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Inflammatory biomarkers and emotional approach coping in men with prostate cancer

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ABSTRACT

Objective: Emotion-regulating coping is associated with improvements in psychological and physical health outcomes. Yet in the context of prostate cancer-related stressors, limited research has characterized associations of emotion-regulating coping processes (emotional expression, emotional processing) and inflammatory processes that are related to disease risk. This investigation examined the relation of Emotional Approach Coping (EAC) with markers of inflammation to test the hypothesis that higher EAC scores at study entry (T1) would be associated with lower proinflammatory markers four months later (T2), specifically sTNF-RII, CRP, and IL-6.

Methods: Forty-one men (M age = 66.62 years; SD = 9.62) who had undergone radical prostatectomy or radiation therapy for localized prostate cancer within two years completed questionnaires, including assessments of EAC, at T1, and provided blood samples for immune assessments at T2.

Results: When controlling for relevant biobehavioral controls, emotional processing predicted lower IL-6 ($B = -.66$, $p < .01$), sTNF-RII ($B = -.43$, $p < .05$), and CRP ($B = -.43$, $p < .10$), whereas emotional expression was significantly associated with higher levels of sTNF-RII ($B = .55$, $p < .05$). Associations of emotional expression and IL-6 ($B = .38$, $p < .10$), and CRP ($B = .44$, $p < .10$) approached significance. Probing interactions of emotional processing and expression (though only approaching significance) suggested that expression of emotion is associated with higher inflammation (CRP and sTNF-RII) only in the context of low emotional processing.

Conclusions: Attempts at emotion regulation via emotional processing appear to modulate inflammatory processes. Understanding, making meaning of, and working through emotional experience may be a promising target of intervention to reduce inflammation with potential effects on psychological and cancer outcomes in men with prostate cancer.

1. Introduction

The experience of cancer diagnosis and treatment exposes individuals to numerous physical and emotional stressors and accounts for increased risk of emotional distress and depression. The first one to two years following radical prostatectomy or completion of radiation treatment for prostate cancer are markedly demanding and characterized by relatively rapid changes in physical functioning (Litwin et al., 2001; Stanford et al., 2000), increased risk for depression (Jayadevappa et al., 2011), sleep disturbance (Savard et al., 2005), worry and anxiety (Sharpley et al., 2008), and declining health-related quality of life (Gore et al., 2009). Emotional perturbations and chronic negative affective states associated with stressors can invoke potent negative effects on inflammatory and other cellular immune processes (Irwin, 2002; Kemeny, 2007; Reiche et al., 2004; Segerstrom and Miller, 2004; Steptoe et al., 2007), which can compound the burden associated with cancer and have a direct and indirect impact on mental and physical health outcomes (Grivennikov et al., 2010; Mantovani et al., 2008; see also Irwin and Cole, 2011 on behavior and inflammation). Coping through avoidance has typically been associated

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with suppression of cellular immune function, as seen in individuals with HIV and cancer (Fawzy et al., 1990; Futterman et al., 1996; Goodkin et al., 1992a,b); however, effects of approach coping on immune parameters have rarely been assessed (see Goodkin et al., 1992a). Use of coping strategies that lead one to focus on and regulate difficult emotions (e.g., emotional approach coping) related to one's cancer experience has potential for modifying the affective response, reducing inflammation (Master et al., 2009), and improving psychological (Hoyt, 2009) and physical (Hoyt et al., 2013) health outcomes in men with cancer.

