Introduction: Body mass index (BMI) has been associated with the risk of oesophageal cancer. However, the influence of BMI on postoperative complications and prognosis has been controversial.

Methods: In total, 2031 consecutive patients who underwent oesophagectomy between 1998 and 2008 were classified according to Asian-specific BMI (kg m⁻²) cutoff values. The impact of BMI on overall survival (OS) was estimated using the Kaplan–Meier method and Cox proportional hazard models. We performed a meta-analysis to examine the association of BMI with OS and postoperative complications.

Results: Patients with higher BMI had more postoperative complications (P = 0.002), such as anastomotic leakage (P = 0.016) and cardiovascular diseases (P < 0.001), but less incidence of chylous leakage (P = 0.010). Logistic regression analysis showed that BMI (P = 0.005) was a confounding factor associated with postoperative complication. Multivariate analysis showed that overweight and obese patients had a more favourable survival than normal weight patients (HR (hazard ratio) = 0.80, 95% CI (confidence interval): 0.70–0.92, P = 0.001). Subgroup analysis showed that the association with higher BMI and increased OS was observed in patients with oesophageal squamous cell carcinoma (ESCC) (P < 0.001), oesophageal adenocarcinoma (EA) (P = 0.034), never-smoking (P = 0.035), ever-smoking (P = 0.035), never alcohol consumption (P = 0.005), weight loss (P = 0.003) and advanced pathological stage (P < 0.001). The meta-analysis further corroborated that higher BMI was associated with increased complication of anastomotic leakage (RR (risk ratio) = 1.04, 95% CI: 1.02–1.06, P = 0.001), wound infection (RR = 1.03, 95% CI: 1.00–1.05, P = 0.039), but decreased incidence of chylous leakage (RR = 0.98, 95% CI: 0.96–0.99, P < 0.001). In addition, high BMI could significantly improved OS (HR = 0.78, 95% CI: 0.71–0.85, P < 0.001).

Conclusion: Preoperative BMI was an independent prognostic factor for survival, and strongly associated with postoperative complications in oesophageal cancer.
Oesophageal cancer is one of the most common cancers in the world, with >480,000 new cases and 400,000 deaths annually, of which about half occurred in China (Jemal et al, 2011). Despite advances of surgical techniques and incorporation of new therapeutic approaches, oesophageal cancer is still a highly devastating disease with poor prognosis (van Hagen et al, 2012). There is a strong evidence that lifestyle factors such as physical activity, diet and obesity may have an effect on survival for some cancers (Davies et al, 2011).

The association between body mass index (BMI) and the risk of oesophageal cancer has been established (Oh et al, 2005; Tran et al, 2005; Kubo and Corley, 2006; Smith et al, 2008; Turati et al, 2012). However, there is no general consensus on the influence of BMI on survival in oesophageal cancer. Some studies suggested that patients with higher BMI had a significantly better prognosis than those with lower BMI (Smith et al, 2008; Hayashi et al, 2010; Melis et al, 2011; Kayani et al, 2012; Scarpa et al, 2012), whereas others yielded conflicting results (Healy et al, 2007; Morgan et al, 2007; Schumacher et al, 2009; Skipworth et al, 2009; Grotenhuis et al, 2010; Madani et al, 2010; Yoon et al, 2011; Blom et al, 2012). In addition, whether patients with higher BMI would have an increased incidence of postoperative complication is still debated. Several studies described no differences in postoperative complications after oesophagectomy (Morgan et al, 2007; Scipione et al, 2007; Melis et al, 2011; Blom et al, 2012), whereas some reported that a higher incidence of severe complications were noted in patients with higher BMI (Healy et al, 2007; Grotenhuis et al, 2010; Hayashi et al, 2010).

Therefore, we analysed a large cohort of Chinese patients with oesophageal cancer and carried out a comprehensive meta-analysis to elucidate these two controversial issues.

**MATERIALS AND METHODS**

**Patients.** We identified consecutive patients with oesophageal cancer who underwent surgical resection at Sun Yat-sen University Cancer Center between December 1998 and December 2008. Patients were excluded if they received neoadjuvant or adjuvant therapy, had an unknown BMI or history of other cancer. Patient characteristics and postoperative complications were collected from retrospective medical record review using a standardized data collection form. Surgical procedure was performed as previously described in our studies (Liu et al, 2012). The most common surgical approaches included the left transthoracic procedure, the Ivor-Lewis approach and the cervicothoracoabdominal procedures. Lymph node dissection including standard or extended dissection of thoracic and abdominal lymph nodes was performed in patients with no evidence of metastatic disease that included cervical or coeliac lymph node metastases. Pathologic stage was determined according to the 7th edition AJCC staging system (Rice et al, 2010). The study was approved by the Ethics Committee of Sun Yat-sen University Cancer Center. All patients provided a written informed consent according to the ethical approval.

