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Whole-body cryotherapy can reduce the inflammatory response in humans: a meta-analysis based on 11 randomized controlled trials

Jun He[1,3]✉, Xinyu Zhang[2], Zhili Ge[2], Jingjing Shi[2], Shuwen Guo[1] & Jun Chen[3]✉

Whole-body cryotherapy (WBC) is increasingly being studied and used in various populations, mainly focusing on improving the body's regenerative capacity. More comprehensive summaries of anti-inflammatory responses are needed. To systemically assess the effect of WBC on the inflammatory response in humans based on randomized controlled trials (RCTs). Articles about RCTs accessing the effects of whole-body cryotherapy on the levels of inflammatory factors in humans published until August 1, 2024 had been searched in PubMed, Web of Science, Embase and Cochrane library databases. The general information of the included articles and exposure mode, the types and levels of inflammatory factors in serum were extracted. The PEDro scale was used to assess the risk of bias, and the GRADE scale was used to assess the level of certainty of evidence. RevMan 5.4 software were used to conduct the meta-analysis. A total of 11 RCTs in 11 articles were included, and the total sample size was 274. The level of IL-1β in serum of people exposed to WBC was lower than that in control group (SMD value was − 2.08pg/mL, *P* < 0.05), and athletes exposed to WBC were more likely to benefit from this. The level of IL-10 in serum of people exposed to WBC was higher than that in control group (SMD value was 0.78 pg/mL, *P* < 0.05), and obese people exposed to WBC were more likely to benefit from this than athletes. WBC effectively reduces inflammation by lowering IL-1β and increasing IL-10 levels, offering significant benefits for athletes and obese individuals.

Keywords Whole-body cryotherapy, Inflammation, Inflammatory factors, Randomized controlled trials

Inflammation underlies a wide variety of physiological and pathological processes. Inflammation can be triggered by a variety of factors[1], including blood clots[2], immune system disorders[3], cancer[4], infections[5], chemical exposures[6] and physical injuries[7]. Chronic or frequent inflammation may contribute to metabolic related diseases, cancers and autoimmune diseases[8], thus reducing the inflammatory response is generally considered beneficial[1]. Inflammatory factors refer to various cytokines involved in inflammatory response. Among them, members of tumor necrosis factor family and interleukin family play a major role in the inflammation. Different inflammatory factors can regulate the inflammatory process by promoting inflammation or inhibiting inflammation[9,10]. Studies have shown that athletes can reduce oxidative stress and inflammation by adding extra exercise[11].

In recent years, there has been a growing trend in the use of cold temperatures for therapeutic, health, and sporting recovery purposes, commonly known as cryotherapy. Cryotherapy is a physiotherapy method that utilizes the organism's response to stimulation through exposure to ice, cold water, and cold air[12]. The primary advantage of cryotherapy lies in its ability to alleviate post-injury pain and soreness[12]. Cryotherapy-induced reductions in inflammation and tissue damage have been evidenced in animal models of muscle injury and in humans[13,14]. Therefore, to limit the inflammation became one of the main goals of cryotherapy.

In cryotherapy, the use of whole-body cryotherapy (WBC) is growing. WBC utilizes compression refrigeration technology to create an environment of extremely low temperatures ranging from − 110℃ to -140℃. The subject is then exposed to this environment for a brief duration, typically 1 to 3 min, in order to achieve therapeutic effects. The extreme cold of WBC has become an emerging tool for sport and exercise recovery[15], demonstrating

[1]China Ordnance Industry Group-machine-environment Key Laboratory, Institute for Hygiene of Ordnance Industry, NO.12 Zhangba East Road, Yanta District, Xi'an 710065, Shaanxi, China. [2]Department of Occupational and Environmental Health, School of Public Health, Jilin University, Changchun 130021, Jilin, China. [3]Sanhang Institute for Brain Science and Technology, Northwestern Polytechnical University, Xi'an 710129, Shaanxi, China. ✉email: hejun152@126.com; junchen_sibst@nwpu.edu.cn

reductions in pain[16], inflammation[17], improved muscle strength recovery and benefits to range of motion[18]. Besides athletes and healthy individuals, WBC provides benefits for obese individuals because of its anti-inflammatory effect[19]. WBC increases plasma concentrations of cortisol, β endorphins, and catecholamines[20], regulates adaptive changes in myocardial and vascular parameters[21], and enhances vagus nerve drive at rest[22]. Some studies have demonstrated that WBC can increase the levels of anti-inflammatory interleukins and decrease the secretion of proinflammatory molecules[23,24]. Physiological mechanisms may involve a variety of factors, including sympathetic excitation triggered by cold stimuli, release of endogenous opioids, and changes in cytokine levels[21]. Cryostimulation can lead to vasoconstriction, lowering local temperatures, thereby reducing blood flow and reducing the release of inflammatory mediators[25]. But the results of some studies are inconsistent. For example, Wilson LJ found that cryotherapy intervention has no positively effect on borne markers of inflammation or structural damage compared to placebo[26]. It is very crucial to provide accurate evidence about the effect of WBC on inflammation.

