Research Progress on Integrated Traditional Chinese and Western Medicine Diagnosis and Treatment of Chronic Critical Illness: Postprint

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Abstract

Chronic critical illness (CCI) is a clinical syndrome in which critically ill patients, after surviving the acute life-threatening phase, still require prolonged life support, and is characterized by high morbidity and high mortality. Modern medicine attributes its core mechanism to the persistent inflammation–immunosuppression–catabolism syndrome (PICS), whereas traditional Chinese medicine (TCM) classifies it under the categories of "deficiency taxation (xulao)" and "collapse syndrome (tuozheng)," considering its fundamental pathogenesis to be "root deficiency with excess in the manifestation," with debilitation of vital qi as the root and toxin, blood stasis, and phlegm as the manifestations. Western medical treatment mainly consists of interventions such as immunomodulation, nutritional support, and rehabilitation therapy. TCM treatment takes pattern differentiation according to the eight guiding principles as the overarching framework, and comprehensively applies zang-fu pattern differentiation, qi-blood-body fluids pattern differentiation, and pattern differentiation based on the six meridians and the defense-qi-nutrient-blood systems, supplemented by characteristic therapies such as acupuncture and external treatments. On this basis, this article further proposes that future efforts should focus on exploring an integrated diagnostic and therapeutic model combining Chinese and Western medicine. Through approaches such as integrating disease diagnosis with TCM pattern identification, promoting synergy between Chinese and Western medicines, and incorporating non-pharmacological therapies, the advantages of integrative Chinese and Western medicine can be fully leveraged to provide patients with more comprehensive diagnostic and therapeutic regimens, thereby improving prognosis and enhancing quality of life.

Full Text

1.1 Epidemiological Characteristics

The prevalence of chronic critical illness (CCI) continues to rise globally, characterized by high mortality, poor long-term prognosis, numerous complications, complex treatment requirements, and a severe imbalance between survival benefits and healthcare resource investment, making it an extremely challenging clinical syndrome in critical care medicine. Kahn et al. analyzed 3,235,741 ICU patients in the United States from 2004–2009 and found that 7.6% met criteria for CCI, with an in-hospital mortality rate as high as 39.5% and an associated increase in healthcare expenditures of approximately $25 billion. Japanese studies showed that CCI patients accounted for about 9.0% of ICU patients from 2011–2018, with in-hospital mortality rates of 28.2%–30.6% and healthcare costs reaching 2.3–2.7 billion USD. Canadian research confirmed that one-sixth of ICU patients developed persistent critical illness, with a 54% increased risk of death compared to patients without persistent critical illness. Spanish studies on trauma patients indicated that 14% of ICU trauma patients progressed to CCI, with significantly prolonged ICU stays and markedly elevated mortality rates. Although large-scale epidemiological data are lacking in China, existing studies reveal a grim situation. Li et al. conducted a multicenter cross-sectional study of ICU patients across 53 hospitals in China on a single day and found that CCI patients accounted for 30.7% (145/472) of the cohort. Zheng et al. conducted a study involving 34 hospitals across 12 provinces in China and found that CCI patients comprised approximately 26.89% of ICU patients, with 59% experiencing multiple organ failure, 58% having multidrug-resistant bacterial infections, and 36% developing sepsis—all significantly higher than in non-CCI patients.

1.2 Diagnostic Criteria and Clinical Manifestations

CCI was first proposed by Girard et al. in 1985, referring to critically ill patients who, after acute-phase treatment in the ICU, remain dependent on long-term life support and whose condition progresses to a chronic stage. For decades, significant differences have existed in academic definitions of CCI. Wiencke et al. summarized findings showing that some studies defined CCI as ICU patients requiring mechanical ventilation for more than 21 days, while others used tracheostomy status or ICU length of stay as criteria, driving exploration for standardized definitions. In 2014, the Research Triangle Institute (RTI) developed a preliminary CCI definition based on U.S. healthcare data, which has been adopted by many subsequent epidemiological surveys and clinical studies. The RTI definition requires ICU stay exceeding 8 days plus at least one of the following clinical manifestations: prolonged mechanical ventilation (96 hours of continuous ventilation), tracheostomy, sepsis and severe infection, severe trauma, or presence of multiple organ failure, ischemic stroke, intracerebral hemorrhage, or traumatic brain injury. In 2017, Loss et al. concluded that pre-

