

EFFECT OF RADIX *SOPHORAE FLAVESCENTIS* EXTRACT ON TREATMENT AND PROGNOSIS OF PATIENTS WITH WILMS TUMOR

WEIXIA MENG¹, MINGJUN ZHENG¹, LING LI^{2*}

¹Department of Pediatrics, China Resources and Wisco General Hospital, 430080 Wuhan, Hubei, China

²Department of Pathology, China Resources and Wisco General Hospital, 430080 Wuhan, Hubei, China

*corresponding author: 15926270264@163.com

Manuscript received: June 2026

Abstract

The study investigated the effects of matrine on Wilms tumour (WT) cells and evaluated the clinical outcomes of matrine injection combined with preoperative transcatheter arterial chemoembolisation (TACE) in children with WT. Primary WT cells were treated with matrine (0 - 1.5 mg/mL), and cell proliferation and apoptosis were assessed using MTT assays and flow cytometry. Additionally, 65 children with WT received either TACE alone (n = 33) or TACE combined with matrine injection (n = 32). Clinical outcomes, serum tumour markers, tumour-free survival (TFS) and adverse reactions were evaluated. Matrine inhibited WT cell proliferation and increased apoptosis in a concentration-dependent manner ($p < 0.05$). Compared with TACE alone, combined treatment was associated with shorter hospitalisation, faster renal function recovery, higher complete tumour resection rates, and reduced serum tumour marker levels ($p < 0.05$). TFS rates were 87.9% and 93.8% in the TACE and combination groups, respectively, while adverse reactions were less frequent with combined treatment. These findings suggest that matrine may enhance the therapeutic outcomes of TACE in children with WT.

Rezumat

Studiul a investigat efectele matrinei asupra celulelor tumorii Wilms (WT) și a evaluat rezultatele clinice ale administrării injectabile a matrinei în asociere cu chemoembolizarea arterială transcater (TACE) preoperatorie la copiii diagnosticați cu WT. Celulele WT primare au fost tratate cu matrină (0 - 1,5 mg/mL), iar proliferarea celulară și apoptoza au fost evaluate prin testul MTT și citometrie în flux. În plus, 65 de copii cu WT au beneficiat fie de TACE în monoterapie (n = 33), fie de TACE asociată cu administrarea injectabilă a matrinei (n = 32). Au fost evaluate rezultatele clinice, markerii tumorali serici, supraviețuirea fără tumoare (TFS) și reacțiile adverse. Matrina a inhibat proliferarea celulelor WT și a stimulat apoptoza într-o manieră dependentă de concentrație ($p < 0,05$). Comparativ cu TACE în monoterapie, tratamentul combinat a fost asociat cu reducerea duratei spitalizării, recuperarea mai rapidă a funcției renale, creșterea ratei de rezecție tumorală completă și scăderea nivelurilor markerilor tumorali serici ($p < 0,05$). Ratele TFS au fost de 87,9% și 93,8% în grupurile TACE și, respectiv, TACE asociată cu matrină, în timp ce reacțiile adverse au fost mai puțin frecvente în grupul cu tratament combinat. Aceste rezultate sugerează că matrina ar putea îmbunătăți rezultatele terapeutice ale TACE la copiii cu WT.

Keywords: matrine, Wilms tumor, transcatheter arterial chemoembolization, tumor markers, tumor-free survival

Introduction

Wilms tumor (WT) is a common malignant solid tumor in children, accounting for more than 80% of pediatric urinary system tumors (1). Currently, surgery, radiotherapy, and chemotherapy are the main methods for WT. Preoperative chemotherapy and systemic chemotherapy combined with surgical treatment can effectively shrink the tumor and create conditions for surgery. Preoperative chemotherapy includes systemic intravenous chemotherapy, Transcatheter Arterial Chemoembolization (TACE), and intratumoral injection (2-4). However, chemoradiotherapy can induce serious complications, and children need to face serious adverse reactions (AR) such as bone marrow suppression (BMS).

Radix Sophorae Flavescens is the dried root of the legume *Sophora flavescens* Ait. (*Fabaceae*), which has the functions of clearing heat and drying dampness, killing insects, and diuresis. Modern pharmacological studies have confirmed that *Radix Sophorae Flavescens* contains a variety of chemical components such as alkaloids, flavonoids, saponins, and volatile oils (5). Matrine alkaloids can be divided into different types of alkaloids, such as matrine, genistein, and amygdalin. Matrine is an extract of the active ingredients of Chinese herbal medicine, such as the root of broad bean, and its chemical molecular formula is $C_{15}H_{24}N_{20}$ (6). Matrine belongs to the quinazoline alkaloid group. Matrine and oxymatrine have the strongest anti-tumor activity and are the main anti-tumor active ingredients in traditional Chinese medicine (TCM) (7). Matrine can reduce the

percentage of cells in S phase and G2/M phase, increase the percentage of cells in G0/G1 phase, block cells from entering S phase, and thus inhibit the proliferation of tumor cells (TCs) (8). Matrine can also reduce the activity of lactate dehydrogenase in TCs, thereby blocking the anaerobic glycolysis of TCs and blocking tumor progression (9). Other studies have confirmed that matrine can inhibit the expression of Vascular Endothelial Growth Factor (VEGF) and fibroblast growth factor, the proliferation of endothelial cells, and the formation of blood vessels, thereby inhibiting the growth of tumors (10). Zhou *et al.* (11) confirmed that matrine could inhibit invasion of osteosarcoma cells through the STAT3 pathway. Matrine has a direct killing effect on TCs and can also induce apoptosis of tumors. Moreover, matrine almost does not affect the life process of normal cells and can even increase the number of white blood cells (WBCs) in the blood and promote the improvement of the body's immune function (12, 13). Various degrees of matrine were used to treat WT cells, and the effects on cells were analyzed. This study aimed to explore the outcome of matrine injection on TACE treatment and prognosis of WT in children, providing a reference for improving the outcome and prognosis of WT in children.

