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# Prognostic and clinicopathological significance of long non-coding RNA UCA1 in colorectal cancer
## Results from a meta-analysis

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## Abstract
**Objective:** Urothelial cancer-associated 1 (UCA1), an oncogenic long non-coding RNA, was aberrantly upregulated in colorectal cancer (CRC). This study aimed to further explore the clinical value of UCA1 in CRC.

**Methods:** Eligible studies were retrieved by searching Pubmed, Embase, Cochrane Library, Web of Science, Chinese National Knowledge Infrastructure, and Wanfang databases. Pooled hazard ratio (HR) and odds ratio (OR) with 95% confidence interval (CI) were applied to assess the prognostic role and clinical significance of UCA1.

**Results:** A total of 7 eligible studies with 775 cancer patients were recruited in the meta-analysis. The results showed that UCA1 overexpression was significantly correlated with poor overall survival in patients with CRC (HR = 2.25, 95% CI: 1.77–2.87, $P < .001$). There was also a significantly negative association between high UCA1 levels and tumor differentiation (OR = 2.84, 95% CI: 1.87–4.31, $P < .001$), lymph node metastasis (OR = 3.48, 95% CI: 2.24–5.41, $P < .001$), distant metastasis (OR = 2.67, 95% CI: 1.32–5.38, $P = .006$), tumor node metastasis stage (OR = 3.01, 95% CI: 2.16–4.18, $P < .001$), tumor invasion depth (OR = 2.18, 95% CI: 1.03–4.61, $P = .04$), and tumor size (OR = 2.27, 95% CI: 1.56–3.32, $P < .001$).

**Conclusions:** Our study revealed that UCA1 overexpression was associated with poor prognosis and more advanced clinicopathological features, suggesting that UCA1 may serve as an indicator for unfavorable outcome of patients with CRC.

**Abbreviations:** ceRNA = competing endogenous RNA, CI = confidence interval, CNKI = Chinese National Knowledge Infrastructure, CRC = colorectal cancer, CREB1 = cyclic adenosine 3′,5′-monophosphate response element binding protein 1, HR = hazard ratio, lncRNA = long non-coding RNA, NOS = Newcastle-Ottawa Scale, OR = odds ratio, OS = overall survival, qRT-PCR = quantitative reverse transcription-polymerase chain reaction, UCA1 = urothelial cancer-associated 1, ZEB1 = zinc finger E-box binding homeobox 1.

**Keywords:** colorectal cancer, long non-coding RNA (lncRNA), meta-analysis, prognosis, urothelial cancer-associated 1

## 1. Introduction

Colorectal cancer (CRC) is not only the fourth most frequent malignancy but also ranks as the fourth leading cause of cancer-related death worldwide, which has threatened human health seriously. According to the GLOBOCAN 2018 database, approximately 1.8 million new cases and 861,600 deaths were caused by CRC in 2018.[1] Although great advances on therapy strategies have been achieved, the clinical outcome of CRC still is far away from satisfaction.[2] Therefore, there is an urgent need to understand the precise molecular mechanisms underlying tumorigenesis as well as to identify new therapeutic targets for CRC. Nowadays, advantage of molecular biomarkers in diagnosis and prognosis of multiple malignancies has been highlighted, which might provide more exact clues for supervising individual therapy and monitoring disease progression.[3,4]

Long non-coding RNAs (lncRNAs), accounting for 70% of the human genome, are defined as a class of RNA molecules with length larger than 200 nucleotides.[5] In the past, lncRNAs were once considered as transcriptional noise in the genomic RNAs. However, a growing body of evidence has suggested the regulation role of lncRNAs on gene expression at the epigenetic, transcriptional, or posttranscriptional levels.[6,7] In particular, the effect of lncRNAs on tumorigenesis has attracted attention recently and become widely acceptable.[8] More importantly, the expression of lncRNAs was indicated to be dysregulated in multiple malignancies, which is responsible for diverse biological processes, such as tumor cell proliferation, apoptosis, invasion, and metastasis.[9,10] Subsequently, emerging evidence has suggested that there was a significant association between aberrant expression of lncRNAs and progression of disease, including clinicopathological features and survival, which indicates that lncRNAs may serve as molecular biomarkers for various malignancies.[11]

Urothelial cancer-associated 1 (UCA1), a novel lncRNA and locating in the chromosome 19p13.12, was originally

discovered to be up-regulated in bladder transitional cell carcinoma in 2006 and could promote cell proliferation and transformation.[12,13] Recently, overexpressed UCA1 has attracted great concerns due to its involvement in diverse malignancies, especially CRC.[14,15] However, these results were limited by small sample scales or inconsistent conclusions. For instance, Han et al[14] demonstrated that UCA1 expression was related with differentiated histology and invasion depth of CRC, whereas Jiang et al[15] illustrated that UCA1 was correlated with differentiation rather than invasion depth. Until now, meta-analysis associated UCA1 has not yet to be performed in CRC. Therefore, with the aim to investigate the potentially clinical value of UCA1, relevant articles were collected to perform this comprehensive meta-analysis for assessing the correlation of UCA1 expression with clinicopathological features and prognosis in patients with CRC.

