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Correlates of violent suicide attempts in patients with bipolar disorder

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ABSTRACT

Background: Suicide is one of the leading causes of death in bipolar disorder (BD); violent suicide attempts are associated with the highest level of lethality. We aimed to evaluate factors related to the risk of violent suicide in a large naturalistic sample of patients with BD; in addition, we analyzed the rates of lifetime suicide attempts and the variables associated with suicidal behavior.
Methods: We recruited 847 patients with BD. Patients were grouped according to whether they had a lifetime history of suicide attempts and, among suicide attempters, subjects who had used a violent suicide method were compared with those who had attempted suicide with a nonviolent method. Comparisons were performed using $\chi 2$ tests for categorical variables and ANOVA for continuous variables. Logistic regression (LogReg) was used to identify explanatory variables associated with violent suicide attempts (dependent variable).
Results: Two hundred and two patients (24%) had a lifetime history of suicide attempts. Subjects with at least one lifetime suicide attempt showed longer duration of illness (22.4 ± 14.1 years vs 19.9 ± 14.2 years: p 0.028), more lifetime hypomanic episodes (3.3 ± 4.3 vs 2.3 ± 3.1: p 0.001), more lifetime depressive episodes (6.0 ± 4.4 vs 4.7 ± 4.1: p < 0.001), higher rates of lifetime psychiatric comorbidities (50.0% vs 41.3%: p 0.029), higher rates of lifetime medical comorbidities (58.0% vs 48.9%: p 0.028) and higher rates of reduced HDL cholesterol (46.2% vs 36.7%: p 0.030). Among suicide attempters, fifty-two patients (30.6%) attempted suicide with a violent method. We found more men in the group of violent suicide attempters than in the group of nonviolent suicide attempters (65% vs 28%; p: <0.001). Moreover subjects with previous violent attempts showed higher mean values of weight (80.5 ± 18.3 vs 69.4 ± 14.7: p < 0.001), body mass index (27.8 ± 5.6 vs 25.2 ± 4.7: p < 0.003) and waist circumference (98.7 ± 18.5 vs 92.4 ± 14.3: p 0.032). The LogReg analysis confirmed the association of violent attempts with male gender (p: <0.001; Phi: 0.35) and higher waist circumference (p: <0.001; Cohen's d: 0.39).
Limitations: In our research we analyzed lifetime suicide attempts, but the sample does not include completed suicides, meaning that we are unable to test whether the results are generalizable to suicide deaths. Moreover, some relevant variables, such as medical comorbidities/metabolic parameters at the time of suicide attempts and previous medication, were not collected. Another limitation concerns the heterogeneity of recruited patients in terms of clinical characteristics (e.g.: medical conditions, drug treatments), with potential confounding factors.
Conclusions: The present study confirms the association between male gender and violent suicide and suggests a correlation between obesity and the use of violent suicide methods. The relationship between obesity and suicidal behaviour is worthy of interest and deserves to be explored by further studies.

1. Introduction

Bipolar disorder (BD) is a recurrent and chronic disease characterized by the occurrence of manic (or hypomanic), depressive, or mixed episodes. According to the World Health Organization, BD is one of the world's ten most disabling conditions [1]. Suicide is one of the leading causes of death in BD: as reported by the most recent

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guidelines [2], approximately 6%–7% of identified patients with BD dies by suicide, 43% report suicidal ideation, 21% suicide plan and 16% suicide attempt within the past year. Existing studies suggest that 13.2%–17.5% of patients with BD with a lifetime history of suicide attempt performs them with violent methods, such as hanging, shooting or jumping from heights; these subjects, despite representing a minority, need to be precociously recognised, as these methods are associated with the highest level of lethality [3].