Materials and Methods

Cell culture and grouping

Five fresh tumor specimens from patients with WT who underwent surgical resection were selected for primary culture of WT cells. This research was approved by the Ethics Committee of China Resources and Wisco General Hospital, and the research subjects were informed and signed the consent form. To confirm cell identity, the morphological characteristics were first examined under an inverted phase-contrast microscope (Olympus IX73, Olympus Corporation, Tokyo, Japan), revealing a polygonal or spindle-shaped appearance consistent with WT cells. Subsequently, flow cytometry (FACSCanto II, BD Biosciences, San Jose, CA, USA) was performed to assess the expression of WT1 (ab89901, Abcam, Cambridge, MA, USA) and Vimentin (#5741, Cell Signaling Technology, Danvers, MA, USA), with positivity rates of 92.6% and 89.3%, respectively, confirming their identity as WT cells. Cell viability, determined using a Muse Cell Analyzer (0500-3115B, Merck-Millipore, Billerica, MA, USA), consistently exceeded 95%. The cells were seeded in RPMI-1640 medium (#11875-093, Gibco, Grand Island, NY, USA) supplemented with 10% fetal bovine serum (#10099-141, Thermo Fisher Scientific, Waltham, MA, USA) and 1% penicillin-streptomycin (Abbott Laboratories, IL, Switzerland). Subsequently, they were cultured at 37°C in a 100% humidified CO₂ incubator (Thermo Fisher Scientific,

USA) with 5% CO₂. The fresh medium was replaced every 3 days. The cells were subjected to short tandem repeat (STR) analysis and Mycoplasma testing. When the cell convergence reached about 90%, subculture was carried out. Matrine powder (purity ≥ 98%, Zhongxin Technology Biotechnology Co., Ltd., Shanghai, China) was dissolved in RPMI-1640 medium to make final concentration solutions of 0.5, 1.0, and 1.5 mg/mL. The primary WT cells in log phase were divided into: (1) Ctrl, complete culture medium was used for cell culture, (2) 0.5 mg/mL matrine included in complete culture medium, (3) 1.0 mg/mL matrine, and (4) 1.5 mg/mL matrine. Cells in each group were set up in 5 compound wells. *MTT assay to detect the cell proliferation inhibition rate*

The primary cultured WT cells in the log phase were seeded in 96-well plates at 1×10^4 cells *per well*. The 24 hrs later, it was replaced by a drug culture medium for culturing for 24, 48, 72 and 96 hrs. Each well was supplemented with 20 µL of methyl thiazolyl tetrazolium assay (MTT) reagent (Sigma-Aldrich, Louis, MO, USA) (5 mg/mL) and then incubated for 4 hrs. After the original supernatant was discarded, 150 µL Dimethyl Sulfoxide (DMSO) reagent (Sigma-Aldrich, USA) was added and mixed for 15 min by shaking. The absorbance of each well was measured at a wavelength of 492 nm using a Multiskan FC microplate reader (Thermo Fisher Scientific, USA).

Apoptotic rate

The primary cultured WT cells were cultured under the above conditions. After 24 hrs, it was replaced by a drug culture medium for culturing for another 24 hrs. The cells were washed twice with 4 °C pre-cooled phosphate-buffered saline (Thermo Fisher Scientific, USA), then centrifuged at 1000 r/min for 10 min, and the supernatant was removed. They were resuspended in 200 µL of 1× binding buffer and 10 µL of Annexin V-FITC reagent (BD Biosciences, Franklin Lakes, NJ, USA) was added, incubated at room temperature in the dark for 15 min. Subsequently, 300 µL of binding buffer (Santa Cruz Biotechnology, Santa Cruz, CA, USA) and 5 µL of propidium iodide (PI) reagent (Invitrogen, Carlsbad, CA, USA) were mixed, and the apoptosis rate of cells was detected using a flow cytometer (Attune NxT, Thermo Fisher Scientific, USA).

Patients and grouping

A total of 65 children with WT treated in the hospital from January 2023 to December 2025 were enrolled. All the children received TCAE chemotherapy before operation and were divided into TACE and TACE + Matrine groups based on the postoperative treatment methods. There were 33 children in the TACE group, including 21 males and 12 females. The median age was 2.6 years (range, 1 - 12). There were 32 patients in the TACE + Matrine group,

including 19 males and 13 females. The median age was 2.3 (1 - 11). The family members of the children were aware of the content of the trial and signed informed consent. This research was approved by the Ethics Committee of China Resources and Wisco General Hospital, and the family members of the children were informed and signed the consent form. Inclusion Criteria: (1) After admission, B-ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI) suggested giant WT and the tumor invaded nearby organs, accompanied by para-aortic lymph node metastasis or ascites, (2) Formation of inferior vena cava tumor thrombus, (3) Distant metastasis such as lung and liver, and (4) Bilateral WT with a maximum diameter of more than 10 cm.

Exclusion Criteria: (1) Poor treatment compliance, (2) Patients who received tumor nephrectomy immediately after admission, and (3) Incomplete follow-up data.

Treatment methods

The children in the TACE group were treated with renal artery TACE before operation, and after general anesthesia, the Seldinger technique (14) was used to percutaneously puncture the femoral artery from the groin and insert a 5F catheter sheath (Abbott Laboratories, IL, Switzerland). The blood supply of the renal artery on the affected side was observed through the catheter, and then chemoembolization was performed. For chemoembolization, 80 mg/m² cisplatin (Teva Pharmaceutical Industries, Petah Tikva, Israel), 40 mg/m² pirarubicin (Sun Pharmaceutical Industries, Mumbai, Maharashtra, India), 3 mg/m² vindesine (Bristol-Myers Squibb, New York, NY, USA) and 5 mL lipiodol (Mylan N.V., Canonsburg, PA, USA) were administered. Adjuvant drugs such as diuretics and antiemetic drugs were applied to prevent and treat AR caused by chemotherapy drugs. Systemic chemotherapy was not used after one-time TACE, but systemic chemotherapy was needed when distant metastasis or peritoneal spread occurred. Retroperitoneal nephrectomy was performed for 2 to 4 weeks following TACE.