**BMI value.** Body mass index (kg m⁻²) was calculated based on a direct measurement of height and weight at diagnosis. Patients were asked whether they had weight loss when compared with their usual weight when their weight was measured at diagnosis. Patients were classified according to Asian-specific BMI cutoff value (Choi et al, 2013) as follows: underweight (<18.5 kg m⁻²); normal weight (18.5–22.9 kg m⁻²) (reference group); overweight and obese (≥23.0 kg m⁻²). These values were chosen because there is evidence that excess risks of mortality from all-cause occur at lower BMI levels in Asians than in Caucasian (Wen et al, 2009). Besides, the mean BMI of Chinese population was relatively low (Smith et al, 2008).

**Definition of postoperative complications.** All complications from surgery to discharge from hospital were prospectively documented. Respiratory diseases complications consisted of pneumonia, respiratory failure. Pneumonia required positive sputum cultures or clear clinical and radiographic evidence of consolidation. Respiratory failure was defined as the requirement for mechanical ventilation for >24 h after surgery. Anastomotic leakage was defined as extravasation of water-soluble contrast medium documented by radiography. Chylous leakage was defined as the milky and elevated triglyceride level drained fluid. Wound infection was defined as purulent discharge from a closed surgical wound, with signs and symptoms of inflammation of the surrounding tissue together with abnormal smell. Vocal cord paresis was defined as hoarseness, pain in the throat when speaking and aspiration (due to poor swallowing reflex) with frequent resultant coughing. Cardiovascular diseases were defined as the myoccardial infarction and arrhythmia detected by electrocardiogram.

The standardized manner of postoperative complications was reported according to the classification system composed by Dindo et al (2003). This system was based on the therapeutic consequences of complications and consists of five grades. Grading of complications was performed according to the most severe complication in each patient.

**Statistical analysis.** Statistical analysis was performed using the SPSS 16.0 for windows software system (SPSS Inc., Chicago, IL, USA). Differences between three groups were tested by the
Table 1. The clinical and pathologic characteristics at baseline, stratified by BMI categories

| Characteristic                  | Overall (n = 2031) | <18.5 kg m⁻² (underweight) (n = 322) | 18.5–22.9 kg m⁻² (normal weight) (n = 1070) | >23.0 kg m⁻² (overweight and obese) (n = 639) | P-value |
|--------------------------------|-------------------|--------------------------------------|-------------------------------------------|---------------------------------------------|---------|
| Hp                             |                   |                                      |                                           |                                             | 0.003   |
| ESCC                           | 1776 (87.4)       | 291 (90.4)                           | 952 (89.0)                               | 533 (83.4)                                 |         |
| EA                             | 201 (9.9)         | 22 (6.8)                             | 96 (9.0)                                 | 83 (13.0)                                  |         |
| Others                         | 54 (2.7)          | 9 (2.8)                              | 22 (2.0)                                 | 23 (3.6)                                   |         |
| Age                            |                   |                                      |                                           |                                             | 0.353   |
| ≤ 58 years                     | 1048 (51.6)       | 156 (48.4)                           | 551 (51.5)                               | 341 (53.4)                                 |         |
| > 58 years                     | 983 (48.4)        | 166 (51.5)                           | 519 (48.5)                               | 298 (46.6)                                 |         |
| Gender                         |                   |                                      |                                           |                                             | 0.367   |
| Female patients                | 481 (23.7)        | 82 (25.5)                            | 240 (22.4)                               | 159 (24.9)                                 |         |
| Male patients                  | 1550 (76.3)       | 240 (74.5)                           | 830 (77.6)                               | 480 (75.1)                                 |         |
| Smoking                        |                   |                                      |                                           |                                             | <0.001  |
| Never                          | 734 (36.2)        | 96 (29.8)                            | 364 (34.0)                               | 274 (42.9)                                 |         |
| Ever (former + current)        | 1296 (63.8)       | 226 (70.2)                           | 706 (66.0)                               | 364 (57.1)                                 |         |
| Alcohol                        |                   |                                      |                                           |                                             | 0.044   |
| Never                          | 1419 (69.9)       | 226 (70.2)                           | 724 (67.7)                               | 469 (73.4)                                 |         |
| Ever (former + current)        | 612 (30.1)        | 96 (29.8)                            | 346 (32.3)                               | 170 (26.6)                                 |         |
| Weight loss                    |                   |                                      |                                           |                                             | <0.001  |
| No                             | 1086 (53.5)       | 141 (43.8)                           | 554 (51.8)                               | 391 (61.2)                                 |         |
| Yes                            | 945 (46.5)        | 181 (56.2)                           | 516 (48.2)                               | 248 (38.8)                                 |         |

