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Age-dependent decline of association between obesity and coronary heart disease: a cohort study in a remote Australian Aboriginal community

Zhiqiang Wang, Wendy E Hoy

ABSTRACT

Objective: To determine whether the association between obesity and coronary heart disease (CHD) in Aboriginal adults depends on age.

Design, setting and participants: A cohort study with up to 20 years of follow-up of 849 participants aged 18–76 years in a remote Aboriginal community in the Northern Territory of Australia.

Main outcome measures: Newly diagnosed CHD cases were identified through hospital records according to ICD codes during the follow-up period. Cox proportional hazard model was used to assess whether the association between obesity and CHD depends on age.

Results: During the follow-up period, 171 participants were diagnosed with CHD. On an average, the incidence rate of CHD increased with the increasing baseline BMI, 11.3%, 16.3% and 20.2% for normal weight, overweight and obese groups, respectively. HRs corresponding to 1 SD increase in BMI were 1.4 (1.0 to 2.0), 1.2 (1.0 to 1.5) and 0.8 (0.5 to 1.2) for those <40, 40–59 and 60+ years, respectively. The interaction terms between age and BMI as category variables or as a continuous variable were statistically significant.

Conclusions: The association between obesity and CHD is stronger for younger adults than for older adults in Aboriginal Australians in the remote community. Our findings suggest that weight control efforts may produce more beneficial effects in CHD prevention in young adults than in older adults.

INTRODUCTION

It has been well established that overweight and obesity increase the risk of mortality and coronary heart disease (CHD) in a number of studies over several decades.1–8 Weight reduction has been found to be beneficial in reducing the CHD risk among overweight and obese people.9–11 It has been suggested the effect of body mass index (BMI) on cardiovascular disease mortality is modified by age.12 A recent analysis by the Emerging Risk Factors Collaboration of a database of over 200 000 participants in 51 studies from 17 countries shows that the strength of the association between BMI and CHD was stronger for younger adults than for older adults.13 On the other hand, a study on obesity and mortality in the USA suggested that the diminishing obesity–mortality association with age was confounded by age at survey and cohort effects, and once those factors were accounted for, the obesity–mortality became stronger with age.14 Understanding the presence of such effect modification by age is important for directing prevention efforts and prioritising public health education. Aboriginal Australians have a high risk of CHD and their CHD is diagnosed at a younger age than non-Aboriginal people.15 It is still not known whether obesity has different effects on CHD risk among Aboriginal people of different ages. The objective of this study was to determine whether age modifies the association between BMI and CHD risk. We analysed the cohort data with up to 20 years follow-up from a remote Aboriginal community in the Northern Territory of Australia.
METHODS

Participants and CHD events

This is a prospective cohort study with up to 20 years of follow-up. Participants were recruited from a remote Aboriginal community in the Northern Territory of Australia from 1992 to 1995. Weight and height were measured for 849 participants aged 18–75 years and who were free from clinically apparent CHD at baseline, representing over 80% of those within the age range in the region. Those participants were followed up until 31 May 2012. During the follow-up period, new CHD events were identified through hospital records using the International Classification of Diseases codes (ICD 9 codes 410–414, and ICD 10 codes I20–I25), including myocardial infarction (410, I21), angina pectoris (411, I20) and other ischaemic heart disease (413, 414, I22, I23, I24 and I25). Deaths and their causes during the follow-up period were determined through a list of death records maintained at the community clinics. For those participants who reached a CHD event or died from non-CHD causes during the follow-up, their follow-up time was the period from the age of their initial screening visit to the age of the first CHD event or death. Others who survived the follow-period were censored at 31 May 2012. Because individual hospital registration numbers which we used to track study participants were unique throughout the Northern Territory, we were able to capture their hospitalisation records even if our study participants had moved outside the local region. The chance of being hospitalised outside the Northern Territory was extremely low, if any, for people in this remote isolated region. Those without hospital and death records were regarded as free from CHD during the follow-up period.

Baseline BMI measurements

Height and weight were measured for study participants at baseline during 1992–1995. Height was measured to the nearest 0.5 cm without shoes. Weight was measured to the nearest 0.1 kg with participants wearing light clothes only and without shoes. BMI was defined as weight divided by height squared (kg/m²). Since those measurements had been taken several years before the development of CHD, BMI readings were not biased by the presence of CHD endpoints.

