are inconsistent with the findings of Contrada et al. [26], Kulik et al. [28], and Krohne et al. [30], but comparable results have been found by two other investigations from cardiovascular surgery [27, 29]. Interestingly, similar to the study at hand, these two studies investigated general perceived social support which refers to the relatively stable, generalized experience of emotional and instrumental support that is performed by significant others [9]. This source of support is, however, under normal circumstances not directly available

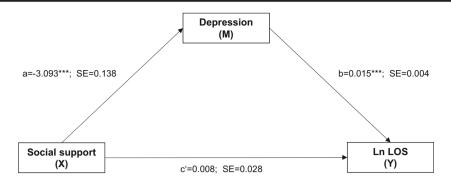
	Depression (M)			Ln LOS (Y)			
	Coefficient (SE)	t	р	Coefficient (SE)	t	р	
Depression ^a	_	_	_	0.015 (0.004)	4.036	< 0.001	
Social support ^b	-3.093 (0.138)	- 22.381	< 0.001	0.008 (0.028)	0.293	0.769	
Feeling of loneliness ^c	2.954 (0.236)	12.495	< 0.001	-0.053 (0.045)	-1.173	0.241	
Living alone ^d	-0.120 (0.145)	-0.825	0.409	-0.052 (0.027)	- 1.964	0.050	
Age	0.002 (0.005)	0.403	0.687	0.005 (0.001)	5.465	< 0.001	
Gender ^e	0.237 (0.130)	1.824	0.068	-0.052 (0.024)	-2.183	0.029	
Physical health (ASA classification) ^f	0.185 (0.197)	0.938	0.348	0.042 (0.036)	1.164	0.245	
Surgical field							
Neuro-, head and neck surgery (reference)	_	_	-	_	-	-	
Abdomino-thoracic surgery	-0.016 (0.171)	-0.091	0.928	0.036 (0.032)	1.153	0.249	
Peripheral surgery	-0.024 (0.176)	-0.137	0.891	0.209 (0.032)	6.472	< 0.001	
Medical comorbidity (CCI) ^g							
0 "none" (reference)	_	-	-	_	-	-	
1 "low"	0.503 (0.177)	2.837	0.005	0.211 (0.033)	6.483	< 0.001	
2 "moderate"	0.371 (0.278)	1.337	0.182	0.325 (0.051)	6.374	< 0.001	
3 "high"	1.009 (0.281)	3.589	< 0.001	0.618 (0.052)	11.923	< 0.001	
Extent of surgical procedure (POSSUM item) ^h							
1 "minor" (reference)	_	-	-	_	-	-	
2 "moderate"	-0.043 (0.163)	-0.263	0.793	0.296 (0.030)	9.859	< 0.001	
4 "major"	0.480 (0.170)	2.817	0.005	0.650 (0.031)	20.720	< 0.001	
8 "major+"	0.441 (0.261)	1.691	0.091	1.099 (0.048)	22.899	< 0.001	

Table 3 Multiple linear regression models for the prediction of the mediator variable depression ($R^2 = 0.30$, F = 75.61 [df: 14; 2472]) and the dependent variable Ln LOS ($R^2 = 0.37$, F = 97.89 [df: 15; 2471]), N = 2487 surgical patients

^a HADS-D (Hospital Anxiety and Depression Scale), subscale depression with higher scores indicating higher depression (range: 0–21). ^b BSSS (Berlin Social Support Scales), subscale perceived social support with higher scores indicating higher social support (range: 1–4). ^c Not feeling lonely (0) versus feeling lonely (1). ^d Not living alone (0) versus living alone (1). ^e Men (0) versus women (1). ^f ASA classification (American Society of Anesthesiologists); ASA I, II (0) versus ASA III, VII (1); ASA I: healthy patients; ASA II: patients with mild systemic disease, no functional limitations; ASA III: patients with severe systemic disease with definite functional limitation; ASA IV: patients with severe systemic disease that is a constant threat to life. ^g CCI (Charlson Comorbidity Index). ^h POSSUM (Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity), item operative severity

in the perioperative setting. Kulik et al. [28] and Krohne et al. [30], instead, did not investigate general social support but context-specific social support during the hospital stay and within the surgical setting. Kulik et al. measured actually received social support that spouses performed by visiting their husbands after the surgery [28], and Krohne et al. developed a questionnaire that assessed perceived social support regarding the stressful situation of the forthcoming surgery [30]. Both of their studies found significant associations between social support and LOS of surgical patients.