Surgical procedures

| Procedure                        | Overall (n = 2031) | <18.5 kg m⁻² (underweight) (n = 322) | 18.5–22.9 kg m⁻² (normal weight) (n = 1070) | >23.0 kg m⁻² (overweight and obese) (n = 639) | P-value |
|----------------------------------|-------------------|--------------------------------------|-------------------------------------------|---------------------------------------------|---------|
| Cervicothoracoabdominal          | 384 (18.9)        | 61 (18.9)                            | 215 (20.1)                               | 108 (16.9)                                 | 0.283   |
| Ivor-Lewis                       | 224 (11.0)        | 29 (9.0)                             | 115 (10.7)                               | 80 (12.5)                                  |         |
| Left transthoracic               | 1423 (70.1)       | 232 (72.1)                           | 740 (69.2)                               | 451 (70.6)                                 |         |
| Radicality of surgery            |                   |                                      |                                           |                                             | 0.063   |
| R0                               | 1885 (92.8)       | 290 (90.1)                           | 993 (92.8)                               | 602 (99.8)                                 |         |
| R1                               | 146 (7.2)         | 32 (9.9)                             | 77 (7.2)                                 | 37 (0.2)                                   |         |
| Differentiation                  |                   |                                      |                                           |                                             | 0.401   |
| G1                               | 1377 (67.8)       | 230 (71.4)                           | 721 (67.4)                               | 426 (66.7)                                 |         |
| G2–3                             | 654 (32.2)        | 92 (28.6)                            | 349 (32.6)                               | 213 (33.3)                                 |         |
| Tumour location                  |                   |                                      |                                           |                                             | 0.012   |
| Upper                            | 334 (16.4)        | 48 (14.9)                            | 176 (16.4)                               | 110 (17.2)                                 |         |
| Middle                           | 1074 (52.9)       | 171 (53.1)                           | 583 (54.5)                               | 320 (50.1)                                 |         |
| Lower                            | 434 (21.4)        | 82 (25.5)                            | 223 (20.8)                               | 129 (20.2)                                 |         |
| EGJ                              | 189 (9.3)         | 21 (6.5)                             | 88 (8.2)                                 | 80 (12.5)                                  |         |
| Pathological stage               |                   |                                      |                                           |                                             | 0.168   |
| Stage I–II                       | 1127 (55.5)       | 168 (52.2)                           | 614 (57.4)                               | 345 (54.0)                                 |         |
| Stage III-IV                     | 904 (44.5)        | 154 (47.8)                           | 456 (42.6)                               | 294 (46.0)                                 |         |
| In-hospital mortality            | 30 (1.5)          | 8 (2.5)                              | 18 (1.7)                                 | 4 (0.6)                                    | 0.101   |
| Postoperative complication       | 277 (13.6)        | 35 (10.9)                            | 130 (12.1)                               | 112 (17.5)                                 | 0.002   |
| Respiratory diseases             | 50 (2.5)          | 6 (1.9)                              | 29 (2.7)                                 | 15 (2.3)                                   | 0.674   |
| Anastomotic leakage              | 110 (5.4)         | 9 (2.8)                              | 55 (5.1)                                 | 46 (7.2)                                   | 0.016   |
| Chylous leakage                  | 17 (0.84)         | 7 (2.2)                              | 8 (0.74)                                 | 2 (0.31)                                   | 0.010   |
| Wound infection                  | 42 (2.1)          | 6 (1.9)                              | 20 (1.9)                                 | 16 (2.5)                                   | 0.669   |
| Vocal cord paresis               | 18 (0.89)         | 1 (0.31)                             | 10 (0.93)                                | 7 (1.1)                                    | 0.458   |
| Cardiovascular diseases          | 40 (2.0)          | 6 (1.9)                              | 8 (0.75)                                 | 26 (4.1)                                   | <0.001  |
| Complications according to Dindo |                   |                                      |                                           |                                             | 0.012   |
| Grade 0                          | 1552 (76.4)       | 263 (81.7)                           | 827 (77.3)                               | 462 (72.3)                                 |         |
| Grade I-IIb                      | 404 (19.9)        | 54 (16.8)                            | 204 (19.1)                               | 146 (22.8)                                 |         |
| Grade IVa-V                      | 75 (3.7)          | 5 (1.5)                              | 39 (3.6)                                 | 31 (4.9)                                   |         |
| Duration of surgery (median, IQR) (min) | 200 (120–405) | 192 (120–350) | 195 (120–410) | 210 (120–420) | <0.001 |
analysed by clinicopathologic parameters or postoperative complication was Kruskal–Wallis test. The association between BMI categories and BMI and oesophageal cancer outcome

