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REVIEW

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Immunonutrition in the perioperative period of ovarian cancer: from molecular mechanism to clinical application

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Abstract

Ovarian cancer is a major disease that poses a serious threat to the life and health of women worldwide, exhibiting the highest mortality rate among all gynaecological tumours. Patients with ovarian cancer often experience malnutrition due to factors such as tumour-related nutritional depletion and stress responses resulting from surgery. This malnutrition status in turn increases complications, mortality, and economic burden; affects treatment efficacy and prognosis; and prolongs hospitalisation time. Therefore, patients with ovarian cancer should be monitored for malnutrition and provided with prompt, adequate nutritional support in addition to surgery. Arginine, glutamine, omega-3 polyunsaturated fatty acids, probiotics, and multiple vitamins are the most widely studied immunonutrients. Moreover, patients with ovarian cancer require individualised nutritional support, with enteral and parenteral nutrition being the presently employed primary methods of nutritional support.

Keywords

Ovarian cancer; Immunonutrition; Pathogenesis; Support pathways; Nutrients

1. Introduction

Ovarian cancer is a gynaecological tumour with the highest mortality rate [1]. Furthermore, the onset of ovarian cancer is insidious, and its clinical manifestations are non-specific. Most patients with ovarian cancer present with symptoms such as loss of appetite, abdominal pain, bloating, bowel habit changes, extreme fatigue, and back pain. Consequently, approximately two-thirds of patients are diagnosed with ovarian cancer at an advanced stage. The current mainstay of treatment for ovarian cancer is surgery supplemented with chemotherapy, whereas radiotherapy is rarely used in clinical practice [2]. Additionally, patients with ovarian cancer have the highest malnutrition rate of all gynaecological tumours, while perioperative malnutrition significantly increases the rates of surgical complications and mortality and affects patient prognosis. Therefore, timely monitoring and providing reasonable nutritional support are required in this patient group. Recent research has indicated that the next-generation sequencing technique has revolutionised the study of metabolic mechanisms, allowing investigation not only at the sample level but also at the cellular level [3]. Various computational methods have also emerged that enable the estimation of metabolic flux in key pathways and metabolites within single cells [4]. This rapidly advancing technology can facilitate the development of personalised nutrition treatment plans for individual patients in clinical settings. This review summarises the recent research progress on immunonutrition in ovarian cancer, offering theoretical guidance for the clinical application of perioperative immunonutrition in this patient population.

2. Pathogenesis of perioperative malnutrition in patients with ovarian cancer

Approximately 24% of patients with gynaecological tumours exhibit malnutrition at diagnosis, with the highest malnutrition incidence among those with ovarian cancer (67%). As the disease progresses, the body enters a state of stress, while the continued tumour proliferation results in a constant consumption of nutrients. All these conditions lead to a gradual escalation of malnutrition [5]. Moreover, the mechanical damage caused by surgery and the fear and anxiety of patients concerning their cancer can aggravate cachexia, increase the rates of surgical complications, morbidity, and mortality, and affect the prognosis.

2.1 Adverse effects of ovarian cancer on patients

Tumours induce the central nervous system to release signals that result in a decreased appetite and anorexia, while advanced tumours often trigger ascite formation. Furthermore, the pain, anxiety, and/or depression in patients with ovarian cancer can cause reduced food intake during the preoperative stage,

eventually leading to insufficient nutrient intake, immunodeficiency and metabolic disorders. Additionally, the catabolic effects of tumours can trigger muscle wasting, increased fat decomposition, and abnormal nutrient metabolism. Moreover, in patients with excessively large or advanced tumours, gastrointestinal metastasis may cause mechanical obstruction of the gastrointestinal tract, ultimately affecting the digestion and absorption of food [6].

2.2 Direct impact of surgery on patients with ovarian cancer

In addition to the tumour-associated adverse effects, surgery, which is the main treatment modality for ovarian cancer, can directly affect patients. For example, the psychological stress response arising from surgical trauma and fear of surgery can result in the excitation of the sympathetic nervous system and the production of various cytokines, including tumour necrosis factor (TNF). Subsequently, these cytokines not only activate the immune system but also induce a serious negative nitrogen balance by activating the hypothalamus–pituitary–adrenal axis, leading to an interaction between the inflammatory and immune responses and the secretion of abundant catecholamines [7].