Emotional approach coping (EAC) (Stanton et al., 1994) is comprised of two distinct but related emotion-regulating strategies: emotional processing and emotional expression. In the case of prostate cancer, emotional processing includes purposive attempts to acknowledge, explore, and understand one's emotions related to prostate cancer; emotional expression represents active verbal and non-verbal efforts to communicate or symbolize cancer-related emotional experiences (Stanton et al., 2000b). Research with breast cancer survivors has characterized a benefit of EAC on physical health and psychological adjustment, including increased vigor, fewer medical visits for cancer-related morbidities, and improved self-reported health (Stanton et al., 2000a, 2002). However, research in men with mixed cancer types (Hoyt, 2009) found that greater use of emotional expression in response to cancer-related stressors was associated with lower levels of psychological distress, whereas emotional processing demonstrated a positive relationship with distress. In an expanded cohort of the current study, Hoyt et al. (2013) found an opposite pattern, with emotional processing associated with improved prostate-specific functioning, but no relationship with emotional expression. Such disparate associations might be better understood by distinguishing the interactions of expressing and processing cancer-related emotions. Expressing emotions without attempts to understand or make meaning from emotional experience might exacerbate affective dysregulation and promote rumination, persistent worry, or other maladaptive repetitive thought patterns.

Little work has attempted to identify biological mechanisms by which EAC operates, including markers of inflammation. In fact, only one study (Master et al., 2009) has examined inflammatory markers in association with dispositional use of EAC. In a sample of young adults undergoing an acute laboratory stressor, higher levels of EAC, particularly emotional processing, were associated with a less pronounced increase in soluble tumor necrosis factor-receptor type-II (sTNF-RII) in oral mucosal transudate (and interleukin-6, though non-significant after controlling for behavioral factors). Those who are less likely to focus on emotions as a means of coping may be at heightened risk for chronic elevations in inflammation and health-related consequences.

To examine whether coping with cancer-related stressors via emotion-regulatory coping processes was associated with markers of inflammation, this study tested the hypothesis that EAC processes would correlate with circulating levels of proinflammatory cytokines within a clinically relevant period following prostate cancer treatment. Prior work supports a benefit to psychological and physical outcomes of emotional expression (Hoyt, 2009) and emotional processing (Hoyt et al., 2013) in men with cancer. Thus, we hypothesized that EAC processes would predict lower inflammation levels during this time period. The interaction of EAC processes (emotional processing $\times$ emotional expression) was also examined. We expected that emotional expression in the presence of emotional processing would exhibit a more pronounced effect on biomarkers.

There is growing evidence that activation of the proinflammatory cytokine network underlies negative psychological states in cancer patients (Irwin and Miller, 2007; Lee et al., 2004; Miller et al., 2008; Musselman et al., 2001). We focus on three inflammatory markers, interleukin-6 (IL-6), C-reactive protein (CRP), and sTNF-RII, which can be reliably assessed in plasma and have been linked to behavioral and cancer-related outcomes in previous research with cancer survivors (Bower et al., 2011, 2009; Collado-Hidalgo et al., 2002; Orre et al., 2009). Evidence from non-cancer populations implicates these markers in emotional disturbance and depression (Dowlati et al., 2010; Howren et al., 2009; O'Brien et al., 2007), and elevations in IL-6 (Jehn et al., 2006; Musselman et al., 2001; Seruga et al., 2009) and TNF-a (Seruga et al., 2009) have been linked to depression in cancer patients. Notably, sTNF-RII reflects TNF-a activity (Spinas et al., 1992) and tends to be more reliably measured than TNF-a (Diez-Ruis et al., 1995). Experimentally induced immune activation with the release of sTNF-RII leads to increased emotional disturbance (Reichenberg et al., 2001) and in cancer samples has been connected to behavioral symptoms including fatigue (Bower et al., 2011). Because IL-6 induces CRP, this biomarker can provide a measure of the cumulative activity of IL-6 and systemic inflammation.

2. Method

2.1. Participants

Men who completed radical prostatectomy or radiation therapy for localized prostate cancer within the prior two years were recruited to take part in a larger study on "health-related quality of life after prostate cancer." Forty-one participants were recruited via physician/clinic referrals ($n = 2$), community outreach and advertisement ($n = 15$), and from an institutional tumor registry database ($n = 24$). Participants were screened to exclude individuals not meeting entrance criteria (e.g., localized disease, time since treatment, English speaking) and those with any cognitive debilitating co-morbidity (e.g., dementia). Participants were also excluded for presence of medical conditions or medications that would likely confound immune evaluation (e.g., autoimmune disorder, inflammatory disease, uncontrolled thyroid disease, active infection, recent myocardial infarction); regular smoker (daily use); or heavy alcohol use (more than 14 drinks per week). Participants were re-screened at each study visit for acute infection, recent vigorous exercise, recent caffeine or cigarette use, and changes in medications, and rescheduled as appropriate.