vious scholars' CCI criteria were all based on a certain length of hospital stay combined with severe organ dysfunction. In 2019, Gardner et al. enriched the diagnostic criteria by refining organ function assessment standards, proposing that patients with persistent organ dysfunction for at least 14 days in the ICU —defined as having one or more abnormal Sequential Organ Failure Assessment (SOFA) scores on day 14 (cardiovascular score 1 or any other organ score 2) —be diagnosed with CCI. Additionally, patients with less than 14 days of ICU stay but persistent organ dysfunction at discharge who were transferred to hospice or other acute care facilities were also included in the diagnostic scope. With deeper understanding of disease characteristics, Chinese experts proposed the new concept of "extensive chronic critical illness (ECCI)" in 2024, referring to patients simultaneously exhibiting five features: disease severity, manifestation diversity, treatment difficulty, prolonged course, and recurrent condition. ECCI breaks through the ICU confinement of CCI diagnosis and extends to a common state of deterioration in chronic patients across various specialties, providing new perspectives for establishing interdisciplinary collaborative diagnosis and treatment systems. Currently, the 2014 RTI and 2019 Gardner criteria are widely adopted, while the newly proposed 2024 Chinese ECCI concept has also attracted extensive attention in the critical care field. The diagnostic procedures are illustrated in Figure 1 [Figure 1: see original paper].

CCI patients exhibit diverse clinical manifestations. Beyond features of the primary disease, they universally show increased susceptibility to infection, multiple organ dysfunction, brain and cognitive abnormalities, and malnutrition. Nelson et al. summarized the core features as ventilator dependence, brain dysfunction, neuromuscular weakness, endocrine and metabolic disorders, malnutrition, impaired skin barriers, and persistent distress symptoms. Additionally, patients often develop post-intensive care syndrome, encompassing physical, cognitive, and psychological impairments including ICU-acquired weakness, swallowing and neuromuscular dysfunction, memory decline, delirium, anxiety, depression, and post-traumatic stress disorder. CCI primarily focuses on somatic symptoms, emphasizing long-term mechanical ventilation and multiple organ dysfunction, further highlighting the chronic and complex nature of the disease, which aligns closely with the characteristics of prolonged course and recurrent condition in China' s "Expert Consensus on Extensive Chronic Critical Illness." These clinical features, together with the required ICU stay duration and series of clinical manifestations in the diagnostic criteria, demonstrate close intrinsic associations.

1.3 Risk Factors and Pathogenesis

Studies indicate that advanced age, sepsis, mechanical ventilation, persistent inflammation, abnormal metabolic indicators, and low immune markers are independent predictors for CCI development and poor prognosis. Mechanical ventilation (OR=3.047, 95%CI=2.303–4.032, P<0.001), elevated temperature (OR=1.493, 95%CI=1.352–1.648, P<0.001), and increased lactate (OR=1.184,

95%CI=1.145-1.224, P<0.001) significantly increase the risk of secondary CCI in elderly sepsis patients, while appropriate antibiotic use (OR=0.348, 95%CI=0.282-0.428, P<0.001) is associated with reduced risk. Elevated APACHE II scores (OR=1.039, 95%CI=1.004-1.074, P=0.027), multiple comorbidities (OR=1.866, 95%CI=1.443-2.412, P<0.001), concurrent infection (OR=3.637, 95%CI=1.995-6.629, P<0.001), thrombocytopenia (OR=0.358, 95%CI=0.209-0.612, P<0.001), and low lymphocyte counts (OR=0.994, 95%CI=0.991-0.997, P<0.001) are also important predictive factors. Loss et al. found that beyond abnormal BMI, mechanical ventilation, sepsis, abnormal Glasgow Coma Scale scores, and inadequate nutrition in the first 7 days, pre-existing neuromuscular disease (OR=4.21, 95%CI=1.63-10.9, P=0.003) may be an early predictor of CCI. Regarding prognosis assessment, Zhao et al. confirmed that mechanical ventilation (OR=4.433, 95%CI=2.192-8.963, P<0.001), elevated mean arterial pressure (OR=4.472, 95%CI=2.156-9.276, P<0.001), and increased respiratory rate (OR=3.364, 95%CI=1.705-6.639, P<0.001) are highly associated with poor outcomes. A prediction model based on these indicators demonstrated excellent performance (development cohort AUC=0.934, 95%CI=0.908-0.960; validation cohort AUC=0.965, 95%CI=0.931-0.999), significantly outperforming traditional scoring systems and facilitating early identification of high-risk patients for targeted interventions to improve prognosis.

