Update on the Obesity Paradox in Aging

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Geriatric Grand Rounds
March 6, 2014

Objectives

1. describe the current definition of the Obesity Paradox in aging
2. evaluate the association between BMI and mortality in the literature
3. begin to understand the complexity behind the question of whether to treat obesity with weight loss in elderly

Outline

• The Aging Obesity Paradox—current definition
• Background on evolving definition of obesity
• Review of BMI vs. mortality literature
• Discuss risks and benefits of weight loss in elderly

Obesity Prevalence among older adults

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>%Men</th>
<th>%Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>26.3</td>
<td>35.4</td>
</tr>
<tr>
<td>50-59</td>
<td>32.2</td>
<td>41.2</td>
</tr>
<tr>
<td>60-69</td>
<td>38.1</td>
<td>42.5</td>
</tr>
<tr>
<td>70-79</td>
<td>28.9</td>
<td>31.9</td>
</tr>
<tr>
<td>&gt;80</td>
<td>9.6</td>
<td>19.5</td>
</tr>
</tbody>
</table>

The “Obesity Paradox” in aging

• Early in life being lean appears optimal for overall health, whereas late in life being overweight to mildly obese appears optimal/protective.
  • Apparent shift in nadir/ideal weight
The “Weight Loss Paradox” in aging

- Early in life weight loss appears to improve overall health, whereas late in life weight loss appears to be less effective or potentially harmful.

Clinical conundrum: to treat or not to treat

- Can we ignore obesity in the elderly?
  - Is ‘normal/healthy’ BMI shifted higher?
  - Is extra fat mass protective?
- Should we treat obesity in the elderly?
  - If so, at what BMI?
  - Is weight loss per se harmful?
  - Does weight loss confer benefits (e.g., function, mobility) that outweigh risks?
- Should we avoid weight loss? Is exercise sufficient?

What is ‘ideal’ body weight?

How do we define obesity?

Then came BMI (kg/m2) charts...

- 1972 – Ancel Keys report in J Chronic Diseases
  BMI is best proxy for %fat

Where did concept of “normal” or “ideal” weight come from?

- 1943 - MetLife introduced ‘desirable’ height-weight tables – based on low mortality risk age 25-59 y

<table>
<thead>
<tr>
<th>Height</th>
<th>Weight (kg)</th>
<th>BMI</th>
<th>Age 25-59</th>
<th>Age 60-69</th>
<th>Age 70-79</th>
</tr>
</thead>
<tbody>
<tr>
<td>5'7&quot;</td>
<td>120-125</td>
<td>22</td>
<td>116-121</td>
<td>123-125</td>
<td>130-135</td>
</tr>
<tr>
<td>5'6&quot;</td>
<td>116-121</td>
<td>23</td>
<td>112-117</td>
<td>119-123</td>
<td>126-131</td>
</tr>
<tr>
<td>5'5&quot;</td>
<td>112-117</td>
<td>24</td>
<td>108-113</td>
<td>115-120</td>
<td>121-126</td>
</tr>
<tr>
<td>5'4&quot;</td>
<td>108-113</td>
<td>25</td>
<td>104-109</td>
<td>110-115</td>
<td>116-121</td>
</tr>
<tr>
<td>5'3&quot;</td>
<td>104-109</td>
<td>26</td>
<td>100-105</td>
<td>106-111</td>
<td>112-117</td>
</tr>
<tr>
<td>5'2&quot;</td>
<td>100-105</td>
<td>27</td>
<td>96-101</td>
<td>102-107</td>
<td>108-113</td>
</tr>
<tr>
<td>5'1&quot;</td>
<td>96-101</td>
<td>28</td>
<td>92-97</td>
<td>98-103</td>
<td>104-109</td>
</tr>
</tbody>
</table>

- 1972 – Ancel Keys report in J Chronic Diseases
<table>
<thead>
<tr>
<th>BMI</th>
<th>Weight Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below 18.5</td>
<td>Underweight</td>
</tr>
<tr>
<td>18.5 - 24.9</td>
<td>Normal</td>
</tr>
<tr>
<td>25.0 - 29.9</td>
<td>Overweight (Obesity Grade I)</td>
</tr>
<tr>
<td>30.0 - 34.9</td>
<td>Obesity Grade II</td>
</tr>
<tr>
<td>35.0 - 39.9</td>
<td>Obesity Grade III</td>
</tr>
<tr>
<td>40.0 and above</td>
<td>Obesity Grade IV ( morbid)</td>
</tr>
</tbody>
</table>

... and BMI-based categorization of overweight and obesity
But... BMI has its limitations

- Adiposity doesn’t scale with BMI exactly
- Proportion of fat:lean mass are not constant

Matching % body fat across age, BMI differs

Drilling down further...

