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Measured Versus Estimated Resting Metabolic Rate in Heart Failure With Preserved Ejection Fraction

Theresa Anderson, MD; Thomas M. Cascino, MD, MSc; Todd M. Koelling, MD; Daniel Perry, MD; Gillian Grafton, DO; Denise K. Houston, PhD; Bharathi Upadhya, MD; Dalane W. Kitzman, MD; Scott L. Hummel, MD, MS

BACKGROUND: Obesity is common in heart failure with preserved ejection fraction (HFpEF), and a hypocaloric diet can improve functional capacity. Malnutrition, sarcopenia, and frailty are also frequently present, and calorie restriction could harm some patients. Resting metabolic rate (RMR) is an essential determinant of caloric needs; however, it is rarely measured in clinical practice. The accuracy of commonly used predictive equations in HFpEF is unknown.

METHODS: RMR was measured with indirect calorimetry in 43 patients with HFpEF undergoing right heart catheterization at the University of Michigan, and among 49 participants in the SECRET trial (Study of the Effects of Caloric Restriction and Exercise Training in Patients With Heart Failure and a Normal Ejection Fraction); SECRET patients also had dual-energy X-ray absorptiometry body composition measures. Measured RMR was compared with RMR estimated using the Harris Benedict, Mifflin-St Jeor, World Health Organization, and Academy for Nutrition and Dietetics equations.

RESULTS: All predictive equations overestimated RMR (by >10%, \( P<0.001 \) for all), with mean (95% CI) differences Harris Benedict equation +250 (186–313), Mifflin-St. Jeor equation +169 (110–229), World Health Organization equation +300 (239–361), and Academy for Nutrition and Dietetics equation +794 (890–697) kcal/day. Results were similar across both patient groups, and the discrepancy between measured and estimated RMR tended to increase with body mass index. In SECRET, measured RMR was closely associated with lean body mass (\( \rho=0.74 \); by linear regression adjusted for age and sex: \( \beta=27 \) [95% CI, 18–36] kcal/day per kg, \( P<0.001 \); \( r^2=0.56 \)).

CONCLUSIONS: Commonly used predictive equations systematically overestimate measured RMR in patients with HFpEF. Direct measurement of RMR may be needed to effectively tailor dietary guidance in this population.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique Identifier: NCT00959660.

Key Words: exercise ■ frailty ■ heart failure ■ malnutrition ■ obesity
WHAT IS NEW?
• Metabolic factors and obesity are believed to be important in heart failure with preserved ejection fraction.
• No previous studies have reported resting metabolic rate in this population.
• Across a diverse cohort of clinical and research study patients with heart failure with preserved ejection fraction, frequently used predictive equations substantially overestimated resting metabolic rate.

WHAT ARE THE CLINICAL IMPLICATIONS?
• Malnutrition is a poor prognostic sign in heart failure, yet a hypocaloric diet can increase exercise capacity and improve quality of life in at least some patients with heart failure with preserved ejection fraction.
• In this study, commonly used predictive equations did not accurately estimate resting metabolic rate, an essential factor in calculating daily caloric needs.
• Measuring resting metabolic rate using indirect calorimetry could help guide effective and safe dietary interventions in heart failure with preserved ejection fraction.

The Academy of Nutrition and Dietetics (AND) recommends assessment of resting metabolic rate (RMR), ideally with indirect calorimetry, for nutritional evaluation of patients with HF. The RMR, combined with a multiplier based on typical physical activity, is then used to accurately calculate individual caloric intake needs. However, in practice, predictive equations are instead frequently used to estimate RMR. Despite the importance of obesity and uncertainty about its management, evidence is currently lacking with regard to measured or estimated RMR among patients with HFpEF.

