

Body mass index stratification in hospitalized Italian adults with congenital heart disease in relation to complexity, diagnosis, sex and age

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Abstract *Background and aims:* Adults with congenital heart disease (ACHD) are at risk of overweight and obesity, two major health problems, though underweight can be a negative prognostic factor too. Awareness of the body mass index (BMI) in ACHD is very limited. The present study describes the use and prevalence of BMI in Italian symptomatic hospitalized ACHD patients in relation to complexity by Bethesda system classification, diagnosis, sex and age.

Methods and results: We classified 1388 ACHD patients, aged 18–69 years, on the basis of their BMI, and compared them to the Italian reference population. In our total ACHD population we found a significantly higher prevalence of underweight compared to the Italian reference population (6.34% vs 3.20%). ACHD women were more underweight than men. Underweight decreased with age. Overweight was significantly less frequent in the total ACHD population (26.73% compared to 31.70%) in the Italian reference population. Men were more likely to be overweight than women. In statistical terms obesity was similar in the Italian reference population (10.50%) and our ACHD population (9.58%). Both overweight and obesity increased with age. Results were comparable using a diagnostic anatomical-functional classification and the Bethesda system classification.

Conclusions: In our cohort of ACHD the prevalence of underweight was double that of the Italian reference population. The prevalence of overweight was lower, while obesity was similar. Since BMI does not account for differences in body fat distribution, a future aim will be to quantify the visceral component of the adipose tissue in ACHD patients and examine their body composition in order to reflect their risk of acquired cardiovascular disease better, and either to maintain or achieve an adequate visceral component.

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Acronyms: CHD, Congenital Heart Disease; ACHD, Adult with Congenital Heart Disease; NCDs, non-communicable diseases; BMI, Body Mass Index; WHO, World Health Organization; PFO, Patent Foramen Ovale.

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Introduction

The prognosis of children with congenital heart disease (CHD) has changed over the last decades, primarily due to improvements in surgical techniques and interventional catheterization. As a consequence, the population of adults with congenital heart disease (ACHD) has increased [1–3] and its prevalence is estimated at four per thousand adults [1,4].

This new population of patients is now exposed to the environmental and behavioral risk factors [5–7] entailed in chronic diseases - also referred to as non-communicable diseases (NCDs), such as overweight and obesity, which have become two major health problems throughout the world [8–10]. However, underweight is a risk factor too, and is associated with increased mortality [8,11]. The body mass index (BMI) is the most widely used measure, defined by the World Health Organization (WHO) to classify weight status, and it correlates with all-causes mortality [8,12].

In Italy, the latest data from the National Health Institute monitoring system called *Passi* declared a prevalence of underweight, overweight and obesity in the adult population as respectively 3.2%, 31.7% and 10.5% [13]. Excessive weight and underweight are important health concerns for ACHD patients, since they can both be markers of increased risk and negative prognostic factors [14]. However, data about the weight status of ACHD patients are few and non-homogenous, maybe reflecting national differences [14–16].

The aim of the present study was to describe, for the first time, the prevalence of underweight, normal weight, overweight and obesity in a wide sample of Italian ACHD patients hospitalized in our Centre, in relation to diagnosis, sex and age.

Methods

We gathered data from the Pediatric and Adult Congenital Heart Centre database and from the Department of Cardiothoracic, Vascular Anesthesia and Intensive Care database at the IRCCS Policlinico San Donato University Hospital (Milan, Italy).

We considered a selected population consisting of patients who were hospitalized for cardiac surgery or for catheterization. Data was obtained at hospital admission before any intervention and comprised information on diagnosis, intervention technique, age, sex, height and weight directly measured. We could therefore calculate patients' BMI, as weight (kg)/height² (m²). As defined by WHO, patients were classified as underweight (BMI <18.5 kg/m²), normal weight (BMI 18.5–24.9 kg/m²), overweight (BMI 25.0–29.9 kg/m²), obese (BMI ≥ 30.0 kg/m²) [12].

We retrospectively collected data on ACHD hospitalized in the IRCCS Policlinico San Donato from 2000 to 2016. We merged the hospital's Cardiac Surgery and Catheterization databases into one. At the time of data extraction

information on 2606 hospitalized ACHD was available. For patients with more than one hospital admission between 2000 and 2016, we used the information on the most recent one for our analysis.

We considered the following exclusion criteria: patients under 18 and over 69 years old, CHD associated with genetic syndromes (Down syndrome) and patent foramen ovale (PFO).

The study focused on ACHD who could be included in the third level of the ESC Guidelines [17], hospitalized in our specialist Centre and presenting a complex clinical situation.

We used the Bethesda system classification based on the complexity of the cardiac defect (COMPLEXITY - Tables 2 and 3) [18], therefore we divided our population into the three categories of complexity "Simple", "Moderate" and "Great".

We also have decided to split all the congenital heart defects into four categories on the basis of the initial diagnosis and in relation to the overall clinical history (DIAGNOSTIC CATEGORIES - Tables 1–3) [17,19,20].

A total of 1388 patients met the diagnosis and age criteria, and had complete data on weight and height.

We compared our ACHD data with data for the Italian population recorded in the Italian National Health

Table 1 Diagnostic categorization of ACHD.

