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Esophageal cancer and body mass index: Results from a prospective study of 220,000 men in China and a meta-analysis of published studies

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Several epidemiological studies have reported on the association between body mass index (BMI) and risk of esophageal cancer, but these were mostly in Western populations where many are overweight or obese. There is little direct evidence about the relationship in China where the mean BMI is relatively low and the disease rate is high. We examined the data from a population-based prospective study of 220,000 Chinese men aged 40–79 without a previous history of cancer (mean BMI 21.7 kg/m^2), which included 1,082 esophageal cancer deaths during 10 years of follow-up. Adjusted hazard ratios for death from esophageal cancer by baseline BMI category were calculated using Cox proportional hazards models. Even among men with good self-assessed health and BMI $\geq$ 18.5 kg/m^2, there was a strong inverse association between BMI and death from esophageal cancer, with each 5 kg/m^2 higher BMI associated with 25% (95%CI: 11–36%) lower esophageal cancer mortality. This inverse association persisted when analysis was restricted to men who had never smoked or when the first 5 years of follow-up were excluded. The strength of the relationship was consistent with the pooled estimate for squamous cell carcinoma of the esophagus in a meta-analysis of prospective studies (31% lower relative risk per 5 kg/m^2 higher BMI; 95% CI: 25–37%), but contrasted with that for adenocarcinoma which showed a positive association with BMI. Together, these data provide reliable evidence that in many populations low BMI is associated with an increased risk of squamous cell carcinoma of the esophagus.

Key words: body mass index; cohort study; mortality; esophageal cancer

Introduction

Esophageal cancer is amongst the most common neoplastic causes of death world wide, accounting for an estimated 400,000 deaths annually, of which about half occur in China.[1,2] Several epidemiological studies have reported on the relationship between esophageal cancer and body fatness, usually measured indirectly by body mass index (BMI). In general, these studies have tended to show that BMI is associated positively with the risk of adenocarcinoma of the esophagus, but inversely with the risk of squamous cell carcinoma,[3–5] which are the two main histological types of the disease. Most were case control studies, so were particularly susceptible to reverse causality bias[6,7] (*i.e.*, an artefact as a result of weight loss due to pre-existing disease at the time of measurement) or other biases as a result of attempting to estimate weight prior to onset of the illness.[8] In the few prospective cohort studies that demonstrated an inverse association between squamous cell carcinoma of the esophagus and BMI,[5,9,10] questions also remain as to whether inadequate control for potential confounding factors such as smoking and heavy alcohol drinking[11] or failure to deal rigorously with reverse causality may have contributed, at least in part, to the observed association.[9]

Most of the previous studies were conducted in Western populations in which the mean BMI is high but the incidence of esophageal cancer is relatively low. There is little reliable epidemiological evidence about the association with BMI in the Chinese population, where the mortality from esophageal cancer (which is predominantly squamous cell carcinoma) is particularly high[12] and mean BMI is relatively low. We report here the findings from a nationally representative prospective cohort study of the association between BMI and mortality from esophageal cancer involving more than 220,000 Chinese men aged 40–79. To put our results into context with those from other populations and to help quantify reliably the magnitude of the potential association with BMI, we also conducted a meta-analysis of the present study and published evidence on BMI and esophageal cancer.

Methods

Baseline survey and follow-up

The study design, field survey methods and participants have been described in detail elsewhere.[13,14] Briefly, 45 areas (23 urban, and 22 rural) throughout China were chosen at random from the 145 Disease Surveillance Points (DSP) which were established during the 1980s by the Chinese Center for Disease Control (China CDC) to provide nationally representative mortality statistics for the entire country.[15,16] A typical surveillance point covers a defined population of about 50,000–100,000 residents in 4–8 geographically defined units (either urban street committees or groups of rural villages). During 1990–91, all men aged over 40 years in 2 or 3 units from each of the 45 selected areas were invited to participate in the survey, and about 80% of those invited took part.

Study participants were interviewed by trained health workers using a standardized questionnaire with detailed information obtained on education, occupation, smoking habits, alcohol consumption and frequency of consumption of some food types. A self-reported medical history was also taken which included the participants' self-assessed health status and whether they had been medically diagnosed with cancer or other chronic disease. Participants' height and weight were measured and BMI was calculated as weight in kilograms divided by the square of the height in meters (kg/m^2).

After the baseline survey the vital status of the study population was followed up by local DSP staff through the death registries previously established in these areas, with annual active confirmation of vital status (or death report) by local residential committees. The underlying cause of each death was sought from official death certificates, supplemented (if necessary) with information from medical records, and coded by trained staff in the central DSP office using the 9th revision of the WHO International Classification of Disease (ICD-9). The results presented here are for the first 10 years of follow-up to January 2002, among men who

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were aged 40–79 at baseline survey and had no reported history of cancer.