## 2. Material and methods

### 2.1. Literature search strategy

To get access to potentially eligible studies, relevant literatures exploring the association of UCA1 with clinicopathological features and prognosis of CRC were systematically retrieved in Pubmed, Web of Science, Cochrane Library, Embase, Chinese National Knowledge Infrastructure (CNKI), and Wanfang databases updated to January 2019. To increase the sensitivity of the search, both MeSH terms and free-text words were used in the retrieval strategy. Relevant retrieval terms are as follows: "UCA1" or "urothelial cancer-associated 1", "cancer" or "carcinoma" or "tumor" or "neoplasm", and "survival" or "prognosis" or "prognostic" or "progression" or "metastasis" or "clinicopathological". In addition, the reference lists in relevant articles were screened manually in case of the omission of any potentially relevant literature. Because the data were obtained from publicly available databases, additional approval by an ethics committee was not applicable.

### 2.2. Inclusion and exclusion criteria

Inclusion and exclusion criteria were formulated to screen the publications. The eligible studies met the following inclusion criteria:

(1) the association of UCA1 with progression of CRC was explored,
(2) the expression of UCA1 in primary cancerous tissues were detected,
(3) patients were grouped according to the expression levels of UCA1, and
(4) relevant clinicopathological parameters were described.

Exclusion criteria included

(1) duplicate publications,
(2) no original articles, reviews, letters, case reports, and commentaries,
(3) studies focusing on UCA1 in other types of cancers rather than CRC,
(4) studies using non-tissue samples, and
(5) studies lack of usable data.

For multiple publications from the same medical center, only the most recent or the most complete study was included in the meta-analysis.

### 2.3. Data extraction

According to the inclusion and exclusion criteria, two investigators (X-QL and X-DL) deliberately reviewed and collected the essential information from the eligible studies independently, For any discrepancy, a consensus was achieved through discussion with a third investigator (T-KQ). For each eligible study, the following information was collected: the first author' name, publication year, country, cancer type, sample size, detection method of UCA1 expression, cut-off value, number of patients in high/low UCA1 expression group, follow-up period, outcome measures, survival analysis methods (univariate or multivariate), and hazard ratio (HR) and corresponding 95% confidence interval (CI) for overall survival (OS). If the HRs with their 95% CIs were provided in the original studies, these available data were extracted directly. When an included study gave only Kaplan–Meier survival curves, the survival data was digitized by the Engauge Digitizer version 4.1 software (http://digitizer.sourceforge.net/) and calculated as described by Tierney et al.[16]

### 2.4. Quality assessment

The quality of all included studies was assessed according to the Newcastle-Ottawa Scale (NOS) criteria for cohort studies.[17] The NOS criteria is scored based on three aspects, including subject selection, comparability of subject, and clinical outcome, with the final scores ranging from 0 (lowest) to 9 (highest). A study with the NOS scores more than 6 was regarded as high quality.

### 2.5. Statistical analysis

Statistical analysis was performed with Review Manager 5.2 (The Cochrane Collaboration, Oxford, UK) and stata SE12.0 (Stata Corporation, TX). HRs and corresponding 95% CIs were used to assess the association between UCA1 and OS in CRC, with HR > 1 indicating that the patients with high UCA1 expression had a poor prognosis. Odds ratios (ORs) and their 95% CIs were used to evaluate the association between UCA1 and clinicopathological features in patients of CRC. The between-studies heterogeneity was assessed with the Chi square-based Q test and $I^2$ statistics. A $P$ value < .05 or $I^2$ > 50% indicated significant heterogeneity, in which case a random-effect model was applied, otherwise, a fixed-effect model was used. Subgroup analysis was performed to further investigate the prognostic value of UCA1 in CRC. Sensitivity analyses were employed to access the stability of the results. The potential publication bias was evaluated with funnel-plot analysis as well as Egger's test. All the $P$ values were determined by two-sided tests, and $P < 0.05$ was considered statistically significant.

## 3. Results

### 3.1. Literature information

As shown in the flow diagram (Fig. 1), a total of 235 records were retrieved by searching Pubmed, Web of Science, Cochrane Library, Embase, CNKI, and Wanfang databases. Initially, 5 records were removed because of duplication. After the title and abstract were screened, 132 articles were excluded due to either no original articles or reviews or case reports or commentaries. Subsequently, full text was assessed carefully and 91 articles were found to be ineligible due to lack of available outcome or inappropriate study design or for focusing on the level of UCA1 from other type of cancers rather than CRC. Finally, 7
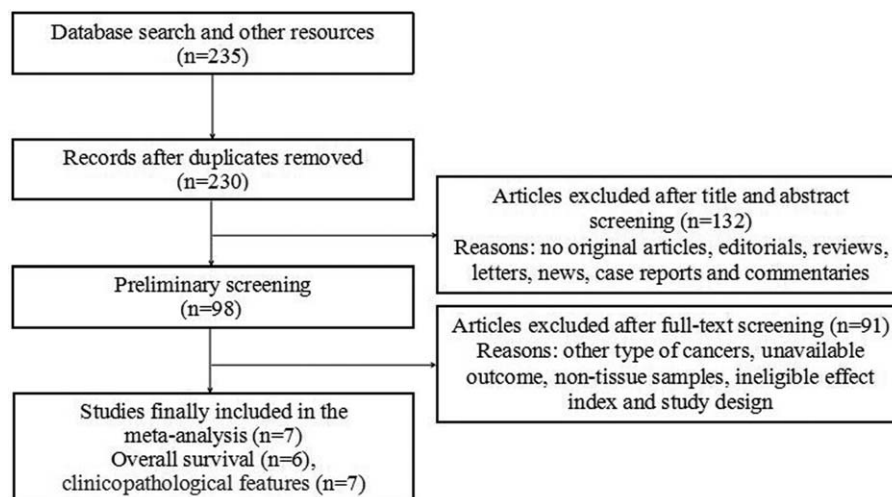
**Figure 1.** The flow diagram for screening eligible publications in the meta-analysis.

