Gender and age differences in cardiovascular complications in anorexia nervosa patients.

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Gender and age differences in cardiovascular complications in anorexia nervosa patients

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ABSTRACT

Background: Anorexia nervosa (AN) is characterized by severe malnutrition and electrolyte imbalances. Differences in cardiovascular complications between males and females with AN have not been studied. Additionally, coronary artery disease (CAD) prevalence and cardiovascular complications in patients with AN >65 years have not been reported.
Methods: AN patients > 18 years were identified in the Nationwide Inpatient Sample 2009–2010 database using the Ninth Revision of International Classification of Disease code 307.1. Demographics, risk factors, and cardiovascular event rates were compared to general population data.
Results: CAD incidence was lower in all AN patients compared to the general population (4.4% vs 18.4%, $p < 0.001$). Despite AN males having higher prevalences of hypertension and diabetes than AN females, there was no difference in CAD. AN males had higher rates of cardiac arrests, arrhythmias, and heart failure. Interestingly, 4.3% of patients with AN were >65 years old. When compared to the general population > 65 years, older AN patients had lower rates of CAD (35% vs 16%; $p < 0.001$). Older AN patients still had higher CAD rates compared to the general population under 65 (8.6%) and AN patients under 65 (4%; $p < 0.001$). Older AN patients had a lower incidence of heart failure (24% vs 16%; $p = 0.04$), and a trend towards less arrhythmias (30% vs 21%; $p = 0.08$).
Conclusions: Our data suggests that male AN patients experienced more cardiac arrests, arrhythmias, and heart failure than female AN patients. Additionally, older AN patients have a decreased incidence of CAD and heart failure compared to the general population > 65 years old.

1. Introduction

Anorexia nervosa (AN) is an eating disorder defined as restriction of energy intake relative to requirement due to intense fear of gaining weight resulting in significantly low body weight [1]. Over the last five decades, both the incidence of AN and the rate of hospitalization have increased [2]. Furthermore, due to severe malnutrition leading to significant medical complications, AN is associated with the highest rate of mortality amongst all psychiatric disorders with 5.1 deaths per 1000 person years [3]. Cardiovascular complications occur in up to 80% of patients with AN, and account for up to 30% of mortality [4]. Cardiac structural alterations, including decreased left ventricular mass and dimension, pericardial effusions, mitral valve prolapse, conduction abnormalities, and hypotension resulting from autonomic dysfunction are all well described.

Cardiovascular complications associated with AN have been derived from studies with limited sample sizes and from predominantly female and adolescent populations. However, with recent changes in diagnostic criteria for AN in DSM-V, the sensitivity to diagnose AN has increased in other populations, including males. The present study therefore aimed to assess cardiac manifestation of AN based on a large, national database and to assess gender and age differences.

2. Methods

2.1. National Inpatient Sample database

We analyzed data from the National Inpatient Sample (NIS) database for the year 2009–2010 which contains data on inpatient hospital stays from states participating in Healthcare Cost and Utilization project. Each year NIS provides data on roughly 8 million hospitalizations from about 1000 hospitals. The NIS is designed to approximate a 20% sample of U.S. community hospitals, defined as "all non-federal, short-term, general, and other specialty hospitals, excluding hospital units of

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institutions," representing more than 95% of the U.S. population. Criteria used for stratified sampling of hospitals into the NIS include ownership, bed size, teaching status, urban/rural location, and U.S. region. All discharges from sampled hospitals are included in the NIS database. The NIS is an all-payer database that covers all patients, including those covered by Medicare, Medicaid, or private insurance, and those who are uninsured. Inpatient stay records in the NIS include clinical and resource use information available from discharge abstracts derived from state-mandated hospital discharge reports. Discharge weights provided by the NIS allow extrapolation to calculate expected national hospitalization rates [NIS online overview].

