Psychological and metabolic risk factors in older adults with a previous history of eating disorder: A cross-sectional study from the Predimed-Plus study

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ABSTRACT

Objectives: To explore affective and cognitive status, later in life, in individuals with and without previous history of ED, and also its association with MetS symptomatology. **Method:** A cross-sectional analysis of 6756 adults, aged 55-75 years with overweight/obesity and MetS participating in the PREDIMED-Plus study was conducted. Participants completed self-reported questionnaires to examine lifetime history of ED, according to DSM-5 criteria, and other psychopathological and neurocognitive factors. Anthropometric and metabolic measurements were also collected. **Results:** Of the whole sample, 24 individuals (0.35%) reported a lifetime previous history of ED. In this subsample, there were more women and singles compared to their counterparts, but they also presented higher body mass index (BMI), higher levels of depressive symptoms and higher cognitive impairment than those without lifetime ED. **Conclusions:** This is one of the first studies to analyze the cognitive and metabolic impact, of a previous history of ED. The results showed that lifetime ED was associated with greater depression and cognitive impairment, but also with higher BMI, later in life. No other MetS risk factors were found, after controlling for relevant variables.

Keywords: eating disorder, neuropsychological profile, depressive symptoms, metabolic syndrome, cardiovascular risk

Key Points:

- This is one of the first studies to analyse the cognitive and metabolic impact of a previous history of ED, later in life.
- Greater levels of depressive symptoms and cognitive impairment were associated with a previous history of ED compared to participants without that condition.
- Those participants with a previous ED presented higher BMI values, later in life, in comparison with participants without a lifetime ED.

INTRODUCTION

Recent research has reported an increased risk of a subsequent medical condition in mental disorders, including eating disorders (EDs) (Momen et al., 2020). In several ED studies, medical complications, such as obesity (OB), gastrointestinal or dermatological alterations have also been described (McCuen-Wurst, 2018; Mehler & Andersen, 2017). Cardiometabolic consequences significantly influence high mortality in EDs (Johnson, 2002), and these constitute a risk factor for developing the Metabolic Syndrome (MetS) (Aguilar, 2015). MetS is a multiplex risk factor that includes increased abdominal circumference, high values of triglycerides and low values of high-density lipoproteins cholesterol (HDLc), hypertension, and increased fasting glycaemia (Alberti et al., 2009). MetS prevalence has become a concern around the world over the last decades (Cameron, 2004), reaching a prevalence that ranges from 7% to 56.7% in the Spanish population aged 35 to 74 years (Fernández-Bergés et al., 2012). Furthermore, MetS has been widely associated with OB (Després & Lemieux, 2006; Weiss et al., 2004).

Some altered and inappropriate eating behaviors, such as lower eating frequency (Ritchie, 2012), eating meals irregularly and meal skipping (Roehrig et al., 2009), gorging eating pattern or faster-eating (Kral, 2001), have been related with increased cardiovascular risk and MetS (Gibson, Workman, & Mehler, 2019; Gleaves, Lowe, Green, Cororve, & Williams, 2000; Winston & Stafford, 2000), even at the genetic level (Watson et al., 2019). In adult cases of bulimia nervosa (BN) and binge eating disorder (BED), binging episodes have been highlighted as a factor with an elevated risk for MetS, associated with high body mass index (BMI) and high blood pressure (Abbott, Dindol, Tahrani, & Piya, 2018; Blom, Guerdjikova, Mori, Casuto, & McElroy, 2015; Hudson et al., 2010; Klatzkin, Gaffney, Cyrus, Bigus, & Brownley, 2015; Roehrig et al., 2009; Udo et al., 2014). Moreover, the chronic use of stimulants, such as methamphetamine, has also been associated with the development of chronic coronary disease as well as cardiomyopathy (Diercks, 2008). These substances have been reported in ED samples in order to lose weight (Neale, Abraham, & Russell, 2009).

Regarding the different components of MetS and their relationship with EDs, abdominal OB is mostly related to BN and BED, being considered as a strong risk factor for MetS and other associated diseases (e.g. type 2 diabetes) in middle-aged patients (Kalra, 2013; Pappachan & Viswanath, 2017; Toplak et al., 2019; Udo et al., 2014) in comparison with anorexia nervosa (AN) (Manna & Jain, 2015). Similarly, blood pressure decrease is described as a medical complication among EDs, especially referred to AN, usually secondary to chronic volume depletion and orthostatic changes (Winston & Stafford, 2000). Nevertheless, those EDs related to high BMI (i.e. BN and BED) may present an increase in blood pressure values, contributing to the increased cardiovascular risk (Klatzkin et al., 2015). Finally, despite the fact that dyslipidemia is a common finding in EDs, its etiology is still unclear, as many studies reveal a wide distribution of lipid levels in this population (Hussain et al., 2019; Johnson et al., 2002; Nakai, Noma, Fukusima, Taniguchi, & Teramukai, 2016). However, the long-term impact of MetS in ED has rarely been explored in the literature.