An extensive literature has deepened socio-demographic, clinical, environmental, genetic and neurobiological factors related to violent suicide methods in psychiatric disorders [4]. It has been well established that men use violent methods more often than women, both in suicide and suicide attempts [5,6]. Furthermore, higher impulsivity and aggression levels as well as substance abuse disorder have been associated with violent suicide [7–10]. A few studies investigated the correlation between violent suicide and environmental factors, including seasonality, temperature, relative humidity, rainfall, hours of sunshine and pressure. A significant positive correlation was found between violent attempts and ambient temperature and number of sunshine hours [11,12]. Recent research works deepened the relation between violent suicide and serotonin axis, including candidate gene studies and gene expression studies. In a candidate gene study with a sample of schizophrenic patients, a significant association was found between violent suicide and the genotype frequencies of promoter of the serotonin-transporter gene (5HTTLPR) polymorphism [13]. Other studies evaluated differences in the promoter polymorphism of the tryptophane hydroxylase (TPH) between violent and nonviolent suicide attempters, with conflicting results [14,15]. In order to identify neurobiological factors related to violent suicide, the implication of cytokines in the pathogenesis of suicide has been recently investigated. Interleukin-6, measured in cerebrospinal fluid (CSF), peripheral blood, and postmortem brain tissue, has shown robust associations with violent suicide and suicide completion [16]. Furthermore, the relationships between metabolic parameters and violent suicide have been extensively studied. A study conducted by Tanskanen and colleagues demonstrated that serum total cholesterol concentration was positively related to violent but not nonviolent suicide; the same trend could be shown for the concentration of high density lipoprotein cholesterol, but not reaching statistical significance [17]. Conversely, two studies performed by Marcincko and colleagues found significantly lower cholesterol serum levels in violent suicide attempters compared with suicide attempters using nonviolent methods [18,19]. A similar case-control study looked at women with a history of suicide attempts and compared the serum cholesterol concentration between violent suicide attempters and nonviolent suicide attempters: again, a lower concentration was predictive of violent methods within this sample of patients [20]. Two postmortem studies, relevant to the question of fatty acid composition and violent suicide, reported the following findings: significantly lower cholesterol levels in the prefrontal cortex of violent suicide attempters, significantly higher cholesteryl ester hydrolase (LIPA) expression in violent suicide attempters, a significantly lower cholesterol/phospholipid level ratio in violent suicide attempters and increased levels of phospholipids in violent suicide attempters when compared with nonviolent suicide attempters [21,22].

Risk factors for violent suicide, with special reference to BD, were investigated by few studies, mainly conducted with small samples and heterogeneous methods. Available data suggest that male gender [23–25], onset of BD with a hypo/manic episode [26,27], S allele of the serotonin transporter gene (5-HTTLPR) polymorphisms [26] and single nucleotide polymorphisms of the CLOCK and TIMELESS genes [27] seem to be correlated with an increased risk of suicide with violent methods. A study performed by our research group analyzed the correlation between metabolic syndrome, lipid profile and suicide with violent methods in bipolar patients, but no significant differences were found in violent suicide attempters compared to nonviolent ones [28].

The primary goal of this study was to evaluate in a large naturalistic sample of patients with BD potential factors related to the risk of suicide with violent methods. In addition, we sought to examine in our sample the rates of lifetime suicide attempts and the variables associated with suicidal behavior.

2. Material and methods

2.1. Study design and patients

Data derive from an independent cross-sectional observational study aimed to analyze course characteristics, medical conditions and response to treatments in patients with BD.

Subjects for this study were recruited from all patients with a principal diagnosis of BD type I, II or Not Otherwise Specified (NOS) (DSM-IV-TR, DSM-5) [29,30] consecutively admitted to the Department of Neuroscience, University of Turin (Italy), from January 2006 to February 2019.

Potential participants were thoroughly explained aims and study procedures and had to give their written consent before participation; exclusion criteria included age <18 and refusal to consent participating in the study. The protocol was approved by the local Ethical Committees.

2.2. Assessments and procedures

All diagnoses were confirmed by means of the Mini-International Neuropsychiatric Interview (MINI) [31]. At the study entry, general socio-demographic information and clinical data were collected for each subject. Clinical characteristics such as age at onset, duration of illness, number of previous manic/depressive episodes, psychiatric comorbidity, psychiatric family history, current medication and psychopharmacological treatments were ascertained either from clinical charts or by direct questioning the study participants. History of suicide attempt, defined as a selft–destructive behavior with the intention of ending one's life, independently of the resulting damage, [32] was retrospectively assessed for each patient, focusing on the modality of suicidal behavior. According to Stenbacka et al. [33], the suicide attempt method was defined violent (hanging, shooting, jumping from heights, moving train, cutting, drowning) or nonviolent (poisoning). Individuals who had made more than one attempt were classified according to the violence of their most violent attempt.