Statistical analysis

The data were partitioned into age bands of <40, 40–59 and 60+ years throughout the follow-up. For those whose age fell into two age bands during the follow-up period, their total follow-up time was subdivided and allocated into the corresponding age bands as described by Clayton and Hills.16 We calculated the incidence rates of CHD according to their baseline BMI values: <25, 25–29.9 and 30+ kg/m². HRs of CHD for obesity and 1 SD increase in BMI were calculated with Cox proportional hazards models adjusting for baseline age and gender. We assessed effect-modification with a formal test of the interaction term between age and BMI (or obesity). To further control the effect of competing risk of non-CHD death, we used a competing-risks regression method17 to estimate the HRs. All analyses were performed with Stata SE V.12.1.18

RESULTS

Table 1 shows the characteristics of the study participants with different baseline BMI levels. Those obese participants were more likely to be women. They also had higher levels of systolic and diastolic blood pressure, and higher prevalence of known diabetes but lower prevalence of cigarette smoking and alcohol drinking at baseline.

During the follow-up period of 12,398 person-years in 849 participants, 128 died from non-CHD causes and 171 were diagnosed with CHD. Table 2 shows the detailed follow-up time and the number of cases by age and BMI groups. On an average, the incidence rates of CHD, which increased with the increasing baseline BMI, were 11.3%, 16.3% and 20.2% for normal weight, overweight and obese groups, respectively.

<table>
<thead>
<tr>
<th>Table 1 Baseline characteristics of study participants by baseline BMI levels: mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline BMI (kg/m²)</strong></td>
</tr>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Male, n (%)</td>
</tr>
<tr>
<td>Age, years</td>
</tr>
<tr>
<td>Weight, kg</td>
</tr>
<tr>
<td>Height, cm</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
</tr>
<tr>
<td>Waist c., cm</td>
</tr>
<tr>
<td>Systolic pressure, mm Hg</td>
</tr>
<tr>
<td>Diastolic pressure, mm Hg</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
</tr>
<tr>
<td>Drinking, n (%)</td>
</tr>
<tr>
<td>Known diabetes, n (%)</td>
</tr>
</tbody>
</table>

A rising trend in CHD risk with increased BMI was observed in younger age groups (figure 1). Estimated HRs with adjustment of baseline age, gender, known diabetes and smoking status are shown in table 3. For those younger than 40 years, adjusted HRs for overweight and obesity were 1.5 (95% CI 0.6 to 3.5) and 2.6 (95% CI 1.1 to 6.3), respectively, with BMI <25 kg/m² as the reference group. For those aged 40–59 years, their HRs of CHD were 1.1 (95% CI 0.7 to 1.8) and 1.2 (95% CI 0.7 to 2.0) for overweight and obesity, respectively. However, for those aged 60 years or older, the CHD risk for normal BMI group was as high as those for overweight and obese groups and no increasing trend in CHD risk with increasing BMI was observed in this age group. To assess whether the association between BMI and CHD risk depended on age and gender, we tested the interaction terms of BMI with age and gender in the Cox proportional hazard models. The overall test for interaction terms between age and BMI categories was statistically significant (p=0.012).

When BMI was treated as a continuous variable, the HRs corresponding to 1 SD increase in BMI decreased with increasing age, 1.4, 1.2 and 0.8 for those younger than 40, 40–59 and 60 years or older, respectively. The interaction term between age and BMI as a continuous variable was also statistically significant (p=0.011).

Further adjusting for competing risk of non-CHD deaths, the pattern of the association between CHD and BMI either as a continuous variable or as categorical variables remained similar (table 4). The association was stronger for younger adults than for older adults with a statistically significant interaction term between age and BMI.

**DISCUSSION**

In this cohort study with up to 20 years follow-up, we found that age is a strong effect modifier for the association between obesity (or BMI) and CHD in Aboriginal people. The association between obesity and CHD declined with age. The younger they are, the stronger the association between BMI and CHD. Among adults under 40 years, the risk of CHD is 2.6 times in obese individuals as in those with BMI <25 kg/m², but there is no significant association between obesity and CHD among those 60 years or older. Our findings suggest that the effect of obesity on development of CHD is stronger in younger people than in older people.

It has been well established that the people with high BMI have a high risk of CHD, but a very few studies have assessed the effect modification of the BMI-CHD association by age. The Emerging Risk Factors Collaboration group suggested that age is a strong effect modifier for BMI-CHD association. They reported that the HRs for CHD associated with per 1 SD increase in BMI decreased with increasing age, from 1.41 for their youngest group (40–59 years) to 1.23 for 60–69 and 1.12 for 70 years or older. In our study, we used different age groups because CHD occurred at younger ages in Aboriginal people. Nevertheless, the pattern of effect modification by age in our study was similar to that reported by the Emerging Risk Factors Collaboration group. To our knowledge, this is the first study to assess effect modification by age in a high-risk indigenous population.