Although prolonged preoperative and postoperative fasting can prevent vomiting and aspiration during anaesthesia and surgery, it can induce psychological and physiological discomfort as well as lower the nutritional intake of patients. Recently, several randomised controlled trials have reported that drinking carbohydrate-rich fluids 2 hours before surgery helps minimise postoperative discomfort and improve insulin resistance, perioperative well-being, immune function, and nutritional status while not increasing the likelihood of events such as aspiration pneumonia and asphyxia linked to the aspiration of gastric contents [8]. Schilder J.M. *et al*. [9] compared the length of hospital stay, duration of postoperative intestinal obstruction, and incidence of adverse effects, such as nausea, vomiting, and postoperative complications, in two groups of patients fed a liquid diet on postoperative day 1. In that study, traditional oral intake was initiated in the patients only after bowel function recovery. Their results demonstrated that patients who received the early feeding regimen had a significantly shorter hospital stay and lower treatment costs. Another investigation by Braga M. *et al*. [10] compared the effects of different formulations of enteral nutrition (EN) administered within 12 h of surgery. The researchers revealed a significant reduction in the severity of postoperative infection and hospital stay in patients fed a nutrient-rich diet. Therefore, patients with ovarian cancer without contraindications such as diabetes are recommended to be provided carbohydrate-rich fluids 2 h before surgery, followed by a nutrient-rich liquid diet as early as possible after surgery to avoid fasting-induced malnutrition.

2.3 Direct effects of chemotherapy on patients with ovarian cancer

Chemotherapy, which often causes side effects such as anorexia, nausea, vomiting, and diarrhoea, is used as an adjuvant treatment in the early stages of ovarian cancer when malnutrition is not likely. Nevertheless, these side effects may result in reduced food intake and insufficient nutrient absorption, leading to anaemia and hypoalbuminemia that seriously affect the quality of life and nutritional status of patients. Additionally, the side effects of chemotherapeutic drugs can cause discomfort in patients. This discomfort can lead to patient resistance to chemotherapy and treatment termination, potentially increasing the severity of cachexia [11].

3. Types and roles of commonly used immunonutritional agents in ovarian cancer

Nutritional therapy has been suggested as the first-line treatment instead of adjuvant treatment for patients with tumours [12]. Immunonutrition not only fulfils the daily requirement of nutrients and energy but also participates in the metabolism and immune regulation of the body as well as improves the immunity, prognosis, and quality of life of patients. To date, the nutrients that have been extensively studied and used in clinical practice include arginine, glutamine, omega-3 polyunsaturated fatty acids (ω-3 PUFAs), probiotics and vitamins.

3.1 Arginine

Arginine is a common non-essential amino acid involved in cell growth and proliferation, immune responses and the maintenance and protection of intestinal mucosal function. This amino acid serves as a nitrogen source for nitric oxide production in endothelial and immune cells during vasodilation and host defence mechanisms as well as for the synthesis of creatine for muscle metabolism and urea for maintaining systemic nitrogen homeostasis [13]. The increased expression of arginase and inducible nitric oxide synthase can lead to decreased arginine concentration, which in turn inhibits the tumour-specific T-cell responses and acquired immune responses. These alterations allow tumour cells to evade the immune system and continue proliferation. Thus, adequate arginine supplementation may enhance T-lymphocyte production, thereby reversing the immunosuppressive state and enabling the optimal functioning of the host immune response. To verify this hypothesis, Paßlack N. [14] conducted an *in vitro* study on cats to assess the effect of amino acids on immune function and found that high arginine doses heightened the secretion of Interleukin (IL)-4, IL-10 and Tumor Necrosis Factor (TNF)-α by T cells and significantly affected T-cell proliferation. In further support of this perspective, a meta-analysis of 11 trials reported a significantly higher proliferative response of Cluster of differentiation (CD)4^+ T cells and a lower incidence of infectious complications in the group supplemented with L-arginine than in the control group [15]. Moreover, several randomised controlled trials demonstrated that arginine increases prealbumin levels, alleviates wound complications, decreases the length of hospital stay, and improves long-term survival in various tumours, including gastric, colorectal and head and neck cancers [16].

