REVIEW

Review, impact, and future of severe and extra-severe burn treatment in China

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ABSTRACT

China began using the colored liquid from tea and tincture to treat burns as early as the sixth century B.C., and records of Chinese medicine for the rescue and treatment of burns date from the Jin Dynasty to the Ming and Qing Dynasties. Modern burn treatment medicine in China began in 1958 when national steel production began. Since then, burn patients have increased dramatically, independent burn departments have been established nationwide, and burn surgery has moved into technological development. With the combined efforts of several generations of burn medical workers in China, the clinical treatment of severe and extra-severe burns has steadily increased. Many fields, such as burn shock prevention and treatment, wound repair, and sepsis, have become world leaders in the 21^{st} century, forming a treatment technology and theoretical system with distinctive Chinese characteristics. Burn medical professionals have conducted numerous clinical and fundamental experimental studies, founded the Burns Surgery Branch of the Chinese Medical Association, established academic journals, and successfully established China Burn Treatment Program. The advancement of science and technology has promoted the development of modern medicine, and 3D virtual reality technology, 3D printing technology, organoid culture, and tissue engineering skin have demonstrated potential advantages and excellent application prospects in the treatment of severe burns, providing new ideas and directions for the discipline's development. In the new journey of development and reform, we should continue to strengthen the systematic construction of the discipline, enhance the innovative treatment capability, and create further triumph.

Key Words: Severe burns, History, Achievements, Shock, Wound repair, Sepsis, Disciplinary development

1. INTRODUCTION

Over the past 74 years, burn surgery in China has developed rapidly. The clinical cure rate of extensive burns consistently ranks among the world's highest, and theoretical research on burns is among the most advanced.[1] Burn injury is a common trauma-like disease, the fourth most common injury in the world, and is one of the most dangerous causes of threats to human life and health, mental health, and disability, both in peacetime and wartime. Despite decreased burns due to modern society's development, significant and severe burns, group injuries, and particular burns occasionally complicate burn treatment. According to the WHO, about 11 million burn patients and about 180,000 deaths worldwide yearly. Complications such as shock, sepsis, and multi-organ failure are important causes of burn deaths.[2,3]

Extensive burns typically refer to patients with severe and

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extra-severe burns in the burn specialty. Severe trauma or inhalation injury, chemical burns, and high-voltage electrical burns complicate severe burns. There are burns identified in the literature as having 30% TBSA (total body surface area), 40%, and more than 50% as large-area burns, and in most of the literature, extensive burns are those with an area greater than 50%.[4, 5]

2. An overview of the history of burn surgery in China

Since fire discovery, burns have been associated with humanity, and the first records date back to 3500 B.C. petroglyphs on Neanderthal cave walls.[7] In the sixth century B.C., the Chinese extracted colored juices and tinctures from tea leaves for burn treatment.[8] In 300 A.D., it was recorded in Ge Hong's "The Handbook of Prescriptions for Emergencies" of the Jin Dynasty that "scalding and fire burns are treated by applying aged lime, or by adding oil and tincture." The experience of treating burns has also been recorded in Liu Juanzi's "Liu Juanzi's Ghost Legacy Formula" in the Southern Qi Dynasty, Sun Simiao's "Important Prescriptions Worth a Thousand Gold for Emergency" in the Tang Dynasty, Chen Shiduo's "Surgical Secrets" of Qing Dynasty, and Wu Qian's "Medical Zong Jinjian (Essentials of Surgical Heart Method," and traditional Chinese medicine has long played a significant role in the treatment of burns in modern Chinese medicine.[9] New medical theories emerged along with the development of modern burn surgery, and new medical theories were enlightened. In 1933, an article on burns and tannins was published in volume 19 of "The National Medical Journal of China." In 1946, in volume 32, in the article "Progress in Surgery in the last decade" written by Shen Kefei and others, burn-related contents such as burn rehydration, wound medication, flesh grafting, and skin removal knives were introduced.[10]

As a milestone in the history of burn surgery, Dr. Everett Evans established the first actual burn unit in 1947 in Virginia, followed in 1949 by the establishment of the first burn center in the world, the "U.S. Army Burn Center" in Texas, USA, marking the establishment of the world's burn department.[11] After the outbreak of the war to resist U.S. aid to North Korea, the treatment of burn injuries by volunteer soldiers prompted burn research work in China. In 1952, the Peking Union Medical College and other schools opened a burn plastic training course, and the Academy of Military Medical Sciences established a burn research group.[1] In 1954, the Surgical Society of the Shanghai Branch of the Chinese Medical Association published a "comprehensive report on burns" in the 4^{th} issue of the "Chinese Journal of Surgery," introducing the experience of 1,021 burn cases treated in 10 hospitals in Shanghai.[12]

