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Research paper

Impact of religiosity/spirituality on biological and preclinical markers related to cardiovascular disease. Results from the SPILI III study

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ABSTRACT

OBJECTIVE: This study aimed at exploring to what extent psychosocial factors, such as religiosity/spirituality and sense of coherence, mediate the negative effects of stress on a variety of cardiometabolic indicators, i.e., hypertension, diabetes, cardiovascular and cerebrovascular disease, and atherosclerotic bio-clinical markers. DESIGN: A total of 220 subjects (66.2±16.0 years) of the SPILI III cohort (1988-2012) attending a primary care setting in Spili, a rural town in Crete, represented the target group for the present study. Of these, 195 (88.6%) participated in the re-examination (67.2±15.2 years). All participants underwent a standardized procedure including evaluation of anthropometric measurements, biochemical indicators of atherosclerosis, stress hormones, in parallel with ultrasound measurements of carotid intima media thickness (IMT). Religiosity, spirituality and sense of coherence were evaluated with the use of international questionnaires translated into the Greek language and linguistically validated. RESULTS: Participants with higher levels of religious and spiritual beliefs presented lower levels of carotid IMT (1.01±0.101 vs 1.53±0.502 mm, p<0.001). Patterns of inverse relationships were also observed between religiosity/spirituality and prevalence of diabetes (35.1% vs. 2%, p<0.001) with an estimated diabetes risk, fully adjusted odds ratio, 95% CI: 0.91 (0.87-0.94). Highly religious participants presented lower serum cortisol levels (12.3±5.8 vs. 18.2±5.1 μg/dl, p<0.001). Sense of coherence was positively associated with religiosity/spirituality [mean SOC (SD): 123±20 vs. 158±15) p<0.001]. CONCLUSIONS: These findings may be associated with a possible favourable effect of religiosity/spirituality on several cardio-metabolic determinants, therefore deserving further attention by healthcare practitioners and researchers.

Key words: Cardiovascular disease, Carotid intima media thickness, Religiosity, Serum cortisol, Spirituality

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INTRODUCTION

The population of Crete has frequently been mentioned in the literature, especially on account of their exceptionally low incidence of CVD,[1,2] and much discussion has been devoted to the role played in Cretans' health and longevity of the Cretan Mediterranean diet. However, it is of great interest also to examine to what extent various psychosocial factors might be partially accountable for this fact, and particularly the strong religious beliefs of this population, which may act as a buffer against stress. Religiosity has been defined as a set of beliefs and practices relating to the transcendent, whilst spirituality is seen as being intimately connected to the mystical.[3]

Current evidence suggests that aspects of religiosity and spirituality may be involved in the regulation of important physiological processes.[4] A critical review of the literature reveals a link between religious involvement and lower blood pressure.[4] Likewise, a longitudinal cohort study reports that older adults with frequent religious attendance in combination with prayer and Bible study tend to have lower blood pressure.[5] In addition, recent findings from a large population-based survey implemented in Norway demonstrate that religious attendance is associated with lower systolic and diastolic blood pressure, after adjustment for relevant confounders.[6] With regard to spirituality, higher levels of spiritual well-being have been significantly associated with lower levels of ambulatory blood pressure and lower high sensitivity C-reactive protein levels.[7] Similarly, practices such as meditation have been related with lower cardiovascular risk and lower cholesterol or blood pressure levels.[4]

In addition to the notions of religiosity and spirituality, the literature also addresses sense of coherence (SOC), a concept that was developed by Aaron Antonovsky in 1987, as studied in association with cardiovascular determinants.[8] Antonovsky's approach introduces a salutogenic perspective of explaining individuals' health outcomes by focusing on what keeps people healthy rather than what makes them ill.[8] SOC represents a stable personality disposition and consists of three components, namely comprehensibility, manageability and meaningfulness.[8] It is proposed that a person characterized by strong SOC is more likely to be able to select suitable coping strategies and to handle life situations appropriately.[8]