In contrast to the above findings, other studies have indicated that adequate arginine levels may contribute to tumour

growth, proliferation, and metastasis, whereas low arginine concentrations can help control tumour growth [17]. A study involving patients with breast cancer who were randomly administered a standard diet or arginine supplements measured the rate of tumour protein synthesis using leucine. The study results revealed that the rate of tumour protein synthesis in the patients receiving arginine supplements was higher than the rate in those on a standard diet, implying that L-arginine stimulates tumour growth and progression *in vivo* [18]. Recently, Nazarian B. *et al*. [19] performed a meta-analysis to investigate the effects of L-arginine on inflammatory biomarkers. The researchers observed that L-arginine supplementation increased C-reactive protein (CRP) levels in patients aged >60 years (baseline CRP levels >3 mg/dL), in those with tumours, and in those with EN support, suggesting that arginine supplementation should be cautiously administered in these patient populations to avoid increasing the infection rate. However, the benefits of adequate arginine supplementation in patients with ovarian cancer remain unclear. Thus, large sample-size studies should be conducted to explore this aspect.

3.2 Glutamine

Glutamine is a non-essential amino acid that serves as the most crucial nitrogen source for maintaining nitrogen homeostasis in the body. This amino acid is also an essential nutrient for the proliferation and cytokine production of lymphocytes, phagocytosis and secretory activity of macrophages, and bacterial killing ability of neutrophils [20]. Further, adequate glutamine is required for maintaining intestinal mucosal function and reducing bacterial translocation and the inflammatory responses of the body [21]. Glutamine is primarily stored in the skeletal muscles, where it lowers negative nitrogen balance and maintains muscle mass and intestinal integrity. During stressful conditions such as tumour development and surgery, the stored glutamine in the plasma and muscles is rapidly depleted owing to its supply to the visceral organs, leading to immunosuppression in critically ill patients and elevated infection risk [22]. Correspondingly, prior randomised controlled trials have reported that glutamine supplementation in patients with cancer can aid in reducing treatment complications, shortening hospital stays and prolonging survival [23].

Ovarian cancer often results in the overproliferation and overexpression of the *MYC* oncogene, leading to adverse effects. Glutamine has been shown to inhibit the *MYC* oncogene to promote the apoptosis of tumour cells and effectively treat tumours [24]. Additionally, glutamine supplementation in patients undergoing radiotherapy can contribute to mitigating the severity of radiation-induced diarrhoea. Another investigation by Anderson *et al*. [25] showed that glutamine supplementation not only alleviates the symptoms and improves the quality of life of patients receiving chemotherapy but also reduces chemotherapy-induced mucosal damage, such as mucositis, stomatitis, pharyngitis, oesophagitis and enteritis. Furthermore, oral glutamine administration can reduce paclitaxel (PAC)-induced peripheral neuropathy, inhibit proteolytic metabolism, and enhance intestinal barrier function [26]. Similarly, Stubblefield, M.D. *et al*. [27] evaluated the neurological signs and symptoms and nerve conduction alterations in 46 patients undergoing PAC chemotherapy, among which 17 received high doses of PAC combined with glutamine, while the remaining 29 were administered a high dose of PAC only. Their findings indicated that the neurological signs and symptoms were significantly alleviated in patients receiving PAC with glutamine. However, contradictory results were reported in a study conducted by Loven D. *et al*. [28] using the same PAC regimen in 43 patients with ovarian cancer, wherein 23 received glutamine supplementation during chemotherapy, and 20 received a placebo with chemotherapy. The results revealed that glutamine supplementation did not prevent PAC-induced peripheral neurotoxicity after six treatment sessions. Yang L. *et al*. [29] also examined the relationship between ovarian cancer cells and glutamine and found that the proliferation of highly invasive ovarian cancer cells significantly depended on glutamine, suggesting the critical role of glutamine in promoting ovarian tumour growth. Moreover, glutamine withdrawal was suggested to induce apoptosis and cell cycle arrest in ovarian cancer cells, indicating that glutamine deficiency might be beneficial for patients with ovarian cancer and that excess supplementation was not required.

