Abstract

Objective: To test the hypothesis that adolescent obesity would be associated with greater risks of adverse health in severely obese adults.

Methods: Before weight loss surgery, adult participants in the Longitudinal Assessment of Bariatric Surgery-2 underwent detailed anthropometric and comorbidity assessment. Weight status at age 18 was retrospectively determined. Participants who were ≥80% certain of recalled height and weight at age 18 (1502 of 2308) were included. Log binomial regression was used to evaluate whether weight status at age 18 was independently associated with risk of comorbid conditions at time of surgery controlling for potential confounders.

Results: Median age and adult body mass index (BMI) were 47 years and 46, respectively. At age 18, 42% of subjects were healthy weight, 29% overweight, 16% class 1 obese, and 13% class ≥2 obese. Compared with healthy weight at age 18, class ≥2 obesity at age 18 independently increased the risk of lower-extremity venous edema with skin manifestations by 435% (P < .0001), severe walking limitation by 321% (P < .0001), abnormal kidney function by 302% (P < .0001), polycystic ovary syndrome by 74% (P = .03), asthma by 48% (P = .01), diabetes by 42% (P < .01), obstructive sleep apnea by 25% (P < .01), and hypertension (by varying degrees based on age and gender). Conversely, the associated risk of hyperlipidemia was reduced by 61% (P < .01).

Conclusions: Severe obesity at age 18 was independently associated with increased risk of several comorbid conditions in adults undergoing bariatric surgery. Pediatrics 2013;132:1098–1104
Although evidence exists documenting a positive relationship between duration of pediatric overweight/obesity and comorbidity later in life,1–5 little information is available describing the long-term health impact of severe adolescent obesity. As the pediatric obesity epidemic continues to unfold, with increasing prevalence of severe pediatric obesity in particular, it is important to understand long-term health consequences.

Severely obese children and adolescents rarely “outgrow” obesity. Longitudinal follow-up of the Bogalusa cohort of children (aged 5–14 years) with body mass index (BMI) values ≥99th percentile for age found that they attain a remarkable adult (mean age 27 years) BMI (mean = 43.6 ± 9), demonstrating childhood severe obesity serves as a useful predictor of adult severe obesity.6 What is not well understood is how adolescent weight status relates to health risks later in life. A useful method to model long-term effects is to retrospectively assess weight status in adults and determine how current health status is related to adolescent weight status. In our previous work,7 we developed an instrument to permit the identification of adults with a history of adolescent obesity through recall.

Our objective was to model the impact of obesity in adolescence on health outcomes later in adulthood. Using adults with severe obesity enrolled in the Longitudinal Assessment of Bariatric Surgery-2 (LABS-2),8 we characterized reported weight status at age 18. We also determined whether weight status at age 18 was independently associated with risk of having major obesity-related comorbid conditions and cardiometabolic risk factors at time of bariatric surgery, while accounting for the potential influence of confounders. We hypothesized that compared with being of healthy weight, severe obesity at age 18 would markedly increase the risk of adverse health conditions for those undergoing bariatric surgery as adults.

METHODS
Participants
LABS-2 is an observational study designed to assess the risks and benefits of bariatric surgery in adults.8 Patients who were ≥18 years old seeking a first bariatric surgical procedure at 10 centers throughout the United States were recruited between February 2006 and February 2009. By close of enrollment, 2458 participants attended a preoperative research visit and underwent a bariatric surgical procedure as part of clinical care. All participating centers had institutional review board approval and all participants provided written informed consent. The LABS-2 study is registered at www.clinicaltrials.gov (#NCT00465829). The current study uses a subsample of this LABS-2 cohort (n = 1502) based on inclusion criteria detailed subsequently.

