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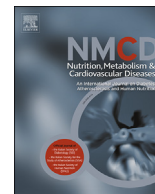
RESEARCH PAPER

Longitudinal trends of body composition in Anorexia Nervosa: Cardiac functioning impacts the restoration of fat-free mass at three-months follow-up

Livio Tarchi [a], Emanuele Cassioli [a], Eleonora Rossi [a], Marco Faldi [a], Eleonora D'Areglia [b], Gaia Maiolini [b], Anita Nannoni [b], Valentina Scheggi [c], Brunetto Alterini [c], Valdo Ricca [a], Giovanni Castellini [a,*]

[a] Psychiatry Unit, Department of Health Sciences, University of Florence, AOU Florence, 50134, Italy
[b] Dietetics Unit, Careggi University Hospital, Florence, 50134, Italy
[c] Division of Cardiovascular and Perioperative Medicine, Careggi University Hospital, Florence, 50134, Italy

Abstract *Background and aims:* Predictors of outcomes are needed in order to improve the clinical management of patients with Anorexia Nervosa (AN). The present study evaluated whether cardiac dysfunction might be associated with different longitudinal outcomes of AN.
Methods and results: A sample of 35 patients with AN (11 restricting, 24 binge-purging– age range 16−28 years old) and 42 healthy controls (18−29 years old) were evaluated in terms of psychometric variables, Body Mass Index (BMI), body composition (by bioimpedance analysis, namely: Fat-Free Mass − FFM, Fat Mass − FM, Body Cell Mass − BCM, Phase Angle - PhA) and cardiac functioning (left ventricular ejection fraction - LVEF; global longitudinal strain − LVGLS). FM was significantly and negatively associated with eating psychopathology (weight and shape concerns, b −0.523, p 0.029; and shape concerns b −0.578, p0.015), while cardiac dysfunction (LVGLS > −18%) was positively associated with dietary restraints (b 1.253, p 0.043). LVEF, in turn, was positively associated with BCM (b 0.721, p 0.008) and FFM (b 0.779, p 0.039). Cardiac dysfunction negatively impacted the effect of nutritional rehabilitation, as those patients reporting reduced LVGLS showed lower FFM (b −4.410, p 0.011), FM (b −1.495, p 0.003) and BCM (b −2.205, p 0.015) at follow-up after three months.
Conclusion: These preliminary results showed that cardiac functioning might represent an early predictor of cachexia and chronicity, while body composition seems to be a more accurate measure for evaluating the recovery process of patients with AN.

1. Introduction

Anorexia Nervosa (AN) is a disabling condition, frequently complicated by a chronic course [1,2]. AN may also be often worsened by severe medical consequences [3−5]. The heterogeneity of treatment response among patients with AN has been attributed to different patterns of psychopathological and clinical presentations of the underlying disorder [6]. A better characterization of these patterns of clinical presentation might identify specific targets of interventions in the perspective of precision medicine [7,8]. In fact, it has been reported that current diagnostic criteria adopted to assess illness severity in AN may not fully align with the burden of reported symptoms [9]. A clinical orientation towards precision medicine could also tackle the issue of medical complications among patients with AN.

In particular, cardiovascular events have long represented a dreaded complication in these patients [10−12]. However, even though cardiac remodeling has been associated with life threatening adverse cardiac events [13], this factor has not still been conceptualized as a prognostic factor in the recovery process of patients with AN. Cardiac remodeling in AN has been mainly studied by the degree of impairment to the Left-Ventricular Ejection Fraction (LVEF).[1] Nonetheless, the current literature has also focused on a novel marker, the Left-Ventricular Global Longitudinal Strain (LVGLS), which is considered a more sensitive estimate of the myocardial deformation along the longitudinal axis of the left ventricle [15−18].

Indeed, LVGLS may be capable of detecting early signs of myocardial dysfunction, prior to clinical abnormalities or objectifiable symptoms [19]. LVGLS has been described as mostly reduced in its absolute value for conditions of frailty, and it has also been shown to have a prognostic potential over several medical conditions, such as aortic stenosis [18], COVID-19 [16], or chemotherapy-induced cardiotoxicity [17,20].