In 1958, the national steel making, burn patients dramatically increased, Shanghai Guangci Hospital (now Ruijin Hospital) successfully treated Qiu Cai Kang, a steelworker with "89.3% burn area and 22% of third-degree burn area,"[10] breaking the foreign claim that "total burn area over 80% cannot be cured" at that time, having begun the successful treatment of extensive burns in China, burn surgery has been developed rapidly throughout the country, independent burn centers have been established, and burn surgery has stepped into the track of specialty development.[13, 14] In 1959, Shanghai Guangci Hospital (now Ruijin Hospital) established the surgical technique of combining large allogeneic (seed) skin openings with tiny autologous skin slice inlays. In 1966, a patient with a total burn area of 98% and a third-degree burn area of 90% was successfully treated using this method, which was gradually promoted clinically and internationally as the "Chinese method" and established its prominent position in domestic and international burn treatment.[15] In the same year, Shanghai Guangci Hospital (now Ruijin Hospital) applied hibernation drugs to assist in the treatment of the shock period and received better results, forming the "hibernation therapy," which effectively reduced the post-burn stress reaction and facilitated the early treatment of critical burns, and simultaneously published the first burn monograph "Treatment of Severe Burns" in China. In October of the same year, the Changhai Hospital of the Second Military Medical University published the "Handbook of Burn Treatment," which promoted the popularization of burn treatment.[16] In 1961, the Department of Histology and Embryology of the Seventh Military Medical University (currently the Army Military Medical University) made simpler the "Chinese nine-point method" for estimating the burned area of Chinese people based on measurements of 450 young and strong men and women.[10] In 1962, at the Third Military Medical University (now Army Military Medical University), the All-Army Burn Specialized Group (later renamed the Burn Specialized Committee) was established. Based on 147 cases of early rehydration in adult patients with severe burns, the "San Medical University formula" for burn fluid rehydration was summarized in the same year.[17] In 1964, the Ruijin Hospital compiled data on rehydration during shock in 600 patients without respiratory burns or other complications. It proposed the "Ruijin formula" for fluid resuscitation in burn shock.[10]

The 1970s National Burn Conference in Shanghai was a significant indicator of the development of modern burn surgery in China. The conference established the "Chinese nine-point method" and the "palm method" for uncomplicated calculations of the burn area, the "third-degree and fourth-degree burn" for classifying burn depth, as well as the classification standard for burn severity. Based on the burn area and body weight as measurement parameters, a general formula for rehydration during burn shock has been established and widely accepted by domestic counterparts in this conference.[10] In the 1990s, the classification of burn depth was revised to "fourth degrees and five divisions."[18,19] The criteria for severe burns are a total area of 31%-50%, a third-degree burn area of 10%-19%, or a burn area of less than 31% with one of the following conditions: (1) severe systemic condition or shock; (2) compound injuries (severe trauma, impact injury, radiation injury, chemical poisoning); and (3) moderate or severe respiratory burns. Extra-severe burns are defined by a total area of at least 50% or a third-degree burn area of at least 20%. In 2006, Yang Zongcheng modified the classification of burn severity in "burn therapy" by defining severe burns as a total area of 51%-80%; deep second and third-degree burn areas of more than 10%; or burn areas of less than 51% but combined with serious combined injuries or complications, and destructive electrical burns, phosphorus burns. Extra-severe burns have a total surface area of 80% or more and are typically accompanied by severe combined injuries or sequelae.[18–20] Common terms for large-area burns are severe and Extra-severe burns.

In 1972, the 304th Hospital of the People's Liberation Army (now the 4th Medical Center of the PLA General Hospital) was the first to establish a skin bank with liquid nitrogen cryogenic storage. Cryogenic refrigerators (-80°C) or liquid nitrogen skin banks were successively established in burn centers across the nation in the 1980s, which significantly improved the success rate of cryopreservation of skin.[21] In 1973, Beijing Jishuitan Hospital successfully treated Jiang Chunlan, a two-year-old whose total burn area reached 98% and 94% of the third-degree burn area, creating a miracle in the annals of burn medicine.[22] In 1978, the Third Military Medical University (now Army Military Medical University) spearheaded the Institute of Burn Injury formation and researched inhalation injury and burn infection. Subsequently, burn treatment centers across the nation established laboratories one by one and conducted a series of studies on early burn damage, shock, infection, wound repair, skin storage, inhalation injury, organ damage, immunity, metabolic nutrition, etc., yielding a wealth of research results.[10,11] Sheng Zhiyong et al. introduced "scab cutting in the shock period" for the first time in 1979. Guo Zhenrong and Sheng Zhiyong used Swan-Ganz catheter hemodynamic testing to perform surgical scabbing during the shock period within 48 hours after injury in 1986, achieving better results and conducting many clinical and experimental investigations.[23] Changhai Hospital of Naval Military Medical University was the first institution in China to research epidermal cell culture and use a combination of autologous and allogeneic epidermal cell culture membranes to repair third-degree burn lesions in 1987.[24,25]