Statistical analysis

All analyses were restricted to deaths occurring between ages 40–79 years, with censoring when men moved away from the original study area or reached age 80 (since it is often difficult to determine reliably the underlying cause of death at older ages). BMI at baseline was categorized into 5 groups: <18.5, ≥ 18.5, ≥ 20, ≥ 22.5 and ≥ 25 kg/m^2, with 154 subjects excluded due to missing or extreme BMI values (<10 or ≥ 50 kg/m^2). These groups include the conventional WHO cut-off points of 18.5 kg/m^2, 20 and 25.0 kg/m^2.[17] Since only 11% of the study population had a BMI $\geq$ 25.0 kg/m^2, this category was not subdivided further.

Cox proportional hazards models were used to estimate the hazard ratio for esophageal cancer in each of the 5 categories of BMI.[18] The analyses were stratified by age at risk (5-year age groups) and individual area, and were adjusted for smoking (never, ex, current) and alcohol consumption (not regular alcohol drinkers; moderate drinkers, <28 units/week; heavy drinkers, ≥ 28 units/week). The 95% confidence interval for each hazard ratio was estimated using the "floating absolute risk" method, which allows comparisons to be made between any pair of groups rather than just with an arbitrarily chosen reference group.[19] Trend tests were conducted by using the mean value for each BMI category as a continuous variable in the model. Departure from log-linearity was tested by a likelihood ratio test between this model and the one with BMI group as a categorical variable. The hazard ratio per 5 kg/m^2 higher BMI, which was chosen to represent the difference between the 2 cut-off points at 20 and 25 kg/m^2, was also calculated by refitting the model with BMI as a continuous covariate, assuming a log-linear relationship between esophageal cancer mortality and BMI. Statistical significance of the coefficient, and also of coefficients arising from trend tests, was evaluated using a Wald test (two-sided p value).

Meta-analysis of published studies

Case control or prospective cohort studies investigating the relation between BMI and esophageal cancers were identified through searches of the Medline and EMBASE databases for articles published in English and entered in the databases during 1980–August 2006, and from hand searches of bibliographies in these studies and other published reviews. A total of 25 studies were identified, of which 11 were eventually excluded from the meta-analysis for the following reasons: reports describing the same study but with different follow-up periods;[20,21] lack of enough information on BMI to calculate a relative risk per unit change in BMI;[22–24] case control studies with BMI measured at interview[6,7] (likely to result in reverse causality bias); case control studies with BMI estimated for 20 years prior to interview or for young adulthood[8,25] (estimates may be biased); and combined outcome with cancer of the esophagogastric junction or the gastric cardia[26,27] (the association with BMI may differ between these sites[28]). For one study[29] only the information on squamous cell cancer was used, as the data on adenocarcinoma was combined with gastric cardia adenocarcinoma.

Most studies reported relative risks for individual BMI categories. We estimated the change in relative risk per 5 kg/m^2 higher BMI from these by fitting an inverse variance weighted regression to the log relative risks and the midpoint for each BMI category. The method used to fit the regressions allows for non-independence of relative risk estimates.[30] In most studies BMI was divided into quartiles and the first and last BMI categories were open-ended. For these the typical BMI was taken as 1.27 standard deviations from the mean. (Assuming BMI follows a normal distribution, the expected value of the upper quartile of a standard normal distribution was calculated by integrating the standard normal distribution for values of the standard normal deviate which lie above the 75th centile [*i.e.*, conditional on $z > 0.67$]. The integration works out as 1.27; hence the expected value of the upper quartile will be 1.27 standard deviations from the mean for other normal distributions.)

Results

A total of 221,156 men aged 40–79 (mean age 54.3) at baseline were included in the present analysis and the overall mean baseline BMI among them was 21.7 kg/m^2 (Table I). The age-adjusted BMI was significantly lower among rural men (21.2 kg/m^2) than among urban men (23.1 kg/m^2). After adjustment for age and area, men with higher BMI tended to be slightly better educated, less likely to work in a manual occupation and less likely ever to have smoked.

