Thyroid cancer (TC) originates from thyroid epithelial cells and is one of the common malignant tumors in the endocrine system (1). It has the characteristics of slow growth and low malignancy (2). It has no obvious symptoms when rising early; in the middle and late stages, it can be manifested as hard masses, dysphagia, vocal cord compression, and neck intercourse (3). Symptoms such as compression of nerve nodules seriously dampen patients’ quality of life. Epidemiological surveys show that TC accounts for 1.3% of the world’s cancer incidence and 0.5% of cancer mortality. TC incidence in China has also been on the rise (4). The number of new cases of TC accounts for 15.6% of the total number of TCs in the world, and the number of deaths accounts for 13.8% of the world’s total (5, 6). A large number of clinical research data show that TC is a malignant tumor with a low degree of malignancy and relatively slow development, and the patient has a long survival period and a good prognosis (7). However, it is worth noting that TC has the characteristics of easy recurrence after surgery, which seriously affects the prognosis of patients (8). Therefore, effective risk stratification of TC patients after surgery, so as to timely intervene in patients with high-risk prognosis, can effectively reduce tumor metastasis and recurrence. The probability of improving the prognosis can also effectively save medical resources (9). The current clinical predictive identification of recurrence/metastasis of TC after surgery mainly depends on the detection of relevant serum tumor markers (10, 11). It is vulnerable to the patient’s age, gender, endocrine status, intraoperative tumor tissue invasion, and whether to receive radionucleus after surgery. Interference of multiple factors such as thyroid therapy, and related markers are not satisfactory for early judgment of recurrence/metastasis of TC after surgery and for risk stratification (12, 13).

In recent years, the relationship between microRNA (miRNA) and TC has gradually attracted the attention of academic circles. miRNA is a type of small (19-25 nucleotides) non-coding single-stranded RNA with a variety of biological functions (14). As a potential oncogene and tumor suppressor gene, it inhibits the expression of target genes through a post-transcriptional regulatory mechanism and involves tumor development (15, 16). Compared with unaffected thyroid tissue, a variety of miRNAs have been shown to be transcriptionally dysregulated in TC (17-19). Among them, miR-105-3p is a highly conserved miRNA, indicating that it has a variety of potential biological effects (20). miR-105-3p is closely related to tumor onset and development, including ovarian cancer, prostate cancer, colon cancer and hepatocellular carcinoma (21-24). In addition, miR-105-3p can be used as an oncogene to affect various biological behaviors of tumor growth (25). However, to date, little is known about the expression pattern and biological functions of miR-105-3p in TC. This study aimed to investigate the dynamic changes of serum miR-105-3p expression after TC surgery and its correlation with clinicopathological manifestations and to evaluate its clinical value as a potential biomarker.
Materials and Methods

General information
This study collected 100 TC patients in our hospital from January 2017 to January 2019, all of whom underwent radical resection of TC and were treated with thyroid-stimulating hormone inhibitory drugs after surgery. Collect patient general information (age, gender), pathological type (papillary carcinoma, follicular carcinoma, and medullary carcinoma), tumor differentiation degree (well-differentiated, moderately differentiated, and poorly differentiated), TNM staging, and lymph node metastasis. This study complies with the Declaration of Helsinki and the relevant laws and regulations of China's clinical trial research. All subjects signed an informed consent form or authorized family members to sign before being selected. The research was approved by the hospital ethics committee and complied with the quality management standard requirements of clinical trial research.

Inclusion and exclusion criteria
Inclusion criteria: (1) TC diagnostic criteria based on the 2015 NCCN diagnostic guidelines for TC; (2) age 20-70 years; (3) confirmed by pathological examination; (4) patient has no history of radiotherapy or chemotherapy and endocrine disease. Exclusion criteria: (1) patients with other thyroid surgery; (2) patients with other malignant tumors; (3) patients with immune function diseases; (4) pathological data missing.

Serum miR-105-3p detection
5 mL of fasting peripheral venous blood was collected from all patients 1d before operation and 1d, 2d, 4d, 8d, and 14d after operation, centrifuged at 3000r/min for 10min, and collected serum. Use the Trizol kit to extract serum total RNA, determine RNA purity and concentration, and refer to the reverse transcription kit instruction manual to reverse transcription of RNA into cDNA. ABI7500 fluorescence quantitative PCR instrument was used to determine serum miR-105-3p content.

Follow-up study
After the patient was discharged from the hospital, follow-up was conducted every 6 months, and serum was collected to detect the level of miR-105-3p. All patients were followed up for 2 years after surgery. Recurrence or metastasis was regarded as a poor prognosis, otherwise, the prognosis was good.

Statistical analysis
All data were statistically analyzed using SPSS 22.0 software, and the data were expressed as mean ± standard deviation and a one-way analysis of variance was performed. GraphPad 8.0 software was used for drawing. p<0.05 is considered statistically different.

Results

General information
Among all 100 TC patients, 29 were males and 71 were females; aged 20-70 years, with an average (51.92±12.62) years old; pathological types: 38 cases of papillary carcinoma, 33 cases of follicular carcinoma, 29 cases of medullary carcinoma; differentiated degree: 43 cases of high differentiation, 28 cases of moderate differentiation, 29 cases of poor differentiation; TNM staging: 28 cases of stage I, 42 cases of stage II, 30 cases of stage III; lymph node metastasis: 58 cases of lymph node metastasis, 42 cases of no lymph node metastasis (Table 1).