In this study, we measured RMR in a heterogeneous group of patients with HFpEF and compared the results to commonly used predictive equations for RMR. We then evaluated these parameters in a well-characterized HFpEF clinical trial cohort, in which we also explored the relationship between RMR and body composition. This work aims to improve our understanding of RMR in HFpEF, which may inform individualized dietary recommendations for patients and eventually provide additional insight into HFpEF pathophysiology.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Design and Patient Selection
We first analyzed clinically obtained data from the University of Michigan (Michigan). The database initially included consecutive patients with HFpEF (EF≥50%) referred for right heart catheterization from 2011 to 2015 (n=110). During this time period, patients underwent measurement of RMR, with the original intent to improve the precision of Fick cardiac output calculations. Chart review was performed (T.A., T.M.C. and S.L.H.) to exclude patients with congenital, infiltrative, hypertrophic, or primary restrictive cardiomyopathy, and 43 patients were included in the final analysis. The study was approved by IRBMED, University of Michigan’s Institutional Review Board, and participants provided informed consent.

We then analyzed baseline data from the SECRET trial (Study of the Effects Caloric Restriction and Exercise Training in Patients With Heart Failure and a Normal Ejection Fraction). In brief, SECRET randomized 100 older adults with obesity (body mass index [BMI] ≥30 kg/m²), self-described sedentary lifestyle, and HFpEF in a 2×2 design to usual care, hypocaloric diet, regular moderate-intensity exercise, or both interventions. Details of the inclusion and exclusion criteria and the primary study results have been previously published. At study baseline, RMR was measured in the 49 participants assigned to the dietary intervention group and used to calculate caloric intake goals. The SECRET trial was approved by Wake Forest University’s Institutional Review Board, and participants provided informed consent.

Demographics, clinical characteristics, and RMR between the 2 study cohorts were compared using 2-sample t testing or \( \chi^2 \) testing as appropriate. In the Michigan cohort, patients who underwent right heart catheterization during hospitalization were treated as New York Heart Association class IV for comparison.

RMR Measurement and Calculation

The RMR in the Michigan cohort was measured before clinically indicated right heart catheterization. Measurements were obtained in a fasting, semi-supine, and nonsedated state after a 10-minute resting period with the use of a canopy hood and a breathing valve apparatus and the Vmax Encore metabolic cart. The RMR was calculated using the Weir formula:

\[
\text{RMR} = 1440 \times (3.94 \frac{\text{VO}_2}{\text{minute}} + 1.11 \times \frac{\text{VCO}_2}{\text{minute}})
\]

kcal/day. In the SECRET trial, the RMR was obtained at the baseline visit with indirect calorimetry using the MCG Ultima CCM system with patients wearing PreVent masks (CCM Express, MGC Diagnostics). SECRET participants also had...

Nonstandard Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AND</td>
<td>Academy of Nutrition and Dietetics</td>
</tr>
<tr>
<td>BMI</td>
<td>body mass index</td>
</tr>
<tr>
<td>HBE</td>
<td>Harris Benedict equation</td>
</tr>
<tr>
<td>MSJE</td>
<td>Mifflin-St. Jeor equation</td>
</tr>
<tr>
<td>RMR</td>
<td>resting metabolic rate</td>
</tr>
<tr>
<td>SECRET</td>
<td>Study of the Effects of Caloric Restriction and Exercise Training in Patients With Heart Failure and a Normal Ejection Fraction</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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Circ Heart Fail. 2021;14:e007962. DOI: 10.1161/CIRCHEARTFAILURE.120.007962
dual-energy X-ray absorption and lower extremity magnetic imaging resonance scans at study baseline.\textsuperscript{6} Estimations of RMR were performed using the Harris Benedict equation (HBE), Mifflin-St Jeor equation (MSJE), and World Health Organization (WHO) equation.\textsuperscript{11–13} In a similar manner, we also evaluated the performance of AND guidance for nonmalnourished patients with chronic HF with reduced ejection fraction (HFrEF), which recommends estimating RMR at 22 kcal/kg per day actual body weight.\textsuperscript{8} The generally accepted threshold for accurately estimated RMR is within 10% of the measured value.\textsuperscript{14} See Table 1 for equations.