Category name	Type of CHD included	Number of subjects (%)
1) Septal Heart defects & lesions with Left-to-Right Shunt	Atrial Septal Defect, Ventricular Septal Defect, Complete Atrioventricular Canal Defect, Partial Atrioventricular Canal Defect, Total Anomalous Pulmonary Venous Return, Partially Anomalous Pulmonary Venous Return, Patent Ductus Arteriosus, Coronary Artery Fistula, Eisenmenger syndrome	No. 864 (62.20)
2) Conotruncal Heart diseases	Tetralogy of Fallot, Pulmonary Atresia with Ventricular Septal Defect, Transposition Of Great Arteries, Truncus Arteriosus, Double Outlet Right Ventricle	No. 209 (15.10)
3) Valve defects, Atrioventricular and/or Ventriculoarterial discordance & Aortic defects	Pulmonary Atresia With Intact Septum, Corrected Transposition Of Great Arteries, Pulmonary Valve Stenosis, Aortic Valve Stenosis, Mitral Valve Stenosis, Ebstein's Anomaly, Coarctation of the Aorta, Vascular Rings, Double Aortic Arch, Paravalvular Leak	No. 247 (17.80)
4) Univentricular Heart	Univentricular Heart	No. 68 (4.90)

Institute's *Passi* Surveillance System. This system is based on a systematic and continuous sample case data collection of self-reported Italian adults' health conditions for surveillance of major behavioral risk factors, and any preventive measures included in the National Prevention Plan. From the *Passi* project we extracted a sample of 145 992 subjects from the list of residents enrolled in each Italian local health unit to select a monthly random sample of persons aged 18–69 years, stratified in sex and age groups (18–34, 35–49, 50–69 years). The last available data was for the three years 2013–2016. We stratified and analyzed our sample the same way, by age and sex.

All patients signed informed consent to the processing of personal data when admitted to the IRCCS Policlinico San Donato. In any case this was a retrospective study, therefore ad hoc consent was not actually required. The study was approved by the competent Ethics Committee (IRCCS San Raffaele Hospital; 100/INT/2017 dated 14/09/2017).

Statistics

Descriptive data are expressed as counts (percentages) for categorical data and as means (SD) for continuous variables. The association between complexity classification, diagnostic categories, weight classes and baseline demographic variables (sex and age in categories) was investigated with the Chi-square or Fisher's exact test, as appropriate. For association in diagnostic categories, a 2-side *P* value of 0.05 was considered statistically significant.

After Bonferroni correction for multiple testing, we considered *P* value of 0.006 to be statistically significant for the comparison between the classes of complexity, diagnostic categories and the reference population. Statistical analysis was done using SAS version 9.4 (SAS Institute, Cary, NC).

Results

The study comprised 1388 adult symptomatic patients with congenital heart defects who were hospitalized for cardiac surgery or catheterization. Their mean \pm SD age was 41.45 ± 13.18 years. [Tables 2 and 3](#) show all the data analyzed, with the stratification by sex and age that follows two different approaches: defect complexity (in accordance with Bethesda system classification) and diagnostic anatomical-functional classification. There were 776 females (55.91%) and 612 males (44.09%); 467 aged 18–34 years (33.65%), 521 aged 35 to 49 (37.54%), and 400 aged 50 to 69 (28.82%).

Through Bethesda classification patients were distributed as follows: simple defects 827 (59.58%), moderate defects 431 (31.05%), great defects 130 (9.37%).

[Table 1](#) shows the diagnostic categories and their distribution.

The BMI distribution of total ACHD population vs the Italian reference population is illustrated in [Fig. 1](#).

[Figure 2](#) sets out the distribution of the total ACHD cohort and of each class of complexity, compared to the Italian reference population for each BMI class.

[Figure 3](#) shows the distribution of the total ACHD cohort and of each diagnostic category, compared to the Italian reference population for each BMI class.

There were significant differences in the distribution of sex and underweight, normal weight, overweight and obesity among the complexity class "Simple" (X^2 test $p < 0.0001$) and "Moderate" (X^2 test $p = 0.02$) ([Table 2](#)). In the same way we found significant differences in the distribution of sex and weight status in the various heart defect categories ([Table 2](#)). In particular, the most evident difference between sexes was seen in Septal heart defects & lesions with Left-to-Right Shunt (X^2 test $p < 0.0001$), where there were 68 obese females (12.69%) versus 21 obese males (6.23%).

There were also significant differences in the distribution of age categories and weight status categories among all the complexity classes and, equally, we found these diversities in the various heart defect categories, except for Univentricular Heart ([Table 3](#)).

Normal weight

In our ACHD population 57.35% were normal weight, similarly to the Italian reference population of 54.60%. Normal weight was significantly close to the figure for the Italian population in every complexity class ([Fig. 2B](#)). Normal weight was more common among women than men ([Table 2](#)).

Normal weight was generally more common in young people (18–30 years old) ([Table 3](#)).

Underweight

In the Italian reference population the figure for underweight is 3.20%. This prevalence was significantly higher in our total ACHD population (6.34%) and in "Simple" (5.80%) and "Great" (16.15%) classes of complexity. The prevalence of underweight was higher, but not significantly, for "Moderate" complexity patients (4.41%) ([Table 2](#) and [Fig. 2A](#)).

Underweight was more common among ACHD women than men ([Table 2](#)).

In our cohort the prevalence of underweight was higher compared to the Italian population in all the complexity classes, except for older patients with moderate complexity defect.

The prevalence of underweight was higher among younger people and tended to decrease with age, in both the Italian cohort and the total ACHD cohort, except for older patients with great complexity defect who were found to be more underweight than the younger ones (27.27% vs 22.06%).

Overweight

We found a significantly lower prevalence of overweight in the total ACHD population (26.73%) and particularly in the great complexity class (16.15%) compared to the Italian reference population (31.70%). The prevalence of

Table 2 BMI distribution by sex.