All subjects received a medical examination; a specific evaluation of metabolic parameters has been conducted for each patient: weight was measured fasting and undressed, height barefoot, waist circumference at midway between the inferior margin of the ribs and the superior border of the iliac crest, at minimal inspiration. Body mass index (BMI) was calculated as the body weight in kilograms divided by the square of the body height in metres. Two blood pressure measurements were obtained by using a mercury sphygmomanometer: the first with the subject in a lying position, the second with the subject in a seated position at least two minutes after the first measurement. The mean blood pressure of the two measurements was used. A blood sample (including cholesterol, glucose, triglycerides and HDL-c) was drawn in the morning (7:00 am), when patients were fasting for previous 10 h. Metabolic syndrome has been evaluated using definition of the International Diabetes Federation (IDF) Task Force on Epidemiology and Prevention, American Heart Association and National Heart, Lung and

Table 1
Socio-demographic and clinical characteristics of the total sample (n = 842) and differences in socio-demographic and clinical characteristics between suicide attempters (n = 202) and non attempters (n = 640).

Characteristics	Total sample (n = 842)	Suicide attempters (n = 202)	Non-suicide attempters (n = 640)	F/χ^2	df	p
Age (years), mean ± *sd*	49.9 ± 15.7	50.8 ± 14.7	49.6 ± 16.0	1.017	1	0.313
Education (years), mean ± *sd*	11.9 ± 4.2	11.8 ± 4.1	11.9 ± 4.2	0.184	1	0.668
Sex, n (%)						
Male	348 (41.3)	77 (38.1)	271 (42.3)	1.130	1	0.288
Female	494 (58.7)	125 (61.9)	369 (57.7)			
Bipolar disorder, type, n (%)						
Bipolar I	352 (41.8)	73 (36.1)	279 (43.6)	5.072	4	0.280
Bipolar II	459 (54.5)	123 (60.9)	336 (52.5)			
Bipolar NOS	28 (3.3)	6 (3.0)	22 (3.4)			
Age of onset (years), mean ± *sd*	29.3 ± 12.4	28.4 ± 11.8	29.6 ± 12.6	1.528	1	0.217
Duration of illness (years), mean ± *sd*	20.5 ± 14.2	22.4 ± 14.1	19.9 ± 14.2	4.858	1	**0.028**
Duration of untreated illness (years), mean ± *sd*	13.2 ± 12.5	14.3 ± 13.0	12.9 ± 12.4	1.804	1	0.180
Manic episodes (number), mean ± *sd*	1.3 ± 2.5	1.0 ± 2.1	1.4 ± 2.6	3.154	1	0.077
Hypomanic episodes (number), mean ± *sd*	2.6 ± 3.4	3.3 ± 4.3	2.3 ± 3.1	11.965	1	**0.001**
Depressive episodes (number), mean ± *sd*	5.0 ± 4.2	6.0 ± 4.4	4.7 ± 4.1	13.741	1	**<0.001**
Lifetime psychiatric comorbidities, n (%)	365 (43.3)	101 (50.0)	264 (41.3)	4.787	1	**0.029**
Family history of mood disorders, n (%)	483 (57.6)	119 (59.2)	364 (57.1)	0.266	1	0.606
Family history of suicide, n (%)	11 (6.5)	3 (6.4)	8 (7.7)	0.080	1	0.774
Lifetime medical comorbidity, n (%)	402 (51.1)	112 (58.0)	290 (48.9)	4.855	1	**0.028**
Weight (kg), mean ± *sd*	72.6 ± 16.0	72.6 ± 16.6	72.6 ± 15.8	0.001	1	0.974
BMI (kg/m^2), mean ± *sd*	28.5 ± 5.8	25.8 ± 5.1	29.5 ± 5.2	0.386	1	0.535
Waist circumference (cm), mean ± *sd*	94.2 ± 16.7	94.6 ± 16.1	94.1 ± 16.9	0.071	1	0.790
Serum lipid levels (mg/dl), mean ± *sd*						
Cholesterol	195.2 ± 44.7	193.5 ± 46.1	195.8 ± 44.2	0.290	1	0.591
Tryglicerides	134.2 ± 77.5	135.3 ± 85.4	133.8 ± 74.7	0.046	1	0.829
HDL cholesterol	51.9 ± 16.5	51.2 ± 18.1	52.1 ± 15.9	0.358	1	0.550
Glycemia (mg/dl), mean ± *sd*	86.4 ± 22.8	88.1 ± 23.0	85.9 ± 22.8	1.214	1	0.271
Systolic arterial pressure (mmHg), mean ± *sd*	122.9 ± 12.5	122.1 ± 12.5	123.2 ± 12.5	1.006	1	0.316
Diastolic arterial pressure (mmHg), mean ± *sd*	79.1 ± 8.8	77.9 ± 8.7	79.4 ± 8.8	3.794	1	0.052
Metabolic syndrome, n (%)	198 (29.3)	58 (33.1)	140 (28.0)	1.654	1	0.198
Abdominal obesity, n (%)	259 (49.4)	73 (51.4)	186 (48.7)	0.306	1	0.580
Low HDL cholesterol, n (%)	256 (39.1)	78 (46.2)	178 (36.7)	4.701	1	**0.030**
Elevated blood pressure, n (%)	321 (47.9)	85 (48.6)	236 (47.7)	0.387	1	0.824
Impaired fasting glucose, n (%)	117 (17.5)	37 (21.5)	80 (16.1)	2.876	1	0.237
Hypertriglyceridemia, n (%)	194 (29.1)	46 (26.7)	148 (29.9)	1.361	1	0.715