In 2004, HUMECA of the Netherlands demonstrated the MEEK skin grafting technique at the Wuhan National Burn Symposium. In 2005, Nanjing Gulou Hospital was the first to apply the technique, which provided a new method for repairing large, deep burn wounds by alleviating the shortage of skin sources in the skin donor region. The MEEK micro dermal grafting technique is a new autologous skin grafting technique for repairing large deep burn wounds, following the large allogeneic (seed) skin open hole autologous small skin grafting and autologous micro dermal grafting.[26,27]

In 1985, the former Third Military Medical University, the Second Military Medical University, the Fourth Military Medical University, the PLA General Hospital, and the 159th Hospital of the PLA received the first Prize in National Science and Technology Progress for their "Study of Burns" project. The first significant project of the National Natural Science Foundation of China, chaired by Li Ao and Shi Jixiang and titled "Study of Early Pathogenesis of Burns and Wound Healing" which promoted the clinical development of burn surgery, received multiple scientific and technological awards in 1991. "Basic and Clinical Research on Systemic Inflammatory Reaction and Sepsis after Burns" declared by Chai Jiake, Sheng Zhiyong, and Xia Zhaofan of the Changhai Hospital of the Second Military Medical University won the first prize of National Science and Technology Progress in 2002. In 2015, the PLA General Hospital research project "nnovative Theory and Key Measures for the Development of New Characteristics and Prevention of Difficult-to-heal Wounds on Chinese Body Surface" led by Fu Xiaobing was awarded the First Prize in National Science and Technology Progress. Shi Jixiang and Li Ao were awarded the Evans Award by the American Burn Society in 1988 and 1994, respectively, specifically for foreign burn specialists in recognition of their achievements in burn surgery. In 1983, the Burns and Plastic Surgery Group of the Chinese Medical Association Branch of Surgery was established, and in 1986, the Chinese Medical Association Branch of Burns Surgery was founded. In 1985, the "Chinese Journal of Plastic and Burn Surgery" was established; in 2000, it was split into the "Chinese Journal of Plastic Surgery" and the "Chinese Journal of Burns," and in 2022, it was renamed the "Chinese Journal of Burns and Wounds." In 2006, the "Chinese Journal of Injury Repair and Wound Healing (electronic version)" was established. In 2013, the Southwest Hospital of Army Medical University established "Burns & Trauma," an internationally oriented English SCI journal for burn specialties with an impact factor of 5.71. These most prestigious academic journals in the field of burns have played a significant role in advancing burn surgery.[10]

In the 21st century, new technologies and methods have been continuously applied to clinical practice, resulting in significant advancements in all aspects of shock resuscitation and complication prevention, respiratory support and management, metabolic and nutritional support, infection control and immune regulation, and rehabilitation and functional reconstruction. With the rapid development of molecular biology and skin tissue engineering, new dressings, cell growth factors, tissue-engineered skin, and stem cells in burn wound repair have made significant strides. The total treatment capacity for extensive burns has been further enhanced.[10,28,29] Through the efforts of several generations of burn medical workers in China, a great deal of basic medical research has been completed, and fruitful results have been obtained; the clinical treatment level has been continuously improved, a large number of patients with severe burns have been successfully treated, rich experience has been accumulated, a complete set of burn treatment theory and technology with our characteristics has been developed, and a Chinese treatment system for burns has been established. It has enriched the world's burn medicinal treasure trove.[30]