	Mean Age (±SD)	N. total	Under weight n (%)	CI 95%	p ^a	Normal weight n (%)	CI 95%	p ^a	Over weight n (%)	CI 95%	p ^a	Obese n (%)	CI 95%	p ^a	p
TOTAL (n%)	41.45 (±13.18)	1388	88 (6.34)	[5.12 -7.75]	<0.0001	796 (57.35)	[54.70 -59.97]	0.042	371 (26.73)	[24.42 -29.15]	<0.0001	133 (9.58)	[8.08 -11.25]	0.272	
Female (55.91%)	42.00 (±12.55)	776	66 (8.51)	[6.64 -10.69]	0.001	468 (60.30)	[56.77 -63.77]	0.853	159 (20.49)	[17.70 -23.50]	0.031	83 (10.70)	[8.61 -13.09]	0.431	<0.0001 ^b
Male (44.09%)	40.76 (±13.92)	612	22 (3.59)	[2.27 -5.39]	<0.0001	328 (53.59)	[49.55 -57.60]	0.011	212 (34.64)	[30.87 -38.56]	0.011	50 (8.17)	[6.00 -10.63]	0.014	
COMPLEXITY															
Simple	43.51 (± 13.06)	827	48 (5.80)	[4.31 -7.62]	< 0.0001	470 (56.83)	[55.38 -60.24]	0.207	227 (27.45)	[24.43 -30.63]	0.009	82 (9.92)	[7.96 -12.16]	0.609	<0.0001 ^b
Female (%)	43.78 (±12.20)	503	42 (8.35)	[6.08 -11.12]	0.015	300 (59.64)	[55.21 -63.96]	0.647	105 (20.87)	[17.40 -24.69]	0.128	56 (11.13)	[8.52 -14.21]	0.330	
Male (%)	43.10 (±14.30)	324	6 (1.85)	[0.68 -3.99]	0.011	170 (52.47)	[46.88 -58.02]	0.148	122 (37.65)	[32.36 -43.18]	0.460	26 (8.02)	[5.31 -11.54]	0.077	
Moderate	39.47 (± 13.20)	431	19 (4.41)	[2.67 -6.80]	0.168	242 (56.15)	[51.32 -60.89]	0.529	123 (28.54)	[24.32 -33.06]	0.168	47 (10.90)	[8.12 -14.24]	0.814	0.0200 ^b
Female (%)	39.13 (±12.90)	216	11 (5.09)	[2.57 -8.93]	0.882	132 (61.11)	[54.26 -67.65]	0.944	47 (21.76)	[16.45 -27.86]	0.523	26 (12.04)	[8.02 -17.14]	0.302	
Male (%)	39.63 (±13.51)	215	8 (3.72)	[1.62 -7.20]	<0.0001	110 (51.16)	[44.27 -58.02]	0.452	76 (35.35)	[28.97 -42.14]	0.209	21 (9.77)	[6.15 -14.54]	0.588	
Great	34.92 (±10.55)	130	21 (16.15)	[10.29 -23.63]	<0.0001	84 (64.62)	[55.75 -72.80]	0.022	21 (16.15)	[10.29 -23.63]	<0.0001	4 (3.08)	[0.84 -7.69]	0.003	0.2402 ^c
Female (%)	36.51 (±10.78)	57	13 (22.81)	[12.74 -35.84]	<0.0001	36 (63.16)	[49.34 -75.55]	0.787	7 (12.28)	[5.08 -23.68]	0.043	1 (1.75)	[0.04 -9.39]	0.041	
Male (%)	33.67 (±10.26)	63	8 (10.96)	[4.85 -20.46]	<0.0001	48 (67.75)	[53.72 -76.47]	<0.0001	14 (19.18)	[10.98 -30.08]	0.004	3 (4.11)	[0.86 -11.54]	0.112	
DIAGNOSTIC CATEGORIES															
Septal Heart defects & lesions with Left-to-Right Shunt	44.31 (± 12.82)	864	46 (5.32)	[3.92 -7.04]	0.001	478 (55.32)	[51.94 -58.67]	0.681	251 (29.06)	[26.04 -32.20]	0.099	89 (10.30)	[8.35 -12.52]	0.868	
Female (62.50%)	43.85 (±12.29)	540	39 (7.22)	[5.19 -9.74]	0.134	312 (57.78)	[53.49 -61.98]	0.171	121 (22.41)	[18.96 -26.16]	0.478	68 (12.59)	[9.91 -15.69]	0.042	<0.0001 ^b
Male (37.50%)	45.07 (±13.65)	324	7 (2.16)	[0.87 -4.40]	0.007	166 (51.23)	[45.65 -56.80]	0.316	130 (40.13)	[34.74 -45.69]	0.909	21 (6.48)	[4.06 -9.74]	0.006	
Conotruncal Heart Diseases	36.53 (± 11.66)	209	23 (11.00)	[7.11 -16.05]	< 0.0001	128 (61.24)	[54.28 -67.89]	0.060	45 (21.53)	[16.16 -27.73]	0.001	13 (6.22)	[3.35 -10.40]	0.042	
Female (46.41%)	36.04 (±11.21)	97	13 (13.40)	[7.33 -21.38]	0.003	67 (69.07)	[58.88 -78.07]	0.097	16 (16.49)	[9.73 -25.40]	0.096	1 (1.03)	[0.00 -3.04]	0.001	0.0053 ^b
Male (53.59%)	36.96 (±12.07)	112	10 (8.93)	[4.36 -15.81]	<0.0001	61 (54.46)	[44.78 -63.90]	0.219	29 (28.89)	[18.08 -35.03]	0.003	12 (10.71)	[5.66 -17.97]	1.000	
Valve defects, Atrioventricular and/or Ventriculoarterial discordance & Aortic defects	38.03 (± 13.52)	247	10 (4.05)	[1.96 -7.32]	0.465	143 (57.89)	[51.47 -64.13]	0.307	66 (26.72)	[21.31 -32.70]	0.100	28 (11.34)	[7.67 -15.97]	0.678	0.0474 ^b

