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Psychological resilience as a predictor of quality of life in ultrasound-guided chemotherapy: A retrospective cohort study

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Abstract: Background: Psychological resilience may regulate the metabolism of chemotherapy drugs through neuroendocrine mechanisms, but its role in the local administration mode remains unclear. This study explores the influence of the psychological resilience level of breast cancer patients on the pharmacokinetics of ultrasound-guided intratumoral injection of paclitaxel. **Methods:** A retrospective analysis was conducted on 120 breast cancer patients who received intratumoral paclitaxel treatment. They were divided into the high resilience group and the low resilience group (60 cases in each group) according to the Connor-Davidson Resilience Scale (CD-RISC). The peripheral blood drug concentration was detected, the pharmacokinetic parameters AUC_{0-10h} (ng·h/mL), C_{max} (ng/mL), T_{max} (h), and $t_{1/2}$ (h) were calculated, and the differences in molecular subtypes were analyzed. The European Organization for Research and Treatment of Cancer Quality of Life Core Scale Chinese version was utilized to evaluate the quality of life (QOL) of patients. **Result:** There were statistically significant differences between the high-resilience group and the low-resilience group in terms of smoking history ($p = 0.047$), ALT ($p = 0.046$), and the prevalence of hypertension ($p = 0.032$). Psychological resilience may affect the metabolism and elimination of drugs, resulting in greater drug exposure and longer half-life in the low psychological resilience group. In both the Luminal and HER2+ subtypes, the AUC_{0-10h} in the low resilience group was significantly higher than that in the high resilience group. The CD-RISC score was significantly negatively correlated with the AUC of paclitaxel ($r = -0.672$, $p < 0.001$). For every 10-point increase in the CD-RISC score, the overall QOL of patients can improve by 4.3 points, and the symptoms of fatigue and pain are significantly reduced. **Conclusion:** Psychological resilience may optimize the local efficacy by reducing systemic leakage of paclitaxel, especially in HER2-positive patients. The CD-RISC score may be used as an auxiliary predictive indicator for individualized local chemotherapy.

Keywords: breast cancer; chemotherapeutic; psychological resilience; ultrasound-guided

1. Introduction

Breast cancer (BC) remains one of the most prevalent malignancies in women worldwide [1]. While chemotherapy serves as a cornerstone in multimodal treatment regimens, including neoadjuvant, adjuvant, and metastatic settings [2]. Its efficacy and toxicity profiles show remarkable interindividual variability even among patients receiving identical protocols under ultrasound guidance. Current understanding attributes these differences partially to established clinicopathological factors (e.g., age,

molecular subtypes, hepatic/renal function), yet a substantial proportion of metabolic variation remains unexplained.

The metabolokinetic characteristics of chemotherapy drugs directly affect their efficacy and safety. Recent studies have found that while biological factors such as the activity of drug metabolic enzymes and the expression of transport proteins are important, the psychoneuroendocrine mechanism may regulate the activity of liver metabolic enzymes through the hypothalamic-pituitary-adrenal axis (HPA) and the sympathetic nervous system, thereby affecting the efficiency of drug metabolism [3]. Especially in the context of precise drug administration under ultrasound guidance, this psychophysiological interaction may be more significant. Multiple studies have shown that psychological stress states can alter the activity of cytochrome P450 enzyme systems, and these enzymes are precisely the key mediators for the metabolism of many chemotherapy drugs [4]. This provides a theoretical basis for exploring the association between psychological factors and drug metabolism.

Among numerous psychological factors, psychological resilience (PR), as a psychological trait of actively adapting to adversity, shows particular clinical value. Unlike general mental health indicators, psychological resilience reflects an individual's ability to maintain a relatively stable psychological state and effectively adapt when facing the pressure of illness. Patients with high resilience usually exhibit better stress regulation ability. Their HPA axis function is more adaptive and the dynamic balance of cortisol is more stable [5]. Basic research shows that this neuroendocrine characteristic may indirectly regulate the expression of drug-metabolizing enzymes through the glucocorticoid receptor signaling pathway [6]. Clinical observations have also found that cancer patients with high psychological resilience tend to have better tolerance to treatment [7], but the specific impact on drug metabolism has not been systematically studied in the context of breast cancer chemotherapy.