It has also been reported that excess body weight increases the risk of death from any cause and from cardiovascular disease and the relative risk with greater body weight is higher among younger participants in a study of US adults. However, a study by Masters et al suggested that survey-based estimates of age patterns in
has been considered to affect CHD risk through its influence on those known risk factors.\(^2^7\) We did not adjust for those known risk factors in our analysis.

There are several limitations in this study. BMI was estimated only once at one age point for each participant and no recent BMI values were taken. Therefore, the effect of BMI changes on CHD risk could not be directly assessed. The CHD cases were identified through routinely documented hospital records during the follow-up period. Under-reporting is possible as some participants with minor CHD events may not be hospitalised and diagnosed as such. However, there is no evidence that such under-reporting could have occurred differently among people with different BMI levels. Another limitation of this study is the small sample size, particularly for the older age group. Although the interaction term for testing the dependence of the BMI–CHD association on age was statistically significant, the association between BMI and CHD in the older age group could not be accurately estimated as reflected by the wide 95% CIs. Finally, the study was conducted in a single relatively homogenous population in one community. It remains to be verified whether our findings can be applied to the general Aboriginal population in Australia.

### CONCLUSION

The association between obesity and CHD declines with increasing age and is stronger in young adults than for older adults in Aboriginal Australians. Our findings imply that the efforts of obesity prevention and weight control are more likely to produce beneficial effects on CHD prevention in younger than in older people. Further interventional studies are needed to quantify

#### Table 3: HRs* of CHD for different baseline BMI levels by age groups

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Overweight† HR (95% CI)</th>
<th>Obese† HR (95% CI)</th>
<th>Interaction p Value‡</th>
<th>BMI (1 SD)* HR (95% CI)</th>
<th>Interaction p Value§</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>1.5 (0.6 to 3.5)</td>
<td>2.6 (1.1 to 6.3)</td>
<td>0.012</td>
<td>1.4 (1.0 to 2.0)</td>
<td>0.011</td>
</tr>
<tr>
<td>40–59</td>
<td>1.1 (0.7 to 1.8)</td>
<td>1.2 (0.7 to 2.0)</td>
<td></td>
<td>1.2 (1.0 to 1.5)</td>
<td></td>
</tr>
<tr>
<td>60+</td>
<td>1.0 (0.5 to 2.5)</td>
<td>0.5 (0.1 to 2.1)</td>
<td></td>
<td>0.8 (0.5 to 1.2)</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for age, gender, known diabetes and smoking status.  
†With BMI <25 kg/m\(^2\) as reference.  
‡Interaction between age and BMI as category variables.  
§Interaction between age and BMI as a continuous variable.

#### Table 4: HRs of CHD for different baseline BMI levels adjusting for competing risk of non-CHD death

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Overweight* HR (95% CI)</th>
<th>Obese* HR (95% CI)</th>
<th>Interaction p Value‡</th>
<th>BMI (1 SD)* HR (95% CI)</th>
<th>Interaction p Value§</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>1.5 (0.6 to 3.6)</td>
<td>2.6 (1.1 to 6.0)</td>
<td>0.026</td>
<td>1.4 (1.1 to 2.0)</td>
<td>0.012</td>
</tr>
<tr>
<td>40–59</td>
<td>1.2 (0.7 to 1.8)</td>
<td>1.3 (0.8 to 2.1)</td>
<td></td>
<td>1.2 (1.0 to 1.4)</td>
<td></td>
</tr>
<tr>
<td>60+</td>
<td>1.2 (0.6 to 2.5)</td>
<td>0.5 (0.1 to 2.1)</td>
<td></td>
<td>0.8 (0.5 to 1.2)</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for competing risk of non-CHD death, age, gender, known diabetes and smoking status.  
†Interaction between age and BMI as category variables.  
‡Interaction between age and BMI as a continuous variable.
the effect of weight reduction on CHD risk in people of different ages.

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Contributors WEH and ZW conceived the idea of the study and were responsible for the design of the study. WEH provided input into the data analysis and was responsible for the acquisition of the baseline data. ZW was responsible for linking baseline and hospital data and for undertaking data analysis. Both WEH and ZW contributed to the first draft, and read and approved the final version.

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Competing interests WEH was supported by Australian Fellowship (#511081) and ZW by NHMRC Fellowship (APP1042345).

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