In psychiatry, LVGLS has been described as altered across a variety of conditions, including post-COVID psychological distress [21], bipolar disorder [22], borderline personality disorder [23], and AN [24−26]. This biomarker may thus offer prognostic novel insight by leveraging on early signs of cardiac dysfunction [27], a significant contribution to morbidity and mortality in AN [28]. However, to the present day, a more accurate description of the relationship between body composition and LVGLS in AN is lacking.

Besides predictors of treatment response, the characterization of patients with AN should also be improved in terms of outcome measures. For instance, bioimpedance analysis (BIA) might offer a better representation than BMI of the clinical conditions in patients with AN. BIA evaluates body composition (the relative levels of fat-free mass − FFM - and fat mass − FM) as well the degree of metabolic distress (body cell mass − BCM − a sum of all metabolically active cells in the body [29,30]; phase angle − PhA,

reflecting hydration status and possibly overall physical activity [31,32]). In fact, BIA has been indicated as a more accurate marker of severity than BMI in patients with AN [33], especially when used to assess longitudinal trajectories of weight restoration [34,35]. BIA, as a clinical instrument, might also be able to better capture the heterogeneity between patients. Indeed, a recent meta-analysis showed that patients with AN could maintain altered values in body composition as assessed by BIA, despite reaching a normalization in BMI, thus indicating that body composition might still be altered even after weight restoration [36].

1.1. Aims

Based on the abovementioned evidence, the present study aimed at exploring the role of cardiac functioning (either by LVEF or LVGLS) as a potential marker of different clinical stages for patients with AN. To test this role, a longitudinal observation of patients assessed before and after a nutritional intervention was performed adopting either BMI, or body composition parameters - as assessed by BIA, as outcome measures.

2. Methods

2.1. Sample

A consecutive series of female patients who attended the Eating Disorders Clinic of Florence University Hospital for the first time seeking outpatient care was enrolled, between March 2020 and December 2022, provided they met the following inclusion criteria: female sex, female gender, age between 18 and 65 years, diagnosis of AN according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [37], as assessed by the Structured Clinical Interview for DSM-5 Disorders, Clinician Version [38]. Exclusion criteria were as follows: illiteracy, intellectual disability, presence of psychotic symptoms, severe depression, or manic state at the time of enrollment, current suicidal ideation, and lack of written informed consent. The sample consisted of 35 patients with AN (11 AN restricting − AN-r, and 24 AN binge/purging − AN-bp).

A sample of 42 women from the general population was also recruited. Healthy controls were sampled within university and higher education settings, in order to tentatively match participants in terms of age. Controls were gender and sex-matched, only cisgender women were enrolled. Controls were screened for psychiatric disorders by the Structured Clinical Interview for DSM-5 Disorders, Clinician Version [38] before enrolment. Body composition and cardiac functioning were investigated, equally than in the clinical group of patients with AN. The inclusion criteria were as follows: female sex, female gender, age between 18 and 65 years, no current diagnosis of psychiatric disorder, no history of Schizophrenia, Bipolar Disorder, Eating Disorder. Exclusion criteria were as follows: illiteracy, intellectual disability, lack of written informed consent.

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[1] A measure of functional efficiency of the heart - and, therefore, one of the most employed markers to classify heart failure [14].

2.2. Study design and assessment

Eligible patients with AN were offered a 3-month clinical program at the University Hospital of Florence. On their first day at the clinic, patients were evaluated for their anthropometric measures from which BMI were calculated. Their body composition was also assessed at the time of first evaluation by the dietician through bio-impedance analysis (BIA). The dietician, in agreement with the patient, formulated a personalized diet to be followed, typically composed of three main meals and two snacks, to be consumed within the clinic. Echocardiography was performed with a maximum latency of two weeks. Patients were then followed up weekly for their BMI and nutritional rehabilitation program by the same dietician, and again after 3 months along BIA.

Patients also received a clinical and psychometric evaluation during the first psychiatric visit. All participants were asked to complete the following self-administered tests using validated Italian versions:

- Symptom Checklist-90-Revised (SCL-90), a 90-item self-reported symptom inventory to assess psychological symptoms and mental distress. It is composed of a global score (Global Severity Index, GSI) to measure overall psychological distress level. Higher scores indicate more severe psychological distress. The Cronbach's alpha value for the general scale containing all items was 0.96 [39].
- Eating Disorder Examination Questionnaire 6.0 (EDE-Q), a 28-item self-reported questionnaire to evaluate the range, frequency, and severity of behaviors associated with an Eating Disorder (ED) diagnosis. EDE-Q provides a global score (EDE Total Score) and is categorized into 4 subscales (EDE Restraint; EDE Eating Concerns; EDE Shape Concern; EDE Weight Concern). Higher scores correspond to higher levels of psychopathology. The Cronbach's alpha for each subscale ranges between 0.79 and 0.94 [40].