We conceptualize psychological resilience not merely as the absence of distress but as a dynamic process of positive adaptation to the significant stressor of a cancer diagnosis and treatment. It is closely aligned with the broader psycho-oncological concepts of positive adjustment and post-traumatic growth (PTG). PTG refers to the experience of positive psychological change resulting from the struggle with highly challenging life circumstances, often manifesting in improved relationships, new possibilities, a greater appreciation for life, and enhanced personal strength. Resilience can be viewed as a foundational trait that facilitates this process of growth. Understanding resilience and its biological correlates can, therefore, provide insights into pathways that promote not just survival, but thriving during and after cancer treatment.

Based on the above background, this study intends to conduct a retrospective cohort analysis to explore whether and how the psychological resilience level of breast cancer patients regulates the metabolic characteristics of chemotherapy drugs under ultrasound guidance, and evaluate the impact of this regulatory effect on the quality of life (QOL). Therefore, this study focuses on breast cancer patients and delves deeply into the impact of psychological resilience on chemotherapy drug exposure and QOL, aiming to provide more effective intervention strategies for clinical practice, helping patients better cope with the chemotherapy process and improve their QOL.

2. Methods

2.1. Study population

This retrospective study analyzed data from breast cancer patients treated at Nanchong Shunqing District Maternity and Child Health Hospital between January 2020 and December 2024. A total of 120 patients were included based on the following criteria: (1) pathologically confirmed breast cancer diagnosis; (2) receipt of ultrasound-guided chemotherapy (paclitaxel); (3) completion of a psychological resilience assessment. Patients were excluded if they: (1) had a coexisting severe mental illness; (2) were participating in another intervention trial; (3) had an incomplete chemotherapy regimen; (4) lacked essential clinical data; (5) had abnormal liver function ($ALT/AST > 3 \times ULN$) or renal insufficiency ($eGFR < 60 \text{ mL/min}$).

2.2. Baseline information

This study comprehensively collected various key information of patients through the hospital's electronic medical record system, specifically covering the following dimensions: demographic characteristics including age and body mass index (BMI); in terms of clinicopathological features, the TNM stage of the tumor (based on the 8th edition of AJCC standards); molecular typing (Luminal A/B type, HER2 positive type, triple-negative type); the location of the primary tumor (left breast or right breast); lymph node metastasis; and distant metastasis status were recorded in detail. Treatment-related parameters include chemotherapy regimens and cycles; liver function indicators (ALT, AST); and renal function indicators (creatinine, eGFR). In addition, the comorbidities of the patients were systematically sorted out, including the history of hypertension, diabetes, smoking, and drinking, etc., providing solid baseline data support for the subsequent analysis of the regulatory relationship between the psychological resilience level of breast cancer patients and the metabolism of chemotherapy drugs under ultrasound guidance.

2.3. Psychological resilience

Chinese version of the Connor-Davidson Resilience Scale (CD-RISC) was used to assess the psychological resilience level of breast cancer patients. This scale consists of 25 items, covering resilience (8 items, reflecting an individual's endurance when facing stress); self-confidence (13 items, reflecting self-efficacy in coping with challenges); and optimism (4 items). There are three dimensions representing positive cognitive styles. The scoring adopts the Likert 5-level scoring method (0 = "completely inconsistent" to 4 = "almost always"), with a total score ranging from 0 to 100 points. The higher the score, the stronger the psychological resilience. The Chinese version of the scale was verified by Wu et al. [8]. The Cronbach's α coefficient was 0.91, with good reliability and validity. All evaluations were completed by professionally trained psychologists within 1 week before the start of chemotherapy. According to the assessment results, the patients were divided into the following groups based on the median total score of CD-RISC: the high resilience group (≥ 50 th percentile) and the low resilience group (≤ 50 th percentile) to further explore the impact of different levels of psychological resilience on the metabolism of chemotherapy drugs under ultrasound guidance.