During about 10 years of follow-up, 6,722 participants died from cancer between the ages of 40 and 79, of which 1,082 (16%) deaths were from esophageal cancer (Table I). There was an inverse association between baseline BMI and mortality from esophageal cancer (mortality rates were standardized by age and area), with the highest mortality rate of 5.7 (SE 0.4) per 10,000 person years in the BMI group of 18.5–20.0 kg/m^2 and the lowest of 3.3 (SE 0.4) per 10,000 among those with BMI $\geq$25 kg/m^2 (Table I). The standardized mortality rates from esophageal cancer were twice as high in rural areas (5.5 per 10,000) as in urban areas (2.6 per 10,000) but the inverse association with BMI was still evident in both urban and rural areas (data not shown).

After further adjustment for smoking and alcohol consumption using Cox proportional hazards models (Fig. 1*a*) this trend of decreasing risk with higher BMI was highly statistically significant among men with BMI $\geq$ 18.5 kg/m^2 (p for trend <0.0001), and it was approximately log-linear (test for deviation from log-linear model: $p = 0.9$). However, the hazard ratio for the BMI $<$ 18.5 kg/m^2 group appeared not to be fully consistent with this inverse log-linear trend. Since underlying causes of death may differ in those who are markedly malnourished, subsequent analyses excluded this group. Among all men with BMI $\geq$ 18.5 kg/m^2, each 5 kg/m^2 higher BMI was associated with a 30% (95%CI: 18–41%) lower risk of death from esophageal cancer.

In the study, 7% of the men considered their health to be poor at baseline (Table I), and it is possible that some could have low body weight associated with undiagnosed esophageal cancer at baseline that could contribute to the observed inverse association with BMI. Indeed, among men with poor self-assessed health at baseline each 5 kg/m^2 higher BMI was associated with a 64% (95%CI: 38–79%; $p = 0.0002$) lower risk of esophageal cancer mortality (test for heterogeneity: $p = 0.01$). Consequently, this group of individuals were further excluded from the main analyses. Figure 1*b* shows the association between BMI and esophageal cancer mortality in men with good self-assessed health. In men with good health who had BMI $\geq$ 18.5 kg/m^2 at baseline, each 5 kg/m^2 higher BMI was associated with 25% (95%CI: 11–36%; $p = 0.0008$) lower risk of esophageal cancer mortality after adjustment for age, smoking, alcohol and area. Further separate analyses of the first and second 5 years of follow-up in this group of individuals did not find any significant difference between follow-up periods (22% and 27% lower risks respectively for each 5 kg/m^2 higher BMI) (Fig. 2), implying that potential bias due to reverse causality has been controlled effectively.

The possibility of residual confounding being responsible for the association of esophageal cancer mortality with BMI was addressed further by considering different adjustments to the model. In the present study, the amount smoked per smoker was largely unrelated to BMI (Table I); hence further adjustment for amount smoked made no material difference to the observed association. Furthermore, when the analysis was restricted to men who were never smokers, the inverse association between BMI and risk of esophageal cancer persisted, with each 5 kg/m^2 higher BMI associated with 38% (95% CI: 15–55%; $p = 0.003$) lower esophageal cancer mortality (Fig. 2). Likewise, alcohol consumption was

TABLE I – CHARACTERISTICS OF THE STUDY POPULATION AT BASELINE AND SUBSEQUENT MORTALITY FROM OESOPHAGEAL CANCER[1], ACCORDING TO BMI CATEGORY AND OVERALL

	BMI (kg/m^2) at baseline					
	<18.5	18.5	20.0	22.5	≥25.0	Overall
Number of participants	20,303	37,721	89,051	49,436	24,645	221,156
Baseline characteristics						
Mean age (years)[2]	58.9	55.4	53.4	53.1	54.4	54.3
Living in an urban area (%)[2]	18.3	15.8	19.5	35.8	64.5	27.4
Mean BMI (kg/m^2)	17.5	19.3	21.2	23.6	27.0	21.7
Mean height (m)	1.66	1.65	1.65	1.64	1.63	1.65
Mean weight (kg)	48.4	53.0	57.8	63.4	72.3	59.0
<6 years of education (%)	67.3	68.7	67.8	65.8	63.4	67.0
Employed in manual occupation (%)	76.2	76.2	74.3	70.9	67.4	73.2
Smoking category (%)[3]						
Never smokers	21.7	23.3	25.8	29.6	33.4	26.7
Ex smokers	6.0	5.2	5.6	6.8	9.9	6.3
Current smokers	72.3	71.5	68.6	63.6	56.7	67.0
Tobacco (g/day/smoker)[4]	20.4	20.7	20.9	20.8	20.6	20.8
Alcohol consumption (%)[3]						
Not regular alcohol	69.3	68.0	66.2	65.3	64.9	66.5
Moderate drinkers: <28 units/week	18.5	18.8	19.7	19.9	20.7	19.6
Heavy drinkers: ≥28 units/week	12.2	13.2	14.1	14.8	14.4	13.9
Poor self-assessed health (%)	13.3	8.4	6.5	5.5	6.6	7.2
Mortality from oesophageal cancer						
Number of deaths	93	218	487	216	68	1,082
Mortality rate (per 10,000 person years)	5.2	5.7	5.0	4.1	3.3	4.7
SE of mortality rate[5]	0.5	0.4	0.2	0.3	0.4	0.1

