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SYSTEMATIC REVIEW

The metabolic syndrome and its components as prognostic factors in colorectal cancer: A meta-analysis and systematic review

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Key words
colorectal cancer, diabetes, glucose intolerance, metabolic syndrome, prognostic.

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Abstract

Background and Aim: Metabolic syndrome (MetS) increases the risk of colorectal cancer (CRC), and the impact of MetS on CRC prognosis remains controversial after the diagnosis of CRC has been established. This study aimed to explore the impact of the individual components and synergies of MetS on the prognosis of patients with CRC.
Methods: We searched articles published before August 3, 2022, in four databases, including PubMed, Embase, Cochrane Library, and ScienceDirect. The random-effects model inverse variance method was used to estimate the summarized effect size.
Results: Patients with CRC with MetS were 1.342 times more likely to experience all-cause mortality than those without MetS, and the 95% confidence interval (CI) of hazard ratio (HR) was 1.107–1.627 ($P = 0.003$). CRC-specific mortality in patients with CRC with MetS was 2.122 times higher than in those without MetS, and the 95% CI of HR was 1.080–4.173 ($P = 0.029$). CRC-specific mortality exhibited an increasing trend of risk with increased metabolic risk factors. The HR of CRC-specific mortality for one, two, and three metabolic risk factors was 1.206 (95% CI, 1.034–1.407; $P = 0.017$), 1.881 (95% CI, 1.253–2.824; $P = 0.002$), and 2.327 (95% CI, 1.262–4.291; $P = 0.007$), respectively.
Conclusions: Metabolic syndrome increased all-cause and CRC-specific mortality in patients with CRC. As a single component of MetS, diabetes mellitus increased overall mortality in patients with CRC, while obesity increased CRC-specific mortality in patients with CRC, with a significant difference from non-MetS. Moreover, the risk of CRC-specific mortality increased with increasing number of metabolic risk factors.

Introduction

Metabolic syndrome (MetS) manifests itself as a group of clinical syndromes, including diabetes or glucose intolerance, hypertension (HTN), obesity, and dyslipidemia, with multiple metabolic diseases occurring simultaneously.[1,2] A sedentary lifestyle, chronic stress, an imbalanced diet, and lipodystrophy may increase the risk of MetS.[3] MetS is associated with a higher risk of metabolic and cardiovascular disorders, including chronic kidney disease, peripheral vascular disease, coronary artery disease, and stroke. The incidence of MetS has increased dramatically worldwide and has become a major public health problem due to aging, urbanization, and lifestyle changes.

In recent years, many lines of evidence have indicated that MetS has hormonal and systemic effects that increase susceptibility to various cancers.[4–6] Epidemiological studies have shown that MetS and its components are associated with an elevated risk of cancer, including colorectal cancer (CRC). CRC is the third most common

neoplasm and the fourth most lethal malignancy worldwide, accounting for 10.2%[7] of all cancers. Although MetS increases the risk of CRC, its impact on CRC prognosis remains controversial after the diagnosis of CRC has been established. Shen *et al*. examined 503 Chinese patients with various stages of CRC and found that overall survival and disease-free survival (DFS) were significantly reduced in patients with combined MetS.[8] Pathophysiological reasons for the association between diabetes mellitus (DM) and a poor prognosis of CRC may be related to insulin resistance, glucose utilization, angiogenesis, adipokine production, and oxidative stress. However, several studies have reached different conclusions. Goulart *et al*.[2] assessed the 30-day prognosis of 134 patients who underwent CRC surgery and found that 46 were eligible for MetS. The authors found no association between MetS or its components and operative complications. A study of 1236 patients showed that MetS had no significant effect on postoperative complications or mortality.[9] To date, the value of MetS as a prognostic indicator has remained controversial, although there may be a link between MetS and CRC prognosis.

The prognostic analysis of CRC is based primarily on clinical factors, such as completeness of surgery, TNM stage, and number of lymph nodes procured, and secondarily on relevant pathologic features, such as microsatellite instability and grade. Despite these prognostic factors, the prognostic and predictive factors that guide treatment strategies are still lacking in many clinical situations. Therefore, these factors must be clinically recognized to improve treatment and outcomes. To address this issue, we carried out a meta-analysis and systematic study to explore whether MetS affects the prognosis of patients with CRC. In this study, we separately investigated the impact of individual components and synergies of MetS on the prognosis of patients with CRC, which will help identify high-risk components and provide ideas for clinical treatment and management.

Materials and methods

Protocol and guidance. This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[10] The study protocol was published in the INPLASY database under registration number INPLASY202280050 (https://inplasy.com/inplasy-2022-8-0050/).