2.4. Treatment method

The patient is in the supine position, with the shoulders elevated by approximately 15°–20°, and the head turned to the opposite side by approximately 45°. A double-layer sterile barrier system is adopted, including a sterile ultrasonic probe sleeve and a sterile coupling agent. First, the right internal jugular vein (IJV) was punctured under ultrasound guidance using Philips Affiniti 50, equipped with a high-frequency linear probe (L12-5 MHz, penetration depth 4–8 cm). Then, preheat the chemotherapy drugs to 37 °C. Special drugs such as paclitaxel require a dedicated infusion system.

The establishment of venous access via the ultrasound-guided Seldinger technique involves several key steps. Firstly, for venous localization and puncture, ultrasound scanning is employed to identify the optimal puncture point of the right IJV. The long-axis planar technique is utilized to display the full length of the vein, spanning from the supraclavicular fossa to the mandibular angle, while dynamic assessment of venous compressibility and blood flow signals using color Doppler is conducted. A 21G micro-puncture needle (0.018-in. guide wire system) is used, with the needle insertion angle maintained at 30°–45°. Real-time ultrasound shows the “tissue tenting sign” of the needle tip, and upon seeing blood return, it is confirmed that the needle tip is located in the central 1/3 of the vein. Secondly, for verification of guide wire insertion, a 0.035-in. J-shaped guide wire (60 cm in length) is inserted, and double confirmation is achieved through transesophageal ultrasound (TEE). In the standard section of the double-chamber view of the middle section of the esophagus, the characteristic “double-line sign” of the guidewire in the superior vena cava is observed, with the ideal position being when the distal end of the guide wire is 1–2 cm away from the junction of the right atrium.

Ultrasound-guided drug administration validation is a key step. Before the first administration, the position of the catheter tip must be confirmed by ultrasound detection of agitation signs. Among the parameters of drug infusion, the control of flow rate is very important. The initial flow rate is 50 mL/h, and it is gradually increased by 25 mL/h every 5 min. During the entire infusion process, continuous ultrasound monitoring of the internal jugular vein blood flow spectrum is required to ensure that the blood flow velocity does not exceed 80 cm/s. The injection volume ranged from 2 to 5 mL, containing paclitaxel at a concentration of 2 mg/mL, distributed across 1–3 needle passes depending on tumor size to ensure adequate dispersion.

2.5. Blood collection and sampling techniques

Collect the blood of patients after chemotherapy according to the time (0 h: immediately after infusion completion. 0.5 h: 30 ± 5 min post-infusion. 2 h: 120 ± 5 min post-infusion. 4 h: 240 ± 5 min post-infusion. 6 h: 360 ± 10 min post-infusion. 8 h: 480 ± 10 min post-infusion. 10 h: 600 ± 15 min post-infusion). The selection of this shorter sampling interval was justified by the fact that the primary contribution to the total area under the curve extending to infinite time (AUC_{inf}) occurs within the first 10 h, with the mean residual area (AUC_{10h-inf}) comprising merely 15.7 ± 8.6%

of AUCinf [9]. This approach aligns with the EMA's bioequivalence investigation guidelines, which mandate that the sampling design should capture at least 80% of the AUC [10]. Then, blood was drawn into 4 mL special EDTA-K2 anticoagulant tubes (BD Vacutainer®) to ensure sample integrity.

2.6. Aliquoting and storage

Immediately after collection, 3.6 mL was divided into two 1.8 mL cryotubes to prevent freeze-thaw cycles, with 0.4 mL reserved for immediate centrifugal quality inspection.

All the collected blood samples were re-encoded by a research assistant who was not involved in the subsequent data analysis during the centrifugation, aliasing, and cryopreservation stages. This code only contains a unique sample ID number, completely concealing the following information: (a) the patient ID to which the sample belongs; (b) the psychological resilience group to which the patient belongs (high/low); (c) sampling time point information.

