Low Perceived Social Support and Post–Myocardial Infarction Prognosis in the Enhancing Recovery in Coronary Heart Disease Clinical Trial: The Effects of Treatment

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Objective: In post hoc analyses, to examine in low perceived social support (LPSS) patients enrolled in the Enhancing Recovery in Coronary Heart Disease (ENRICHD) clinical trial ($n = 1503$), the pattern of social support following myocardial infarction (MI), the impact of psychosocial intervention on perceived support, the relationship of perceived support at the time of MI to subsequent death and recurrent MI, and the relationship of change in perceived support 6 months after MI to subsequent mortality. **Methods:** Partner status (partner, no partner) and score (<12 = low support; >12 = moderate support) on the ENRICHD Social Support Instrument (ESSI) were used post hoc to define four levels of risk. The resulting 4 LPSS risk groups were compared on baseline characteristics, changes in social support, and medical outcomes to a group of concurrently enrolled acute myocardial infarction patients without depression or LPSS (MI comparison group, $n = 408$). Effects of treatment assignment on LPSS and death/recurrent MI were also examined. **Results:** All 4 LPSS risk groups demonstrated improvement in perceived support, regardless of treatment assignment, with a significant treatment effect only seen in the LPSS risk group with no partner and moderate support at baseline. During an average 29-month follow-up, the combined end point of death/nonfatal MI was 10% in the MI comparison group and 23% in the ENRICHD LPSS patients; LPSS conferred a greater risk in unadjusted and adjusted models (HR = 1.74–2.39). Change in ESSI score and/or improvement in perceived social support were not found to predict subsequent mortality. **Conclusions:** Baseline LPSS predicted death/recurrent MI in the ENRICHD cohort, independent of treatment assignment. Intervention effects indicated a partner surrogacy role for the interventionist and the need for a moderate level of support at baseline for the intervention to be effective. **Key words:** social support, acute coronary syndrome, clinical trials.

CAD = coronary artery disease; **CHD** = coronary heart disease; **AMI** = acute myocardial infarction; **MI** = myocardial infarction; **ENRICHD** = Enhancing Recovery in Coronary Heart Disease; **LPSS** = low perceived social support; **ESSI** = ENRICHD Social Support Instrument; **UC** = usual care; **INT** = intervention; **DISH** = Diagnostic Interview and Structured Hamilton; **ECG** = electrocardiogram; **BDI** = Beck Depression Inventory; **HR** = hazard ratio; **CI** = confidence interval.

INTRODUCTION

A large and consistent body of evidence involving both community and patient populations has demonstrated the beneficial effects of supportive social relationships on health (1). The effect of social support on the prognosis of patients with coronary artery disease (CAD) remains one of the strongest findings in this literature. This effect was first demonstrated clearly in the Beta Blocker Heart Attack Trial (2), in which myocardial infarction (MI) patients who reported both social isolation and high levels of stress had greater than 4 times the mortality risk of those who were neither isolated nor suffering from stress.

Subsequent studies have shown a variety of social support indicators to be important predictors of prognosis in CAD patients. Measures assessing the presence, degree and quality of intimate social ties—including measures of marital status, whether the person lives alone or with others, and the availability of various sources of emotional support—have been linked with mortality in patients with CAD or after MI (3–6). Indices of social network size, frequency of social activity, group membership, and perceived support have also been found to predict survival (7–10). The replication of this association across a large number of studies despite the variety of social support measures used and the fact that the association remains strong even when controls for sociodemographic and disease severity indicators are included in the analyses attest to the robustness of the phenomenon.

While the relationship between social support and cardiovascular outcomes is strong and consistent, relatively few studies have investigated the stability of social support over time and whether different long-term patterns of support influence medical prognosis, either in healthy community samples or in patients with existing CAD. Cerhan and Wallace (11) examined the relationship between long-term change in social support and mortality in elderly individuals living in rural communities. Social ties were assessed twice over a 3-year period, and participants were followed for 8 years. In multivariate models adjusting for demographic and medical variables and for depression, increased mortality was associ-

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ated with reports of consistently low social ties over time, but not with decline in social ties, for both men and women. In contrast, the Health Professionals Follow-up Study found that for men over age 65, an increase in friends over the period of assessment was associated with lower 2-year mortality, thereby demonstrating the benefit of an increase in social network (12).