- Lipid stored appropriately (subcutaneously) vs. where we don’t want it (ectopically)

What does this have to do with age-related changes in BMI vs. Mortality?

- With aging, for the same BMI we:
  - Are shorter
  - Have less lean mass
    - Less and poorer quality muscle
    - Less and poorer quality bone
  - Have more fat mass
    - Centrally/viscerally
    - Ectopically
    - Poorer quality subcutaneous tissue
Trajectories of weight gain throughout life often differ: Duration of obesity varies

BMI often varies from mid- to late-life: History of obesity varies

Reasons BMI may be a poor indicator of risk of mortality with increasing age

- **Reverse causation bias**
  - Unintentional weight loss caused by illness/chronic disease
- **Healthy participant bias**
  - Surveys rarely include institutionalized, often exclude older and unhealthy outright
  - More aggressive pharmacologic treatment in younger, healthier patients
- **Birth cohort bias**
  - Steady decline in US mortality with time (age and birth cohort - collinearly related)
- **BMI not sensitive marker**
  - High variability in adiposity, nutritional status, disability, chronic disease

**BMI vs. Mortality Curves**

Prospective cohort >1M US adults

Multivariate RR of death from all causes by BMI, smoking, and disease

- **Men**
  - n=457,785
  - Follow-up 14y
  - Deaths 201,622
- **Women**
  - n=588,369
  - Mean age 57y
  - Cancer Prevention Study II cohort

No history of disease or smoking

Multivariate RR of death from CVD, Cancer, or other causes

- **Men**
  - Cancer prevention
  - All other causes
- **Women**
  - Cancer prevention
  - All other causes
By Age Group

Multivariate RR of death from all causes – no history of smoking or disease

Pooled 57 cohorts - W Europe & N America

RR of death from all causes – adj. for age, smoking, study

Men Women

Total n=852,824
Deaths n=72,749
Mean age 46y

Prospective Studies Collaboration Lancet 2009

All-cause mortality - by Age Group

HR for death from any cause per 5kg/m² increase in BMI – no history of smoking, excluding deaths in 1st 5y follow-up, adjusted for sex

Disease-specific mortality - by age Group within upper BMI range (25-50kg/m²)

HR for death from all causes by BMI, and smoking

Pooled 19 cohorts >1.4M US adults

Men n=613,200
Women n=846,800
Deaths n=160,087

Berrington de Gonzalez et al NEJM 2010

Adapted from Calle E. et al NEJM 1999

Prospective Studies Collaboration Lancet 2009

Prospective Studies Collaboration Lancet 2009

Prospective Studies Collaboration Lancet 2009

Adapted from Prospective Studies Collaboration Lancet 2009
By Age Group

HR for death from any cause – no history of smoking

BMI & Mortality among adults shortly before diagnosis of Type 2 Diabetes: Combined Nurses Health and Health Professionals Follow-up Studies

BMI & all-cause Mortality by sex and age at time of Type 2 DM diagnosis - Never smokers

Systematic Review & Meta-analysis
Is there an “Obesity Paradox” at all ages?

Meta-analysis among older (≥65y) adults only: All-cause mortality

What if we adjust for some epidemiologic biases impacting the age effect?
Interaction between obesity status and age at survey- National Health Interview Survey Linked Mortality Files (n>820,000)

Grey line – Proportional HR vs. BMI 18.5-29.9
Black bars – Age-specific HR vs. BMI 18.5-29.9

BMI 30-34.9
BMI 35-39.9
BMI >40

Interaction between obesity status and age at survey- National Health Interview Survey Linked Mortality Files (n>820,000)

Linear reduction in mortality by birth cohort

Summary of BMI vs. Mortality Curves

- Curves differ by
  - Age group
  - Birth cohort
  - Women vs. men
  - Smoking vs. non-smoking
  - All-cause vs. disease-specific mortality
  - Duration of follow-up
  - Measured vs. self-reported BMI

Risk of CHD by BMI, Waist, or Waist:Hip

Emerging Risk Factor Collaboration Lancet 2011

Mediators?
Risk of Stroke by BMI, Waist, or Waist:Hip

Emerging Risk Factor Collaboration Lancet 2011

Age-related differences in the Hazard Ratio for CHD or Stroke per 1SD higher baseline BMI

Emerging Risk Factor Collaboration Lancet 2011

Pooled 97 cohorts (1.8M global) - What mediates risk b/w BMI and CHD?