The TACE + Matrine group received matrine injection (10 mL in 250 mL normal saline) in addition to TACE, once a day, for 21 days as a cycle, and 2 cycles were carried out.

Observation indicators

The length of intensive care unit (ICU) stay, length of hospital stay, and renal function recovery time were recorded. Normal renal function was defined as a serum creatinine level recovered to 24.9 - 69.7 μmol/L. Based on imaging examination, the tumor volume was measured, the necrotic area of the maximum enhanced tumor slice was calculated, and the tumor reduction rate, capsule integrity, and complete tumor resection rate were observed. Fasting venous blood (3 mL) was collected, and the serum levels of Carcinoembryonic Antigen (CEA), Carbohydrate Antigen (CA125), CA19-9, Cytokeratin 19 fragment

(CYFRA21-1), β2-Microglobulin (β2-MG), and Squamous Cell Carcinoma Antigen (SCC-Ag) were detected by electrochemiluminescence immunoassay. The AR of the children during treatment was recorded. The patients were followed mainly by imaging examination. The survival time and survival outcome of the patients following the treatment were recorded.

Statistical analysis

SPSS 26.0 (IBM Corp., Armonk, NY, USA) was employed for information processing. The count data were expressed as rates. The χ^2 test was adopted. Measurement data were presented as means $\pm$ SD, and a *t*-test was adopted. A *p*-value < 0.05 was considered statistically significant.

Results and Discussion

Effect of matrine on the proliferation of human WT cells

The effect of different concentrations of matrine on the proliferation inhibition rate of human renal cell carcinoma cells was evaluated using the MTT assay (Figure 1). The results indicated that the proliferation inhibition rates of human renal cell carcinoma cells treated with 0.5, 1.0, and 1.5 mg/mL matrine were higher than those of the Ctrl group (*P* < 0.05). Furthermore, the proliferation inhibition rates of cells treated with 0.5, 1.0, and 1.5 mg/mL matrine showed a gradual increase (*P* < 0.05).

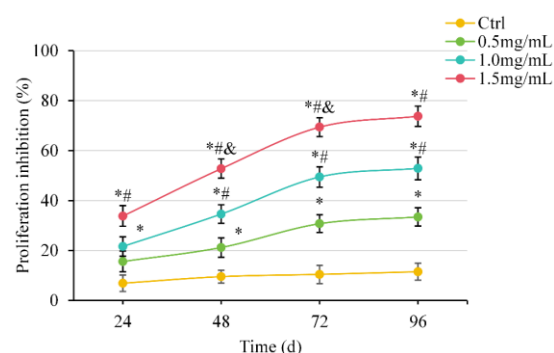
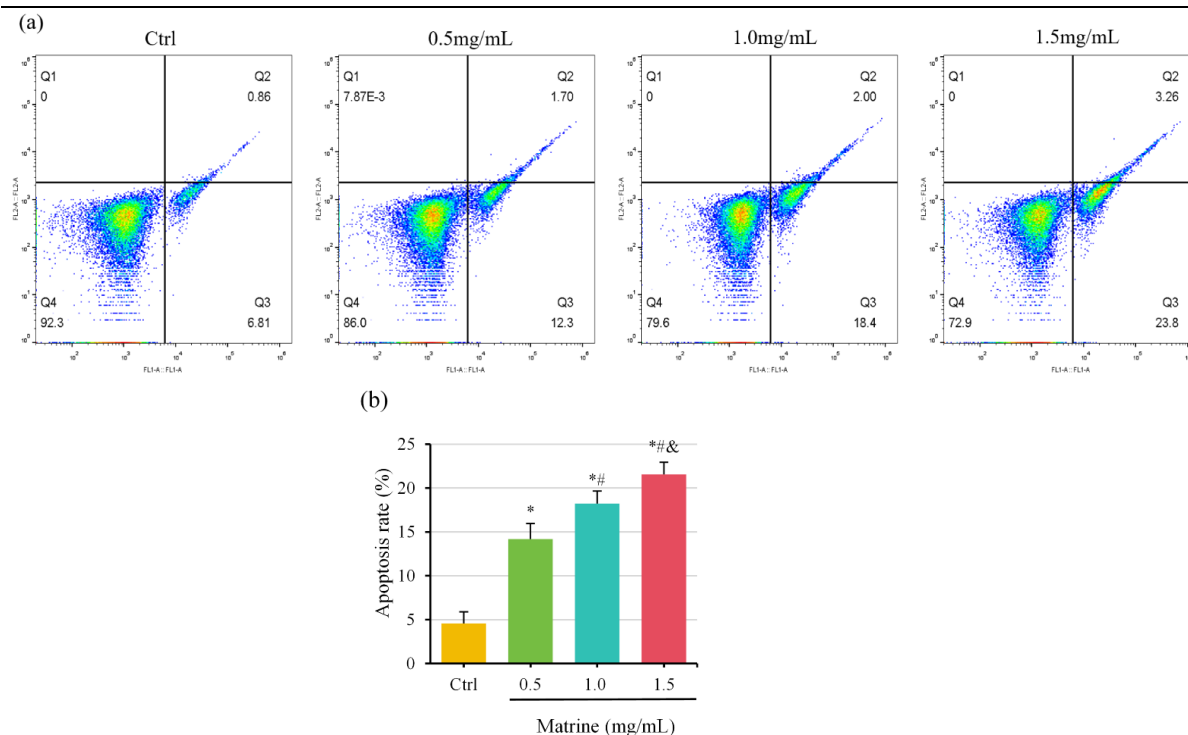


Figure 1.