[1]Baseline data and mortality rates are standardized to the overall area and 5-year age group structures in the study population (excluding those with prior cancer).–[2]Unstandardized mean or percentage.–[3]Hazard ratios for esophageal cancer death (unfloated 95% CI) for ex and current smokers relative to never smokers were 1.10 (0.83–1.45) and 1.23 (1.07–1.43): for moderate and heavy drinkers compared to nondrinkers they were 1.10 (0.93–1.30) and 1.21 (0.98–1.49). These hazard ratios were adjusted for area and 5-year age group, and, as appropriate, for smoking or alcohol.–[4]Estimated consumption, for current smokers only.–[5]The standard error (SE) is estimated as the mortality rate divided by the square root of the number of deaths.

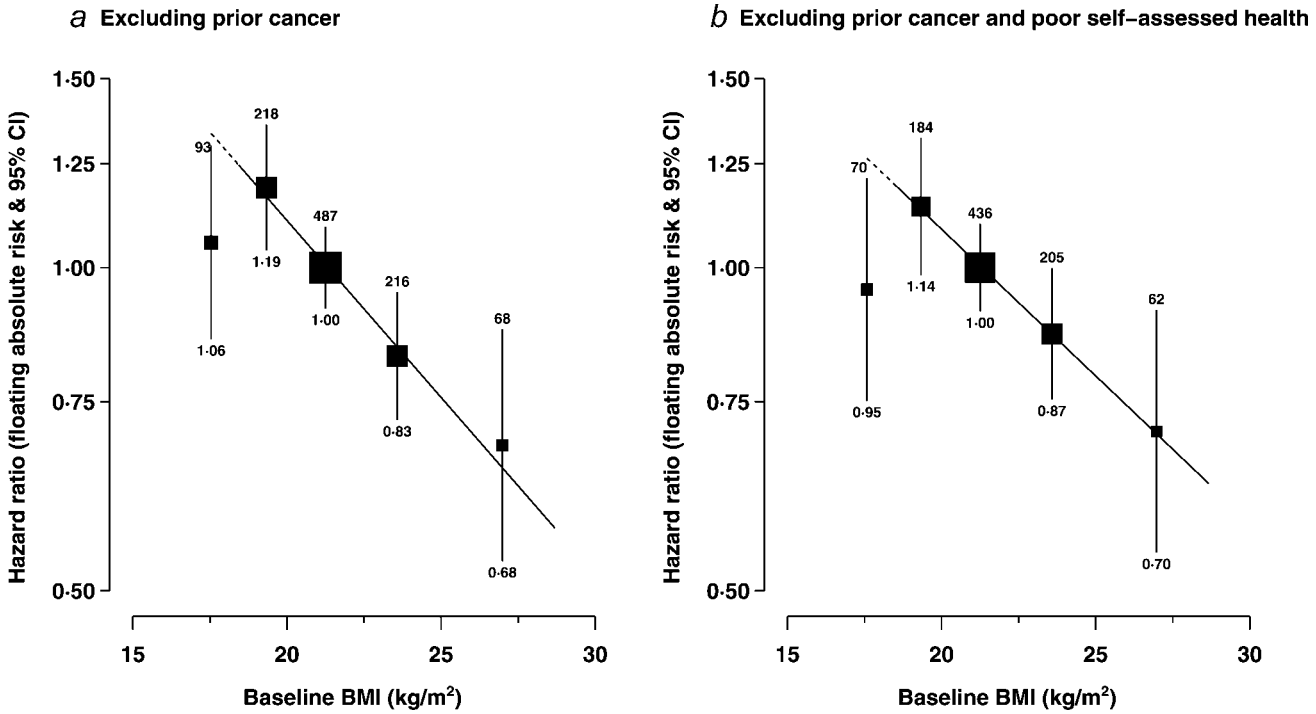

FIGURE 1 – China Prospective Study: hazard ratios (and 95% CI) for death from esophageal cancer in men at ages 40–79 *versus* the mean BMI in each category, adjusted for area, age, smoking and alcohol consumption. (*a*) In men with no history of cancer at baseline. Relative risk in men with BMI ≥ 18.5 kg/m^2 0.70 (95%CI: 0.59–0.82; $p < 0.0001$) per 5 kg/m^2 higher BMI. (*b*) In men with no history of cancer or poor self-assessed health at baseline. Relative risk in men with BMI ≥ 18.5 kg/m^2 0.75 (95%CI: 0.64–0.89; $p = 0.0008$) per 5 kg/m^2 higher BMI. Ratios are plotted on a floated absolute risk scale, and the area of each square is inversely proportional to the variance of the log relative risk. Numbers above confidence intervals are deaths, and those below the confidence intervals are hazard ratios. The trend lines were fitted excluding the group with BMI < 18.5 kg/m^2.