Less is known about how social support changes over the weeks and months following MI, though clinical lore suggests that such change does occur. For example, it is thought that social support is at its highest during hospitalization and immediately following discharge, with family and friends responding to the "crisis" of the acute event. As the saliency of the medical event decreases, it may be that those in the social network assume a return to normalcy and are less vigilant of or responsive to the needs of the patient. In addition, compromised health may adversely affect social relationships (11), as patients may be less effective in seeking support. Few studies, however, have attempted to characterize the social support trajectory following MI. Rankin (13) described time period effects for emotional support among women at 6 weeks, 6 months, and 12 months following MI. Although post hoc tests were not reported, inspection of mean responses reveals the highest values at 6 weeks, with levels declining at 6 months. Others have also reported a decline in support in the months after acute medical illness such as MI (14). Hence, the question of how change in social support after MI affects subsequent medical prognosis may be important.

A number of explanations have been offered for the beneficial effects of social support on cardiovascular health. For example, social contacts may foster better health habits, treatment adherence, and proper use of health care resources (15). There is also evidence that social isolation may be accompanied by potentially deleterious physiological activity involving the autonomic nervous system and immune function (1). Finally, social support has been shown to reduce psychological distress, which is associated with elevated mortality risk (cf, 16) and is high in cardiac patients. The existence of these plausible mechanisms, coupled with strong epidemiologic evidence, makes social support a prime candidate for psychosocial interventions (INTs) designed to improve prognosis.

The Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) study was a multicenter, randomized control clinical trial sponsored by the National Heart, Lung and Blood Institute. Patients with acute myocardial infarction (AMI) and comorbid low perceived social support (LPSS), depression, or both were enrolled in the trial to test whether treating these psychosocial factors following AMI reduces the risk of reinfarction and death (17). The INT significantly improved both depression and low social support; however, rates of reinfarction and death did not differ between INT and usual care (UC) arms. The size of the ENRICHD sample and the length of follow-up present a unique opportunity to examine changes in social support after MI and to investigate whether these changes are associated with differences in medical outcomes. Thus, the purpose of this report is to (1) examine the pattern of social support following AMI in patients with LPSS enrolled in the ENRICHD study; (2) examine the impact of the ENRICHD psychosocial INT on subsequent perceived social support for these patients; (3) examine the relationship of perceived social support at the time of MI to the patients' future medical morbidity and mortality; and (4) determine whether change in perceived social support after MI was related to subsequent mortality. These questions and the analytic approach used to address them are post hoc in nature and designed as hypothesis generating.

METHODS

Study Population and Measurement

The sample reported on here is limited to the 1503 AMI patients (833 males; 670 females) of the total ENRICHD cohort ($N = 2481$) who were enrolled because of LPSS ($N = 648$) or dual LPSS and depression ($N = 855$), and to a comparison group of AMI patients (MI comparison group, $N = 408$) meeting the same medical eligibility criteria but not depression or LPSS criteria, who were recruited for an ENRICHD ancillary study of heart rate variability at the same time (18). All patients were recruited between October 1996 and October 1999 from 73 hospitals affiliated with 8 clinical centers, as described in detail elsewhere (17,19). AMI eligibility was determined by characteristic elevation of one or more biomarkers of myocardial injury plus symptoms compatible with AMI and/or characteristic electrocardiogram (ECG) changes. Patients with AMI subsequent to revascularization, with noncardiac conditions likely to be fatal within 1 year, with major psychiatric comorbidity, active substance abuse or severe dementia, or who could not be enrolled within 28 days of the AMI were excluded. Approval of the protocol was obtained from all local institutional review boards before initiating recruitment, and written informed consent was obtained from all participants.

LPSS was determined by the ENRICHD Social Support Instrument (ESSI; see Table 1), which is composed of 6 items that other studies had found individually predictive of MI/death in cardiac patients and a seventh item regarding partner status (20). Each item is endorsed on a 1 (none of the

TABLE 1. ENRICHD Social Support Instrument (ESSI)

For each of the following questions, mark your answer by placing a number in the space provided.

Answer:

1 for none of the time
2 for a little of the time
3 for some of the time
4 for all of the time

_____1. Is there someone available to you who you can count on to listen to you when you need to talk?
_____2. Is there someone available to give you good advice about a problem?
_____3. Is there someone available to you who shows you love and affection?
_____4. Is there someone available to help you with daily chores?
_____5. Can you count on anyone to provide you with emotional support, such as talking over problems or helping you make difficult decisions?
_____6. Do you have as much contact as you would like with someone you feel close to, someone you can trust and confide in?

