

# Serum Lipid Levels in Patients with Eating Disorders

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## Abstract

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**Objective** To evaluate some risk factors for cardiovascular diseases in feeding and eating disorders, the degree of lipid abnormalities was investigated in a large Japanese cohort of different groups of feeding and eating disorders, according to the Japan Atherosclerosis Society Guidelines for the Prevention of Atherosclerotic Cardiovascular Diseases 2012 (JAS Guidelines 2012).

**Methods** Participants in the current study included 732 women divided into four groups of feeding and eating disorders: anorexia nervosa, restricting type (AN-R); anorexia nervosa, binge-eating/purging type; bulimia nervosa (BN); and binge-eating disorder (BED). We measured the serum levels of total cholesterol, high-density-lipoprotein (HDL) cholesterol, and triglyceride in these participants. Low-density-lipoprotein (LDL) cholesterol and non-HDL cholesterol levels were also calculated.

**Results** The concentrations of LDL cholesterol and non-HDL cholesterol were widely distributed in all groups. When the LDL cholesterol risk was defined as  $\geq 120$  mg/dL and the non-HDL cholesterol risk as  $\geq 150$  mg/dL, according to the JAS Guidelines 2012, the proportion of LDL cholesterol risk ranged from 29.6% (BN) to 38.6% (AN-R), and the proportion of non-HDL cholesterol risk ranged from 17.8% (BN) to 30.1% (BED).

**Conclusion** The present findings suggest the existence of LDL cholesterol risk and non-HDL cholesterol risk in all groups of eating disorders. Given the chronicity of this condition, the development of elevated concentrations of LDL cholesterol and non-HDL cholesterol at an early age may increase the risk of cardiovascular diseases.

**Key words:** LDL cholesterol, non-HDL cholesterol, eating disorders, risk factors

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## Introduction

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The number of patients with eating disorders has increased ten-fold in clinical and community samples in Japan from 1980 to the present (1, 2). Eating disorders remain an important social health concern in Japan (1), as in Western countries (3).

The mortality rate associated with anorexia nervosa (AN) is high (5.9-18%), and death is mainly attributed to cardiac events (3-5). It is well known that individuals with AN demonstrate cardiac structural (decreased left ventricular mass and wall thickness), functional (left ventricle dysfunction),

and electrical (prolonged QT interval and bradycardia) problems. Episodes of sudden death induced by hypokalemia and arrhythmia are common in patients with AN and bulimia nervosa (BN) (6).

We previously conducted an outcome study in Japanese women with an eating disorder, followed from 4 to 9 years, and found that 14 (10.2%) out of 137 patients with AN died primarily due to cardiac events (5). Although we could not determine whether cardiac death was due to hypercholesterolemia, all of the 10 patients who had died due to cardiac events had high levels of serum total cholesterol, ranging from 233 mg/dL to 312 mg/dL. It is well known that cholesterol levels are one of the risk factors for cardiovascular

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diseases.

Recently, guided by recent research on risk factors of cardiovascular diseases in the United States (7, 8), the Japan Atherosclerosis Society published the Japan Atherosclerosis Society Guidelines for the Prevention of Atherosclerotic Cardiovascular Diseases 2012 (JAS Guidelines 2012), in which the levels of low-density-lipoprotein (LDL) cholesterol, high-density-lipoprotein (HDL) cholesterol, triglyceride (TG), and non-HDL cholesterol are included as risk factors of cardiovascular diseases (9).

There are some reports on the lipid levels in patients with AN in Japan (10, 11). However, to the best of our knowledge, there is no report on the lipid levels in BN and binge-eating disorder (BED) in Japan. In this study, to evaluate some risk factors for cardiovascular diseases in eating disorders, the degree of lipid abnormalities was investigated in a large Japanese cohort of different groups of feeding and eating disorders according to the JAS Guidelines 2012.