More research is needed on WBC in healthy, injured, or clinical populations with musculoskeletal conditions, particularly concerning its anti-inflammatory effects. This understudied topic requires further exploration to determine how WBC can be applied to individuals with inflammatory diseases. A systematic review can guide future research efforts by mapping these evidence gaps and help ensure that WBC interventions are optimized across a broader range of conditions and populations. Therefore, the present meta-analysis was undertaken to systemically assess the effect of whole-body cryotherapy on the inflammatory response in humans based on RCT. It is important for the prevention and treatment of the inflammation-related diseases.

Methods

Search strategy

Two independent authors (ZXY and GZL) searched for articles about randomized controlled trials to assess the effects of whole-body cryotherapy on the levels of inflammatory factors in humans published from January 1, 2000 to January 1, 2024 in PubMed, Web of Science, Embase and Cochrane library databases. The search term adopts the form of subject word combined with free word. Search terms include whole body cryotherapy, whole body cryostimulation, cryotherapy, cryostimulation, cold exposure, cold stress, cold therapy, inflammation, inflammatory factors, IL-6, IL-1β, TNF-α, etc. The search strategy combinations in the Chinese database was "inflammation OR inflammatory factors" "IL-6 OR IL-1β OR TNF-α" "cryotherapy OR cold exposure OR cold stress OR cryostimulation". The English search strategy takes the PubMed database as an example: ((("inflammation"[MeSH Terms] OR "Inflammations"[Title/Abstract] OR "inflammatory factors"[Title/Abstract]) AND "cryotherapy"[MeSH Terms]) OR "Cryotherapies"[Title/Abstract] OR " whole body cryotherapy "[Title/Abstract] OR "cold therapy"[Title/Abstract] OR "cold therapies"[Title/Abstract] OR "Cryostimulation"[Title/Abstract]) AND (randomized controlled trial[Filter]). The connectives were adjusted based on the retrieval requirements of different databases. In addition, the reference listed in relevant reviews were manually retrieved to supplement the literature.

Selection criteria

Two independent authors (ZXY and HJ) selected and excluded the searched articles. Any studies that clearly deviate from the research objectives are excluded by reviewing the title and abstract of the literature. The remaining literature is thoroughly assessed through a comprehensive reading of the full text based on the inclusion criteria and exclusion criteria. Their differences were decided by the third author (ZLT).

The inclusion criteria includes: subjects are people who have had no major illnesses or surgeries recently, do not take any medication, and have no unhealthy habits, and the gender, age, region are not limited; the intervention mode of the experimental group must be WBC, and the control group did not receive any intervention but with the similar baseline data; the outcome index included at least one inflammatory factor level; studies were designed as RCT; the language is English or Chinese.

The exclusion criteria includes: subjects were animals; there was no control group or the baseline data of the control group was significantly different from that of the experimental group; studies were unable to accurately extract data on valid exposure conditions or inflammatory markers; the types of articles are reviews, meeting minutes, book chapters, pathology reports, etc.; for repeated published studies, only the one with the most comprehensive reports is retained.

Data extraction

Two independent authors (ZXY and HJ) separately extracted data from the included literature, and the disagreement was ruling by the third author (ZLT). The extracted data includes: the general information of the included articles such as the title, first author, publish year, country; the general information of the subjects such as sex, age, occupation, health status; the information of exposure such as exposure temperature, exposure time, exposure methods; the types and levels of inflammatory factors in serum (mean and standard deviation).

For studies that only provide data such as the median and interquartile distances, if the research results conform to normal distribution, the statistical tool Mean Variance Estimation (hkbu.eu.hk) was used to convert the median and interquartile distances into the mean and standard deviation; if they do not conform to normal distribution, the data will be discarded. Input the extracted data into Excel table, and check the extracted data to ensure the accuracy of the data.

Quality assessment

Two authors (ZXY and HJ) conducted quality assessment for eligible studies independently based on the Physiotherapy Evidence Database (PEDro)[27]. All RCTs included in this Meta-analysis are assessed for methodological quality using the 10-point PEDro scale. Except for item 1, which is not scored, 1 point will be awarded for each of the other items, for a total of 10 points. The score ranged from zero to three is considered of low quality. The score ranged from 4 to 5 is considered of medium quality. The score ranged from 6 to 8 is considered of high quality, and a score of 9 or above is considered of very high quality.

The strength of the evidence was evaluated using the Grade of Recommendations Assessment, Development and Evaluation (GRADE) standard[28], and the strength of the evidence was divided into four levels: high, moderate, low, and very low according to five factors: risk of bias, heterogeneity, indirectness, precision, and publication bias.

Statistical analyses

RevMan 5.4 software were used to conduct the meta-analysis. The levels of inflammatory factors in the control group and the experimental group were shown as mean ± standard deviation ($\overline{x} \pm s$). Weighted mean differences (WMDs) and 95% confidence intervals (CIs) were computed when the unit of an inflammatory factor was the same, otherwise standardized mean difference (SMD) and 95% CIs were computed. I-squared (I^2) was used to assess the heterogeneity. When $I^2 < 50\%$, a fixed-effect model was used for the meta-analysis. When $I^2 \geq 50\%$, a random-effect model was used for the meta-analysis. When heterogeneity is high, random-effects models are able to better reflect the true variability between studies, providing more reliable and generalizable results. Subgroup analyses were performed to identify the potential sources of the heterogeneity when there were multiple reports of populations in different countries or different physical conditions, or multiple reports of different control types. Sensitivity analysis was used to evaluate the stability of the results. Egger test was used to evaluate the publication bias, and $P < 0.05$ was considered as the existence of publication bias.