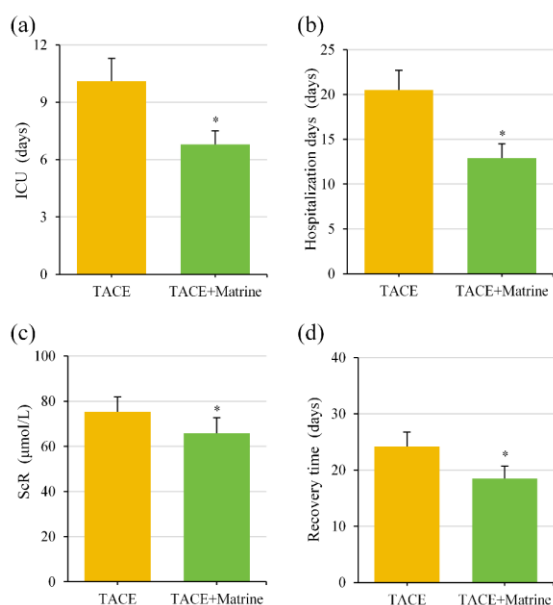
Effect of various degrees on the suppression rate of human Wilms tumor (WT) cells. **P* < 0.05 compared to Ctrl, #*P* < 0.05 compared to dose at 0.5, &*P* < 0.05 compared to dose at 1.0

Effect on apoptosis of human WT

The effect of different concentrations of matrine on the apoptosis rate of human renal cell carcinoma cells was assessed using flow cytometry (Figure 2a, b). The results revealed that the apoptosis rates of human renal cell carcinoma cells treated with 0.5, 1.0, and 1.5 mg/mL matrine were significantly higher than those of the Ctrl group (*P* < 0.05). Additionally, the apoptosis rates of cells treated with 0.5, 1.0, and 1.5 mg/mL matrine exhibited a gradual increase (*P* < 0.05).

**Figure 2.**

Impact of various degrees on the apoptotic rate of human WT. (a) Flow cytometry and (b) Apoptotic rate. * $P < 0.05$ compared to Ctrl, # $P < 0.05$ compared to does at 0.5, & $P < 0.05$ compared to does at 1.0

**Figure 3.**

Influence on recovery outcomes in children with WT. (a) Length of intensive care unit (ICU) stay, (b) Total length of stay, (c) Serum creatinine level, and (d) Time to recovery of renal function. Compared with the Transcatheter Arterial Chemoembolization (TACE) method, * $P < 0.05$ compared to TACE

Influence on the therapeutic outcome in children with WT

The study evaluated the efficacy of TACE combined with matrine injection in the treatment of pediatric

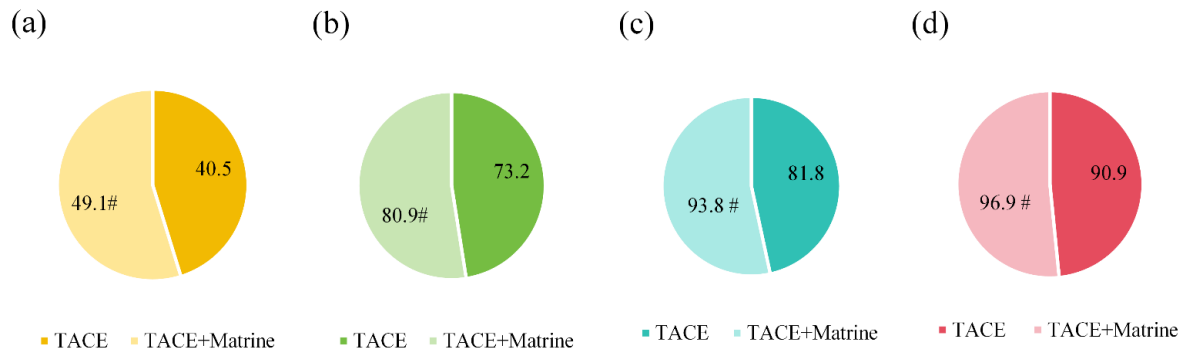
renal cell carcinoma (Figure 3a–d). The results indicated that compared to the TACE group, the TACE + Matrine group exhibited significantly shorter ICU stay duration, total hospital stay duration, and time for renal function recovery, along with markedly lower levels of serum creatinine ($P < 0.05$).

Impact on tumor shrinkage, tumor necrosis, capsule integrity and total tumor resection rate in children with WT

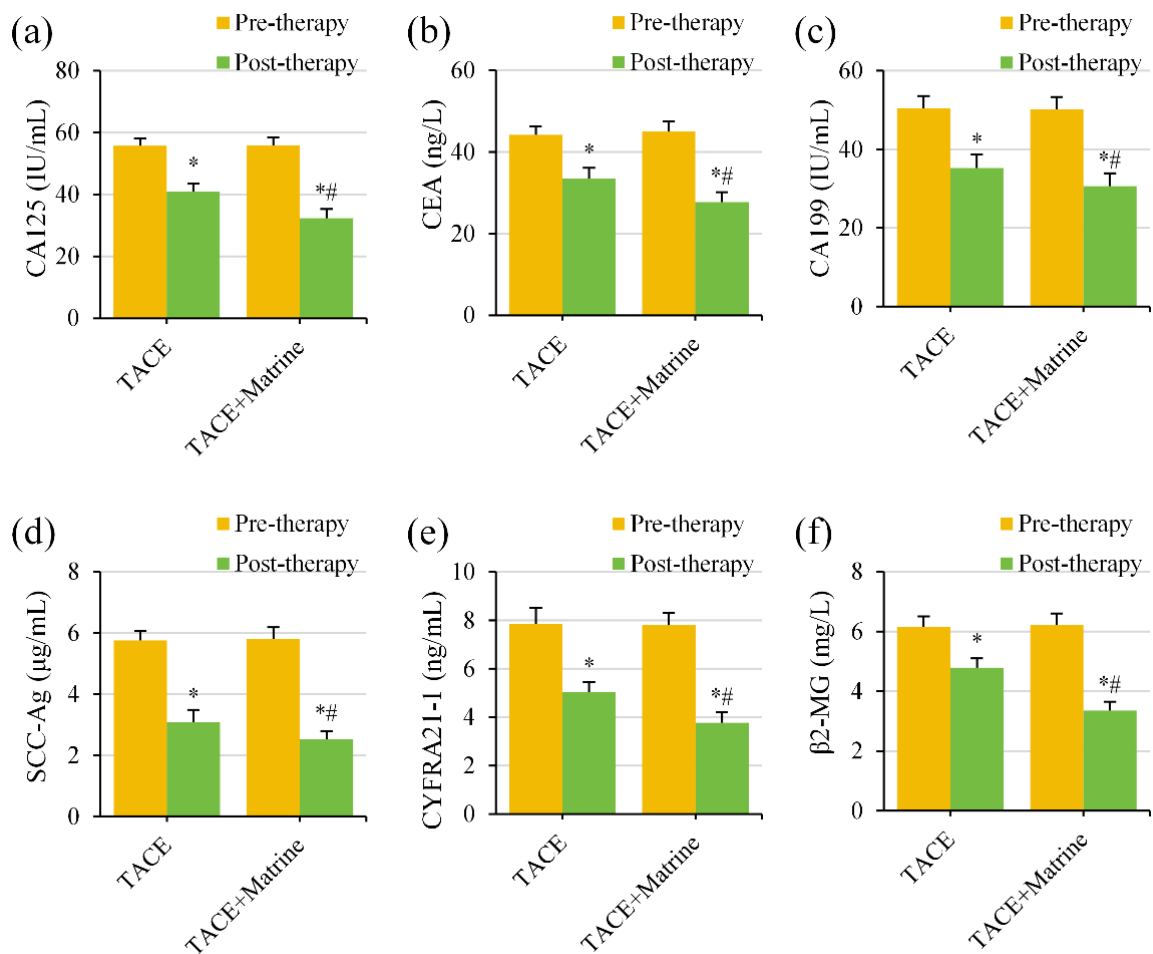
The study employed imaging techniques to evaluate the clinical efficacy of TACE combined with Matrine injection in the treatment of pediatric renal cell carcinoma (Figure 4a–d). The results revealed that compared to the TACE group, the TACE + Matrine group exhibited significantly higher rates of tumor volume reduction, tumor necrosis, intact capsule preservation, and complete tumor resection ($P < 0.05$).