Measures
Cincinnati Weight History Questionnaire
The Cincinnati Weight History Questionnaire (CWHQ) is a self-report measure designed to assess obese respondents’ perception of their weight status at various time points earlier in life7 (see online Supplement Information). The 20-item instrument consists of questions related to recall of body weight, height, and size (eg, perceived size compared with age mates, clothing size) at age 18, as well as perceived duration of excess weight status. The initial validation study for the CWHQ suggested moderate sensitivity for recall of height and weight at age 18. Therefore, for the current study, the CWHQ was modified such that each item was also yoked to a follow-up question that further assessed a respondent’s level of certainty (range 0%–100%) for each recalled response. Only 2 CWHQ questions/confidence ratings were included in the present analyses: those targeting recall of height and (non-pregnant) weight at age 18. Only those respondents whose confidence rating was 80% or higher for both height and weight were included. Of the 2458 LABS-2 subjects, 2308 completed the CWHQ by November 15, 2012, of whom 65% (n = 1502) met these criteria. Their estimated BMI at age 18 was calculated as weight (kg)/height (meters)2 and used to determine adolescent weight status (healthy weight: BMI <25; overweight: BMI 25 to <30; class 1 obese: BMI 30 to <35; class 2 obese: BMI 35 to <40; class 3 obese: BMI ≥40).

Demographics, BMI, and Health Status at Time of LABS-2 Enrollment
Gender, race, ethnicity, marital status, education, employment status, household income, and smoking status were assessed by questionnaire as previously described.8,9 Age was determined from date of birth and date of surgery. Height and weight were measured according to standard protocol, and BMI was calculated.10 The following major comorbidities and cardiometabolic risk factors were assessed: diabetes, hypertension, ischemic heart disease, dyslipidemia, hyperlipidemia, polycystic ovary syndrome (PCOS), obstructive sleep apnea, asthma, abnormal renal function, microalbuminuria, urinary incontinence, lower extremity venous edema with skin manifestations (venous edema), and severe walking limitation. Data sources for comorbidity assessment included self-report, abstraction from medical records, patient interview, physical examination, and laboratory assays. Laboratory assays were performed by the Northwest Lipid Metabolism and Diabetes Research Laboratories (Seattle, WA). Detailed comorbidity definitions are available in the online Supplemental Information,
and the technical details pertaining to assays have also been previously described.\(^9\)

Excluding PCOS, which only applies to female patients, and hyperlipidemia, which is a subset of dyslipidemia, the number of major comorbidities was summed (possible range: 0–11) to provide a rough estimate of disease burden. Disease severity was not taken into account and all diseases were weighted equally.

**Statistical Analyses**

Potential selection bias was examined by comparing preoperative characteristics of LABS-2 participants in the analysis sample (\(n = 1502\)) to those excluded (\(n = 956\)) using Pearson’s \(\chi^2\) test (categorical variables) and Wilcoxon rank-sum test (continuous variables). Pearson’s correlation was used to examine the relationship between BMI at age 18 and age at time of surgery. Multiple log-bionomial regression was used to evaluate whether weight status at age 18 (overweight, class 1 obese, and class 2 or 3 obese vs normal weight) was independently associated with health outcomes, controlling for age (which is analogous to controlling for years since age 18) and change in BMI from age 18 to time of surgery (which were centered at their mean), as well as gender and race, if they were independently related to the outcome (\(P < .05\)). Models for abnormal kidney function and microalbuminuria also controlled for diabetes and hypertension status. Higher-order terms and all possible interactions within the main effects model were considered and kept if significant at \(\alpha = .05\) and their inclusion improved the model fit.\(^11,12\)

We present adjusted relative risks (ARR) and 95% confidence intervals (95% CI) for weight status at age 18 and years since age 18. Statistical analyses were performed with SAS (version 9.3; SAS Institute Inc, Cary, NC).

**RESULTS**

**Characteristics of Study Participants**

At the time of surgery, age for the 1502 participants ranged from 19 to 76 (median age 47 years); BMI ranged from 34 to 94 (median 46; Table 1). Most (96%) exhibited obesity-related comorbid conditions, with almost two-thirds (64.5%) having ≥3 comorbidities or cardiometabolic risk factors of the 11 that were considered. Hypertension (66.9%), dyslipidemia (63.3%), obstructive sleep apnea (55.5%), urinary incontinence (44.4%), hyperlipidemia (36.9%), and diabetes (33.2%) were relatively common conditions in the cohort (Table 1).

