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Medical comorbidity in complicated grief: Results from the HEAL collaborative trial

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ABSTRACT

Objective: To describe medical comorbidity in persons with Complicated Grief (CG) and to test whether medical comorbidity in individuals with CG is associated with the severity and duration of CG, after adjusting for age, sex, race, and current depressive symptoms.

Methods: In exploratory analyses, we compared data from participants in an NIMH-sponsored multisite clinical trial of CG ("HEAL": "Healing Emotions After Loss") to archival data from participants matched on age, gender, and race/ethnicity, stratified by the presence or absence of current major depression. We used the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) as a measure of medical polymorbidity. We investigated the association between CG and medical comorbidity via multiple linear regression, adjusting for sociodemographic and clinical variables, including severity of depressive symptoms.

Results: Chronological age and severity of co-occurring symptoms of major depression correlated with cumulative medical polymorbidity in persons with Complicated Grief. The severity of CG and the time since loss did not correlate with global medical polymorbidity (CIRS-G score). Nor was there an interaction between severity of depressive symptoms and severity of CG symptoms in predicting global CIRS-G score. Cumulative medical comorbidity, as measured by CIRS-G scores, was greater in subjects with current major depression ("DEPRESSED") than in CG subjects, and both DEPRESSED and CG subjects had greater medical morbidity than CONTROLS.

Conclusion: Medical comorbidity is prevalent in Complicated Grief, associated with increasing age and co-occurring depressive symptoms but apparently not with chronicity and severity of Complicated Grief per se. This observation suggests that treating depression in the context of CG may be important to managing medical conditions in individuals with Complicated Grief to attenuate or prevent the long-term medical sequelae of CG.

1. Introduction

Complicated Grief (CG) is a chronic and debilitating condition estimated to occur in 7% of bereaved people, thus affecting tens of millions of people worldwide (Kersting et al., 2011). Studies have shown that CG can reliably be distinguished from major depression both in response to treatment and primary symptomatology (Cozza et al., 2016; Shear et al., 2016, 2014; Supiano and Luptak, 2014). CG symptoms include prolonged yearning, longing, sorrow, persistent thoughts of the deceased, and difficulty imagining a future with purpose and meaning, together with impairment in social and occupational function (Kersting et al., 2011).

There is a strong association between bereavement, especially CG, and negative health outcomes. CG is known to shorten life expectancy, due to death from heart disease and/or cancer

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(Prigerson et al., 2002). CG has also been associated with physiologic symptoms, such as shortness of breath, palpitations, digestive difficulties, loss of appetite, weight loss, poor treatment adherence, sleep issues including restlessness, insomnia, and low sleep quality, and a 10-fold greater risk for hypertension and heart disease (Lannen et al., 2008; H. G. Prigerson et al., 1995a,b; Prigerson et al., 1997; Shear, 2015; Stroebe et al., 2011).

CG also frequently co-exists with major depression, which is similarly associated with shortened life expectancy across a range of medical and neurological disorders (Gallo et al., 2013). Evidence-based treatment of depression in older primary care adults leads to substantial reduction in mortality risk (24% over eight years), secondary to reductions in cancer-related deaths (Gallo et al., 2013). We do not know whether evidence-based treatment of CG to remission also leads to reductions in mortality risk. However, to test whether evidence-based treatment of CG to remission also leads to reductions in mortality risk, we must first develop an understanding of the type, extent, and severity of medical comorbidity in persons with CG, with and without depression. Thus, this study addresses the following aims:

1. To describe medical comorbidity in persons with complicated grief, as compared with non-bereaved depressed subjects with current major depression and with non-bereaved, non-depressed control participants.
2. To test whether medical comorbidity in complicated grief is associated with the severity and duration of CG, after adjusting for the effects of age, sex, race, and severity of depressive symptoms.

2. Methods

2.1. Design

We analyzed data from a multisite clinical trial of CG ("HEAL": "Healing Emotions After Loss") (Shear et al., 2016), sponsored by the National Institute of Mental Health. HEAL is a double-blind, placebo-controlled, randomized clinical trial that evaluated the efficacy of antidepressant pharmacotherapy, with and without complicated grief psychotherapy, in the treatment of CG. Participants were recruited from four communities in the United States: Boston, MA; New York, NY; Pittsburgh, PA; and San Diego, CA. Further details of design, data collection, and outcomes are available in Shear et al. (2016). The present study used baseline (pre-intervention) data collected between 2010 and 2014. We also used data from comparison subjects without CG, but with current major depression from the Pittsburgh site of HEAL, collected under the auspices of an NIMH-sponsored center for the prevention and treatment of major depression in older adults (ACISR: P30 MH90333; PI: Reynolds CF; for further description of depressed subjects, see Reynolds et al., 2006). These archival data (1995–2016) were used as a benchmark to provide additional context for comparable measures in HEAL participants.