A significant difference was declared if the P-value was 0.05 and 0.10, respectively. A significant difference was performed using Cox’s proportional hazards regression model with a forward stepwise procedure (the entry and removal probabilities were 0.05 and 0.10, respectively). Multivariate analysis was performed using Cox’s proportional hazards regression model with a forward stepwise procedure (the entry and removal probabilities were 0.05 and 0.10, respectively). A significant difference was declared if the P-value from a two-tailed test was <0.05.

Meta-analysis. Two reviewers independently performed systematic literature search of the following databases: PubMed, Embase, Web of Science and CNKI database (last search up to December 2012). The following search terms were used: ‘oesophageal cancer or oesophageal neoplasms’, ‘body mass index or overweight or obesity’ and ‘survival or prognosis’. All potentially eligible studies were retrieved. Studies were included if they met all of the following criteria: (1) patients with oesophageal cancer who underwent surgery, (2) BMI as an exposure interest, (3) information provided for estimating parameters and (4) published in English, German and Chinese with English abstract. Disagreements between reviewers were resolved by a third reviewer or by discussion and consensus. We assessed and quantified statistical heterogeneity for each pooled estimate using the I2 statistic. If heterogeneity existed, a random effects model was adopted; otherwise, a fixed effects model was used. Pooling analysis was performed using the Mantel–Haenszel model and reported as hazard ratio (HR) with 95% confidence intervals (CIs) for the assessment of the influence of BMI on OS and risk ratio (RR) with 95% CIs for the association between BMI and postoperative complication. Where possible, the HR and associated variance were obtained directly from each study. When the association between BMI and HRs of survival was not reported, HRs were calculated by the methods of Parmar et al. (1998) and Tierney et al. (2007). The Begg’s funnel plot and Egger’s test were employed to estimate the potential publication bias. Sensitivity analysis was conducted to re-evaluate the overall results by omitting specific studies. The significance of the pooled HR or RR was determined by the Z-test and P<0.05 was considered as statistical significance. All analyses were performed with the software STATA version 12 (StataCorp, College Station, TX, USA).

RESULTS

Patient characteristics by BMI. After excluding patients who receiving neoadjuvant or adjuvant therapy or with unknown BMI, 2031 consecutive patients with oesophageal cancer were included in the study and were divided into three groups according to BMI (Figure 1). Patient characteristics were shown in Table 1. Patients with higher BMI were more likely to be diagnosed with oesophageal adenocarcinoma (EA) and less likely to be oesophageal squamous cell carcinoma (ESCC) (P=0.003). Besides, overweight and obese patients were less likely to be smoker (P<0.001) and alcohol consumers (P=0.044), had lower likelihood of weight loss (P<0.001) when compared with normal weight.

Postoperative complication. With respect to perioperative complication, overweight and obese patients had more postoperative complication (P=0.002), such as anastomotic leakage (P=0.016) and cardiovascular disease (P<0.001). In addition, they had a longer operative time (P<0.001) than those with normal weight. Interestingly, overweight and obesity was associated with less incidence of chylous leakage in comparison to normal weight (P=0.010). There was significant difference in the rate of postoperative complication for different surgical procedures, 29.2% for cervicotraheacoldiabomal procedure, 12% for the Ivor-Lewis and 8% for the left transthoracic procedure (P<0.001) (data not shown). Logistic regression analysis showed that BMI (P=0.005), surgical procedures (P<0.001) and age (P=0.046) were confounding factors associated with postoperative complication (Supplementary Table 1). When all postoperative complications were categorised according to the Dindo classification, there were also significant differences between patients with underweight, normal weight, overweight and obesity (P=0.012, Table 1).