Eligibility criteria. This study evaluated MetS and its components as prognostic factors for CRC. The inclusion criteria were as follows: (i) patients with CRC; (ii) intervention: MetS; (iii) control: without MetS; (iv) outcome: hazard ratio (HR) of survival or odds ratio (OR) of postoperative complications; and (v) study design: prospective or retrospective observational cohort studies.

Information sources and search strategy. We searched articles published before August 3, 2022, in four electronic databases, including PubMed, Embase, Cochrane Library, and ScienceDirect, using the following search terms: metabolic syndrome, colorectal cancer, colon cancer, rectal cancer, bowel cancer, rectal carcinoma, mortality, complication, prognosis, postoperative, death, prognosis, survival, readmission, length of stay, metastases, and recurrence.

Study selection. Two well-trained independent reviewers screened all abstracts. By applying inclusion/exclusion criteria to the information contained in the abstracts, we reduced the number of potentially eligible articles. The full-text articles retrieved were evaluated using the same inclusion and exclusion criteria as the abstracts. Any disagreements that arose during the selection process were discussed among the reviewers until a consensus was reached.

Data extraction. For all studies, two investigators extracted the study design, sample size, publication year, study country, participant characteristics (age and sex), follow-up time, and results of interest. In the case of multiple publications, we included the latest or comprehensive information. If there was no HR value in numeric format, we obtained it from the Kaplan–Meier plots in the original study using the methods suggested by Tierney *et al*.[11]

Definition of outcomes. Survival outcomes were HRs of overall mortality, CRC-specific mortality, and DFS. The HR for survival between patients with and without MetS was calculated.

Postoperative outcomes were ORs of postoperative complications and postoperative mortality.

We also meta-analyzed the effects of any single component of MetS, including DM, HTN, dyslipidemia, and obesity.

We also meta-analyzed all-cause mortality, CRC-specific mortality, and DFS of each component to determine which of the aforementioned prognostic outcomes was associated with each component. However, we pooled only those studies that had been included to assess MetS and provided single-component prognostic results and did not search separately for studies that assessed only the impact of a single component on CRC.

Survival outcomes were pooled based on the number of metabolic risk factors to assess whether the risk of death increased with the addition of metabolic risk factors.

Statistical analysis. A random-effects model inverse variance method was used to estimate the summarized effect size, assuming that heterogeneity always exists. We reported the pooled estimates as the weighted mean difference and their respective 95% confidence interval (CI). Heterogeneity between studies was assessed using the Cochran Q test and a P-value < 0.10 was considered significant. We also calculated the I^2 statistic as a measure of inconsistency between studies. Heterogeneity was considered significant if I^2 values were $> 50\%$. Publication bias was examined using the Begg[12] and Egger[13] regression tests. STATA version 15.0 (College Station, TX, USA) was used for all analyses.

Quality assessment. To assess the risk of bias in observational studies, we used the Newcastle–Ottawa Quality Assessment Scale. The scale assigns stars (up to nine stars) based on the quality of selection, comparability, exposure, and outcome of the study participants.

Results

Study characteristics. We initially screened 944 studies and, after eliminating duplicate studies, 296 studies were obtained for the next step of title and abstract screening. Ninety-three articles were evaluated in full text for eligibility, and 70 were excluded for the following reasons: 52 had no outcome measure of interest, 4 were duplicate trials, 9 reported only relative risk for a single component, and 5 were healthy controls. The final number of articles included in this meta-analysis was 23 (Fig. 1). The total sample size was 399 773 participants, and the number of patients with MetS was 38 910; 39% of the studies were conducted in North America, 26% in Europe, and 35% in Asia. The 23 studies were observational, including 8 prospective, 14 retrospective, and 1 cross-sectional study. Each included article was awarded at least six stars according to the Newcastle–Ottawa Scale (NOS). Table 1 summarizes the characteristics and NOS scores of the included studies.

Synthesis of results

Association between metabolic syndrome and survival of patients with colorectal cancer. First, the pooled results of the 13 studies showed that patients with CRC with MetS were 1.342 times more likely to experience all-cause mortality than patients with CRC without MetS, and the 95% CI of the HR was 1.107–1.627 (P = 0.003) (Fig. 2). Second, the pooled results of the two studies showed that CRC-specific mortality in patients with CRC with MetS was 2.122 times higher than that of patients with CRC without MetS, and the 95% CI of HR was 1.080–4.173 (P = 0.029) (Fig. 3a). Third, the pooled results of the seven studies showed significant differences in DFS between patients with CRC with and without MetS (HR, 1.574; 95% CI, 1.086–2.281; P = 0.017) (Fig. 3b).