3. China's significant achievements in the rescue and treatment of large-area burns

3.1 Comprehensive measures for the prevention and treatment of shock

Burn shock is one of the most significant complications of severe burns, and prevention and treatment of shock are administered throughout the entirety of the burn treatment process. Shock is the body's response to a reduction in adequate circulating blood volume, which is a pathological process of metabolic and cellular injury resulting from inadequate tissue perfusion. The focus of the prevention and treatment of early burn shock is timely and effective rehydration, with fluid therapy as the core of the more developed treatment measures, using the rehydration formula to calculate the estimated amount of rehydration, along with clinical monitoring indicators for adjustment, individualized treatment. The focus of rehydration is on "quantity," and the characteristics of rehydration are on "quality," restoring adequate circulating blood volume, enhancing microcirculation and tissue metabolism, and allowing patients to pass the shock period without incident.[31] Shen Chuanan[32] proposed the "ten-fold rehydration formula for prehospital emergency resuscitation of adults with large-area burns," which is: rehydration rate (%TBSA/ml/h) = total burn area (%TBSA) $\times$ 10 (ml/h), and the recommended fluid for infusion is an electrolyte solution such as sodium lactate Ringer's solution. This formula is straightforward to calculate and is ideally suited for use by non-specialists in burn care for the prehospital resuscitation of adults with extensive burns, particularly in groups of burn patients, and can enhance the quality of prehospital care.[33]

Burn shock is caused not only by hypovolemic factors but also by burn peritonitis and cardiac insufficiency, and significant progress has been made in pathophysiological research on burn shock. Glycocalyx damage in vascular endothelial cells is an essential factor in microcirculatory disorders. Improving organ function by repairing the glycocalyx of vascular endothelial cells can preserve the integrity of vascular endothelial cells in patients with septic shock, reduce capillary leakage, and diminish micro thrombosis. In burn shock, there is a similar phenomenon of macrocirculatory-microcirculatory decoupling, in which the macrocirculation and microcirculation are not coordinated, and microcirculatory perfusion and tissue oxygenation remain inadequate even after the target value of the macrocirculatory parameters has been reached. Therefore, burn shock and septic shock resuscitation strategies that only target the macrocirculatory parameters are ineffective, and the functional status of the microcirculation must be evaluated. Moreover, in vasodilatory or intractable shock manifested by hypovascular tone or even vascular paralysis, high doses of vasoactive medications are ineffective, and the microcirculatory impairment is exacerbated. The mechanisms of vascular hyporesponsiveness involve abnormal vasoactive receptors, steroidal corticosteroid insufficiency, and increased nitric oxide release; these essential research findings are crucial guidelines for the clinical management of extensive burns.[34] With the advancement of science and technology, improved methods for monitoring shock and new instruments for the rescue and treatment of burn shock have become available. Pulse contour cardiac output (PiCCO) monitoring is a new hemodynamic monitoring technique developed in recent years that enables comprehensive monitoring of patient hemodynamics, cardiac function, and pulmonary water content.[35] PiCCO helps guide shock resuscitation and fluid management. Clinical evidence indicates that most patients with severe burns have a persistently high extravascular pulmonary water index, which has a significant negative correlation with pulmonary dysfunction. Therefore, the researchers propose a fluid management strategy that may reduce organ complications and increase the success rate of burn rescue. Along with restrictive fluid rehydration, cardiac support measures such as enhancing positive myocardial muscle strength, reducing anterior and posterior cardiac load, and mitigating myocardial damage maximize the efficacy of minimal fluid rehydration and achieve a more effective fluid resuscitation.[36]

3.2 Treatment and repair of wounds

Essential components of burn treatment include treating and repairing burn wounds, determining burn area and profundity before treatment, and the progressive implementation of intelligent devices in the clinic. For instance, the BurnCalc human 3D scanning system developed by Changhai Hospital of Naval Medical University evaluates the burn area. The BurnCalc human 3D scanning system consists of a handheld 3D scanning device Kinect II, a 3D model reconstruction system, and an interactive display system, which has good stability and accuracy in measuring the area of standard cubes and can accurately assess the extremity and torso burn areas of burn patients.[37]

In China, a comprehensive treatment system for large burn wounds has been established, including surgical, chemical, enzymatic, biological, and multiple methods of wound debridement such as waterjet, ultrasound, and plasma, as well as various methods for cutting scabs, autologous skin grafts after abrasive scabbing, allogeneic and mixed allogeneic skin grafts, natural and synthetic biomaterial grafts, tissue-engineered skin graft, and new products of genetic engineering and modern dressings, as well as bio-3D printing technology, trauma closure, and negative pressure drainage technology, hyperbaric oxygen therapy technology, direct current therapy technology, photon therapy technology, traditional Chinese medicine treatment technology, and other comprehensive trauma management measures, have created a suitable treatment plan for severe burns.[30]

Early scabbing is the gold standard for deep burn treatment.[38] For extensive burns, it is essential to remove the deep burn scab as "early and completely" as possible and to close the wound effectively; the timing and size of the first excision, as well as the success of the operation, primarily determine the patient's subsequent stability and prognosis.[5] In the clinical treatment of sizeable deep burn wounds, Meek micro-dermis grafting improved the survival rate and first-stage healing rate compared to micro-dermis grafting, shortened the operation, wound healing, and hospitalization time, and reduced the treatment cost.[39]