To summarize, the extent to which social relationship factors are directly associated with surgical outcomes seems to be far from clear. In their extensive review of psychosocial factors and surgical outcomes, Rosenberger et al. examined 11 studies that investigated the prediction of 16 diverse surgical outcomes by social support, social isolation, and social activity. The authors found that only four out of 16 outcomes were predicted by social relationship factors [19]. Following a suggestion of Rosenberger et al. [19], one might assume that general perceived social support and the feeling of belonging and connectedness (as the opposite of loneliness) are only weakly directly related to short-term surgical outcomes, although they are significantly associated with long-term health outcomes and mortality. Psychological distress like depression, in turn, seems to be substantially predictive for both surgical short-term outcomes and general long-term health outcomes [17-23, 60]. Social relationship factors have proven to be substantial risk factors for depression [6-8, 16, 24], and major theoretical models suggest the decrease of depression as a possible pathway through which higher social support has a positive influence on physical health [1, 9–11]. Thus, it is plausible to suggest that the association of social support and loneliness with surgical outcomes is predominantly indirect by mediation of depression.



Indirect effect: ab = -0.046, SE=0.012; Cl₉₅ (-0.070, -0.023)

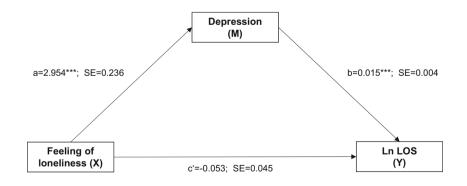
Fig. 3 Mediation model of the effect of social support (*X*) on Ln LOS (*Y*) through depression (*M*); N = 2487. The regression model includes the independent variable social support and the covariates living alone, feeling of loneliness, age, gender, physical health (ASA classification), surgical field, medical comorbidity (CCI), and extent of surgical

Limitations and Future Directions

This study assessed perceived social support, loneliness, and living alone in surgical patients. Despite the ambiguity of living alone, these variables are established social relationship factors, and in previous research, they showed substantial effects in predicting general health outcomes and mortality [1–13, 16, 24]. However, the applied social relationship measures do not explicitly refer to the context of the hospital stay, and as a consequence, it is not clear how the patients experienced the quality of their social relations during the perioperative and postoperative period. Although previous research showed that single-item measures and established loneliness questionnaires correlate substantially [8, 61], it cannot be ruled out that the use of a single-item measure of loneliness may have limited the results of this study. It should also be kept in mind that in this study, social relationship factors and

procedure (POSSUM operative severity item). *X* independent variable; *M* mediator; *Y* dependent variable; *a*, *b*, and *c'* unstandardized OLS regression coefficients; *Ln LOS* log-transformed length of hospital stay (days); *SE* standard error; *CI*₉₅ 95% bootstrap confidence interval of the product $a \times b$; *p < 0.05; **p < 0.01; ***p < 0.001

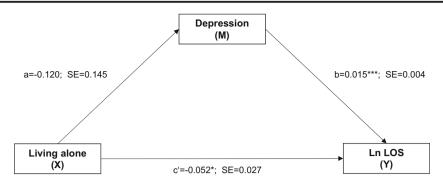
depression were both assessed preoperatively at the same time. Hence, based on this data, no conclusions can be drawn concerning the causality of the relationship between social support, loneliness, and depression, and as a consequence, from a methodologically strict perspective, the indirect effects of these social relationship factors on LOS should be seen as statistically mediated by preoperative depression. Furthermore, LOS is an outcome indicator that can reliably be assessed in a large sample of patients from diverse surgical fields. Although LOS is a valid and robust multiplydetermined indicator of recovery time [25], the assessment of additional outcomes would have contributed to evaluate the predictive ability of social relationship factors in the surgical setting, e.g., postoperative complications, as well as subjective patient ratings of postoperative pain and quality of life. Finally, depressive symptoms were measured with the HADS-D, a standardized, validated, and widely used depression