Yes/no 7. Are you currently married or living with a partner?

time) to 4 (all of the time) Likert scale. A score <3 on 2 or more items and a total score <18, or a score of 2 on 2 items without regard to total score, classified a patient as meeting LPSS eligibility for the trial; psychometrics of the ESSI demonstrate its reliability and validity (20). Depression was determined by the Depression Interview and Structured Hamilton (DISH), a semistructured diagnostic interview utilizing Diagnostic and Statistical Manual, version 4 criteria and providing a severity rating based on the Hamilton Rating Scale for Depression (21).

Demographic information, medical history, physical examination data, and reference ECGs were collected immediately after enrollment. In addition to the qualifying scores on the ESSI and DISH, patients completed the Beck Depression Inventory (BDI), a 21-item self-report measure of depression symptoms (22) that has been found predictive of post-AMI prognosis (23).

INT

Patients were assigned randomly to either a cognitive therapy INT or to UC treatment arms. The primary treatment goal for LPSS patients was to alter perception of social support by modifying the environmental, behavioral and/or cognitive factors contributing to LPSS. The individually tailored treatment was based on a qualitative and quantitative assessment that identified instrumental and emotional needs, cognitions, attitudes, and beliefs relating to social ties and network availability, the degree of social integration, current satisfaction with specific sources of support, and preference for and importance of specific types of support. It also determined social planning, communication, and problem-solving skills and identified whether social anxiety or phobia was contributing to the experience of insufficient support. INT components addressed behavioral/social skill deficits, cognitive factors contributing to the perception or maintenance of unsatisfying levels of social support, and social outreach and network development, in a manner that was informed by the assessment (24). For patients with both depression and LPSS, the INT combined this focus with traditional Beck cognitive therapy for depression (25). Adjunctive pharmacotherapy was available for patients with severe and/or treatment resistant depression. Both treatment arms received the AHA *Active Partnership* booklet (26), which offers education on coronary heart disease (CHD) risk factors, though no explicit instructions were given to either arm regarding use of this booklet. Patients assigned to UC were provided no further information after hospital discharge and received the care usually provided by their physicians.

Follow-up Evaluations and End-Point Ascertainment

Follow-up evaluations were conducted 6 months after enrollment and annually thereafter, except for the MI comparison group, which underwent all but the 6-month evaluation. Average follow-up for the total cohort was 29 months (range, 18–54 months). Follow-up evaluations were composed of medical history, including ascertainment of hospitalizations/deaths that had occurred since the previous follow-up, physical examination with resting ECG, and readministration of the ESSI, the BDI, and the DISH.

The primary end point for the ENRICHD clinical trial was combined recurrent AMI or all-cause mortality, with a secondary end point solely of all-cause mortality. The records of every identified hospitalization were obtained for review, along with follow-up ECGs. Classification of primary end points was made using standardized criteria by an end-point ascertainment committee that was masked to treatment assignment. All study staff involved in end-point data collection, verification, and classification or involved in the follow-up psychosocial assessments were also masked to treatment assignment.

Data Reduction

Four LPSS risk groups were defined post hoc for ENRICHD LPSS patients, as a function of partner status (partner, no partner) and baseline ESSI score ($\leq$12 = low support; >12 = moderate support). A score of 12 on the ESSI for determination of risk-group membership was selected so that the distribution of patients was comparable to that seen in the extant social support literature. LPSS patients who died (n = 69) or who were lost to follow-up (n = 344) before the 6-month evaluation was completed were excluded from analyses regarding initial change in social support as change was not ascertainable. For the same reasons, LPSS patients who died (cumulative n = 126) or were lost to follow-up (cumulative n = 318) between baseline and second follow-up were excluded from analysis of late change in LPSS reported here. Exclusions from analyses for the MI comparison group included nine deaths and 75 lost to follow-up. For analyses concerning the effects of treatment, remission of LPSS at follow-up was defined as an ESSI score above the threshold for ENRICHD eligibility.

Statistical Analysis

Change in ESSI Score: INT Versus UC

Random-effect regression models (27) were used to examine change in ESSI score from baseline to 6- and 12-month follow-up and probability of remission in LPSS during this period for the 4 LPSS risk groups. A random subject effect was specified to account for the lack of independence for the repeated observations on the same subject. The fixed effects were treatment, time, risk group, treatment × time, and treatment × time × risk group.