A research project, known as the SPILI project, has been in progress since 1988 in the rural area of the village of Spili on Crete, Greece, with the aim of monitoring the long-term health status of the population.[9,10] The first literature reports revealed that, in spite of the negative risk factor profile of the Spili cohort, the prevalence of coronary heart disease remained surprisingly low.[9,10] In the absence of a specific explanation for these findings, we formulated a hypothesis stating that the existence of specific health assets of the local community may contribute to a form of resilience against CVD by counterbalancing negative neuroendocrine consequences of stress. The current study, named the SPILI III study,[11] investigates further this hypothesis. Although the Cretan population remains highly religious, research efforts regarding the effects of religiosity/spirituality on health have only focused on the Orthodox Christian lifestyle and specifically on the beneficial effects of adherence to the Greek Orthodox religious tradition of periodic fasting on participants' lipids profile and obesity.[12] With regard to SOC, a previous study showed that Cretan males of the Spili cohort achieved higher SOC scores compared with a reference group from northern Europe.[13]

Aside from the above, the study of potential connections between psychosocial characteristics and health, in terms of disease prevention, healing or coping, has received limited attention among this population. We therefore assumed that religiosity/spirituality and sense of coherence could represent positive coping mechanisms, possibly associated with decreased chronic inflammation.[11] On this basis, the SPILI III study was designed with the aim of exploring potential mediating effects of religious/spiritual beliefs and sense of coherence on the cardiovascular health of this well-defined population, who have been continuously monitored for over two decades. The set of data reported here demonstrates associations between religiosity/spirituality and a variety of cardiovascular biochemical, clinical and imaging indicators.

METHODS

Study sample and sampling procedure

The Spili project represents a cohort study initially established in 1988 (Spili I). The study sample of Spili I consisted of n=432 subjects (205 males, 227 females).[9] A follow-up study was carried out 12 years after the initial examination (Spili II).[10] The target population of Spili II consisted of 248 persons and 200 inhabitants were finally included.[10] The current phase of the Spili project (Spili III) was designed to include all of the participants of the Spili II study (n=248) plus the ex-inhabitants who had participated in Spili I (n=37), not evaluated in Spili II. Of all these, sixty-five persons were no longer alive (n=220). Therefore, a total of 220 subjects represented the target group for the second follow-up. All subjects received an invitation letter and were approached by telephone. A total number of 195 participants (97 males, 98 females), mean age 67.2±15.2 (not significant gender difference, p= 0.054), were re-examined, representing 88.6% of the target group. Twenty-five individuals, reporting "good health", declined our invitation. In regard to gender, non-participants did not differ in comparison to participants [males: 8.5% (9) vs. 91.5% (97) and females: 14% (16) vs. 86% (98), p=0.195]. The mean age of the non-participants was more likely to be lower than the mean age of participants [58.48 (SD: 20.236) vs. 67.16 (SD: 15.19), p=0.021]. The project was launched in September 2009 at the primary healthcare center located in the Cretan village of Spili and was gradually completed over an 18-month period.

Bioethics

The study protocol was approved by the Institutional Ethics Committee of the University Hospital of Heraklion, Crete (No 9989/02.09.2008). All individuals were informed about the aims of the study and written informed consent was obtained from all participants prior to any data or sample collection. Laboratory and health examinations results were made available to the participants

Disease definitions and diagnostic criteria

Participants were interviewed with the help of a previously used questionnaire,[10] utilising questions regarding age, gender, marital and occupational status, a detailed medical history and information on smoking habits. With regard to smoking, we grouped participants as non-smokers, current smokers and former smokers (cessation for more than 12 months). For current smokers, we recorded the average number of cigarettes smoked daily.

Height was measured in centimeters, using a portable stadiometer, to the nearest 0.5 cm, without shoes and with eyes looking straight ahead. Weight was measured with a SECA 815 electronic scale with the subjects wearing light clothing and without shoes. Body mass index (BMI) was calculated as weight (in kilograms) divided by squared standing height in meters squared. According to standard guidelines, overweight was defined as BMI between 25.0-29.9 kg/m^2 and obesity as ≥30.0 kg/m^2.

Blood pressure (BP) measurements were performed after the end of the interview following a standardized protocol according to the Joint National Committee (JNC) 7 guidelines.[14] The patients were seated quietly for at least 5 minutes on a chair with feet on the floor and arms supported at heart level. The BP was measured in both arms and, in the event of a difference, the reading from the arm with the higher BP was retained. Three BP measurements were acquired from each patient with a more than 1-min interval between them and the mean value was recorded.

Data regarding previous myocardial infarction, cerebrovascular disease and congestive heart failure were obtained for all participants, both through the personal interview and by reviewing medical records stored in the database of the primary healthcare center, which is responsible for continuous contact with all SPILI project participants.