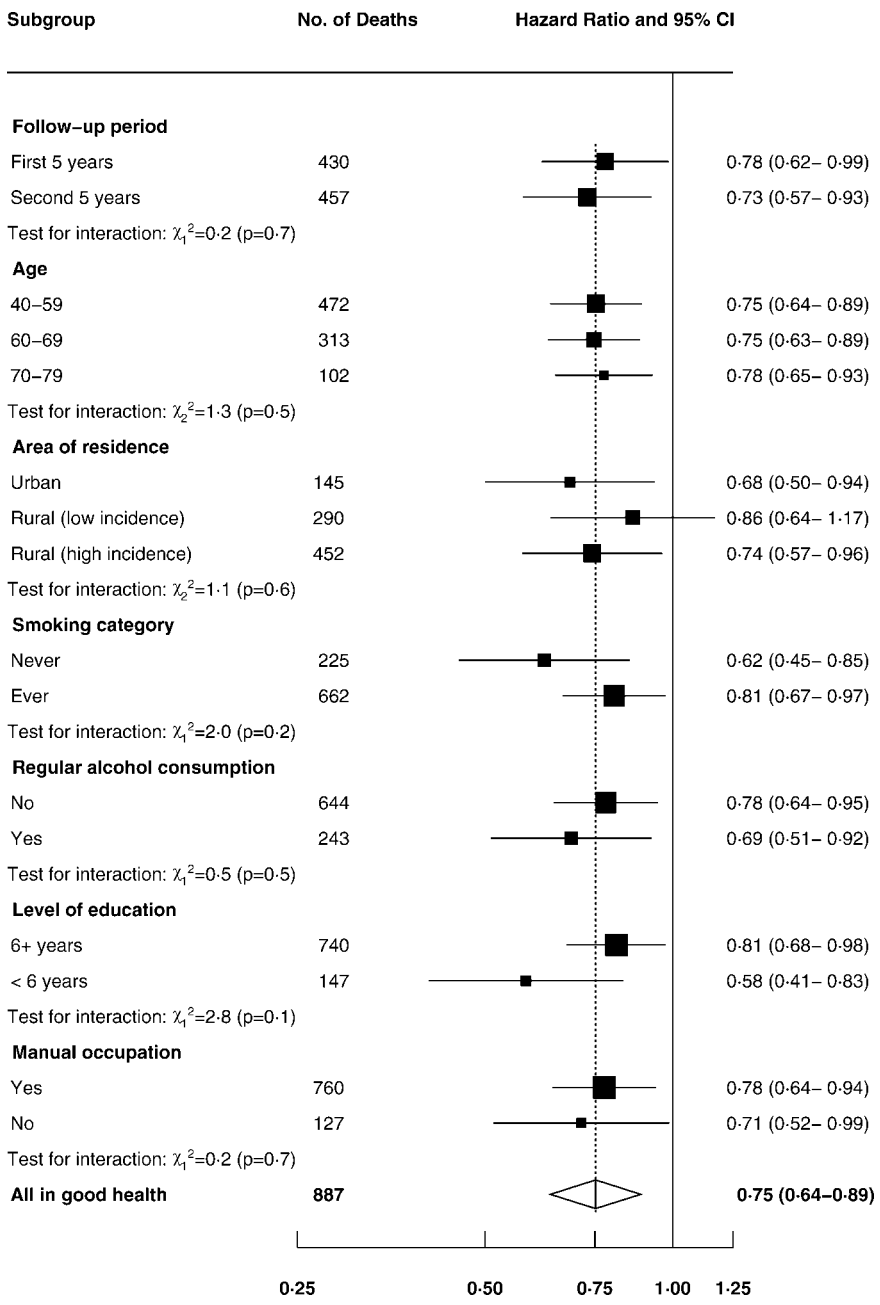

FIGURE 2 – China Prospective Study: hazard ratios (and 95% CI) for death from esophageal cancer per 5 kg/m^2 increase in baseline BMI by major population subgroup at baseline (in men with BMI $\geq$ 18.5 kg/m^2, aged 40–79 at risk with no history of cancer or poor self-assessed health). The interaction term was included in the model and its significance ascertained by the difference in log likelihood from the model without the interaction term. For area of residence and follow-up period the model was fitted separately to the subgroups of the data, and interaction tested with a χ^2 heterogeneity test. Area of residence was divided into urban and rural categories, and rural areas were divided further according to the esophageal cancer mortality rate in each area ($<$10 or $\geq$10 deaths/10,000 years). The area of the squares (■) is proportional to the variance of the log relative risk, and the diamond (◆) indicates the overall hazard ratio.