Perceived Social Support and Medical Outcomes

Cox proportional hazards modeling was used to estimate the risk (hazard ratios, [HRs], 95% confidence intervals [CIs]) for the primary end point of death or nonfatal MI (modeled for the first event per patient only), and for all-cause mortality for ENRICHD LPSS patients versus MI comparison group patients. Initial models were calculated comparing all LPSS patients against MI comparison group patients. Subsequent analyses compared the 4 LPSS risk groups to the MI comparison group. Two models were examined for each set of analyses: model 1 was an unadjusted; model 2 was adjusted for important demographic and medical variables found to be significantly ($p <$ .05) associated with both the exposure variable (LPSS risk group) and the medical outcomes (a "confound" model). Significance for tests of equality of responses across LPSS risk groups was set at $\alpha = 0.05$. If significant, a Bonferroni correction (α/k, where k is the number of comparisons) was applied for subsequent pairwise comparisons. All statistical analyses were conducted using SAS software, Version 8.2 (28).

RESULTS

Thirteen of the 1503 LPSS patients enrolled in the trial were excluded from analysis due to missing item-level responses on the ESSI. Of the remaining 1490 patients, 805 (54%) were neither married nor living with a partner, and of these, 327 (41%) scored $\leq$12 on the ESSI (no partner/low support LPSS risk group) and 478 (59%) scored >12 (no partner/moderate support LPSS risk group). Of the 685 LPSS patients with a partner, 189 (28%) scored $\leq$12 on the ESSI (partner/low support LPSS risk group) and 496 score >12 (partner/moderate support LPSS risk group). In the MI comparison group, 22% (n = 87) of patients were neither married nor living with a partner. Table 2 shows the distribution of baseline characteristics across the 4 LPSS risk groups and the MI comparison group. These groups differed significantly on age, gender, minority status, use of β-blockade in medication regimen, and the medical comorbidities of diabetes, hypertension, previous percutaneous revascularization, previous stroke/TIA, and history of heart failure (all $p <$ .05).

Change in ESSI Score: INT Versus UC

All 4 LPSS risk groups demonstrated some degree of improvement from baseline to 6-, and 12-month follow-up, regardless of treatment assignment. No partner/moderate support patients assigned to UC demonstrated the least improvement (6-month $\Delta = 1.18$; 12-month $\Delta = 1.52$), while partner/low support patients assigned to INT demonstrated the

TABLE 2. Comparison of Baseline Characteristics for MI Comparison Group and Four LPSS Risk Group

Demographic Characteristics	No./(%)					p^a
	MI Comparison Group (n = 408)	Partner		No Partner		
		LPSS Moderate ESSI (n = 496)	LPSS Low ESSI (n = 189)	LPSS Moderate ESSI (n = 478)	LPSS Low ESSI (n = 327)	
Age ≥ 60	54	49	46	59	55	.005
Gender (female)	32	34	37	59	44	<.001
Race (minority)	21	30	43	43	38	<.001
Married or living with partner	78	100	100	N/A	N/A	<.001
College education	24	23	22	16	19	.044
Medications						
ACE inhibitors	49	47	45	51	48	.684
Aspirin	91	91	85	86	88	.035
β Blockers	85	80	77	75	73	.001
Calcium channel blockers	12	16	14	19	17	.124
Vasodilators	40	36	40	40	43	.329
Medical comorbidities						
Diabetes	23	30	27	35	33	.003
History of hypertension	52	57	62	69	63	<.001
Ever smoker	69	61	74	64	65	.017
Creatinine >1.3	15	17	14	18	22	.158
Renal insufficiency	6	9	9	12	9	.048
Pulmonary disease	13	14	19	20	21	.011
Previous MI	20	26	30	27	28	.054
Previous stroke/TIA	6	6	12	10	10	.005
Previous CABG	11	15	10	12	12	.183
Previous PTCA	10	15	19	15	12	.045
History of heart failure	5	9	10	18	15	<.001
Killip class III–IV	4	5	6	9	7	.102
Ejection fraction (EF)						
Normal (EF ≥ 50)	54	53	53	52	54	.220
Moderate (40 < EF < 50%)	23	28	20	23	21	
Severe (EF < 40%)	23	19	27	25	25	

[a] p Values are based on χ^2 tests.
MI = myocardial infarction; LPSS = low perceived social support; ESSI = ENRICHD Social Support Instrument; CHF = congestive heart failure.