NOS: Not Otherwise Specified.
BMI: Body Mass Index.
Bold values indicate statistically significant values.

Blood Institute [34]: metabolic syndrome was present if three or more of the following five criteria were met:

- Abdominal obesity: waist circumference ≥94 cm in men and ≥80 cm in women;
- High blood pressure: systolic pressure ≥130 mmHg and/or diastolic pressure ≥85 mmHg or on antihypertensive medication;
- High fasting glucose: ≥100 mg/dl or on glucose-lowering medication;
- Hypertriglyceridemia: ≥150 mg/dl or on lipid-lowering medication;
- Low HDL-C: <40 mg/dl in men and <50 mg/dl in women.

2.3. Statistical analysis

Socio-demographic and clinical features of the patients were summarized as mean and standard deviation (SD) for continuous variables and frequency and percentage for categorical variables. Patients were grouped according to whether they had a lifetime history of suicide attempts or they had never attempted suicide in their life. Further, patients who had used a violent suicide method were compared with those who had attempted suicide with a nonviolent method.

The normality of data distribution was evaluated by using Shapiro-Wilk and Kolmogorov-Smirnov tests. Comparisons were performed using $\chi 2$ tests for categorical variables and ANOVA for continuous variables. Furthermore, logistic regression (LogReg) was used to identify explanatory variables associated with violent suicide attempts (dependent variable).

The results from every statistical comparison of the treatment groups were presented as 2-sides p values rounded to 3 decimal places. The criterion for statistical significance in all comparison was a p value < 0.05.

All statistical analyses were performed by SPSS software version 22.0.

3. Results

Eight-hundred fifty-three patients with BD were asked to participate; six refused their consent. Among the 847 patients recruited, 5 (0.6%) were excluded from the research due to lack of data about lifetime suicide attempts.

Ultimately, we completed the analysis using 842 subjects. The demographic and clinical characteristics of the total sample are given in Table 1. The sample is representative for the population of patients with BD: 58.7% of the patients were females, the majority of the sample (54.5%) had bipolar II disorder, the mean age at onset of BD was 29.3 ± 12.4 years, the mean duration of illness was 20.5 ± 14.2 years. Two hundred and two patients (24%) had a lifetime history of suicide attempts; among suicide attempters, 22 subjects (10.9%) had made more than one attempt in their life. The demographic and clinical differences between suicide attempters and non attempters are summarized in Table 1: subjects with at least one lifetime suicide attempt showed longer duration of illness (22.4 ± 14.1 years vs 19.9 ± 14.2 years: p 0.028), more lifetime

Table 2
Differences in socio-demographic and clinical characteristics between violent (n = 52) and nonviolent (n = 118) suicide attempters.