Associations between metabolic syndrome and postoperative outcomes of patients with colorectal cancer. The pooled results of the six studies and three studies did not show significant differences in the incidence of postoperative complications and postoperative mortality between patients with CRC with and without MetS, with ORs of 1.138 (95% CI, 0.909–1.424; P = 0.259) and 0.809 (95% CI, 0.311–2.106; P = 0.664), respectively (Fig. 4).

Association between a single component of metabolic syndrome and survival of patients with colorectal cancer. Associations between the four components of MetS (DM, HTN, dyslipidemia, and obesity) and the three types of survival

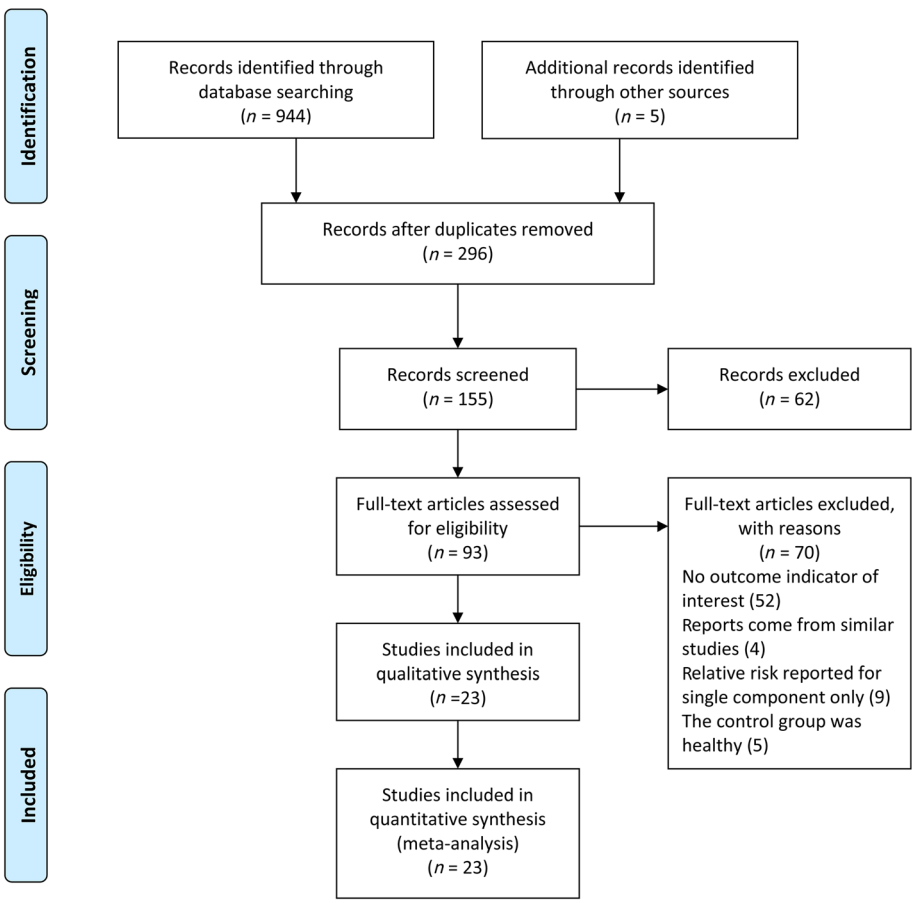


Figure 1 Flowchart of study selection.