Indirect effect: ab = 0.044, SE=0.012; Cl₉₅ (0.023, 0.070)

Fig. 4 Mediation model of the effect of feeling of loneliness (X) on Ln LOS (Y) through depression (M); N = 2487. The regression model includes the independent variable feeling of loneliness, and the covariates social support, living alone, age, gender, physical health (ASA classification), surgical field, medical comorbidity (CCI), and extent of surgical procedure (POSSUM operative severity item). X

independent variable; *M* mediator; *Y* dependent variable; *a*, *b*, and *c'* unstandardized OLS regression coefficients; *Ln LOS* log-transformed length of hospital stay (days); *SE* standard error; *Cl*₉₅ 95% bootstrap confidence interval of the product $a \times b$; *p < 0.05; **p < 0.01; ***p < 0.001



Indirect effect: ab = -0.002, SE=0.002; CI₉₅ (-0.007, 0.002)

Fig. 5 Mediation model of the effect of living alone (*X*) on Ln LOS (*Y*) through depression (*M*); N = 2487. The regression model includes the independent variable living alone and the covariates social support, feeling of loneliness, age, gender, physical health (ASA classification), surgical field, medical comorbidity (CCI), and extent of surgical

questionnaire. Whereas the HADS can correctly identify clinically significant depression, it cannot establish diagnoses of mood disorders according to ICD-10 or DSM-5.

Taken together, future studies that aim to investigate the associations between social relationships, depression, and surgical outcomes should also include factors that measure social relationships within the context of the hospital stay. Additionally, it would be of interest to assess further outcomes that may be more sensitive to the influence of psychosocial factors and that may have interesting mediator or moderator effects including both medical and patient self-report data. Future studies should also establish temporal precedence of the assessment times such that the measurement of the independent variables precedes the measurement of the mediator, which precedes the measurement of the outcomes. Given the clear empirical evidence for a moderate association between self-reported depressive symptomatology and LOS in surgical patients, prospective investigations would be important that compare the predictive ability of self-reported depressive symptomatology and clinical diagnoses of depressive disorders.

Implications and Conclusions

The study at hand may contribute to the understanding of the complex and, in many aspects, yet unexplored relationships of psychosocial factors and surgical outcomes by providing the first findings on significant indirect effects of general social support and loneliness on LOS. The results suggest that social support and loneliness are not directly, but indirectly related with shortterm surgical outcomes by an association with depression which in turn is related to worse medical outcomes. This finding may add to the development and investigation of empirically supported approaches that procedure (POSSUM operative severity item). X independent variable; M mediator; Y dependent variable; a, b, and c' unstandardized OLS regression coefficients; Ln LOS log-transformed length of hospital stay (days); SE standard error; CI_{95} 95% bootstrap confidence interval of the product $a \times b$; *p < 0.05; **p < 0.01; ***p < 0.001

aim to decrease psychological distress by explicitly improving of social relationships [31]. Depression seems to be pivotal for understanding the associations between psychosocial factors and surgical outcomes [60], emphasizing the need to integrate proactive psychological treatment programs in acute medical settings including anesthesiology and surgery [25]. A possible approach to make use of the positive effects of social relationships in these settings would be to involve the patients' significant other people to a stronger degree. They are the major sources of general social support in the daily life of the patients, and thus, they may exert this function also effectively in acute medical settings.