From a pathogenesis perspective, persistent inflammation-immunosuppression-catabolism syndrome (PICS) is currently considered the core pathophysiological mechanism of CCI. Its essence is a vicious cycle of interaction among organ dysfunction, inflammatory response, and catabolism, directly leading to pathological changes such as sarcopenia and immunosuppression, and further triggering secondary consequences including recurrent infections, metabolic disorders, and bone marrow dysfunction. During the progression of critical illness, early intense inflammatory responses can induce multiple organ failure (MOF). Although intensive care technology has significantly reduced early mortality in MOF patients, some survivors enter a PICS state due to persistent immunosuppression and incomplete organ function recovery. This state continuously reinforces itself through the vicious cycle of "inflammation, immunity, and metabolism," ultimately driving disease progression to CCI.

Additionally, the "CCI pathogenesis theory"proposed by the U.S. Sepsis and Critical Illness Research Center in 2018, centered on damage-associated molecular patterns (DAMPs), has also received widespread attention. DAMPs are non-microbial molecules from the cell nucleus or cytoplasm released after host cell damage, which trigger non-infectious inflammatory responses by activating the immune system, leading to systemic inflammation, organ injury, and even death. Meanwhile, when pathogen-associated molecular patterns (PAMPs) trigger inflammatory responses through Toll-like receptors, pro-inflammatory cytokines such as IL-1 and IL-6 can clear pathogens but also cause tissue damage, leading to continuous DAMPs release and forming a "inflammation-injury-inflammation" vicious cycle that drives progression from acute infection to CCI. For exam-

ple, after traumatic injury, mitochondrial DNA as a typical DAMP exacerbates immune dysregulation through activation of the cGAS-STING signaling pathway, further resulting in hyper-catabolic and hyper-metabolic states that cause comprehensive failure of the patient' s immune and metabolic systems, necessitating dependence on extracorporeal life support and entry into a CCI state. The development and progression of PICS are closely related to the vicious cycle and functional exhaustion among inflammation, immunity, and metabolism triggered by continuous DAMPs release (Figure 2 [Figure 2: see original paper]).

2.1 Traditional Chinese Medicine Disease Name

As a clinical syndrome proposed by modern medicine, CCI' s dual attributes of "chronicity"and "critical illness"align with the TCM understanding of "prolonged disease inevitably leads to deficiency, extreme deficiency causes damage"and the critical state of "Yin-Yang separation and essence depletion." Although TCM has no direct corresponding disease name, based on the cognitive methods of "inferring internal conditions from external signs and categorizing by analogy," we can construct a TCM explanatory framework "centered on consumptive disease with multiple disease categories" from its characteristics of long-term life support dependence, multi-organ functional decline, recurrent condition, and mixed deficiency-excess patterns, laying a theoretical foundation for subsequent syndrome differentiation and treatment from multiple dimensions including Zang-fu organs, Qi-blood-fluid, and six meridians.

"Xulao" (consumptive disease), as the overarching category for various chronic deficiency syndromes, has a pathological core of Qi-blood-Yin-Yang deficiency and Zang-fu organ functional decline, which highly matches the essence of CCI—exhaustion of vital Qi and prolonged non-healing. The *Suwen · Tongping Xushi Lun* states, "When essence and Qi are taken away, there is deficiency," where the character "taken away" vividly summarizes the process of acute vital Qi consumption. The *Yizong Jinjian* further clarifies: "Deficiency refers to insufficiency of Yin-Yang, Qi-blood, nutrition-defense, essence-spirit, bone marrow, and fluids; damage refers to consumption of external skin, vessels, flesh, tendons, and bones, and internal lung, heart, spleen, liver, and kidney," elucidating the evolution from Qi-blood-fluid deficiency to Zang-fu organ structural damage.

Furthermore, the core contradictions vary across different CCI stages, often manifesting as multiple disease categories coexisting. For instance, consciousness disturbance belongs to "Jue syndrome" (reversal syndrome), acute deterioration to multiple organ failure constitutes "Tuo syndrome" (collapse syndrome), ventilator dependence falls under "Chuan syndrome" (panting syndrome), ICU-acquired weakness resembles "Wei disease" (flaccidity syndrome), and various bleeding tendencies belong to "Xue syndrome" (blood syndrome). This "one disease, multiple syndromes" model not only reflects TCM' s dynamic grasp of pathological priorities at different disease stages but also suggests that clinical practice requires further syndrome differentiation based on overall disease identification, such as using Zang-fu organ syndrome differentiation to treat

"Xulao," "Chuan syndrome," and "Wei disease," Qi-blood-fluid syndrome differentiation for "Xue syndrome," and six-meridian and Wei-Qi-Ying-Xue syndrome differentiation for critical conditions like "Jue syndrome" and "Tuo syndrome."