Results

Literature selection and exclusion

A total of 3760 articles were searched out based on the search strategy. Five hundred and forty-two duplicate articles were deleted through EndNote literature management software. Three thousand and seventy-six articles were excluded through reading titles and abstracts. Forty-one articles were excluded through reading the full text. Finally, 11 articles were included. The flowchart of the literature selection and exclusion is shown in Fig. 1.

Characteristics of the included literatures

A total of 11 RCTs in 11articles were included in this study, including 2 parallel controlled trials, 4 cross-controlled trials, and 5 self-controlled trials. The total sample size of the included articles was 274, with a minimum sample size of 5 and a maximum sample size of 32. There are 4 articles reported the effect of WBC on the level of IL-1β, 9 articles reported the effect of WBC on the level of IL-6, 4 articles reported the effect of WBC on the level of IL-10, 5 articles reported the effect of WBC on the level of TNF-α, and 4 articles reported the effect of WBC on the level of CRP. The detail characteristics of the included literatures were shown in Table 1.

Quality of the studies included

The average PEDro score of the 11 studies included was 6.6, indicating a high overall quality. Baseline data were similar across all literatures. All studies reported more than 85% subjects abide by the intervention, and provides point estimates and intergroup analyses for each effect size. The quality of the studies included was shown in Table 2.

The results of meta-analysis and sensitivity analysis

(1) The effect of WBC on the level of IL-1β.

There are 4 studies reported the effect of WBC on the level of IL-1β, including 72 people exposed to the extremely low temperatures ranging from − 110℃ to -140℃ for a brief duration, and 70 controls. Heterogeneity test results showed that $I^2 = 89\%$ ($P < 0.001$), which means high heterogeneity. This may be due to the small number of studies on this indicator or the presence of other heterogeneous sources. Random-effect model was adopted. The results of meta-analysis showed that the level of IL-1β in serum of people exposed to WBC was lower than that in control group, and the SMD was − 2.08pg/mL (95% CI: -3.43, -0.73) (Fig. 2A). The results of subgroup analysis showed that individuals exposed to WBC had lower serum IL-1β levels regardless of control mode; athletes exposed to WBC were more likely to benefit from this than the general population (Fig. 2B). Sensitivity analysis showed that the results were stable (Fig. 2C).

(2) The effect of WBC on the level of IL-6.

There are 9 studies reported the effect of WBC on the level of IL-6, including 126 people exposed to the extremely low temperatures ranging from − 110℃ to -140℃ for a brief duration, and 125 controls. Heterogeneity test results showed that $I^2 = 88\%$ ($P < 0.001$), which means high heterogeneity. The high heterogeneity may be due to differences in region, population type, or duration of exposure. Random-effect model was adopted. The results of meta-analysis showed that there was no significant difference in the level of IL-6 in serum of people exposed to WBC with that in control group, and the SMD was − 0.48pg/mL (95%CI :-1.29, 0.34) (Fig. 3A). Subgroup analysis found that heterogeneity can be reduced in self-controlled studies ($I^2 = 69\%$, $P = 0.020$), in healthy people ($I^2 = 40\%$, $P = 0.170$), or in obese people ($I^2 = 77\%$, $P = 0.040$) (Fig. 3B). Sensitivity analysis showed that the results were stable (Fig. 3C).

(3) The effect of WBC on the level of IL-10.

There are 4 studies reported the effect of WBC on the level of IL-10, including 39 people exposed to the extremely low temperatures ranging from − 110℃ to -140℃ for a brief duration, and 39 controls. Heterogeneity test results showed that $I^2 = 52\%$ (P -0.100), and random-effect model was adopted. The results of meta-analysis showed that the level of IL-10 in serum of people exposed to WBC was higher than that in control group, and the SMD was 0.78 pg/mL (95%CI :0.08, 1.48) (Fig. 4A). Subgroup analysis found that heterogeneity can be reduced