Hypertension was defined as systolic BP (SBP) ≥140 mmHg or diastolic BP (DBP) ≥90 mmHg or current treatment with antihypertensive drugs, according to JNC 7.[14] Hypercholesterolaemia was defined as total serum cholesterol levels greater than 200 mg/dl or the use of lipid lowering agents.[15] Diabetes mellitus was defined as a fasting blood sugar >125 mg/dl or the use of antidiabetic medication.[16]

Biochemical analyses

Blood samples were obtained from the antecubital

vein between 6:00 and 8:00 a.m., in a sitting position after overnight fasting and alcohol abstinence, and after 30 min resting. Serum total cholesterol, high density lipoprotein cholesterol, triglycerides and blood glucose were measured using an enzymatic method in an Olympus automated analyzer (AU5400 high-volume chemistry analyzer; Olympus, Inc., Melville, New York).

Low density lipoprotein (LDL) cholesterol was calculated with the Friedewald formula: total cholesterol– (HDL cholesterol + 1/5 x triglycerides).[17] Serum cortisol concentration was measured with the use of a chemiluminescent immunoassay analyzer (ARCHITECT Cortisol Reagent Kit, Abbott Laboratories), with reagent from the same company (Cortisol Reagent Kit). Interleukin 1β and interleukin 6 were assayed with a chemiluminescent immunometric analyzer (Immulite 1000; DPC-Siemens), with reagents from the same company (Siemens Healthcare Hellas). Plasma fibrinogen was measured on Diagnostica Stago analyzers (STA-R Evolution and STA-Compact) using STA Fibrinogen reagent (Diagnostica Stago). The inter- and intra-assay coefficients of variation for these parameters were less than 5%. The laboratories of Clinical Chemistry-Biochemistry and Clinical Immunology-Experimental Endocrinology of the University Hospital of Heraklion follow both internal and external quality control procedures. Internal quality control is carried out routinely twice daily in two levels, while external quality assessment is performed by two programmes: 1) External Quality Assurance Services, Clinical Chemistry Program (EQAS) (BioRad) performed every 15 days and 2) National System of External Quality evaluation in Clinical Chemistry (NSEQCC) carried out every month.

Carotid artery ultrasound analysis

Scans were performed by two senior residents who were instructed on the protocol technical details by a qualified specialist expert in vascular ultrasound techniques. Measurements were made with a portable ultrasound unit that consisted of a General Electric Logiq book e and a high resolution 10-15 MHz linear array broadband transducer. Sonographers were blinded to all patients' clinical information. Subjects were examined in the supine position. Images of the distal 1 cm of the right and left common carotid artery and the carotid bulb were recorded, and intima media thickness (IMT) measurements on the far wall 1 cm proximal to the carotid bulb were obtained.[18]

Psychosocial factors' assessment

Although both spirituality and religiosity are important concepts in explaining changes in healthcare, there are certain difficulties in their definition. Definitions for spirituality and religiousness require attention prior to any assumptions made during research. Definitions stated by Koenig et al[3] put forward the view that religion may be seen as a set of beliefs, practices and rituals related to the transcendent, often involving the mystical. This may include rules about conduct within a specific social group, and beliefs and behaviours that are derived from traditions that have developed over time within a community. Religion is also seen as an organized system of beliefs to facilitate closeness to the transcendent and to foster an understanding of one's relationship to other community members. Spirituality is seen as being distinguished by its connection to that which is sacred, being intimately connected to the mystical and to organized religion, although extending beyond organized religion.[3] There is a definite connection between the two; however, it is argued that although all religions involve spirituality to some extent, not all forms of spirituality are religious.[19]

Assessment of religiosity/spirituality of all participants was performed using the Royal Free Interview for Spiritual and Religious Beliefs (RFI-SRB) that has been translated and validated in the Greek language.[20, 21] This instrument (designed for use across a variety of religions) focuses on the strength and consequences of faith.[21] Strength of religious/spiritual belief is calculated via six questions with continuous responses, each scored on a 0-10 scale (total range 0-60). Higher values of the RFI-SRB indicate that strength of religious and spiritual faith is high. The six questions of the Royal Free Survey are presented in Appendix 1. The questionnaire includes additional questions with categorical responses (not included in the score calculation, but used for the validation of response consistency) on prayer and attendance at worship services. Furthermore, participants completed the 29-item Sense of Coherence (SOC) scale

developed by Antonovsky,[22] which was translated into Greek and validated at the Clinic of Social and Family Medicine of the University of Crete.[23] The original instrument consists of 29 items scored on a 7-point Likert scale format with two fixed responses, 'never' and 'very often'. Total scores range from 29-203. Higher scores indicate a stronger SOC. Cronbach's alpha coefficient of the SOC scale was equally very high (a=0.888). Partial correlation coefficient between SOC and RFI was r=0.0773, p<0.001 controlling for gender, age and family status.