Influence on serum tumor marker levels in children with WT

The levels of serum CA125, CA19-9, CEA, SCC-Ag, CYFRA21-1 and β 2-MG were measured before and after treatment in both the TACE group and the TACE + Matrine group (Figure 5a–f). The results indicated that compared to pre-treatment levels, the post-treatment levels of serum CA125, CA19-9, CEA, SCC-Ag, CYFRA21-1 and β 2-MG were significantly lower in both groups of patients ($P < 0.05$). Furthermore, compared to the TACE group, the post-treatment levels of serum CA125, CA19-9, CEA, SCC-Ag, CYFRA21-1, and β 2-MG were significantly lower in the TACE + Matrine group ($P < 0.05$).

**Figure 4.**

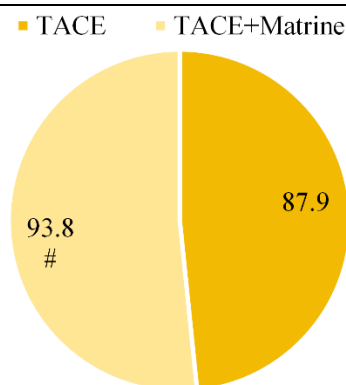
Impact on tumor-related parameters. (a) Tumor shrinkage rate, (b) Tumor necrosis rate, (c) Capsule integrity rate, and (d) Rate of complete tumor resection. # $P < 0.05$ compared to TACE subjects

**Figure 5.**

Differences in serum tumor markers before and following the remedy. (a) Serum Carbohydrate Antigen (CA125), (b) Serum Carcinoembryonic Antigen (CEA), (c) Serum CA19-9, (d) Serum Squamous Cell Carcinoma Antigen (SCC-Ag), (e) Serum Cytokeratin 19 fragment (CYFRA21-1), and (f) β2-Microglobulin (β2-MG). * $P < 0.05$ compared to same group pre-remedy, # $P < 0.05$ compared to TACE subjects

Influence on the survival rate of children with WT
The tumor-free survival (TFS) outcomes of the two groups of patients during the follow-up period were recorded (Figure 6). The TFS rate was 87.9% (29/33) in the TACE group, with 2 cases of tumor recurrence and 2 deaths. In contrast, the TFS rate

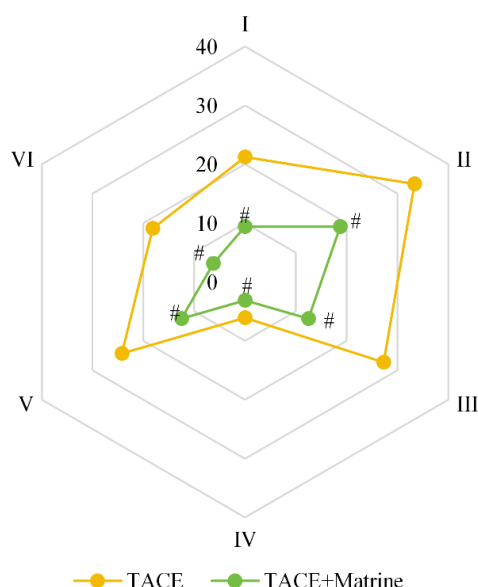
was 93.8% (30/32) in the TACE + Matrine group, with 1 case of tumor recurrence and 1 death. Upon comparison, the TFS rate of patients in the TACE + Matrine group was significantly higher than that of the TACE group ($P < 0.05$).

**Figure 6.**

Analysis of tumor-free survival (TFS) in WT children. [#]P < 0.05 compared to TACE subjects

Comparison of AR rates in children with WT

The occurrence of AR in the two groups of pediatric patients was recorded and compared (Figure 7). In the TACE group, the incidence rates of leukopenia, gastrointestinal reactions, bone marrow suppression, anemia, fever and alopecia were 21.2, 33.3, 27.3, 6.1, 24.2, and 18.2%, respectively. In the TACE + Matrine group, the incidence rates of leukopenia, gastrointestinal reactions, bone marrow suppression, anemia, fever, and alopecia were 9.4, 18.8, 12.5, 3.1, 12.5, and 6.3%, respectively. It can be observed that compared to the TACE group, the incidence rates of AR, including leukopenia, gastrointestinal reactions, bone marrow suppression, anemia, fever, and alopecia, were significantly lower in the TACE + Matrine group ($P < 0.05$).