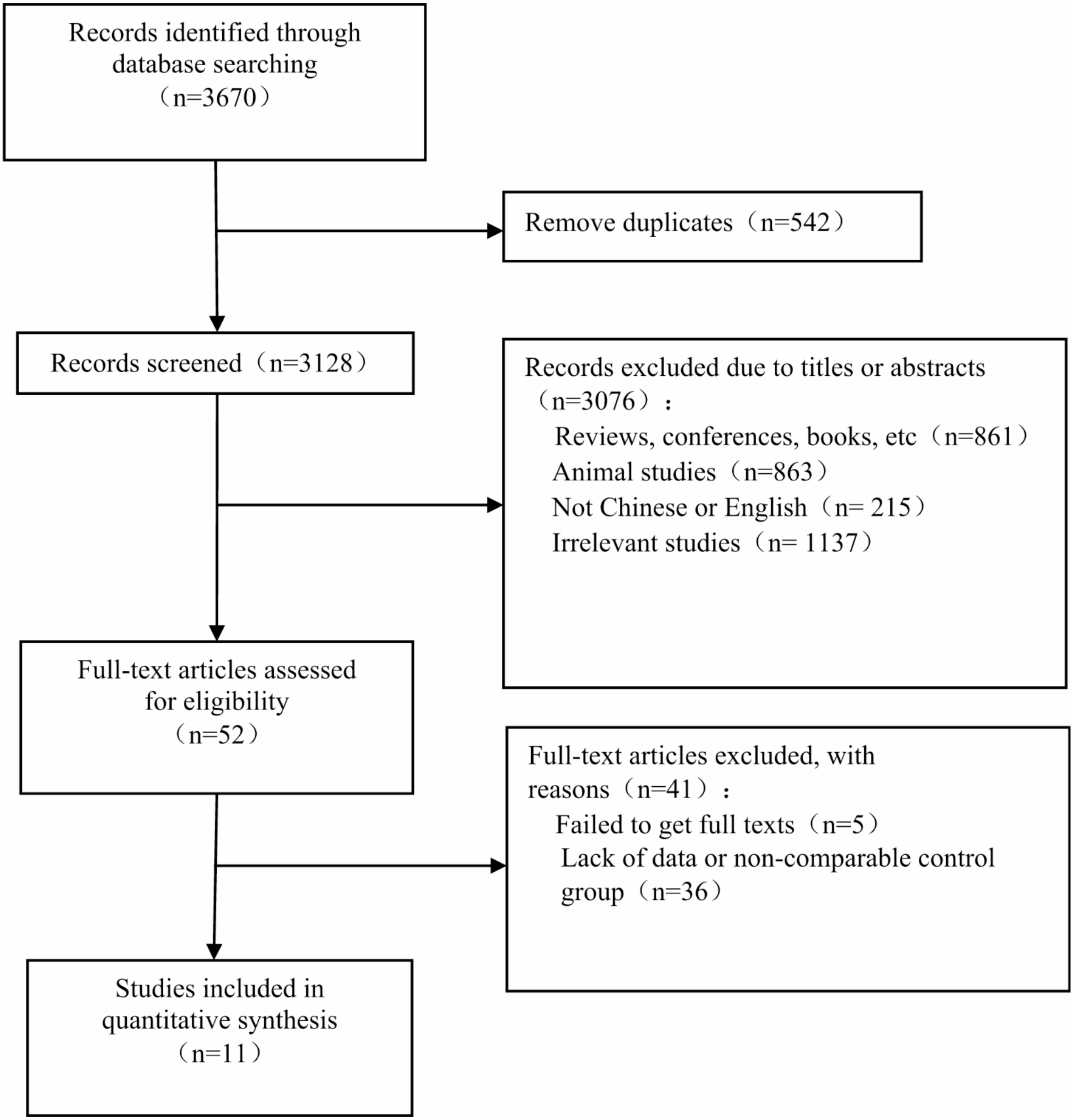

Fig. 1. Literature screening flow chart.

in cross-control studies (I^2 = 0%, P = 0.80) or in self-controlled studies (I^2 = 0%, P = 0.69), in athletes (I^2 = 44%, P = 0.170) (Fig. 4B). The results of subgroup analysis also showed that obese people exposed to WBC were more likely to benefit from this than athletes (Fig. 4B). Sensitivity analysis showed that the results were stable (Fig. 4C).

(4) The effect of WBC on the level of TNF-α.

There are 5 studies reported the effect of WBC on the level of TNF-α, including 79 people exposed to the extremely low temperatures ranging from − 110℃ to -140℃ for a brief duration, and 77 controls. Heterogeneity test results showed that I^2 = 72% (P = 0.006), which means high heterogeneity. High heterogeneity may be due to different exposure times, population types, or control types. Random-effect model was adopted. The results of meta-analysis showed that there was no significant difference in the level of TNF-α in serum of people exposed to WBC with that in control group, and the SMD was − 0.64pg/mL (95%CI :-1.31, 0.06) (Fig. 5A). Subgroup analysis found that heterogeneity can be reduced in cross-control studies (Fig. 5B). Sensitivity analysis showed that the results were stable (Fig. 5C).