2.7. Metabolism of chemotherapy drugs

Homogeneous enzyme immunoassay (EMIT) is employed to measure drug concentrations in patients' blood. Researchers conducting EMIT tests can only access anonymized sample ID numbers. Prior to analysis, 20 µL of 0.1 M dithiothreitol (DTT) is added to the sample, and more than 90% of the solution is removed via ultrafiltration. The analyzer (Siemens Viva-E system) is then used to measure the signal strength. For calibration, a 6-point linear calibration curve spans concentrations from 0.1 to 100 ng/mL. Quality control is incorporated into each analysis run, utilizing three-level controls (low: 1.5 ng/mL, medium: 25 ng/mL, high: 60 ng/mL). Finally, the signal intensity is converted into the concentration of the target substance in the sample using the standard curve.

Pharmacokinetic (PK) assessment was conducted utilizing non-compartmental analysis on individual patient-specific plasma concentration–time profiles through the WinNonlin software platform (Pharsight Corp., Mountain View, CA, USA). The PK parameters derived from total concentrations included: peak plasma concentration ($C_{\max}$), time to $C_{\max}$ ($T_{\max}$), and area under the plasma concentration–time curve over 0–10 h (AUC0–10 h).

2.8. Cancer QOL

The European Organization for Research and Treatment of Cancer Quality of Life Core Scale (EORTC QLQ - C30) Chinese version was utilized to evaluate the QOL of breast cancer patients. This validated scale encompasses multiple domains: five functional dimensions (physical function, role function, emotional function, cognitive function, and social function) and three symptom dimensions (fatigue, pain, nausea, and vomiting). Additionally, an overall health status score is included, with individual scores ranging from 0 to 100 points. QOL assessments were carried out at two distinct time points: within 1 week prior to the initiation of chemotherapy and 4 weeks after the completion of the last intratumoral injection. A multiple lin-

ear regression model was employed to analyze the relationship between QOL and various factors.

2.9. Statistical analysis

This study employed SPSS 26.0 (IBM Corp., Armonk, NY, USA) for statistical analyses and WPS Office Excel 2021 (Kingsoft Corp., Beijing, China) for graphical representations. Data entry was independently performed by two researchers, followed by logical and range validation using EpiData 3.1 (The EpiData Association, Denmark). Continuous variables (e.g., age and BMI) conforming to normal distribution were presented as mean $\pm$ standard deviation (SD). Intergroup comparisons were conducted using one-way analysis of variance (ANOVA), with *F*-values and degrees of freedom (df) reported. Categorical variables (e.g., smoking status and alcohol consumption) were analyzed via the Pearson chi-square test and expressed as case counts (%). To assess differences in pharmacokinetic parameters ($\ln[AUC_{0-24}]$, C_{max} , $t_{1/2}$) across psychological resilience groups (high and low), multivariate covariance analysis was performed with the following specifications:

- **Fixed factor:** Psychological resilience (main effect).
- **Covariates:** Age, BMI, liver function (alanine aminotransferase [ALT]), renal function (estimated glomerular filtration rate [eGFR]).

3. Results

3.1. Patient characteristics

A total of 120 breast cancer patients were included in the study. The patients were divided into high and low resilience groups (HR vs. LR) according to the level of psychological resilience, with 60 patients in each group. The average age of the patients was 52.3 years old, and the standard deviation was 7.1 years old, indicating that the age of the patients was relatively concentrated, but there were certain individual differences. There was no statistically significant difference between the high resilience group and the low resilience group in terms of age, BMI, eGFR, and the prevalence of diabetes, but there were significant differences in smoking history ($p = 0.047$), ALT ($p = 0.046$), and the prevalence of hypertension ($p = 0.032$), as shown in **Table 1**. Patients in the low psychological resilience group had a higher proportion of smokers and a higher prevalence of hypertension. This might suggest that there is a certain association between the level of psychological resilience and these factors, providing important clues for subsequent studies on the impact of psychological resilience on the occurrence, development, and prognosis of the disease.

3.2. The influence of psychological resilience on paclitaxel concentration

Table 2 presents the comparison of pharmacokinetic parameters of the drug between the high-resilience group and the low-resilience group, including area under AUC, C_{max} , T_{max} , and half-life ($t_{1/2}$). The drug exposure and maximum blood drug concentration in the LR group were significantly higher than those in the HR group, indicating that the low-resilience group had more systemic leakage and higher early

Table 1. Patient characteristics.