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Table 1. General information on patients with thyroid cancer.
TC patients of different genders, ages, pathological types and TNM stages (Figure 1A-C and Figure 1E); the serum miR-105-3p level of well-differentiated patients was significantly higher than that of moderately differentiated and poorly differentiated patients (Figure 1D); the serum miR-105-3p level of patients with lymph node metastasis was significantly higher than that of non-metastatic patients (Figure 1D and Figure 1F).

Changes in serum miR-105-3p levels after TC surgery
To study changes in miR-105-3p levels after TC surgery, we detected serum miR-105-3p levels of all patients on the 1d, 2d, 4d, 8d, and 14d post-operatively. The results showed that compared with preoperatively, serum miR-105-3p levels in TC patients showed a decreasing trend after surgery; and with the passage of time after surgery, serum miR-105-3p levels gradually decreased; 4 days after surgery, the patient's serum miR-105-3p level was significantly different from that before surgery (Figure 2).

The relationship between serum miR-105-3p level and prognosis after TC
In order to further explore the relationship between the changes in serum miR-105-3p levels after TC surgery and the patient’s prognosis, we conducted a 2-year follow-up of all patients and collected patients’ serum for miR-105-3p levels every 6 months, 4 times in total. The results showed that 47 patients had recurrence or metastasis 2 years after surgery, which was a poor prognosis; 53 patients had a good prognosis. Comparing the changes in serum miR-105-3p levels of postoperative patients, it was found that from 8 days after TC surgery, serum miR-105-3p levels can significantly distinguish between patients with poor prognosis and patients with good prognosis (Figure 3A), and during the 2-year follow-up period, the serum miR-105-3p level of patients with poor prognosis was significantly higher than that of patients with good prognosis (Figure 3B).

Discussion
TC is currently one of the fastest-growing malignant tumors, and its specific pathogenesis is not clear (26, 27). It can be related to many factors such as diet, genetic inheritance, ionizing radiation and chemical substances (28). Current studies believe that the occurrence of TC is related to environmental factors and genetic factors, involving the inactivation of tumor suppressor genes and the excessive
activation of oncogenes, and multiple signal transduction pathways cause excessive proliferation and apoptosis of tumor cells, thereby promoting tumor development, and the signal transduction pathways in tumor cells are regulated by multiple factors (29). With the gradual development of diagnosis and treatment methods, studies have found that the prognosis of TC is relatively good, but its postoperative evaluation of the prognosis still lacks specific non-invasive detection markers (19, 30). Therefore, this study explored the dynamic changes of serum miR-105-3p expression after TC surgery and its correlation with clinical manifestations and evaluated its clinical value as a potential biomarker after TC surgery.

miRNA is an important molecule that regulates gene expression discovered in recent years (31). Its properties are relatively stable in tumors and the expression of miRNA in different tumor cells or tumor tissues may be different, but they are the same in the same individual. In different tumors, miRNA plays the role of promoting or suppressing cancer, which mainly depends on the downstream transcription RNA, and the relationship between miRNA and its target gene in the body is regulated by various factors (32). The diagnostic value of miRNA in TC has been confirmed (33). It can not only distinguish malignant tissues from normal tissues but also has differential expression in different stages of TC. Assessing serum miRNA levels is a practical method for follow-up patients after non-invasive thyroidectomy (34). Our study found that serum miR-105-3p levels were significantly increased in patients with well-differentiated TC and lymph node metastasis, suggesting that serum miR-105-3p levels are closely related to the degree of differentiation of TC patients and lymph node metastasis. Within 14 days after the operation, the serum miR-105-3p level gradually decreased over time, suggesting that the reduction of serum miR-105-3p level can predict the improvement of the prognosis of TC after surgery.

Postoperative recurrence or metastasis not only increases the treatment difficulty and causes the body to be injured twice, but it is also the main reason for the decrease in the survival rate of patients (35-41). Early prediction of the risk of postoperative recurrence or metastasis of TC helps clinicians formulate effective preventive measures, thereby significantly improving the prognosis of patients and improving the quality of life after surgery (42). Our study found that serum miR-105-3p levels can significantly distinguish patients with poor prognosis and good prognosis 4 days after TC surgery, and the diagnostic value of serum miR-105-3p levels gradually increases with the passage of time after surgery, suggesting that serum miR-105-3p level has a good diagnostic value for the prognosis of TC after surgery and has potential for the diagnosis of TC after surgery.

Conclusion
The level of serum miR-105-3p is closely related to tumor differentiation and lymph node metastasis in TC patients, and its level gradually decreases with the passage of time after surgery. It has a good diagnostic value for the prognosis of TC after surgery and is expected to become a TC surgery. Potential biomarkers for post-diagnosis.

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Competing interests
All authors declare that there is no conflict of interest.

Ethics approval and consent to participate
For human study, written informed consent and approval documents from the Ethics Committee of Shaanxi Provincial People’s Hospital were obtained. Written informed consent was obtained from all patients.

Availability of data and materials
The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

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