First author (Year of publication)	Country	Crowd type	Control type	Sample size (C1/C2,*n*)	Age(years)	Exposure temperature (C1/C2,℃)	Exposure time (C1/C2,min)	Exposure method	Other measures	Detection method	Outcome measures
Malte Krueger(2019[29]	Germany	male athletes	Cross-control	11/11	25.9 ± 2.1	-110/(21.7 ± 0.8)	3/3	temperature-controlled cryochamber	Rapidly transitioning through − 10 °C and − 60 °C	ELISA	bce
Agnieszka Zembron-Lacny(2020[15]	Poland	elite male wrestlers	Parallel control	11/9	24.27 ± 3.35(C1) 25.00 ± 2.83(C2)	-120/23	3/3	cryogenic chamber	2 times/day, 7 days	ELISA	ad
Adnan Haq(2022[20]	U.K.	healthy male volunteers	Parallel control	9/8	37.0 ± 13.3	-120/(20 ± 0.5)	3/10	cryogenic chamber	30s adaptation to -60 °C	Bio-Plex Multiplex Immunoassays	b
Ewa Ziemann(2013[30]	Poland	obese men	Self-control	7/7	40.0 ± 4.0	-110/NR	3/NR	cryogenic chamber	20 ~ 30s adaptation to -60 °C, 1 time/day	ELISA	bcd
Katarzyna Dulian(2015[31]	Poland	obese men	Self-control	5/5	38.4 ± 8.2	-110/NR	3/NR	cryogenic chamber	20 ~ 30s adaptation to -60 °C	ELISA	b
Magdalena Wiecek(2020[32]	Poland	healthy female	Self-control	18/18	60.28 ± 3.63	-130/NR	3/NR	cryogenic chamber	30s adaptation to -60 °C, 4 times/day	ELISA	be
Banfi Giuseppe(2009)[33]	Italy	male rugby players	Self-control	10/10	26.0 ± 2.5	-110/NR	2/NR	cryogenic chamber	30s adaptation to -60 °C	ELISA	ce
Anna Lubkowska(2010)[34]	Poland	healthy men	Self-control	15/15	21.0 ± 0.7	-130/NR	3/NR	cryogenic chamber	30s adaptation to -60 °C	ELISA	b
Celestyna Mila-Kierzenkowska(2013)[35]	Poland	professional male volleyball players	Cross-control	18/18	28.32 ± 4.01	-130/NR	0 ~ 2/45	"Arctica" cryochamber	10 ~ 20s adaptation to -60 °C	ELISA	abd
Alicja Jurecka(2023)[36]	Poland	male athletes	Cross-control	32/32	25.20 ± 2.37	-130/NR	0 ~ 2/NR	cryogenic chamber	10 ~ 20s adaptation to -60 °C	ELISA	abd
Hervé Pournot(2011)[25]	France	male runners	Cross-control	11/11	31.80 ± 1.96	-110/24	3/30	temperature-controlled unit	NR	ELISA	abcde

Table 1. Basic information of the included literature. Note: C1: Low temperature exposure group; C2: Control group. a: IL-1β; b: IL-6; c: IL-10; d: TNF-α; e: CRP. NR: Not reported.

Included literature	A	B	C	D	E	F	G	H	I	J	K	Score
Malte Krueger(2019)[29]	Yes	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6
Agnieszka Zembron-Lacny(2020)[15]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Adnan Haq(2022)[20]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Ewa Ziemann(2013)[30]	Yes	Yes	No	Yes	No	Nor	No	Yes	Yes	Yes	Yes	7
Katarzyna Dulian(2015)[31]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Magdalena Wiecek(2020)[32]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Banfi Giuseppe(2009)[33]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Anna Lubkowska(2010)[34]	Yes	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6
Celestyna Mila-Kierzenkowska(2013)[35]	Yes	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6
Alicja Jurecka(2023)[36]	Yes	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6
Hervé Pournot(2011)[25]	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	7

Table 2. Quality evaluation of the included literature. Note: A: Subject eligibility; B: Randomization; C: Assign hidden; D: Baseline similar; E: Subjects are blinded; F: Therapist blinding; G: Appraiser blinding; H: Dropout rate<15%; I: Intention-to-treat analysis; J: Statistical analysis was performed between groups; K:Point measurements and variance values.