Acknowledgements The authors wish to thank the teams of the preoperative anesthesiological assessment clinics and of BRIA (Bridging Intervention in Anesthesiology), Department of Anesthesiology and Operative Intensive Care Medicine (CCM, CVK), Charité -Universitätsmedizin Berlin, for the excellent help with patient care, data collection, and analysis.

Funding This study was supported by the DFG (German Research Foundation, Bonn, Germany; Grant KR 3836/3-1). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Compliance with Ethical Standards

Conflicts of Interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

References

- Cohen S. Social relationships and health. Am Psychol. 2004;59: 676–84.
- 2. Eisenberger N. An empirical review of the neural underpinnings of receiving and giving social support: implications for health. Psychosom Med. 2013;75:545–56.
- Holt-Lunstad J, Smith T, Layton J. Social relationships and mortality risk: a meta-analytic review. PLoS Med. 2010;7:e1000316. https://doi.org/10.1371/journal.pmed.
- Holt-Lunstad J, Smith T, Baker M, Harris T, Stephenson D. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. Perspect Psychol Sci. 2015;10(2):227–37.
- Holt-Lunstad J, Smith T. Loneliness and social isolation as risk factors for CVD: implications for evidence-based patient care and scientific inquiry. Heart. 2016;102(13):987–9.
- Marroquín B. Interpersonal emotion regulation as a mechanism of social support in depression. Clin Psychol Rev. 2011;31:1276–90.
- Santini Z, Koyanagi A, Tyrovolas S, Mason C, Haro J. The association between social relationships and depression: a systematic review. J Affect Disord. 2015;175:53–65.
- Stickley A, Koyanagi A. Loneliness, common mental disorders and suicidal behavior: findings from a general population survey. J Affect Disord. 2016;197:81–7.
- 9. Thoits P. Mechanisms linking social ties and support to physical and mental health. J Health Soc Behav. 2011;52(2):145–61.
- Uchino B. Social support and health: a review of physiological processes potentially underlying links to disease outcomes. J Behav Med. 2006;29(4):377–87.
- Uchino B, Bowen K, McKenzie C, Birmingham W. Psychological pathways linking social support to health outcomes: a visit with the "ghosts" of research past, present, and future. Soc Sci Med. 2012;74:949–57.
- Valtorta N, Kanaan M, Gilbody S, Ronzi S, Hanratty B. Loneliness and social isolation as risk factors for coronary heart disease and stroke: systematic review and meta-analysis of longitudinal observational studies. Heart. 2016;102(13):1009–16.
- Pinquart M, Duberstein P. Associations of social networks with cancer mortality: a meta-analysis. Crit Rev Oncol Hematol. 2010;75:122–37.
- Livhits M, Mercado C, Yermilov I, Parikh J, Dutson E, Mehran A, et al. Is social support associated with greater weight loss after bariatric surgery? A systematic review. Obes Rev. 2011;12:142–8.
- Luttik M, Jaarsma T, Moser D, Sanderman R, van Veldhuisen D. The importance and impact of social support on outcomes in patients with heart failure: an overview of the literature. J Cardiovasc Nurs. 2005;20(3):162–9.
- Gariépy G, Honkaniemi H, Quesnel-Vallée A. Social support and protection from depression: systematic review of current findings in Western countries. Br J Psychiatry. 2016;209:284–93.
- Evans D, Charney D, Lewis L, Golden R, Gorman J, Krishnan K, et al. Mood disorders in the medically ill: scientific review and recommendations. Biol Psychiatry. 2005;58:175–89.
- Sotelo J, Nemeroff C. Depression as a systemic disease. Pers Med Psychiatry. 2017;1-2:11–25.
- Rosenberger PH, Jokl P, Ickovics J. Psychosocial factors and surgical outcomes: an evidence-based literature review. J Am Acad Orthop Surg. 2006;14(7):397–405.
- Linnen H, Krampe H, Neumann T, Weiss-Gerlach E, Heinz A, Wernecke K-D, et al. Depression and essential health-risk factors in surgical patients in the preoperative anesthesiological assessment clinic. Eur J Anaesthesiol. 2011;28(10):733–41.
- Kerper LF, Spies CD, Buspavanich P, Balzer F, Salz A-L, Tafelski S, et al. Preoperative depression and hospital length of stay in surgical patients. Minerva Anestesiol. 2014;80(9):984–91.