3.3 Omega-3 polyunsaturated fatty acids

ω-3 PUFAs, primarily including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are an important class of nutrients mostly found in fish oil. These fatty acids exert pro-apoptotic and anti-angiogenic effects as well as potentially induce ovarian cancer cell death via the restoration of T-cell function by mainly activating the reactive oxygen species-dependent Mitogen-Activated Protein Kinase (MAPK) pathway and inhibiting arginase to increase the concentration of available arginine [30]. Oral administration of ω-3 PUFA-rich supplements 5 days before surgery has been shown to not only improve the preoperative nutritional status but also alleviate the preoperative and postoperative inflammatory and immune responses in patients with cancer [31]. Zajdel A. *et al*. [32] reported that DHA inhibits cell viability and proliferation, accelerates cell death, and induces caspase-3/7 activation, thereby significantly enhancing the cytotoxic effects of cisplatin in ovarian cancer cells. Zhao Y. *et al*. [33] also demonstrated that EPA functions as a tumour suppressor in ovarian cancer by inducing apoptosis via the fatty acid receptor G Protein-coupled Receptor 30 (GPR30). Moreover, DHA has been suggested to be more effective than EPA in impeding the growth of ovarian cancer cells [34]. A study by Eilati E. *et al*. [35] indicated that the long-term consumption of a flaxseed-rich diet could reduce ovarian cancer severity and lower prostaglandin E2 levels in hens. Furthermore, PUFA-rich flaxseeds produce methoxyestradiol, which promotes P38 phosphorylation, mediates glycolipid metabolism, and eventually induces apoptosis in ovarian cancer cells [36]. Therefore, ω-3 PUFAs are a nutritional agent with established clinical efficacy in killing ovarian cancer cells.

3.4 Probiotics

Probiotics are essentially used to inhibit the growth of harmful bacteria and improve the intestinal microenvironment.

Chemotherapy can increase intestinal permeability and lead to the transfer of intestinal microorganisms outside the gut. This translocation of intestinal microorganisms triggers a systemic immune response to cause chronic inflammation, metabolic dysfunction, malnutrition, and cachexia. Therefore, maintaining intestinal barrier function may help to counteract the symptoms of cachexia in patients with cancer [37]. Sipos A. *et al*. [38] also reported that signalling through bacterial metabolites could be involved in ovarian cancer pathogenesis. For example, the upregulation of pro-inflammatory metabolites, such as lipopolysaccharides and lysophospholipids, and the downregulation of tryptophan metabolites can inhibit tumour growth. Currently, probiotics are used in clinical practice to treat diseases as well as in daily life to regulate the balance of intestinal flora, promote nutrient absorption, maintain intestinal health and improve immunity [39]. Furthermore, consulting a registered dietitian or healthcare professional can help formulate an individualised probiotic combination or identify a probiotic type best suited for each person. However, attention should be paid when using probiotics in immunocompromised patients, and the possible risks linked to probiotic consumption should be considered.

3.5 Vitamins

3.5.1 Vitamin A

Vitamin A is a fat-soluble vitamin associated with night vision, with its deficiency being the primary cause of night blindness. Moreover, all-trans retinoic acid, an intermediate metabolite of vitamin A, has been shown to inhibit the proliferative and invasive abilities of ovarian cancer cells via S100A10-dependent and -independent mechanisms [40]. Wang Q. *et al*. [41] conducted a meta-analysis including 4882 cases to examine the association between vitamin A and ovarian cancer and found that a higher dietary intake of vitamin A might contribute to a lower ovarian cancer incidence. Similarly, several randomised controlled trials have highlighted that vitamin A metabolism promotes tumorigenesis and that vitamin A supplementation is beneficial for patients with ovarian cancer [42].

3.5.2 Vitamin B

Vitamin B9, also known as folic acid or folate, is a B vitamin critically involved in the methylation, synthesis and repair of DNA and maintaining normal cellular function. Approximately 90% of patients with ovarian cancer overexpress the folate receptor. This receptor facilitates the transport of folate to cells, leading to the depletion of folate levels and interfering with their ability to drive cancer progression [43]. In support of this notion, Arthur R.S. *et al*. [44] determined that the dietary intake of folic acid or vitamin B6 at specific concentrations lowers the risk of ovarian cancer. Conversely, some studies have suggested that folic acid intake and ovarian cancer risk are not significantly correlated [45]. Therefore, these contrasting findings on the potential benefits of folic acid supplementation should be resolved by conducting large sample-size studies to validate the relationship between folate and ovarian cancer.