Participants were English-speaking men who ranged in age from 51 to 87 years ($M = 66.62$, $SD = 9.62$) and on average, completed treatment 15.63 months prior ($SD = 7.53$; range = 2 to 24 months) to study completion. Clinical and socio-demographic variables are reported in Table 1. No men were on active hormonal therapy at the time of participation. Notably, an additional three men completed the initial assessment but not the T2 session (not reported on here). These men did not differ significantly from those who completed the T2 assessment on sociodemographic or cancer-related variables.

2.2. Procedures

After providing written informed consent, participants attended an individual session (T1) to complete questionnaire and interview assessments and returned for a follow-up session 4 months later (T2) where they provided blood samples. Their height and weight as well as other relevant biobehavioral variables were recorded at each session. All assessments were conducted in the morning (before 11 am). Participants received $25 after each session. The institutional review board at the University of California, Los Angeles approved study procedures.

Table 1
Participant characteristics ($N = 41$).

Characteristic, mean (SD) or %		Characteristic, mean (SD) or %	
Age, in years	66.62 ($SD = 9.62$)	*Job status*:	
		Full-time employment	39.0%
Ethnicity:		Part-time employment	9.8%
White (non-Hispanic)	80.5%	Retired	46.3%
African American/Black	12.2%	Unemployed/disability	4.9%
Hispanic/Latino	4.9%	*Relationship status*:	
Other	2.4%	Married/partnered	87.8%
Education:		Widowed/divorced	7.3%
High school	7.2%	Single, never married	4.9%
Some post-high school	22.0%	*Treatment*:	
2-year college degree	9.8%	Prostatectomy/surgery	78.0%
4-year college degree	22.0%	Radiation therapy	22.0%
Advanced degree	39.0%	Previous hormone therapy	4.9%
Annual household income:		Months since diagnosis	22.24 (SD = 10.90)
$15,000 or less	2.5%		
$15,001-$45,000	2.5%	Months since treatment	15.63 (SD = 7.53)
$45,001-$75,000	27.5%		
$75,001-$100,000	20.0%	Gleason sum	5.7 (SD = 1.39)
$100,001 or more	47.5%		

2.3. Measures

Emotional approach coping

Use of EAC processes in response to prostate cancer-related stressors were measured at T1 using Stanton and colleagues' (Stanton et al., 1994, 2000a,b) EAC scales, which consist of the 4-item emotional processing (e.g., "I take time to figure out what I'm really feeling", "I delve into my feelings to get a thorough understanding of them") and 4-item emotional expression (e.g., "I feel free to express my emotions", "I let my feelings come out freely") scales. Participants were instructed to complete items to reflect the degree to which they engaged in EAC in response to cancer problems and experiences on a 4-point scale (1 = I don't do this at all; 4 = I do this a lot). As measured by the EAC scales, EAC processes may include verbal or nonverbal attempts at expression and intrapersonal or interpersonal coping efforts. Both EAC scales have been shown to demonstrate sound internal consistency and predictive validity [see Austenfeld and Stanton, 2004 for a review of the psychometric properties]. In the current study, Cronbach's alphas were 0.82 for emotional processing and 0.90 for emotional expression.

Assessment of inflammatory markers

Blood samples for circulating inflammatory markers were collected by venipuncture into EDTA tubes, placed on ice, centrifuged for acquisition of plasma, and stored at -80 degrees Celsius for subsequent batch testing. Plasma levels of IL-6 were determined by high sensitivity enzyme-linked immunosorbent assay (ELISA; R&D Systems, Minneapolis, MN) according to manufacturer's protocols, with a lower limit of detection of 0.2 pg/mL. sTNF-RII levels were determined by regular-sensitivity ELISA (R&D Systems, lower limit 234 pg/mL). CRP levels were determined by a high-sensitivity ELISA (Immundiagnostik, ALPCO Immunoassays, Salem, NH) according to the manufacturer's protocol, but with an extended standard curve to a lower limit of detection of 0.2 mg/L. All samples were run in duplicate; intra-assay and inter-assay precision of all tests were less than or equal to 10%.