greatest improvement (6-month Δ = 6.28; 12-month Δ = 7.00). The effect of treatment assignment on the change in ESSI score from baseline to 6- and 12-months was compared for the 4 LPSS risk groups by testing for treatment × risk group interactions at each time point. The treatment effect on change in ESSI score was found to differ significantly across groups at the 6-month (p = .04), but not at the 12-month (p = .57) follow-up visit. Relative to the group with the greatest baseline support (partner/moderate support), the groups with no partner showed significantly greater improvement in ESSI score at 6 months (moderate support: treatment difference [INT-UC] = 2.22, p = .005), or a trend toward greater improvement (low support: treatment difference [INT-UC] = 1.24, p = .081) (see Figure 1). Although the treatment effects were not significantly different across the 4 LPSS risk groups at 12 months, the trends toward greater treatment benefit in the no partner risk groups were in a similar direction (moderate support: treatment difference in [INT-UC] = 0.88, p = .22; low support: treatment difference [INT-UC] = 0.95, p = .24) (see Figure 2).

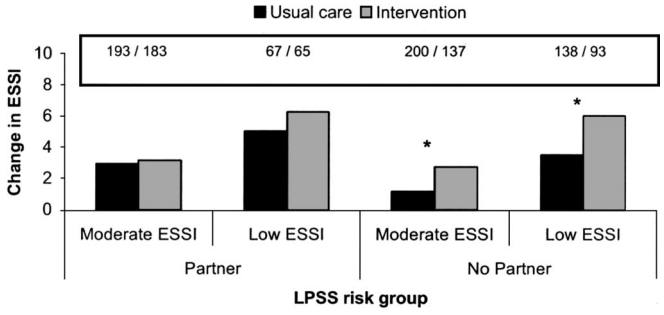

Figure 1. Baseline to 6-month change in ESSI score for each LPSS risk group. Textbox contains N = . * Indicates significance at the p < .05 level.

Remission of LPSS

Depending on LPSS risk group, 21% to 59% of UC patients and 33% to 66% of INT patients no longer met ENRICHD LPSS criteria at 6 months. These percentages remained stable at 12 months (21% to 62% for UC patients and 28% to 71% for INT patients). The effect of treatment assignment on the probability of remission of LPSS (no longer meeting ENRICHD LPSS criteria) was not found to differ

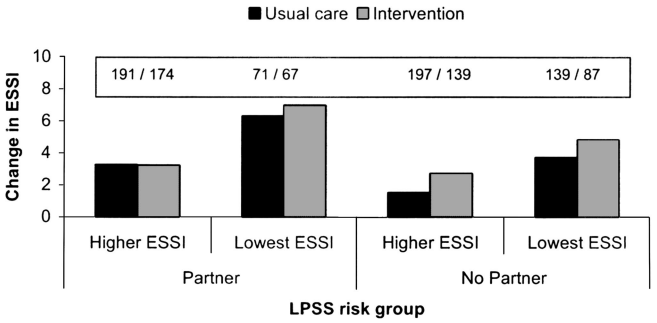

Figure 2. Baseline to 12 month change in ESSI score for each LPSS risk group. Textbox contains $N =$.

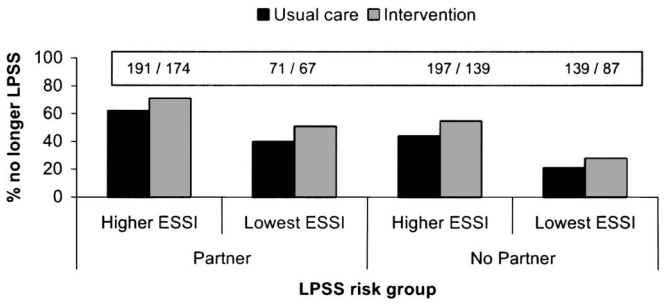

Figure 4. Percent of patients in each LPSS risk group no longer meeting LPSS criteria at 12 months. Textbox contains $N =$.

significantly across the 4 LPSS risk groups at 6 ($p = .88$) or 12 months ($p = .99$) (see Figures 3 and 4). The only significant effect of treatment assignment on LPSS remission was for patients in the no partner/low support LPSS risk group at 6 months (INT 33% vs UC 21%, $p < .05$). Thus, a large percentage of ENRICHD patients in both the UC and INT conditions demonstrated improvements over time in levels of perceived social support sufficient to render them no longer eligible for the trial.

Baseline ESSI Score and Subsequent Death and/or Recurrent MI

During an average follow-up period of 29 months, there were 183 patients with recurrent MI, 130 deaths without recurrent MI, and 71 patients with recurrent MI who subsequently died. The event rates for the combined end point of death or nonfatal MI were 23% among ENRICHD LPSS patients and 10% among MI comparison group patients; mortality rates were 12.5% and 3.5%, respectively.