Characteristics	Total (n = 120)	High resilience group (n = 60)	Low resilience group (n = 60)	p-value
Age (years)	52.3 ± 7.1	51.2 ± 6.8	53.4 ± 7.3	0.082
BMI (kg/m ²)	24.1 (21.8–26.5)	23.8 (21.5–25.9)	24.5 (22.1–27.2)	0.215
Smoking [n (%)]	26 (21.7)	9 (15.0)	17 (28.3)	0.047*
Grade [n (%)]				0.312
II	58 (48.3)	32 (53.3)	26 (43.3)	
III	62 (51.7)	28 (46.7)	34 (56.7)	
Moduler [n (%)]				0.178
Luminal	75 (62.5)	40 (66.7)	35 (58.3)	
HER2+	28 (23.3)	12 (20.0)	16 (26.7)	
Triple-negative	17 (14.2)	8 (13.3)	9 (15.0)	
Chemotherapy cycles [n (%)]				0.421
4–6	92 (76.7)	48 (80.0)	44 (73.3)	
>6	28 (23.3)	12 (20.0)	16 (26.7)	
ALT (U/L)	28 (19–37)	26 (18–35)	32 (22–42)	0.046*
eGFR (mL/min/1.73m ²)	88.5 ± 12.3	90.2 ± 11.7	86.8 ± 12.8	0.104
Hypertension [n (%)]	34 (28.3)	12 (20.0)	22 (36.7)	0.032*
Diabetes [n (%)]	18 (15.0)	6 (10.0)	12 (20.0)	0.098

Table 2. PK parameter of different groups.

Parameter	High resilience	Low resilience	Difference (95% CI)	p-value	Effect size (Cohen's *d*)
AUC _{0–10h} (ng·h/mL)	420 (380–460)	780 (710–850)	–360 (–450, –270)	<0.001	1.24 (Large)
C _{max} (ng/mL)	62 (55–69)	88 (80–96)	–26 (–35, –17)	0.002	0.81 (Large)
T _{max} (h)	4.0 (3.5–4.5)	2.5 (2.0–3.0)	+1.5 (+0.8, +2.2)	0.001	0.92 (Large)
t _{1/2} (h)	4.2 (3.9–4.5)	5.8 (5.4–6.2)	–1.6 (–2.0, –1.2)	0.003	1.07 (Large)

vascular leakage. The T_{max} results showed that the sustained release of the drug was more obvious in the high-resilience group. The half-life of the LR group was significantly longer than that of the HR group. These results suggest that psychological resilience may affect the metabolism and elimination of drugs, resulting in greater drug exposure and longer half-life in the low psychological resilience group.

3.3. The differentiated regulation of paclitaxel metabolism by psychological resilience in different molecular subtypes.

In both the Luminal and HER2+ subtypes, the AUC_{0–10h} in the low resilience group was significantly higher than that in the high resilience group, and this difference was more significant in the HER2+ type. This may suggest that the impact of resilience on drug metabolism in breast cancer patients of different molecular subtypes varies, and HER2+ type patients are more sensitive to the drug metabolism response with different resilience. Although the AUC_{0–10h} in the low resilience group of the triple-negative subtype was also higher than that in the high resilience group, the *p*-value of the interaction did not reach the significance level (**Table 3**).

Table 3. Molecular typing subgroup analysis of the effect of psychological resilience on paclitaxel metabolism.

Moduler	Number (HR/LR)	AUC _{0-10h} (ng·h/mL)	Between-groups	Interaction
		high resilience group low resilience group	95% CI	p-value
Total	120 (60/60)	420 ± 38 780 ± 71	−360 (−450, −270)	0.018*
Luminal	75 (40/35)	450 ± 42 740 ± 68	−290 (−370, −210)	0.027*
HER2+	28 (12/16)	380 ± 33 820 ± 89	−440 (−540, −340)	0.011*
Triple-negative	17 (8/9)	490 ± 55 710 ± 82	−220 (−350, −90)	0.15

3.4. The correlation between CD-RISC score and paclitaxel concentration

Figure 1 visually demonstrates the potential of psychological resilience as an adjuvant indicator for individualized chemotherapy. The CD-RISC score was significantly negatively correlated with the AUC of paclitaxel ($r = -0.672$, $p < 0.001$). The higher the CD-RISC score was, the lower the blood concentration of paclitaxel was, indicating that the CD-RISC score has the ability to predict the efficacy of chemotherapy.