Table 1 Characteristics of included studies

Study	Year	Study design	Age	Male%	Sample size	MetS	Country	Follow up (months)	Criteria for the definition of MetS	NOS		
										Selection	Comparability	Outcome
Akinyemiju[14]	2018	Cross-sectional	—	—	152 952	10 543	USA	0.0	ATP III	★★★★	★★	★★
Anderson[15]	2016	Retrospective	64.1 (10.3)	67.0%	102	6	USA	0.0	ATP III	★★★	★	★
Bhome[16]	2021	Prospective	72.4 (25–93)	59.0%	1066	177	UK	50.0	Self-defined	★★★★	★★	★★★
Cespedes Feliciano[17]	2016	Prospective	64 (11)	51.0%	2446	897	USA	72.0	ATP III	★★★★	★★	★★★
Chen[18]	2018	Retrospective	51.8 (12.6)	100.0%	838	215	China	60.0	The Diabetes Society of Chinese Medical Association	★★★	★	★★★
Colangelo[19]	2002	Retrospective	40.0 (12.5)	57.4%	35 582	—	USA	314.4	Self-defined	★★★★	★★	★★★
Croft[20]	2019	Retrospective	68.9	—	142	53	Canada	59.6	Self-defined	★★★	★★	★★★
Feng[21]	2021	Retrospective	59	55.3%	2046	682	China	92.0	IDF	★★★★	★★	★★
Feng[22]	2021	Retrospective	65 (60–74)	60.7%	1271	201	China	24	Chinese Diabetes Society (CDS, 2004)	★★★★	★★	★★★
Goulart[2]	2017	Prospective	67.9 (12.9)	—	134	46	Portugal	1.0	ATP III	★★★	★	★★
Lohsiriwat[23]	2010	Prospective	61 (29–91)	56.1%	114	42	Thailand	1.0	2005AHA/NHLBI	★★★	★	★★
Matthews[24]	2010	Prospective	47.2 ± 9.8	100.0%	33 230	9268	USA	172.8	ATP III	★★★★	★★	★★★
Ottaiano[25]	2016	Prospective	31–78	47.1%	102	—	Italy	46.0	ATP III	★★★	★	★★★
Peng[26]	2016	Prospective	56 (45, 67)	58.3%	1318	213	China	58.6	The Diabetes Society of Chinese Medical Association	★★★★	★★	★★★
Reed[27]	2019	Retrospective	70.1	66.4%	122	43	Canada	72.0	Self-defined	★★★	★	★★★
Shariq[28]	2019	Retrospective	65.5 ± 13.5	—	91 566	7603	USA	1.0	A modification of the NCEP-ATP III	★★★★	★★	★★
Shen[8]	2010	Retrospective	64.13	—	507	179	China	45.1	Self-defined	★★★★	★★	★★★
Silva[29]	2021	Retrospective	70 (12)	58.3%	168	85	Portugal	60	The Harmonized Criteria	★★★	★	★★★
Trevisan[30]	2001	Retrospective	20–69	57.1%	37 302	1174	Italy	84.0	Self-defined	★★★★	★★	★★★
Yang[31]	2013	Retrospective	77.1 (6.5)	42.6%	36 079	7024	USA	60.0	ATP III	★★★★	★★	★★★
You[32]	2015	Retrospective	68.8 ± 10.8	56.6%	1069	221	China	59.6	The Diabetes Society of Chinese Medical Association	★★★★	★	★★★
Zarzavadjian Le Bian[9]	2018	Prospective	70 (51–88)	68.2%	1236	85	France	3.0	ATP III	★★★	★	★★
Zhou[33]	2020	Retrospective	65 (16)	61.4%	381	153	China	1.0	AHA/NHLBI	★★★	★★	★★
Total 23 studies				399 773	38 910							

MetS, metabolic syndrome; NOS, Newcastle–Ottawa Scale.

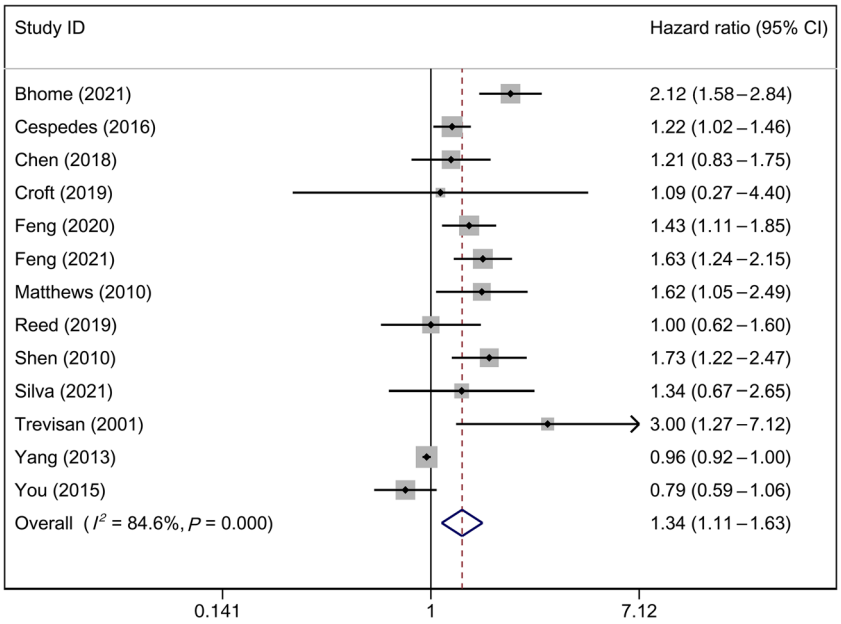
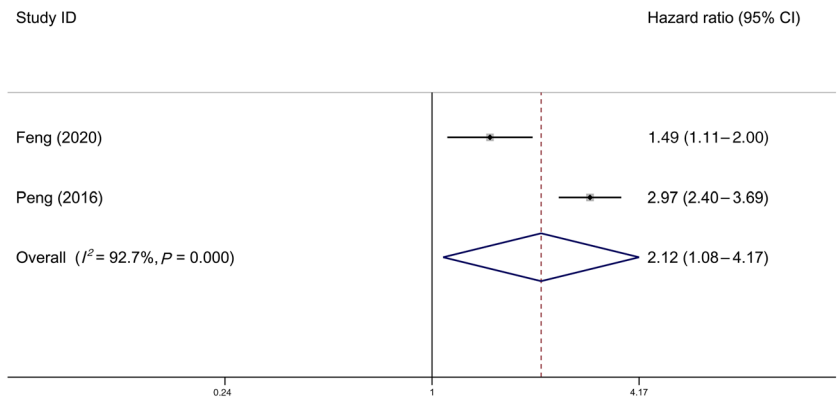


