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Acupuncture for Crohn's disease: current status and future perspectives

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Crohn's disease (CD), a type of inflammatory bowel disease, is a chronic, recurrent inflammatory disease of the intestine, with the main clinical manifestations including abdominal pain, diarrhea, and loss of body mass. The disease is common in Europe and the United States, and its incidence has increased in recent years in newly industrialized countries in Asia, Africa, and South America[1]. The exact pathogenesis of this disease remains unclear; however, it is thought to be related to immune, genetic, environmental, and psychiatric factors. Current pharmacological treatments for this disease are based on immunosuppressive agents and biologics; however, at least 30% of patients do not receive effective treatment because of poor response or drug intolerance[2]. In recent years, an increasing number of domestic and international clinical studies have demonstrated the advantages of acupuncture in the treatment of CD[3]. Our group conducted a randomized controlled trial (RCT) and confirmed that acupuncture is a safe and effective treatment for mild-to-moderate CD, especially for patients with CD who do not respond well or are intolerant to traditional medications. We demonstrated that acupuncture can improve clinical symptoms and induce and maintain long-term remission of CD, which is related to the regulation of the intestinal microbiota structure, intestinal barrier function, and peripheral circulation of Th1/Th17 cytokines in patients[4–5]. Our group has also demonstrated that acupuncture can reduce the clinical recurrence rate in patients with CD. These results were presented at the Digestive Disease Week 2023 conference[6]. In addition, an RCT conducted in Germany demonstrated that acupuncture significantly improved intestinal inflammation and general health status in patients with mild-to-moderate active CD compared with sham acupuncture[7]. Italian scholars confirmed that electroacupuncture is more effective in reducing fatigue scores than waiting lists in patients with CD[8]. This evidence suggests that the international recognition of acupuncture for the treatment of CD is increasing.

The mechanism of acupuncture in the treatment of CD is also being elucidated, which mainly includes two aspects: local regulation inside the intestines and neuromodulation outside the intestines. The former refers to the regulation of intestinal microbiota, intestinal epithelial cell function, and local intestinal immune cells[9]. In regulating the intestinal microbiota, acupuncture increased the abundance of anti-inflammatory and short-chain fatty acid-producing bacteria, decreased serum Interferon-γ (IFN-γ), Interleukin-17A (IL-17A), Interleukin-1β (IL-1β), and Tumor Necrosis Factor-α (TNF-α) levels, and enhanced the integrity of the intestinal barrier in patients with mildly and moderately active CD, realizing a long-term remission of the disease[4]. The regulation of intestinal epithelial cell function mainly includes protection of the intestinal epithelial mechanical barrier, as well as inhibition of epithelial-mesenchymal transition[10–11]. The regulation of local intestinal immune cells mainly includes inhibiting aberrant immune activation, regulating immune cell homeostasis, modulating the activation of inflammasome pathways, and inhibiting pro-inflammatory cytokine secretion[12–13]. Neuromodulation outside the intestines is mainly the regulation of brain function and neurotransmitters in the brain-gut axis. Regarding the former, some studies have shown that both electroacupuncture and moxibustion treatments improved cortex-subcortical coupling in patients with CD in remission, but electroacupuncture regulated homeostatic afferent processing network, whereas moxibustion mainly regulated the default mode network of the brain[14]. Regarding the latter, studies have confirmed that moxibustion significantly reduced the expression of dopamine and receptor dopamine receptor 1 in the colon, dorsal horn of the spinal cord, and hypothalamus as well as downregulates the overexpression of substance P and neurokinin 1 receptor in the colonic mucosa of rats with CD[15]. Therefore, the effect of acupuncture on CD is a multi-pathway, multi-target, and multi-level holistic regulatory effect.

However, many challenges remain in the study of acupuncture for CD, and several gaps remain to be addressed. Firstly, because the prevalence of CD is low, the sample sizes of the existing studies are generally small, and studies based on large sample populations are lacking. As studies on acupuncture for CD are mainly performed in large cities, there is an obvious

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uneven regional distribution of patients. Insufficient accessibility to acupuncture therapy leads to difficulties in conducting studies with larger samples. Secondly, the efficacy evaluation and outcomes were not sufficiently standardized, and the accuracy of the trial needs to be improved. Most current studies use the Crohn's Disease Activity Index (CDAI) as one of the outcomes that relies on patients' self-reported symptoms and feelings. This may not objectively and reliably reflect the severity of the disease and intestinal inflammation, making it difficult to correlate strongly with colonoscopic and imaging results. Thirdly, patients with CD tend to take Western medicine for long periods. To take advantage of the respective strengths of acupuncture and Western medicine, selecting appropriate treatments for patients with different disease subtypes and different disease periods, flexibly using acupuncture, moxibustion, and medicine, and continuously improving and optimizing the treatment protocols to better promote and maintain long-term remission of the disease are clinical issues that require urgent research. Fourthly, the clinical efficacy of acupuncture is influenced by the parameters of acupuncture or moxibustion stimulation (electrical stimulation intensity and frequency, treatment period, moxibustion temperature, and duration)[16]. Few studies have been conducted to determine optimal parameters for acupuncture stimulation. There have also been a few studies on long-term follow-up and efficacy assessments. Finally, the mechanisms underlying acupuncture have not been systematically or thoroughly elucidated.

