DOI: 10.66069/ojspub.27450706

Exploring the Syndrome Differentiation and Treatment of Colorectal Cancer Based on the Yin-Yang Theory of the Yellow Emperor's Inner Canon

Gang Tang[1], Yami Zhang[2,*]

[1]Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
[2]Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China
**Correspondence Author*

Abstract: ***Colorectal cancer (CRC), as one of the most common malignant tumors of the digestive tract, poses a serious threat to the health of the Chinese population and imposes a substantial burden on society. However, most existing Western medical treatment modalities are accompanied by unavoidable adverse effects. The incorporation of Traditional Chinese Medicine (TCM) interventions represents a breakthrough in the diagnosis and treatment of CRC. In TCM, there is a diversity of perspectives regarding the etiology and pathogenesis of CRC, with numerous clinical syndrome types that render syndrome differentiation challenging. Upon in-depth study of the traditional Chinese philosophical concept of Yin-Yang and the theory of Yin-Yang pathogenesis as articulated in the Yellow Emperor's Inner Canon, the author posits that the fundamental pathogenesis of CRC is "Yin-Yang imbalance with impeded circulation." "Circulation" constitutes the fundamental principle governing the movement of Yin and Yang; impeded circulation leads to either local Yang-heat accumulation or Yin-cold aggregation, thereby inducing the coalescence of stasis, toxin, phlegm, and turbidity, which in turn triggers tumorigenesis. It is proposed that the pathogenesis of impeded Yin-Yang circulation can facilitate clinical syndrome differentiation in CRC and enhance the precision of TCM diagnosis and treatment. Furthermore, the feasibility of discerning the Yin-Yang pathogenesis of CRC from clinical manifestations of cold and heat as well as tumor microscopic phenotypes is discussed. In terms of clinical treatment, a strategy that integrates local and systemic considerations, with a primary focus on moderating cold and heat and promoting Yin-Yang circulation, is recommended. Medication should be tailored according to the individual's predominant Yin-Yang inclination and proportional balance, with the goal of achieving "Yin tranquility and Yang firmness" (Yin Ping Yang Mi). By adhering to "Yin-Yang" as the fundamental principle of treatment, emphasizing classical thinking, reducing the difficulty of clinical syndrome differentiation, improving therapeutic efficacy, and enhancing the quality of life for CRC patients, this approach offers new avenues for TCM-based antitumor strategies.***

Keywords: Colorectal cancer, Traditional Chinese Medicine, Yellow Emperor's Inner Canon, Yin-Yang.

1. Introduction

Cancer is the second leading cause of death worldwide, with both morbidity and mortality showing a progressive upward trend [1]. Among these, colorectal cancer (CRC) is one of the most frequently diagnosed malignant tumors of the digestive tract. According to statistics, the incidence and mortality rates of CRC in China rank second and fifth, respectively, among all malignant tumors [2]. CRC has thus become a major risk factor threatening the health of the Chinese population.

Contemporary treatment modalities for CRC include surgery, radiotherapy, chemotherapy, targeted therapy, and immunotherapy. However, all these approaches are associated with significant and often severe adverse effects [3]. Therefore, exploring the application of TCM pattern differentiation and treatment in the management of CRC is of considerable importance. In TCM, CRC falls within the categories of "intestinal accumulation" (chang ji), "intestinal fungus" (chang xun), "visceral toxin" (zang du), and "abdominal masses" (ju ju). Throughout history, physicians have held divergent views on the nature of these conditions, and no unified consensus has been reached. Nevertheless, most practitioners concur that the pathogenesis is fundamentally attributable to the intermingling of phlegm, qi, blood stasis, dampness, heat, and toxic pathogens [4]. These theories are grounded in Zang-Fu pattern differentiation combined with the differentiation of qi, blood, and body fluids, yet they essentially remain analyses from the perspective of pathogenic qi versus healthy qi and deficiency versus excess [5].

However, the pathogenesis of neoplastic diseases is often exceedingly complex, characterized by concurrent deficiency and excess, as well as intertwining pathogenic and healthy qi, all of which mutually influence one another. This complexity imposes high demands on the clinician's diagnostic acumen, rendering clinical syndrome differentiation and medication selection difficult to achieve with precision, thereby substantially impeding the application of TCM interventions in oncological practice. To address this, the author has conducted an in-depth investigation of the Yin-Yang pathogenic theory in the Yellow Emperor's Inner Canon and the concept of Yin-Yang in ancient Chinese philosophy, concluding that approaching the pathogenesis of CRC through the lens of Yin-Yang offers the advantage of simplification and direct access to the fundamental nature of the disease. Based on the principles governing Yin-Yang movement, the fundamental pathogenesis of CRC can be encapsulated as "Yin-Yang imbalance with impeded circulation."