Pooled 97 cohorts (1.8M global) - What mediates risk b/w BMI and Stroke?


Prospective cohort followed at Cooper Institute (Dallas, TX)

Table 2. Age- and sex-adjusted hazard ratios (95% CI) of cardiovascular disease and all-cause mortality by body mass index (BMI) and waist:hip ratio (WHR). Cohort: Multiple Risk Factor Intervention Trial (US), MRFIT 1970-1984.

<table>
<thead>
<tr>
<th>Mortality Predictor</th>
<th>Normal Weight</th>
<th>Overweight</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease</td>
<td>1.0 (95% CI 1.0, 1.6)</td>
<td>1.3 (95% CI 1.0, 1.6)</td>
<td>1.6 (95% CI 1.2, 2.0)</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td>1.0 (95% CI 1.0, 1.6)</td>
<td>1.3 (95% CI 1.0, 1.6)</td>
<td>1.6 (95% CI 1.2, 2.0)</td>
</tr>
<tr>
<td>All deaths (except CVD)</td>
<td>1.0 (95% CI 1.0, 1.6)</td>
<td>1.3 (95% CI 1.0, 1.6)</td>
<td>1.6 (95% CI 1.2, 2.0)</td>
</tr>
</tbody>
</table>

Men n=25,714 Follow-up 10y
Deaths n=1025 (639 CVD) Mean age 44y Aerobic Center Longitudinal Study cohort

Wei, M. et al JAMA 1999

Independent association of low muscle mass and high central adiposity with mortality

<table>
<thead>
<tr>
<th>No. of deaths</th>
<th>Rate per 1000 person years</th>
<th>Adjusted relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist circumference (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low MAMC&lt;74 (n=470)</td>
<td>150</td>
<td>40.9</td>
</tr>
<tr>
<td>74-102 (n=375)</td>
<td>150</td>
<td>55.2</td>
</tr>
<tr>
<td>103-126 (n=94)</td>
<td>150</td>
<td>58.4</td>
</tr>
<tr>
<td>For trend</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Higher MAMC&lt;74 (n=470)</td>
<td>150</td>
<td>21.7</td>
</tr>
<tr>
<td>74-102 (n=375)</td>
<td>150</td>
<td>55.2</td>
</tr>
<tr>
<td>103-126 (n=94)</td>
<td>150</td>
<td>58.4</td>
</tr>
<tr>
<td>For trend</td>
<td>0.03</td>
<td></td>
</tr>
</tbody>
</table>

N=4,107 men aged 60-79y
MAMC = mid-arm muscle circumference
Wannamethee AJCN 2007
Sarcopenic obesity and risk of CVD and mortality among men age 60-79y (n=4,252)

<table>
<thead>
<tr>
<th>Waist (cm)</th>
<th>Arm (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>&lt;102</td>
</tr>
<tr>
<td>Sarcopenic</td>
<td>&lt;25.9</td>
</tr>
<tr>
<td>Obese</td>
<td>&gt;102</td>
</tr>
<tr>
<td>Sarcopenic-obese</td>
<td>&gt;25.9</td>
</tr>
</tbody>
</table>

Atkins, J. AMJ 2014

What about weight loss?

Review and meta-analysis of weight loss and all-cause mortality (26 prospective studies)

- Overall relative risk according to Reason for weight loss x Baseline health
  - Intentional RR 1.01 (0.93 - 1.09)
    - Healthy (n=12) RR 1.11 (1.0 - 1.22)
    - Unhealthy (n=7) RR 0.87 (0.77 - 0.99)
  - Unintentional RR 1.22 (1.09 - 1.37)
    - Healthy (n=6) RR 1.27 (1.09 - 1.47)
    - Unhealthy (n=5) RR 1.16 (0.97 - 1.38)

Harrington, M. Natl Revs 2009

Impact of current vs. mid-life obesity on mortality: Framingham Heart Study cohort