Characteristics	Violent attempt (n = 52)	Nonviolent attempt (n = 118)	F/χ^2	df	p
Age (years), mean ± *sd*	49.9 ± 15.9	50.2 ± 14.1	0.062	1	0.831
Education (years), mean ± *sd*	11.8 ± 3.8	11.5 ± 4.1	0.179	1	0.673
Sex, n (%)					
Male	34 (65.4)	33 (28.0)	21.16	1	**<0.001***
Female	18 (34.6)	85 (72.0)			
Bipolar disorder, type, n (%)					
Bipolar I	17 (32.7)	44 (37.3)	0.69	2	0.707
Bipolar II	34 (65.4)	70 (59.3)			
Bipolar NOS	1 (1.9)	4 (3.4)			
Age of onset (years), mean ± *sd*	28.7 ± 13.7	27.9 ± 11.5	0.138	1	0.711
Duration of illness (years), mean ± *sd*	21.3 ± 14.3	22.4 ± 13.6	0.222	1	0.638
Duration of untreated illness (years), mean ± *sd*	14.7 ± 14.3	14.7 ± 12.9	0.001	1	0.976
Manic episodes (number), mean ± *sd*	0.8 ± 1.5	1.2 ± 2.3	0.839	1	0.361
Hypomanic episodes (number), mean ± *sd*	3.1 ± 3.8	3.1 ± 4.5	0.001	1	0.994
Depressive episodes (number), mean ± *sd*	5.7 ± 4.0	6.2 ± 4.8	0.460	1	0.499
Lifetime psychiatric comorbidity, n (%)	23 (44.2)	56 (47.4)	0.151	1	0.697
Family history of mood disorders, n (%)	28 (53.8)	71 (60.7)	0.69	1	0.405
Family history of suicide, n (%)	3 (6.4)	8 (7.7)	0.080	1	0.774
Current psychopharmacological treatment, n (%)					
Monotherapy	6 (11.5)	21 (17.8)			
Combination therapy	45 (88.5)	97 (82.2)	3.240	2	0.198
None	1 (1.9)	0 (0)			
Lithium, n (%)	31 (59.6)	76 (65.0)	0.442	1	0.506
Anticonvulsivants, n (%)	27 (51.9)	53 (44.9)	0.771	1	0.399
First-generation antipsychotics, n (%)	8 (15.4)	7 (5.9)	4.009	1	0.074
Second-generation antipsychotics, n (%)	30 (57.7)	60 (50.8)	0.679	1	0.410
Antidepressants, n (%)	19 (36.5)	48 (40.7)	0.259	1	0.611
Lifetime medical comorbidity, n (%)	32 (61.5)	70 (59.3)	0.044	1	0.083
Weight (kg), mean ± *sd*	80.5 ± 18.3	69.4 ± 14.7	16.6	1	**<0.001***
BMI (kg/m^2), mean ± *sd*	27.8 ± 5.6	25.2 ± 4.7	9.34	1	**0.003***
Waist circumference (cm), mean ± *sd*	98.7 ± 18.5	92.4 ± 14.3	0.968	1	**0.032***
Serum lipid levels (mg/dl), mean ± *sd*					
Cholesterol	190.6 ± 49.2	194.6 ± 45.0	0.234	1	0.629
Tryglicerides	154.2 ± 95.1	131.6 ± 83.2	2.272	1	0.134
HDL cholesterol	47.6 ± 15.4	52.0 ± 18.9	1.955	1	0.164
Glycemia (mg/dl), mean ± *sd*	89.1 ± 23.8	86.9 ± 23.3	0.296	1	0.587
Systolic arterial pressure (mmHg), mean ± *sd*	124.1 ± 11.9	120.8 ± 12.4	2.529	1	0.114
Diastolic arterial pressure (mmHg), mean ± *sd*	78.9 ± 8.8	77.5 ± 8.8	0.958	1	0.327
Metabolic syndrome, n (%)	20 (35.7)	36 (64.3)	1.13	1	0.288
Abdominal obesity, n (%)	21 (40.4)	49 (41.5)	1.704	1	0.300
Low HDL cholesterol, n (%)	19 (36.5)	54 (45.8)	0.605	1	0.437
Elevated blood pressure, n (%)	27 (51.9)	50 (42.4)	1.006	1	0.316
Impaired fasting glucose, n (%)	12 (23.1)	20 (16.9)	0.789	1	0.374
Hypertriglyceridemia, n (%)	13 (25.0)	31 (26.3)	0.124	1	0.724

NOS: Not Otherwise Specified.
BMI: Body mass index.
* Remained significant after Bonferroni correction: p < 0.0017.

