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On the status of renal function and renal ultrasound manifestations in women with initially diagnosed breast cancer: a cross-sectional study from China

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Abstract

Purpose

Kidney diseases substantially increase breast cancer (BC)-related mortality. This study explored the status of renal function and ultrasound manifestations in Chinese women with initially diagnosed BC.

Methods

A total of 7,052 female patients with initially diagnosed BC and 70,520 age-matched controls from the health screening population during the same period were included from 2012 to 2020. Renal function data, including estimated glomerular filtration rate based on serum creatinine (eGFRcr), and renal ultrasound data were collected. Group differences were analyzed using the Mann-Whitney U test and the chi-square test.

Results

(1) BC patients had poorer renal function than controls, manifested by higher rates of: hypercreatinemia (7.69% vs. 5.53%), hyperuremia (5.80% vs. 3.96%), eGFRcr < 90 ml/min/1.73m^2 (21.27% vs. 17.08%), and eGFRcr < 60 ml/min/1.73m^2 (1.66% vs. 1.22%); all $P < 0.001$. (2) BC patients showed lower proportions of hyperuricemia (2.78% vs. 2.92%, $P = 0.006$). (3) BC patients had higher rates of hypocalcemia (7.07% vs. 4.09%), hyperphosphatemia (2.36% vs. 0.88%), and hypoalbuminemia (20.24% vs. 0.68%), all $P < 0.001$. (4) Abnormal renal ultrasound manifestations were more common in BC patients: renal cysts: 12.06% vs. 7.85%, renal/ureteral stones: 4.23% vs. 3.13%, hydronephrosis: 0.90% vs. 0.44%, all $P < 0.001$.

Conclusion

Chinese women with initially diagnosed BC exhibit poorer renal function, lower serum uric acid, and higher rates of hypocalcemia, hyperphosphatemia, hypoalbuminemia, and renal ultrasound abnormalities such as cysts and stones.

Introduction

Breast cancer (BC) remains the most prevalent malignancy in females globally[1]. By 2050, the number of new BC cases and deaths is expected to rise by 38% and 68%, respectively[2]. Thus, reducing BC incidence and improving prognosis are paramount. Studies show comorbidities at BC diagnosis greatly impact survival. BC patients with one or more comorbidities have lower survival rates[3]. Among these comorbidities, renal diseases are highly prevalent[4] and linked to increased BC death risk[5]. Several observational studies demonstrate that more than half of BC patients have estimated glomerular

filtration rate based on serum creatinine (eGFRcr) below 90 ml/min/1.73m^2[6–8]. In solid tumor cohorts, including breast cancer, the prevalence of chronic kidney disease (CKD, eGFR < 60 ml/min/1.73 m2) ranges from 12% to 25%[9]. Notably, BC patients with an eGFR < 60 mL/min/1.73 m2 face a 1.99-fold higher risk of cancer-specific mortality compared with those with an eGFR ≥ 60 mL/min/1.73 m2[10], a poor prognosis that can be largely attributed to the clinical challenges renal diseases poses for standard radical BC treatment. Severe renal impairment complicates standard radical BC treatments. In such cases, therapy may be inadequate, increasing BC-specific mortality. Even with guideline-recommended standard therapy, if the renal mortality risk is high, survival may not justify the therapy[3]. As a result, cancer patients complicated by kidney disease exhibit inferior outcomes and diminished opportunities to benefit from curative therapy[9]. These clinical challenges have spurred the emergence of breast onconephrology[11].

Despite the growing recognition of breast onconephrology as an interdisciplinary field integrating BC and nephrology, critical gaps remain in the current evidence base. Most available data come from Europe and the Americas[9], with no large-scale studies from China or Asia. China has a high CKD burden (156 million CKD patients)[12], yet only 10% are aware[13]. Most onconephrology studies focus on renal function and blood markers, such as serum creatinine (Scr) and eGFRcr, and few studies include morphological data[14]. However, ultrasonography remains key in CKD assessment[15]. Two major debates exist in onconephrology. First, while most studies find higher breast cancer incidence in CKD patients[9, 16, 17], some report no difference[18]. Second, since cancer is more common in people over 65, it is unclear whether the tumor and mild CKD association is age-related or due to kidney disease[9].