Statistical analysis

Mean values, standard deviation and frequencies were used to describe the studied characteristics of the participants. Differences with regard to age-group and gender were tested with the use of the chi-square or Student-t test. For the classification of subjects according to religious/spiritual beliefs based on the RFI score, a dichotomous classification was used, calculated as follows: median values were extracted (age-gender specific categorization); scores below the median value were considered as low or moderate, while scores equal to or above the median value were considered as moderate-to-high religiosity/spirituality. The odds ratios for the subjects' having high religiosity/spirituality were estimated based on participants' characteristics. Logistic regression analysis was applied controlling for gender, age, family status, smoking habits and body mass index. Furthermore, differences between mean values of sense of coherence scale levels, body mass index, intima media thickness and other biological markers were evaluated in relation to religiosity/spirituality categories using analysis of covariance (ANCOVA); gender, age, family status, smoking and body mass index were used as covariates. Heterogeneity was tested by the Levene test. Data were analyzed using the Statistical Package for the Social Sciences software (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp).

RESULTS

The total sample of the present work was 195 subjects (50% women) with a mean age of 67±15 years. The median (quartiles) RFI-SRB score was 48 (11, 51); mean ±SD: 32.2± 19.6). Our data produced a Cronbach's alpha coefficient for RFI[20] of a=0.978, indicating a high level of internal consistency. The studied sample was separated into two groups according to the RFI-SRB score (i.e., score higher and lower than median), as detailed in the Methods section. Analysis of the two groups revealed several differences, in particular in the prevalence of CVD risk factors: people with a lower RFI-SRB score showed higher presence of smoking (37.1% vs 1%), p<0.001), hypertension (60.2% vs 80.4%, p=0.002) and diabetes mellitus (35.1% vs 2%, p<0.001), while the presence of myocardial infarction was more frequent among people with a lower RFI-SRB score (Table 1). Moreover, people with a higher RFI-SRB score also had a higher SOC score (total, as well as sub-scores) (Table 1).

As far as atherosclerotic related biomarkers are concerned, people with a higher RFI score had lower intimae media thickness (1.01±0.101 vs. 1.53±.0.502 mm, p<0.001) and lower serum cortisol levels (12.3±5.8 vs. 18.2±5.1 μg/dl, p<0.001). Additionally, fasting blood glucose levels were higher in people with a lower RFI-SRB score (106±44 mg/dl vs. 91±11 mg/dl, p=0.003). The other biomarkers studied did not show any difference between groups (Table 2).

Multivariable analysis was further applied in order to evaluate the association between the RFI-SRB score and the development of hypertension, diabetes mellitus and cardiovascular disease (i.e., congestive heart failure or coronary heart disease). All analyses, i.e., unadjusted, age-sex only adjusted and fully adjusted (i.e., for age, gender, family status, smoking habits and body mass index) showed that the RFI-SRB score was inversely associated with the development of these conditions (Table 3).

DISCUSSION

Main findings

The main finding of this observational study was that highly religious participants, as indicated by a high RFI-SRB score, showed results that were inversely associated with the development of hypertension, diabetes mellitus and cardiovascular disease, whilst they presented a lower level of carotid IMT and lower serum cortisol levels in comparison with the participants who were not highly religious. In

Table 1. Descriptive characteristic of the n=195 participants of the study by level of Spiritual and Religious Beliefs