Female (44.53%)	40.05 (±13.02)	110	6 (5.45)	[2.03 -11.49]	1.000	71 (64.55)	[54.85 -73.43]	0.436	20 (18.18)	[11.47 -26.67]	0.180	13 (11.82)	[6.45 -19.36]	0.520
Male (55.47%)	36.41 (±13.73)	137	4 (2.92)	[0.80 -7.31]	0.015	72 (52.55)	[43.85 -61.14]	0.347	46 (33.58)	[25.74 -42.14]	0.162	15 (10.95)	[6.26 -17.42]	1.000
Univentricular Heart	32.75 (± 9.21)	68	9 (13.24)	[6.23 -23.64]	< 0.0001	47 (69.12)	[56.74 -79.76]	0.020	9 (13.24)	[6.23 -23.64]	0.001	3 (4.41)	[0.92 -12.36]	0.114
Female (42.65%)	34.93 (±10.06)	29	8 (27.59)	[12.73 -47.24]	<0.0001	18 (62.07)	[42.26 -79.31]	1.000	2 (6.90)	[0.85 -22.77]	0.029	1 (3.45)	[0.09 -17.76]	0.357 0.0003 ^c
Male (57.35%)	31.13 (±8.29)	39	1 (2.56)	[0.06 -13.48]	0.234	29 (74.36)	[57.87 -86.96]	0.001	7 (17.95)	[7.54 -33.53]	0.005	2 (5.13)	[0.00 -12.05]	0.312
Italian reference Population		145 992	4672	[3.09 -3.31]		79 712	[54.27 -54.93]		46 279	[31.40 -32.00]		15 392	[10.30 -10.80]	
Female		71 536	4049	[5.46 -5.86]		43 408	[60.22 -61.14]		17 026	[23.39 -24.21]		7053 (9.86)	[9.57 -10.16]	
Male		74 455	506	[0.61 -0.75]		36 029	[47.92 -48.86]		29 559	[39.23 -40.17]		8369	[10.93 -11.55]	

CI 95% = 95% Confidence Interval.

Bold type is used to indicate the sum of subgroups.

^a p for comparison with Italian reference Population.

^b p calculated with X² test to evaluate the association between weight status categories and sex.

^c p calculated with Fisher test to evaluate the association between weight status categories and sex.

overweight was lower, but not significantly, for simple (24.45%) and moderate (28.54%) complexity classes (Fig. 2C).

Men were more overweight than women in the total ACHD population (34.64% vs 20.49%) and in every complexity class (Table 2).

Overweight tended to increase with age in every complexity class (Table 3).

Obesity

Obesity was statistically similar in the Italian reference population and in the total ACHD population (10.50% vs 9.58%), so as in simple (9.92%) and moderate (10.90%) complexity classes. For the great complexity class the prevalence of obesity was significantly lower (3.08%) (Fig. 2D).

Considering stratification by sex, the levels of obesity were higher in ACHD women than in men (10.70% vs 8.17%).

The distribution of obesity by sex was not homogeneous in the different complexity classes (Table 2).

Obesity increased with age in our total sample, as well as in all the complexity classes (Table 3).

Using a diagnostic anatomical-functional classification, the prevalence of each weight status was the following.

Normal weight

We found that normal weight was similar to the Italian population in every diagnostic category (Fig. 3B).

Underweight

The prevalence of underweight was significantly higher than the Italian reference population particularly for Univentricular heart, Conotruncal heart diseases and for Septal heart defects & lesions with Left-to-Right Shunt.

The prevalence of underweight was higher, but not significantly, for Valve defects, Atrioventricular and/or Ventriculo-arterial discordance & Aortic defects (Table 2 and Fig. 3A).

ACHD women were more underweight than men in every diagnostic category (Table 2).

Underweight tended to increase with age in every diagnostic category (Table 3).

Overweight

We found a significantly lower prevalence of overweight particularly in the Conotruncal heart diseases category (21.53%) and in the Univentricular heart category (13.24%) compared to the Italian reference population (31.70%). The prevalence of overweight was lower, but not significantly, for Septal heart defects & lesions with Left-to-Right Shunt (29.06%) and Valve defects, Atrioventricular and/or Ventriculoarterial discordance & Aortic defects (26.72%) (Fig. 3C).

Table 3 BMI distribution by age class.