In 1996, the first synthetic dermis, Integra®, was approved for clinical use. In 2007, the first domestic tissue-engineered skin product, AntifuTM, was developed by the Fourth Military Medical University and used successfully in clinical trials.[40] Lando® double-layer artificial dermis was granted a Class III medical device registration certificate by the National Pharmaceutical Administration (NMPA), filling a void in China. The artificial dermis provides a new method for deep trauma restoration that can partially supplant skin grafts and slivers.[41] According to reports, the Chinese bilayer skin product "AntifuTM" has been licensed for production.[42]

Platelet concentrates (PC) products are abundant in high concentrations of growth factors that modulate the inflammatory response, anti-infection, induce vascularization, etc. According to their maturation process, PC products can be divided into three generations: platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and growth factor concentrate (CGF).[43,44] PRP has the function of promoting wound healing, and its participation in the re-epithelialization process by affecting the length and thickness of new epithelium improves the quality of wound healing and has a significant repair effect; it has been widely used in the treatment of difficult-to-heal wounds after burns as well as in multidisciplinary trauma repair treatment, and research on PRP has been intensified.[45,46]

Exosomes (Exo) are a current research hotspot, and they serve a crucial role in various aspects of human health and disease. Studies have demonstrated that adipose mesenchymal stem cells (ADSC), with self-renewing proliferative and multidirectional differentiation potential, can significantly accelerate wound healing alone or in conjunction with novel materials laden with ADSC-Exo.[47] Extracellular vesicles derived from mesenchymal stem cells (MSC-EV) have a high potential to promote angiogenesis in diabetic ulcers and, thus, wound repair.[48] Using exosomes from human adipose stem cells with Mg^{2+} and gallic acid (GA) to create novel nano-scaffold materials can enhance the material's osteogenic, angiogenic, and anti-inflammatory properties.[49] Exo research is in its infancy and confronts numerous challenges from clinical application; additional in-depth research is still required.

3.3 Burn infections and sepsis

The largest organ in the human body is the skin. The maintenance of the immune homeostasis of the skin depends on good regulation among the epithelial cells, stromal cells, immune cells, and the microbial community of the skin surface. Studies have shown that the skin's immune system plays an essential regulatory role in skin injury repair.[50] The skin immune system indirectly affects wound healing by regulating important direct effector cells for wound repairs, such as epidermal stem cells, vasculitis-associated macrophages, and neutrophils.[51] During burn treatment, infection accompanies the entire burn wound healing process, and burn infection prevention and control is an integral part of the burn treatment process. Measures such as active treatment of wounds, early fluid resuscitation, rational application of antimicrobial drugs, and vital organ support have become the basis of burn infection prevention and control. Alternative therapies such as microbial therapy, phototherapy, and stem cell therapy are also used to prevent and control burn infections. In addition, immune modulation has opened up new avenues for the intervention of burn infection and its complications. It is essential to gain a deeper understanding of its inflammatory immune response and regulatory mechanisms and investigate new early warning biomarkers, immune prevention, and treatment strategies to improve clinical burn infection treatment and patient prognosis.[52, 53] Studies have demonstrated a close relationship between systemic immune and inflammatory responses and prognosis in patients with severe burns. Patients with lower counts of CD8+T cells, $\gamma\delta$T cells, B cells, and iNKT in peripheral blood at admission are more susceptible to bacterial infections, delayed recovery of HLA-DR/monocytes, and dysregulation of late cytokine secretion is associated with the development of septic shock.[54]

Frederick Twort discovered phages in 1915. In 2011, the FDA approved the first food additive composed of phages. In 2014, the American Institute of Allergy and Infectious Diseases identified phage therapy as one of the measures for treating drug-resistant bacteria. 11 units in France, Belgium, and Switzerland conducted the first multinational clinical trial of phages for the treatment of P. aeruginosa and E. coli infections following burns in the same year.[55] In 2017, a scholar reported using phages to treat two patients with sepsis successfully, and in 2019, the European Union and the United States launched a standardized protocol for phage clinical trials. In China, the Shanghai Institute of Phage and Drug Resistance successfully used phages to treat infections induced by drug-resistant bacteria, paving the way for a new era in phage therapy.[56] Because the host spectrum of phages is too restricted, it severely restricts the promotion and application of phage therapy, and there is an urgent need for a breakthrough. Nevertheless, phage therapy may be the most effective treatment for super-resistant bacterial infections.[57]