2.2.1. Nutritional status and Bioelectrical Impedance Analysis (BIA)

A multi-frequency segmental body composition analyzer (Akern© BIA 101, BIVA PRO) was used to obtain whole and compartmental body composition data. Data were collected while participants lied on a flat mattress, with foot and hand-electrodes in place. Four indices of body composition were calculated: PhA, BCM, FM, FFM. PhA is an index of hydration and possibly physical activity [31,32]. BCM is an indicator of nutritional status, and assesses the weight of metabolically active mass, offering the possibility of discerning between total body weight and the effect of extracellular water [41]. FM and FFM represent the body weight of the respective components [30]. Normalized ratios were then computed according to the literature on the topic [42,43], firstly dividing the absolute value for height (FFM/m, FM/m and BCM/m), then as a percentage (FFM and FM divided by total weight — FFM% and FM%,

respectively, multiplicative inverses of each other; BCM divided by FFM — BCM%).

2.2.2. Echocardiography

In order to minimize inter-rater variability, a single medical doctor, expert in the field of cardiac imaging (V.S.), evaluated each patient by 2D speckle tracking. A General Electric VIVID E9 (General Electric, Fairfield, Connecticut) device was used. Images were analyzed using the EchoPAC Software package (GE Healthcare) with a 17 segments model. Left ventricular mass was calculated with the Devereux formula as

$$0.8 \times 1.04 \times [(LVeDD + IVS + PW) - LVeDD] + 0.6$$

Left ventricular systolic function was estimated by calculating the LV ejection fraction (LVEF, %) following the biplane approach. In healthy individuals, LVEF ranges between 50 and 65% [44], and a LVEF below 50% is currently conceptualized as moderately reduced for what concerns heart failure [45].

The left ventricular global longitudinal strain (LVGLS) was obtained through standard echocardiographic evaluation by analyzing the peak values of longitudinal strain (ΔL) in the left ventricle, which measures the degree of left ventricle deformation through the cardiac cycle and, therefore, myocardial function in this region. In healthy patients, the average peak GLS ranges from -18% to -20% [25]. The degree of peak GLS is mostly reduced in its absolute value for conditions of frailty (i.e. a higher strain - lower in absolute values - represents worse cardiac function). Myocardial longitudinal strain (ΔL) was calculated using the following formula:

$$\Delta L = (L_s - L_d)/L_d$$

where L_s is the end-systolic length of a segment and L_d is its end-diastolic length. The overall LVGLS derives from ΔL data of six individual segments (i.e. basal, mid, and apical interventricular septum, as well as apical, mid, and basal lateral wall).

Cardiac functioning was then dichotomized as categorical, dividing the sample by clinical cut-offs (above -18% for LVGLS, below 50% for LVEF). The dichotomization was performed as the effect of cardiac dysfunction was not hypothesized to be continuous, but rather categorical in nature, affecting only those patients beyond a severity threshold. In other words, the effect given by cardiac dysfunction was not hypothesized as dimensional and gradual, but as impacting recovery only when pathological, in line with the empirical evidence on the topic [46].

2.3. Power analysis

The sample size was calculated a priori by G*Power 3.1.9.7. The following settings were used: model ANOVA repeated measures, within-between interactions; effect size 0.25; alpha 0.05; power 0.95; number of groups 2; number of measurements 2; correlation among repeated measures

0.7. The sample size derived from this calculation was a total sample of 34 patients.

2.4. Statistical analysis

Sample descriptives were illustrated by means and standard deviations, their mean difference computed, and their statistical difference calculated by ANCOVA. Associations between body composition and psychopathological characteristics or cardiac functioning were estimated by linear regressions, adjusted for age, BMI, and duration of illness. Cardiac functioning was described both as a continuous and categorical variable (dichotomous, according to clinical cut-offs: above −18% for LVGLS and below 50% for LVEF; [17,46]). No patient in the sample was found with LVEF below 50% (minimum 55%, maximum 68%). By contrast, 17 patients exhibited LVGLS above −18% (48.57%; maximum −14.4%, minimum - 23.2%). Longitudinal mixed models were computed to estimate longitudinal trends for body composition parameters. Analyses of interaction between effects were similarly computed, with time, diagnostic subtype or cardiac functioning, and an interaction term with time as fixed effects. Significant effects were graphically represented. An a priori threshold of p = 0.05 was chosen for statistical significance. Analyses were performed using R 4.3.3 [47], with the support of the following libraries: *tidyverse* [48], s*ciplot* [49].