Clinical characteristics, sociodemographics, and biobehavioral factors

Participants reported their age, level of education, income, employment status, ethnicity, and other socio-demographic variables. This included information regarding health history, health behaviors, diagnosis and treatment factors, and level of prostate-specific functioning (as measured by The UCLA Prostate Cancer Index (UCLA-PCI) (Litwin et al, 1998).

2.4. Data analyses

Descriptive statistics were computed for key study variables including sociodemographic and relevant clinical characteristics. Distributions of inflammatory markers were non-normal. Thus, all inflammatory markers were transformed prior to analyses using a natural log transformation; non-transformed values are shown in tables and figures for ease of interpretation. Zero-order correlations among predictor and dependent variables were also computed. Several covariates were identified a priori based on recommendations for treating biobehavioral factors in the assessment of circulating inflammatory markers (O'Connor et al., 2009). These included participants' age, ethnicity (White non-Hispanic vs. ethnic minority), body mass index, and number of months since completing primary cancer treatment. Covariates were controlled in subsequent analyses.

Multiple linear regression was used to test study hypotheses. T2 inflammatory markers were separately regressed on EAC measures at T1, controlling for identified variables. Control variables were entered in the first step, EAC processes were entered in step 2, and the interaction term of emotional expression and emotional processing was entered in the final step. Moderator analyses allowed for examination of the possibility that emotional processing efforts are conditioned by emotional expression (and vice versa) as observed in previous research (Stanton et al., 2000a) and were conducted in accordance with procedures outlined by Aiken and West (1991).

3. Results

Sociodemographic and cancer-related variables are reported in Table 1. Descriptive statistics and correlations for key study variables are reported in Table 2. Mean values of emotional expression and emotional processing were slightly higher than those documented by Hoyt (2009) in men with mixed cancer types for emotional expression (M = 2.46, SD = .91) and emotional processing (M = 2.41, SD = .81), and slightly lower than those documented by Stanton et al. (2000a) in women with breast cancer, which were 2.95 (SD = .84) and 3.00 (SD = .80) for emotional expression and emotional processing, respectively.

Men in the sample reported notable difficulty with sexual function ($M = 40.18$; range = 0–93) and psychological bother of sexual symptoms ($M = 43.05$; range = 0–100), as well as with urinary function ($M = 73.32$; range = 6.60–100) and psychological bother of urinary symptoms ($M = 53.05$; range = 0–100). These reflect

Table 2
Descriptive statistics and correlations for key variables.

Variable	Descriptive statistics			Correlations				
	Mean	SD	Range	1	2	3	4	5
Emotional processing	2.79	.80	1.00–4.00	–	.64***	−.20	−.50**	−.04
Emotional expression	2.62	.81	1.00–4.00		–	−.04	−.18	−.15
IL-6, pg/mL[a]	1.92	1.88	.48–11.10				–	−.08
CRP, mg/L	2.85	4.24	.23–18.23					
sTNF-RII, pg/mL	2754.43	812.15	1634.20–4817.10					

[a] Descriptive statistics for inflammatory markers show non-transformed values; all analyses were performed on natural-log transformed values.
** $p < .01$.
*** $p < .001$.

variation in prostate cancer treatment-related physical and psychological demands at levels similar or lower than samples of men treated for localized disease (Gore et al., 2009).