studies[14,15,18–22] comprising 775 patients were identified as eligible for the present quantitative analysis, including 6 on OS and 7 on clinicopathological features.

### 3.2. Study characteristics

The main characteristics and data of the inclusion studies were summarized in Table 1. As shown, all studies were conducted in China and published between 2014 and 2018 with sample scales ranging from 54 to 185. Tumor node metastasis (TNM) staging ranged from stage I to IV. The longest follow-up period was up to 120 months. The UCA1 expression was detected with quantitative reverse transcription-polymerase chain reaction (qRT-PCR) in all studies. The cut-off value of UCA1 levels was based on median value in 4 studies, mean value in 2 studies, and fourth quartile value in 1 study. With inconsistent cut-off value due to different criteria, all participants in the inclusion studies were categorized into high and low UCA1 expression groups. HRs with corresponding 95% CIs were extracted from multivariate analysis in 5 studies and univariate analysis in 5 studies (estimated effects collected from Kaplan–Meier survival curve in 2 studies). All of the included studies got 7 scores or more according to the NOS criteria, which indicated their high quality of methodology.

### 3.3. Association between UCA1 and OS

A total of 6 studies of 715 patients reported the association between UCA1 expression levels in cancer tissues and OS of CRC. As shown in Figure 2, the fixed-effect model was applied to calculate the pooled HR and its 95% CI since no significant heterogeneity was found among these studies ($I^2 = 0\%$, $P = .44$). The results revealed that high UCA1 expression was significantly associated with poor OS (HR = 2.25, 95% CI: 1.77–2.87, $P < .001$). Although there was no significant between-studies heterogeneity, the subgroup meta-analysis was conducted based on analysis type, sample size, and cut-off value for a subsequent investigation of potential heterogeneity. From the subgroup results by analysis type (Fig. 3A), we found that UCA1 similarly was a significantly prognostic indicator of OS in multivariable analysis subgroup (HR = 2.39, 95% CI: 1.80–3.16, $P < .001$) and univariable analysis subgroup (HR = 2.65, 95% CI: 1.93–3.63, $P < .001$), without statistically significant heterogeneity in the two subgroups ($I^2 = 8.0\%$, $P = .36$ and $I^2 = 25\%$, $P = .25$, respectively). Then, elevated UCA1 was also found to be significantly associated with OS of patients in studies with sample sizes both equal or greater than 90 (HR = 2.17, 95% CI: 1.62–2.91, $P < .001$) and less than 90 (HR = 2.44, 95% CI: 1.59–3.74, $P < .001$), with significant heterogeneity in the former ($I^2 = 59\%$, $P = .09$) but not in the latter ($I^2 = 0\%$, $P = .87$) (Fig. 3B).

| Table 1 |
|---|

**Main characteristics of all enrolled studies in this meta-analysis.**

| Study | Year | Region | Tumor type | Sample size | Tumor stage | Follow-up (months) | Survival | Detection method | Cut-off value | Analysis type | NOS score |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Bian-1 et al[18] | 2016 | China | CRC | 90 | I–IV | Up to 80 | OS | qRT-PCR | Median value | M/U | 7 |
| Bian-2 et al[18] | 2016 | China | CRC | 105 | I–IV | Up to 120 | OS | qRT-PCR | Median value | U | 7 |
| Cui et al[19] | 2019 | China | CC | 60 | I–IV | NR | NR | qRT-PCR | Mean value | NR | 7 |
| Han et al[14] | 2014 | China | CRC | 80 | I–IV | Mean 42.6 | OS | qRT-PCR | Mean value | U | 7 |
| Jiang et al[15] | 2016 | China | CRC | 121 | I–IV | Up to 60 | OS | qRT-PCR | Median value | M | 8 |
| Ni et al[20] | 2015 | China | CRC | 54 | I–IV | Up to 50 | OS | qRT-PCR | Median value | M/U | 8 |
| Tao et al[21] | 2015 | China | CC | 80 | I–IV | Up to 72 | OS | qRT-PCR | Fourth quartile | M/U | 8 |
| Yao et al[22] | 2018 | China | CRC | 185 | I–IV | Up to 36 | OS | qRT-PCR | Median value | M/U | 9 |