Univariate and multivariate analysis. The median of follow-up was 64 months. Univariate survival analysis showed a strongly significant difference in OS among three groups of patients. The 5-year OS and 10-year OS of patients with higher BMI were significantly longer than those of patients with lower BMI (P<0.001, Table 2, Figure 2). In addition, there was also significant difference in 5-year DFS among three groups of patients, 34.7% for underweight group, 37.3% for normal weight and 40.7% for

Table 1. (Continued)

| Characteristic | Overall (n=2031) | <18.5 kg m

°2 (underweight) (n=322) | 18.5–22.9 kg m

°2 (normal weight) (n=1070) | ≥23.0 kg m

°2 (overweight and obese) (n=639) | P-value |
|-----------------|--------------|-----------------|-----------------|-----------------|-----------------|
| Perioperative blood loss (median, IQR) (ml) | 200 (100-400) | 200 (100-400) | 200 (100-400) | 200 (100-500) | 0.195 |
| In-hospital stay, median (IQR) (day) | 21 (18–26) | 21 (13–24) | 21 (14–27) | 21 (14–26) | 0.131 |
| ICU stay, median (IQR) (day) | 2 (1–6) | 2 (1–4) | 1 (1–5) | 1 (1–6) | 0.233 |
| No. of collected lymph Nodes (median, IQR) | 13 (3–35) | 12 (3–32) | 13 (3–36) | 13 (3–34) | 0.530 |
| No. of metastatic lymph node (median, IQR) | 0 (0–2) | 1 (0–2) | 0 (0–2) | 1 (0–2) | 0.163 |
| Lymph node ratio, median (IQR) | 0.00 (0.00–0.64) | 0.045 (0.00–0.63) | 0.00 (0.00–0.67) | 0.035 (0.00–0.62) | 0.092 |

Abbreviations: BMI = body mass index; HP = histopathology; EA = oesophageal adenocarcinoma; EGJ = esophagogastroduodenal junction; ESCC = oesophageal squamous cell carcinoma; G = grade; IQR = interquartile range.
overweight and obese ($P = 0.009$, Supplementary Table 2). As given in Table 2, patients with old age, male, advanced pT category, lymph node metastasis, oesophagogastric junction tumour location, weight loss, a history of smoking and alcohol consumption and poor histologic differentiation were found to have a significantly shorter OS. In the final multivariate survival analysis with adjustment for covariates, we found that overweight and obese patients had a 20% lower risk of dying from any cause including oesophageal cancer when compared with normal weight patients ($HR = 0.80$, 95% CI: 0.70–0.92, $P = 0.001$).

In order to reduce possible effects of reverse causality due to prior diagnosed diseases or undiagnosed diseases, the sensitivity analyses were performed by excluding patients with prior diagnosed diseases ($HR = 0.86$, 95% CI: 0.78–0.95, $P = 0.003$) or died during the first year of follow-up ($HR = 0.85$, 95% CI: 0.78–0.92, $P < 0.001$). The results did not substantially differ from the main results. We re-run the univariate survival analysis using a traditional BMI value 25 for overweight and obese instead of 23, and the increased OS for overweight and obese patients was also found ($HR = 0.83$, 95% CI: 0.71–0.98, $P = 0.031$) when compared with normal weight ($BMI < 25.0\text{kg m}^{-2}$).