2.2 Traditional Chinese Medicine Etiology and Pathogenesis

The TCM etiology of CCI can be summarized into three categories: external contraction, internal injury, and iatrogenic factors. External contraction primarily involves warm-epidemic toxins that penetrate into the nutrient-blood level, consuming genuine Yin and sinking into Zang-fu organs, serving as the initiating factor. Internal injury mainly results from prolonged severe diseases leading to exhaustion of genuine Qi in the five Zang organs and loss of Qi-blood-fluid generation, representing the internal basis for disease occurrence. Iatrogenic factors include surgical trauma, mechanical ventilation-induced Qi consumption, and Qi stagnation-blood stasis from prolonged bed rest, further exacerbating vital Qi deficiency and meridian obstruction. These three categories of etiological factors intertwine and collectively contribute to disease development.

Under these etiological factors, CCI develops a core pathogenesis of "deficiency in root and excess in branch," with overall Eight-Principle attributes of mixed deficiency-excess, intermingled cold-heat, and simultaneous interior-exterior disease. Deficiency involves comprehensive Qi-blood-Yin-Yang deficiency, while excess involves phlegm-turbidity, blood stasis, and toxin accumulation; cold manifests as Yang Qi decline, while heat represents toxin hyperactivity; the disease initially affects the lung-defense level, but over time penetrates internally to the five Zang organs. This Eight-Principle framework provides the basic structure for subsequent specific syndrome differentiation.

"Deficiency in root" is based on Qi-blood-Yin-Yang deficiency, with lung, spleen, and kidney as the core affected organs, representing the internal foundation for the disease' s prolonged and recurrent nature. "Excess in branch" refers to pathological products such as phlegm-turbidity, blood stasis, and heat-toxins generated on the basis of vital Qi deficiency. Between deficiency and excess forms a vicious cycle of "deficiency leading to excess, and excess pathogen injuring the genuine," further obstructing Qi flow and consuming Zang-fu organ function, constituting clinically common mixed deficiency-excess patterns such as Qi deficiency with blood stasis, Yin deficiency with heat-toxin, and Yang collapse with phlegm obstruction.

The pathological evolution often follows the transmission pattern from Qi to blood, from meridians to collaterals, and from one organ to multiple organs. The acute exacerbation phase commonly presents critical signs of "Jue syndrome" and "Tuo syndrome" with pathogen sinking and genuine deficiency, Yin-Yang separation, which in Eight-Principle terms mostly belong to interior-deficiency-cold or true deficiency with false heat patterns, closely related to six-meridian and Wei-Qi-Ying-Xue syndrome differentiation. The chronic persistent phase

is based on "Xulao," complicated by mixed deficiency-excess patterns such as "Chuan syndrome," "Wei disease," and "Xue syndrome," mostly characterized by coexistence of Zang-fu organ functional decline and Qi-blood-fluid disharmony. This dynamic evolution process reflects the complex interplay between continuous vital Qi consumption and pathogenic turbidity accumulation, providing the core pathological basis for subsequent "disease-syndrome combination and stage-based treatment" from the perspective of Eight-Principle syndrome differentiation combined with Zang-fu organs, Qi-blood-fluid, six meridians, and other multi-level approaches.

3.1.1 Immunometabolic Regulation and Nutritional Support

CCI clinical treatment faces major challenges, as its complex pathophysiological mechanisms make single-modality treatment difficult to achieve significant efficacy. The CHADDA team proposed a comprehensive intervention framework targeting the three core components of persistent inflammatory response, immunosuppression, and catabolism, using mitochondrial biogenesis activators and antioxidants to regulate excessive inflammation, myeloid-derived suppressor cell inhibitors and interferon- to reverse immunosuppression, and proteasome inhibitors combined with testosterone to improve catabolic imbalance, implementing treatment from multiple aspects including immunomodulation, anti-inflammatory and antioxidant therapy, early rehabilitation, and nutritional-metabolic support.

Nutritional support is a key measure to improve CCI patient outcomes. A multinational multicenter observational study covering 202 ICUs and 2,853 patients on mechanical ventilation for 4 days found that high-risk patients receiving high-calorie and high-protein intake protocols had reduced mortality and shorter hospital stays. Patients receiving high protein intake in the first 4 days after admission had a 7% reduced mortality risk (OR=0.93, 95%CI=0.89–0.98, P=0.003), which further decreased to 10% if continued for 12 days (OR=0.90, 95%CI=0.84–0.96, P=0.003). High energy intake showed similar trends, with mortality risk reductions of 7% in the first 4 days (OR=0.93, 95%CI=0.89–0.97, P<0.001) and 12% over 12 days (OR=0.88, 95%CI=0.83–0.94, P<0.001). This nutritional protocol was also associated with shorter hospital stays, with high protein intake shortening stays by 5% in surviving patients at 4 days (HR=1.05, 95%CI=1.01–1.09, P=0.01) and 9% at 12 days (HR=1.09, 95%CI=1.03–1.16, P=0.002). Zheng et al. systematically summarized CCI nutritional support strategies, including identifying high-risk patients, rational nutritional support, maintaining adequate protein intake, early mobilization as much as possible, and antibiotic stewardship, lung-protective strategies, and palliative care, emphasizing that CCI nutritional support must focus on protein supplementation while controlling initial calorie intake levels.