Compared with LABS-2 participants excluded from this analysis (\(n = 956\)), included participants (\(n = 1502\)) were slightly older (median age 47 vs 45 years; \(P < .01\)), and a greater percentage were male (23% vs 19%; \(P = .03\)), white (88% vs 83%; \(P < .0001\)), and had obstructive sleep apnea (56% vs 48%; \(P < .001\)) and PCOS (15% vs 11% among females; \(P < .01\)), whereas a smaller percentage had venous edema (6% vs 8%; \(P = .0499\)). There were no significant differences between included and excluded groups with respect to ethnicity, BMI, number of comorbidities, or the percentage with diabetes, hypertension, ischemic heart disease, dyslipidemia, hyperlipidemia, asthma, abnormal kidney function, microalbuminuria, urinary incontinence, and severe walking limitation.

**Weight Status at Age 18**

BMI at age 18 ranged from 14.5 to 69.7 kg/m\(^2\). Median BMI at age 18 was 25.9 (interquartile range: 22.5–31.0), with 42% normal weight, 29% overweight, and 29% obese (16% class 1 obese, 7% class 2 obese, and 6% class 3 obese). BMI at age 18 was significantly inversely correlated with age at time of surgery (\(r = -0.44\); \(P < .0001\)). As indicated in Table 2, it was relatively rare for older adults to have severe obesity in adolescence (eg, 0.5% of those aged ≥60 years vs 36% of those aged <30 years), whereas it was relatively rare for younger adults to have normal weight in adolescence (eg, 7% of those <30 years vs 64% of those ≥60 years).

| TABLE 1 Preoperative Characteristics of Adults Undergoing Bariatric Surgery |
|----------------|----------------|----------------|
| Male           | 344 (22.9)     |                |
| Age, y, median (IQR) | 47 (38–55)   |                |
| Race           |                |                |
| White          | 1317 (88.2)    |                |
| African American | 123 (8.2)   |                |
| Other          | 54 (3.6)       |                |
| Hispanic       | 69 (4.6)       |                |
| BMI, median (IQR) | 45.8 (41.7–51.3) |        |
| Diabetes       | 474 (33.2)     |                |
| Hypertension   | 973 (66.9)     |                |
| Ischemic heart disease | 90 (6.1) |                |
| Dyslipidemia   | 760 (53.3)     |                |
| Hyperlipidemia | 445 (35.9)     |                |
| PCOS           | 167 (15.2)     |                |
| Obstructive sleep apnea | 832 (55.5) |            |
| Asthma         | 388 (25.3)     |                |
| Abnormal kidney function | 111 (7.7) |            |
| Microalbuminuria | 164 (12.2)  |                |
| Urinary incontinence | 630 (44.4) |            |
| Venous edema   | 93 (6.2)       |                |
| Severe walking limitation | 99 (7.2)  |                |

Frequency (% reported unless otherwise indicated. IQR, interquartile range.

\(a\) Missing: race, n = 8; ethnicity, n = 1; diabetes, n = 74; n = 60; hypertension, n = 47; ischemic heart disease, n = 26; dyslipidemia, n = 302; hyperlipidemia, n = 295; PCOS (of 1158 women), obstructive sleep apnea, n = 2; asthma, n = 27; abnormal kidney function, n = 63; microalbuminuria, n = 159; urinary incontinence, n = 85; venous edema, n = 2; severe walking limitation, n = 123; number of comorbid conditions, n = 535.

\(b\) Hyperlipidemia was defined as all individuals taking a lipid-lowering medication or with a high level of LDL cholesterol (≥160 mg/dL). Dyslipidemia was defined as having either hyperlipidemia, a low level of high-density lipoprotein (<40 mg/dL), or high triglycerides (≥200 mg/dL).

\(c\) Includes all comorbidities listed above except PCOS, which applies only to women, and hyperlipidemia, which is a subset of dyslipidemia.
Relationship Between Weight Status at Age 18 and Adult Health Status

The adjusted relative risks of having comorbidities and cardiometabolic risk factors associated with weight status at age 18 are shown in Table 3. After adjustment, compared with healthy weight at age 18, class 2 or 3 adolescent obesity independently increased the risk for venous edema (435%), severe walking limitation (321%), abnormal kidney function (302%), PCOS (74%), asthma (48%), diabetes (42%), obstructive sleep apnea (25%), and hypertension (25% among females at mean age 46) in adulthood. Compared with healthy weight, class 1 adolescent obesity also increased the risk for venous edema (202%), abnormal kidney function (83%), PCOS (75%), diabetes (37%), obstructive sleep apnea (20%), and hypertension (16% for women and 42% for men at mean age 46). Even overweight at age 18 significantly increased the risk for venous edema (120%) and severe walking limitation (116%) in adults undergoing bariatric surgery.