3.1. Relationships between emotional approach coping and inflammatory markers

To test the hypothesis that men reporting greater levels of emotional expression and emotional processing would evidence lower levels of proinflammatory markers at T2, multiple regression analyses were conducted using EAC processes as predictors and inflammatory markers as dependent variables. Analyses included identified control variables for each outcome. Consistent with hypotheses, T1 emotional processing was significantly associated with lower circulating levels of IL-6 ($B = -.66$, $p < .01$) and sTNF-RII ($B = -.43$, $p < .05$) at T2. The relationship with CRP was in the same direction and approached significance ($B = -.43$, $p < .10$). However, contrary to hypotheses, T1 emotional expression was related to increased levels of sTNF-RII ($B = .55$, $p < .05$), and a similar pattern approached significance for IL-6 ($B = .38$, $p < .10$) and CRP ($B = .44$, $p < .10$).

3.2. Interaction of emotional processing and emotional expression

To assess the possibility that emotional processing and emotional expression have combined effects, interaction terms were also included in analyses. Though only approaching significance, interactions were observed for effects on T2 sTNF-RII and CRP (see Table 3). Because these interactive effects accounted for 7–8% of the variance and might help explain the unexpected influence of emotional expression on inflammatory markers, moderated effects were probed and plotted at 1 SD above and below the mean of emotional processing. At relatively low levels of emotional processing, high emotional expression was significantly associated with higher CRP ($B = .73$, $p < .01$) (see Fig. 1a) and sTNF-RII ($B = .81$, $p < .01$) (see Fig. 1b). However, this effect is buffered (no longer significant) in the presence of high levels of emotional processing in both the case of CRP ($B = .13$, *ns*) and sTNF-RII ($B = .23$, *ns*).

4. Discussion

Research has demonstrated that, under particular conditions, coping with stressful circumstances through emotional approach confers benefit to health and well-being (see Stanton, 2011), yet few studies have examined correlated physiological processes. The goals of this study were to examine relationships of the use of EAC processes (i.e., emotional expression, emotional processing) to regulate responses to emotion-laden stressors associated with prostate cancer and biological markers of inflammation (i.e., IL-6, sTNF-RII, CRP) during a period of known high demand for prostate cancer survivors. T1 EAC processes and their interaction accounted for 18–22% of the variance in T2 inflammatory markers.

Hypotheses regarding longitudinal effects of emotional processing were generally supported. Emotional processing of prostate cancer-related stressors predicted lower levels of inflammation

Table 3
Predictors of inflammatory markers at time 2.

	T2 inflammatory marker											
	IL-6				CRP				sTNF-RII			
Variable[a]	ΔR^2	*B*	SE	β	ΔR^2	*B*	SE	β	ΔR^2	*B*	SE	β
Block 1	.27*				.17				.23†			
Age		.02	.01	.33*		−02	.02	−.13		.01	.01	.28†
Ethnicity[b]		.13	.27	.08		−.23	.53	−.08		−.17	.11	−.24
Body mass index		.04	.03	.23		.11	.06	.31		.01	.01	.18
Time since treatment completion		.01	.01	.16		.02	.02	.11		<.01	.01	−.01
Block 2	.17*				.10				.15*			
Emotional processing		−.59	.19	−.66**		−.69	.38	−.43†		−.16	.06	−.43*
Emotional expression		.31	.16	.38†		.63	.32	.44†		.18	.07	.55*
Block 3	.03				.08†				.07†			
Emotional processing X Emotional expression		−.17	.14	−.18		−.52	.29	−.31†		−.11	.06	−.27†
	$F(7, 35) = 3.48^{**}$; $R^2 = .47$				$F(7, 34) = 2.12^{\dagger}$; $R^2 = .35$				$F(7, 35) = 3.23^{*}$; $R^2 = .45$			

[a] Regression coefficients reflect values at the end of Block 3, with all variables entered into the equation.
[b] 0 = White (non-Hispanic); 1 = ethnic minority.
† $p < .10$.
* $p < .05$.
** $p < .01$.