From a psychopathological perspective, higher levels of depression have been observed in obese people with and without EDs (Stunkard, 2003). It is worth noting that some studies suggest that the presence of OB and EDs is a risk

factor for the development and maintenance of depression (Linde et al., 2004). With regards to cognitive function, several studies have reported an association between EDs and cognitive impairment in patients with obesity and cardiovascular risk (Fillit, Nash, Rundek, & Zuckerman, 2008; Mallorquí-Bagué et al., 2018). However, although some authors have studied eating behavior in people with cognitive impairment (Zakzanis, Campbell & Pollsinelli, 2010), there is less literature linking EDs to the level of dementia (Woolley et al., 2007). However, numerous studies have focused on cognitive impairment in populations with overweight and OB in midlife, indicating a greater dysfunction in cognitive aspects and higher risk of dementia in these subjects compared to people with normal weight (Fitzpatrick et al., 2009; Xu et al., 2011). Controversial results have been found in relation to later-life population (Fitzpatrick et al., 2009; Stewart et al., 2005).

This is one of the first studies to analyze the negative impact of having a previous history of an ED, in a middle-old age MetS population. The main aim of this study was to explore the association between previous history of ED and metabolic, affective and cognitive potential consequences, in adult/elderly MetS patients. We hypothesized that those subjects with a history of ED will present a greater vulnerability in terms of neuropsychological factors, so that the variables of current depression and cognitive functions may be significantly impaired compared to the rest of the sample. Besides, participants with an ED background are expected to present higher cardiometabolic risk, given the physical consequences that such disorders may have in the medium to long term, as reported previously.

METHODS

Study design and participants

This cross-sectional study was conducted in the context of the PREDIMED-Plus study cohort, which included 6874 older adults enrolled between 2013 and 2016 by 23 Spanish centers from different universities, hospitals and research institutes working in collaboration with 208 Primary Care Health Facilities belonging to the Spanish National Health System. Participants were men and women aged 55 and 75 years, free of cardiovascular disease at enrolment, with a BMI over 27kg/m^2 and who met criteria of MetS according to the International Diabetes Federation and the American Heart Association and National Heart, Lung and Blood Institute (Alberti et al., 2009). More details of the study cohort, inclusion and exclusion criteria, and methods are specified elsewhere (Salas-Salvadó et al., 2019; Martínez-González et al., 2019) and the protocol is available at http://predimedplus.com. Among the whole sample, 118 participants were excluded due to missing data in the variables analysed in this work, so the final sample was composed of 6756 individuals. Figure S1 (supplementary material) contains the flowchart for the sampling. All participants provided written informed consent, and the study protocol and procedures were approved according to the ethical standards of the Declaration of Helsinki by the Research Ethics Committees from all the participating institutions. The PREDIMED-Plus study was registered at the International Standard Randomized Controlled Trial (ISRCT; http://www.isrctn.com/ISRCTN89898870).

Assessment of the outcome and covariates

At baseline, trained staff collected participants' information through questionnaires regarding sociodemographic characteristics (sex, age, level of education, marital status and employment status). Additionally, participants

completed a self-reported questionnaire for assessing eating disturbances. A depression symptomatology scale [*Beck Depression Inventory–II (BDI-II)]* and a test to measure cognitive impairment [*The Mini-Mental State Examination* (*MMSE*)] were administered by trained personnel.

Clinical and psychometric assessment

The ED diagnostic criteria interview is a short-structured interview for the diagnosis of ED according to the DSM-5 criteria (American Psychiatric Association, 2013). This interview allows the diagnosis of lifetime or current ED (within the last 3 months). It also provides specific information regarding the eating symptomatology displayed (e.g.: number of binge eating episodes/vomits per week). Medical records from those participants which reported a lifetime ED were reviewed in order to ensure the correct diagnosis. None of the patients reported a current ED.