Figure 2 Forest plot of hazard ratio of all-cause mortality among patients with CRC, MetS *versus* non-MetS. *Note*: Weights are from random-effects analysis. CI, confidence interval; CRC, colorectal cancer; MetS, metabolic syndrome.

a



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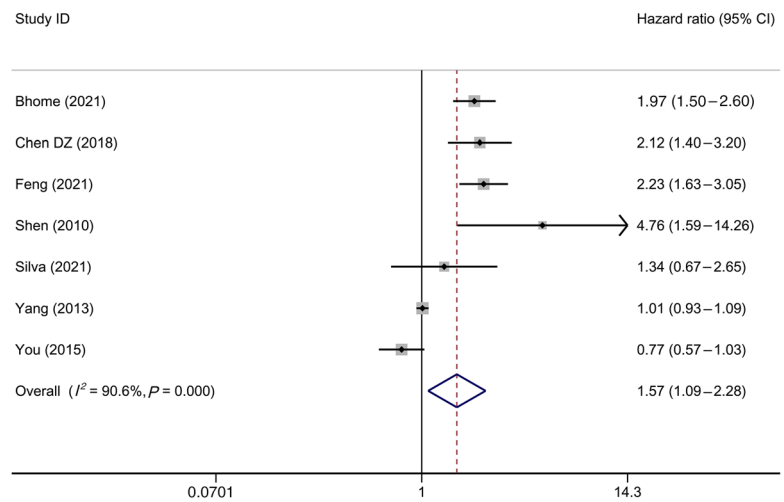

Figure 3 Forest plot of hazard ratio of (a) CRC-specific mortality among patients with CRC, MetS *versus* non-MetS, and (b) disease-free survival among patients with CRC, MetS *versus* non-MetS. *Note*: Weights are from random-effects analysis. CI, confidence interval; CRC, colorectal cancer; MetS, metabolic syndrome.