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## Materials and Methods

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### Participants

The original cohort consisted of 878 patients who consecutively sought treatment for an eating disorder at Karasuma Oike Nakai Clinic in Kyoto City between 2005 and 2012. All patients were assessed using the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I) (12) by an eating disorder specialist prior to treatment, as described previously (13). Questions that appear in Module H of the SCID-I were administered to all patients without following skip rules (e.g., patients were asked about fear of gaining weight whether or not anorexic underweight was present), making it possible to evaluate alternative eating disorder diagnostic criteria. In addition to the DSM-IV criteria for AN and BN, the SCID-I asks about the criteria for BED if binge eating is present, but not compensation. The DSM-5 diagnostic criteria (14), based on SCID-I interviews, were used to generate the DSM-5 diagnoses of feeding and eating disorders. We used a body mass index (BMI) cut-off of less than 17.5 kg/m<sup>2</sup> for AN diagnosis, according to the published norms for Japanese women aged between 16 and 30 (13). All patients met the DSM-5 criteria for feeding and eating disorders. Ten men (2 AN, 6 BN, and 2 BED) and 136 patients with other specified feeding or eating disorders were excluded. Accordingly, the participants in the current study included 732 women with a feeding or eating disorder, aged 15-45 years, and consisted of 145 cases (19.8%) of AN, restricting type (AN-R); 140 cases (19.1%) of AN, binge-eating/purging type (AN-BP); 304 cases (41.5%) of BN; and 143 cases (19.5%) of BED. All patients were of Japanese ethnicity.

Objective weight and height were measured and current BMI was calculated for all patients. The premorbid BMI, maximum BMI and minimum BMI in adult, and duration of illness were assessed by self-reporting during the first con-

sultation. Age of onset was defined as the age at which eating behavior changed. All patients provided their informed consent for the use of their data in an anonymous form. Ethical approval for this study was obtained from the Ethics Committee of Kyoto University Graduate School and Faculty of Medicine.

### Methods

Fasting blood samples were obtained from all participants in the morning (between 8 AM and 10 AM). The concentrations of total cholesterol, HDL cholesterol, and TG were measured enzymatically by Falco Bio-systems Ltd., Kyoto, Japan. LDL cholesterol was calculated using the Friedewald formula (15). Non-HDL cholesterol was calculated by subtracting HDL cholesterol from total cholesterol. Cut-off points for high levels of total cholesterol ( $\geq 220$  mg/dL) were based on the Japan Atherosclerosis Society Guidelines for the Prevention of Atherosclerotic Cardiovascular Diseases 2002 (16). Cut-off points for high levels of LDL cholesterol ( $\geq 140$  mg/dL), non-HDL cholesterol ( $\geq 170$  mg/dL), and TG ( $\geq 150$  mg/dL), and low levels of HDL cholesterol ( $< 40$  mg/dL) were based on the JAS Guidelines 2012 (9). In addition, cut-off points for borderline levels of LDL cholesterol ( $\geq 120$  mg/dL) and non-HDL cholesterol ( $\geq 150$  mg/dL) were based on the JAS Guidelines 2012 (9).

### Statistics

All statistical analyses were performed with the SPSS (ver. 13.5) software program. The significance of group differences was tested using an analysis of covariance controlling for age and BMI or a logistic regression analysis controlling for age and BMI, with the level of statistical significance set at  $p < 0.05$ . Spearman's correlations were used to evaluate the relationships among different variables.

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## Results

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Table 1 shows group differences in clinical variables across the four groups of eating disorders. Significant group differences were found for current age, the duration of illness, current BMI, premorbid BMI, maximum BMI, and minimum BMI.

Table 2 shows group differences in the lipid levels across the four groups. The levels of total cholesterol, LDL cholesterol, HDL cholesterol, non-HDL cholesterol, and TG were widely distributed in all groups. Significant group differences were found for the mean levels of total cholesterol, LDL cholesterol, HDL cholesterol, non-HDL cholesterol, and TG.