CC = colon cancer, CRC = colorectal cancer, M = multivariate, NR = not report, OS = overall survival, qRT-PCR = quantitative real-time-polymerase chain reaction, U = univariate.
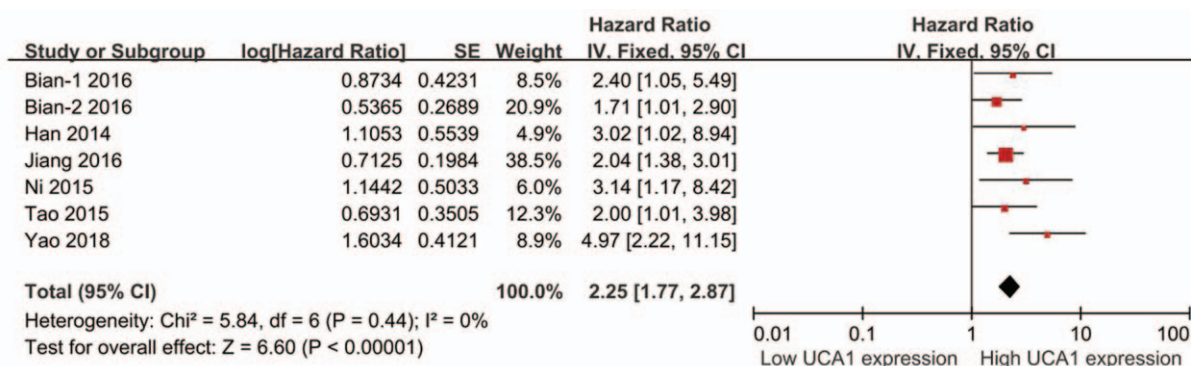
**Figure 2.** Forest plot of meta-analysis for the association between high UCA1 expression with overall survival (OS). CI = confidence interval, HR = hazard ratio, UCA1 = urothelial cancer-associated 1.

Meanwhile, a significant relationship between UCA1 expression and OS of patients was observed in studies with median as cut-off value (HR = 2.25, 95% CI: 1.73–2.93, $P < .001$) and non-median as cut-off value (HR = 2.25, 95% CI: 1.26–4.02, $P = .006$), without evidence of significant heterogeneity across the two subgroups ($I^2 = 27\%$, $P = .24$ and $I^2 = 0\%$, $P = .53$, respectively) (Fig. 3C). Results from the above analysis indicated that high UCA1 expression was significantly correlated with poor OS in CRC patients, suggesting that UCA1 was an indicator of decreased survival rate in CRC.

### 3.4. Association between UCA1 and clinicopathological features

In order to determine whether the expression of UCA1 was related to clinically pathological characteristics, the clinicopathological data were further collected for the meta-analysis. As shown in Table 2, a total of 7 studies including 670 cases reported the association of UCA1 overexpression with clinicopathological features of CRC. Except for tumor invasion depth ($I^2 = 72\%$, $P = .007$), there was no significant heterogeneity among studies for age ($I^2 = 49\%$, $P = .12$), gender ($I^2 = 2\%$, $P = .41$), location ($I^2 = 0.0\%$, $P = .80$), tumor size ($I^2 = 47\%$, $P = .11$), lymph node metastasis ($I^2 = 0.0\%$, $P = 1.0$), distant metastasis ($I^2 = 25\%$, $P = .26$), TNM stage ($I^2 = 36\%$, $P = .16$), histopathological grade

($I^2 = 26\%$, $P = .23$), lymphatic invasion ($I^2 = 0.0\%$, $P = .73$), and venous invasion ($I^2 = 0.0\%$, $P = .78$). The pooled results revealed that high UCA1 transcription levels were significantly associated with tumor differentiation (OR = 2.84, 95% CI: 1.87–4.31, $P < .001$), lymph node metastasis (OR = 3.48, 95% CI: 2.24–5.41, $P < .001$), distant metastasis (OR = 2.67, 95% CI: 1.32–5.38, $P = .006$), TNM stage (OR = 3.01, 95% CI: 2.16–4.18, $P < .001$), tumor invasion depth (OR = 2.18, 95% CI: 1.03–4.61, $P = 0.04$), and tumor size (OR = 2.27, 95% CI: 1.56–3.32, $P < .001$). However, no significant correlation was found with gender (OR = 0.81, 95% CI: 0.58–1.13, $P = .21$), age (OR = 0.91, 95% CI: 0.61–1.37, $P = .66$), lymphatic invasion (OR = 1.56, 95% CI: 0.88–2.75, $P = .13$), venous invasion (OR = 0.85, 95% CI: 0.39–1.85, $P = .69$), and nervous invasion (OR = 0.59, 95% CI: 0.18–1.95, $P = .39$). Taken together, the above results revealed that UCA1 overexpression was significantly correlated with poorer differentiation, deeper tumor invasion (T3 stage or more), higher risk of metastasis, and more advanced TNM stage in CRC patients, suggesting that UCA1 may serve as a risk factor for these unfavorably clinicopathologocal features of CRC.