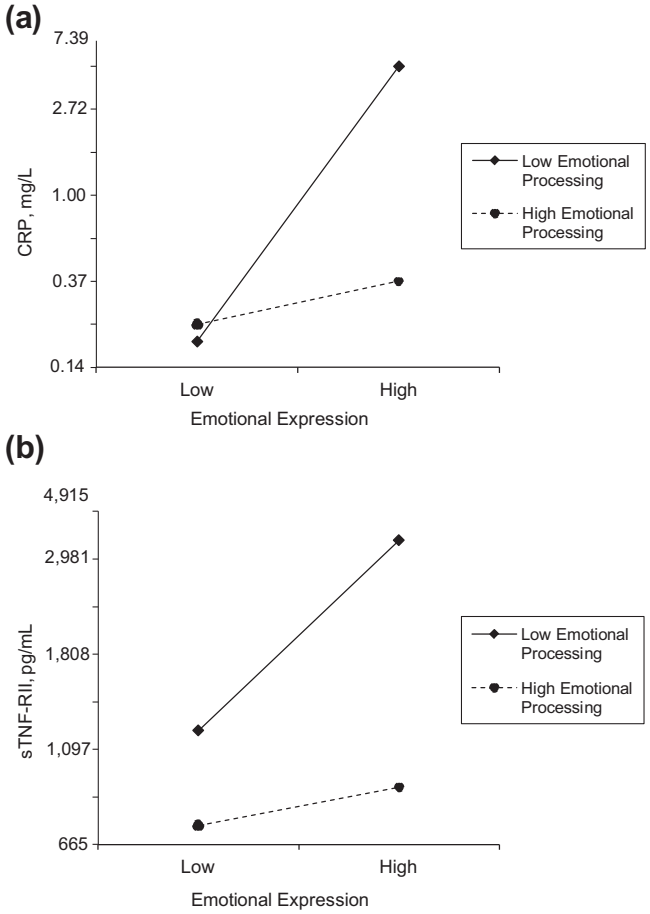

Fig. 1. Figure displays interaction effects for (a) T2 CRP and (b) T2 sTNF-RII. Analyses controlled for age, body mass index, ethnic status, and time since completion of primary cancer treatment (radiation therapy, surgery). Dashed line denotes non-significant simple slopes.

over time, providing support for the prospect that processing of emotions associated with prostate cancer-related stressors modulates changes in inflammatory responses and lending insight into the possibility that inflammatory mechanisms have the potential to contribute to the benefits of emotional processing on psychological and physical outcomes observed across studies. It may be that the process of "working through" or making meaning from difficult emotions provides adaptive regulation of emotion and greater likelihood of a declining trajectory of chronic systemic inflammation following treatment for prostate cancer, though examination of changes over time is required. Prior work on emotional approach has shown that emotional processing supports adaptive emotion regulation by fostering positive cognitive reappraisals (Creswell et al., 2007), improving interpersonal support (Lichtenthal et al., 2006), and promoting physiological habituation to emotional stressors through sustained exposure (Low et al., 2006, 2008), which may then influence inflammatory responses.

In contrast to those for emotional processing, hypotheses regarding the links between emotional expression and inflammatory markers were not supported. The association of emotional expression with higher levels of inflammation was unexpected. However, examination of the interactions with emotional processing offers a possible explanation. Although the relevant interactions did not attain statistical significance at $p < .05$, they accounted for seven to eight percent of the variance in the inflammatory markers. Explorations of the interactions suggest that emotional expression is associated with higher levels of inflammation only when used in relative isolation of emotional processing. Expressing one's emotions without efforts to understand them might promote emotion dysregulation by extending maintenance of negative affect (Rude et al., 2007), impairing cardiovascular habituation (Low et al., 2008), or preventing adaptive processing allowing one to maintain distance from emotional stressors and thus blocking attempts at cognitive change or active coping. Expressive writing or similar interventions that also prompt cognitive processing of emotions may be optimal in promoting affect regulation and associated downstream immune changes. In fact, avoidance of processing of HIV-related emotional content has been associated with a trend toward lower CD4+ percentages (Lutgendorf et al., 1997) and cognitive processing after loss predicts less rapid declines in CD4+ cells in HIV positive men (Bower et al., 1996).