- Orri M, Boleslawski E, Regimbeau J, Barry C, Hassler C, Gregoire E, et al. Influence of depression on recovery after major noncardiac surgery. Ann Surg. 2015;262(5):882–90.
- Kim S, Duncan P, Groban L, Segal H, Abbott R, Williamson J. Patient-reported outcome measures (PROM) as a preoperative assessment tool. J Anesth Perioper Med. 2017;4(6):274–81.
- Graven L, Grant J. The impact of social support on depressive symptoms in individuals with heart failure: update and review. J Cardiovasc Nurs. 2013;28(5):429–43.
- Laderman M, Mate K. Behavioral health integration in acute medical settings: an opportunity to improve outcomes and reduce costs. Jt Comm J Qual Patient Saf. 2016;42(7):331–6.
- Contrada RJ, Boulifard DA, Hekler EB, Idler EL, Spruill TM, Labouvi EW, et al. Psychosocial factors in heart surgery: presurgical vulnerability and postsurgical recovery. Health Psychol. 2008;27(3):309–19.
- Contrada RJ, Goyal TM, Cather C, Rafalson L, Idler EL, Krause TJ. Psychosocial factors in outcomes of heart surgery: the impact of religious involvement and depressive symptoms. Health Psychol. 2004;23:227–38.
- 28. Kulik J, Mahler H. Social support and recovery from surgery. Health Psychol. 1989;8(2):221–38.
- Sorensen EA, Wang F. Social support, depression, functional status, and gender differences in older adults undergoing first-time coronary artery bypass graft surgery. Heart Lung. 2009;38:306–17.
- Krohne H, Slangen K. Influence of social support on adaptation to surgery. Health Psychol. 2005;24(1):101–5.
- Cacioppo S, Grippo AJ, London S, Goossens L, Cacioppo JT. Loneliness: clinical import and interventions. Perspect Psychol Sci. 2015;10(2):238–49.
- Cacioppo JT, Cacioppo S. Social relationships and health: the toxic effects of perceived social isolation. Soc Personal Psychol Compass. 2014;8(2):58–72.
- Perissinotto C, Covinsky K. Living alone, socially isolated or lonely - what are we measuring? J Gen Intern Med. 2014;29(11):1429– 31.
- Cacioppo JT, Cacioppo S, Capitanio JP, Cole SW. The neuroendocrinology of social isolation. Annu Rev Psychol. 2015;66:733–67.
- Heinrich L, Gullone E. The clinical significance of loneliness: a literature review. Clin Psychol Rev. 2006;26:695–718.
- Kerper LF, Spies CD, Salz A-L, Weiß-Gerlach E, Balzer F, Neumann T, et al. Effects of an innovative psychotherapy program for surgical patients - bridging intervention in anesthesiology: a randomized controlled trial. Anesthesiology. 2015;123(1):148–59.
- 37. Krampe H, Salz A-L, Kerper L, Krannich A, Schnell T, Wernecke K-D, et al. Readiness to change and psychotherapy outcomes of an innovative psychotherapy program for surgical patients: results from a randomized controlled trial. BMC Psychiatry. 2017;17(417):417. https://doi.org/10.1186/s12888-017-1579-5.
- Zigmond A, Snaith R. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67:361–70.
- Herrmann C, Buss U, Snaith R. HADS-D Hospital Anxiety and Depression Scale: Deutsche Version. Bern: Verlag Hans Huber; 1995.
- 40. Smarr KL, Keefer AL. Measures of depression and depressive symptoms: Beck Depression Inventory-II (BDI-II), Center for Epidemiologic Studies Depression Scale (CES-D), Geriatric Depression Scale (GDS), Hospital Anxiety and Depression Scale (HADS), and Patient Health Questionnaire-9 (PHQ-9). Arthritis Care Res. 2011;63(S11):S454–S66.
- Brennan C, Worrall-Davies A, McMillan D, Gilbody S, House A. The hospital anxiety and depression scale: a diagnostic metaanalysis of case-finding ability. J Psychosom Res. 2010;69:371–8.
- 42. Schulz U, Schwarzer R. Soziale Unterstützung bei der Krankheitsbewältigung: die Berliner social support Skalen