### 3.5. Sensitivity analysis

In order to assess the stability of the pooled results, sensitivity analysis was performed using stata SE12.0 software to assess the

### Table 2

**Association between high levels of UCA1 and characteristics of patients with CRC.**

| Clinicopathological parameters | Studies (n) | Patients (cases) | OR (95% CI) | Z value | P | Heterogeneity $I^2$ (%) | P | Model |
|---|---|---|---|---|---|---|---|---|
| Gender (female vs. male) | 6 | 610 | 0.81 (0.58–1.13) | 1.26 | 0.21 | 2 | 0.41 | Fixed effects |
| Age (<60 vs. ≥60) | 4 | 389 | 0.91 (0.61–1.37) | 0.44 | 0.66 | 49 | 0.12 | Fixed effects |
| Location (CRC vs. CC) | 3 | 291 | 0.77 (0.48–1.24) | 1.08 | 0.28 | 0 | 0.80 | Fixed effects |
| Tumor size (<5 vs. ≥5) | 5 | 495 | 2.27 (1.56–3.32) | 4.27 | <0.001 | 47 | 0.11 | Fixed effects |
| Tumor differentiation (Moderate/well vs. poor) | 7 | 670 | 2.84 (1.87–4.31) | 4.89 | <0.001 | 26 | 0.23 | Fixed effects |
| Depth of tumor (T1–T2 vs. T3–T4) | 5 | 556 | 2.18 (1.03–4.61) | 2.03 | 0.04 | 72 | 0.007 | Random effects |
| Lymph node metastasis (positive vs. negative) | 4 | 440 | 3.48 (2.24–5.41) | 5.55 | <0.001 | 0 | 1.00 | Fixed effects |
| Distant metastasis (positive vs. negative) | 4 | 345 | 2.67 (1.32–5.38) | 2.73 | 0.006 | 25 | 0.26 | Fixed effects |
| TNM stage (I–II vs. III–IV) | 7 | 670 | 3.01 (2.16–4.18) | 6.56 | <0.001 | 36 | 0.16 | Fixed effects |
| Lymphatic invasion | 3 | 224 | 1.56 (0.88–2.75) | 1.52 | 0.13 | 0 | 0.73 | Fixed effects |
| Venous invasion | 2 | 134 | 0.85 (0.39–1.85) | 0.41 | 0.69 | 0 | 0.78 | Fixed effects |
| Nervous invasion | 1 | 80 | 0.59 (0.18–1.95) | 0.86 | 0.39 | NA | NA | Random effects |

CC = colon cancer, CI = confidence interval, CRC = colorectal cancer, NA = not applicable, OR = odds ratio, TNM = tumor node metastasis.

$I^2 > 50\%$ with the random-effects model.

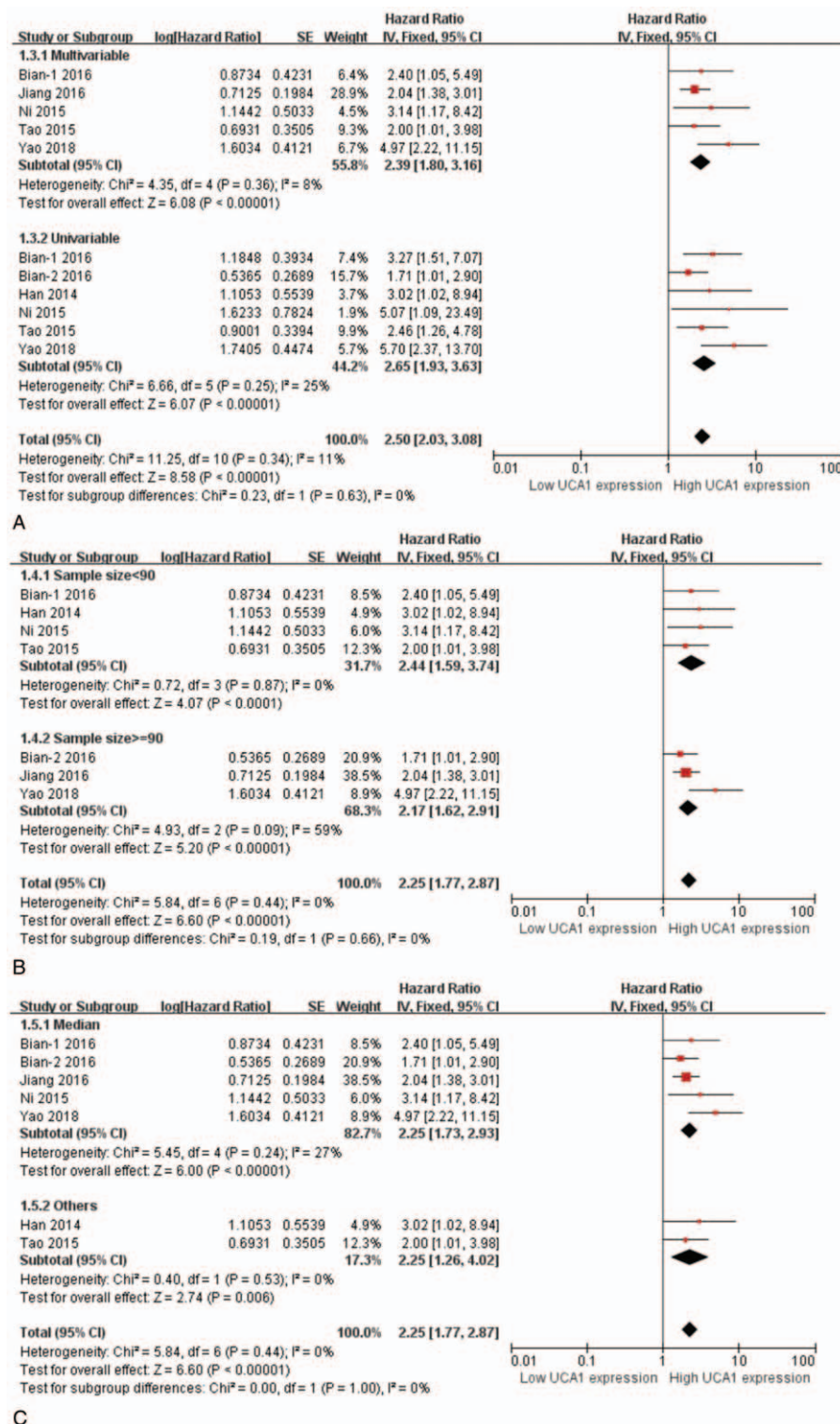$I^2 \leq 50\%$ with the fixed- effects model.