2. The Operational Principles of Yin-Yang in Ancient Chinese Philosophical Thought

Ancient Chinese philosophers posited that movement and change are the normal states of the universe [6]. The Dao De Jing states: "There is a thing inherently complete, born before heaven and earth. Soundless and formless, it stands alone and does not change, circulates universally and does not wane. It may be regarded as the mother of all under heaven. I do not know its name; I style it 'Dao'." The Dao circulates universally and operates without cease. The Guo Yu·Yue Yu states: "When Yang reaches its extreme, Yin emerges; when Yin reaches its extreme, Yang emerges. The sun wanes and returns; the moon wanes and then waxes." The Zhou Yi·Xi Ci states: "One Yin and one Yang constitute the Dao." Even in the Dream of the Red Chamber, it is mentioned that "qi differentiates into Yin and Yang; when Yin is exhausted, Yang manifests; when Yang is exhausted, Yin manifests." It is evident that in the view of the ancients, Yin-Yang served as an essential instrument for comprehending the world and constituted the fundamental source of the unceasing generation and transformation of all things under heaven [7]. Their operation is characterized by ceaseless cyclical movement. From mountains, rivers, and the cosmos above to the flow of qi and blood and cellular metabolism in the human body below, all phenomena conform to the cyclical patterns of Yin and Yang.

3. The Theory of Yin-Yang Pathogenesis in the Yellow Emperor's Inner Canon

The Yellow Emperor's Inner Canon, as the earliest extant medical classic in China, places great emphasis on the theory of Yin-Yang. The Su Wen·Treatise on the Corresponding Manifestations of Yin and Yang states: "Yin and Yang are the Dao of heaven and earth, the fundamental principles of all things, the parents of transformation and change, the root of generation and destruction, and the abode of the divine intelligence. In treating disease, one must seek its root in Yin-Yang." The Su Wen·Treatise on Vital Communication with Heaven states: "The root of life lies in Yin-Yang." These passages reflect the early recognition of the critical importance of Yin-Yang to human health and vitality. The Su Wen·Treatise on Vital Communication with Heaven further states: "When Yin is tranquil and Yang is firm, the spirit is properly regulated; when Yin and Yang separate and diverge, the essential qi is exhausted." "Yin tranquility and Yang firmness" refers to the state of Yin-Yang balance. The Su Wen·Treatise on the Eight Principles and the Divine Light states: "When Yin and Yang are intermingled in disorder, true qi and pathogenic factors are indistinguishable, stagnation settles and remains fixed, external deficiency and internal chaos ensue, and excessive pathogens arise." "The intermingling of Yin and Yang in disorder" here refers to the disruption of Yin-Yang circulation. The Su Wen·Treatise on the Separation and Union of Yin and Yang states: "Yin and Yang may be counted as ten, extrapolated to a hundred, counted as a thousand, extrapolated to ten thousand—indeed, their manifestations are innumerable, yet their essential principle is one." The "one" here likewise points to the centrality of circulation. The Inner Canon contains numerous passages expounding the significance of Yin-Yang to the human body, as well as the principles of balance and cyclical movement. Hence, in treating disease, one must first distinguish Yin and Yang, for the crux of Yin-Yang lies in circulation and balance.

4. Feasibility of Applying "Yin-Yang Imbalance with Impeded Circulation" as the Fundamental Pathogenesis in CRC Syndrome Differentiation

In clinical practice, the syndrome differentiation of CRC is characterized by a multitude of divergent approaches, with most physicians treating patients based on their individual clinical experience. Owing to differences in areas of expertise and diagnostic reasoning, therapeutic outcomes vary considerably. According to statistical data, the major TCM syndrome types of CRC include: spleen-kidney Yang deficiency, spleen deficiency with mixed pathogens, dampness-heat pouring downward, liver-kidney Yin deficiency, qi deficiency and blood depletion, stasis-toxin internal accumulation, spleen deficiency type, qi stagnation and blood stasis, and dampness-heat with accumulated toxins [8]. This profusion of syndrome types not only hinders the widespread application of therapeutic modalities but also adversely affects the treatment and prognosis of CRC patients. The exploration of more intuitive and simplified approaches to syndrome differentiation is essential for enhancing the precision and efficacy of TCM-based diagnosis and treatment of CRC.