**Figure 7.**

Incidence of adverse events in WT patients. I, Leukopenia; II, Gastrointestinal reaction; III, BMS; IV, Anemia; V, Fever; VI, Hair loss. [#]P < 0.05 compared to TACE subjects

Wilms tumor, also known as nephroblastoma, is a common malignant tumor in children. Matrine is an effective, low-toxicity, anti-tumor drug with demonstrated efficacy against various types of cancer cells, including leukemia, hepatocellular carcinoma, and lung cancer (15-17). Matrine exhibits anticancer activity by inhibiting tumor cell proliferation, inducing apoptosis and differentiation, and reversing tumor cell drug resistance (18).

Matrine is a bioactive alkaloid extracted from *Radix Sophorae Flavescens*, known for its anticancer properties. Studies noted that oxidative bitter bioactive matrine derived from it can ameliorate liver cell damage and fibrosis, inhibit the production of the inflammatory cytokine IL-1 by inflammatory cells, and suppress the generation of IL-2 by Th cells, thereby attenuating T lymphocyte proliferation (19,20). In this study, it was found that the proliferation inhibition rate and apoptosis rate of human renal cell carcinoma cells significantly increased after matrine treatment compared to the Ctrl group, indicating that matrine can markedly suppress the proliferation of human renal cell carcinoma cells and promote apoptosis. Zhou *et al.* (21) demonstrated that treatment with different concentrations of matrine induced apoptosis in human neuroepithelial tumor D341 cells. Yan *et al.* (22) found that matrine could inhibit the proliferation of human rhabdomyosarcoma cells and promote apoptosis by downregulating the extracellular signal-regulated kinase pathway. Wang *et al.* (23) confirmed that treatment with matrine in HepG2 cells could mediate the reactive oxygen species (ROS)/ c-Jun N-terminal Kinase (JNK)/Tumor Protein p53 (p53) signaling pathway to promote apoptosis. Moreover, with increasing concentrations of matrine, both proliferation inhibition rate and apoptosis rate gradually increased, suggesting a dose-dependent effect of matrine on tumor cells.

For surgical treatment of pediatric WT in stages III–V, where tumors are large or have metastasized, surgery is challenging with a high rate of intraoperative complications (24). Therefore, neoadjuvant chemotherapy is crucial. TACE is a common chemotherapy method for liver tumors. It involves directly injecting chemotherapy drugs and embolic agents into the tumor artery, increasing local drug concentration, targeting tumor cells, enhancing tumor killing, and reducing systemic AR (25-27). Neoadjuvant chemotherapy can rapidly reduce tumor volume and promote the formation of a fibrous capsule around the tumor, creating a protective barrier to prevent rupture during surgery, which is essential for preoperative treatment (28, 29). Matrine has been shown to inhibit cancer cell metastasis and adhesion, confirming its role in tumor suppression (30).

In this study, combined treatment with matrine was found to significantly reduce ICU stay duration, total hospital stay duration, and time for renal function

recovery compared to the TACE group. Additionally, levels of serum creatinine, tumor volume reduction rate, tumor necrosis rate, intact capsule preservation rate, and complete tumor resection rate were significantly lower in the TACE + Matrine group. These findings indicate that the TACE + Matrine regimen facilitates faster recovery during postoperative rehabilitation, effectively reduces tumor burden, and improves the success rate and prognosis of surgical treatment. Zhang *et al.* (31) demonstrated that matrine can reduce the expression of VEGF and vascular endothelial growth factor receptor (VEGFR), thereby inhibiting angiogenesis in breast cancer. The study revealed that compared to the TACE group, children in the TACE + Matrine group exhibited significantly lower incidences of AR, including leukopenia, gastrointestinal reactions, bone marrow suppression, anemia, fever, and alopecia. This suggests that matrine injection markedly alleviates AR in children with nephroblastoma undergoing TACE treatment. Chemotherapy, while effective in targeting tumor cells, also inflicts damage on host tissues, leading to varying degrees of AR that impede patient survival and treatment tolerance (32). Matrine, however, has been shown to enhance patients' immune function post-chemotherapy, augment chemotherapy sensitivity, and mitigate toxic side effects (33). Moreover, due to the high propensity of tumors for metastasis and invasion, coupled with their exceedingly complex and dynamic nature, this study analyzed the impact of matrine on cancer cell migration and invasion. Adhesion and motility are pivotal factors in tumor cell metastasis, wherein cytoskeletal linker proteins play significant roles in tumor invasion and metastasis (34). Sun and Xu (35) demonstrated that treatment with matrine notably downregulated the expression levels of matrix metalloproteinases matrix metalloproteinase-2 (MMP-2) and MMP-9 in NPC-039 cells, suggesting matrine's capability to suppress cancer cell migration and invasion. The current study observed a significantly higher tumor-free survival rate in children in the TACE + Matrine group compared to the TACE group, indicating that TACE combined with matrine injection enhances the therapeutic efficacy against pediatric nephroblastoma and improves tumor-free survival in affected children. Duan *et al.* (36) corroborated that matrine, in combination with Irinotecan, when used against human colon cancer cells, effectively suppressed cell proliferation and induced apoptosis. Additionally, it was found that after treatment in the TACE + Matrine group, serum levels of CA125, CA19-9, CEA, SCC-Ag, CYFRA21-1, and β 2-MG markedly decreased. Among these, CA125 and CA19-9 are primary markers of tumor cells closely associated with the clinical staging and severity of cancer patients (37). The CEA serves as a broad-spectrum tumor marker, while SCC-Ag is found in various

cancers, particularly in epithelial cell carcinomas such as esophageal, lung, and renal carcinomas (38). Research indicated that serum levels of SCC-Ag are significantly elevated in patients with chronic kidney disease compared to healthy individuals, serving as a diagnostic biomarker for kidney-related conditions (39). CYFRA21-1 is expressed at higher levels in cancer patients and is a substance released after degradation of epithelial-origin tumor cells (40). The β 2-MG is primarily generated by platelets and lymphocytes, with increased serum levels of β 2-MG occurring when tumor cells undergo necrosis (41). Studies indicated that serum levels of β 2-MG are significantly higher in patients with early-stage kidney damage compared to healthy individuals, suggesting its utility in the assessment of early-stage kidney dysfunction (42). Consequently, matrine can further reduce serum levels of tumor markers in patients with nephroblastoma after chemotherapy, which is crucial for improving treatment outcomes.