Additional research has conducted in-depth studies on CCI nutritional-metabolic therapy, indicating that combined supplementation of adequate

protein with immunonutrients has dual effects of regulating inflammatory response and enhancing anabolism, while recommending probiotic supplementation to improve intestinal microecological balance and early resistance training combined with high-protein diet to synergistically improve nutritional status and maintain long-term support effects. Studies show that combined supplementation of adequate protein with immunonutrients such as arginine and leucine can increase lymphocyte proliferation rate by 25%–30%, raise prealbumin levels by 20%–25%, and reduce pro-inflammatory cytokine levels by 25%–35%. Probiotic supplementation can increase beneficial gut bacteria abundance by over 40% and significantly improve nutritional indicators such as serum total protein and albumin. Early resistance training combined with high-protein diet can improve physiological function scores by 18%–22% and increase muscle fiber thickness by 10%–12% after 3–6 months, synergistically enhancing nutritional levels and maintaining long-term effects.

3.1.2 Multimodal Rehabilitation and Discharge Management

CCI patients often suffer from post-intensive care syndrome, manifesting as motor dysfunction, cognitive impairment, and psychological disorders. Renner et al. found that symptoms can appear within 48 hours of ICU admission and persist for 5–15 years, with 64% and 56% of ICU survivors having at least one functional impairment at 3 and 12 months, respectively, and 25% and 21% having two or more functional impairments. Based on these findings, their team developed multimodal rehabilitation guidelines for PICS patients, proposing systematic assessment of exercise capacity, cognitive function, and psychological status in CCI patients, improving motor function through early mobilization, emphasizing delirium prevention and treatment to improve cognitive impairment, and recommending tools such as ICU diaries for psychological reconstruction. Nelson et al. proposed five major therapeutic goal systems for comprehensive CCI patient care, including ventilator weaning, nutritional support, cognitive and functional recovery, complication prevention, and palliative care implementation, also emphasizing the importance of developing multimodal rehabilitation treatment plans. Muscle mass loss due to prolonged catabolism is a core pathological feature of CCI patients, and muscle dysfunction, due to its significant manifestation and slow recovery, often becomes a critical link in the rehabilitation process. For patients with ICU-acquired weakness, studies recommend a combined passive and active muscle rehabilitation strategy, encouraging patients to actively get out of bed for activities on the basis of bedside bicycle-assisted training to promote motor function recovery.

To improve CCI patient prognosis and quality of life, research teams have conducted more systematic and comprehensive explorations of CCI treatment models. Liu et al. used ECCI patient discharge as an entry point to construct a structured whole-course management plan, such as using evidence-based tools to quantitatively assess discharge indications, establishing ventilator configura-

tion standards and airway care training plans, introducing family collaborative operation assessment mechanisms, and strengthening out-of-hospital care connections through multi-mode follow-up systems combined with standardized guidelines and information technology integration. Additionally, studies found that only about 20% of CCI patients are discharged directly home, with the majority remaining in skilled nursing facilities or long-term acute care hospitals for subsequent care. Based on this, Lin et al. proposed a closed-loop whole-cycle management approach, advocating for policy support through improving respiratory therapist certification systems, constructing regional collaborative treatment networks, establishing coordinated diagnosis and treatment mechanisms between tertiary hospitals and primary institutions, and forming seamless management systems from in-hospital emergency care to community rehabilitation.

3.2 TCM Syndrome Differentiation and Treatment of CCI

CCI TCM treatment emphasizes "disease-syndrome combination," using Eight-Principle syndrome differentiation as the overarching framework. On the basis of clarifying the fundamental attributes of Yin-Yang, interior-exterior, cold-heat, and deficiency-excess, it comprehensively applies Zang-fu organ syndrome differentiation, Qi-blood-fluid syndrome differentiation, and six-meridian and Wei-Qi-Ying-Xue syndrome differentiation to form a hierarchical diagnosis and treatment system that addresses both root and branch.