4.1 Differentiating the Yin-Yang Pathogenesis of CRC through the Lens of Cold and Heat Pathogenic Factors

The Su Wen·Treatise on the Corresponding Manifestations of Yin and Yang states: "Excessive Yin necessarily gives rise to Yang; excessive Yang necessarily gives rise to Yin." "Extreme cold generates heat; extreme heat generates cold." The Ling Shu·Examination of Disease and Measurement of the Cubit states: "Severe cold then engenders heat; severe heat then engenders cold." These passages effectively elucidate the close relationship between Yin-Yang and cold-heat, wherein cold and heat are in fact concrete manifestations of the predominance or decline of Yin and Yang in the body. While changes in Yin and Yang are difficult to perceive with the naked eye, manifestations of cold and heat are relatively intuitive. Thus, discerning Yin-Yang pathogenesis through the lens of cold and heat may serve as a critical clinical entry point.

Contemporary physicians often approach CRC from the perspective of toxic pathogens. For instance, the theory of "latent toxin" (fu du) posits that latent toxins readily transform with heat, scorching the intestinal tract and giving rise to symptoms such as bloody purulent stools and tenesmus [9]. Treatment in such cases is predominantly centered on detoxifying and combating cancer, or clearing heat and removing toxins. In fact, the association of toxin with tumors has ancient roots. The Jingyue Quanshu states: "Carbuncles arise from heat accumulating externally; it is the qi of Yang-toxin, characterized by high swelling, red coloration, and severe pain." The Waike Qixuan·Treatise on the Roots and Manifestations of Sores and Ulcers states: "Sores are

injuries; when muscle tissue becomes necrotic, accompanied by pain and itching, and ulceration ensues, they are called sores. The term 'sore' encompasses a broad range of conditions. Although they are designated by various names—such as carbuncles, deep abscesses, furuncles, scrofula, scabies, and eruptions—these are only general classifications." It is noteworthy that toxic pathogens may be differentiated into cold-toxin and heat-toxin, just as tumors may be classified according to Yin and Yang. The Ling Shu·Treatise on the Origins of All Diseases states: "When accumulation first arises, it is engendered by cold; cold then gives rise to 厥 (reversal/cold-induced stagnation), which in turn forms accumulation." The Ling Shu·Water and Abdominal Distension states: "What is intestinal fungus? Qibo said: Cold qi lodges outside the intestine and contends with the defensive (Wei) qi. When qi cannot be nourished, it becomes constrained, accumulating inwardly; evil qi then arises and polyps are generated." These passages indicate that not only heat-toxin but also cold-toxin constitutes a pathogenic factor in tumorigenesis. Both cold-induced congelation and heat-induced stagnation can give rise to endogenous tumors. Notably, in CRC and gastric cancer—both gastrointestinal malignancies—the pathogenesis frequently manifests as cold-heat complex with Yin-Yang imbalance. Treatment is often directed at concurrently addressing cold and heat, with the aim of moderating Yin-Yang. For example, Banxia Xiexin Decoction has been employed in the treatment of colorectal cancer [10]. Furthermore, therapeutic strategies should be tailored according to the stage of disease progression: in the early stage, when heat-toxin is rampant, the primary approach is to clear heat, remove toxins, and drain dampness; in the later stage, when spleen Yang is insufficient, the focus should shift to protecting healthy qi and warming and supplementing spleen Yang [11]. All of these considerations suggest the potential applicability of using cold and heat as surface markers to probe the root of Yin-Yang and regulate Yin-Yang balance in the treatment of CRC.

4.2 Differentiating the Yin-Yang Pathogenesis of CRC through Tumor Phenotypes

The Ling Shu·Yin-Yang and the Sun and Moon states: "Yin and Yang have names but are formless." This indicates that Yin-Yang refers to formless qi and constitutes a relatively abstract concept. With the advancement of modern medicine, in cases where there is "no syndrome to differentiate," where manifestations are indistinct, or where syndromes are too complex to differentiate with ease, we can perform pattern differentiation by investigating the microscopic manifestations of the disease [12]. Gan Zuwang proposed the diagnostic approach of "five diagnostic methods combined." Taking laryngitis as an example, physicians throughout history have often summarized the pathogenesis of hoarseness as "solid metal does not resound" or "broken metal does not resound." With the aid of laryngoscopy, modern practitioners have observed vocal cord nodules and polyps, many of which do not conform to patterns of lung excess or lung deficiency, yet may be effectively treated with methods that resolve phlegm and transform stasis [13]. Similarly, for patients with nasopharyngeal carcinoma or laryngeal cancer, this approach to pattern differentiation may also be referenced.