not strongly associated with BMI in this population (Table I); therefore further adjustment for amount of alcohol consumed did not change the relationship. Adjusting for variables associated with low socioeconomic status (educational level or manual occupation) or frequency of intake of individual dietary components (meat/poultry, fish, milk, eggs, fruit, salted/pickled vegetables or fresh vegetables) also did not alter the association. There was also little evidence that the strength of the association was significantly modified by locality or background rate of disease (urban, rural areas with low mortality [$<$10 per 10,000], rural areas with high mortality [$\geq$10 per10,000]), age, smoking, alcohol drinking, level of education or type of occupation (Fig. 2), although the statistical power to detect potentially important modifications was limited.

Meta-analysis of published studies

Figure 3 summarizes the study population, the main features of data analysis and estimated relative risks associated with 5 kg/m^2 higher BMI, stratified by study design and histological types of cancer (adenocarcinoma and squamous cell), for other studies and the present study. Of the 14 published studies, 5 were prospective cohort studies,[5,9,10,31,32] with 1 having separate data on both types of histology.[5] The other 9 were case control studies,[3,4,29,33–38] including 1 nested in a research database of patient records[4] and 4 with separate data on both types of histology.[3,4,37,38] Six were of North American populations, 5 were European, and 3 were Asian. BMI was slightly lower in the Norwegian prospective study[5] than for other European and North American studies and it was also estimated considerably earlier (1963–1975 compared to the 1980s and 1990s in most studies). Only 2 studies did not adjust for smoking,[5,10] although one[5] did investigate the effects of adjustment in subsidiary analyses and found no effect. Similarly, of the studies that did not adjust for alcohol consumption,[5,10,35,37] one[37] reported no effect of additionally adjusting for alcohol. Of the 5 prospective studies only one[10] excluded follow-up (approximately 2 years), although the Norwegian study[5] and our own found no