**Statistical Analysis**

Statistical analysis was performed using STATA 15.1 (STATA, Inc, College Station, TX), and \(P<0.05\) denotes statistical significance. Demographics, clinical characteristics and RMR were compared between the 2 study cohorts using 2-sample \(t\) testing, Wilcoxon rank-sum testing, or \(\chi^2\) testing as appropriate. Measured RMR and estimations of RMR were compared using paired \(t\) tests. Bland-Altman plots were created to assess the differences and potential biases between measured and estimated RMR. Using the SECRET cohort, univariable and multivariable generalized linear regression was performed to evaluate the relationships between lean body mass (from dual-energy x ray absorption), lower extremity skeletal muscle mass (from magnetic imaging resonance), and RMR.

Last, we also evaluated how using estimated RMR would have affected the SECRET dietary intervention groups by comparing calorie targets determined using indirect calorimetry versus predictive equations for RMR.

**RESULTS**

Demographic and selected clinical characteristics for both patient cohorts are shown in Table 2. Patients in the Michigan cohort \((n=43)\) were 53% women, 88% White, 58% with diabetes and other comorbidities, notably 60% with atrial fibrillation, and had median (interquartile range) B-type natriuretic peptide level 381 (81–489) pg/mL. Patients in the SECRET cohort \((n=49)\) were 82% women, 49% White, had lower New York Heart Association class, and lower B-type natriuretic peptide level at 30 (19–34) pg/mL.

Measured versus estimated RMR are shown in Table 3 and illustrated in Figure 1. Indexed for body weight, the measured RMR across the combined cohort was 14.7±3.5 kcal/kg per day. The measured and estimated RMR were moderately well correlated for all 4 estimation equations (\(r=0.64–0.70\), all \(P<0.001\)). However, in both patient groups and across the cohort as a whole, all 4 predictive equations significantly overestimated RMR when compared with the measured RMR (>10% mean difference, \(P<0.001\) for all comparisons; see Bland-Altman plots in Figure 2). The MSJE had the closest range of agreement to the measured RMR, and the AND guidance for patients with HFrEF\textsuperscript{22} kcal/kg actual body weight/day was the least accurate, overestimating measured RMR by a mean of 59%. All 4 equations overestimated RMR by >10% in half or more of participants (HBE 57%, MSJE 50%, WHO 68%, AND 95%) while rarely underestimating RMR by >10% (HBE 5%, MSJE 10%, WHO 3%, AND 2%). The overestimation of RMR by all 4 equations increased along with BMI, particularly for the AND equation (Figure 3).

Across the cohort as a whole \((n=92)\), RMR was inversely associated with age \((\beta=−10\) kcal/day per y of age, \(P=0.02)\) and female sex \((\beta=326\) kcal/day, \(P<0.001)\) but was unrelated to self-reported race or

### Table 1. Measured and Estimating Equations for Calculating Resting Metabolic Rate

<table>
<thead>
<tr>
<th>Method</th>
<th>Resting metabolic rate equation, kcal/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weir</td>
<td>1440×(3.94 VO(_2) [l/min] +1.11×VO(_2) [l/min])</td>
</tr>
<tr>
<td>Harris-Benedict*</td>
<td>Men: 66.5+(13.75×weight [kg])+(5×height [cm])−(6.78×age [y])</td>
</tr>
<tr>
<td></td>
<td>Women: 555.1+(9.56×weight [kg])+(1.85×height [cm])−(4.68×age [y])</td>
</tr>
<tr>
<td>Mifflin-St. Jeor*</td>
<td>Men: [9.99×wt [kg]]+[(6.25×height [cm])−(4.92×age [y])] + 5</td>
</tr>
<tr>
<td></td>
<td>Women: [9.99×wt [kg]]+[(6.25×height [cm])−(4.92×age [y])−161]</td>
</tr>
<tr>
<td>WHO*</td>
<td>[15.4×Wt [kg]]+[(0.27×Ht [cm])+717]</td>
</tr>
<tr>
<td>AND*</td>
<td>Normally nourished patients: 22 kcal/kg×actual body wt [kg]</td>
</tr>
<tr>
<td></td>
<td>Malnourished patients: 24 kcal/d×actual body wt [kg]</td>
</tr>
</tbody>
</table>

AND indicates Academy of Nutrition and Dietetics; and WHO, World Health Organization.

*Estimating equation.