2.5. Data availability, ethics approval

The data and code supporting the present study can be shared upon reasonable request to the corresponding author, as they can contain potentially sensitive clinical information. The study protocol was approved by the ethics committee of the local institution (Comitato Etico Regione Toscana—Area Vasta Centro, protocol code OSS.14.162). The study was conducted in accordance with the guidelines of the Declaration of Helsinki of 1964 and subsequent amendments.

3. Results

3.1. Descriptive statistics

Patients with AN showed a lower BMI in comparison to controls. Patients and controls did not differ for age and education. Patients exhibited a lower BCM, FM, FFM and higher PhA in comparison to controls (both in terms of normalized weights and percentage of total mass). No difference was observed between AN-r and AN-bp for duration of illness. However, AN-bp reported higher eating concerns (Hedges' g 0.715, F-value 121.164, p < 0.001) and higher PhA (Hedges' g 0.790, F-value 4.930, p 0.033) in comparison to AN-r. As expected, AN patients scored significantly higher on the EDE questionnaire and the SCL-90 in comparison to healthy controls. Moreover, LVGLS was significantly elevated in controls in comparison to patients with AN. See Table 1 for further details.

3.2. Body composition, cardiac functioning, and psychopathology

Body composition was not associated with general psychopathology. However, a significant association between BMI and eating concerns was observed. By contrast, FM/m and FM% were significantly associated with weight and shape concerns, as well as EDE total score (β −0.483, p 0.027, β 0.592, p 0.018; respectively). Cardiac dysfunction (as assessed by LVGLS above −18%) was significantly and positively associated with EDE Restraint scores (β 1.253, p

Table 1 Sample descriptives.

	AN	Controls	Hedges' g	F-Value	p-value
N	35	42	/	/	/
Age (years)	21.65 (±3.03)	22.27 (±2.32)	0.163	1.033	0.313
Education (years)	13.69 (±2.08)	13.54 (±1.62)	0.081	0.127	0.723
Duration of illness (years)	4.28 (±5.77)	/	/	/	/
BMI	15.96 (±1.77)	21.77 (±2.23)	2.856	155.707	<0.001
EDE Restraint	4.00 (±1.64)	0.84 (±1.06)	2.333	103.972	<0.001
EDE Eating Concern[a]	3.87 (±1.22)	0.51 (±0.67)	3.503	234.235	<0.001
EDE Shape Concern	4.69 (±1.26)	1.82 (±1.33)	2.210	93.229	<0.001
EDE Weight Concern	3.98 (±1.34)	1.50 (±1.26)	1.912	69.812	<0.001
EDE Total Score	4.13 (±1.16)	1.17 (±0.99)	2.765	145.984	<0.001
SCL-90 GSI	1.84 (±0.67)	0.84 (±0.67)	1.493	42.528	<0.001
Fat-Free Mass (FFM, kg/m)	23.50 (±2.63)	27.82 (±1.66)	2.005	76.751	<0.001
Fat Mass (FM, kg/m)	2.91 (±1.77)	7.82 (±3.32)	1.799	61.813	<0.001
Body Cell Mass (BCM, kg/m)	12.16 (±1.93)	15.20 (±1.23)	1.917	70.133	<0.001
Phase Angle (deg)[a]	5.47 (±0.57)	6.19 (±0.41)	1.472	41.377	<0.001
Fat-Free Mass (FFM, % on total body weight in kg)	89.40 (±5.22)	78.02 (±7.38)	1.753	58.689	<0.001
Fat Mass (FM, % on total body weight in kg)	10.59 (±5.22)	21.14 (±7.05)	1.678	53.762	<0.001
Body Cell Mass (BCM, % on FFM in kg)[a]	51.71 (±5.50)	54.59 (±1.98)	0.701	9.986	0.002
Left Ventricular Ejection Fraction (LVEF, %)	62.16 (±3.47)	63.57 (±4.15)	0.366	2.552	0.114
Left Ventricular Global Longitudinal Strain (LVGLS, %)[a]	−19.04 (±2.32)	−20.33 (±1.84)	0.623	7.404	0.008

Note: F-value by ANOVA. All significant differences were observed for both for AN-r and AN-bp in comparison to controls.
[a] Post-hoc statistically significant difference, AN-bp > AN-r (p < 0.05, after Tukey correction for multiple comparisons).