In 2016, “Sepsis 3.0” defined sepsis as a life-threatening organ dysfunction resulting from dysregulation of the body’s immune response to infection. This revision of the definition of sepsis eliminates the concept of SIRS and replaces it with the severity of organ injury as the primary diagnostic reference point. Sepsis is diagnosed in patients with suspicion of infection and SOFA ≥ 2.[58, 59] Due to its specificity, burn sepsis necessitates the ongoing refinement of diagnostic criteria and treatment modalities in clinical practice to achieve individualized and refined diagnosis and treatment.[71] More advances in research on the mechanism of sepsis have led to the development of novel clinical treatment strategies. Patients with sepsis, for instance, are susceptible to increased vascular permeability. Numerous factors and mediators are involved in modulating sepsis vascular permeability, which is anticipated to be a target in the clinical treatment of sepsis.[60] Cytokines play an important role in developing sepsis and are involved in the immune and inflammatory regulation of sepsis; they are also utilized as biomarkers for early detection, diagnosis, and prognostic assessment of sepsis and as therapeutic targets for preventing and treating sepsis.[61] In addition, the study of the role of dendritic cells in the immune defense of the body, antigen presentation, activation of the acquired immune response, induction of autoantigen immune tolerance, and other processes involved in the immune disorder of sepsis, leading to the development of targeted immunomodulatory drugs or the exploration of new immunotherapeutic approaches, has become a significant challenge in sepsis research.[62]

3.4 Protection of burned organ function

Respiratory and circulatory failure are the most life-threatening complications of treating severe burns. The Extracorporeal Membrane Pulmonary Oxygenation (ECMO) technique can partially replace the heart’s pumping function and the gas exchange function of the lungs, allowing the heart and lungs to rest with less burden.[63] 5 patients with burn injuries and ARDS were treated with ECMO at the Southwest Hospital of the Army Medical University in 2021; three were successfully deconditioned, and one survived. Four patients passed away due to MODS and sepsis shock. 295 burn patients received ECMO, including 157 adults and 138 children, according to a review of 13 foreign publications; the overall morbidity and mortality rate was 48.8%, including 83 deaths in adult burn patients with a morbidity and mortality rate of 52.9% and 61 deaths in children with burns with a rate of 44.2%. The use of ECMO in the field of burns is still in its infancy, and numerous controversies are challenging to resolve.[64]

Continuous renal replacement therapy (CRRT) has been widely used in extensive, severe burns. CRRT helps improve the patient’s stress response, high catabolism, and continuous removal of toxins, and maintaining the patient’s internal environment’s stability, stabilizing the patient’s clinical status and enhancing the prognosis.[65] In recent years, the concept of CRRT in patients with severe burns has progressively shifted from renal replacement therapy to non-renal field therapy, and its application in the early stages of burns has been advocated with positive therapeutic outcomes.[66]

Inhalation injury is one of the challenges in the treatment of burns. According to the literature, the incidence of inhalation injury in hospitalized burn patients in China ranges from 4.89% to 11.28%. The morbidity and mortality rate of patients with inhalation injuries has ranged from 5.17% to

24.75% since 2000.[67] In recent years, attention has been paid to early airway management of inhalation injury, and the application of fiberoptic bronchoscopy in diagnosis and treatment, early tracheotomy, and mechanical ventilation has led to a gradual decline in the morbidity and mortality rate of patients with inhalation injury. Severe burns frequently accompany inhalation injury, and patients with moderate to severe inhalation injury require comprehensive treatment, including trauma treatment, prevention and treatment of ventilator-associated pneumonia (VAP), prevention and treatment of burn sepsis, rational use of antibiotics, burn care, and prevention and control of infection in the intensive care unit (ICU). Numerous obstacles exist in diagnosing and treating inhalation injuries.[6,68] The mortality and morbidity rate increases to 40% if pneumonia is also present in burn patients with combined smoke inhalation and lung injury. Both inhalation lung injury and pneumonia are independent risk factors that influence the morbidity and mortality of burn patients.[69]

Prone position therapy (PPT) and prone ventilation (PPV) garner increasing attention in adult burn patients on a turning bed. PPV using a burn turning bed can improve oxygenation, pulmonary compliance, and hemodynamic indices, facilitate carbon dioxide expulsion and sputum drainage, and improve pulmonary compliance and proper heart function in adult burn patients with moderate to severe ARDS due to various causes and resulting in intractable hypoxemia.[70,71]