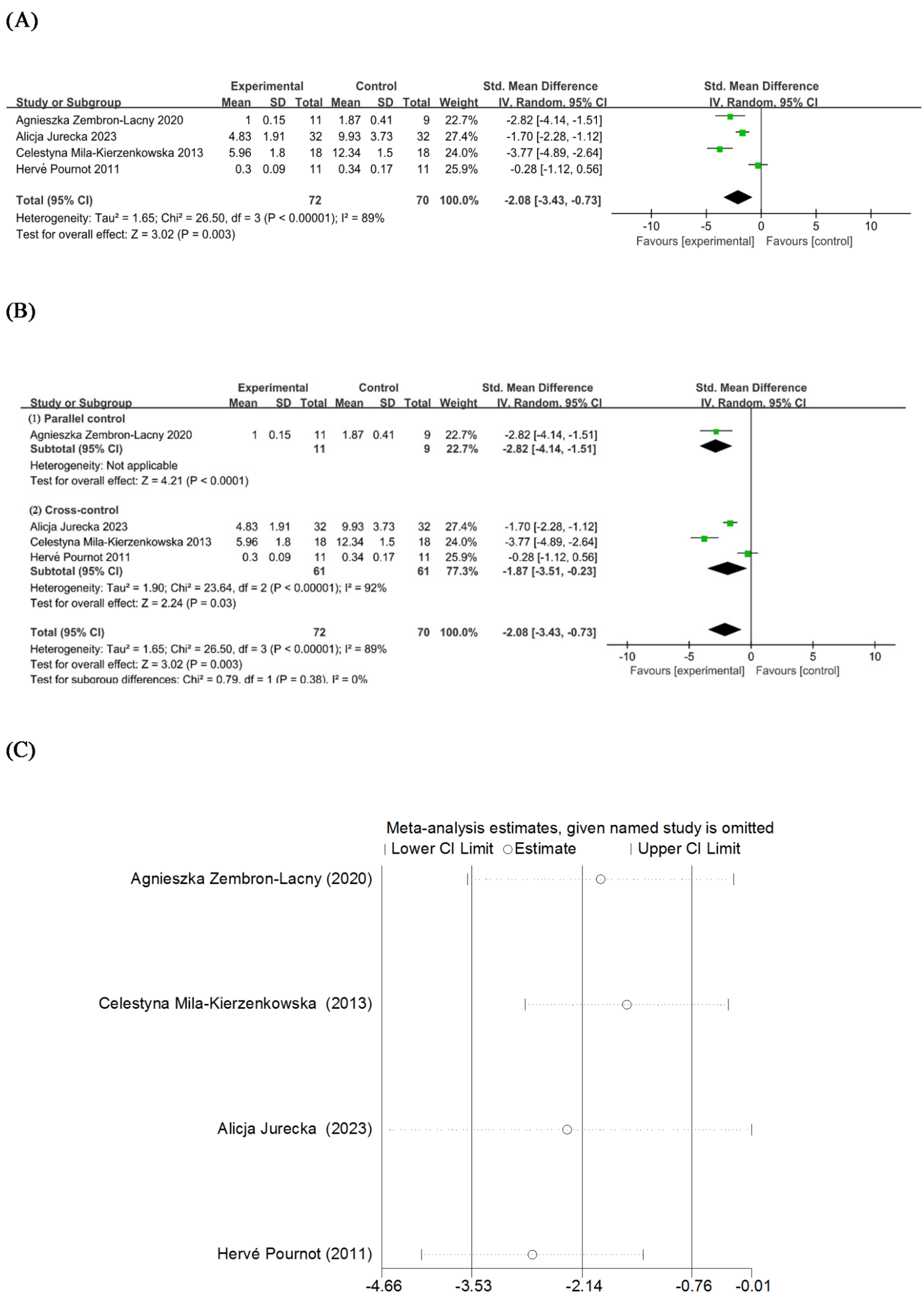

Fig. 2. The effect of WBC on serum IL-1β levels. (**A**) Results of meta-analysis of total effects; (**B**) Results of control subgroup analysis; (**C**) Sensitivity analysis plot. The positions of the rhombus on the abscissa represented weighted mean differences (WMD) from random effect meta-analysis. Horizontal lines represent 95% confidence intervals (CIs).