**Table 2. Univariate and multivariate survival analysis for OS in patients with oesophageal cancer**

| Prognostic factor | Mean 5-year OS (%) | Median 5-year OS (%) | 10-year OS (%) | HR (95% CI) | P-value | HR (95% CI) | P-value |
|-------------------|-------------------|---------------------|----------------|-------------|---------|-------------|---------|
| **Age**           |                   |                     |                |             |         |             |         |
| $\leq$ 58 years   | 84.5              | 41.0                | 38.3           | 36.3        | 1.20    | 1.07–1.35   | 0.002   |
| $>$ 58 years      | 69.9              | 34.0                | 31.0           | 27.1        | 1.23    | 1.10–1.38   | 0.001   |
| **Gender**        |                   |                     |                |             |         |             |         |
| Male              | 72.3              | 34.0                | 38.6           | 28.2        | 0.72    | 0.62–0.83   | $< 0.001$ |
| Female            | 93.5              | 56.0                | 49.6           | 43.1        | 0.86    | 0.74–0.98   | 0.04    |
| **pT category**   |                   |                     |                |             |         |             |         |
| T1–2              | 100.4             | 82.0                | 55.8           | 45.1        | 1.78    | 1.56–2.01   | $< 0.001$ |
| T3–4              | 66.6              | 29.0                | 34.6           | 25.5        |         |             |         |
| **pN category**   |                   |                     |                |             |         |             |         |
| N0                | 103.3             | 95.0                | 57.5           | 47.3        | 2.50    | 2.22–2.82   | $< 0.001$ |
| N1–3              | 49.5              | 22.0                | 23.6           | 15.4        | 1.51    | 1.34–1.70   | $< 0.001$ |
| **Differentiation**|                 |                     |                |             |         |             |         |
| G1                | 85.1              | 47.0                | 46.6           | 36.2        |         |             |         |
| G2–3              | 61.2              | 26.0                | 29.7           | 23.0        | 1.09    | 1.01–1.16   | 0.019   |
| **Tumour location**|                 |                     |                |             |         |             |         |
| Upper             | 66.4              | 40.0                | 41.0           | 30.0        | 0.89    | 0.83–0.95   | 0.001   |
| Middle            | 57.7              | 41.0                | 43.7           | 34.4        | 1.19    | 1.02–1.39   | 0.024   |
| Lower             | 34.6              | 32.0                | 39.4           | 29.6        | 0.85    | 0.75–0.97   | 0.019   |
| EGJ               | 41.4              | 31.0                | 30.3           | 0.00        | 1.31    | 1.17–1.47   | $< 0.001$ |
| **BMI**           |                   |                     |                |             |         |             |         |
| $< 18.5\text{kg m}^{-2}$ (underweight) | 63.7 | 28.0 | 36.5 | 22.8 | 1.19 | 1.02–1.39 | 0.024 |
| 18.5–22.9 $\text{kg m}^{-2}$ (normal weight) | 77.4 | 34.0 | 40.3 | 32.9 | 1.01 | 1.00–1.02 | 0.999 |
| $\geq 23.0\text{kg m}^{-2}$ (overweight and obese) | 86.7 | 44.0 | 45.8 | 35.8 | 0.85 | 0.75–0.97 | 0.019 |
| **Weight loss**   |                   |                     |                |             |         |             |         |
| No                | 85.5              | 43.0                | 45.5           | 36.2        | 1.35    | 1.19–1.52   | $< 0.001$ |
| Yes               | 68.5              | 32.0                | 36.3           | 26.9        | 1.15    | 1.01–1.31   | 0.038   |
| **Smoking**       |                   |                     |                |             |         |             |         |
| Never             | 90.3              | 52.0                | 47.4           | 40.6        | 1.39    | 1.23–1.57   | $< 0.001$ |
| Ever (former + current) | 70.0 | 33.0 | 37.7 | 26.6 |         |             |         |
| **Alcohol**       |                   |                     |                |             |         |             |         |
| Never             | 84.0              | 42.0                | 44.6           | 35.8        | 1.23    | 1.08–1.40   | 0.002   |
| Ever (former + current) | 61.2 | 27.0 | 33.1 | 22.1 |         |             |         |

**Abbreviations**: BMI = body mass index; EGJ = oesophagogastric junction; G = grade; HR = hazard ratio; 95% CI = 95% confidence interval.

Subgroup analysis. Univariate survival analyses stratified by histology, smoking status, alcohol consumption, weight loss and pathological stage were performed. We found that the association with higher BMI and increased OS were observed in patients with ESCC ($P < 0.001$), EA ($P = 0.034$), never-smoking ($P = 0.035$), ever-smoking ($P = 0.035$), never alcohol consumption ($P = 0.005$), weight loss ($P = 0.003$) and advanced pathological stage ($P < 0.001$) (Supplementary Table 3).

Meta-analysis of BMI and postoperative complication. As the search flow diagram showed (Figure 3), 14 studies including the current study, were included in our meta-analysis (Table 3) (Trivers et al, 2005; Healy et al, 2007; Morgan et al, 2007; Schumacher et al, 2009; Skipworth et al, 2009; Grotenhuis et al, 2010; Hayashi et al, 2010; Madani et al, 2010; Melis et al, 2011;
Of the 14 studies, 7 studies were conducted in Europe, 4 in the United States, 2 in China and 1 in Canada, 1 study published in German, 1 in Chinese with English abstract and others were all in English. Only patients with oesophageal cancer in one study which enrolled both of oesophageal and gastric cancer were included in our meta-analysis (Trivers et al., 2005). Owing to the varied cutoff of BMI in each study, we pooled estimate of comparison of the highest BMI group with the lowest group for consistency (Table 3).