0.033). A significant association at baseline between body composition and cardiac functioning was observed (LVEF and BCM, LVEF and FFM). A reduced LVEF was associated with lower FFM and BCM at baseline (β 0.779, p 0.011, β 0.721, p 0.006; respectively). No significant association between LVGLS and body composition was found. See Supplementary Materials Tables S1 and S2 for further results.

3.3. Longitudinal trends of BMI and body composition

A significant difference across time was observed for the whole group of patients, in terms of BMI restoration (Fig. S1, Table S3), while no significant effect was observed for FFM, BCM, and FM. Considering that the lack of significant improvement in the whole sample was hypothesized to be due to heterogeneity of the sample, further analyses were performed dividing the sample on the basis of either: i) diagnostic subtype; ii) cardiac function at baseline. Indeed, according to this last analysis, different trends of changes in body composition were observed across time for LVGLS (significant interaction effect, Table S4).

No significant effect on body composition changes was observed assessing diagnostic subtypes (*BMI as the outcome measure*: timepoint β 0.317, p < 0.001; AN-r β −1.107, p 0.310; *FFM as the outcome measure*: timepoint β 0.071, p 0.865; AN-r β −2.345, p 0.106; *FM as the outcome measure*: timepoint β −0.556, p 0.509; AN-r β −1.288, p 0.640; *BCM as the outcome measure*: timepoint β −0.150, p 0.963; AN-r β −1.609, p 0.132; *PhA as the outcome measure*: timepoint β −0.047, p 0.749; AN-r β −1.96, p 0.414).

No significant effect was observed in terms of body composition in patients without cardiac dysfunction (LVGLS ≤ −18%). On the contrary, for those patients with cardiac dysfunction (LVGLS > −18%), despite an increase in BMI being observed, diverging trends for body composition were noticed, with FM, FFM and BCM showing a reduction across time (FM interaction term with time β −1.495, p 0.003; FFM interaction term with time β −4.410, p 0.011; BMC β −2.205, p 0.015). See Fig. 1 for a graphical representation of results and Supplementary Materials Table S3 for a comparison with the baseline longitudinal model.

4. Discussion

To the best of our knowledge, this is the first study evaluating the role of cardiac impairment as a predictor of outcome in AN, considering the longitudinal variation of body composition. According to the main results, LVGLS was associated with clinical severity of AN before entering the acute treatment and rehabilitation program. Moreover, LVGSL was found to predict the trajectory of body composition restoration in patients with AN after treatment and partial weight restoration.

As previously mentioned, in psychiatry, LVGLS has been described as altered across a variety of conditions, including post-COVID psychological distress [21], bipolar disorder [22], borderline personality disorder [23], and AN [24–26]. This transdiagnostic potential of LVGLS has been mainly interpreted in light of the concept of "allostatic load" [50]. This theoretical framework posits that chronic and repeated stress exerts a somatic burden, disturbing physiological homeostatic mechanisms [51]. For this reason, a higher risk of developing cardiovascular disease may be associated with most psychiatric conditions [51]. In AN, LVGLS might then represent an early biomarker of increased risk for cardiovascular disease [27], a crucial parameter in light of the potential somatic burden exerted by malnutrition and/or possible compensatory behaviors [52]. An early marker of somatic distress may be of crucial importance for the clinical staging of AN, as well as for correctly postulating prognostic outcome at the individual level for affected individuals. In fact, it can be posited that a patient exhibiting alterations in cardiac function (e.g. LVLGLS) may have crossed a threshold of severity, its recovery being potentially compromised.