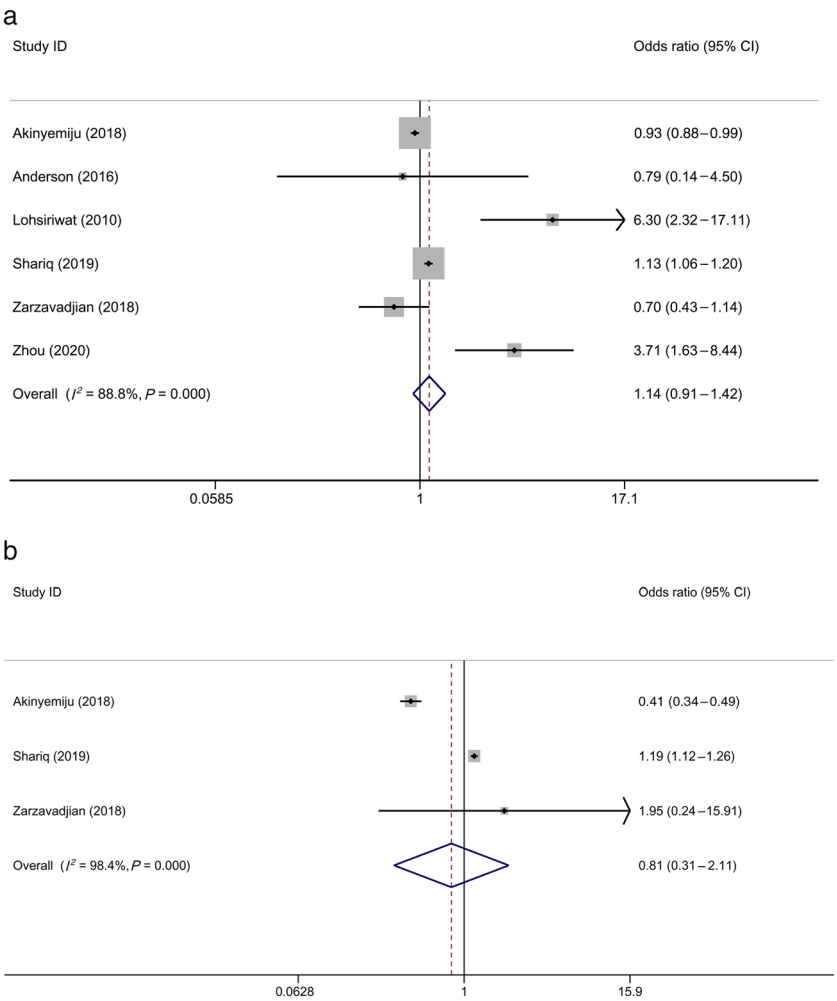

Figure 4 Forest plot of odds ratio of (a) postoperative complications among patients with CRC, MetS *versus* non-MetS, and (b) postoperative mortality among patients with CRC, MetS *versus* non-MetS. *Note*: Weights are from random-effects analysis. CI, confidence interval; CRC, colorectal cancer; MetS, metabolic syndrome.

(all-cause mortality, CRC-specific mortality, and DFS) were assessed. The results showed that the associations between DM and overall mortality, obesity, and CRC-specific mortality were significantly different compared with patients without MetS, with HRs of 1.170 (95% CI, 1.127–1.214; $P < 0.000$) and 1.333 (95% CI, 1.157–1.537; $P < 0.000$), respectively (Table 2).

Association between the number of metabolic risk factors and survival of patients with colorectal cancer. First, CRC-specific mortality exhibited an increasing trend with increasing metabolic risk factors. The HR of CRC-specific mortality for one, two, and three metabolic risk factors was 1.206 (95% CI, 1.034–1.407; $P = 0.017$), 1.881 (95% CI, 1.253–2.824; $P = 0.002$), and 2.327 (95% CI, 1.262–4.291; $P = 0.007$), respectively. Second, as the number of metabolic risk factors increased, no pattern was found for overall mortality risk. The HR of overall mortality for one, two, and three metabolic risk factors was 1.140 (95% CI, 1.08–1.204; $P < 0.000$), 1.558 (95% CI, 0.896–2.708; $P = 0.116$), and 1.384 (95% CI, 0.852–2.246; $P = 0.189$), respectively (Fig. 5).

Sensitivity analysis. Comparisons of postoperative mortality and postoperative complications between patients with CRC with and without MetS included a cross-sectional study[14]; therefore, we excluded this study from the sensitivity analysis.

Table 2 Associations between single component of the MetS and survival of patients with CRC

Component	CRC-specific mortality	DFS	Overall mortality
DM	1.903 (0.632–5.728)	1.263 (0.933–1.711)	1.170 (1.127–1.214)
HTN	1.242 (0.97–1.591)	1.089 (0.803–1.477)	1.315 (0.879–1.966)
Dyslipidemia	1.381 (0.982–1.942)	0.818 (0.624–1.073)	1.029 (0.816–1.298)
Obesity	1.333 (1.157–1.537)	1.087 (0.812–1.455)	1.041 (0.914–1.186)

CRC, colorectal cancer; DFS, disease-free survival; DM, diabetes mellitus; HTN, hypertension; MetS, metabolic syndrome.

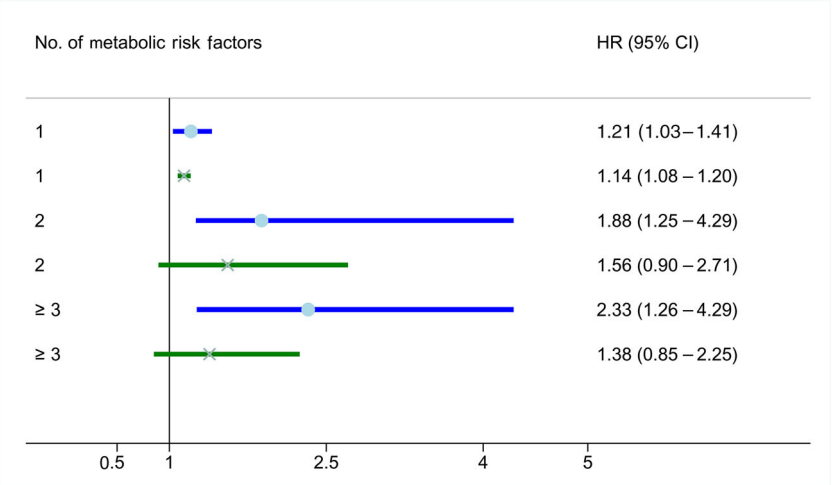

Figure 5 Plot of associations between number of metabolic risk factors and survival of patients with CRC. ■, Overall mortality; ■, CRC mortality. CI, confidence interval; CRC, colorectal cancer; HR, hazard ratio.