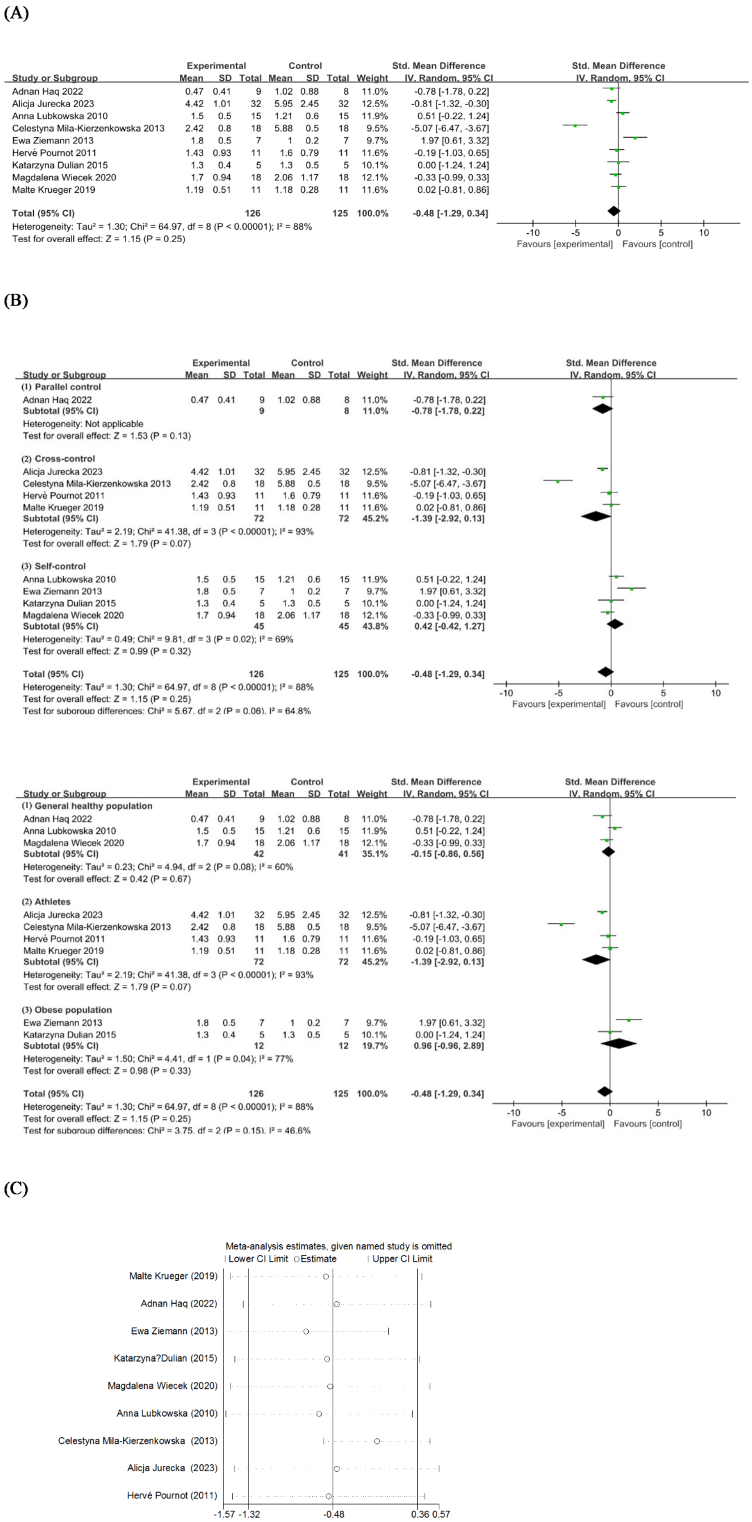

Fig. 3. The effect of WBC on serum IL-6 levels. (**A**) Results of meta-analysis of total effects; (**B**) Results of control subgroup analysis; (**C**) Sensitivity analysis plot. The positions of the rhombus on the abscissa represented weighted mean differences (WMD) from random effect meta-analysis. Horizontal lines represent 95% confidence intervals (CIs).

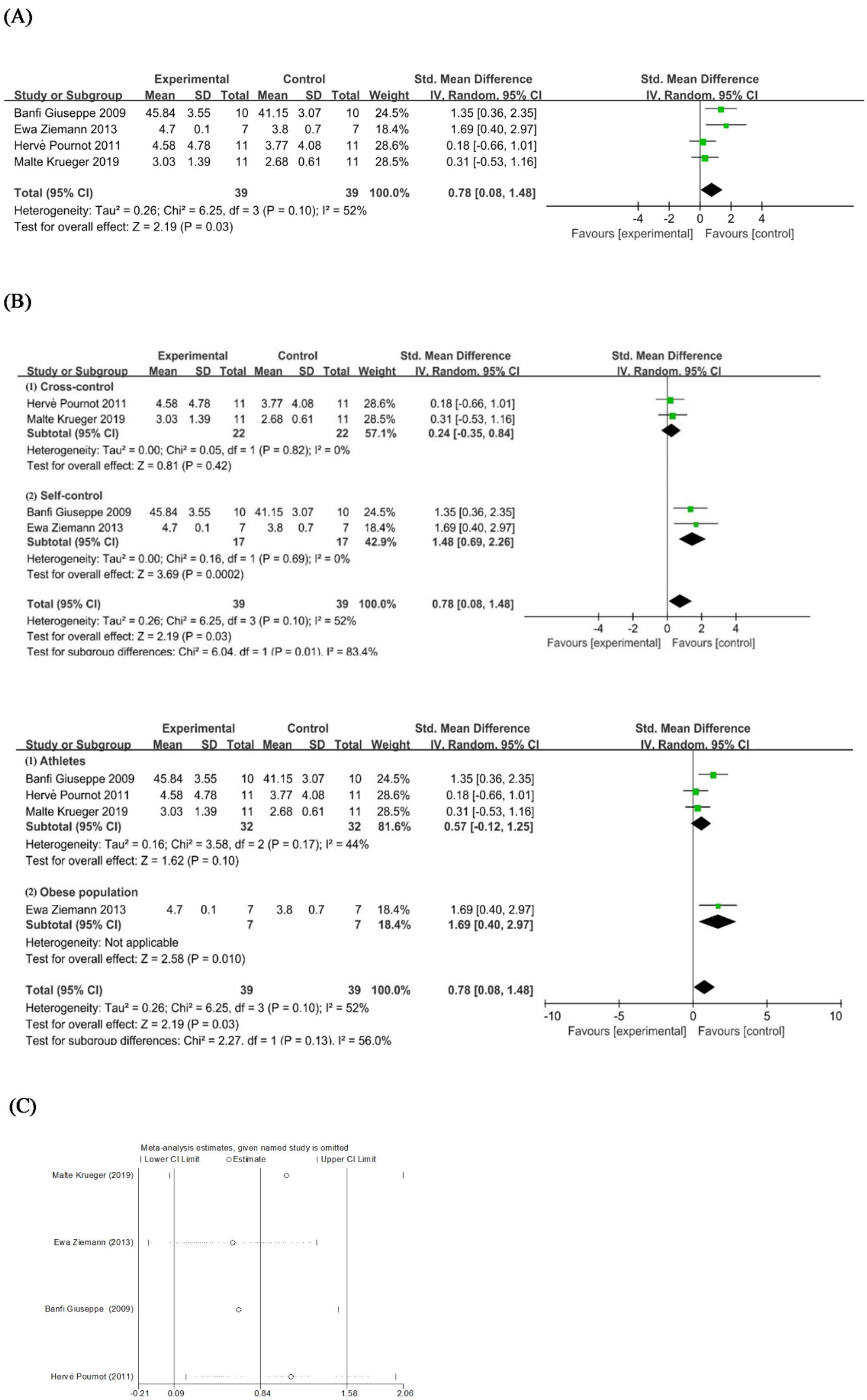

Fig. 4. The effect of WBC on serum IL-10 levels. (**A**) Results of meta-analysis of total effects; (**B**) Results of control subgroup analysis; (**C**) Sensitivity analysis plot. The positions of the rhombus on the abscissa represented weighted mean differences (WMD) from random effect meta-analysis. Horizontal lines represent 95% confidence intervals (CIs).