This study is the first to examine renal function and renal ultrasound manifestations in Chinese women with initially diagnosed BC in a large cohort. We compared these women with age-matched females from the health screening population during the same period. Our aim was to determine whether renal dysfunction or structural abnormalities are present in women with newly diagnosed BC prior to treatment. This provides clinical evidence on whether a initial BC diagnosis is associated with renal dysfunction or abnormal ultrasound findings.

Materials and Methods

Study population

This retrospective single-center cross-sectional study included BC patients with renal function data from the China Database for Concomitant Disease of Breast Cancer (CDCDBC)[19] at Chongqing Breast Cancer Center (2012–2020). It also included a concurrent control population from the Health Management Center of the First Affiliated Hospital of Chongqing Medical University. Variables included: (1) demographic data, medical and family history, and treatment plans (from electronic records and follow-ups); (2) both breast and abdominal ultrasound imaging for BC patients and the controls; (3) blood tests including Scr, eGFRcr, blood count, liver function, blood glucose, and lipids for all; (4) pathology for BC

patients. Exclusion criteria for the BC group included: (1) distant metastasis at diagnosis; (2) bilateral BC; (3) male BC; (4) age under 18; (5) other cancer history; (6) specific pathology. Exclusion criteria for the age-matched controls group included: (1) missing gender; (2) missing age; (3) no creatinine data. In total, 7,052 initially diagnosed female BC patients and 70,520 age-matched female controls (1:10) were included (see Supplementary Material 1 for details). The study was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University. As a retrospective study under Article 39 of the "Measures for the Ethical Review of Biomedical Research Involving Human Subjects", consent was waived because subjects could not be located and the research did not involve privacy or commercial interests.

Data collection

Experienced healthcare professionals collected demographic and medical information using standard procedures. Body Mass Index (BMI) was calculated as weight (kg) divided by height (m) squared. All data were stored in the electronic medical record system of Chongqing Breast Cancer Center.

Experienced laboratory technicians from the Department of Laboratory Medicine at the First Affiliated Hospital of Chongqing Medical University (Chongqing Medical Laboratory Quality Control Center) analyzed all hematological parameters including renal function data. These included blood count, liver function, and serum calcium, magnesium, and phosphorus. Renal function measures included Scr, eGFRcr, urea, and serum uric acid (SUA). The laboratory is the College of American Pathologists (CAP)-accredited (number: 7215494). Blood samples were collected after an 8-hour fast. Samples from BC patients were taken before treatment. Units, reference ranges, and test methods are in Supplementary Material 2. For abnormal albumin, serum calcium would be corrected. The formula used: corrected calcium = serum calcium + 0.02 * (40 - albumin). Scr was in μmol/L[20], and eGFRcr used the 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula[21], validated in cancer cohorts[22]. No evidence shows that any new tumor-specific formulas outperform CKD-EPI[9, 23]. For comparison with previous studies, we also employed both the Cockcroft-Gault[9] and the abbreviated Modification of Diet in Renal Disease (aMDRD)[24] formulas in Supplementary Material 3. During eGFRcr calculation, creatinine results were converted to mg/L (1 mg/L = 8.84 μmol/L) and rounded to two decimals. CKD was classified by the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) criteria. Population monitoring could not be reassessed after 3 months, so we used a single-measurement approach, which supports risk assessment and public health planning[25].

All breast and renal ultrasonography in this study were performed using standard ultrasound scanners. All procedures were performed and evaluated by licensed, experienced ultrasonographers from the Department of Ultrasound at the First Affiliated Hospital of Chongqing Medical University. The test results were derived from specific instruments and population parameters and were ultimately classified and diagnosed by licensed, experienced clinicians.

All BC patients enrolled in this study underwent pathological diagnosis through histopathological examination and immunohistochemical methods conducted by the Pathology Center of Chongqing Medical University, with final confirmation by a certified pathologist. The center has been accredited by the CAP. Immunohistochemical assays were performed on tumor tissue samples, with results interpreted according to the joint guidelines established by the American Society of Clinical Oncology (ASCO) and the CAP.

Statistical analysis

All data were processed using Microsoft Office 2021, with statistical analysis performed using R 4.3.3 and Python 3.13. This study did not impute or delete missing values. For each variable, analyses were based on available data (the effective sample size for each variable is detailed in Supplementary Material 3). Normality testing was conducted using the Kolmogorov-Smirnov test (K-S test) for independent samples. Normally distributed measurement data were expressed as mean ± standard deviation (Mean ± SD), while non-normally distributed measurement data were expressed as median (lower quartile, upper quartile) [M(Q1, Q3)]. Categorical data were presented as counts (proportions) [n (%)]. Descriptive statistics were based on valid samples. Between-group analyses were performed using the Mann-Whitney U test for ordinal data and the chi-square test for unordered categorical data. Except for P-values, which were retained with three decimal places, all other data were retained with two decimal places. A two-sided $P < 0.05$ was considered statistically significant.