To evaluate the association of higher BMI with increased incidence of postoperative complication, several studies reporting postoperative complication were included. As shown in Supplementary Table 4, higher BMI was significantly associated with increased complication of anastomotic leakage (RR = 1.04, 95% CI: 1.02–1.06, \( P = 0.001 \), Figure 4a), wound infection (RR = 1.03, 95% CI: 1.00–1.05, \( P = 0.031 \), Figure 4b) and cardiovascular diseases (RR = 1.02, 95% CI: 1.00–1.05, \( P = 0.039 \), Figure 4c). More interestingly, patients with higher BMI inversely had a significantly decreased incidence of chylous leakage (RR = 0.98, 95% CI: 0.96–0.99, \( P < 0.001 \), Figure 4d). But with respect to the incidence of respiratory diseases and in-hospital mortality, there was no significant difference between the highest BMI group and lowest group. In all above pooled estimates, no significance of heterogeneity and publication bias was detected (Supplementary Table 4).

**Figure 2. Kaplan–Meier curves of OS according to BMI categories.** Abbreviation: BMI = body mass index.

**Figure 3. Flowchart of study selection for inclusion in the meta-analysis.**

Yoon et al., 2011; Zhu et al., 2011; Blom et al., 2012; Scarpa et al., 2012). Of the 14 studies, 7 studies were conducted in Europe, 4 in the United States, 2 in China and 1 in Canada, 1 study published in German, 1 in Chinese with English abstract and others were all in English. Only patients with oesophageal cancer in one study which enrolled both of oesophageal and gastric cancer were included in our meta-analysis (Trivers et al., 2005). Owing to the varied cutoff of BMI in each study, we pooled estimate of comparison of the highest BMI group with the lowest group for consistency (Table 3).

To evaluate the association of higher BMI with increased incidence of postoperative complication, several studies reporting postoperative complication were included. As shown in Supplementary Table 4, higher BMI was significantly associated with increased complication of anastomotic leakage (RR = 1.04, 95% CI: 1.02–1.06, \( P = 0.001 \), Figure 4a), wound infection (RR = 1.03, 95% CI: 1.00–1.05, \( P = 0.031 \), Figure 4b) and cardiovascular diseases (RR = 1.02, 95% CI: 1.00–1.05, \( P = 0.039 \), Figure 4c). More interestingly, patients with higher BMI inversely had a significantly decreased incidence of chylous leakage (RR = 0.98, 95% CI: 0.96–0.99, \( P < 0.001 \), Figure 4d). But with respect to the incidence of respiratory diseases and in-hospital mortality, there was no significant difference between the highest BMI group and lowest group. In all above pooled estimates, no significance of heterogeneity and publication bias was detected (Supplementary Table 4).

**Meta-analysis of BMI and survival.** All 14 studies were included to estimate the association of BMI and survival in oesophageal cancer. We found that patients with higher BMI had a significantly favourable OS (HR = 0.78, 95% CI: 0.71–0.85, \( P < 0.001 \), Figure 5a), there was no evidence of heterogeneity between the studies (\( P = 0.188 \), \( I^2 = 24.7\% \)). The Begg’s funnel plots
showed no evidence of obvious asymmetry (Supplementary Figure 1), and Egger’s test indicated no significance of publication bias (P > 0.05). Sensitivity analysis was carried out to assess the influence of individual studies on the summary effect. Removal of one study published in German, one in Chinese with English and our current study, did not alter the overall result (HR = 0.80, 95% CI: 0.72–0.89, P < 0.001). To examine whether the association of higher BMI and increased OS was observed when using a traditional BMI cutoff value 25, five studies with the same BMI cutoff value 25 were included. We also found the similar result (HR = 0.82, 95% CI: 0.72–0.94, P = 0.004, Figure 5b).

**DISCUSSION**

Body mass index has been associated with the risk of oesophageal cancer. Nevertheless, the effect of BMI on postoperative complication and prognosis of oesophageal cancer remains controversial. The main reasons can be summarised as follows: lack of large-scale clinical studies; different BMI cutoff values in different studies; some patients receiving neoadjuvant or adjuvant therapy were enrolled in some studies. Therefore, in our large-scale cohort study, patients were classified according to Asian-specific BMI cutoff values. In addition, patients who received neoadjuvant or adjuvant therapy were excluded. To our knowledge, our study consisting of 2031 Chinese patients cohort and meta-analysis was the first time to systematically elucidate the association of BMI with postoperative complication and prognosis in oesophageal cancer.