	N. total	Under weight n (%)	CI 95%	p ^a	Normal weight n (%)	CI 95%	p ^a	Over weight n (%)	CI 95%	p ^a	Obese n (%)	CI 95%	p ^a	p
TOTAL (n%)	1388	88 (6.34)	[5.12–7.75]	< 0.0001	796 (57.35)	[54.70–59.97]	0.042	371 (26.73)	[24.42–29.15]	< 0.0001	133 (9.58)	[8.08–11.25]		0.272
18–34 years (33.65%)	467	50 (10.71)	[8.05–13.87]	<0.0001	320 (68.52)	[64.10–72.71]	0.801	75 (16.06)	[12.85–19.71]	0.036	22 (4.71)	[2.98–7.05]	1.000	<0.0001 ^b
35–49 years (37.54%)	521	24 (4.60)	[2.97–6.78]	0.024	310 (59.50)	[55.15–63.75]	0.120	142 (27.26)	[23.47–31.30]	0.046	45 (8.64)	[6.37–11.39]		0.457
50–69 years (28.82%)	400	14 (3.50)	[1.93–5.80]	0.002	166 (41.50)	[36.63–46.50]	0.577	154 (38.50)	[33.71–43.46]	0.506	66 (16.50)	[13.00–20.51]		0.531
COMPLEXITY														
Simple	827	48 (5.80)	[4.31–7.62]	< 0.0001	470 (56.83)	[53.38–60.24]	0.207	227 (27.45)	[24.43–30.63]	0.009	82 (9.92)	[7.96–12.16]		0.609 <0.0001 ^b
18–34 years (%)	230	23 (10.00)	[6.45–14.63]	0.019	155 (67.39)	[60.92–73.41]	0.617	39 (16.96)	[12.34–22.44]	0.282	13 (5.65)	[3.04–9.47]		0.540
35–49 years (%)	315	15 (4.76)	[2.69–7.73]	0.042	189 (60.00)	[54.36–65.45]	0.172	84 (26.67)	[21.86–31.91]	0.077	27 (8.57)	[5.72–12.23]		0.567
50–69 years (%)	282	10 (3.55)	[1.71–6.42]	0.008	126 (44.68)	[38.78–50.69]	0.578	104 (36.88)	[31.24–42.80]	0.102	42 (14.89)	[10.95–19.59]		0.934
Moderate	431	19 (4.41)	[2.67–6.80]	0.168	242 (56.15)	[51.32–60.89]	0.529	123 (28.54)	[24.32–33.06]	0.168	47 (10.90)	[8.12–14.24]		0.814 <0.0001 ^b
18–34 years (%)	169	12 (7.10)	[3.72–12.07]	0.520	122 (72.19)	[64.79–78.80]	0.405	28 (16.57)	[11.30–23.05]	0.290	7 (4.14)	[1.68–8.35]		0.857
35–49 years (%)	155	6(3.87)	[1.43–8.23]	0.460	84 (54.19)	[46.01–62.21]	0.686	48 (30.97)	[23.80–38.88]	0.931	17 (10.97)	[6.52–16.98]		0.586
50–69 years (%)	107	1 (0.33)	[0.00–2.27]	1.000	36 (36.64)	[24.80–43.42]	0.063	47 (43.93)	[34.34–53.85]	0.695	23 (21.50)	[13.71–29.28]		0.081
Great	130	21 (16.51)	[10.29–23.63]	< 0.0001	84 (64.62)	[55.75–72.80]	0.022	21 (16.15)	[10.29–23.63]	< 0.0001	4 (3.08)	[0.84–7.69]		0.003 0.0030 ^c
18–34 years (%)	68	15 (22.06)	[12.90–33.76]	<0.0001	43 (63.24)	[50.67–74.61]	0.296	8 (11.76)	[5.22–21.87]	0.096	2 (2.94)	[0.36–10.22]		0.775
35–49 years (%)	51	3 (5.88)	[1.23–16.24]	0.178	37 (72.55)	[58.26–84.11]	0.023	10 (19.61)	[9.82–33.12]	0.071	1 (1.96)	[0.00–5.77]		0.059
50–69 years (%)	11	3 (27.27)	[6.02–60.97]	<0.0001	4 (36.36)	[7.94–64.79]	0.767	3 (27.27)	[6.02–60.97]	0.379	1 (9.09)	[0.00–26.08]		1.000
DIAGNOSTIC CATEGORIES														
Septal Heart defects & lesions with Left-to-Right Shunt	864	46 (5.32)	[3.92–7.04]	0.001	478 (55.32)	[51.94–58.67]	0.681	251 (29.06)	[26.04–32.20]	0.099	89 (10.30)	[8.35–12.52]		0.868
18–34 years (25.46%)	220	22 (10.00)	[6.37–14.75]	0.023	153 (69.55)	[63.00–75.55]	0.942	33 (15.00)	[10.56–20.42]	0.075	12 (5.45)	[2.85–9.33]		0.639 <0.0001 ^b
35–49 years (38.20%)	330	12 (3.64)	[1.89–6.27]	0.403	201 (60.90)	[55.41–66.21]	0.084	91 (27.58)	[22.82–32.74]	0.137	26 (7.88)	[5.21–11.33]		0.304
50–69 years (36.34%)	314	12 (3.82)	[1.99–6.58]	0.002	124 (39.49)	[34.05–45.13]	0.230	127 (40.45)	[34.97–46.10]	0.954	51 (16.24)	[12.34–20.80]		0.638
Conotruncal Heart diseases	209	23 (11.00)	[7.11–16.05]	< 0.0001	128 (61.24)	[54.28–67.89]	0.060	45 (21.53)	[16.16–27.73]	0.001	13 (6.22)	[3.35–10.40]		0.042