Results

Basic characteristics of participants

This study ultimately enrolled 7,052 initially diagnosed female BC patients with pathologically confirmed diagnosis and renal function data, including Scr and eGFRcr from the CDCDBC database. The median age was 50.00 (44.00, 58.00) years, and the median BMI was 23.23 (21.21, 25.34). Of these patients, 4,236 completed renal ultrasonography. For comparison, a control group consisting of 631,895 individuals undergoing health screening during the same period was identified, including 322,309 males (51.01%) and 309,586 females (48.99%) with available Scr and eGFRcr data. After randomization, 70,520 female health screening controls without a history of BC were matched at a 1:10 ratio by age and included in the control group. The age-standardized difference between the 70,520 control subjects and the 7,052 female BC patients was 0. A Mann-Whitney U test was performed to compare the two groups' ages, yielding no significant difference ($P = 1$). The median age of the control group was 50.00 (44.00, 58.00) years, and the median BMI was 22.60 (20.89, 24.67). Among them, 45,963 age-matched controls completed renal ultrasonography. Detailed baseline characteristics of the participants are summarized in Supplementary Material 3.

Comparison of renal function between initially diagnosed female BC patients and age-matched female health screening controls

The median level of Scr in BC patients was significantly higher than that in the control group [59.00 (53.00, 65.00) vs. 57.00 (51.00, 63.00) μmol/L, $P < 0.001$], and the proportion of hypercreatinemia in BC patients was also significantly higher than that in the control group (7.69% vs. 5.53%, $P < 0.001$). The median level of serum urea in BC patients was significantly higher than that in the control group [4.90 (4.00, 5.90) vs. 4.80 (4.00, 5.70) mmol/L, $P = 0.001$], and the proportion of hyperuremia in BC patients was also significantly higher than that in the control group (5.80% vs. 3.96%, $P < 0.001$). The median level of SUA in BC patients was significantly lower than that in the control group [267.00 (229.00, 311.00) vs. 274.00 (236.00, 317.00) μmol/L, $P < 0.001$], and the proportions of high-normal uric acid (7.54% vs. 8.82%) and hyperuricemia (2.78% vs. 2.92%) in BC patients were also significantly lower than those in the control group ($P = 0.006$). Compared with the control group, the median eGFRcr in BC patients was significantly lower [101.67 (92.02, 109.12) vs. 103.69 (94.61, 110.95) ml/min/1.73m^2]. After KDIGO stratification, the proportion of patients with eGFRcr ≥ 90 ml/min/1.73m^2 was lower (78.73% vs. 82.92%), while the proportion with eGFRcr < 90 ml/min/1.73m^2 was higher (21.27% vs. 17.08%). Additionally, the proportion with eGFRcr < 60 ml/min/1.73m^2 (defined as renal impairment or CKD) was significantly higher (1.66% vs. 1.22%), with a statistically significant difference ($P < 0.001$). See Table 1 for details.

Comparison of calcium, magnesium, and phosphorus levels between initially diagnosed female BC patients and age-matched female health screening controls

Compared with the control group, the median serum calcium level was significantly lower in BC patients [2.29 (2.23, 2.36) vs. 2.33 (2.26, 2.39) mmol/L, $P < 0.001$]. Hypocalcemia was present in 7.07% of BC patients at initial diagnosis, significantly higher than the 4.09% in the age-matched controls ($P = 0.003$). After albumin correction, the median corrected calcium level in BC patients rebounded to 2.24 (2.18, 2.29) mmol/L, higher than the median level of 2.19 (2.13, 2.25) mmol/L in the controls ($P < 0.001$). Serum magnesium in BC patients was 0.88 (0.84, 0.92) mmol/L, higher than 0.87 (0.83, 0.90) mmol/L in the controls ($P < 0.001$). The median serum phosphorus level in BC patients was 1.19 (1.09, 1.30) mmol/L, higher than 1.15 (1.05, 1.24) mmol/L in the controls ($P < 0.001$). Hyperphosphatemia was present in 2.36% of BC patients at initial diagnosis, significantly higher than the 0.88% in the controls ($P = 0.007$). See Table 2 for details.