The Beck Depression Inventory–II (BDI-II) (Beck, 1996) is a 21-item self-report measure for assessing the severity of depressive symptoms in adults and adolescents (ages from 13 to 80 years). The BDI-II reflects the diagnostic criteria for Major Depressive Disorder listed in the DSM-5 (American Psychiatric Association, 2013). Scores for each item range from 0 to 3; the total score is the sum of all responses. Higher total scores indicate more severe depressive symptomatology. The standardized cut-offs are as follows: 0–13 indicates minimal depression, 14–19 mild depression, 20–28 moderate depression, 29–63 severe depression. The Cronbach's alpha in our sample shows a very good internal consistency (α= 0.883).

The Mini-Mental State Examination (*MMSE*; Folstein, 1975)*; Spanish version* (Blesa et al., 2001) is a valid indicator of general cognitive impairment which assesses orientation, attention, memory, language and visual-spatial skills. It is commonly used to screen for dementia, but also to estimate the severity and progression of cognitive impairment. The score ranges from 0 to 30, a lower score being an indicator of greater impairment.

Anthropometric and biochemical measurements

Al baseline, weight, height, and waist circumference were measured in duplicate by trained personnel following a pre-established protocol. BMI was calculated by dividing the weight (kg) by the square of height (m2). Waist circumference was determined midway between the lowest rib and the iliac crest. Blood pressure was measured with a validated semiautomatic oscillometer (Omron HEM-705CP, Hoofddorp, the Netherlands). Fasting blood samples were obtained to determine serum glucose, HbA1c and lipid profile (total cholesterol, high-density lipoprotein cholesterol (HDLc) and triglycerides) using standard enzymatic methods. Low-density lipoprotein cholesterol (LDLc) was calculated by the Friedwald formula whenever triglycerides were inferior to 300 mg/dL.

Statistical analysis

Statistical analysis was carried out with Stata16 for Windows (StataCorp, 2019). The comparison between the two groups of the study (defined by the absence/presence of ED) for the sociodemographics was based on t-test for quantitative variables and chi-square tests ($\chi 2$) for categorical variables. Clinical measures were compared between the groups adjusted by the participants' sex, through logistic regression for categorical measures and analysis of covariance (ANCOVA) for quantitative variables.

No statistical deviation from normality was found for absence-ED group in the Kolmogorov-Smirnov test obtained for the quantitative measures (p>.05 for all the variables), and exact p-value was obtained for contingency tables with at least 1 cell with expected count less than 5.

The effect size for the mean differences was based on the standardized Cohen's-d coefficient, considering null for |d|<0.20, low-poor for |d|>0.20, moderate-medium for |d|>0.50 and large-high for |d|>0.80 (Cohen, 1988; Kelley, 2012). For the proportion differences, the effect size was based on the Cohen's-h coefficient, calculated as the difference of the arcsine transformation for the two proportions obtained in the groups and with an interpretation equivalent to the Cohen's-d measure: |h|=0.20 as small effect size, |h|=0.50 as mild-medium, and |h|=0.80 as high-large effect size (Cohen, 1988; Granero et al., 2020).

RESULTS

Table 1 displays the distribution of the sociodemographic variables in the sample. Most participants were from Europe (97.5%), married (76.7%), with primary or less education levels (49.0%) and retired (56.3%). Mean age was 65 years old (SD=4.9). Comparison between the groups defined by the absence-presence of lifetime ED achieved statistical differences in the distribution of the sex (higher proportion of women within the group who reported presence of a lifetime ED, 70.8% versus 48.4%, *p*=.028) and the marital status (lower proportion of married participants within the group who reported presence of ED, 70.8% versus 76.7%, *p*=.043).

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Table 2 shows the comparison between participants with and without a previous history of an ED for the clinical variables analyzed in this work, adjusted by the covariate sex. No differences between the groups were found for cardiovascular diseases, total cholesterol, HDLc, LDLc, triglycerides, hypertension, and diabetes risk. However, the presence of an ED background was related to a higher prevalence of overweight (*p*=.046), higher BMI (*p*=.047), higher levels of depression symptoms (*p*<.001) and lower scores in the MMSE (*p*=.001).

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DISCUSSION

In this large cohort study, including nearly 6,756 middle-old age (55-75 years old) participants, we explored affective and cognitive status, later in life, in individuals with and without previous history of ED, but also its association with MetS symptomatology. To our knowledge, this is one of the first studies to analyze the cognitive and metabolic impact, of a previous history of ED.