Future work might also explore the neural correlates of EAC that might be associated with upstream processes of the central nervous system affecting downstream immune regulation. For instance, Master et al. (2009) revealed that higher levels of emotional expression were associated with greater resting left-sided frontal electroencephalography asymmetry, an indicator of approach-oriented motivation and lower likelihood of negative affectivity in response to stressors. Such patterns of cerebral activation have been associated with increased immunocompetence including smaller decrements in natural killer cell activity following an emotional stressor (Davidson et al., 1999), and a larger antibody titer rise after influenza vaccination (Rosenkranz et al., 2003).

Several assumptions underlie the conceptual model under investigation in this study. One assumption is that emotion-regulating coping processes have the potential to interrupt affective pathways to proinflammatory cytokine activity. However, it is also possible that cytokine signals communicate with the brain and ultimately influence emotional response (Miller et al., 2005). A second assumption is that heightened cytokine levels are maladaptive. The body's attempt at tissue repair following surgical intervention and exposure to radiation involves up-regulation of proinflammatory cytokine responses (Barcellos-Hoff, 1998; Goldfarb et al., 2010; Stone et al., 2003) to promote tissue repair. Indeed, positive affect was associated with increased levels of proinflammatory cytokines in a study of men with prostate cancer undergoing radiation therapy (Sepah and Bower, 2009). However, all the men in this study had completed treatment, and persistently elevated proinflammatory markers have been associated with treatment-related toxicities following treatment for prostate cancer (Christiansen et al., 2007).

Study limitations should be noted. This study relied on a relatively small and relatively homogenous sample of primarily white, highly educated men with localized disease and had limited statistical power. Examination of samples with diversity across race, ethnicity, socioeconomic status, age, cultural experience, and disease characteristics will extend this research. This study also utilized a somewhat arbitrary window of 4 months in which to detect changes in a sample of patients with varied durations since treatment completion. However, longitudinal studies of men treated for prostate cancer have reported detectable changes in prostate-specific functioning in as little as 3-month re-assessments within the 2-year period following treatment (Litwin et al., 2001; Namiki et al., 2008). Further, men reported being bothered by urinary and sexual symptoms (via responses on the UCLA-PCI) at notably higher proportions than reports in larger longitudinal population studies. Stanford et al. (2000) reported minor to severe bother related to urinary problems in 62.2% of men with localized prostate cancer ($N = 1291$), and minor to severe bother related to sexual problems in 86.0% of men at 24 months post-surgery. This compares to 73.2% and 92.7%, respectively, in the current study. Finally, the current study offers a preliminary examination of

measures of inflammation utilizing a traditional ELISA approach to examine a limited set of biomarkers. Other approaches should be utilized in future research to explore the possibility of associations of coping with other inflammatory markers, including anti-inflammatory cytokines. Despite these limitations, this is the only study to examine emotion-regulating coping processes on inflammation in men with prostate cancer and these results inform our limited understanding of the influence of these coping processes in this population. Results from this study are correlational, and although consistent with our conceptual framework, causal conclusions cannot be made.

The present study implicates emotional processing as an effective coping strategy by which regulation of emotion modulates inflammatory processes. Over time, coping through emotional processing might be protective against chronic inflammatory processes, which have been associated with a variety of adverse health outcomes, including overall and disease-related mortality (Shafique et al., 2012). Identifying the degree to which coping processes account for changes in immune regulation will contribute to the growing knowledge base regarding psychosocial influences on cancer-related morbidity, progression, recurrence, and mortality (Lutgendorf and Sood, 2011). Studies that examine trajectories of dynamic relationships of coping and immune activity will make a significant contribution. Further, as psychosocial interventions continue to identify inflammatory processes as primary outcomes (Cohen et al., 2011), more precise identification of psychological and behavioral processes that underlie signaling of inflammatory biomarkers is increasingly critical. Prostate cancer often presents unique circumstances to patients and the degree to which these findings generalize to other populations and contexts warrants further investigation. Additional research is needed to characterize the effect on varied and prolonged immune responses, and most importantly, to prostate-specific outcomes.

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