Comparison of renal ultrasound manifestations between initially diagnosed female BC patients and age-matched female health screening controls

The proportion of no significant abnormalities in renal ultrasound was lower in BC group than in control group (81.73% vs. 86.99%, $P < 0.001$); the proportion of renal cysts in BC group was significantly higher than in control group (12.06% vs. 7.85%, $P < 0.001$); the proportion of renal/ureteral stones in BC group was significantly higher than in control group (4.23% vs. 3.13%, $P < 0.001$); the proportion of renal cysts with calcification in BC group was higher than in control group (0.97% vs. 0.45%, $P < 0.001$); the proportion of hydronephrosis in BC group was significantly higher than in control group (0.90% vs. 0.44%, $P < 0.001$). No statistically significant differences were observed in other specific renal ultrasound classifications, as detailed in Table 3.

Comparison of other baseline characteristics between initially diagnosed female BC patients and age-matched female health screening controls

The age of the BC study population and the female age-matched controls, after 1:10 age matching, was 50.00 (44.00, 58.00) years. The BMI of the BC group was higher than that of the control group [23.23 (21.21, 25.34) vs. 22.60 (20.89, 24.67)]. The median serum albumin level in the BC group was lower than that in the control group [43.00 (40.00, 46.00) vs. 46.00 (44.00, 48.00) g/L]. Approximately 20.24% of women with BC had hypoalbuminemia at initial diagnosis, significantly higher than the 0.68% in the age-matched controls. All comparisons except for age ($P = 1$) were statistically significant ($P < 0.001$), as detailed in Table 4.

Discussion

This retrospective cross-sectional study was the first to incorporate renal function indicators and renal ultrasound classification data from a large sample of Chinese women with initially diagnosed BC, and to compare them with age-matched female health screening controls to explore renal health status in these women. The study data results showed that 21.27% of women with BC had a 2009 CKD-EPI eGFRcr below 90 ml/min/1.73m^2 at initial diagnosis, 1.66% had a 2009 CKD-EPI eGFRcr below 60 ml/min/1.73m^2, 7.07% had concurrent hypocalcemia, 2.36% had concurrent hyperphosphatemia, 20.24% had concurrent hypoalbuminemia, 12.06% had concurrent renal cysts, 4.23% had concurrent renal/ureteral stones, and 0.90% had concurrent hydronephrosis. These data were significantly higher than those of age-matched female health screening populations, but the median level and proportion of elevated SUA in women with initially diagnosed BC were lower than those in age-matched controls. This suggests that Chinese women with initially diagnosed BC exhibit poorer renal function, lower SUA levels, and higher rates of hypocalcemia, hyperphosphatemia, hypoalbuminemia, and renal ultrasound abnormalities such as cysts and stones. Meanwhile, since the control group comprised age-matched female health screening population, age was controlled as a confounding variable. This suggests that the nephrological characteristics of BC in these initially diagnosed women may not be age-related, but rather reflect intrinsic renal changes or other factors directly or indirectly related to BC. The underlying mechanisms of this association warrant further investigation.

The renal function of Chinese women with initially diagnosed BC is significantly lower than that of age-matched women in routine physical examinations, possibly because a considerable proportion of BC patients may have pre-existing reduced renal function and its risk factors. First, renal impairment may be an indirect result of common comorbidities such as diabetes and hypertension[9]. On one hand, the kidneys are target organs attacked by common comorbidities of BC, including diabetes, hypertension, and obesity[5, 15, 26]; on the other hand, to treat these comorbidities, some individuals begin taking nephrotoxic drugs before being diagnosed with BC[27, 28]. Due to limited endogenous repair capacity[29], damaged kidney cells cannot fully restore normal function, leading to gradual progression toward CKD[30], which in turn reduces renal function. Second, unlike in other countries, traditional Chinese herbal

medicine, as a Chinese method for treating breast diseases, has a history of thousands of years and is still widely used in the early observation of suspicious breast nodules[31–36]. However, the active components of natural compounds in Chinese herbal medicine are relatively complex, and some herbal ingredients exhibit varying degrees of nephrotoxicity[37].