Although preliminary in nature, the present study also suggested an interplay between body composition and eating psychopathology, namely an association between increased shape concern and increased FFM/decreased FM. This result could be interpreted in light of the reduced dietary intake correlated with eating psychopathology, along with a higher likelihood to engage in physical exercise [53], thus driving the increase in FFM and decrease in FM. Although a biomarker of hydration and possibly physical activity, no significant correlation between PhA and compensatory behaviors was here observed. Future research may thus be interested in further exploring psychopathological or behavioral correlates of PhA in AN. In fact, PhA is consistently observed as decreased in AN in comparison to the general population (Table 1), and PhA may also correctly differentiate patients with worse nutritional status in cross-sectional designs [54,55].

For what pertains to the clinical presentation of patients with AN, a reduced LVEF was associated with a lower FFM and BCM at baseline. Instead, LVGLS, previously described as a sensitive marker of frailty [46], was here able to detect the portion of patients with AN exhibiting a worse longitudinal trajectory of FFM restoration. The role of LVGLS in predicting longitudinal FFM restoration might be better interpreted as a function of diagnostic sensitivity. In fact, as previously mentioned, no single patient was observed below the clinical cut-off for LVEF, almost half of the sample (17/35, 48.57%) showed a LVGLS above the threshold of −18%. From a theoretical perspective, the results of the present study are conceptually coherent with previous observation on different disorders [56–61], namely that once specific threshold of severity is overtaken, the outcome trajectory can be compromised, as a higher effort might be needed to restore homeostasis and respond to metabolic or general distress at the somatic level.

Muscle catabolism is a consistent finding in AN [62], with several empirical results suggesting reduced muscle strength in patients with AN [63,64], possibly correlated to the degree of reduced lean mass [33,64–66]. BIA may be
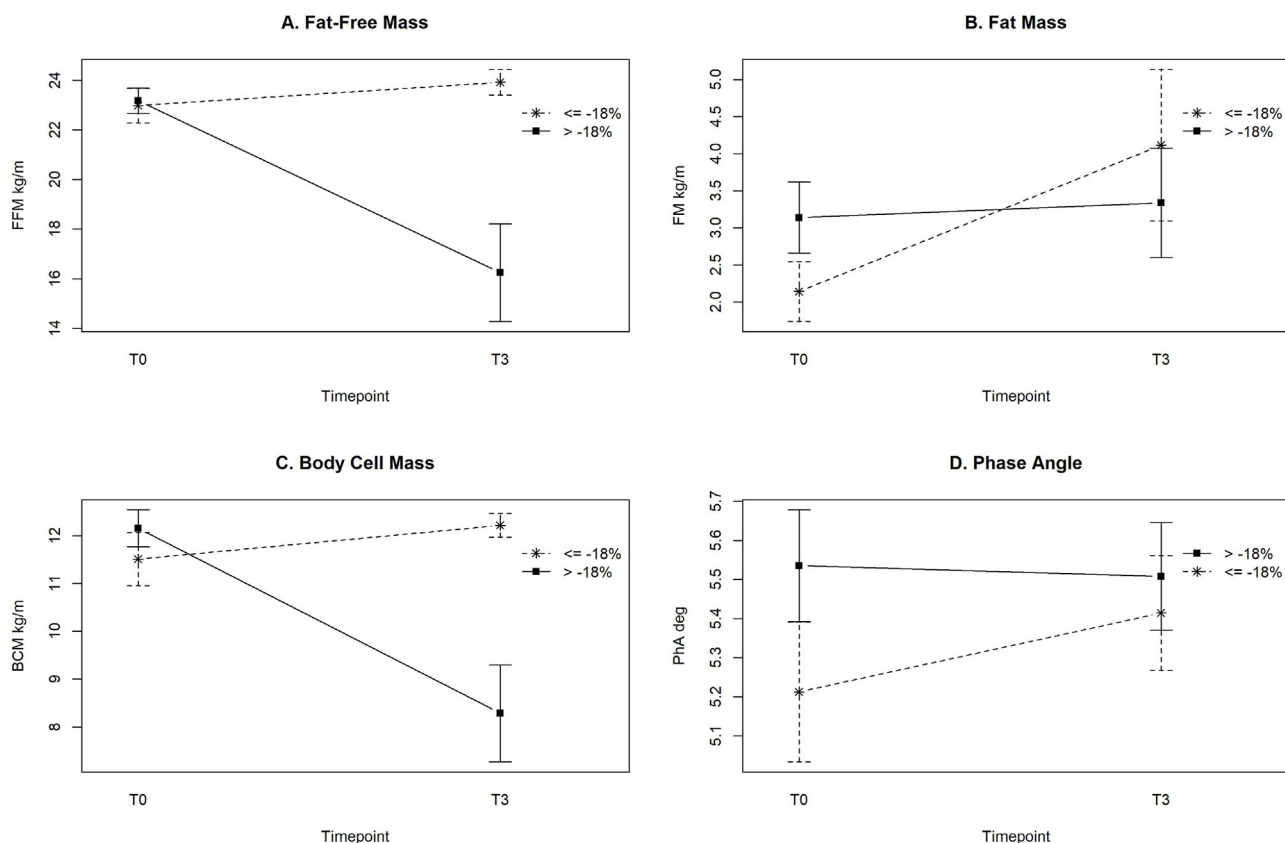
Figure 1 Longitudinal trends of body composition in patients with Anorexia Nervosa, in light of cardiac functioning (Left Ventricular Global Longitudinal Strain − LVGLS − below or above −18%; above −18%, solid line, representing cardiac dysfunction). Error bars represent standard errors.