**Figure 3.** Forest plots of subgroup analysis for the association between high UCA1 expression with overall survival (OS) based on (A) analysis type, (B) tumor size, and (C) cut-off value. CI = confidence interval, HR = hazard ratio, UCA1 = urothelial cancer-associated 1.

effect of any single study on OS and clinicopathologic characteristics by omitting individual study at a time in total population. As shown in Figure 4, when each study was removed sequentially, none of the residual results were dramatically altered each time. Because of the limited number

of studies and without between-studies heterogeneity, the sensitivity analysis was not performed in these groups of clinicopathologic covariates including age, location, lymph node metastasis, distant metastasis, lymphatic invasion, venous invasion, and nervous invasion.
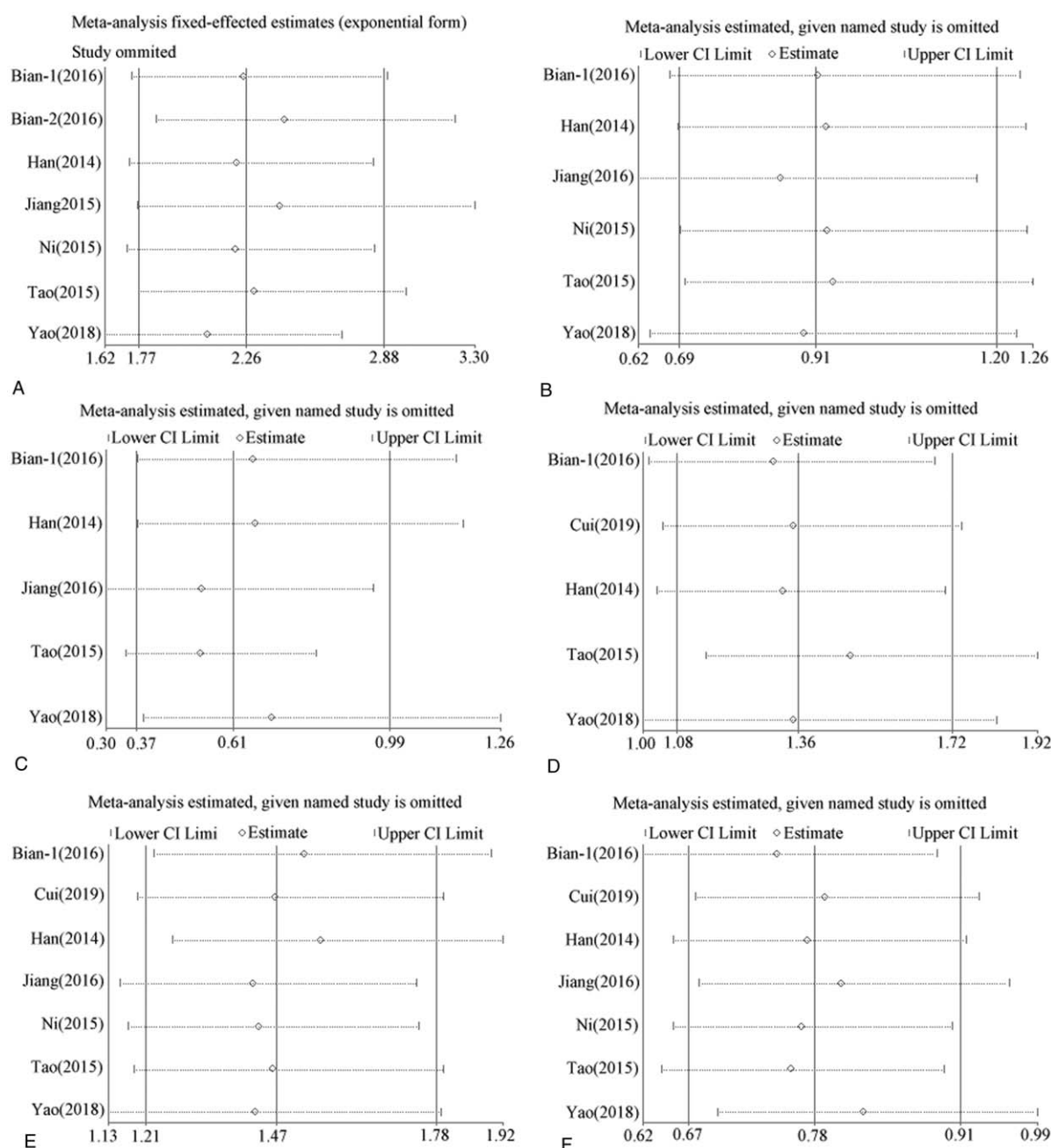
Figure 4. Results of sensitivity analysis in groups with (A) overall survival (OS), (B) gender, (C) depth of tumor, (D) tumor size, (E) TNM stage, and (F) tumor differentiation.