		Royal Free Interview score for Spiritual and Religious Beliefs (RFI-SRB)		
		<median	**≥median**	***p***
N		97	98	
Age, years, mean (SD)		66 (16)	69 (15)	0.424
Age group, %				0.277
	<65	42.3	34.7	
	65+	57.7	65.3	
Family status, %				0.862
	married	72.2	75.5	
	not married, divorced	2.1	2.2	
	widowed	25.8	22.4	
Religion, %				0.504*
	Christian Orthodox	99.0	98.0	
	Christian Evangelist	1.0	2.0	
Smoking, %	current	37.1	1.0	<0.001
Obesity status, %	overweight, obese	85.6	77.6	0.149
Hypertension, %		80.4	60.2	0.002
Diabetes mellitus, %		35.1	2.0	<0.001
Cerebrovascular event, %		3.1	0.0	0.121*
Congestive heart failure, %		7.2	1.0	0.058*
Myocardial infarction, %		6.2	0.0	0.014*
SOC (range: 82-194), mean (SD)		123 (20)	158 (15)	<0.001
Comprehensible score		45 (9.5)	58 (7.6)	<0.001
Manageable score		40 (8.7)	54 (7.5)	<0.001
Meaningful score		38 (8.4)	46 (5.6)	<0.001

Values are mean±SD or relative frequencies (%). *P*-values derived using chi-square or Fisher exact test (*) and analysis of variance

Table 2. Analysis of atherosclerotic related biochemical and ultrasound results by level of Spiritual and Religious Beliefs

	Royal Free Interview score for Spiritual and Religious Beliefs (RFI-SRB)		
	<median	**≥median**	***p***
N			
Carotid artery IMT, mm	1.53(0.502)	1.01(0.101)	**<0.001**
Serum cortisol, mg/dL	18.2(5.1)	12.3(5.8)	**<0.001***
Plasma fibrinogen, mg/dL	314(64)	303(69)	0.251
Serum glucose, mg/dL l	106(44)	91(11)	**0.003**
Serum Total cholesterol, mg/dL	211(41)	208(36)	0.610
Serum Triglycerides, mg/dL	96(29)	103(29)	0.798*
Serum HDL-C, mg/dL	55(26)	54(17)	0.740
Serum LDL-C, mg/dL	136(37)	131(32)	0.299
Serum Interleukin 1 beta, pg/mL	5(0.5)	7.15(2.45)	0.429*

Values are mean±SD or relative frequencies (%). *P*-values derived using Student's t-test, Mann-Whitney test (*) and analysis of variance

Table 3. Results from simple and multiple logistic regression analyses that evaluated the association between Royal Free Interview for Spiritual and Religious Beliefs (RFI-SRB) score (independent) on various clinical characteristics (i.e., hypertension, diabetes, and CVD) of the participants (dependent covariates)

Dependent outcome	Unadjusted Odds Ratio (95%CI)	Age, gender adjusted Odds Ratio (95%CI)	Fully adjusted* Odds Ratio (95%CI)
Hypertension			
RFI-SRB score (*by 1 unit*)	0.37 (0.19-0.70)	0.93 (0.91-0.96)	0.96 (0.92-0.99)
Age (*by 1 year*)	-	1.13 (1.09-1.17)	1.14 (1.09-1.19)
Gender (*males vs. females*)	-	0.43 (0.18-1.00)	0.47 (0.18-1.21)
Family status *(married vs. widowed/not married/divorced)*	-	-	1.05 (0.25-4.50)
Smoking (*current vs. ex/never*)	-	-	5.80 (1.06-31.89)
Body mass index (*per 1 kg/m^2*)	-	-	1.22 (1.05-1.42)
Diabetes mellitus			
RFI-SRB score (*by 1 unit*)	0.04 (0.01-0.17)	0.90 (0.87-0.93)	0.91 (0.87-0.94)
Age (*by 1 year*)	-	1.06 (1.02-1.10)	1.06 (1.02-1.11)
Gender (*males vs. females*)		2.29 (0.85-6.14)	2.69 (0.90-8.06)
Family status *(married vs. widowed/not married/divorced)*	-	-	0.75 (0.22-2.55)
Smoking (*current vs. ex/never*)	-	-	1.54 (0.45-5.49)
Body mass index (*per 1 kg/m^2*)	-	-	1.09 (0.95-1.25)
Cardiovascular disease**			
RFI-SRB score (*by 1 unit*)	0.06 (0.01-0.48)	0.93 (0.90-0.97)	0.92 (0.89-0.96)
Age (*by 1 year*)	-	1.06 (1.02-1.12)	1.05 (0.99-1.11)
Gender (*males vs. females*)		1.50 (0.47-4.82)	1.89 (0.46-7.87)
Family *(married vs. widowed/not married/divorced)*	-	-	0.73 (0.16-3.27)
Smoking (*current vs. ex/never*)	-	-	0.41 (0.08-1.99)
Body mass index (*per 1 kg/m^2*)	-	-	0.97 (0.82-1.16)