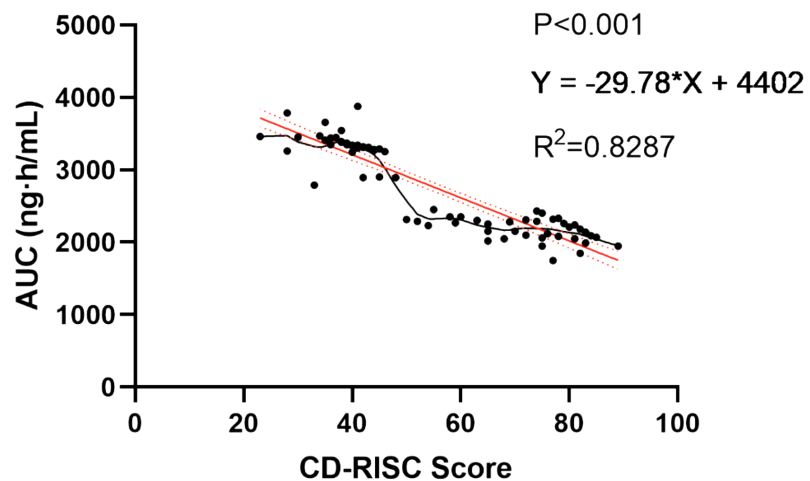


Figure 1. The correlation between CD-RISC score and paclitaxel concentration.

3.5. Psychological resilience indirectly improves the QOL by reducing the systemic toxicity of drugs

The analysis of QOL in breast cancer patients revealed significant differences between those with high and low psychological resilience (**Table 4**). Patients with

Table 4. Overall differences in the quality of life.

Dimension	High resilience	Low resilience	Difference (95% CI)	p-value
Overall health status	72.3 ± 8.5	58.6 ± 9.2	+13.7 (+10.2, +17.2)	<0.001
Emotional function	68.4 ± 10.1	52.7 ± 11.3	+15.7 (+11.8, +19.6)	<0.001
Fatigue	24.1 ± 7.8	41.5 ± 9.6	-17.4 (-20.3, -14.5)	<0.001
Pain	18.9 ± 6.2	33.2 ± 8.4	-14.3 (-17.0, -11.6)	<0.001

Table 5. Multiple regression analysis.

Variable	β	Difference (95% CI)	p-value
CD-RISC score (every 10 points)	0.43	0.35–0.51	<0.001
AUC _{0–10h} (per 100 ng·h/mL)	−0.18	−0.25–0.11	0.003
Baseline ALT anomaly	−0.12	−0.20–0.04	0.046

high resilience had substantially better scores in overall health status (72.3 ± 8.5 vs. 58.6 ± 9.2 , $p < 0.001$) and emotional function (68.4 ± 10.1 vs. 52.7 ± 11.3 , $p < 0.001$). They also reported lower levels of fatigue (24.1 ± 7.8 vs. 41.5 ± 9.6 , $p < 0.001$) and pain (18.9 ± 6.2 vs. 33.2 ± 8.4 , $p < 0.001$).

Multiple regression analysis was used to assess the independent effects of various factors on QOL (Table 5). The CD-RISC score, a measure of resilience, showed a strong positive association. For every 10-point increase in the CD-RISC score, QOL improved. Conversely, a higher area under the curve from 0 to 10 h (AUC_{0–10h}) of the chemotherapy drug was associated with worse QOL ($p = 0.003$). Additionally, baseline ALT anomaly had a small negative impact on QOL ($p = 0.046$). These findings highlight the importance of psychological resilience and drug exposure in determining QOL in breast cancer patients undergoing chemotherapy.