In our study, higher BMI was proved to be a risk factor for postoperative complication, such as anastomotic leakage and cardiovascular diseases. Previous studies reported that patients with higher BMI had a higher incidence of anastomotic leakage (Healy et al, 2007; Grotenhuis et al, 2010; Blom et al, 2012). The potential mechanisms might be summarised as follows: overweight and obese patients were performed a more challenge of a cervical anastomosis procedure and had higher rate of diabetes mellitus which could adversely affect the growth of anastomosis (Blom et al, 2012). Interestingly, we found that patients with higher BMI had less incidence of chyloous leakage when compared with lower BMI. This result was in accordance with some previous studies (Morgan et al, 2007; Blom et al, 2012). However, the underlying mechanisms were rarely elucidated and in need to be further studied. The number of event for postoperative complication in each study was rarely elucidated and in need to be further studied. The number of event for postoperative complication in each study was rarely elucidated and in need to be further studied.
The clinical cohort study and meta-analysis both suggested that patients with higher BMI had a favourable survival when compared with lower BMI. In our cohort study, overweight and obese patients had an apparently longer 5-year OS than normal weight. Multivariate survival analysis showed that BMI was an independent prognostic factor in oesophageal cancer. Sensitivity analysis by excluding patients with prior diagnosed diseases or who died within the first 1 year of follow-up showed the similar result. Given most studies used a traditional BMI value 25 for overweight and obese, we re-run the univariate survival analysis using 25 as BMI cutoff. And we found that higher OS for overweight and obese patients was still noted. What is more, meta-analysis by pooling five studies with the same BMI cutoff 25 confirmed this result. Our finding was similar to some previous studies (Smith et al, 2008; Hayashi et al, 2010; Melis et al, 2011; Scarpa et al, 2012), including one meta-analysis based on small sample size (Kayani et al, 2012). In addition, a survival advantage in patients with higher BMI has been repeatedly described for renal cancer and sporadically reported for gastric cancer (Dindo et al, 2003; Mullen et al, 2008).

The mechanism by which overweight and obese patients might improve survival is not well understood. The prognostic advantage for overweight and obese patients might be attributed to the fact that overweight and obese was associated with never-smoking, never alcohol consumption and no weight loss in our present study. All of these factors were proved to affect survival not only in our study but also in other studies (Thrift et al, 2012). Besides, patients with overweight and obese were more likely to be diagnosed with EA and less likely to be ESCC when compared with normal weight. Patients with EA were reported to have a better prognosis than those with ESCC (Holscher et al, 1995). However, when we performed univariate survival analyses stratified by smoking status, alcohol consumption, weight loss and histology, the association with higher BMI and increased OS were observed in patients with never-smoking, ever-smoking, never alcohol consumption, weight loss, ESCC and EA subgroup. The findings indicated that weight loss rather than smoking or alcohol consumption status or histology might be responsible for the survival difference. In essence, the decreased oesophageal cancer death leaded to the better prognosis for higher BMI patients because higher DFS for them was noted in our study.

In addition, a recent study indicated that preoperative nutritional deficiency was associated with poor survival in cancer patients (Morgan et al, 2011). Overweight and obese patients might have a better nutritional status and potential survival advantage because they had large appetites and high lipid concentration, and could adequately preserve their fat and muscle mass (Davos et al, 2003). We should acknowledge that the association between BMI and survival might be influenced by unmeasured confounding factors such as selection criteria and specially the socioeconomic status. Patients with overweight and obese were thought to be

Figure 4. Forest plot of RR for postoperative complication of patients with highest vs lowest BMI category. (A) Anastomotic leakage. (B) Wound infection. (C) Cardiovascular diseases. (D) Chylous leakage. Abbreviation: RR = risk ratio.
associated with higher income and higher education condition in China. They were more likely to receive chemotherapy and/or radiotherapy after recurrence than patients with lower BMI because of the financial support.

In conclusion, our larger scale Chinese cohort study and meta-analysis provided more definite and quantitative evidence that higher BMI was associated with favourable survival and some postoperative complications including anastomotic leakage, wound infection and cardiovascular diseases in oesophageal cancer.

**ACKNOWLEDGEMENTS**

We would like to thank the authors of the studies included in our manuscript. This work was supported by of Chinese Ministry of Health Key Program grant (No. 179).

**CONFLICT OF INTEREST**

The authors declare no conflict of interest.

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