18–34 years (45.93%)	96	15 (15.63)	[9.02 –24.46]	0.001	63 (65.62)	[55.23 –75.02]	0.507	17 (17.71)	[10.67 –26.83]	0.701	1 (1.04)	[0.03–5.67]	0.093	0.0172 ^c
35–49 years (38.76%)	81	7 (8.64)	[2.52 –17.00]	0.009	47 (58.02)	[46.54 –68.91]	0.738	19 (23.46)	[14.75 –34.18]	0.150	8 (9.88)	[4.36 –18.54]	0.852	
50–69 years (15.31%)	32	1 (3.12)	[0.00–9.15]	0.370	18 (56.25)	[37.66 –73.64]	0.153	9 (28.13)	[13.75 –46.75]	0.207	4 (12.50)	[3.51 –28.99]	0.809	
Valve defects, Atrioventricular and/or Ventriculoarterial discordance & Aortic defects	247	10 (4.05)	[1.96–7.32]	0.465	143 (57.89)	[51.47 –64.13]	0.307	66 (26.72)	[21.31 –32.70]	0.100	28 (11.34)	[7.67 –15.97]	0.678	
18–34 years (44.13%)	109	6 (5.50)	[2.05 –11.60]	1.000	75 (68.81)	[59.22 –77.34]	1.000	21 (19.27)	[12.34 –27.93]	1.000	7 (6.42)	[2.62 –12.78]	0.499	0.0108 ^c
35–49 years (34.41%)	85	3 (3.53)	[0.73–9.97]	0.737	45 (52.94)	[41.81 –63.87]	0.586	27 (31.76)	[22.08 –42.76]	1.000	10 (11.76)	[5.79 –20.57]	0.465	
50–69 years (21.46%)	53	1 (1.89)	[0.05 –10.07]	0.534	23 (43.40)	[29.84 –57.72]	1.000	18 (33.96)	[21.52 –48.27]	0.402	11 (20.75)	[10.84 –34.11]	0.256	
Univentricular Heart	68	9 (13.24)	[6.23 –23.64]	< 0.0001	47 (69.12)	[56.74 –79.76]	0.020	9 (13.24)	[6.23 –23.64]	0.001	3 (4.41)	[0.92 –12.36]	0.114	
18–34 years (61.76%)	42	7 (16.67)	[6.97 –31.36]	0.013	29 (69.05)	[52.91 –82.38]	1.000	4 (9.52)	[2.66 –22.62]	0.120	2 (4.76)	[0.58 –16.16]	1.000	0.6803 ^c
35–49 years (36.76%)	25	2 (8.00)	[0.98 –26.03]	0.159	17 (68.00)	[46.50 –85.50]	0.314	5 (20.00)	[6.83 –40.70]	0.283	1 (4.00)	[0.1–20.35]	0.507	
50–69 years (1.47%)	1	0 (0.00)			1 (100.00)	[2.5 –100.00]	0.430	0 (0.00)			0 (0.00)			
Italian reference Population	145 992	4672 (3.20)	[3.09–3.31]		79 712 (54.60)	[54.27 –54.93]	46 279 (31.70)		[31.4–32.0]		15 392 (10.50)	[10.3–10.8]		
18–34 years	39 272	2392 (6.09)	[5.81–6.38]		27 121 (69.06)	[68.43 –69.67]	7839 (19.96)		[19.42 –20.51]		1924 (4.90)	[4.60–5.21]		
35–49 years	50 075	1427 (2.85)	[2.68–3.03]		28 057 (56.03)	[55.46 –56.60]	15 729 (31.41)		[30.88 –31.95]		4857 (9.70)	[9.35 –10.07]		
50–69 years	56 499	808 (1.43)	[1.32–1.55]		24 272 (42.96)	[42.44 –43.48]	22 758 (40.28)		[39.75 –40.81]		8667 (15.34)	[14.95 –15.73]		

CI 95% = 95% Confidence Interval.

Bold type is used to indicate the sum of subgroups.

^a p for comparison with Italian reference Population.

^b p calculated with X² test to evaluate the association between weight status categories and age categories.

^c p calculated with Fisher test to evaluate the association between weight status categories and age categories.

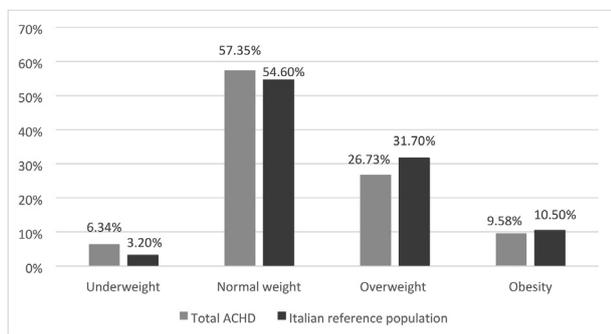


Figure 1 BMI distribution in ACHD population versus Italian reference population.

ACHD men were more overweight than women in every diagnostic category (Table 2). Overweight tended to increase with age in every diagnostic cluster, except for Univentricular heart (Table 3).

Obesity

Obesity was statistically similar in the Italian reference population, in Valve defects, Atrioventricular and/or Ventriculoarterial discordance& Aortic defects (11.34%) and in Septal heart defects & lesions with Left-to-Right Shunt (10.30%). For Conotruncal heart diseases (6.22%) and even Univentricular heart (4.41%) the percentages were lower, but not significantly (Fig. 3D).

The distribution of obesity by sex was not homogeneous in the different diagnostic categories (Table 2).

Obesity increased with age in all the diagnostic subgroups except for Univentricular heart (Table 3).

Discussion

To the best of our knowledge, this is the first retrospective study in Italy focusing on BMI of ACHD hospitalized patients, who represent a selected population of symptomatic ACHD.

This could affect the generalizability to the total ACHD population, which is estimable in Italy in 80.000–100.000 individuals [21].