### Table 2. Clinical Characteristics of University of Michigan and SECRET Trial Participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Michigan ((n=43))</th>
<th>SECRET ((n=49))</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>62±12</td>
<td>66±5</td>
<td>0.026</td>
</tr>
<tr>
<td>Women</td>
<td>23 (53%)</td>
<td>40 (82%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White</td>
<td>38 (88%)</td>
<td>24 (49%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>34.9±11.0</td>
<td>39.0±5.0</td>
<td>0.022</td>
</tr>
<tr>
<td>BNP</td>
<td>381 (81–489)</td>
<td>30 (19–34)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>7 (16%)</td>
<td>31 (63%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>III</td>
<td>18 (42%)</td>
<td>18 (37%)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>18 (42%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.7±1.1</td>
<td>0.9±0.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>132±25</td>
<td>137±14</td>
<td>0.27</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>71±11</td>
<td>79±8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>25 (58%)</td>
<td>16 (33%)</td>
<td>0.021</td>
</tr>
<tr>
<td>Hypertension</td>
<td>22 (51%)</td>
<td>46 (94%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>26 (60%)</td>
<td>2 (4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>16 (37%)</td>
<td>7 (14%)</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Values are percentage reflected as (%) or mean±SD, except for BNP, which is presented as median (IQR). BMI indicates body mass index; BNP, B-type natriuretic peptide; IQR, interquartile range; NYHA, New York Heart Association; and SECRET, Study of the Effects of Caloric Restriction and Exercise Training in Patients With Heart Failure and a Normal Ejection Fraction.
New York Heart Association class. The measured RMR was greater in patients on beta-blockers than in those who were not ($\beta=+201$ kcal/day [95% CI, 41–361] kcal/day), but the differences between measured and estimated RMR were not significantly affected by beta-blocker use ($\beta$ range = $-49$ to $-6$ kcal/day for all 4 equations tested, all $P>0.46$). The measured RMR and the differences from estimated RMR were not affected by thyroid hormone replacement.

In the SECRET cohort ($n=46$ of 49 with available body composition data), RMR was strongly associated with total lean body mass by dual-energy X-ray absorption ($\rho=0.74$; by linear regression adjusted for age and sex: $\beta=27$ [95% CI, 18–36] kcal/day per kg, $P<0.001$; $r^2=0.56$) and more weakly associated with lower extremity skeletal muscle mass ($\rho=0.48$; by linear regression adjusted for age and sex: $\beta=5$ [95% CI, 1–9] kcal/day per kg, $P=0.02$; $r^2=0.26$).

In the SECRET trial, the calorie intake recommendations were based on daily total energy expenditure, derived from measured RMR multiplied by an activity factor (most commonly 1.3, consistent with sedentary lifestyle). In women ($n=40$) calculated total energy expenditure was $1801 \pm 497$ kcal/day and in men ($n=9$) total energy expenditure was $2141 \pm 306$ kcal/day (mean±SD). The intervention aimed for a $-400$ kcal/day deficit in the diet-only group and a $-350$ kcal/day deficit in the diet + exercise group and achieved $-388 \pm 55$ and $-355 \pm 23$ kcal/day (mean±SD), respectively. The SECRET participants assigned to hypocaloric diet lost an average of 7 kg of weight over 20 weeks of participation. If predictive equations for RMR had instead been used to calculate daily energy needs, recommended changes in calorie intake would have been: HBE: $-65 \pm 346$, MSJE: $-149 \pm 342$, WHO: $-20 \pm 347$, AND: $+748 \pm 497$ kcal/day (mean±SD). All of these would have been insufficient to produce adequate weight loss, and in some instances, a total caloric surplus rather than deficit may have occurred.

**DISCUSSION**

Our study found that predictive equations for RMR in patients with HFpEF systematically and substantially overestimate RMR measured by indirect calorimetry. We found similar results across a variety of commonly used equations in a heterogeneous clinical HFpEF cohort, then validated these observations in the well-characterized SECRET clinical trial sample. As in other studies, we found inverse relationships between measured RMR and age as well as female sex. In the SECRET cohort, lean body mass by dual-energy X-ray absorption was closely associated with RMR.