2.2. Participants

The original HEAL sample included 395 persons who ranged in age from 19 to 89 (Shear et al., 2016). Of these, we matched 149 with subjects from our Advanced Centers for Interventions and Services Research (ACISR), on age, gender, and race/ethnicity. Then, in order to address Aim 1, we compared HEAL participants to two groups of ACISR participants; those who were 1) non-bereaved and non-depressed (CONTROLS; n = 98); and 2) non-bereaved but depressed, with current major depression (DEPRESSED; n = 149). Diagnoses were made using the structured clinical interview for DSM-IV (SCID) (APA, 1994). To match HEAL participants with ACISR participants, we created seven age categories: 18–30, 31–40, 41–50, 51–60, 61–70, 71–80, and 81–90; two gender categories: women and men; and four race/ethnicity categories: White, Black, Asian Pacific, and Other/Unknown. Each participant was then assigned a number that corresponds to a specific combination of categories of age, gender, and race. One hundred forty-nine HEAL participants were matched for the DEPRESSION comparison; of these, ninety-eight were matched for the CONTROL comparison. T tests, chi-square tests and Fisher exact tests were used to test whether comparison groups were comparable in terms of age, gender and race (Table 1). The same group of HEAL participants served in both comparisons. We did not account for family-wise comparison because each comparison was specified a priori as part of our hypothesis and not as part of a post-hoc analysis. We did not adjust for site in the analysis because we detected no site × treatment interactions in the parent clinical trial reported in JAMA Psychiatry (Shear et al., 2016). We chose to match instead of adjusting for covariates (age, sex, racial/ethnic group) because matching ensures that the proportion of covariates is roughly equal across groups, whereas with covariate adjustment, one may end up with a strong imbalance which can lead to balance and power issues. Moreover, our choice of covariates was done to achieve simple, clearly defined, and clearly bounded categories that result in minimizing contamination among matching variables. These variables tend to be strongly related to depression outcome (e.g., age,

Table 1
Participant characteristics in comparisons of medical comorbidity in Complicated Grief, Major Depression, and Controls.

Covariate	Descriptive statistics				Statistics for pairwise comparison		
	$Cg^{(1)}$ (n = 98)	Control (n = 99)	$Cg^{(2)}$ (n = 149)	Depressed (n = 150)	$Cg^{(1)}$ vs control	$Cg^{(2)}$ vs depressed	Control vs depressed
Age (years), mean (SD)	68.5 (7.9)	68.8 (8.0)	63.8 (11.9)	64.1 (11.9)	t (195) = 0.330,p = 0.74	t (297) = 0.19, p = 0.85	t (246.9) = -3.77, p = 0.0002
Gender, n (%)					X^2 (1) = 0.0153,	X^2 (1) = 0.01,	X^2 (1) = 0.0002,
Men	24 (24.5)	25 (25.3)	37 (24.8)	38 (25.3)	p = 0.90	p = 0.92	p = 0.99
Women	74 (75.5)	74 (74.8)	112 (75.2)	112 (74.7)			
Race, n (%)					X^2 (1) = 0.0006,	Fisher Exact, p = 1	Fisher Exact, p = 1
Black	10 (10.2)	10 (10.1)	14 (9.4)	14 (9.3)	p = 0.98		
White/Hispanic	88 (89.8)	89 (89.9)	134 (89.9)	135 (90.0)			
Asian Pacific			1 (0.7)	1 (0.7)			
Global CISRS-G Medical comorbidity, mean (SD)	8.2 (4.5)	6.4 (3.8)	7.6 (4.4)	8.7 (4.4)	t (195) = -3.08, p = 0.0024	t (297) = 2.19, p = 0.029	t (247) = 4.17, p < 0.0001

Note: $CG^{(1)}$ is the sample used in $CG^{(1)}$ vs CONTROL comparison, and $CG^{(2)}$ is the sample used in $CG^{(2)}$ vs DEPRESSED comparison. People with complicated grief are selected separately to match with CONTROL group and DEPRESSED group in age, gender and race.