Some studies have tried to describe the long-term medical consequences (e.g. cardiovascular) associated with abnormal eating behaviors, mostly based on young and middle-age population (Chen, Wang, & Cheskin, 2016; Dobrescu et al., 2020; Kärkkäinen, Mustelin, Raevuori, Kaprio, & Keski-Rahkonen, 2018; Ritchie, 2012; St-Onge et al., 2017; Udo et al., 2014) and early onset EDs (Gibson et al., 2019; Johnson et al., 2002). Within the cardiovascular negative effects, some of them are related to MetS components (González-Cantú et al., 2018; Hudson, 2010; Nakai, 2016; Nieto-Martínez et al., 2017; Paz-Graniel, 2019). Considering that all the participants present a minimum BMI of 27kg/m^2, in terms of weight, those patients with a history of EDs reported lower levels of overweigh and higher levels of BMI in comparison with the rest of the sample. This finding is consistent with other studies highlighting that EDs

and OB have shared risk factors (Baños et al., 2014) and that the presence of one of these two variables is also a risk factor for the development of the other (Zigman & Elmquist, 2003). Therefore, many authors have suggested a continuum from the underweight inherent in AN to the OB characteristic of BED (Fagundo et al., 2012). In contrast to previous studies, that observed a link between MetS and lifetime ED, associated with secondary OB but also with obesity-independent factors (Hudson et al., 2010; Manna & Jain, 2015; Nieto-Martínez et al., 2017), the current study failed to identify a significant association between EDs and cardiovascular risk factors, such as high blood pressure, glucose abnormalities, type 2 diabetes, hypercholesterolemia and hypertriglyceridemia, later in life.

According to one of the stated hypothesis, another finding to emerge from the present study is the current higher level of depression in the group with a history of ED. The comorbidity between EDs and mood disorders is well known, particularly depression (Fernandez-Aranda et al., 2007; Fichter, 2004) and that the presence of both pathologies hinders the recovery of eating and mood symptoms (Berkman, 2007). Both disorders are characterized by low self-esteem and altered eating patterns (Konttinen, 2010). We can therefore hypothesize that this tendency to underestimate oneself and this vulnerability to present a lower mood is increased in patients who have suffered from an ED and endures later in life.

We also identified a lower score on the MMSE by patients with a history of ED, indicating that they have a greater cognitive impairment than those participants with MetS who have never met criteria for being diagnosed with an ED. As there is a lack of studies evaluating cognitive impairment in patients with EDs through the MMSE, it could be postulated that the lower scores in that test are mediated by other variables such as overweight or OB or the greater presence of depressive symptoms. Also, this observation dovetails with other research finding that cognitive dysfunction is common among obese people (Miller, 2014; Xu et al., 2011) and it is associated with poorer weight loss outcomes (Spitznagel et al., 2013). In this line, an interesting study carried out with patients with high cardiovascular risk found a significant association between MMSE scores and OB, stating that for every one point increase in BMI above 30, the chances of having cognitive impairment increased 27%. Nevertheless, they did not observe an association between OB and depressive symptoms (Costa et al., 2010). In other psychiatric illnesses, such as bipolar disorder or schizophrenia, a significant association has also been observed between cardiovascular risk and obesity, and impaired neurocognition functions (Bora, Akdede, & Alptekin, 2017). Along these lines, some research has been carried out with the aim of reducing obesity by strengthening cognitive functions (Forcano, Mata, de la Torre, & Verdejo-García, 2018).

The results of this study should be considered in light of its limitations. Despite the large total sample size, there is a notable heterogeneity of sample size and the number of patients with presence of ED is quite small. At this point, it should be noted that the comparison between the groups was based in both null-hypothesis significance tests and estimations of the effect size through the Cohen's-*d* measure (a standardized coefficient independent on the sample sizes), In addition, despite the low sample size for a group in the study, significant results have been obtained, which provides empirical evidence regarding the existence of real relationships in the original populations. Another limitation to highlight would be the use of a non-validated instrument to assess the presence of an ED. Future studies should employ validated and commonly used structured interviews in which the different types of EDs are evaluated. The cross-sectional nature of the study and the retrospective self-reported data collection might affect the reliability of

the present study. Additional prospective and longitudinal analyses and intervention trials are warranted with careful consideration of the long-term cardiovascular implications of EDs, which are less clear.

Conclusion

To conclude, this is one of the first studies to analyze the cognitive and metabolic impact, of a previous history of ED. The results showed that lifetime ED was associated with greater depression and cognitive impairment, but also with higher BMI, later in life. These results suggest the relevance of identifying specific vulnerability factors among patients with MetS, such as an ED, in order to develop preventive strategies and personalized treatment approaches.