Tumor functional phenotypes represent an important means of understanding tumors at the microscopic level. The integration of microscopic tumor phenotypic characteristics with macroscopic TCM pattern differentiation serves as a supplement to TCM diagnostic methodology and may potentially contribute to the construction of a new TCM holistic view. In 2000, Weinberg of the Massachusetts Institute of Technology summarized the six biological functions acquired during the multistage development of human tumors, and subsequently updated and expanded these in 2011 [14-15]. Since then, research on tumor phenotypes has continued to achieve breakthroughs. Some studies have found that the characteristics of tumor phenotypes also conform to the Yin-Yang theory of the Inner Canon, and that the divisibility of tumor phenotypes aligns with the infinite divisibility of Yin-Yang [16]. We may utilize tumor phenotypes to differentiate the Yin-Yang pathogenesis of tumors. The activation of tumor cell proliferation and morphogenesis in situ pertains to Yin, while hyperplasia, invasion, metastasis, and replication may be regarded as Yang. This corresponds precisely to the Inner Canon principles: "Yang transforms qi; Yin shapes form," "Yin is quiescent; Yang is dynamic," and "Yang governs killing; Yin governs storing." In clinical practice for CRC, detecting phenotypic changes in circulating tumor cells (CTCs) and studying the dynamic trends of mesenchymal CTCs (M+ CTCs) before and after treatment can provide important evidence for tumor recurrence assessment and therapeutic response evaluation. Research has shown that mesenchymal cells, which constitute an important component of the body's physiological functions, are closely associated with cancer cell metastasis and invasion [17]. From the perspective of Yin-Yang, this reflects the dynamic changes of Yin-Yang predominance and decline between the organism as a whole and the localized tumor proliferation. Owing to the complexity and interconnectedness of the internal environment, this may be understood as the obstruction of Yin-Yang circulation at the local level, leading to localized tumor cell proliferation.

5. Analysis of Yin-Yang Pathogenesis and Therapeutic Principles in CRC as a Case Study

In TCM, the Zang-Fu organs are not merely anatomical structures but also encompass concepts of physiological functions. In the human body, that which is superior and external pertains to Yang, while that which is inferior and internal pertains to Yin. In terms of the Zang-Fu organs, the five Zang (solid organs) pertain to Yin, while the six Fu (hollow organs) pertain to Yang, and each may be further subdivided into Yin and Yang. The large intestine is one of the six Fu organs; functionally, it is characterized by free flow and unimpeded movement. It is internally-externally paired with the Taiyin Lung, with ascending and descending mutually dependent—this constitutes one Yin-Yang cycle. Additionally, it connects with the small intestine, which governs reception and transformation, as well as the separation of pure from turbid, while the large intestine governs the conduction of waste products—this constitutes another Yin-Yang cycle. Thus, in the Yin-Yang circulation of the human body, the large intestine commonly manifests with Yang attributes. When Yin-Yang circulation is obstructed and

manifests as Yang deficiency constitution, this becomes a risk factor for colorectal cancer [18]. At this stage, the toxic pathogen is predominantly Yin in nature, congealing locally and potentially manifesting as polypoid protrusions without ulceration or infiltration. The therapeutic approach should integrate local and systemic considerations, with a primary focus on warming Yang to transform qi and moderating cold and heat. Of course, the fundamental pathogenesis of CRC lies in Yin-Yang imbalance with impeded circulation. Although the local toxic pathogen is predominantly Yin in nature, the degree of Yin-Yang predominance varies among patients and across different stages of disease progression. In clinical practice, the predominant inclination and proportional balance of Yin-Yang imbalance should be comprehensively considered in selecting the appropriate therapeutic principles, formulas, and medicinals.

6. Conclusion

Yin-Yang is the fundamental principle of treatment emphasized by the Inner Canon and constitutes the root pathogenesis underlying the occurrence and development of disease. It represents a dynamic equilibrium theory grounded in the holistic view of Qi monism. The differentiation of Yin-Yang pathogenesis through the lens of cold and heat is an important method consistent with the TCM principle of "observing the subtle to discern the overt." The differentiation of Yin-Yang pathogenesis through microscopic tumor phenotypes represents an organic integration of modern scientific and technological approaches with traditional Chinese medicine. Exploring the clinical syndrome differentiation of CRC from the fundamental pathogenesis of "Yin-Yang imbalance with impeded circulation" assists clinicians in returning to the distinctive roots of TCM, facilitates the precision and simplification of clinical treatment for CRC, and may serve as a promising direction for contemporary TCM research on CRC.