The pooled results of postoperative mortality showed significant differences; the OR was 1.186 (95% CI, 1.118–1.258; $P < 0.000$), while when the study by Akinyemiju *et al*. was included, the original pooled result was 0.809 (95% CI, 0.311–2.106; $P = 0.664$). This suggests that the study by Akinyemiju *et al*.[14] is sensitive to this outcome; the results of postoperative mortality between patients with CRC with and without MetS should be interpreted with caution.

There was no substantial change in the pooled results of postoperative complications after excluding the study by Akinyemiju *et al*.[14]

Publication bias. The Egger test was the best for synthesizing results with 10 or more datasets. Only data on overall mortality (MetS *vs* non-MetS) were included. The Egger test showed $P = 0.007$, which was inconsistent with the Begg test ($P = 0.714$). Based on a visual inspection of the funnel plots (Fig. S1), we adopted the detection results of the Egger test and believed that publication bias existed.

Discussion

This meta-analysis included 21 studies with a total sample size of 398 334 subjects. Our study revealed the following: (i) Patients with CRC with MetS were more significantly associated with all-cause mortality and CRC-specific mortality than those without MetS; (ii) the associations between DM and overall mortality, obesity, and CRC-specific mortality were significantly different compared with patients without MetS, but the association between DM and obesity and DFS was not significant; (iii) CRC-specific mortality increases with increased metabolic risk factors; and (iv) the incidence of postoperative complications and mortality in patients with CRC with MetS was not significantly different from those without MetS.

Studies have shown that MetS is associated with CRC prognosis. A meta-analysis indicated that MetS is associated with reduced survival in patients with CRC.[34] To determine the relationship between MetS and CRC prognosis, we examined the relationship between MetS and the survival of patients with CRC. We found that patients with CRC with MetS had significantly higher all-cause mortality and CRC-specific mortality. Currently, it is widely accepted that the pathogenesis of MetS and CRC may be associated with certain endocrine hormone abnormalities such as hyperinsulinemia and insulin resistance. MetS causes hyperinsulinemia and insulin resistance, leading to elevated levels of insulin-like growth factor-1 (IGF-1). The activation of the insulin/IGF-1 system by increased levels of circulating insulin through the ligation of the insulin receptor A (IR-A) expressed in CRC cells can promote the activity of the MEK/Raf/Ras and PI3K/Akt pathways. When these axes are dysregulated, they induce cancer-promoting effects, such as the promotion of angiogenesis, inhibition of apoptosis, and proliferation. Many patients with MetS have visceral obesity. As visceral fat is metabolically more active than subcutaneous fat, visceral adipocytes can release potentially harmful levels of tumor necrosis factor-α and interleukin 6, leading to a chronic proinflammatory state and insulin resistance.[28] Moreover, recent studies have shown that MetS is associated with gut microbiota dysfunction.[35–37] Disorders in the gut microbiota can affect fat intake and lead to weight gain, which, in turn, is a source of cytokines that induce carcinogenesis and low-grade, chronic inflammation.[38–40] Obesity itself can also affect the ecology of the intestinal flora.[41] Several studies have revealed that MetS increases the risk of mortality in many diseases. Ju *et al*. found that MetS was associated with an increased risk of all-cause and cardiovascular disease mortality in adults aged ≥ 60 years. They observed a 24% increase in the risk of cardiovascular disease mortality and a 23% increase in the risk of all-cause mortality among older adults with MetS compared with those without MetS.[42] The meta-analysis included 19 studies that revealed that MetS was significantly associated with a higher risk of prostate cancer-specific death (relative risk [RR], 1.12; 95% CI, 1.02–1.23).[43] Pre-existing MetS among patients with coronavirus disease was significantly associated with a higher risk of short-term mortality (OR, 2.30; 95% CI, 1.52–3.45).[44] MetS was associated with an increased risk of all-cause death in patients with breast cancer.[45] End-stage renal disease patients with MetS had a significantly increased risk of all-cause mortality (RR, 1.92; 95% CI, 1.15–3.21) compared with those without MetS.[46] These findings are consistent with those of the present study. Our study showed that patients with CRC with MetS had significantly higher all-cause mortality (HR, 1.342; 95% CI, 1.107–1.627) and

CRC-specific mortality (HR, 2.122; 95% CI, 1.080–4.173). However, there is a lack of comparison between the effects of MetS on mortality from various diseases.