The results are presented as OR (odds ratio) and 95% confidence intervals for the 1-unit increase of RFI-SRB score.
*Fully adjusted for age, gender, family status, smoking habits and body mass index; **Congestive heart failure or Myocardial infarction

addition, we report that high levels of religious/spiritual beliefs are positively associated with a sense of coherence. Our data indicate a positive correlation between religiosity/spirituality, sense of coherence and a favourable cardiovascular profile, expressed via decreased preclinical predictors of atherosclerosis and cardiovascular health conditions, independently of other aggravating factors, as identified in the present study or in previous studies.[9,10]

Interpreting the results of the study

To the best of our knowledge, this is the first report in Europe of an inverse association between religiosity/spirituality in relation to carotid IMT. Findings from a North-American multi-ethnic cohort study suggested no significant association between dimensions of religiosity and carotid IMT.[24] In regard to the link between religion and body weight, it is noteworthy that the majority of evidence derives from the United States (US) cross-sectional studies. For example, in a study that examined the association between religion and BMI, Protestant males presented higher body weight compared to those with no religious affiliation.[25] Similarly, data from a cross-sectional survey (Pawtucket Heart Health Program) reported that church members presented a greater likelihood of

being twenty per cent overweight compared to non-church members.[26] In parallel with this, Ferraro, using individual level data, reported a positive association of religious practice with BMI.[27] Different findings have been reported more recently by Cline and Ferraro[28] on the relationship between different measures of religious life and obesity. Surprisingly, attendance at religious services has been associated with a lower risk of obesity among American females, while religious media practice (reading religious books, watching or listening to religious programs on the television or radio) has been found to increase obesity risk and prevalence.[28] Direct access to aliments and beverages of people practicing religion in their own environment has been reported to be the most plausible explanation for this association.[28]

Another finding of the Spili III study suggests a benefit of religiosity to cardiovascular health; remarkably, our study points to a significantly lower frequency of diabetes mellitus among highly religious subjects. It is also of interest that higher scores of religiosity/spirituality were related to lower cortisol levels, suggesting a lower stress impact among religious/spiritual individuals. Consistent with this finding, in a study among a cohort of 60 undergraduate students, religiosity was also associated with lower cortisol levels.[29] Interestingly, the authors discussed the existence of physiological pathways that link religious and spiritual factors with health.[29] Additionally, Ironson, et al, in a study among HIV-positive patients, supported the association of religiosity with favourable physiological outcomes, reporting significantly lower levels of urinary cortisol levels, less distress and more optimism among subjects with strong religious/spiritual beliefs.[30] Urinary cortisol concentration was reported to be the basic mediator for this association.[30] Notably, a study of immune system function among a sample of older adults reported a relatively weak association between church attendance and healthier immune system indicators,[31] a result not verified in our group.

Explanatory mechanisms to account for these associations are difficult to establish. An interesting hypothesis suggests that experiences of worship activities and feelings of group membership may inhibit the production of stress hormones that impair the function of the immune system.[32] Indirectly, religious involvement confers a protective effect on shaping positive health behaviours and personal lifestyles (dietary restrictions, prohibition against tobacco use).[32,33] The Orthodox Christian diet, in particular, is characterized by high consumption of fibre, fruits, vegetables and legumes and low intake of saturated fatty acids, forming a nutritional model that mimics a Mediterranean dietary pattern,[34] well known for its protective effects on human health.[35] Interestingly, findings from a Greek study show a significant reduction of LDL cholesterol after adherence to Greek Orthodox Christian church fasting.[12] However, evidence regarding a potential lowering effect of Greek Orthodox fasting on blood pressure levels is inconsistent. Reports from a study in Greece revealed that, compared to a control group, those engaging in fasting presented higher levels of systolic and diastolic blood pressure.[36]