There was a significant interaction between weight status at age 18 and both gender and age relation to hypertension, such that class 2 or 3 obesity at age 18 had a greater effect in women versus men and in younger versus older adults. For example, among women, class 2 or 3 obesity at age 18 increased risk of hypertension by 25% at the mean age of 46 years, whereas risk was increased by 48% at age 30 (data not shown).

Class 2 or 3 obesity at age 18 independently reduced the risk of hyperlipidemia by 61% and overweight at age 18 reduced the risk by 16%. However, weight status at age 18 was not significantly associated with dyslipidemia, or ischemic heart disease, urinary incontinence, or microalbuminuria. Because of the low prevalence of ischemic heart disease (6.1%), this study had adequate power to detect only a large increase in risk.

Relationship Between Age and Adult Health Status

We also examined whether there was an independent effect of age on adult health outcomes (eg, controlling for adolescent BMI or change in BMI from age 18 to adulthood). Each decade since age 18 was associated with an increased risk of ischemic heart disease (ARR = 2.16; 95% CI = 1.76–2.64; P < .0001), asthma (ARR = 1.17; 95% CI = 1.07–1.28 in female subjects; AR = 0.87; 95% CI = 0.70–1.07 in male subjects; P < .01), abnormal kidney function (ARR = 1.92; 95% CI = 1.60–2.31; P < .0001), abnormal kidney function (ARR = 1.99; 95% CI = 1.68–2.36; P < .0001), abnormal kidney function (ARR = 1.01; 95% CI = 1.00–1.02 in female subjects; ARR = 1.04; 95% CI = 1.02–1.06 in male subjects; P < .01), venous edema (ARR = 1.80; 95% CI = 1.47–2.20; P < .0001), and severe walking limitation (ARR = 1.99; 95% CI = 1.68–2.36; P < .0001). Age was also associated with an increased risk of diabetes, hypertension, hyperlipidemia, and obstructive sleep apnea (all Ps < .05), although the nature of these relationships was quadratic and some differed by gender or weight status (Supplemental Table 4 and Supplemental Figs 1–4). Interestingly, increasing decade beyond age 18 was negatively associated with PCOS (ARR = 0.71; 95% CI = 0.61–0.83; P < .0001), whereas age was not related to microalbuminuria (ARR = 0.97; 95% CI = 0.83–1.13; P = .70).

DISCUSSION

The aging process and cumulative effects of various exposures over time have health impacts that result in development of detrimental health conditions in adults not commonly seen in pediatric age groups. Not unexpectedly, our findings support this concept. Each decade beyond age 18 incrementally increased risk of 11 of the 13 comorbidities evaluated in this study. However, not widely appreciated is the impact of adolescent obesity on longer-term outcomes and especially the impact of severe adolescent obesity, independent of other confounding variables. The risk of numerous comorbid conditions was significantly elevated by adolescent obesity, independent of the change in BMI since adolescence. These comorbid conditions included diabetes, PCOS, hypertension, obstructive sleep apnea, asthma, abnormal kidney function, venous edema, and severe walking limitation.

Indicative of a secular trend of increasing BMI in younger birth cohorts compared with older birth cohorts, the youngest adults in this analysis had