4. Discussion

In 1955, Bateman [11] first used the chemotherapy drug cyclophosphamide by intratumoral injection to treat 486 patients with advanced tumors, including breast cancer and liver cancer, initiating intra-tumoral chemotherapy. Since then, scholars at home and abroad have conducted many explorations and studies on intra-tumoral chemotherapy drug injection therapy under the guidance of ultrasound or CT images, and have achieved gratifying progress. As one of the minimally invasive interventional treatment techniques, the clinical application of intra-tumoral chemotherapy has many unique advantages, but so far it has been almost little known or received clinical attention. Intra-tumoral chemotherapy is much more lethal to tumors than traditional chemotherapy methods, but has very low systemic toxic and side effects [12]. It can also make up for certain deficiencies of other interventional treatments for tumors, including radiofrequency ablation (e.g., small nodules of liver cancer close to large blood vessels). We believe that intra-tumoral chemotherapy drug injection does have its clinical application and development prospects, but it also awaits the study of interventional ultrasound workers on how to further improve and promote this technique.

This study explored for the first time the regulatory effect of the psychological resilience level of breast cancer patients on the metabolism of paclitaxel chemotherapy drugs under ultrasound guidance. By retrospectively analyzing the clinical data of 120 patients, we found that psychological resilience was significantly correlated with the pharmacokinetic parameters (AUC, clearance rate, half-life) of paclitaxel, and this association showed heterogeneity in different molecular subtypes. Patients in the high psychological resilience group showed a lower paclitaxel AUC and a higher clearance rate, suggesting a stronger ability to metabolize paclitaxel. Under the state

of stress, a series of changes occur in the endocrine system of the body, including the activation of the two main physiological systems [13]: the hypothalamic-pituitary-adrenal cortex (HPA) axis and the sympathetic-adrenal medulla (SAM) axis. The norepinephrine and a large amount of catecholamine hormones released by SAM put the body in an alert state, manifested as an increased heart rate, increased cardiac output, elevated blood pressure, and a redistribution of blood volume throughout the body (reduced blood flow to the skin, mucous membranes, and internal organs, and increased blood flow to the heart, brain, and skeletal muscles) [14]. This is consistent with the increase in blood pressure in the low psychological resilience group in the results of this study. On the other hand, the endocrine system also responds to acute stress by activating the HPA axis, and then releases cortisol from the adrenal cortex. The endocrine system responds to psychological stress by activating the HPA axis, prompting the adrenal cortex to release cortisol. Cortisol regulates the expression of the *CYP3A4* gene in the liver through the glucocorticoid receptor (GR), thereby affecting systemic drug metabolism [15]. However, under the local administration mode of intratumoral injection of paclitaxel under ultrasound guidance, the pharmacokinetics of the drug show significant differences:

1) Local retention effect dominates the drug efficacy:

The hydrophobicity of paclitaxel prolongs its retention time in tumor tissues, and only a small amount slowly penetrates the systemic circulation through capillaries [16]. Therefore, the contribution of liver metabolism to overall drug clearance is significantly reduced.

2) Psychological resilience affects local efficacy and systemic leakage:

- Patients in the high psychological resilience group had stable HPA axis function and less fluctuation in cortisol levels. The local drug distribution might be optimized through the following mechanisms: enhancing the normalization of tumor blood vessels and reducing drug extravasation into the systemic circulation [17]. Regulate the tumor microenvironment (such as reducing IL-6) and decrease inflammation-mediated drug clearance [18].
- In the low psychological resilience group, the imbalance of the HPA axis led to the disorder of the cortisol rhythm, causing the following phenomena: the local efficacy was reduced because the vascular permeability of the tumor increased, and paclitaxel leaked into the systemic blood more quickly [19]. The drugs that penetrate the whole body are metabolized by CYP3A4, resulting in an increase in ALT levels and an increased burden on liver metabolism.