ENRICHD LPSS Patients Versus MI Comparison Group Patients (See Table 3)

Model 1 revealed that LPSS conferred significant risk (HR = 2.38; 95% CI, 1.71–3.33) without inclusion of any covariates. This remained significant in model 2 with inclusion of post hoc covariates (HR = 1.80; 95% CI, 1.26–2.58). When examining the end point of death alone, results were comparable for each model.

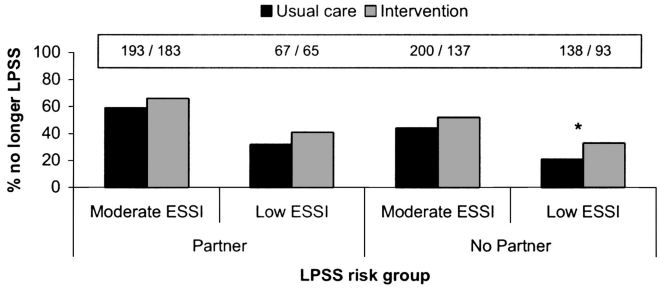

Figure 3. Percent of patients in each LPSS risk group no longer meeting LPSS criteria at 6 months. Textbox contains $N =$. * Indicates significance at the $p < .05$ level.

4 LPSS Risk Groups Versus MI Comparison Group (See Table 4)

Analyses examining the combined end point of death or recurrent MI revealed significant (using Bonferroni corrected $\alpha = 0.05/4 = 0.0125$) HRs ranging from 1.80 to 2.96 (95% CI, 1.23–4.23) for the 4 LPSS risk groups without inclusion of any covariates (model 1). With the exception of the partner/moderate support group, all LPSS risk groups remained significant in model 2 with inclusion of post hoc covariates (HR range = 1.51–2.12; 95% CI, 1.02–3.11; $p < .006$). Models examining the end point of death alone reveal significant HRs ranging from 2.41 to 4.71 (95% CI, 1.25–8.31) for the 4 LPSS risk groups without inclusion of any covariates (model 1). Effects were attenuated with inclusion of post hoc covariates (HR range = 2.13–3.14; 95% CI, 1.14–5.72), and only the no partner/moderate support LPSS risk group remained significant ($p = .0002$) after Bonferroni adjustment. Hence, when examining the combined end point of death or recurrent MI, 3 of the 4 LPSS risk groups remained at significantly greater risk than the MI comparison group, regardless of the adjustments to the model. When examining the end point of death alone, only the no partner/moderate support group remained at significantly greater risk than the MI comparison group after adjusting for potential confounders.

TABLE 3. Effect of LPSS on the Risk of Death or Recurrent MI, or Death Alone[a]

Event	Hazard Ratio (95% CI)	
	MI Comparison Group ($n = 408$)	All LPSS Risk Groups ($n = 1490$)
Death or recurrent MI		
Model 1: unadjusted	1.00	2.39 (1.72, 3.33)
Model 3: risk factor adjustment	1.00	1.80 (1.26, 2.58)
All-cause mortality		
Model 1: unadjusted	1.00	3.40 (1.97, 5.85)
Model 3: risk factor adjustment	1.00	2.50 (1.41, 4.45)

[a] Model 2 includes covariate adjustment for age, sex, BDI score, previous stroke/TIA, heart failure, pulmonary disease, and diabetes.
CI = confidence interval; MI = myocardial infarction; LPSS = low perceived social support.

TABLE 4. Effect of ESSI Score and Partner Status Estimated From Models for Death or Recurrent MI, or All-Cause Mortality[a]

Event	Hazard Ratio (95% CI)				
	MI Comparison Group (n = 408)	Partner		No Partner	
		LPSS Moderate ESSI (n = 496)	LPSS Low ESSI (n = 189)	LPSS Moderate ESSI (n = 478)	LPSS Low ESSI (n = 327)
Death or recurrent MI					
Model 1: unadjusted	1.00	1.80 (1.23, 2.62)	2.35 (1.52, 3.62)	2.96 (2.07, 4.23)	2.54 (1.74, 3.72)
Model 2: risk factor adjustment	1.00	1.51 (1.02, 2.25)	1.91 (1.20, 3.04)	2.12 (1.44, 3.11)	1.76 (1.16, 2.67)
All-cause mortality					
Model 1: unadjusted	1.00	2.41 (1.32, 4.39)	2.51 (1.25, 5.05)	4.71 (2.67, 8.31)	3.58 (1.97, 6.54)
Model 2: risk factor adjustment	1.00	2.13 (1.14, 3.99)	2.02 (0.97, 4.20)	3.14 (1.72, 5.72)	2.24 (1.18, 4.26)

[a] Model 2 includes covariate adjustment for age, sex, BDI score, previous stroke/TIA, heart failure, pulmonary disease, and diabetes.
CI = confidence interval; MI = myocardial infarction; LPSS = low perceived social support.