capable of assessing the degree of muscle catabolism at the individual level in AN, capturing body composition alterations across different stages of illness. LVGLS, on the other hand, may be a sensitive marker of severity, indicating when the individual patient has started to exhibit not only skeletal muscle catabolism, but also myocardial distress. The predictive value of LVGLS might then be tentatively interpreted in terms of muscle catabolism. In other words, LVGLS sensitivity in detecting differential longitudinal trends of body composition might reflect its capability to detect when muscle catabolism has started to impact on the myocardium [36]. Indeed, muscle catabolism can impact either peripheral or central tissues, and over a certain threshold of sarcopenia, myocardial cells might incur metabolic distress [67]. The authors posit that muscle catabolism, and consequent body composition alterations, might be associated with different stages of the illness and outcome trajectories, which are not adequately detected by BMI [34].

As previously mentioned, LVGLS alterations − here posited to also reflect the degree of distress imposed on the myocardium - seem to be able to predict FFM longitudinal trajectories in patients with AN. In particular, patients with AN reporting a relevant alteration for LVGLS showed a decrease of FM, FFM and BCM even though a modest BMI restoration was observed. These results are in line with what was previously described by Hubel and colleagues, namely that body composition may not be fully restored in

weight-recovered patients with AN [36]. However, a significant heterogeneity can be described for what concerns body composition in weight-restored patients (i.e., I^2 - a measure of heterogeneity between studies - observed as above 90% [36]). Interestingly, a cross-sectional study suggested that weight-recovered patients exhibit reduced muscle strength even after long-term weight-stability (~ 27 years) [68]. The authors postulate that addressing the individual degree of cardiac impairment may shed light into potential personalized predictions of outcome. A working hypothesis might be that once cardiac remodeling takes place, a worse trajectory of recovery can be posited, as schematically reported in the model shown in Fig. 2.

In summary, the authors postulate that once the general state of malnutrition starts to tackle not only peripheral muscles, but also visceral lean mass (in particular, the myocardium), the likelihood of recovery is reduced. LVGLS and BIA might then represent affordable and accessible tools for prognosis in AN, assessing whether the patient has crossed its own individual threshold of severity at the time of evaluation for what concerns the somatic burden of pathological eating behaviors.