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Conflicts of Interest

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Table 1

Descriptive for the sample at baseline

		Total (*n*=6,756)		ED: absent (*n*=6,732)		ED: present (*n*=24)		
		n	%	*n*	%	*n*	%	*p*
Sex	*Women*	3,278	48.5%	3,261	48.4%	17	70.8%	**.028***
	Men	3,478	51.5%	3,471	51.6%	7	29.2%	
Origin	*Europe*	6,587	97.5%	6,565	97.5%	22	91.7%	.245
	South-America	151	2.2%	149	2.2%	2	8.3%	
	Africa	15	0.2%	15	0.2%	0	0.0%	
	Asia	3	0.0%	3	0.0%	0	0.0%	
Marital status	*Single*	338	5.0%	334	5.0%	4	16.7%	**.043***
	Married	5,183	76.7%	5,166	76.7%	17	70.8%	
	Widowed	701	10.4%	701	10.4%	0	0.0%	
	Divorced-separated	531	7.9%	528	7.8%	3	12.5%	
Education	*Primary or less*	3,313	49.0%	3,302	49.0%	11	45.8%	.888
	Secondary	1,948	28.8%	1,940	28.8%	8	33.3%	
	University	1,495	22.1%	1,490	22.1%	5	20.8%	
Employment	*Employed*	1,401	20.7%	1,395	20.7%	6	25.0%	.053
	Incapacity	165	2.4%	163	2.4%	2	8.3%	
	Work at home	1,001	14.8%	994	14.8%	7	29.2%	
	Unemployed	384	5.7%	383	5.7%	1	4.2%	
	Retired	3,805	56.3%	3,797	56.4%	8	33.3%	
		Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*p*
Age (years-old)		64.95	4.91	64.95	4.91	64.79	5.53	.876

Note. ED: eating disorder. SD: standard deviation. *Bold: significant comparison.

Table 2

Association of cardiovascular risk and related variables with presence of ED lifespan

Total sample	Total (*n*=6,756)		ED: absent (*n*=6,732)		ED: present (*n*=24)			
	n	%	*n*	%	*n*	%	*p*	|*d*|
Cardiovascular risk	1,007	14.9%	1,001	14.9%	6	25.0%	.184	0.26
Hypercholesterolemia	4,943	73.2%	4,925	73.2%	18	75.0%	.925	0.04
Hypertension	5,835	86.4%	5,815	86.4%	20	83.3%	.677	0.09
Diabetes	1,906	28.2%	1,897	28.2%	9	37.5%	.261	0.20
Group of weight								
Over-weight (27-29.9 kg/m^2*)*	1,812	26.8%	1,808	26.9%	4	16.7%	**.046***	0.25
Obesity I (BMI 30-34.9 kg/m^2*)*	3,308	49.0%	3,298	49.0%	10	41.7%		0.15
Obesity II (BMI 35-39.9 kg/m^2*)*	1,577	23.3%	1,568	23.3%	9	37.5%		0.31
Obesity III (BMI>40 kg/m^2*)*	59	0.9%	58	0.9%	1	4.2%		0.23
	Mean	SD	*Mean*	SD	*Mean*	SD	*p*	|*d*|
BDI (depression)	8.50	7.42	8.48	7.40	15.04	8.84	**<.001***	**0.81†**
MMSE (cognitive impairment)	28.20	1.89	28.21	1.89	26.93	2.55	**.001***	**0.57†**
	Mean	SD	*Mean*	SD	*Mean*	SD	*p*	|*d*|
Cholesterol total (mg/dL)	197.14	37.26	197.15	37.28	196.10	33.47	.888	0.03
HDLc (mg/dL)	48.11	11.77	48.09	11.75	51.46	16.45	.132	0.24
LDLc (mg/dL)	120.98	32.97	120.98	32.99	122.13	26.76	.864	0.04
Triglycerides (mg/dL)	151.36	72.44	151.41	72.47	136.38	59.39	.309	0.23
Mean systolic pressure (mmHg)	139.53	16.70	139.53	16.68	139.24	20.63	.932	0.02
Mean diastolic pressure (mmHg)	80.86	9.88	80.86	9.89	80.85	8.37	.995	0.00
Blood pressure (mmHg)	110.19	11.70	110.19	11.70	110.04	12.52	.950	0.01
Glucose (mg/dl)	113.35	28.87	113.33	28.86	118.58	30.68	.373	0.18
HbA1c (%)	5.89	0.71	5.89	0.71	5.90	0.54	.903	0.03
BMI (kg/m^2)	32.56	3.45	32.55	3.45	33.86	4.02	**.047***	0.35

Note. ED: eating disorder. BMI: body mass index (kg/m^2).

*Bold: significant comparison. †Bold: effect size into the range mild-moderate (|*d*|>0.50) to large-high (|*d*|>0.50).