Patients with BC often exhibit impaired renal function, which may be attributed to the inherent association between declining renal function and an elevated risk of malignant breast tumors[9]. Multiple studies have identified diverse intersection points between breast and kidney diseases: Obesity and insulin resistance may share a common pathological basis for endocrine-related disorders such as CKD and BC[38]; the breast cancer susceptibility gene BRCA1 plays a pivotal role in renal repair following injury[39]; tumors themselves may exert direct, remote damage to the kidneys by secreting specific factors. A 2023 study by Wenhao Xu's team, published in Nature, revealed a novel antidiuretic pathway mediating cross-species tumor-kidney crosstalk that directly acts on renal tubules to inhibit their drainage function, leading to fluid retention and renal dysfunction[40]. Additionally, tumors can induce paraneoplastic glomerulopathy[41], allowing tumor-associated immune complexes to deposit in the glomeruli, triggering in situ immune inflammation manifested as IgA nephropathy and causing direct renal damage[42]. Furthermore, preclinical studies have demonstrated that even in the absence of renal metastases, certain types of BC can independently alter the physiology and function of the kidneys in mice, independent of strain and gender, providing direct biological evidence for the observed early decline in renal function[43]. Lastly, as regulators of systemic metabolic homeostasis, the kidneys are susceptible to electrolyte imbalances, malnutrition, and reduced muscle mass during cancer development and remodeling, which can impair renal function[9].

Pre-existing renal impairment can serve as a risk factor for increased BC risk, resulting in significantly lower renal function in China's female BC patients compared to age-matched female health screening populations. This is because declining renal function can have multiple effects on the body, such as: residual uremic toxins in CKD patients can inhibit the operation of various genes and normal functions[44], potentially elevating the risk of BC; during CKD, the composition of gut microbiota changes[45], which can modulate circulating estrogen levels and thereby influence the pathogenesis of estrogen-driven breast tumors[46]. These systemic changes, caused by renal impairment, may significantly impact the occurrence, progression, and detection of BC. Taken together, these findings suggest a bidirectional relationship where renal impairment predisposes to BC, and BC may accelerate subsequent renal function deterioration.

BC patients had significantly lower median SUA levels and fewer cases of elevated SUA compared to the control group, supporting the hypothesis that SUA may be negatively correlated with or a potential protective factor for BC[47]. This may be because uric acid provides antioxidant defense in the human body, which can counteract the effects of oxidants and free radicals on aging and cancer[48]. However, several studies indicate that SUA concentration is not linked to BC incidence[49], or that elevated SUA are

associated with a higher risk of BC[50]. Among studies hypothesizing a dose-response relationship between SUA and cancer risk and survival[51–54], some suggest a "J"-shaped relationship[52], others propose a "U"-shaped relationship[53], and still others indicate a linear relationship[54]. Although the kidneys excrete only 10% of SUA, the remaining 90% is reabsorbed, making the kidneys the primary site of SUA excretion[55]. In patients with CKD, each 10 mL/min/1.73m² decline in eGFR was associated with an average SUA elevation of approximately 20 μmol/L[54]. In studies evaluating the correlation between SUA and BC, a significant proportion of cohorts did not control for, correct for, or stratify by renal function[49, 51–53], which may be one of the underlying reasons for the current controversy regarding the association between SUA and BC. This suggests that link between SUA and BC risk is likely influenced by other variables, such as renal function, which require further investigation.

Patients with BC are at higher risk of hypocalcemia, hyperphosphatemia, and malnutrition (hypoproteinemia) at initial diagnosis. However, after albumin correction, the proportion of BC patients with normal corrected calcium levels was significantly elevated compared to the control group, indicating that hypocalcemia in female BC patients at initial diagnosis is largely due to hypoproteinemia. Therefore, when assessing serum calcium levels in cancer patients, corrected calcium should be used instead of uncorrected calcium. Previous studies have also found that patients with malignant tumors often exhibit reduced protein intake, malnutrition, decreased muscle mass, and various serum electrolyte abnormalities such as hypocalcemia, hypercalcemia, hyperphosphatemia, and hypermagnesemia[9]. In many cases, these electrolyte disturbances are caused by common etiologies rather than by underlying malignancies. However, in other cases, these electrolyte disturbances serve as signals of neoplastic processes, indicating a poor prognosis[56]. Thus, in cancer patients with abnormal albumin levels, the use of albumin-corrected calcium is crucial for accurate assessment of serum calcium.