The main observations on this population are the following:

- Underweight was double that of the Italian reference population. ACHD women were more underweight than ACHD men. Underweight was more prevalent in younger patients and decreased with age.
- The prevalence of overweight was lower than the Italian reference population, but similar for obesity. Men were more overweight than women and both overweight and obesity increased with age.
- When we considered the Bethesda classification, we found that the highest prevalence of underweight and the lowest prevalence of overweight and obesity have been observed in the complex cardiac diseases.
- Comparing the different anatomical-functional categories the results were similar. In particular, ACHD with Univentricular heart and Conotruncal heart diseases

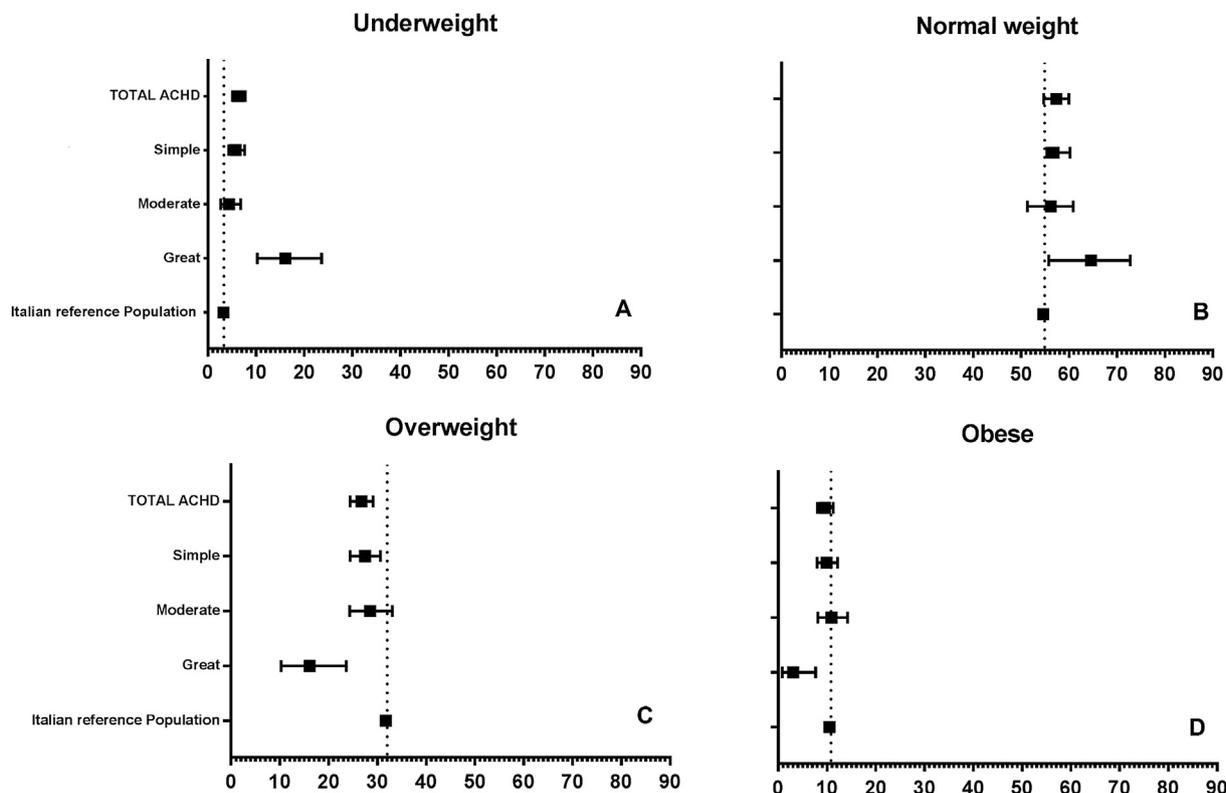


Figure 2 Distribution of ACHD complexity classes by Bethesda classification in each BMI class (underweight, normal weight, overweight, obese) compared to the Italian reference population.

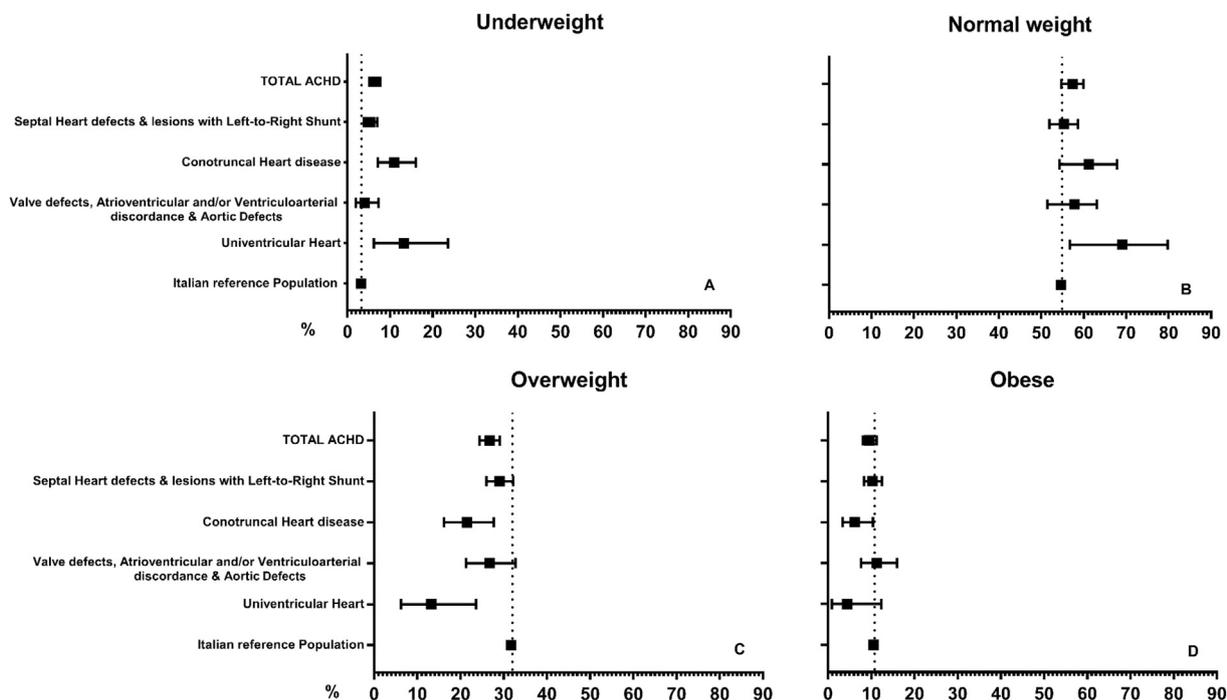


Figure 3 Distribution of ACHD diagnostic categories in each BMI class (underweight, normal weight, overweight, obese) compared to the Italian reference population.