### 3.6. Publication bias

The funnel plots were employed to assess the potential publication bias of the present meta-analysis. As shown, no publication bias was found in the studies with OS (Fig. 5A) or gender (Fig. 5B) or depth of tumor (Fig. 5C) or tumor differentiation (Fig. 5D) or TNM stage (Fig. 5E) or tumor size (Fig. 5F), which was confirmed in Egger's linear regression test using stata SE12.0 software (Table 3). Because of the small number of studies and little heterogeneity, the publication bias was not analyzed in the remaining clinicopathologic co-variate groups.

## 4. Discussion

Nowadays, CRC constitutes a major part of human cancers and still remains an important health challenge worldwide, especially in China.[1] Typically, due to lacking specific symptoms in the early stage of CRC, most patients are diagnosed in an advanced stage, which is responsible for an undesirable five-year survival rate.[23] Thus, it is urgent to identify more precise and specific biomarkers for improving diagnosis and evaluating prognosis.

Accumulating evidence demonstrated that the initiation and progression of malignant tumors was a multi-step process involving in aberrant expression of lncRNAs of multiple
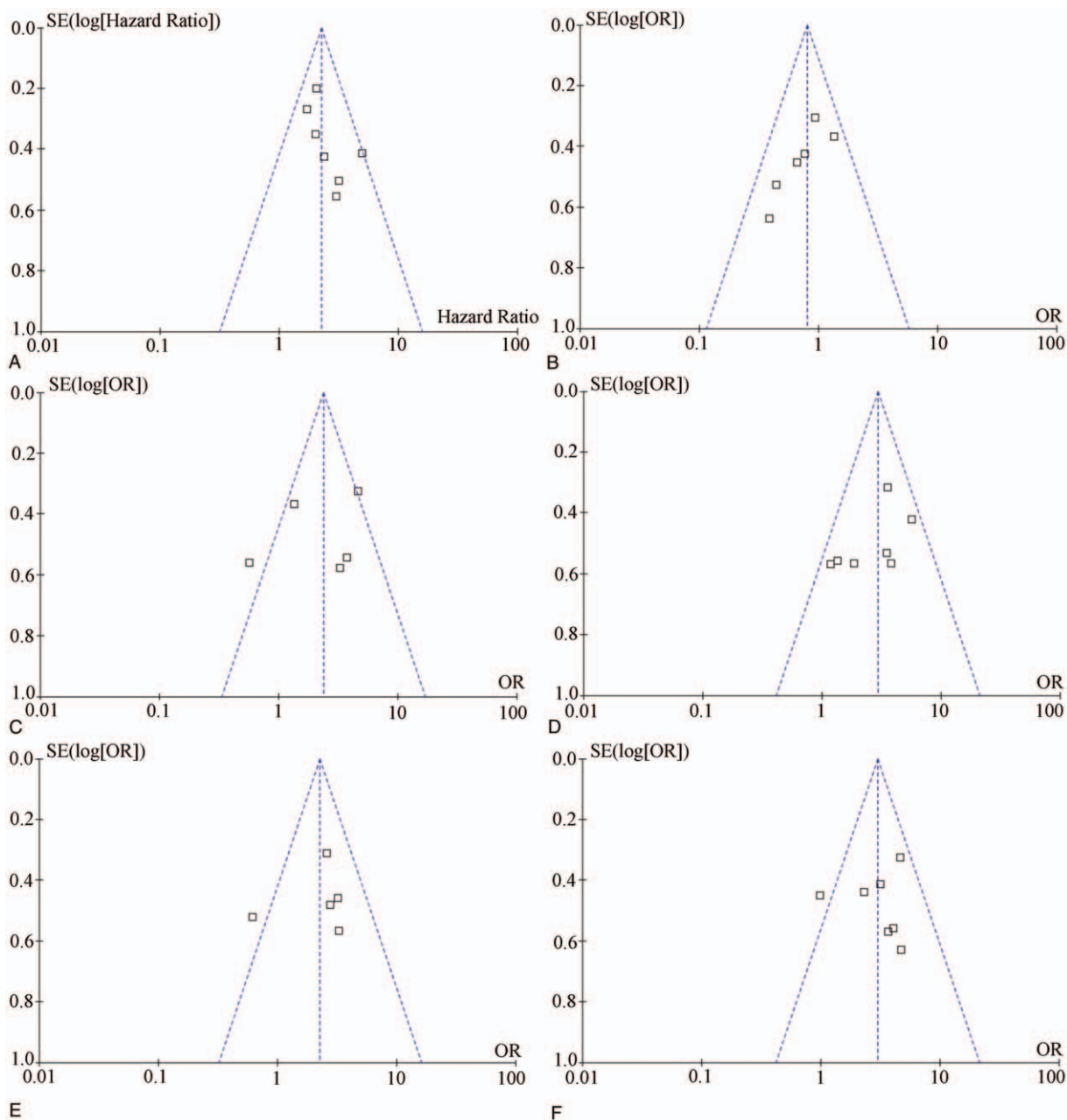
**Figure 5.** Funnel plot analysis of potential publication bias in groups with (A) overall survival (OS), (B) gender, (C) depth of tumor, (D) tumor differentiation, (E) TNM stage, and (F) tumor size.