Table 3
Relationship between potential explanatory variables and violent suicide methods: results from the logistic regression analysis.

Dependent variables	B	S.E.	Wald	ORa	95% CI OR	p
Gender (Male)	1.820	0.545	11.147	6.174	(2.121-17.972)	**0.001**
Body weight	−0.002	0.033	0.004	0.998	(0.935-1.065)	0.948
Body Mass Index	0.086	0.096	0.807	1.090	(0.903-1.315)	0.369
Abdominal circumference	−0.037	0.018	4.309	0.964	(0.931-0.998)	**0.036**

Bold values indicate statistically significant values.

hypomanic episodes (3.3 ± 4.3 vs 2.3 ± 3.1: p 0.001), more lifetime depressive episodes (6.0 ± 4.4 vs 4.7 ± 4.1: p < 0.001), higher rates of lifetime psychiatric comorbidities (50.0% vs 41.3%: p 0.029), higher rates of lifetime medical comorbidities (58.0% vs 48.9%: p 0.028) and higher rates of reduced HDL cholesterol (46.2% vs 36.7%: p 0.030).

The suicide attempters' group was further analyzed according to whether they had employed a violent or a nonviolent suicide attempt; within the attempters' group 32 subjects (15.8%) were excluded due to lack of data about the modality of suicidal behavior. The results are shown in Table 2. Fifty-two patients (30.6%) attempted suicide with a violent method. Violent suicidal attempts consisted respectively in jumping from heights (n = 17), hanging (n = 13), abdominal knife wounds (n = 7), gunshot wounds (n = 4), gas poisoning (n = 4), car accident (n = 3), others (n = 4). In our sample, nonviolent method was drug overdose (n = 118). There was a statistically significant difference in sex distribution (p: <0.001), with more men in the group of violent suicide attempters than in the group of nonviolent suicide attempters (65% vs 28%; p: <0.001). Moreover, we found significant differences within metabolic parameters: subjects with previous violent attempts, in comparison to patients with nonviolent attempts, showed higher mean values of weight (80.5 ± 18.3 vs 69.4 ± 14.7: p < 0.001), BMI (27.8 ± 5.6 vs 25.2 ± 4.7: p < 0.003)

and waist circumference (98.7 ± 18.5 vs 92.4 ± 14.3: p 0.032). There were no further significant differences within other sociodemographic and clinical characteristics between the two groups. The LogReg analysis confirmed the association of violent attempts with male gender (p: <0.001; Phi: 0.35) and with higher waist circumference (p: <0.001; Cohen's d: 0.39). The results of the LogReg analysis are described in Table 3; independent variables included were gender, BMI, weight, abdominal circumference. The LogReg model was statistically significant, $\chi 2$ (4) = 29.590, p < .001. The model explained 28.0% (Nagelkerke R2) of the variance in response and correctly classified 71.6% of cases. Since the LogReg ruled out weight and BMI as independent risk factors, monovariate analyses have been conducted in gender subgroups. In male subgroup no differences emerged between violent and nonviolent suicide attempters; in female subgroup there are statistically significant differences between violent and nonviolent suicide attempters in terms of higher mean body weight (73,2 kg ± 14,5 vs 65,65 ± 12,9: p = .034) and BMI (27,7 ± 4,3 vs 25,1 ± 4,9: p = .047).

4. Discussion

The main objective of this study was to analyze sociodemographic and clinical factors related to violent suicide attempts in a large naturalistic sample of patients with BD; in addition, we analyzed the rates of lifetime suicide attempts and the variables associated with suicidal behavior.

The prevalence of lifetime suicide attempts found in our sample (24%) is consistent with those reported by previous studies [35–37]. Some clinical variables (longer duration of illness, more lifetime hypomanic and depressive episodes, higher rates of lifetime psychiatric and medical comorbidities) were showed to be associated with greater likelihood of lifetime suicide attempts: these results were expected and confirm the most important studies recently carried out on this topic [38,37]. Furthermore, a correlation emerged between reduced HDL cholesterol and lifetime suicide attempts: to date, two studies reported lower serum total cholesterol levels in BD patients with history of suicide attempt [38,39], while no association was identified in a previous Italian study [28]. Therefore, our finding is noteworthy and deserve further investigation in future studies.