3.2.1 Eight-Principle Syndrome Differentiation as the General Framework

Eight-Principle syndrome differentiation runs through the entire CCI diagnosis and treatment process. Yin-Yang differentiation is primary—the disease generally involves Yin-Yang disharmony, with Yin-Yang separation commonly seen in critical phases and dual Yin-Yang deficiency in persistent phases. Interior-exterior differentiation determines disease location—this disease belongs to interior patterns involving the five Zang organs, six Fu organs, Qi-blood, and marrow. Cold-heat differentiation clarifies disease nature—this disease shows intermingled cold-heat, with Yang Qi decline manifesting as cold limbs and toxin-heat accumulation manifesting as fever and restlessness. Deficiency-excess differentiation determines primary-secondary relationships—this disease shows mixed deficiency-excess, with genuine deficiency as the root and pathogenic excess as the branch. These Eight Principles guide subsequent specific differentiations: Zang-fu organ differentiation focuses on identifying interior deficiency locations, Qi-blood-fluid differentiation details the proportion of deficiency-excess, while six-meridian and Wei-Qi-Ying-Xue differentiation emphasize cold-heat transformation and disease depth.

3.2.2 Zang-Fu Organ Syndrome Differentiation

This differentiation applies to CCI patients with Zang-fu organ functional decline as the core pathogenesis, commonly seen in "Xulao," "Chuan syndrome," and "Wei disease," with lung, spleen, and kidney deficiency as the core. The lung governs Qi and respiration, the spleen is the source of Qi-blood generation, and the kidney governs Qi reception and essence storage. When these three organs are deficient, Qi has no source for generation and essence has no basis for transformation. Treatment should tonify lung, spleen, and kidney; boost Qi and nourish blood; and assist with phlegm-resolving, stasis-dispelling, and collateral-unblocking to restore flaccidity.

The *Nanjing· Shisi Nan* states: "For lung damage, tonify Qi; for spleen damage, regulate diet and adapt to cold-heat; for kidney damage, tonify essence," establishing the theoretical foundation for treating organ deficiency. The *Jingyue Quanshu· Chuangcu* states: "Excessive panting has pathogen, which is excess; deficient panting has no pathogen, which is vital Qi deficiency," requiring clinical differentiation of panting' s deficiency-excess priority, mostly related to lung, spleen, and kidney deficiency, with lung-spleen-kidney deficiency as the root and wind-phlegm-stasis as the branch. The treatment principle is to tonify lung, strengthen spleen, and benefit kidney to address the root, and to dispel wind, resolve phlegm, and remove stasis to address the branch. Xu et al., based on "Xulao" theory for treating ICU ventilator dependence, advocate adopting methods such as strengthening genuine Qi and dispelling pathogen, clearing and penetrating with tonification, tonifying lung and kidney with Qi-astringing and panting-stabilizing, resolving phlegm and removing stasis, soothing liver and nourishing heart, and calming with heavy sedatives, while simultaneously strengthening spleen-stomach and boosting Qi-blood, supplemented by external treatment and rehabilitation training to improve nutritional status and diaphragm function. "Wei disease" treatment can follow the principle of "treating flaccidity primarily through Yangming," using Huqian Pill combined with acupuncture to improve muscle strength in ICU-acquired weakness patients.

3.2.3 Qi-Blood-Fluid Syndrome Differentiation

This differentiation applies to patients with Qi deficiency-blood stasis and fluid depletion-phlegm coagulation as the main pathogenesis, commonly seen in sarcopenia, cognitive impairment, and delirium, belonging to "Xue syndrome,""Wei disease," and "Jue syndrome" categories. Qi-blood deficiency and phlegm-stasis intermingling are mutually causal, forming a complex state of genuine deficiency with pathogen lingering and mixed deficiency-excess, requiring treatment to boost Qi and activate blood, resolve phlegm and unblock collaterals, and open orifices to restore consciousness.

For example, bleeding complications belong to "Xue syndrome." Due to prolonged course, Qi-blood deficiency and bleeding are mutually causal—Qi fails to contain blood, exacerbating bleeding, while continuous bleeding further con-

sumes Qi-blood, forming a vicious cycle that worsens the condition. Treatment must address both root and branch by boosting Qi to contain blood, resolving stasis to stop bleeding, or clearing heat and cooling blood, thereby supporting genuine Qi to stop bleeding, dispelling stasis, and generating new blood. Historical physicians mostly treated consciousness disorders such as ischemic stroke from perspectives of external wind affecting collaterals, Qi deficiency-blood stasis, phlegm-stasis obstruction, and genuine decline with accumulation. Modern research using blood-activating and stasis-resolving, Qi-tonifying and blood-activating, blood-activating and stasis-resolving, and phlegm-resolving and Fu-organ-unblocking methods has achieved outstanding results.