<table>
<thead>
<tr>
<th>Age of BMI</th>
<th>Se-adjusted deaths per 10,000 person-years (95% confidence intervals)</th>
<th>Hazard ratios (95% confidence intervals)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>(n = 1,387)</td>
<td>1.0</td>
</tr>
<tr>
<td>Overweight</td>
<td>(n = 1,489)</td>
<td>1.0</td>
</tr>
<tr>
<td>Obese</td>
<td>(n = 1,403)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Harrington, M. Natl Revs 2009

Mid-life weight change and mortality during long-term follow-up in Finnish men

Table 3: All-cause mortality in Finnish men of 65+ years with non-cardiovascular disease in the year 2008

Janssen, I. Obesity 2008

Among obese 70y/o:
43% were not obese at 50y (late gainers)
57% were already obese at 50y (early gainers)

Impact of current vs. mid-life obesity on mortality: Framingham Heart Study cohort

Table 4: All-cause mortality in Framingham Heart Study participants who lived for at least 70 years of age according to BMI at age 50 years

Janssen, I. Obesity 2008

Current vs. mid-life mortality among elderly: Framingham Heart Study cohort

Table 6: All-cause mortality in Framingham Heart Study participants who lived past 70 years of age

Janssen, I. Obesity 2008

Mid-life weight change and mortality during long-term follow-up in Finnish men

Table 5: All-cause mortality in Finnish men of 65+ years with non-cardiovascular disease in the year 2008

Strandberg, T. Eur Heart J 2009

![Graph showing Kaplan-Meier survival for different weight trajectories (2000-2012): Helsinki Businessmen Study.]

Weight trajectories over the life course (1974-2000): Helsinki Businessmen Study

Potential adverse effects of diet-induced weight loss
- Loss of lean mass (muscle and bone)
- Malnutrition
- Reduced energy reserve
- Depression
- Rebound fat gain

Intentional weight loss and all-cause mortality: 12y follow-up of 1RCT (n=585)

Fat loss improves self-reported mobility disability and walking speed

![Graph showing Fat loss improves self-reported mobility disability and walking speed.]

- Mean age = 66 y
- Mean BMI = 33 kg/m²
- Mean weight loss = 4.4 kg

![Graph showing Fat loss improves self-reported mobility disability and walking speed.]

- Mean age = 66y
- Mean BMI = 33 kg/m²
- Mean weight loss = 8 kg

Strandberg, T Eur Heart J 2009

Strandberg, T Am J Epidemiol 2013

Strandberg, T Am J Epidemiol 2013

Shea, MK AJCN 2011

Beaumier, R.J Gerontol 2013
Weight loss and/or exercise in elderly improve physical function (n=107)

Mean age ~70y
Mean BMI = 37 kg/m²
Mean weight loss in diet groups ~9kg (10%)

PPT = Physical Performance Test
FSQ = Functional Status Questionnaire

Review of existing literature of exercise (Ex) and/or diet-induced weight loss

- 5 RCT (n=198) of adults age>65y, BMI>30kg/m², measured body composition (DXA, CT, MRI, UW)
  1. N=27; 1y Diet+Ex vs. Control
  2. N=30; 6m Diet+Resistance Ex vs. Control
  3. N=16; 3m Diet vs. Ex
  4. N=18; 6m Diet+Ex vs. Control
  5. N=107; 1y Diet vs. Ex vs. Diet+Ex vs. Control

Summary of Diet and Exercise RCT data

- 10% weight loss is achievable, primarily through caloric restriction
- 70-80% fat mass, 15-30% fat-free mass
- Exercise attenuates, but doesn’t stop, loss of fat-free mass
- Physical function is improved
- Long-term health implications remain unknown

Conclusions

- The increasing prevalence of obesity among elderly is becoming a critical health challenge
- The epidemiologic data suggest the ideal BMI for older adults may be shifted higher and the risk of obesity-associated mortality blunted
- Yet, correction for critical statistical biases suggest obesity-associated mortality among elderly may in fact be increasing with age

Conclusions

- Mediators of the association between BMI and Mortality - The usual suspects
  - Existing CVD
  - Existing T2DM
  - Smoking
  - Hypertension
  - High cholesterol
  - Low fitness
  - Low muscle mass, high central adiposity

Conclusions

- Unintentional weight loss among obese elderly is associated with increased mortality
- Late-life development of obesity does not appear to increase mortality
- Intentional weight loss in obese elderly does not appear to increase mortality,
- Weight loss does improve physical function, particular when exercise is included
- Exercise helps to preserve muscle and bone in the context of diet-induced weight loss