Change in Social Support and Subsequent Death

Change in social support was modeled in two ways. We first examined change from baseline to 6 and 12 months in overall ESSI score. For both adjusted and unadjusted models, change in ESSI score was not found to predict subsequent death. We then examined improvement in social support status by examining whether at 6 and 12 months the patient still met LPSS study inclusion criteria. Again, improvement status was not found to predict subsequent death.

DISCUSSION

The aims of this paper were to examine the pattern of social support following MI in LPSS patients enrolled in the ENRICHD clinical trial and the effect of treatment on this pattern. Secondary aims were to examine the relationship of social support at the time of MI to future medical morbidity and mortality, and determine whether change in social support after MI was related to subsequent mortality. We discuss these results in 2 sections.

Pattern of Social Support and INT

A significantly higher level of perceived social support 6 months post-AMI was found for the INT arm of the trial than for the UC arm; however, at subsequent follow-up, differences between arms decreased, largely due to the continued increase in social support seen in the UC arm (17). This was unanticipated and contrary to findings from other, observational studies, which demonstrate a decline in social support 12 months after MI (cf, 13,14,29,30). Of note, we also found that at 12 months, patients in the MI comparison group—patients with neither depression nor LPSS in the immediate post-MI period—showed a decline in ESSI score, whereas we find that the LPSS risk groups with the lowest ESSI scores demonstrated the greatest improvement. These findings taken together may represent a "regression to the mean" on the ESSI, with the highest scorers—the MI comparison group—showing a decrement over time, and the lowest scorers—the ENRICHD LPSS cohort—an improvement. Alternatively, findings for the MI comparison group may demonstrate the previously reported natural history of social support in the aftermath of a health crisis, whereas findings for the ENRICHD LPSS cohort demonstrate some general effect of being a participant in a clinical trial, regardless of treatment assignment. Similar general, trial-participant effects have been reported for depression in ENRICHD (31) and for behavioral risk factors in MRFIT (32). The AHA *Partnership* booklet that was provided to all ENRICHD patients regardless of treatment arm may have further enhanced this general effect. Clinical trial enrollment, in which a participant is informed that they are at high risk for some untoward outcome, may therefore be a powerful INT in its own right, an effect that can complicate the conduct of behavioral clinical trials.

In the analyses reported here, a significant treatment effect from baseline to 6 months is seen for the no partner/moderate support group, and this effect is maintained over the long term. The no partner/low support group also shows a significant treatment effect at 6 months; however, the significance of effect is lost by the next follow-up. The partner/moderate and partner/low support groups show no significant treatment effects at either follow-up. These findings must be interpreted with caution, being post hoc in nature. Yet, they might speculatively be interpreted to reflect the positive and negative effects of a partner or significant other and the need for a minimal threshold of support resources for a treatment targeting LPSS to work. Following this interpretation, the study interventionists may have served as "significant other surrogates" for the no partner/moderate and no partner/low support groups during the 6 months of treatment and as such were able to encourage patients in the social outreach and network development activities of the INT. For the moderate support group, as reflected in their higher baseline ESSI scores, the social environment may have met the threshold necessary for the patients to both implement the lessons of treatment and consolidate their gains after the 6-month treatment was terminated. In contrast, for the low support group, as reflected in their lower baseline ESSI scores, the social environment may not have met this threshold. Therefore, although these patients were able to implement treatment lessons initially, they were not able to consolidate their gains over the long term and, because their "significant other surrogate" was gone, lost their

gains once treatment ended. With regard to the partner/moderate and partner/low support groups, the lack of treatment effect may reflect that, in the presence of a partner, the interventionist was unable to serve as a surrogate of any kind and, to the extent that they attempted to influence social support factors, may have been at odds with the wishes, intentions, or efforts of the true partner. In that way, the INT, when delivered to an LPSS patient with a partner, was unable to overcome social support obstacles posed by that partner.