3.2.4 Six-Meridian and Wei-Qi-Ying-Xue Syndrome Differentiation

This differentiation applies to CCI resulting from externally contracted febrile diseases, such as sepsis-related "Jue syndrome" and "Tuo syndrome," which in Eight-Principle terms mostly belong to interior-deficiency-cold or interior-excess-heat patterns, representing critical conditions of pathogen sinking with genuine deficiency and Yin-Yang separation. Clinically, we observe complex patterns such as lingering heat-toxin with Qi-Yin damage, or Yang collapse with phlegm obstruction, requiring treatment to clear residual pathogen, strengthen genuine Qi and consolidate collapse, while also addressing detoxification, Fu-organ-unblocking, and stasis resolution.

The *Sepsis TCM Syndrome Differentiation Diagnostic Criteria (2025)* classifies sepsis into excess and deficiency patterns, with excess patterns including phlegm-heat obstructing lung, intense heat-toxin, Yangming Fu-organ excess, and stasis-toxin obstructing collaterals, and deficiency patterns encompassing lung Qi deficiency, Yin deficiency with internal heat, Qi-blood dual deficiency, and Yin exhaustion with Yang collapse, providing standardized basis for six-meridian and Wei-Qi-Ying-Xue differentiation. The previously proposed "four patterns and four methods" classified sepsis into toxin-heat pattern, blood stasis pattern, acute deficiency pattern, and Fu-organ obstruction pattern, treated respectively with heat-clearing and toxin-resolving, blood-activating and stasis-resolving, genuine Qi-tonifying and root-consolidating, and interior-unblocking and purgation. Research indicates that the six-meridian differentiation system can systematically reveal the dynamic transmission pattern from exterior to interior and from Yang to Yin, while Wei-Qi-Ying-Xue differentiation excels at analyzing complex pathomechanisms such as "Qi-Ying dual disease," providing a clearer hierarchical framework for critical illnesses like sepsis when combined.

3.2.5 Application of Characteristic TCM Therapies in CCI

Characteristic TCM therapies include acupuncture, external TCM treatment, five-element music therapy, and traditional rehabilitation therapies. Through individualized syndrome differentiation and treatment combined with various characteristic therapies, TCM can improve nutritional status, prevent complications, and relieve anxiety in critically ill patients, holding important appli-

cation value in ICU management. In recent years, the implementation rate of appropriate TCM techniques has gradually increased. A survey of 256 ICU patients showed that the implementation rate of appropriate TCM techniques reached 95.31%, with press-needle, application therapy, auricular point pressing, and acupoint plaster ranking highest at 40.23%, 37.11%, 27.34%, and 26.95%, respectively, plus external TCM application, herbal fumigation-washing, and herbal hot compress therapies.

Acupuncture regulates Qi-blood-Yin-Yang through meridians and acupoints, serving as an important external treatment to improve CCI patient symptoms and functional status. Studies show that acupuncture can regulate immune function and improve inflammatory and immunosuppressive states, holding positive significance for delaying PICS progression. For sepsis' s complex immune dysregulation pathological features, electroacupuncture at Zusanli (ST36) can exert holistic regulation and dual-direction balancing effects throughout the disease course, suitable for complex pathomechanisms of genuine Qi deficiency with pathogen sinking. Additionally, acupuncture can promote immune balance and gastrointestinal function recovery, embodying the therapeutic characteristics of "regulating spleen-stomach, supplementing original Qi, and unblocking meridians and collaterals." External TCM treatment methods include herbal fumigation and application, allowing transdermal drug absorption to directly reach the lesion, beneficial for reducing local blood stasis and improving lower extremity deep venous blood circulation in ICU patients with outstanding efficacy. Five-element music therapy combined with auricular point pressing can shorten recovery time and improve sedation quality in ICU delirium patients. Traditional exercises such as Tai Chi and Baduanjin combined with breathing training help enhance patient constitution and promote functional recovery. These therapies have high safety and broad applicability, can be combined with internal administration and acupuncture in multimodal approaches, and can construct an integrated TCM-Western medicine collaborative rehabilitation system.

4 Prospects for Integrated TCM-Western Medicine Diagnosis and Treatment of CCI

CCI remains an incompletely conquered challenge in critical care medicine, with complex pathological mechanisms and poor clinical outcomes, posing continuous pressure on global public health. Currently, Western medicine has made certain progress in CCI diagnosis, pathogenesis, risk factors, and clinical management, while TCM has accumulated experience in syndrome differentiation, holistic regulation, and functional rehabilitation. However, neither has achieved ideal whole-course management within a single system. Therefore, constructing a new integrated TCM-Western medicine diagnosis and treatment model spanning "prevention-treatment-rehabilitation" is not only an urgent clinical need but also a strategic pathway to elevate CCI treatment levels.