3.5.3 Vitamin C

Vitamin C can kill tumour cells by producing hydrogen peroxide to exert local pro-oxidant effects and interfere with the tumour cell cycle. Vitamin C deficiency in patients with ovarian cancer impairs the activity of natural killer (NK) cells [46], whereas supplementation with high vitamin C doses not only kills cancer cells without harming normal tissues but also enhances chemotherapy sensitivity and minimises chemotherapy-related toxicity in ovarian cancer [47]. Similarly, Drisko J. *et al*. [48] demonstrated that chemotherapy combined with vitamin C supplementation could enhance the efficacy of chemotherapy and effectively treat cancer. However, vitamin C should be administered intravenously to achieve optimal efficacy because the oral supplementation of vitamin C can result in severely low final plasma concentrations of vitamin C due to its limited absorption and renal excretion. Nevertheless, vitamin C is vital in maintaining the cytotoxicity of NK cells, and its supplementation represents an alternative modality for ovarian cancer treatment.

3.5.4 Vitamin D

Vitamin D is a fat-soluble vitamin that promotes the absorption of calcium and magnesium in the intestine. Under normal conditions, mesothelial cells serve as a barrier in the peritoneal cavity to prevent cancer cell adhesion. However, the microenvironment formed by tumour-associated mesothelial cells in ovarian cancer supports tumour metastasis, with advanced ovarian cancer often spreading to the peritoneum. A previous investigation by Kitami K. *et al*. [49] showed that vitamin D normalises the peritoneum microenvironment and strengthens the barrier function of endothelial cells, thereby reducing tumour metastasis. Additionally, vitamin D can exert anticancer effects by suppressing Colon Cancer Associated Transcript 2 (*CCAT2*) gene expression in ovarian cancer cells via the active metabolite osteotrol and by directly interfering with Gal-3 protein to restrict the proliferative, invasive, and migratory abilities of these cancer cells [50]. Lastly, vitamin D has been demonstrated to induce cancer cell apoptosis and help predict ovarian cancer prognosis [51].

3.5.5 Vitamin E

Vitamin E possesses the highest anticancer activity and strong antioxidant properties. Additionally, it is involved in certain immune-related processes, including promoting T-lymphocyte proliferation and cytokine secretion by monocytes. Among the various types of vitamin E, gamma-tocotrienol (γ-TT) and delta-tocotrienol (δ-TT) are the two activated forms exhibiting the most potent anticancer effects [52]. These two vitamin E types can induce G1–S-phase arrest in the ovarian cancer cell cycle and mitochondrial apoptosis, synergise with cisplatin to enhance its cytotoxicity, and sensitise ovarian cancer cells to platinum treatment [53]. In line with these results, Thomsen C.B. *et al*. [54] demonstrated that Tocotrienol (TT) combined with bevacizumab had relatively greater efficiency in killing tumour cells in chemotherapy-refractory ovarian cancer. Argyriou A.A. *et al*. [55] performed a randomised controlled trial comparing patients who received oral vitamin E during chemotherapy with those who did not receive vitamin

E supplementation with chemotherapy after 3 months of treatment cessation. Their findings showed that the incidence of neurotoxicity was significantly higher among patients who did not receive vitamin E supplementation, indicating that vitamin E can prevent chemotherapy-induced neuropathy. Therefore, vitamin E supplementation is a suitable option to be used in combination with chemotherapy. This combined therapy not only enhances the efficacy of chemotherapy but also prevents its side effects. Vitamin E has also been found to inhibit cancer cell invasion, metastasis and angiogenesis [56]. Furthermore, vitamin E has been theorised to promote gonadotropin secretion, activate ovarian function, and prevent ovarian cancer. In contrast, a recent meta-analysis reported that high vitamin E intake was not significantly associated with ovarian cancer risk [57] (Table 1 and Fig. 1).

4. Pathways of nutritional support for patients with ovarian cancer

Oral feeding is advocated in patients having early-stage ovarian cancer with no indicators suggesting malnutrition and with good nutritional screening and assessment results. However, the caloric content of the food should be increased to meet nutrient consumption by the tumour. Moreover, oral nutrition supplements should be considered after oral intake alone is rendered inadequate to support the increased calorie and protein requirements, with EN support as the preferred method. Additionally, in cases where the gastrointestinal tract cannot tolerate EN support as the disease progresses, parenteral nutrition (PN) support via the intravenous route is the favoured strategy.