Conclusions

The combination of TACE and matrine injection before operation in children with WT can markedly reduce the level of serum tumor markers, promote tumor shrinkage, and create favorable conditions for surgical resection. Matrine injection can reduce the AR rate, promote postoperative rehabilitation, and improve the TFS rate in children with TACE. The results of this article can provide a reference for the optimization of clinical remedies for WT children.

Acknowledgement

Not applicable.

Funding

Not applicable.

Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article. The other data generated in the present study may be requested from the corresponding author.

Ethics approval and consent to participate

All experimental procedures were approved by the Ethics Committee of China Resources and Wisco General Hospital. Informed consent was obtained from all patients included in the study.

AI use disclosure

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

References

- Shyirambere C, Villaverde C, Nguyen C, Ruhangaza D, Umwizerwa A, Nsanzimana O, et al. Nephroblastoma treatment and outcomes in a low-income setting. *JCO Glob Oncol*. 2022;8:e2200036.
- Lopyan NM, Ehrlich PF. Surgical management of Wilms tumor (nephroblastoma) and renal cell carcinoma in children and young adults. *Surg Oncol Clin N Am*. 2021;30(2):305-323.
- Rădulescu FM, Nedea MI, Dascălu AM, Eugen T, Năstăsescu TI, Vălean D, et al. Antibiotherapy in pediatric oncological patients with positive bacterial infection post-treatment. *Farmacia*. 2025;73(3):686-695.
- Meier CM, Fuchs J, von Schweinitz D, Stein R, Wagenpfeil S, Kager L, et al. Surgical factors influencing local relapse and outcome in the treatment of unilateral nephroblastoma. *Ann Surg*. 2023;278(2):e360-e367.
- Chen MH, Gu YY, Zhang AL, Sze DMY, Mo SL, May BH. Biological effects and mechanisms of matrine and other constituents of *Sophora flavescens* in colorectal cancer. *Pharmacol Res*. 2021;171:105778.
- Moise G, Geamantan-Sîrbu A, Vlad CS, Vlad D, Dumitrescu C, Sima L. Quercetin enhances the anti-tumor activity of doxorubicin in IMR-32 neuroblastoma cells. *Farmacia*. 2024;72(4):785-793.
- Li S, Zhang H, Jiao Y, Song X, Wei L, Liu X. Oxymatrine induces anti-tumor response in cervical cancer by modulating circ_0008460/miR-197-3p/ribonucleotide reductase subunit M2 (RRM2). *Bioengineered*. 2022;13(5):12912-12926.
- Liu J, Guo Y, Cao J. Matrine triggers colon cancer cell apoptosis and G0/G1 cell cycle arrest via mediation of microRNA-22. *Phytother Res*. 2020;34(7):1619-1628.
- Li Q, Xu J, He Z, Wen X, Wang F, Zhang P, et al. The effects of matrine in combination with docetaxel on castration-resistant (androgen-independent) prostate cancer. *Cancer Manag Res*. 2019;11:10125-10133.
- Khan A, Shal B, Naveed M, Nasir B, Irshad N, Ali H, et al. Matrine alleviates neurobehavioral alterations via modulation of JNK-mediated caspase-3 and BDNF/VEGF signaling in a mouse model of burn injury. *Psychopharmacology (Berl)*. 2020;237:2327-2343.
- Zhou H, Chen S, Yang Y, Yang C, Chen D, Yao Z, et al. Matrine enhances the efficacy of adriamycin chemotherapy in osteosarcoma cells by the STAT3 pathway. *Anticancer Drugs*. 2019;30(10):1006-1012.
- Xu PL, Cheng CS, Jiao JY, Chen H, Chen Z, Li P. Matrine injection inhibits pancreatic cancer growth via modulating carbonic anhydrases - a network pharmacology-based study with in vitro validation. *J Ethnopharmacol*. 2022;287:114691.
- Dou M, Chu Y, Zhou X, Wang M, Li X, Ma R, et al. Matrine mediated immune protection in MS by regulating gut microbiota and production of SCFAs. *Mol Neurobiol*. 2024;61(1):74-90.
- Hsu CCT, Kwan GNC, Evans-Barns H, Rophael JA, van Driel ML. Venous cutdown versus the Seldinger technique for placement of totally implantable venous access ports. *Cochrane Database Syst Rev*. 2016;2016(8):CD008942.
- Zhang PP, Zhang F, Zhu K, Zhu JF, Yuan Y, Yang YL, et al. Matrine exerted an anti-tumor effect on acute myeloid leukemia via the lncRNA LINC01116/miR-592-mediated JAK/STAT pathway inactivation. *Neoplasma*. 2022;69:123-135.
- Huang Z, Li H, Li Q, Chen X, Liu R, Chang X. Matrine suppresses liver cancer progression and the Warburg effect by regulating the circROBO1/miR-130a-5p/ROBO1 axis. *J Biochem Mol Toxicol*. 2023;37(10):e23436.
- Luo D, Dai X, Tian H, Fan C, Xie H, Chen N, et al. Sophflarine A, a novel matrine-derived alkaloid from *Sophora flavescens* with therapeutic potential for non-small cell lung cancer through ROS-mediated pyroptosis and autophagy. *Phytomedicine*. 2023;116:154909.
- Chen F, Pan Y, Xu J, Liu B, Song H. Research progress of matrine's anticancer activity and its molecular mechanism. *J Ethnopharmacol*. 2022;286:114914.
- Shi J, Han G, Wang J, Han X, Zhao M, Duan X, et al. Matrine promotes hepatic oval cells differentiation into hepatocytes and alleviates liver injury by suppression of Notch signalling pathway. *Life Sci*. 2020;261:118354.
- Xu Y, Lin H, Zheng W, Ye X, Yu L, Zhuang J, et al. Matrine ameliorates adriamycin-induced nephropathy in rats by enhancing renal function and modulating Th17/Treg balance. *Eur J Pharmacol*. 2016;791:491-501.
- Zhou K, Ji H, Mao T, Bai Z. Effects of matrine on the proliferation and apoptosis of human medulloblastoma cell line D341. *Int J Clin Exp Med*. 2014;7:911-918.
- Yan P, Huang Z, Zhu J. Matrine inhibits cell proliferation and induces apoptosis of human rhabdomyosarcoma cells via downregulation of the extracellular signal-regulated kinase pathway. *Oncol Lett*. 2017;14:3148-3154.
- Wang X, Zhang S, Han K, Wang L, Liu X. Induction of apoptosis by matrine derivative ZS17 in human hepatocellular carcinoma BEL-7402 and HepG2 cells through ROS-JNK-P53 signalling pathway activation. *Int J Mol Sci*. 2022;23(24):15991.
- Higgs EF, Bao R, Hatogai K, Gajewski TF. Wilms tumor reveals DNA repair gene hyperexpression is linked to lack of tumor immune infiltration. *J Immunother Cancer*. 2022;10.
- Qari W, Alzahrani A, Alzahrani M, Saleh Y, Almasabi A, Bawazir O. Bilateral Wilms' tumor with different responses to preoperative chemotherapy. *Cureus*. 2022;14(10):e30593.
- Suceveanu AI, Mazilu L, Katsiki N, Parepa I, Voinea F, Pantea-Stoian A, et al. NLRP3 inflammasome biomarker-could be the new tool for improved cardiometabolic syndrome outcome. *Metabolites*. 2020;10(11):448.
- Li MJ, Zhou YB, Huang Y, Tang DX, Xu S, Wu DH, et al. A retrospective study of the preoperative