4.1 Construction of Integrated TCM-Western Medicine Diagnosis and Treatment Model for CCI

Research shows that ICU patients receiving integrated TCM-Western medicine rehabilitation had shorter hospital stays [(8.76±0.97) days] and lower hospitalization costs [(6545.61±28.59) yuan] compared to control groups receiving conventional care [(13.24±1.32) days, (8786.34±33.42) yuan], with superior scores in nursing quality, nursing service capacity, and quality of life ($P<0.05$), demonstrating significant advantages of integrated rehabilitation in shortening hospital stays.

As an important challenge in critical care medicine, CCI' s high incidence and complex pathological mechanisms pose severe challenges to global healthcare systems. Western medicine plays an irreplaceable role in acute-phase CCI management, particularly in organ function maintenance, infection control, internal environment stabilization, and life support, with precise and rapid "branch-treating" advantages. However, Western medicine still has limitations in long-term functional recovery, immune homeostasis reconstruction, and overall condition regulation. TCM, focusing on the holistic perspective, enhances human genuine Qi through "supporting genuine and dispelling pathogen" strategies, holding "root-treating" strengths in improving internal environment, strengthening constitution, reducing complications, and promoting long-term rehabilitation. Constructing an integrated diagnosis and treatment model combining both can achieve whole-course, stratified intervention with "Western medicine as primary in acute phases, TCM-Western medicine equally important in stable phases," forming a complementary therapeutic pattern.

The integrated TCM-Western medicine model can be constructed through the following pathways (Figure 3 [Figure 3: see original paper]): First, promote the establishment of a "disease-syndrome combination" diagnostic system that integrates TCM syndrome differentiation into existing Western diagnostic and grading systems to form more refined patient stratification. Second, strengthen research on synergistic application of Chinese and Western medicines, focusing on key nodes in the inflammation-immunity-metabolism network to conduct studies on compatibility, dosage, and timing optimization of Chinese herbal formulas and Western drugs—using "anti-infection + heat-clearing and toxin-resolving, Fu-organ-unblocking" in acute phases, "nutritional support + spleen-strengthening and Qi-boosting, kidney-tonifying and essence-filling" in stable phases, and "rehabilitation training + blood-activating and stasis-resolving / tendon-strengthening and bone-fortifying" in rehabilitation stages to achieve stage-adapted, pattern-corresponding treatment. Third, deepen the integrated application of non-pharmacological therapies, incorporating acupuncture, external TCM treatment, and traditional exercises into rehabilitation pathways to synergize with Western rehabilitation techniques, forming a comprehensive treatment plan with both "pharmacological and non-pharmacological" approaches.

4.2 Challenges and Future Prospects

Although integrated TCM-Western medicine shows potential in CCI treatment, constructing such models still faces challenges including non-unified diagnostic standards, large individual differences, and lack of standardized treatment protocols. Non-unified diagnostic standards significantly increase study heterogeneity and hinder clinical intervention effect evaluation. Individual differences in multi-organ dysfunction make it difficult to form unified frameworks for pathological mechanism research. The standardization and normalization of integrated treatment protocols need improvement. In this context, constructing systematic new-era integrated TCM-Western medicine diagnosis and treatment models is not only an urgent clinical need but also a strategic pathway to elevate CCI treatment levels.

Future breakthroughs should focus on the following directions: In basic research, utilizing omics technologies and systems biology methods to deeply elucidate the multi-target regulatory mechanisms of Chinese medicine and acupuncture in immune, metabolic, and neuro-endocrine networks, providing scientific connotation for "disease-syndrome combination."In clinical research, actively conducting high-quality, multicenter randomized controlled trials to evaluate the impact of integrated models on patient survival, organ function recovery, and quality of life, gradually forming recommendations and pathways. In standardization and intelligentization, promoting the development of integrated diagnosis and treatment consensus and guidelines, and exploring the construction of AI-assisted diagnosis and treatment platforms that fuse Western objective indicators with TCM syndrome characteristics to achieve stratified diagnosis and prognosis prediction, driving the iterative evolution of the diagnosis and treatment system toward standardization and intelligence.

In summary, the integrated TCM-Western medicine diagnosis and treatment model provides a new paradigm for "prevention-treatment-rehabilitation" integrated management of CCI. Through deep integration of the advantages of both medical systems and construction of a whole-cycle intervention system with clear stages, distinct pathways, and TCM-Western medicine synergy, not only can we enhance overall rehabilitation and quality of life for CCI patients, but we can also contribute Chinese wisdom and solutions with distinctive features to the development of global critical care medicine.

Note: Figure translations are in progress. See original paper for figures.