It is essential to guide treatment decisions in many clinical CRC scenarios. Currently, CRC prognosis is mainly based on clinical factors. Despite these prognostic factors, there is still a lack of readily available, replicable, and inexpensive prognostic factors that can guide patients or therapeutic decisions. MetS data are usually available or easily accessible and do not require additional molecular pathology studies that may be specialized and expensive. They are easily obtainable, reusable, inexpensive, and well suited for guidance and adjuvant therapy. We expected a significant increase in all-cause and CRC-specific mortality in patients with CRC with MetS. This finding may provide ancillary information to guide treatment decisions, discuss the prognosis with patients, and guide lifestyle changes after cancer diagnosis.

This study not only focused on the prognostic impact of MetS as a syndrome but also examined the impact of obesity, DM, and other components of MetS (e.g. HTN and dyslipidemia) on survival outcomes in patients with CRC separately. Our goal was to further discuss whether individual factors can provide stronger predictions than the combined effects of these factors. The measures of MetS components are available for all patients, and if each component validates its prognostic significance, it will facilitate more precise treatment guidance and help guide lifestyle changes after cancer diagnosis. Most current findings agree that DM may be a major prognostic factor for progression-free survival in CRC. A meta-analysis of 36 studies and approximately 2.3 million participants on the association between DM and CRC revealed a moderate adverse effect of DM on overall survival.[47] This might be because patients with DM often have diabetic gastrointestinal motility dysmotility. End products of metabolism remain in the intestine for a long time, resulting in a prolonged action of toxins and carcinogens in colorectal mucosal cells, which are prone to malignant transformation and have a high degree of infiltration. One study found that in patients with CRC who received adjuvant chemotherapy with capecitabine and oxaliplatin, obesity promoted chronic neurotoxicity and stimulated the development of micrometastases.[25] The mechanism by which obesity affects the prognosis of CRC may involve an imbalance in the adipokine spectrum. Adipose tissue is a highly active participant in the innate immune system, and adipokines are responsible for the paracrine cycle between macrophages and adipocytes. This interaction leads to low-level chronic inflammation throughout the body, providing an enabling environment for the development of tumors. Several studies have revealed that serum adiponectin levels are negatively correlated with CRC.[48–50] Interestingly, MetS, as a whole, affects CRC outcomes, but HTN or dyslipidemia as a single component does not. We speculate that these components may work synergistically. Although individual factors may not work, they can produce synergies when combined. For example, when obesity is combined with insulin resistance, it promotes chronic inflammation, leading to more malignant tumors and a poorer prognosis.[25,51] Our study also found that the risk of CRC-specific mortality increased with the number of metabolic risk factors, confirming a synergistic effect between them.

Many patients with CRC require surgical treatment, and a significant number of them have MetS. DM is generally believed to increase perioperative morbidity and mortality. Patients with DM who undergo surgery are more prone to poor wound healing, hematoma, wound infection, admission to the intensive care unit, and prolonged hospitalization. Due to its effects on immunity and blood vessels, DM has been identified as a risk factor for poor healing. DM is a major component of MetS and has increased perioperative complications. However, the effect of MetS on the postoperative outcome of CRC still lacks a description. We also analyzed the incidence of postoperative complications and mortality in this group of patients. Our pooled results from seven studies showed that the incidence of postoperative complications and mortality in patients with CRC with MetS were not significantly different from those in patients with CRC without MetS. Although our findings suggest that MetS does not affect postoperative complications, more in-depth research is needed due to the paucity of studies.

This study has some limitations. First, we included MetS cases defined by different organizations in this meta-analysis, which may have led to the heterogeneity of the study. Second, because all studies we included were related to MetS, the pooled effect size of the relationship between the MetS single component and prognosis outcomes did not incorporate the results of those studies that examined a single component (such as diabetes) of MetS, although there are more than enough of such studies. Third, although adjustments were made for known risk factors and potential confounding variables (age, sex, smoking, alcohol consumption, family history, year of CRC diagnosis, tumor site, and TNM stage) in almost all included studies, the adjustment varied with each study. This adjustment did not occur in one study because they believed that there were no statistical differences between the two groups of patients at baseline. Therefore, the findings of this study should be interpreted with caution.

Conclusions

Overall, our findings suggest that MetS increases all-cause and CRC-specific mortality in patients with CRC. As a single component of MetS, DM increased overall mortality in patients with CRC, while obesity increased CRC-specific mortality in patients with CRC, with a significant difference from non-MetS. Moreover, the risk of CRC-specific mortality increased with increasing number of metabolic risk factors. This study might provide physicians with useful information to help guide lifestyle changes or treatment strategies after cancer diagnosis.

Data availability statement. The datasets generated during and/or analyzed during the current study are available from the corresponding authors on reasonable request.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1 Funnel plot of hazard ratio of all-cause mortality among patients with CRC, MetS vs non-MetS.