Social Support, Mortality, and Cardiovascular Outcomes

Consistent with results from other studies, baseline LPSS was found to predict medical outcomes, independent of medical comorbidity or other conditions that might confound this association. When examining the 4 LPSS risk groups, however, it was found that not having a partner was a more significant predictor of bad outcome than was ESSI score. Hence, regardless of model adjustment, the absence of a partner predicted medical outcomes, and overall ESSI score did not significantly moderate this finding. These results would appear to again emphasize the importance of partner in both the experience of social support and the impact that support has on medical outcomes. In previous studies of post-MI patients, both emotional support and the presence of a spouse or confidant have been associated with reduced mortality risk (cf, 3,4,6). In long-term population-based studies in which mortality is the primary end point, however, structural characteristics of social networks appear to be more strongly predictive of mortality (cf, 12,33–35). The findings from the current study also suggest that structural components of social ties, as represented by having a partner, may be critical to mortality risk. Structural support features may influence health outcomes through a number of pathways (36), including the buffering of physiological stress responses through the provision of emotional support and via more behavioral pathways such as by encouraging better adherence to post-MI treatment recommendations.

Improvement in social support, regardless of treatment arm, did not affect long-term survival. Although LPSS has been shown to incur risk for poor medical outcome after AMI, the amount of improvement in social support needed to affect post-MI survival has not previously been demonstrated, nor has the relationship of LPSS duration to medical outcomes. These relationships of LPSS to post-MI risk may be mediated by factors that are of a longstanding nature whereby moderate changes in LPSS over a relatively short time frame are not sufficient to influence medical outcomes. Further, treatments or natural influences that mitigate LPSS might not reduce cardiac morbidity and mortality unless they also influence the underlying factors, physiologic and/ or behavioral, that tie LPSS to cardiac outcomes.

Study Limitations

The analyses reported here are post hoc in nature and hence must temper the interpretation of the findings. In addition, the difference in comorbidities between MI comparison group patients and LPSS patients is notable, though the effect of LPSS on medical outcomes remains pronounced with statistical adjustment for these factors. Indeed, the HR for LPSS is robust, though this should come as no surprise, given recent case-control findings regarding the contribution of LPSS and similar psychosocial factors to CHD incidence and prognosis (37). The generalizability of findings to the overall population of post–cardiac-event patients can also be questioned, though the large number of geographically dispersed hospitals from which patients were recruited and the high representation of women and minorities mitigate this concern. The differential loss to follow-up across the 4 LPSS risk groups, ranging from 17% to 33%, raises other questions regarding the veracity of our findings. Rather than drawing conclusions, however, the intention here is to explore the results of ENRICHD as a way of identifying key factors that could inform the design of future LPSS clinical trials. Toward that end, these results provide several promising avenues.

Implications for Future Research

Several questions are raised by the findings presented in this paper. One question concerns the social support improvements seen in the UC patients (in contrast to social support decrements in the MI comparison group). To pursue this issue, future studies should methodically explore the range of factors by which enrollment in a clinical trial can improve outcomes, whether by placebo effects, identification as an "at-risk" patient, provision of even minimal additional resources (e.g., the *Partnership for Health* booklet or brief follow-up contacts), or other factors.

A second question concerns the best treatment approaches for post-MI patients with LPSS. The divergent treatment effects noted for patients with and without a partner and for those with moderate versus low support suggest that the matching of treatment to the LPSS presentation of the patient should be studied in smaller, exploratory trials. For example, insufficient support in the presence of a partner may best be addressed with couples therapy, which would additionally address the partner's concerns and thereby bring him/her in as an ally for improving the patient's perceived level of support. When no partner is available, the individual therapy approach taken for ENRICHD may only be viable for the patient with a threshold level of social resources, whereas those patients without a partner and with very low support may require group therapy, whereby the group serves as a both a temporary network resource, and potentially a resource in the form of new friendships/relationships when treatment ends may be preferable. Another approach to this question may be to first examine "vulnerabilities" or "proximal causes" of LPSS. This would provide a different focus, vulnerability, for matching of treatment to patient. Further, the identification of factors or vulnerabilities that are prognostically significant both with regard to social support and to medical outcomes could provide for better targeting of treatment to those factors.

A final question concerns the importance of LPSS duration to post-MI survival and the amount of improvement in perceived support necessary to affect medical outcomes. Studies that identify the pathophysiological pathway(s) that tie LPSS to outcomes could provide important surrogate markers that could then be used as outcomes in smaller trials focusing on these issues.

Appendix

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