In the United States, >$80\%$ of patients with HFpEF have a BMI in the overweight or obese range, making the obese/metabolic phenotype by far the most common. Obesity is believed to drive pathophysiology not just via associated comorbidities such as hypertension and diabetes but also through multifactorial effects of excess adipose tissue on plasma volume, capillary rarefaction, inflammation, and pericardial restraint. $^6,15$ Maintaining a healthy body weight across the lifespan is one of the most effective preventive strategies for HFpEF. $^6$ Observational studies suggest that weight loss and metabolic improvements following bariatric surgery can reduce the incidence and severity of HF. $^{17,18}$ A small but growing body

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**Table 3. Measured and Estimated Resting Metabolic Rate Within the University of Michigan Cohort and SECRET Trial Cohort**

<table>
<thead>
<tr>
<th>RMR method</th>
<th>Michigan ($n=43$)</th>
<th>SECRET ($n=49$)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD, kcal/d</td>
<td>95% CI</td>
<td>Mean±SD, kcal/d</td>
</tr>
<tr>
<td>Weir (measured)</td>
<td>1614±479</td>
<td>1367–1661</td>
<td>1449±289</td>
</tr>
<tr>
<td>Harris-Benedict</td>
<td>1783±530</td>
<td>1621–1947</td>
<td>1682±233</td>
</tr>
<tr>
<td>Mifflin-St. Jeor</td>
<td>1685±457</td>
<td>1545–1826</td>
<td>1617±233</td>
</tr>
<tr>
<td>WHO</td>
<td>1817±485</td>
<td>1667–1968</td>
<td>1747±209</td>
</tr>
<tr>
<td>AND</td>
<td>2229±800</td>
<td>1983–2478</td>
<td>2311±371</td>
</tr>
</tbody>
</table>

AND indicates Academy of Nutrition and Dietetics; RMR, resting metabolic rate; and WHO, World Health Organization.
of literature suggests that dietary modification can benefit ambulatory patients with HFpEF and obesity. While data on hospitalization and mortality are lacking, positive effects can include improved cardiovascular function, enhanced quality of life, and increased functional capacity. Proposed mechanisms of various strategies include improvement in ventricular-vascular coupling and other hemodynamic factors as well as reduction in visceral fat content, inflammation, and oxidative stress. In addition, dietary calorie restriction in otherwise healthy younger adults with overweight has pleomorphic benefits on aging-related biomarkers, intriguing in a geriatric syndrome such as HFpEF.

However, a hypocaloric diet could have potential negative consequences in some patients with HFpEF. Despite increased body weight, many patients have significantly reduced muscle mass (termed sarcopenic obesity) as well as poorer muscle quality with fatty infiltration and alteration in muscle fiber types. Physical frailty is common in HFpEF and is associated with functional decline and hospitalization burden. Malnutrition frequently overlaps with frailty in older adults and is a major risk factor for death and readmission in patients with HF. In hospitalized patients with HF, insufficient calorie intake is associated with poor postdischarge quality of life and increased readmission burden.

Given the potential benefits (and risks) of calorie restriction in HFpEF, accurate assessment of RMR is essential for tailored dietary guidance. Current AND guidance on energy intake, was developed from indirect calorimetry data obtained from relatively young patients with HFrEF who were not obese, and who had a higher RMR than controls matched for age, activity level, and weight. Data addressing energy intake and RMR in older patients with obesity and HFpEF are currently lacking, and the AND advises against applying the same guidelines in this population. In this HFpEF cohort, the AND recommendation of 22 kcal/kg actual body weight for normally nourished patients profoundly overestimated measured RMR, which averaged well below even the AND guidance for severe HFrEF of 18 kcal/kg actual body weight. Other commonly used predictive equations for RMR also performed poorly.
These discrepancies have many potential causes in patients with HFpEF. Excess fluid volume could increase nonmetabolizing body weight and bias weight-based equations, even in patients with compensated HF. Obesity was almost universally present in this study cohort, and the discrepancy between measured and estimated RMR tended to increase with BMI (Figure 3). These observations are aligned with a recent systematic review, which found that the HBE, MSJE, and WHO predictive equations slightly overestimated RMR in otherwise healthy young to middle-aged adults with overweight or obesity.14 The measured RMR was similar between groups despite a higher BMI in the SECRET cohort. We speculate this may relate to differences in illness severity (eg, higher B-type natriuretic peptide and worse symptom burden in the Michigan cohort) or sex distribution (82% women in SECRET versus 53% in Michigan cohort), since RMR tends to be lower in women than men even after controlling for body composition and fitness level.29