Participation in a religious group can enhance social resources through social coherence and by creating perceptions of a supportive environment and feelings of connection within a homogenous social network sharing common characteristics and values.[32,33] In accord with this finding, our study revealed a significant positive association between religiosity and sense of coherence. To our knowledge, reports regarding the association of SOC with religiosity are scarce. It is interesting that this correlation is to be found in a Mediterranean area with robust traditional links between church and society. The salutary effects of SOC on health outcomes are documented in numerous publications. In a study among 20,500 participants, a strong SOC was associated with a significant reduction in all-cause mortality.[37] Further work in this domain established that greater SOC is associated with higher self-esteem and improved adaptive responses to a stressor situation.[38] In this line, Svartnic et al reported that weak SOC presented a statistically significant association with low levels of HDL and high levels of triglycerides.[39] With regard to the effects of SOC on obesity status, another study revealed a statistically significant negative association between SOC and BMI.[40] A coherent explanation for this association could be the less favourable dietary preferences and food selections of individuals with low SOC scores.[41] In terms of the relationship between SOC and diabetes, in a cross-sectional study among black South Africans, a positive relationship has been

reported between low levels of SOC and diabetes in females.[42] Similarly, findings from a cohort study in Finland showed an increased risk of diabetes among young males with low SOC.[43] It is also interesting that an independent association has been observed between weak SOC and poorer glycaemic control along with the presence of microvascular complications (nephropathy) among males.[44]

Based on the above, we can hypothesize that positive psychological factors may buffer the detrimental effects of the human reaction to psychological stress by mediating physiological processes regulated by the hypothalamic-pituitary-adrenal axis including cortisol hypersecretion and elevation of circulating catecholamines.[45] In a recently published review, Boem and Kubzansky draw the conclusion that optimism is associated with a decreased risk of cardiovascular events, regardless of the presence of traditional risk factors and ill-being.[46] Positive psychological well-being seems to be positively related to health behaviour restoration processes and biological function, such as cardiovascular, inflammatory and metabolic processes.[46] This is also likely to be inversely associated with deteriorative health behaviours and biological functioning.[46] Further prospective investigations are needed, since research on multiple components of psychological well-being and ill-being determinants is promising but still limited.[46,47]

Strengths and limitations

The Spili cohort is certainly highly homogeneous in terms of ethnicity and religion and this characteristic may confer a solid effect on the studied variables. However, although we have analyzed 195 subjects our sample still remains limited. Our findings provide evidence to inform a high demand study protocol which explores a psychosocial dimension of cardiovascular risk within primary care in conditions of extreme research funding limitations. Due to the cross-sectional design of the Spili III study, etiological and direct explanations of the associations between religiosity/spirituality, SOC and cardiovascular disease parameters cannot be established. Furthermore, our findings derive from a restricted geographic area; in this respect, 'occult' but shared biological traits conditioning the overall cardiovascular well-being of the entire village cannot be excluded. The absence of a control group from another location represents a point for consideration. Notably, in the present study we did not examine possible covariates such as praying time, church attendance, fasting and dietary habits and confession that may offer additional insights to our future work.

CONCLUSIONS

This observational study attempted to establish a link between psychosocial factors and cardiovascular health within a rural primary care setting in Greece. Sense of coherence, body mass index, carotid artery IMT, serum cortisol and blood glucose levels showed a significant inverse correlation with the intensity of the religious and spiritual beliefs of the participants. These findings underline the hypothesis that sense of coherence and religiosity may be associated with the low prevalence of cardiovascular disease within this Mediterranean cohort.

AUTHORS' CONTRIBUTIONS

CL conceived the research idea. CL, DA and EKS were involved in the design of the study protocol. DA recruited and assessed the patients based on the study protocol requirements. DA was responsible for performing the data acquisition. EKS provided information on organizational matters. DA and EKS prepared the first draft of the manuscript. EC and MV provided insights on laboratory testing issues. DBP added further statistical information and assisted in revising the article. EC, CL and MV helped in revising the article for important intellectual content and technical details. DT supervised the ultrasound measurements and provided technical input. SS provided useful suggestions on content and editing issues. All authors have read and approved the final manuscript.

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CONFLICT OF INTEREST DECLARATION

All authors declare that they do not have any conflict of interest.

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APPENDIX

APPENDIX 1. Questions with continuous responses from Royal Free Survey

Question 3	How strongly do you hold to your religious/spiritual view of life?
Question 7	How important to you is the practice of your belief in your day to day life?
Question 8	Do you believe in spiritual power or force other than yourself that can influence what happens to you in day-to-day life?
Question 9	Do you believe in spiritual power or force other than yourself that enables you to cope personally with events in your life?
Question 10	Do you believe in spiritual power or force other than yourself that influences world affairs?
Question 11	Do you believe in a spiritual power or force other than yourself that influences natural disasters, like earthquakes and floods?

Source: Reference 21

APPENDIX 2. Sense of Coherence – 29 items.

C: comprehensibility; Ma: manageability; Me: meaning; R: before calculating the total score this should be reversed.