3.5 Nutritional metabolism and rehabilitation

In 1968, Dudrick et al. created total parenteral nutrition, which was introduced to China in the early 1970s and gradually applied to the nutritional treatment of critically ill patients, from surgery to burns. Since 2010, the nutrition of burns has been innovated, and a new "nutritional support therapy" system has been developed, which places greater emphasis on the proper timing of nutrition initiation and administration. The concept of an endogenous heat source has been proposed, and the body's ability to tolerate nutrition has received more attention. We have reached a consensus on "nourishing enteral nutrition" and have implemented enteral nutrition as soon as feasible to improve gastrointestinal motility and blood flow. When 60% of the target caloric and protein cannot be met with enteral nutrition, parenteral nutrition should be initiated as soon as possible. The formation of a more comprehensive burn nutrition theoretical system and treatment strategy has played an essential role in the rescue and treatment of burns, particularly the rescue and treatment of severe burns.[72]

The prevention and treatment of post-burn scarring have received growing attention. The rehabilitation of patients and their reintegration into society are considered concurrently with preserving life in the initial phases of burn injury. The treatment of scars no longer focuses solely on restoring function but also on enhancing appearance.[73] With the advancement of theoretical research, treatment technology, and clinical application of optoelectronic therapy, new devices are continuously being developed, and the outlook for optoelectronic scar treatment is improving. Particularly, the treatment with a 595 nm or 585 nm pulsed dye laser targeting the rich blood flow characteristics in the early stage of scar growth and the clinical application of carbon dioxide or Er: YAG fractional laser is expected to restore scarred skin to nearly normal skin.[74]

Pain has become the fifth vital sign, following temperature, pulse, respiration, and blood pressure, and nitrous oxide (commonly known as laughing gas) mixed with oxygen for inhalation has a rapid onset of analgesia, good analgesic effect, easy control of sedation depth, rapid and complete metabolism, and few and mild toxicity and adverse effects, which can effectively relieve pain during the treatment and rehabilitation of burns, and has a more excellent prospect of application in it.[75,76] It is essential to intervene in burn patients' physical, psychological, and social rehabilitation and establish a multifaceted social support system to assist burn patients in getting out of trouble, returning to society, and reshaping their lives.[77,78]

4. Prospects for the rescue and treatment of extensive burns in China

Technological innovation is evolving rapidly, and digitalization, networking, and intelligence are advancing in-depth, propelling society's rapid development. The medical industry is highly active in technological innovation, and new technologies are emerging to provide human-machine-linked medical services to patients using virtual technology. The meta-universe epoch, which has the potential to transform human society, has arrived. Implementing concepts, methods, technologies, and processes of complexity through the combination of human-machine virtual and real parallelism[79] will transform the current medical and health system and continuously enhance service capabilities through artificial intelligence to aid in solving complex tasks in the medical field. For instance, the application of virtual reality technology in medical imaging, surgical assistance, medical education, telemedicine, rehabilitation training, drug development, etc., with the help of imaging data displayed in holographic/virtual reality, the details of the lesion can be observed comprehensively, reducing the likelihood of misdiagnosis. At the same time, patients can understand the condition of the lesion and the treatment plan more intuitively, fostering doctor-patient communication. In addition, there is tremendous potential for the application of drone technology in clinical rescue operations. Doctors' surgical work is heavy, and surgical efficiency can be improved through VR/AR/MR and other technologies, such as holographic imaging technology that can holographically display effects and full-image display to compensate for problems such as limited field of view in minimally invasive surgery, reducing intraoperative risks and postoperative complications.[80,81] In addition, there is an excellent prospect of application through drone technology to serve clinical rescue work.[82] Medical and health care must maintain pace with the progression of time and make full use of new scientific and technological advancements to expand the horizons of medicine.

Burn surgery is a professional emergency team in significant public health emergencies and wartime, and how strengthening the discipline requires serious consideration. When many burns occur, a country or region's burn treatment level and disaster emergency response capability are tested.[83,84] Academician Xia Zhaofan[85] summarized the care given to 260 Kunshan aluminum dust detonation victims in 2014 and suggested lessons to be observed. (1) develop a more targeted emergency plan for group burns; (2) improve the overload capacity of medical institutions; (3) pay attention to the leading position of burn societies in the treatment of group burns and enhance interdisciplinary communication and collaboration; (4) improve the efficiency of resource utilization in the treatment of group burns; (5) focus on post-disaster psychological intervention, rehabilitation treatment, and long-term care. Academician Fu Xiaobing[86] proposed establishing a networked traumatic burn treatment system in China and applying network theory, technology, and methodologies to address the challenges associated with traumatic burn treatment.