4.1 Oral feeding

Most patients with ovarian cancer who are fed orally do not have the nutritional intake to fulfil the body's needs and tumour-related depletion. Consequently, the energy intake of patients with ovarian cancer should be increased by elevating calorie supply and adjusting nutrition content. Paxton R.J. *et al*. [58] examined the dietary habits of survivors of stage II–IV ovarian cancer and determined that a low-fat and high-fibre diet with a high intake of soy, fruits, and vegetables might increase the survival probability in ovarian cancer and satisfy the required nutrition levels. However, no specific dietary factors have shown a consistent association with ovarian cancer risk [59].

4.2 Enteral nutritional support

EN support is a relatively safer and inexpensive form of nutritional support that helps maintain the integrity of the gastrointestinal mucosa by providing patients with the required nutrients primarily using oral or tube feeding without the need to pour the feed. Compared to standard enteral formulas, EN feeds augment defence mechanisms and modulate inflammation after elective major cancer surgery. Additionally, this method is more physiologically beneficial and less risky than EN support and is commonly used in patients with an intact gastrointestinal tract. Hence, EN is possibly the best approach to providing nutritional support [60].

Chapman J.S. *et al*. [61] revealed that patients who received postoperative EN experienced fewer wound complications and a lower incidence of grade 2 and 3 surgical site infections than those who did not receive EN. Following this study, Buzquurz F. *et al*. [62] conducted a meta-analysis of 22 randomised controlled trials and highlighted that patients on EN exhibited lesser overall infection complications than the controls, further supporting the notion that EN can serve as an approach to minimise surgical site infections. EN can also contribute to diminishing the toxicity and adverse effects associated with cancer treatment and improving the nutritional and clinical status of patients. In patients undergoing major surgery, preoperative EN may ameliorate the cancer-bearing state, while early postoperative EN may reduce infections and wound complications, enhance immunity, and lower treatment

TABLE 1. Molecular mechanism and clinical application of nutrients.

Nutrients	Molecular mechanisms	Clinical application
Arginine	Increase T lymphocyte	Reduce infection complications
Glutamine	Suppresses the *MYC* oncogene	Reduce the side effects of radiotherapy and chemotherapy
Omega-3 polyunsaturated fatty acids	Pro-apoptotic and anti-angiogenic	Improve preoperative nutritional status and postoperative inflammation, immune response
Probiotics	Inhibit the growth and harmful bacteria	Prevent or relieve radiation-induced diarrhea
Vitamin A	S100A10-dependent and independent, mechanism	Reduce the side effects of radiotherapy
Vitamin B	Consume folate receptors	Interferes with cancer progression
Vitamin C	Pro-oxidant effects	Kill tumor cells and improve the sensitivity of chemotherapy
Vitamin D	Inhibit the expression of CCAT2 gene and Gal-3 protein	inhibit the ability of proliferation, invasion, and migration
Vitamin E	Anti-oxidant and promotes T lymphocyte proliferation	Prevent chemotherapy-induced neuropathy

CCAT2: Colon Cancer Associated Transcript 2.