Additionally, several studies document an age related progression in the disparity between measured and estimated RMR.30,31 These differences persist after adjustment for the decrease in lean body mass with aging and are thought to stem from metabolic changes in constitutively active organs such as brain, kidneys, liver, and heart.30 Interestingly, the discrepancy between measured and predicted RMR was approximately twice as large in our study as that found using organ-mass based estimation in healthy older adults.30,31 Whether this relates to methodological or metabolic differences is unclear. Potential contributors specifically linked to HFpEF pathophysiology include sarcopenia, adipose tissue infiltration of musculature, reduced delivery of oxygen, and metabolic substrates due to microvascular dysfunction, and decrease in the number or function of mitochondria.15,22,24,32–35

Our findings address a critical gap in the HF and nutrition literature and have several important implications. The SECRET trial6 demonstrates the powerful potential of diet-related weight loss to improve quality of life and functional capacity in patients with HF. However, if estimated RMR had guided calorie recommendations in SECRET, weight loss and its attendant benefits might

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**Figure 3.** Plots depicting the relationship between body mass index (in kg/m²) and the difference between measured and estimated resting metabolic rate (in kcal/d).

RMR indicates resting metabolic rate; and SECRET, Study of the Effects of Caloric Restriction and Exercise Training in Patients With Heart Failure and a Normal Ejection Fraction.
have been greatly attenuated. Perhaps just as important, avoiding excessive calorie restriction in frail or malnourished patients may help preserve functional capacity and improve outcomes. Hand-held indirect calorimeters to measure RMR have not previously been evaluated in HF, but performance among patients with obesity and/or hospitalized patients suggests this method may not be more accurate than estimation equations. Standard indirect calorimetry is inexpensive, available at most medical institutions, and presents minimal burden and no risk to the patient.

Routine measurement of RMR via indirect calorimetry could facilitate individualized, effective, and safe dietary guidance in HFpEF, translating the potential benefits of hypocaloric diet into practice. Another benefit of measuring RMR would be to increase the accuracy of Fick cardiac output calculations. Moreover, personalized O₂ pathway analysis can identify the dominant pathophysiological mechanisms for exercise intolerance in individual patients with HFpEF. Since HFpEF is a heterogeneous syndrome, such phenotyping may also help select appropriately targeted treatments.

Study Limitations

Limitations in this study include the relatively small patient cohort and the heterogeneity of the sample. The consistency of results across a broad range of demographics, illness severity, and comorbidities suggests good generalizability, although these results may not apply to all patients with HFpEF. Only 5% of patients in this study had body mass index below 25 kg/m², and 82% had body mass index above 30 kg/m². Given this, our findings may not be applicable to patients suffering from heart failure with cardiac cachexia.

Body composition measurements were not available in the Michigan cohort, which could have added more insight into the relationship between lean body mass and RMR. Our analysis of body composition included only lean body mass and appendicular skeletal muscle. While lean mass is the major determinant of RMR, we could not derive the individual contributions of constituatively active tissues such as brain, heart, liver, and kidneys to RMR. We chose to analyze 3 of the most commonly used predictive equations for RMR. It is possible that another published equation would perform better in HFpEF, or that one could be derived from this or other cohorts.

Conclusions

Commonly used predictive equations systematically overestimate measured RMR in patients with HFpEF. Accurate assessment of RMR is needed to realize the benefits and avoid the potential harms of caloric restriction in HFpEF. Mechanistic studies are needed to understand the discrepancy between predicted and measured RMR, which may also provide insight into HFpEF pathophysiology and phenotyping.

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