2.2. Study population

In 2009–10, a total of 7,810,762 hospital records corresponding to a national estimate of 39,434,956 hospital discharges in the United States were analyzed. We extracted all patients greater than 18 years with all listed diagnosis of AN using the International Classification of Diseases-Ninth Edition-Clinical Modification (ICD-9-CM) code 307.1 ($n = 9502$). We chose all listed diagnosis to include all patients with a diagnosis of AN. Patient characteristics including demographics, risk factors, and cardiovascular event rates were collected on these patients using corresponding ICD codes. Subgroup analysis was performed comparing males vs females with AN to assess for gender differences. We also performed analysis comparing patients with AN age greater than 65 years and without AN age greater than 65 years.

2.3. Statistical analysis

Categorical variable was presented as number (percentage), while continuous variable was presented as mean ± SD for normally distributed variables and median (IQR) for others. p value was calculated by chi-square test for categorical variables and t-test for continuous variable. p value < 0.05 was considered statistical significant. All statistical analysis was performed using STATA 10.0.

3. Results

3.1. AN vs general population

The prevalence of AN out all hospital discharges was 0.02% ($n = 9502$). Mean age of the population was 32.3 ± 0.4 years with 4.3% of patients greater than 65 years of age ($n = 415$). Patients with AN were younger when compared to the general population without AN (32.3 ± 0.4 vs 48 ± 0.1, $p < 0.001$). Diabetes (5% vs 15%, $p < 0.0001$), hypertension (6% vs 39%, $p < 0.0001$) and hyperlipidemia (3% vs 21%, $p < 0.0001$) were less prevalent in AN compared to the general population without AN. The prevalence of CAD (4.4% vs 18.4%, $p < 0.001$) and CHF (2.1% vs 6.4%, $p < 0.001$) was also significantly lower in patients with AN compared to the general population.

3.2. Gender differences

AN was more common in females (91%). Males with AN had increased prevalence of hypertension (12.7% vs 4.9%, $p < 0.0001$) and diabetes mellitus (9% vs 4.3%, $p < 0.01$) compared to females with AN (Table 1) with no significant difference in other traditional risk factors. Also, there was no significant difference in the prevalence of CAD between genders. Males with AN did, however, have significantly higher rates of arrhythmias (25% vs 14.8%, $p < 0.001$), cardiac arrests (1.2% vs 0.2%, $p = 0.03$), and heart failure (4.3% vs 1.9%, $p = 0.04$) in comparison to females with AN.

3.3. Age differences

Interestingly, 4.3% of patients with AN were >65 years old (Table 2). When compared to the general population > 65 years old, older AN patients had significantly lower rates of CAD (35% vs 16%; $p < 0.001$). However, older AN patients still had higher CAD rates when compared to the general population under 65 (8.6%) and AN patients under 65 (4%; $p < 0.001$). Additionally, when compared to the general population > 65 years old, older AN patients had a lower incidence of heart failure (24% vs 16%; $p = 0.04$), as well as a trend towards less arrhythmias (30% vs 21%; $p = 0.08$).

4. Discussion

Utilizing the Nationwide Inpatient Sample database, we found that male patients with AN (9% of all AN patients) experienced significantly more cardiac arrests, arrhythmias, and heart failure than female patients with AN. Additionally, older AN patients (surprisingly 4.3% of all AN patients) have a significantly decreased incidence of both CAD and heart failure compared to the general population > 65 years old. The incidence of CAD is higher in older AN patients compared to younger AN patients.

Over the last five decades, both the incidence of AN and the rate of hospitalization have increased [2]. Furthermore, due to severe malnutrition leading to significant medical complications, AN is associated with the highest rate of mortality amongst all psychiatric disorders with 5.1 deaths per 1000 person years [3].

Table 1
Baseline demographic and cardiovascular risk factors in patients with anorexia nervosa.