### Table 2: Age at Time of Bariatric Surgery by Weight Status at Age 18

<table>
<thead>
<tr>
<th>Wt status at age 18</th>
<th>Total</th>
<th>Age at time of surgery (y)</th>
<th>&lt;30 (n = 124)</th>
<th>30 to &lt;40 (n = 338)</th>
<th>40 to &lt;50 (n = 413)</th>
<th>50 to &lt;60 (n = 440)</th>
<th>≥60 (n = 187)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal wt</td>
<td>628 (41.8)</td>
<td>9 (7.3)</td>
<td>85 (25.2)</td>
<td>174 (42.1)</td>
<td>240 (54.6)</td>
<td>120 (64.2)</td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>436 (29.0)</td>
<td>17 (13.7)</td>
<td>109 (32.3)</td>
<td>130 (31.5)</td>
<td>129 (29.3)</td>
<td>51 (27.3)</td>
<td></td>
</tr>
<tr>
<td>Class 1</td>
<td>239 (15.9)</td>
<td>31 (25.0)</td>
<td>81 (24.0)</td>
<td>65 (15.7)</td>
<td>49 (11.1)</td>
<td>13 (7.0)</td>
<td></td>
</tr>
<tr>
<td>Class 2</td>
<td>102 (6.8)</td>
<td>22 (17.7)</td>
<td>41 (12.1)</td>
<td>24 (5.8)</td>
<td>13 (3.0)</td>
<td>2 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Class 3</td>
<td>97 (6.5)</td>
<td>45 (36.3)</td>
<td>22 (6.5)</td>
<td>20 (4.8)</td>
<td>9 (2.1)</td>
<td>1 (0.5)</td>
<td></td>
</tr>
</tbody>
</table>

V (column %) shown.
TABLE 3  Risk of Comorbidities at Time of Bariatric Surgery Attributed to Weight Status at Age 18*

| Weight Status at Age 18 | Normal | Overweight | Class 1 | Class2/3 | P
|------------------------|--------|------------|---------|----------|---
| Venous edema           | 1 (reference) | 2.20 (1.38–3.51) | 3.02 (1.64–5.58) | 5.35 (2.57–11.14) | <.0001
| Severe walking limitation| 1 (reference) | 2.16 (1.37–3.42) | 1.60 (0.81–3.18) | 4.21 (2.13–8.35) | <.001
| Abnormal kidney function| 1 (reference) | 1.49 (0.97–2.28) | 1.83 (1.05–3.20) | 4.02 (2.52–6.42) | <.0001
| PCSD (women only)      | 1 (reference) | 1.46 (0.98–2.16) | 1.75 (1.14–2.69) | 1.74 (1.06–2.89) | .06
| Ischemic heart disease  | 1 (reference) | 1.37 (0.87–2.17) | 1.63 (0.87–3.07) | 1.53 (0.64–3.63) | .39
| Asthma                 | 1 (reference) | 1.02 (0.82–1.28) | 1.25 (0.97–1.61) | 1.48 (1.08–2.02) | .051
| Diabetes               | 1 (reference) | 1.07 (0.90–1.27) | 1.37 (1.12–1.68) | 1.42 (1.09–1.84) | <.01
| Microalbuminuria       | 1 (reference) | 0.93 (0.66–1.31) | 0.96 (0.81–1.52) | 1.35 (0.82–2.22) | .47
| Obstructive sleep apnea| 1 (reference) | 1.05 (0.95–1.16) | 1.20 (1.08–1.34) | 1.25 (1.09–1.44) | <.0001

* Relative risks and 95% CIs for weight status are adjusted for age and change in BMI, which were centered at their mean; gender and race, if significantly related to the outcome; and significant interactions. Models for abnormal kidney function and microalbuminuria also controlled for diabetes and hypertension.

b P value for overall effect.

c There was a significant interaction between weight status at age 18 and both gender and age. Relative risks are presented at mean age, 46 y.

We found a strong effect of adolescent overweight and class 1 obesity on risk of conditions related to physical/anatomic effects of weight, including venous edema and severe walking limitation. Only 1 study has examined walking limitation, and no studies have examined risk of venous edema, as a function of duration of obesity. Whether the effect on walking ability in our study was attributable to weight alone or in combination with other medical conditions is not clear. One major factor limiting our ability to assess the importance of this finding is that only 6% to 7% of the cohort was affected with either severe walking limitation or venous edema.

Adults with adolescent obesity had a markedly elevated risk of abnormal kidney function. This association was seen after controlling for likely confounders such as diabetes and hypertension, as well as years since age 18, suggesting that the risk was independent of these factors. Although numerous studies have related obesity to abnormal kidney function, few have examined the effect of early onset or duration of obesity on kidney outcome.

the highest prevalence of adolescent obesity and severe obesity. However, although adolescent obesity was less common among older adults, it was still represented (ie, 69 adults aged ≥40 reported class 2 or 3 obesity at age 18). Thus, we were able to evaluate the effect of severe obesity in adolescence among younger and older adults. Additionally, because analysis controlled for both years since age 18 and change in BMI since age 18, we were able to investigate the independent effect of adolescent weight status.