Figure indicates group differences in the proportion of risk lipid levels across the four groups. When the LDL cholesterol risk was defined as  $\geq 120$  mg/dL, according to the JAS Guidelines 2012 (25), the proportions of LDL cholesterol risk were 38.6% in AN-R, 31.4% in AN-BP, 29.6% in BN, and 36.4% in BED. No significant group differences were found in the proportion of LDL cholesterol risk. When

**Table 1. Demographic Data of the Four Groups of Eating Disorders.**

	AN-R	AN-BP	BN	BED	Statistics
Number of subjects	145	140	304	143	
Current age (years)	21.1 ± 7.3	24.6 ± 5.7	24.5 ± 5.8	24.1 ± 6.2	F(3, 720)=10.8 p<0.001
DI (months)	40.0 ± 52.1	77.5 ± 65.4	82.6 ± 68.0	63.6 ± 55.6	F(3, 720)=16.2 p<0.001
Current BMI (kg/m <sup>2</sup> )	14.5 ± 1.5	15.3 ± 1.6	20.6 ± 2.1	23.1 ± 3.9	F(3, 720)=462.8 p<0.001
Premorbid BMI (kg/m <sup>2</sup> )	19.3 ± 1.9	19.5 ± 2.2	20.7 ± 2.5	20.6 ± 2.6	F(3, 720)=16.6 p<0.001
Maximum BMI (kg/m <sup>2</sup> )	20.4 ± 2.5	21.1 ± 2.4	23.5 ± 2.9	24.5 ± 4.0	F(3, 720)=63.2 p<0.001
Minimum BMI (kg/m <sup>2</sup> )	13.7 ± 1.7	14.0 ± 1.7	17.4 ± 2.2	17.6 ± 2.7	F(3, 720)=171.5 p<0.001

Data are expressed as the mean ± SD.

BMI: body mass index, DI: duration of illness

AN: anorexia nervosa, R: restricting type, BP: binge-eating/purging type, BN: bulimia nervosa, BED: binge-eating disorder

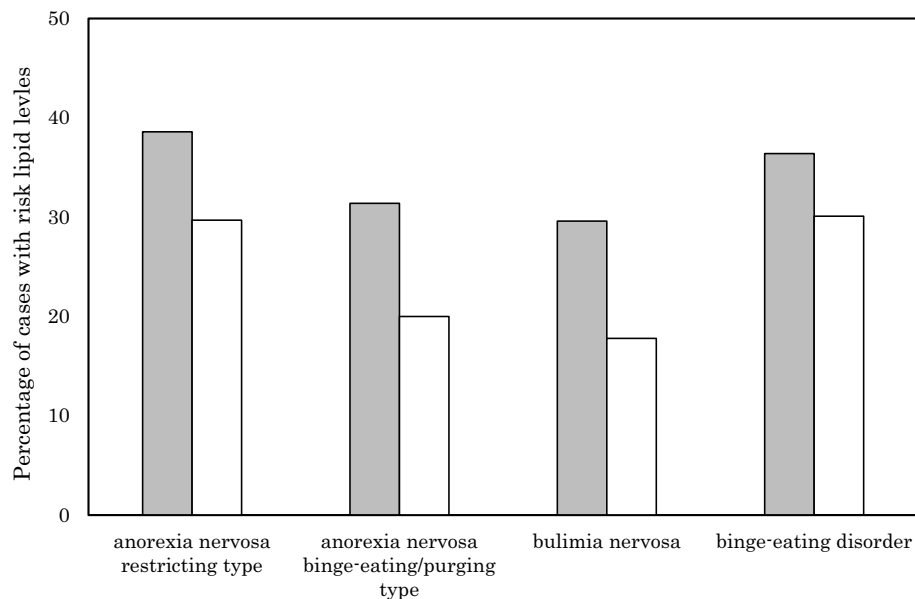
**Table 2. Lipid Levels in the Four Groups of Eating Disorders.**