(BSSS) [social support in coping with illness: the berlin social support scales]. Diagnostica. 2003;49(2):73–82.

- 43. American Society of Anesthesiologists. New classification of physical status. Anesthesiology. 1963;24:111.
- Wolters U, Wolf T, Stuetzer H, Schröder T. ASA classification and perioperative variables as predictors of postoperative outcome. Br J Anaesth. 1996;77:217–22.
- 45. Lange LF, Spies CD, Weiß-Gerlach E, Neumann T, Salz A-L, Tafelski S, et al. Bridging intervention in anaesthesiology: first results on treatment need, demand and utilization of an innovative psychotherapy program for surgical patients. Clin Health Promot. 2011;1(2):41–9.
- 46. Kerper LF, Spies CD, Lößner M, Salz A-L, Tafelski S, Balzer F, et al. Persistence of psychological distress in surgical patients with interest in psychotherapy: results of a 6-month follow-up. PLoS One. 2012;7:e51167.
- Charlson ME, Pompei P, Ales K, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373–83.
- Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi J-C, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care. 2005;43(11):1130–9.
- Copeland GP, Jones D, Walters M. POSSUM: a scoring system for surgical audit. Br J Surg. 1991;78:356–60.
- Noordzij PG, Poldermans D, Schouten O, Bax JJ, Schreiner FAG, Boersma E. Postoperative mortality in the Netherlands: a population-based analysis of surgery-specific risk in adults. Anesthesiology. 2010;112:1105–15.
- German Institute of Medical Documentation and Information. German procedure classification OPS. http://www.dimdi.de/static/ de/klassi/ops/index.htm; 2010.

- Hayes AF. Introduction to mediation, moderation, and conditional process analysis: a regression-based approach. New York: Guilford Press; 2013.
- Hayes AF, Rockwood NJ. Regression-based statistical mediation and moderation analysis in clinical research: observations, recommendations, and implementation. Behav Res Ther. 2017;98:39–57.
- Tabachnick BG, Fidell LS. Using multivariate statistics. 4th ed. Boston: Allyn & Bacon; 2001.
- Hayes AF. Supplementary PROCESS documentation http:// afhayes.com/public/docaddendum.pdf; 2016.
- Beresnevaite M, Rimantas B, Taylor G, Jureniene K, Kinduris S, Barauskiene V. Depression predicts perioperative outcomes following coronary artery bypass graft surgery. Scand Cardiovasc J. 2010;44:289–94.
- Oxlad M, Stubberfield J, Stuklis R, Edwards J, Wade T. Psychological risk factors for increased post-operative length of hospital stay following coronary artery bypass graft surgery. J Behav Med. 2006;29(2):179–90.
- Törer N, Nursal TZ, Caliskan K, Ezer A, Colakoglu T, Moray G, et al. The effect of the psychological status of breast cancer patients on the short-term clinical outcome after mastectomy. Acta Chir Belg. 2010;110:467–70.
- Kitagawa R, Yasui-Furukoi N, Tsushima T, Kaneko S, Fukuda I. Depression increases the length of hospitalization for patients undergoing thoracic surgery: a preliminary study. Psychosomatics. 2011;52:428–32.
- Ghoneim M, O'Hara M. Depression and postoperative complications: an overview. BMC Surg. 2016;16:5.
- Fokkema T, De Jong Gierveld J, Dykstra PA. Cross-national differences in older adult loneliness. Aust J Psychol. 2012;146(1–2): 201–28.