had the highest prevalence of underweight and the lowest prevalence of overweight and obesity, particularly among the youngest women.

These findings confirm that hospitalized ACHD are more likely to be underweight than the general population, as reported by others [14–16].

In particular we found underweight to be more common in patients with complex cardiac diseases, as already observed by Brida et al. [15]. In a similar way, considering the anatomical-functional diagnostic classification, patients affected by Univentricular Heart and Conotruncal heart diseases had the greatest prevalence of underweight.

In contrast with Sandberg’s report [14], we found that women tended more to be underweight than men, and this mirrored the general trend in Italy. Furthermore, as also reported by Lerman [16], in our cohort underweight was clearly more common in younger people than in the oldest age class. We can speculate that in some CHD patients the functional cardiac defect, starting in early childhood, might affect growth and development [22,23] and this could be borne out by our findings.

Underweight is an established negative prognostic factor in acquired heart failure [23] and for mortality [8,24]. In Brida’s study [15] underweight ACHD had worse outcomes. They also found that weight loss in complex ACHD was linked to even higher mortality. Patients with a low BMI probably have less muscle mass and consequently could be at higher risk of sarcopenia and cachexia. One possible cause of the reduced muscle mass could be a low level of physical activity. In fact, inactivity is generally common among ACHD and sport is not properly prescribed, though not always actually discouraged [25–27].

In our ACHD hospitalized cohort, the prevalence of overweight was lower than the Italian reference population, although it was still considerable. However, obesity was statistically similar. From published data [15,16] it would seem that our ACHD population was less overweight than the English ACHD population studied by Brida [15], and also the ACHD of the Icahn School of Medicine at Mount Sinai, New York, studied by Lerman [16]. Moreover, our ACHD men were more often overweight than women, and both overweight and obesity increased with age, as already noted by Brida and Lerman [15,16]. Globally, excess weight constitutes a cardiovascular and metabolic risk factor. Adiposity and particularly abdominal fat are associated with an increased risk of metabolic syndrome, hypertension, insulin resistance, diabetes mellitus and dyslipidemia, each of which raises the risk of myocardial infarction and may thus boost the risk of heart failure [28].

To date there are only few studies in the world – and none in Italy - that have dealt with weight status in ACHD, and the data are conflicting [14–16,29,30]. The link between BMI and long-term prognosis is still not clear. Brida et al. [15] found in their ACHD cohort that overweight or moderate obesity was associated with lower mortality. This would seem consistent with the so-called “obesity paradox”, even though on the whole the lifetime risk of cardiovascular diseases and morbidity seems to be associated with BMI in obese and overweight persons [31].

On the other hand, Lui et al. stated that ACHD patients are particularly vulnerable to atherosclerotic cardiovascular disease risk factors with aging [5,32]. In addition, Deen et al. [33] found metabolic syndrome was more common among ACHD than in the general population. Furthermore, specific corrected heart defects in ACHD might not be well

tolerated or might deteriorate more rapidly in the presence of additional cardiovascular risk factors, and obesity-correlated complications might have dramatic consequences over time on repaired hearts [7]. Therefore, modifiable risk factors, such as physical inactivity, obesity, systemic hypertension, dyslipidemia, diabetes and smoking, should be carefully screened and managed [5,32].

In the future, it would be recommendable for clinicians and health providers always to record carefully their patients' anthropometric parameters - weight and height - in order to calculate BMI, and to continuously monitor the prevalence of underweight, overweight and obesity in ACHD. Thus, it might also be possible to improve the prognostic role of BMI. BMI is the most widely used measure of obesity, but it does not account for body composition and fat distribution. A future goal will therefore be to quantify the visceral component of the adipose tissue in ACHD, especially in underweight patients. Besides BMI, a simple way to evaluate the central distribution of adipose tissue - which is an independent indicator of cardiovascular risk - would be to check an anthropometric parameter such as waist circumference. The assessment of body composition will be essential to measure fat-free and fat mass, so as to plan better and verify the effectiveness of educational interventions on nutrition and physical activity. Lifestyle and nutritional counseling would in all probability be beneficial in all CHD patients. It could help underweight patients to gain weight and avoid malnutrition and sarcopenia, and help overweight or obese patients, particularly those with abdominal obesity, to improve their body composition and reduce cardio-metabolic risks.

Limitations

In our register, like in some others, there is no data for the moment on body composition and waist circumference as simple measures of visceral obesity. This was an observational study with no prognostic purpose but simply illustrates the weight status of an ACHD sample.

Our study refers to a selected population of symptomatic patients who needed a surgical intervention or interventional catheterization and this could affect the generalizability to the total ACHD population.

As regard the Italian reference population, the fact that anthropometric data were self-reported may constitute a further limitation.

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Conflicts of interest

The authors declare they have no competing interests to declare.

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