Duration of obesity is a risk factor for mortality, independent of adult BMI. Framingham found that 2 decades of obesity duration increased mortality risk 2.5-fold. This relationship is mediated in part by obesity-related comorbid conditions. In Israeli military recruits followed from late adolescence to adulthood, high adolescent BMI increased adult diabetes and coronary artery disease risks by nearly threefold and fivefold, respectively. Similarly, several studies have shown “excess BMI-years” increase risk of diabetes21,15–17 and cardiovascular risks.17

Gelber18 studied the association between weight status and glomerular filtration rate (GFR) in 11,000 men and found that high BMI (>26) increased risk of chronic kidney disease (GFR <60 mL/min/1.73 m²) by 26% after 14 years. However, this was an older cohort with average age of 52 years at baseline that was not selected on the basis of BMI. Vivante examined the effect of adolescent obesity on risk of end-stage renal disease (ESRD) 25 years later; adolescent obesity conferred a 3.4-fold increased risk of nondiabetic ESRD and a sevenfold greater risk of diabetic ESRD in adulthood.18 Our finding of a detrimental effect of adolescent BMI on estimated GFR is congruent with these findings. It is a reasonable assumption that over time, obesity-associated metabolic or hemodynamic effects result in kidney injury even with modest elevations in BMI and is more apparent in those with more severe obesity early in life. Although dramatic weight loss seen with bariatric procedures certainly does reverse many of the comorbid conditions associated with severe obesity, the plasticity/reversibility of other conditions, such as abnormal kidney function, remains uncertain.

Our analysis suggests that there is a protective effect of adolescent obesity on hyperlipidemia, but not dyslipidemia, in adults undergoing bariatric surgery. Although most studies of obesity duration point to greater cardiovascular risks for those with longer-standing obesity, including higher risks of dyslipidemia, others have found an equivocal or, as suggested by our data, a negative association between obesity in younger years and hyperlipidemia later in life. This finding of a possible protective effect of adolescent obesity on development of high level of LDL cholesterol later in life is enigmatic at present. It is reassuring from a methodologic standpoint that, controlling for the effects of adolescent weight status, age
did independently predict a significant increase in risk of hyperlipidemia in this same cohort.

This study provides some insight into long-term health risks for adolescents who carry obesity forward in life. A notable strength of this study is the high-quality and uniform assessments of comorbidities in a large sample of severely obese adults across 10 hospitals in the United States. However, the fact that these individuals were highly selected and motivated to undergo a surgical weight loss intervention represents a limitation. This group is not representative of the general population of obese adults because surgical selection criteria generally preclude individuals with BMI <40 or <35 without comorbidities. Another important limitation of this study is the absence of information regarding the actual duration of obesity in this cohort because we did not collect information about which specific age each subject became obese nor the extent to which cycling between obese and nonobese status occurred before bariatric surgery. Thus, these current data cannot be used to define the outcome of “pound-years” per se, which would require more detailed knowledge of weight status over the life of the participants. Finally, another potential limitation of the study is the reliance on recalled weights and heights for defining adolescent BMI and weight status in this cohort. Others authors have noted remarkably good recall of weight history over 3 decades,22,23 but long-term recall of weight by obese men and women may result in underestimation of previous weight by as much as 7 kg.24 Accordingly, the present data may reflect an underestimation of true adolescent BMI and the extent of adolescent excess weight severity in this adult cohort. By limiting analyses to those who were most confident in their recalled height and weight at age 18, we likely increased the validity of these self-reported data.

CONCLUSION

These findings demonstrate that higher weight status at age 18 was associated with undergoing bariatric surgery at an earlier adult age and was independently associated with increased risk of several common comorbid conditions. It will be important for future studies to document whether these individuals who were severely obese as adolescents experienced similar or different outcomes of surgery (surgical safety, improvements in comorbidities, or reduction in BMI) compared with those with a healthier adolescent weight status.

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(Continued from first page)

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1104 INGE et al
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