Psychological resilience has a positive impact on the physical and mental health of patients. During chemotherapy, patients with high psychological resilience can better cope with the physical discomfort and emotional fluctuations brought about by treatment, reduce the occurrence of negative emotions such as anxiety and depression, and improve treatment compliance. Psychological resilience reduces the levels of inflammatory factors (such as IL-6) by inhibiting the excessive activation of the HPA axis and reducing the abnormal release of cortisol [18]. It is known that IL-6 can induce fatigue and pain sensitization [20], which explains the phenomenon that the fatigue and pain scores are lower in the high-elasticity group. High AUC means longer systemic drug exposure, directly leading to an increased risk of bone mar-

row suppression (such as leukopenia) [21] and neurotoxicity [22]. Multiple regression analysis revealed that for every 100 ng·h/mL increase in paclitaxel AUC_{0-10 h}, the QOL score decreased by 0.18 points. Combined with the negative correlation between psychological resilience and AUC, it is suggested that drug metabolism is the key mediating pathway through which psychological resilience affects the quality of life.

Furthermore, relevant studies have shown that insufficient social support is associated with an increased cancer mortality rate [23]. A study evaluated 79 lung cancer patients aged 65 and above who had completed the geriatric assessment (GA). The results showed that white ethnicity was positively correlated with ES scores, and higher BMI, depression, and anxiety were associated with poorer ES [24]. A higher BMI is associated with a higher/better TS score, and living alone is associated with a lower/poorer TS score. The completion of platinum-based dual-drug chemotherapy combined with immunotherapy, as planned was associated with higher ES and TS scores, and disease progression was associated with lower ES scores. This indicates that social support may affect the clinical outcomes of elderly patients with lung cancer. Given that the prognosis of lung cancer is often poor, social support may be an important prognostic indicator. In the future, the combined role of social support and psychological resilience in the treatment and prognosis of elderly patients with lung cancer can be further explored.

From a clinical perspective, the CD-RISC scale could serve as a simple, cost-effective tool for risk stratification. Patients identified with low resilience pre-chemotherapy could be prioritized for targeted psychosocial interventions, such as cognitive-behavioral therapy or mindfulness-based stress reduction, which are known to enhance resilience skills [citation]. Furthermore, for these high-risk patients, clinicians could consider more intensive supportive care measures, such as proactive management of expected side effects, more frequent follow-up, or even consultation with clinical pharmacology services to optimize drug dosing based on anticipated metabolic differences. This approach aligns with the movement toward personalized, whole-person cancer care.

Despite the intriguing findings, this study has several limitations. First, as a retrospective study conducted at a single institution, our patient cohort may have inherent homogeneity in terms of demographic characteristics, standardized treatment protocols, and socioeconomic status. This may limit the generalizability of our findings to broader, more diverse populations. However, this design was instrumental in ensuring a high level of internal validity by minimizing inter-institutional variations in nursing care and data collection procedures. Second, the measurement of systemic blood drug concentration, while standardized, cannot fully represent the intratumoral drug metabolism and distribution, which is the ultimate determinant of therapeutic efficacy. The association between local drug uptake and psychological factors remains a critical black box to be opened.

Building upon these limitations, we propose two primary directions for future research:

- 1) Multi-center validation: A prospective, multi-center study is essential to verify the universality of our findings across different healthcare systems and cultural

contexts. This will help establish whether psychological resilience exerts a consistent influence on drug pharmacokinetics.

- 2) Exploring local mechanisms: Future investigations should employ advanced techniques (e.g., dynamic contrast-enhanced ultrasound or analyses of biopsy specimens) to directly assess intratumoral drug concentrations and explore their correlation with systemic levels of stress hormones (e.g., cortisol) and psychological resilience scores. This will be crucial for elucidating the precise biological pathway through which the mind influences the body at the disease site.

In conclusion, this study, despite its single-center nature, reveals the significant role of psychological resilience as a regulatory factor of paclitaxel metabolism in breast cancer patients, providing empirical evidence for the application of the “bio-psycho-social” medical model in tumor treatment. It establishes a novel paradigm for precision medicine by translating psychological resilience, a “psychological energy indicator,” into quantifiable pharmacokinetic regulatory parameters. To translate this paradigm into broader clinical practice, its generalizability must be confirmed in diverse populations through multi-center collaborations, and the underlying local pharmacological mechanisms must be further dissected.

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Ethical approval: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of Clinical Trial Ethics Committee of Nanchong Shunqing District Maternal and Child Health Care Hospital (protocol code KN2025188 and date of approval 25 May 2025).

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