- treatment of advanced Wilms tumor in children with chemotherapy versus transcatheter arterial chemoembolization alone or combined with short-term systemic chemotherapy. *J Vasc Interv Radiol*. 2011;22:279-286.
28. Zhao W, Xu J, You Y, Guo Z, Xiang Y, Ha K, et al. Thermoresponsive hydrogel for transcatheter arterial chemoembolization of hepatocellular carcinoma. *Chem Commun (Camb)*. 2023;59:9352-9355.
 29. Chintagumpala MM, Perlman EJ, Tornwall B, Chi YY, Kim Y, Hoffer FA, et al. Outcomes based on histopathologic response to preoperative chemotherapy in children with bilateral Wilms tumor: a prospective study (COG AREN0534). *Cancer*. 2022;128(13):2493-2503.
 30. Rashid HU, Xu Y, Muhammad Y, Wang L, Jiang J. Research advances on anticancer activities of matrine and its derivatives: an updated overview. *Eur J Med Chem*. 2019;161:205-238.
 31. Zhang S, Guo S, Gao XB, Liu A, Jiang W, Chen X, et al. Matrine attenuates high-fat diet-induced in vivo and ox-LDL-induced in vitro vascular injury by regulating the PKC α /eNOS and PI3K/Akt/eNOS pathways. *J Cell Mol Med*. 2019;23:2731-2743.
 32. Thomsen JA, Nielsen Dominiak H, Lindgren MS, Jensen JB. Adverse events of hyperthermic intravesical chemotherapy for non-muscle invasive bladder cancer patients. *Scand J Urol*. 2021;55:281-286.
 33. Koch GE, Smelser WW, Chang SS. Side effects of intravesical BCG and chemotherapy for bladder cancer: what they are and how to manage them. *Urology*. 2021;149:11-20.
 34. Liu J, Ding C, Liu X, Kang Q. Cytoskeletal protein 4.1R in health and diseases. *Biomolecules*. 2024;14(2):214.
 35. Sun B, Xu M. Matrine inhibits the migratory and invasive properties of nasopharyngeal carcinoma cells. *Mol Med Rep*. 2015;11:4158-4164.
 36. Duan L, Deng L, Wang D, Ma S, Li C, Zhao D. Treatment mechanism of matrine in combination with irinotecan for colon cancer. *Oncol Lett*. 2017;14:2300-2304.
 37. Lin S, Wang Y, Peng Z, Chen Z, Hu F. Detection of cancer biomarkers CA125 and CA199 via terahertz metasurface immunosensor. *Talanta*. 2022;248:123628.
 38. Chen W, Xiu S, Xie X, Guo H, Xu Y, Bai P, et al. Prognostic value of tumor measurement parameters and SCC-Ag changes in patients with locally-advanced cervical cancer. *Radiat Oncol*. 2022;17(1):6.
 39. Yu X, Xu X, Ye Z. Effect of renal function and hemodialysis on the serum tumor markers in patients with chronic kidney disease. *Front Med China*. 2007;1:308-311.
 40. Wang Q, Zheng H, Hu F, Zhang H, Hu Y, Li J, et al. Serum CYFRA21-1 is correlated with the efficacy of epidermal growth factor receptor-tyrosine kinase inhibitor in non-small cell lung cancer patients harboring EGFR mutations. *Zhongguo Fei Ai Za Zhi*. 2016;19:550-558.
 41. Satarug S, Vesey DA, Nishijo M, Ruangyuttikarn W, Gobe GC. The inverse association of glomerular function and urinary β 2-MG excretion and its implications for cadmium health risk assessment. *Environ Res*. 2019;173:40-47.
 42. Zhang L, Sun J, Zhang M, Lin Y, Fang L, Fang X, et al. The significance of combined detection of CysC, urinary mAlb and β 2-MG in diagnosis of the early renal injury in pregnancy-induced hypertension syndrome. *Saudi J Biol Sci*. 2019;26(8):1982-1985.