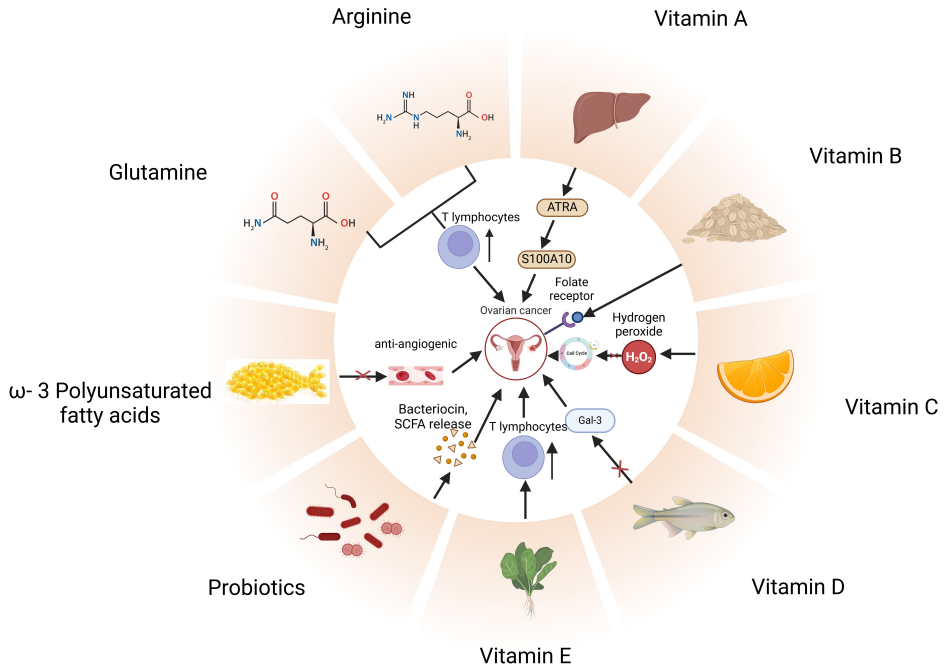

FIGURE 1. Molecular mechanisms of nutrients. ATRA: All-trans-retinoic acid; S100A10: Recombinant S100 Calcium Binding Protein A10; SCFA: Short Chain Fatty Acids; Gal-3: Galectin-3.

costs [63]. However, EN has demonstrated side effects such as gastrointestinal reactions, with one study reporting a higher incidence of postoperative diarrhoea in the immunonutrition group than in the control group [62]. Therefore, patients should be closely observed during nutritional supplementation to detect adverse reactions early and promptly cease oral or tube feeding of immunonutrition preparations.

4.3 Parenteral nutritional support

A study by Heidegger C.P. *et al.* [64] indicated that EN supplementation had slow efficacy and could not adequately manage the nutritional needs of patients, whereas EN combined with PN support led to increased survival and improved quality of life. Thus, PN, mainly consisting of total PN (TPN) support and partial PN support, could serve as a crucial method of malnutrition support by facilitating the intravenous infusion of arginine, glutamine, ω-3 polyunsaturated fatty acids, and vitamins required by patients. Considering that patients with ovarian cancer have reduced intestinal blood flow due to tumour-induced pain, surgery, chemotherapy and other stressful conditions, EN administration may further aggravate gastrointestinal mucosal ischemia. PN can be advantageous in such situations, particularly in patients with advanced ovarian cancer, where the nutritional needs can only be met by PN due to restricted oral nutrition intake caused by the development of malignant bowel obstruction. However, Mendivil A.A. *et al.* [65] compared the effects of TPN and conservative treatment in 147 patients with ovarian cancer undergoing reduction surgery and bowel resection and observed that patients with TPN had more extended bowel function recovery periods and significantly longer hospital stays. These findings could be attributed to the lower preoperative albumin levels in the patients, emphasising that TPN should be cautiously administered in such patients. Moreover, PN is no longer the first choice of nutritional support because long-term PN can lead to intestinal mucosal atrophy and decreased intestinal function.

Home parenteral nutrition (HPN) is a continuation of PN support therapy after hospital discharge and is commonly used for patients requiring long-term PN. This approach involves joint decision-making between the physician and the patient, allowing the patient to receive nutritional support at home and even fulfilling the nutritional needs of those with advanced intestinal obstruction; however, HPN cannot replace the non-nutritional function of food [66]. Vashi P.G. *et al.* [67] investigated 52 adult patients with cancer who received HPN and demonstrated that HPN enhanced the quality of life and nutritional status and reduced the medical costs and financial burden in these patients.

5. Summary and conclusions

Ovarian cancer has the highest mortality rate among all gynaecological tumours. In addition to surgery and chemotherapy, immunonutrition is a crucial treatment modality for tumours, offering broad application prospects. Although the ESPEN and ERAS guidelines are recognised in reference centres, the types of nutrients that can be used, their supplementation routes, and their safety are still debated. Therefore, clinical studies with large sample sizes and more comprehensive epidemiological surveys are warranted to assess and validate the clinical implementation of nutritional support in patients with ovarian cancer.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

FYL—conceptualization. LJC and JM—investigation. YW—writing-original draft preparation. CJ—writing-review and editing. XYX—visualization. HYC—supervision. JC and DKL—project administration. All authors have read and agreed to the published version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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