4.1. Limitations

Although all patients fulfilling inclusion criteria were enrolled, according to the study design, the clinical setting within a University Hospital could bias the selection
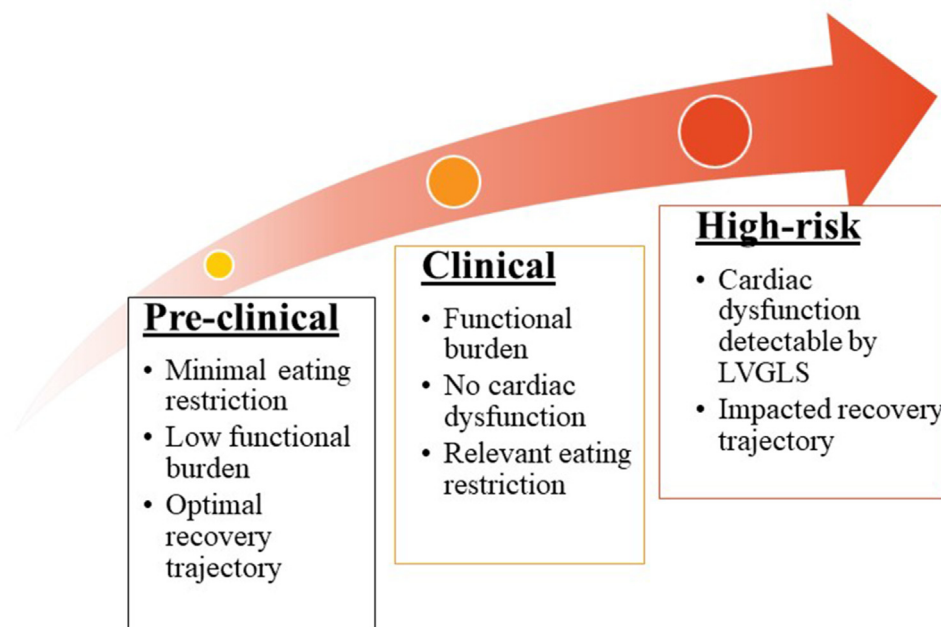
Figure 2 Proposed clinical staging model for the role of body composition and echocardiography in the management of Anorexia Nervosa.

towards more severe patients. This bias, towards the inclusion of more severe patients, could explain the relatively high variability between timepoints, and the modest weight restoration at three months observed using either BMI or body composition parameters. A relatively small number of AN-r patients were included in the study. Future studies might be interested in better understanding sub-diagnostic differences between AN-r and AN-bp, as well as better describing potential differences between sub-diagnostic groups for what concerns longitudinal outcome trajectories.

Nonetheless, previous studies used longer time periods of evaluation, showing significant differences in body composition in patients with AN after a follow-up of three years [69]. For this reason, the modest restoration of FFM, FM and BMI in the enrolled cohort could derive from the shorter adopted time of follow-up (three months). Furthermore, as previously mentioned, a recent meta-analysis showed how FFM might not be fully recovered even after weight restoration in this clinical population [36]. The same meta-analysis suggested that the effect size for FFM restoration in AN might not be considered moderate nor high: with estimates of 4.98 kg of lower FFM before treatment in comparison to controls, 2.98 kg of increase in FFM during treatment, and yet still 1.27 kg of lower FFM after long-term weight-recovery [36].

The sample size in the current study was limited, and the clinical population was gathered within a single center. Future research involving multiple sites may be necessary, in order to establish a normative sample for clinical populations of patients suffering from AN. Finally, only female individuals were here enrolled. While this limitation is in line with the literature on the topic [70], future research might be interested in tackling potential gender differences for current results.

5. Conclusions

Diverging trajectories of recovery can be observed in patients with AN. The current study supports previous attempts to better define clinical severity in AN besides BMI, as this measure may not be used as a reliable predictor of outcome alone. BIA and LVGLS seem more suitable for the purpose of clinical staging in AN. BIA and LVGLS may better account for different stages of severity in AN. Current results show how once cardiac function is impacted at the individual level, a divergent point of equilibrium for the patient can be described. A higher effort (i.e., time) may then be required to overcome metabolic distress (BCM) and promote FM/FFM restoration.

Ethics approval

The study protocol was approved by the local ethics committee (Comitato Etico Regione Toscana—Area Vasta Centro, protocol code OSS.14.162), and the study was conducted in accordance with the guidelines of the Declaration of Helsinki of 1964 and subsequent amendments.

Funding details

Authors contributions

G.C. conceived and planned the experiments. Data collection was performed by M.F., L.T., E.R., E.C, E.D., G.M. Material preparation and statistical analysis were performed

by L.T. with the contribution of E.C. A contribution to the interpretation of the results was given by all the authors, in particular E.D., G.M., A.N., V.S., B.A., G.C., V.R. The first draft of the manuscript was written by L.T with the supervision of G.C. and V.R. All authors provided critical feedback and helped shape the manuscript. All authors read and approved the final version of the manuscript.

Data and code availability statement

The data and code supporting the present study can be shared upon reasonable request to the corresponding author.

Patient consent

Informed consent was obtained from all subjects involved in the study.

Declaration of competing interest

The authors report there are no competing interests to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2024.08.021.

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