	AN-R	AN-BP	BN	BED	Statistics
Number of subjects	145	140	304	143	
Total cholesterol (mg/dL)	215.1 ± 59.4 [111-429]	208.4 ± 42.2 [110-368]	200.7 ± 35.6 [123-315]	210.6 ± 41.4 [130-385]	F(3, 728)=3.8 p=0.010
LDL cholesterol (mg/dL)	122.6 ± 53.2 [37-309]	107.8 ± 34.3 [37-221]	105.2 ± 30.3 [40-205]	114.4 ± 35.7 [54-290]	F(3, 728)=6.8 p<0.001
HDL cholesterol (mg/dL)	79.0 ± 18.3 [37-127]	84.8 ± 20.7 [44-168]	78.3 ± 17.7 [43-140]	75.5 ± 20.4 [35-148]	F(3, 728)=3.5 p=0.016
non-HDL cholesterol (mg/dL)	136.1 ± 54.4 [45-370]	123.1 ± 37.2 [35-243]	122.4 ± 32.5 [52-229]	135.4 ± 39.8 [65-322]	F(3, 728)=7.5 p<0.001
Triglyceride (mg/dL)	77.6 ± 42.0 [19-301]	83.1 ± 52.1 [20-448]	86.1 ± 55.5 [16-448]	113.5 ± 127.7 [3-945]	F(3, 728)=2.7 p=0.044

Data are expressed as the mean ± SD. Numbers in parentheses represent the range in the lipid levels.

LDL: low-density lipoprotein, HDL: high-density lipoprotein.

AN: anorexia nervosa, R: restricting type, BP: binge-eating/purging type, BN: bulimia nervosa, BED: binge-eating disorder



**Figure.** Proportion of the risk levels of LDL cholesterol and non-HDL cholesterol across the four groups of eating disorders. Gray bars indicate the proportion of LDL cholesterol risk (≥120mg/dL). White bars indicate the proportion of non-HDL cholesterol risk (≥150mg/dL).

the non-HDL cholesterol risk was defined as  $\geq 150$  mg/dL, according to the JAS Guidelines 2012 (25), the proportions of non-HDL cholesterol risk were 29.7% in AN-R, 20.0% in AN-BP, 17.8% in BN, and 30.1% in BED. Significant group differences were found in the proportion of non-HDL cholesterol risk.

No significant correlations were found between age at intake and total cholesterol, LDL cholesterol, or non-HDL cholesterol levels; between the duration of illness and total cholesterol, LDL cholesterol, or non-HDL cholesterol levels; or between the BMI at intake and total cholesterol, LDL cholesterol, or non-HDL cholesterol levels in any of the eating disorder groups. No significant correlations were found between the maximum BMI and the levels of total cholesterol, LDL cholesterol, or non-HDL cholesterol in any of the eating disorder groups with the exception that a significant correlation was found between the maximum BMI and non-HDL cholesterol levels in the BED group ( $r = 0.359$ ,  $p < 0.01$ ).

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## Discussion

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We showed the degree of lipid abnormalities in a large Japanese cohort of different groups of feeding and eating disorders, according to the JAS Guidelines.

Klinefelter first reported increased total cholesterol levels in the sera of patients with AN (17). However, the serum total cholesterol values in patients with AN in previously published papers were widely distributed (10, 11, 17-21). Although the frequency of cardiac events in patients with BN is not clear, the serum cholesterol values in patients with BN were also widely distributed (22-26). Small numbers of subjects studied and/or different definitions of hypercholesterolemia in previous reports may account for the different results in the percentages of hypercholesterolemia in these patients. Accordingly, we investigated the degree of lipid abnormalities in a large Japanese cohort according to the JAS Guidelines 2012, the standard guidelines in Japan.

BED is an eating disorder characterized by binge eating without subsequent compensatory behaviors. Recently, BED has been included in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) as its own category of eating disorders (14). Mitchell et al. reported that 22 (6.4%) out of 350 patients with BED had cardiovascular diseases (27). There are some reports on the lipid levels in obese BED patients with BMIs greater than 30.0 kg/m<sup>2</sup> (28, 29). However, to the best of our knowledge, there is no report on the lipid levels in non-obese BED patients. We therefore investigated the lipid levels in non-obese BED patients in the present study.