In our sample about one-third of patients (30.6%) with history of suicidal behavior used violent methods, while previous studies showed lower rates of violent suicide attempts in BD (13.2%–17.5%) [40,41,28]. There are possible explanations for the lack of correspondence between our results and available literature data. Firstly, the sample consists of patients with a high severity of illness, as our Department is a tertiary referral center located within the University General Hospital. Furthermore, investigations on suicidal behaviors in BD, including the present study, are heterogeneous, in terms of characteristics of the samples (e.g.: medications, psychiatric comorbidities), instruments used to assess suicidality and definition of violent or nonviolent methods. Comparing the subjects according to whether they had employed a violent or a nonviolent suicide method, we found significant differences across gender, with more men in the group of violent suicide attempters. Our result is consistent with previous studies that have demonstrated that the main differences in suicidal behavior between men and women is the method chosen to attempt suicide [23,24,28]. No further differences regarding socio-demographic and psychopathological features were found between the two groups. Concerning medical comorbidities and metabolic disorders, our results showed higher mean values of weight, BMI and waist circumference in the group of violent suicide attempters, while no significant difference was found in terms of serum lipid levels, glycemia, blood pressure and metabolic syndrome. The LogReg analysis confirmed also abdominal circumference as independent variable associated with violent suicide attempts; results from monovariate analyses conducted in gender subgroups showed in female group higher mean body weight and BMI values in violent attempters. To our knowledge only one previous study, performed by our research group, with a smaller sample size, specifically evaluated the correlation between violent suicide attempts and metabolic parameters in BD: the results did not show any significant difference between violent and nonviolent suicide attempters. [28]. The methodological limitations of the present study, discussed in the following paragraph, make it difficult to interpret the association between higher BMI/abdominal obesity and violent suicide methods: data on metabolic parameters at the time of suicide attempts and previous pharmacological treatments would be needed to distinguish whether BMI and waist circumference may directly influence the use of violent methods or whether subjects with history of violent attempts are more likely to be prescribed medication that leads to weigth gain and abdominal obesity (e.g.: second generation antipsychotics). The hypothesis of a causal relationship between obesity and violent suicide methods could be explained by the association between obesity and impulsivity. Indeed, impulsive personality traits are prevalent characteristics in obese BD patients and some studies suggest that obesity and impulsivity together may lead to severe course of illness and worse prognosis [42]. Therefore, the relationship between obesity and suicidal behaviour is worthy of interest and deserves to be explored by further methodologically rigorous studies.

Our study presents several limitations, mostly due to the cross-sectional design and to the fact that data derives from a study aimed to investigate clinical characteristics of BD and not suicidal behavior specifically. First, in our research we analyzed lifetime suicide attempts, but the sample does not include completed suicides, meaning that we are unable to test whether the results are generalizable to suicide deaths; then suicidal intent to die is difficult to ascertain retrospectively and information could be biased. Moreover, some patients have missing data about the modality of suicidal attempts and some relevant variables, such as medical comorbidities and metabolic parameters at the time of suicide attempts. Furthermore, in our analysis the impact of pharmacological treatment on suicidal behavior and on metabolic parameters was not evaluated, due to the lack of data on medications prior to study entry. Another limitation concerns the heterogeneity of recruited patients in terms of clinical characteristics (e.g.: medical conditions, drug treatments), with potential confounding factors.

Instead, the large sample size is a strength of the study. Furthermore, subjects enrolled for this study were representative of "real-world" in and outpatients with BD: this should be considered a point of strength in terms of generalizability and external validity.

5. Conclusions

In conclusion, the present study confirms the association between male gender and violent suicide; moreover, our findings suggest a correlation between obesity and the use of violent suicide methods, especially in female patients, but further research is awaited to explore and clarify this relationship. Considering that suicide is regrettably frequent in patients with BD future studies on this issue could help detecting individuals at risk of suicide attempt and take appropriate actions as early as possible.

Declaration of Competing Interest

Gianluca Rosso is /has been a speaker and/or has received research grants from Angelini, Janssen, Lundbeck, Otsuka.

Umberto Albert is /has been a speaker and/or has received research grants from Angelini, Innova Pharma, Neuraxpharm, Janssen, Lundbeck.

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