Variables	Total $n = 9502$	Male $n = 760$ (9%)	Female $n = 8742$ (91%)	p value
Demographic factors				
Age	32.3 ± 0.4	35.4 ± 1.8	32.1 ± 0.4	0.06
In-hospital clinical outcomes				
In hospital death	73 (0.7)	15 (2)	58 (0.6)	0.08
Cardiac arrest	30 (0.3)	9 (1.2)	21 (0.2)	0.03
Repolarization and conduction abnormalities				
Cardiac dysrhythmia	1491 (16)	190 (25)	1301 (14.8)	<0.001
Conduction abnormalities	76 (0.8)	15 (2)	61 (0.7)	0.07
Structural complications				
Heart failure	200 (2.1)	33 (4.3)	167 (1.9)	0.04
Chronic CAD	418 (4.4)	40 (5.2)	378 (4.3)	0.61
Traditional risk factors				
Diabetes mellitus	447 (4.7)	69 (9)	378 (4.3)	<0.01
Hypertension	532 (5.6)	97 (12.7)	435 (4.9)	<0.0001
Hyperlipidemia	257 (2.7)	34 (4.5)	223 (2.6)	0.14
Tobacco use	1473 (15.5)	87 (11.5)	1386 (15.9)	0.12

Table 2
Baseline demographic and cardiovascular risk factors in patients with Anorexia Nervosa and age more than 65.

Variables	Total n = 13,044,315	AN n = 415 (0.003%)	Controls n = 13,043,900 (99.997%)	p value
Demographic factors				
Age	78.2 ± 0.1	74.2 ± 0.9	78.2 ± 0.1	<0.001
In-hospital clinical outcomes				
In hospital death	3.9	7.3	3.9	0.13
Cardiac arrest	0.7	1.2	0.7	0.60
Repolarization and conduction abnormalities				
Cardiac dysrhythmia	29.5	20.7	29.5	0.08
Conduction abnormalities	4.6	1.2	4.6	0.18
Structural complications				
Heart failure	23.9	15.9	23.9	0.04
Chronic CAD	35.3	15.9	35.3	<0.001
Acute coronary syndrome	5.7	2.4	5.7	0.15

Cardiovascular complications occur in up to 80% of patients with AN and account for up to 30% of the mortality [4]. Cardiac structural alterations, including decreased left ventricular (LV) mass and dimension, are well established in this population and can lead to heart failure (HF) [4]. Several theories have been proposed for this manifestation including increased vagal tone, a physiologic adaptation to conserve energy, which results in decreased contractility and preload and eventually cardiac atrophy to compensate for volume depletion [5–7]. Electrolyte depletion and hormonal changes have also been associated with decreased LV mass and size [8–11]. Histologically, interstitial fibrosis and edema, mononuclear infiltration, and loss of cross striations and myofibrils occur in protein-calorie malnutrition [12]. A recent study showed a strong association between AN and myocardial fibrosis on cardiac magnetic resonance [13]. Mitral valve prolapse (MVP) is another structural manifestation affecting 33 to 66% of AN patients [14] and is a result of the mismatch between mitral valve annular size and LV size, known as valvuloventricular disproportion [15]. Pericardial effusions are also prevalent in the AN population with incidence rates reported up to 71% [8,16–18]. Conflicting data has been reported regarding both its cause [4] and relationship with body mass index (BMI) [13,19].

Conduction abnormalities can occur in AN. Sinus bradycardia, seen most commonly [20], is a result of vagal hypersensitivity, and is directly related to percent of weight lost [5,21]. Increased QT dispersion and QT prolongation also occur due to electrolyte abnormalities [22]. QT prolongation is recognized as the main cause of sudden cardiac death in the AN population.

Vascular changes have been reported in AN. Hypotension resulting from autonomic dysfunction along with lack of normal circadian variations in blood pressure is noted in this population [23]. Additionally, peripheral vasoconstriction as a heat-conserving mechanism has also been demonstrated in patients with AN [24,25].

This is a retrospective review of a large patient database of hospital discharge diagnoses. We cannot comment on severity of disease, medications or other treatments, or temporal relationship of events. The strength of this analysis lies in the large number of patients included given the size of this national inpatient sample.

Conflicts of interests

None.

5. Conclusion

Utilizing the Nationwide Inpatient Sample database, we found that male AN patients experienced more cardiac arrests, arrhythmias, and heart failure than female AN patients. Additionally, older AN patients (surprisingly 4.3% of all AN patients) have a decreased incidence of CAD and heart failure compared to the general population > 65 years old.

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