In China, the incidence of burns has decreased in recent years, while the incidence of trauma has increased. In addition to trauma, wounds, and infections, the incidence of trauma caused by diabetes, metabolic diseases, geriatric diseases, and tumors is rising.[87] The burn department has technical advantages in trauma repair, which presents opportunities for developing the burn discipline; so, the emphasis on discipline development should be modified for some departments with inadequate business volume. Academician Fu Xiaobing[87] proposed the discipline management and construction concept of "treating trauma in peacetime and burns in wartime" and encouraged burn departments to treat patients with chronic hard-to-heal trauma in a specific period so that a large number of patients with chronic hard-to-heal trauma could be effectively treated without establishing a trauma repair department. Burn care and trauma care are both similar and distinct. A burn injury is a "local injury caused by disease." In contrast, a body surface lesion caused by disease is a "disease that causes local injury." In 2019, the National Health Care Commission (NHC) requested that medical facilities with certain conditions establish trauma repair centers to treat trauma resulting from underlying diseases or injuries, which is a different system of prevention and control than the repair of acutely injured, traumatic burn surfaces.[88] Burn surgery is a disaster medicine and a military medicine with a special status that can "rush on and save" when there are groups and significant burn incidents and bears the dual responsibilities of medical treatment and social stability. The focus of burn surgery discipline construction is still to strengthen the quality construction and internal development of the burn discipline, to strengthen further the construction of the regional emergency medical rescue system, and to actively invest in the construction of an integrated emergency medical rescue system to respond to major catastrophic accidents and severe trauma (burns and warfare) injuries and to play an influential role in burn medicine.[89]

In recent years, several novel technologies and techniques have emerged in the field of burn surgery, contributing to the growth of burn medicine. With the development of tissue engineering technologies, such as the successful clinical use of tissue-engineered skin, the research results on stem cells, the abundance of natural and synthetic scaffold materials, and the maturation of in vivo and in vitro 3D printing technologies, new treatment tools have become available for trauma repair. With the advancement of 3D printing technology, cell biology, and materials science, 3D bioprinting has become widely used in the medical field, creating new opportunities for extensive burn wound repair.[90] Michael[91] transplanted a 3D-printed epidermis onto the burn of a mouse. The healthy wound healing demonstrated that the 3D bio-printed skin performed similarly to normal skin. According to a study by Chao Zhang,[92] the use of 3D printed ink (Bioink) containing human adipose-derived protein complex (ADPC) could speed up the healing of full skin defect wounds in hairless rodents. The team of academician Xiaobing Fu[93] showed that the 3D bioprinting model allows precise induction of targeted cell differentiation, promotes cell proliferation and matrix secretion, and causes functional regeneration of sweat glands. It offers novel concepts and technical solutions for the in vitro construction of organs and advances the fields of trauma repair and tissue regeneration.

An Organoid is a three-dimensional micro-organ cultured from stem cells under in vitro matrix material support conditions that resemble the primary tissue organ in great detail. Organoid technology provides a new robust research case and technical means for fundamental research, drug screening, and regenerative medicine. Since the team of Dutch scientists Clevers[94] developed intestinal organoid technology in 2009, several organoid models have been established. Skin organoids are anticipated to become a new therapeutic option for wound repair. 55% of skin-like organs transplanted on the traumatic surface of mice displayed outward-growing hairs, the traumatic surface was repaired, and there were no indications of tumor-like growth of the grafts in the host during follow-up.[95] The team of academician Fu Xiaobing[96] used HaCaT cells as seed repair cells, upregulated the expression of endogenous EDA using CRISPR/dCas9 technology, and induced their cross-spectrum reprogramming into sweat-like cells. Matrigel was then used as the primary scaffold to mix with the reprogrammed sweat-like cells to construct sweat-like organs in vitro. Transplantation experiments determined that sweat-like organs contributed to the re-epithelialization of traumatized surfaces and repaired and regenerated the histological structures of sweat glands in hairless mice. Although organoid culture technology is maturing, its clinical application still faces numerous obstacles. Cell and tissue transplantation, organoid transplantation, and organ transplantation will form the basis of regenerative transplantation and advance regenerative medicine alongside organ support therapy and others.[97]

Regarding allograft transplantation for severely disfiguring burn wounds, Devauchelle performed the world's first human facial allograft in Amiens, France, on November 27, 2005, and Xijing Hospital's plastic surgery team performed the first (Second case in the world) partial allograft facial transplant in China on April 13, 2006. In 2018, Rifkin summarised forty facial transplantation cases, discussing their accomplishments, significant challenges, and future directions. Nonetheless, the immune rejection after transplantation and the numerous side effects associated with using immunosuppressive medications prevent this technique's widespread clinical implementation.[98–100]

Conflicts of Interest Disclosure

The authors declare they have no conflicts of interest.

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