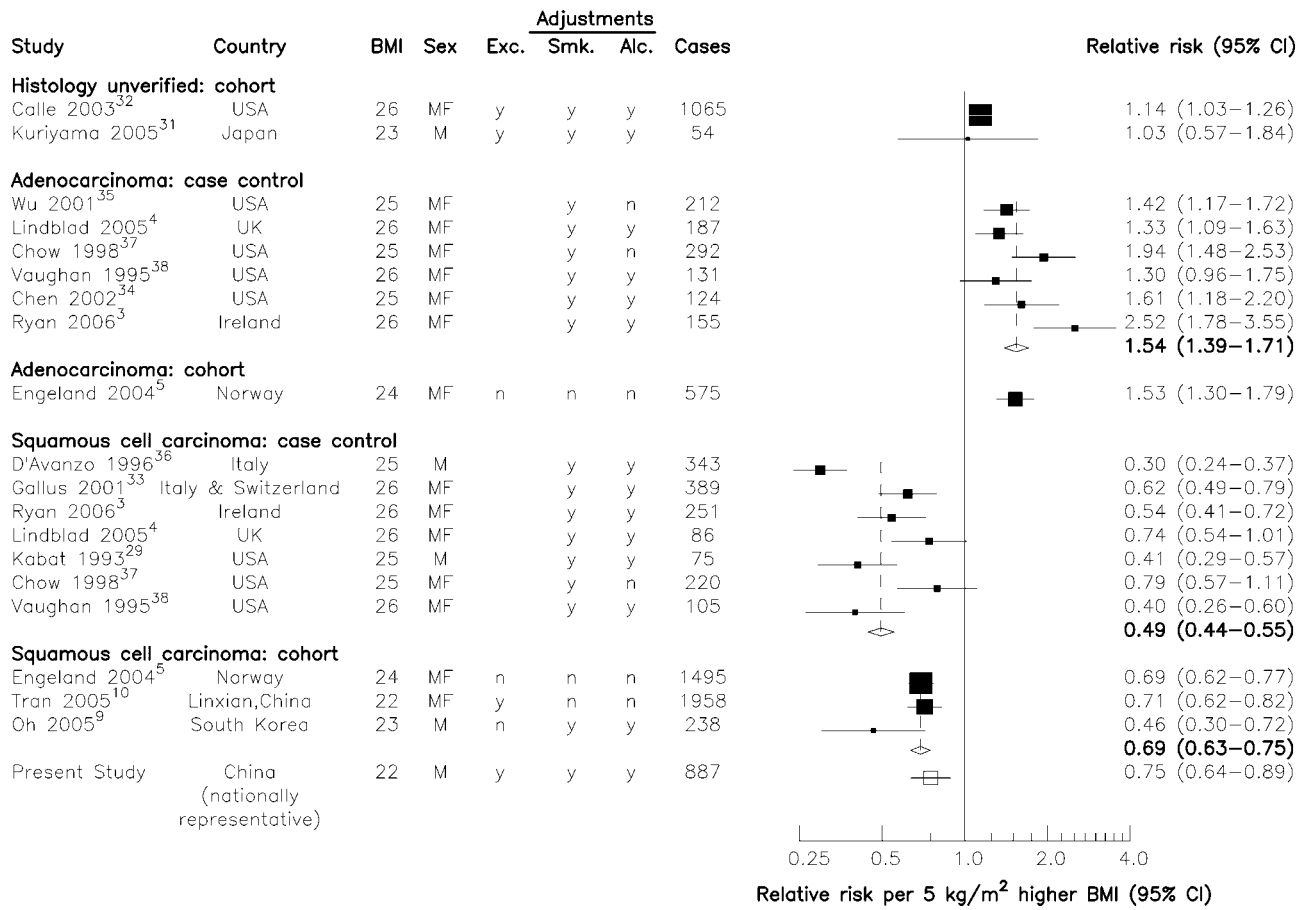

FIGURE 3 – Meta-analysis of epidemiological studies of esophageal cancer and BMI, by study type and cancer histology. Squares (■, □) indicate the change in relative risk per 5 kg/m^2 higher BMI (and 95% CI) for individual studies, with the area of the square inversely proportional to the variance of the log relative risk, and diamonds (◇) represent summary relative risks for each group. Within categories relative risks are ordered according to their standard error. Key to symbols used: BMI, estimated mid-BMI (kg/m^2); Sex, estimate based on males only (M), females only (F), males and females (MF); Exc., (cohort studies only) exclusion of early follow-up or subjects with indicators of undiagnosed disease *e.g.*, BMI $<$ 18.5 kg/m^2, recent weight loss or other poor health (all cohort studies excluded subjects with prior esophageal cancer or prior cancer); Smk., adjusted for smoking; Alc., adjusted for alcohol consumption.

effect in subsidiary analyses which excluded 5 or more years of follow-up. All the prospective studies excluded subjects with a prior cancer diagnosis, but 3[10,31,32] and our own also excluded those with low BMI or other indicators of ill health.

The relationship of BMI with risk of esophageal cancer differed qualitatively between the 2 main types of histology, with a positive association for esophageal adenocarcinoma but a negative one for squamous cell carcinoma (Fig. 3). For adenocarcinomas, there was no evidence that the strength of the relationship with BMI differed significantly between different types of study design, with each 5 kg/m^2 higher BMI associated with 53% (95% CI: 30–79%) and 54% (95% CI: 39–71%) higher risk of cancer respectively for the cohort study and the case-control studies. For squamous cell cancer, the overall strength of the association with BMI was more extreme in case-control studies than in cohort studies, with each 5 kg/m^2 higher BMI associated with 51% (95% CI: 45–56%) and 31% (95% CI: 25–37%) lower risk of esophageal cancer, respectively. Within case-control studies, there was also evidence of statistical heterogeneity between different studies for both adenocarcinomas ($p = 0.01$) and squamous cell carcinomas ($p < 0.001$). However, there were too few studies in the meta-analysis to further investigate the sources of this heterogeneity.

The present study and another similarly large prospective cohort study in the United States[32] did not have any information on tumor histology. In that large US study, there was a weak positive association between esophageal cancer and BMI, suggesting that adenocarcinomas could just have predominated in this population.[39] By contrast, the magnitude of the inverse association in the present study is similar to that in other prospective studies involving squamous cell carcinomas. This is consistent with most esophageal cancer in the present Chinese population being squamous cell carcinomas.[21,40]

Discussion

The present study is one of the largest prospective studies of the relationship between BMI and mortality from esophageal cancer, and it involves a nationally representative population of men with low BMI and large numbers of esophageal cancer deaths. In this relatively lean male population, there was an inverse association between BMI and mortality from esophageal cancer, with each 5 kg/m^2 higher BMI associated with about 25% lower risk of death from the disease. There was little evidence that the strength of the relationship was significantly modified by age, smoking, alcohol drinking, socioeconomic status or background rate of the disease.