Meanwhile, this study also revealed the potentially significant role of renal cysts in oncology and nephrology. As a common disease, the incidence of renal cysts rises with advancing age[57]. Currently, there is limited research on simple renal cysts[58], which may be attributed to the previous belief that solitary or few renal cysts lack clinical significance[59], and that simple renal cysts are often asymptomatic and rarely receive clinical intervention or attention[60]. However, emerging evidence suggests that renal cysts may correlate with various diseases, such as hypertension, diabetes, vascular diseases, proteinuria, renal sclerosis, renal/ureteral stones, and hyperuricemia, and may represent an early manifestation of renal dysfunction[59–64]. No prior studies have investigated the correlation between renal cysts and BC. This is the first study to report a significantly higher proportion of renal cysts in BC patients. This may be attributable to the lower renal function observed in the breast cancer group. Another possible reason is that many comorbidities of BC are also risk factors for renal cysts[5, 65], meaning a considerable proportion of initially diagnosed BC patients already have renal cysts and their risk factors. This suggests that clinicians and researchers in oncology and nephrology should pay closer attention to renal cysts and conduct more in-depth studies of their mechanisms.

This study has several strengths: (1) As the first large-scale study in China focusing on renal function and ultrasound manifestations in initially diagnosed BC patients, it fills the evidence gap in Asian onconephrology; (2) The large sample size (7,052 BC patients and 70,520 age-matched controls) ensures sufficient statistical power; (3) Rigorous age-matching minimizes age-related confounding and improves group comparability; (4) Integration of renal function indicators and ultrasound data enables comprehensive renal assessment; (5) Standardized data collection and statistical methods ensure result reproducibility; (6) Focusing on pretreatment patients avoids anti-tumor therapy-related confounding. This study may also have certain limitations: (1) As a cross-sectional observational study, it can only reveal associations but cannot establish causal relationships; (2) The urine albumin/creatinine ratio is also an important indicator for CKD assessment[66], but this study only provided evidence related to eGFRcr; (3) eGFRcr is derived from serum creatinine levels, which are subject to various confounding factors. This retrospective data may not fully capture all potential serum creatinine confounders, such as diet, hydration status, muscle mass, and history of over-the-counter medication use; (4) In this study, comorbidities potentially influencing renal function—including diabetes, hypertension, and cardiovascular disease, were not excluded or adjusted for as confounders; (5) Due to sample and data limitations, other variables in this study, apart from Scr and eGFRcr, had missing values, which may lead to selection bias. Future studies could further conduct cohort studies or randomized controlled trials to control for confounders, incorporating more sensitive biomarkers such as urinary protein, urine albumin/creatinine ratio, cystatin C, and β2 microglobulin, as well as more comprehensive imaging studies like computed tomography (CT) of the urinary system, and more precise pathological evidence of the kidneys. Long-term follow-up of these indicators could provide a more accurate assessment of renal health in BC patients.

Conclusion

Chinese women with initially diagnosed BC exhibit poorer renal function, lower SUA levels, and higher rates of hypocalcemia, hyperphosphatemia, hypoalbuminemia, and renal ultrasound abnormalities such as cysts and stones. Moreover, the aforementioned renal characteristics of initially diagnosed female BC may not be caused by age but rather by intrinsic renal changes or other factors directly or indirectly related to BC, and the specific mechanisms warrant further investigation. This understanding requires clinicians to pay attention to renal conditions at the initial stage of BC diagnosis and treatment, and integrate them into individualized treatment and long-term follow-up plans to improve patients' overall prognosis and quality of life.

Declarations

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Author contribution B.-Q.P., Z.-H.B., X.-Q.Q., L.-Y.M., X.-C.C., and X.-R.L. collected and analyzed the data. B.-Q.P. drafted the original manuscript. L.-Q.K. conceived and supervised the study. Q.P. and D.-L.L.

contributed to data interpretation and manuscript revision. All authors reviewed and approved the final manuscript.

Data availability The data that support the findings of this study are available from the first author upon reasonable request. The data are not publicly available due to privacy or ethical restrictions.

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Competing interests The authors declare no competing interests.

Ethics approval and consent to participate This study was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University. All procedures performed involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Declaration of Helsinki and its later amendments. Informed consent was not obtained as this was a retrospective study, meeting the requirements for the informed consent waiver.

Consent for publication All authors consented to publication.

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Tables

Tables 1 to 4 are available in the supplementary files section

Supplementary Files

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