The JAS Guidelines 2012 emphasize the importance of LDL cholesterol and non-HDL cholesterol as predictors of cardiovascular risk. In the current study, the LDL cholesterol levels were widely distributed in all the groups of eating disorders. When the LDL cholesterol risk was defined as  $\geq 120$  mg/dL, according to the JAS Guidelines 2012 (9), the

present findings revealed the existence of LDL cholesterol risk in 30-39% of the patients with eating disorders. Non-HDL cholesterol levels were widely distributed in all the groups of eating disorders. The percentage of non-HDL cholesterol risk was lower than that of LDL cholesterol risk in all the groups of eating disorders. Non-HDL cholesterol risk was defined as  $\geq 150$  mg/dL, according to the JAS Guidelines 2012 (9). However, a recent study (30) suggested that an LDL cholesterol level of +30 mg/dL may be above the optimal cut-off value, as 15.7% of US adults with a high LDL cholesterol level are categorized as having a normal non-HDL cholesterol level using this cut-off value. Further research is thus needed to identify the optional cut-off values for the non-HDL cholesterol level.

Non-HDL cholesterol is thought to better encapsulate the total risk from atherogenic lipoproteins in patients with metabolic syndrome in whom LDL cholesterol is characteristically normal and TG concentrations are modestly elevated (7, 8). However, the frequency of hypertriglyceridemia was not high in all the eating disorder groups, ranging from 4.1% (AN-R) to 16.8% (BED). Accordingly, the measurement of non-HDL-cholesterol may not be necessary in eating disorders, except in some patients with hypertriglyceridemia.

Despite these findings, non-HDL cholesterol has many benefits beyond LDL cholesterol in eating disorders in the clinical setting. The non-HDL cholesterol level is easy to calculate and does not require fasting, suggesting that this level may be a valuable tool for cardiovascular risk assessment in patients with eating disorders because they often fail to maintain their fast before blood sampling due to episodes of abnormal eating behaviors (21, 24, 28).

The exact etiology of cholesterol elevation in eating disorders remains unclear. Available evidence suggests that cholesterol elevation in AN may be due to liver dysfunction, dehydration, reduced cholesterol turnover (18), decreased triiodothyronine concentrations (10), and delayed cholesterol metabolism (11). Raised cholesterol concentrations in BN may be associated with the feeding pattern (22) and dietary intake of cholesterol and fat during binge-eating episodes (24). In these studies, the researchers examined the differences in the etiological factors between patients and normal subjects. However, the current study revealed the wide distribution of lipid levels in eating disorders. Accordingly, we must examine these differences between patients with high lipid levels and patients with low or normal lipid levels. Although binge eating is thought to result in hypercholesterolemia, to the best of our knowledge, there is no report on the etiology of hypercholesterolemia in BED.

There are several limitations associated with the current study, including its cross-sectional nature and the inability of correlations to establish causation. To understand the implications of these findings of LDL cholesterol risk and non-HDL cholesterol risk in all groups of eating disorders, an assessment of the cardiac status in relation to these risk markers is needed, in addition to a long-term follow-up of



this population in relation to an increased risk of cardiovascular diseases. Related to this, we measured the lipid levels at intake only. The lipid levels during and after treatment should also be measured.

In summary, the present findings revealed the existence of LDL cholesterol risk and non-HDL cholesterol risk in a large Japanese cohort of different groups of feeding and eating disorders. The implications of the long-term elevation of cholesterol influencing the morbidity in eating disorders must not be neglected. Given the chronicity of this condition, the development of elevated concentrations of cholesterol at an early age may increase the risk of atheroma formation and ischemic heart disease (20, 31).

**The authors state that they have no Conflict of Interest (COI).**

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