High BMI is known to be associated with cancer at several specific sites.[41] However, the apparent inverse associations of BMI with some other types of cancer (particularly lung cancer) shown in a few studies have generally been attributed to confounding

(especially by smoking), recent weight loss due to undiagnosed illness (reverse causality), or both.[42] The present study involves a large number of esophageal cancer deaths among men with relatively low BMI, and detailed information is available not only for a range of potential confounding factors but also about prior disease history and general health status, thus providing a good opportunity to minimize the potential effects of confounding and reverse causality on this association.

In the present study, no information is available about the histological type of esophageal cancer, but there is other evidence that the main type of esophageal cancer in Chinese populations is squamous cell carcinoma.[21,40] Given the positive association between BMI and adenocarcinomas, the inclusion of some adenocarcinoma of the esophagus in the present population could have weakened the inverse association. Similarly, misdiagnosis of gastric cardia cancers, which are relatively common[10] and have traditionally been classified with esophageal cancer in China,[43] would also be expected to attenuate the association further as cancers at this site probably have a weak positive or no association with BMI.[28] Nevertheless, our estimate of a 25% lower risk of esophageal cancer death per 5 kg/m^2 higher BMI is highly consistent with that estimated from other cohort studies involving squamous cell carcinoma, in particular the 2 large studies, 1 in China[10] and the other on a Western population.[5] In case control studies of squamous cell carcinoma some bias may still remain, despite attempts to control for reverse causality by estimating BMI before disease onset. Consequently, the strength of the inverse association (51%) from the pooled results of case-control studies could have been overestimated as compared with that from cohort studies (31%).

The observed inverse association between BMI and esophageal cancer in China (as well as in other populations) is probably real, though not necessarily causal. High consumption of fruit and vegetables has been reported to be inversely associated with incidence of sqamous cell esophageal cancer.[23,44] Therefore it has been proposed that a low calorie diet which causes low BMI is likely also to be restricted in micronutrients such as vitamins C and E, riboflavin and β-carotene,[23,45] and that these deficiencies could lead to increased risk of squamous cell carcinoma (although there is no reliable evidence that these micronutrients really are protective). Although adjusting for different dietary variables in the present study had little effect on the association, the dietary information collected at baseline was rather crude and there have been large changes in the main dietary patterns in China during recent decades.[46] So, it is possible that low BMI may be a better indicator of long-term poor nutrition in these or other factors than that provided by baseline data on individual dietary components. It has also been suggested that low BMI may be a marker for some other risk factor related to socioeconomic status.[10,47] But, this was not supported by the findings in the present study, in which the strength of the association was consistent between different socioeconomic groups (albeit defined quite simply by education level or occupation) and also between urban/rural areas. Future studies of the association of common genetic variants with BMI or other measures of adiposity among individuals with and without the disease may help elucidate the nature of the association.[48] With regard to esophageal adenocarcinoma, the increased risk with high BMI probably represents a causal effect. There is good evidence that increased body fatness is associated with increased gastroesophageal reflux, perhaps as a result of increased intra abdominal pressure or hiatal hernia, and reflux in turn can lead to Barrett's esophagus, a known potential precursor to adenocarcinoma.[49,50]

Mortality rates from esophageal cancer in China are currently at least 2 or 3 times higher than those typically seen in many Western countries, and they are characterized by a low rate of adenocarcinoma and a high rate of squamous cell carcinoma, resembling the pattern in the United States until about the 1970s.[45] Over the last few decades, the incidence of squamous cell carcinoma has been stable or has declined in many Western countries, whereas the incidence of adenocarcinoma has risen,[51] particularly in the United States, a trend that has been attributed largely to an increase in the proportion of people who are overweight or obese in these populations.[45] Similarly, the mean BMI in the Chinese population has also risen steadily as a result of changes in dietary patterns and physical activities,[46] and indeed, there is evidence that mortality from squamous cell esophageal cancer is starting to decline, particularly in some Chinese cities.[43,52] However, further increases in the prevalence of overweight and obesity in China[46] is likely to be associated with increased mortality from various conditions, especially cardiovascular disease.[53] The rate of esophageal adenocarcinoma mortality may also rise consequently,[54] and this alone could potentially offset any advantageous effects of improved population nutrition on squamous cell carcinoma.

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