oncogenes and anti-oncogenes.[24,6] As one of oncogenic lncRNAs, UCA1 was showed extensive regulatory functions in diverse biological processes including cell proliferation, apoptosis, invasion, and cell cycle progression in various types of cancer.[25,26] In addition, UCA1 can also act as a competing endogenous RNA (ceRNA) by sponging to miR-204-5p and regulate the expression of miR-204-5p target genes, such as CREB1 and ZEB1, which is associated with migration and

| Table 3 | | | | | | |
|---|---|---|---|---|---|---|
| **The results of Egger's test (bias) in various groups.** | | | | | | |
| | **Groups** | | | | | |
| **Egger's test (bias)** | **OS** | **Gender** | **Depth of tumor** | **Tumor size** | **TNM stage** | **Tumor differentiation** |
| t value | 2.40 | 2.83 | 0.31 | 1.71 | 2.12 | 2.34 |
| p value | 0.097 | 0.053 | 0.775 | 0.186 | 0.087 | 0.066 |

OS = overall survival, TNM = tumor node metastasis.

invasion.[27] Recently, a growing number of studies have uncovered that UCA1 expression was markedly upregulated in CRC tissues compared to adjacent normal tissues.[25,28] Furthermore, upregulated UCA1 has been found to play important roles in CRC occurrence and progression via exerting oncogenic function.[29,30] Meanwhile, it was also reported that a high level of UCA1 expression was closely correlated with a larger tumor size, poorer differentiated histology, and greater tumor depth.[14,18,21] More importantly, patients with high UCA1 expression had a poorer prognosis compared to patients with low UCA1 expression.[14,15,18,20–22]

The above-mentioned results suggested that UCA1 played a crucial regulatory role in the biological process of carcinogenesis and might serve as a potential target for treatment of CRC. However, the sample sizes in most studies were relatively small. Even, it was distinctive about the association between UCA1 overexpression and progression of CRC, such as invasion and metastasis. With the intent to identify the clinical value of UCA1 expression, a comprehensive meta-analysis was performed to investigate the relationship between UCA1 expression and clinicopathologic characteristics and assess prognosis role of UCA1 for CRC patients.

To our knowledge, this is the first meta-analysis to explore the clinical significance and prognostic value of UCA1 overexpression in CRC. Here, this meta-analysis on 7 eligible studies with a total of 775 patients was evaluated to provide evidences that UCA1 overexpression could predict advanced clinicopathological features and serve as an unfavorably risk factor for survival of patients with CRC. In these findings, the elevated UCA1 expression was negatively correlated with poor OS in patients with CRC. Meanwhile, subgroup analysis was performed and the pooled results would not be altered by other factors, such as sample size, analysis type, and cut-off value. In addition, the association between UCA1 expression and clinicopathological features was evaluated in patients with CRC. Totally, the results verified that high UCA1 expression was associated with worse histopathological grade, deeper tumor invasion, and more advanced TNM stage. Furthermore, the patients with UCA1 overexpression may have a higher risk of developing lymph node metastasis and distant metastasis. Besides, the sensitivity analysis also indicated the stability of this results.

Otherwise, it should be emphasized that several limitations existed in the current meta-analysis. First, all available studies were performed in Chinese population rather than worldwide population, suggesting that the clinical role of UCA1 should be taken cautiously in other regions and ethnicities. Second, the data of HR and 95% CIs estimated from Kaplan–Meier survival curves might be less accurate than that obtained directly from published statistical data, which might increase the potential bias. Third, the limited databases were used for retrieval and the included studies were of relatively small numbers as well as an inconsistent cut-off value of UCA1 expression, which might result in some heterogeneity. In addition, the power of the study was not defined and the statistical analysis measuring that the sample size is adequate enough to make any conclusions was not performed in our present study. Based on these limitations, the predictive significance of assessed UCA1 in these unfavorably clinicopathological covariates and poor prognosis of CRC patients might be overestimated to some extent.

Taken together, the present study revealed that UCA1 overexpression not only might predict a poor prognosis in CRC but also was associated with advanced tumor stage and high

risks of metastasis, especially in Chinese population. In another word, UCA1 may serve as a promising biomarker to predict prognosis and progression of CRC. Considering the limitations existing in the present study, more large-scale and better designed studies should be required to conduct for further updating the findings of this analysis.

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## Author contributions

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