1. When you talk to people, do you have the feeling that they don't understand you? (C)

R 1 2 3 4 5 6 7

Never Always have this feeling

2. In the past, when you had to do something which depended upon cooperation with others, did you have the feeling that it: (Ma)

1 2 3 4 5 6 7

Surely wouldn't get done Surely would get done

3. Think of the people with whom you come into contact daily, aside from the ones to whom you feel closest. How well do you know most of them? (C)

1 2 3 4 5 6 7

You feel that they're strangers You know them very well

4. Do you have the feeling that you don't really care about what goes on around you? (Me)

R 1 2 3 4 5 6 7

Very seldom or never Very often

5. Has it happened in the past that you were surprised by the behaviour of people whom you thought you knew well? (C)

R 1 2 3 4 5 6 7

Never happened Always happened

6. Has it happened that people whom you counted on disappointed you? (Ma)

R 1 2 3 4 5 6 7

Never happened Always happened

7. Life is: (Me)

R 1 2 3 4 5 6 7

Full of interest Completely routine

8. Until now your life has had: (Me)

1 2 3 4 5 6 7

No clear goals or purpose at all Very clear goals

9. Do you have the feeling that you're being treated unfairly? (Ma)

1 2 3 4 5 6 7

Very often Very seldom or never

10. In the past ten years your life has been: (C)

1 2 3 4 5 6 7

Full of changes without your knowing what will happen next — Completely consistent and clear

11. Most of the things you do in the future will probably be: (Me)

1 2 3 4 5 6 7

Completely fascinating — Deadly boring

12. Do you have the feeling that you are in an unfamiliar situation and don't know what to do? (C)

1 2 3 4 5 6 7

Very often — Very seldom or never

13. What best describes how you see life: (Ma)

R 1 2 3 4 5 6 7

One can always find a solution to painful things — There is no solution to painful

14. When you think about your life, you very often: (Me)

R 1 2 3 4 5 6 7

Feel how good it is to be alive — Ask yourself why you exist at all

15. When you face a difficult problem, the choice of a solution is: (C)

1 2 3 4 5 6 7

Always confusing and hard to find — Always completely clear

16. Doing the things you do every day is: (Me)

R 1 2 3 4 5 6 7

A source of deep pleasure and satisfaction — A source of pain and boredom

17. Your life in the future will probably be: (C)

1 2 3 4 5 6 7

Full of changes without Without knowing what will happen next — Completely consistent and clear

18. When something unpleasant happened in the past your tendency was: (Ma)

1 2 3 4 5 6 7

"To eat yourself up" about it — To say "ok that's that, I have to live about it with it" and go on

19. Do you have very mixed-up feelings and ideas? (C)

1 2 3 4 5 6 7

Very often — Very seldom or never

20. When you do something that gives you a good feeling: (Ma)

R 1 2 3 4 5 6 7

It's certain that you'll go on feeling good — It's certain that something will happen to spoil the feeling

21. Does it happen that you have feelings inside you would rather not feel? (C)

1 2 3 4 5 6 7

Very often — Very seldom or never

22. You anticipate that your personal life in the future will be: (Me)

1 2 3 4 5 6 7

Totally without meaning or purpose — Full of meaning and purpose

23. Do you think that there will always be people whom you'll be able to count on in the R future? (Ma)

1 2 3 4 5 6 7

You're certain there will be — You doubt there will be

24. Does it happen that you have the feeling that you don't know exactly what's about to happen? (C)

1 2 3 4 5 6 7

Very often — Very seldom or never

25. Many people – even those with a strong character – sometimes feel like sad sack (losers) in certain situations. How often have you felt this way in the past? (Ma)

1 2 3 4 5 6 7

Never — Very often

26. When something happened, have you generally found that: (C)

1 2 3 4 5 6 7

You overestimated or underestimated proportion — You saw things in the right it's importance

27. When you think of the difficulties you are likely to face in important aspects of your life,
R do you have the feeling that: (Ma)

1 2 3 4 5 6 7

You will always succeed in overcoming the difficulties — You won't succeed in overcoming the difficulties

28. How often do you have the feeling that there's little meaning in the things you do in your daily life? (Me)

1 2 3 4 5 6 7

Very often — Very seldom or never

29. How often do you have feelings that you're not sure you can keep under control? (Ma)

1 2 3 4 5 6 7

Very often — Very seldom or never

Source: Reference 8