References

[1] Wild CP, Weiderpass E, Stewart BW. World Cancer Report: Cancer Research for Cancer Prevention [M]. Lyon: International Agency for Research on Cancer, 2020: 16.

[2] Liu Zongchao, Li Zhexuan, Zhang Yang, et al. Interpretation of the 2020 Global Cancer Statistics Report [J]. Electronic Journal of Integrated Tumor Therapy, 2021, 7(2): 1-14.

[3] Xue Siqi, He Jing, Tang Yong. Advances in the treatment of colon cancer [J]. China Medicine and Pharmacy, 2022, 12(9): 58-61.

[4] Peng Qifeng, Chang Jun, Wang Chengchuan, et al. Application of precision TCM treatment in colorectal cancer [J]. Chinese Journal of Coloproctology, 2018, 38(01): 52-55.

[5] Fu Li, Wang Feiye, Xu Yun, et al. Study on the distribution and evolution patterns of TCM syndromes in colorectal cancer [J]. Journal of TCM Oncology, 2024, 6(01): 63-69. DOI:10.19811/j.cnki.ISSN2096-6628.2024.01.010.

[6] Peng Jing. A study on the category of "transformation" in ancient Chinese aesthetics [D]. Sichuan Normal University, 2010.

[7] Cui Zhizhong. An insight into the characteristics of early Chinese thought from the category of "Yin-Yang" [J]. Journal of Hunan Institute of Engineering (Social Science Edition), 2015, 25(03): 59-62.

[8] Chen Ye, Liu Jintao, Zhu Yuan, et al. Overview of TCM syndrome differentiation and treatment of colorectal cancer [J]. China Cancer, 2015, 24(04): 319-324.

[9] Li Yu, Li Cheng, Shi Haoyang, et al. Etiological treatment of colorectal cancer based on the theory of "latent toxin" [J]. Tianjin Traditional Chinese Medicine, 2024, 41(6): 714-718. DOI:10.11656/j.issn.1672-1519.2024.06.08.

[10] Kong Weiwei, Zhao Nini, Wang Xinwen. Experience of Wang Xixing in treating colorectal cancer with harmonization therapy [J]. China's Naturopathy, 2020, 28(09): 28-29+74. DOI:10.19621/j.cnki.11-3555/r.2020.0912.

[11] Cao Jing. A brief exploration of the prevention and treatment of digestive system tumors guided by the Yellow Emperor's Inner Canon [J]. Guangming Journal of Chinese Medicine, 2013, 28(11): 2248-2249.

[12] Shen Ziyin. Micro-syndrome differentiation and the microscopicization of syndrome differentiation [J]. Journal of Traditional Chinese Medicine, 1986, (02): 55-57. DOI:10.13288/j.11-2166/r.1986.02.038.

[13] Wang Dongfang, Gan Zuwang, Qin Du'an. Etiological investigation of laryngeal cough and its pathophysiological basis [J]. Liaoning Journal of Traditional Chinese Medicine, 1995, (04): 145-146. DOI:10.13192/j.ljtcm.1995.04.145.wangdf.001.

[14] Hanahan D, Weinberg RA. The hallmarks of cancer [J]. Cell, 2000, 100(1): 57-70.

[15] Hanahan D, Weinberg RA. Hallmarks of cancer: The next generation [J]. Cell, 2011, 144(5): 646-674.

[16] Sun Leitao, Yu Jieru, Zhang Leyin, et al. Exploration of tumor phenotype identification from the perspective of TCM Yin-Yang concept [J]. Journal of Traditional Chinese Medicine, 2019, 60(12): 1030-1034. DOI:10.13288/j.11-2166/r.2019.12.009.

[17] Erdogan B, Webb DJ. Cancer-associated fibroblasts modulate growth factor signaling and extracellular matrix remodeling to regulate tumor metastasis [J]. Biochem Soc Trans, 2017, 45(1): 229-236.

[18] Zhao Hongbo, Wu Xiaojing, Yang Yun, et al. Correlation of colon polyps' endoscopic morphological characteristics and pathological types with TCM syndrome types [J]. World Chinese Journal of Digestology, 2020, 28(21): 1068-107.