Future research should focus on establishing the efficacy of acupuncture for CD by conducting clinical trials with larger sample sizes. The effectiveness and methods of acupuncture for the treatment of CD should be widely introduced and promoted to doctors in the departments of Chinese medicine, acupuncture, and gastroenterology in hospitals at all levels, so that doctors in small- and medium-sized cities will use it in patients with CD, which will help expand the sample sizes for studies and eventually benefit more patients. Additionally, a long-term follow-up program should be established to determine the long-term efficacy of acupuncture in the treatment of CD. Different combinations of acupuncture, moxibustion, and medicines are reasonably applied to different disease subtypes and disease periods of CD with the goal of maintaining long-term remission and non-recurrence of the disease and exploring the combination of acupuncture, moxibustion, and medicines for the long-term treatment of CD. To evaluate the differences in the efficacy of different acupuncture treatments, acupuncture stimulation parameters, acupoints, and their optimal combinations should be explored to develop the most appropriate treatment plan to improve the efficacy of acupuncture. At present, the clinical efficacy of acupuncture for CD is mainly evaluated using the CDAI, Inflammatory Bowel Disease Questionnaire, endoscopic manifestations, and intestinal histology. Validated efficacy models should be introduced and a combination of intestinal computed tomography (CT)/magnetic resonance imaging (MRI), colonoscopy, histology, and peripheral inflammatory markers with CDAI scores should be used for subjective and objective assessments. Simultaneously, internationally recognized evaluation methods should be introduced, and standardized RCTs should be conducted in strict compliance with the Consolidated Standards of Reporting Trials (CONSORT) statement to evaluate the efficacy and safety of acupuncture for CD more scientifically and precisely and to promote the entry of acupuncture therapy into international inflammatory bowel disease consensus opinions and guidelines. Moreover, the differences in the efficacy of different acupuncture therapies should be compared with an aim of clarifying the characteristics of the effects of different therapies so that the mechanism of acupuncture can be interpreted more precisely based on the quantified efficacy.

It has been shown that the involved pain sites may be high-prevalence areas for acupoint sensitization in patients with CD[17]. In the future, more attention should be paid to CD disease response points and acupoint sensitization to elucidate the manifestations and objective laws of CD acupoint sensitization. Acupuncture interventions should also be conducted to observe the superiority of sensitized points compared with traditional acupuncture interventions and to elucidate the quantitative effect of acupuncture-sensitized points. On this basis, the mechanism of action of acupuncture-sensitized points should be elucidated. In addition, machine learning and other emerging technologies should be actively introduced to build acupuncture efficacy prediction models to predict the clinical efficacy of acupuncture, screen the appropriate population for acupuncture treatment of CD, so as to guide doctors in their decision-making, reduce the waste of healthcare resources, and promote the application and promotion of precision medicine of acupuncture, as well as to promote the use and dissemination of the "Artificial Intelligence Acupuncture" one of the new modernized modalities of acupuncture (Figure 1).

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

Chunhui Bao drafted the manuscript. Jinrong Zhang revised the manuscript. Huangan Wu proposed revisions to the important intellectual content of the manuscript. All authors reviewed and approved the manuscript.

Ethical approval of studies and informed consent

Not applicable.

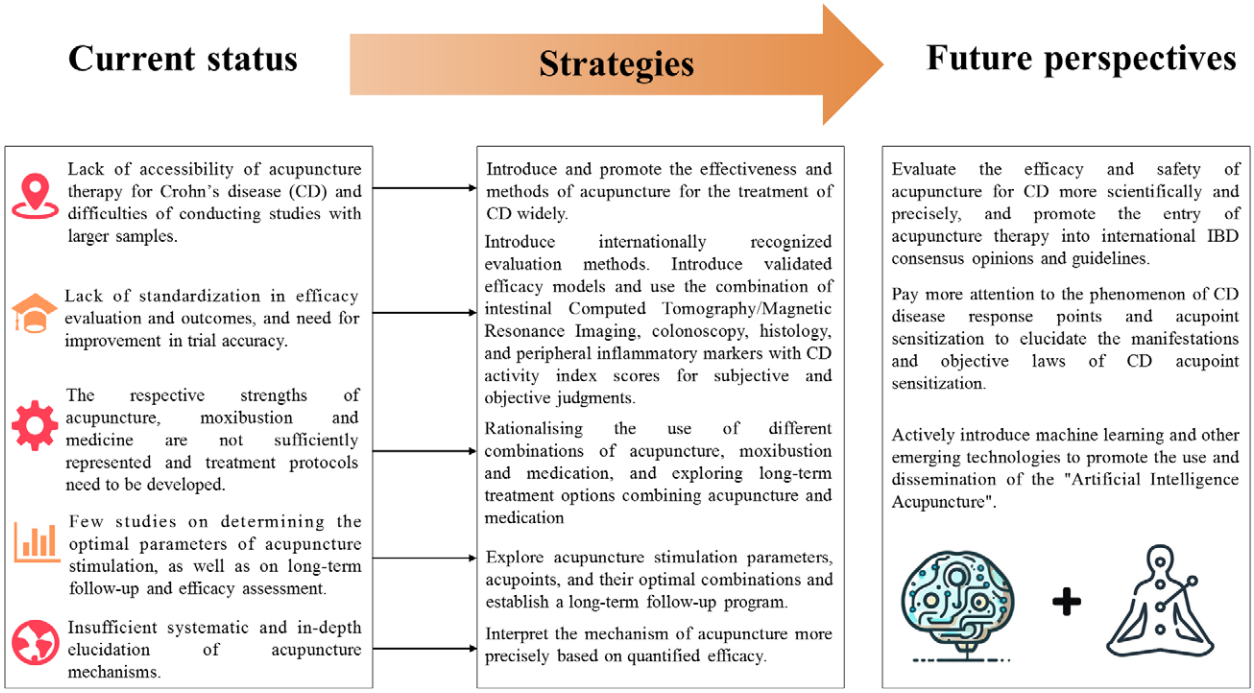

Figure 1. Roadmap of the current status, countermeasures, and outlook of acupuncture treatment for Crohn's disease.

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Data availability

Not applicable.

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