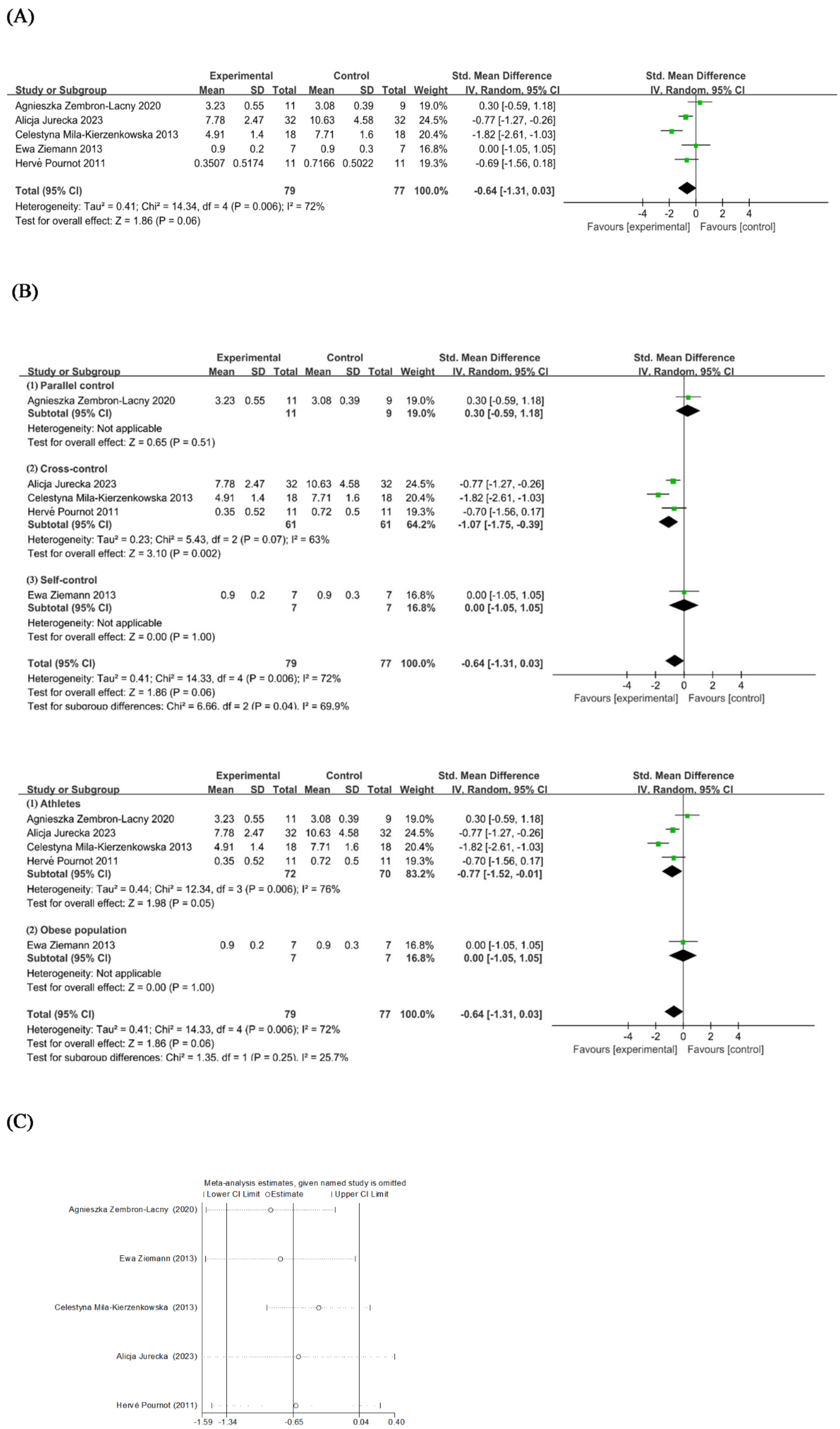

Fig. 5. The effect of WBC on serum TNF-α levels. (**A**) Results of meta-analysis of total effects; (**B**) Results of control subgroup analysis; (**C**) Sensitivity analysis plot. The positions of the rhombus on the abscissa represented weighted mean differences (WMD) from random effect meta-analysis. Horizontal lines represent 95% confidence intervals (CIs).

Inflammatory factor	SE	t	P>|t|	95%CI
IL-1β	5.248	-0.81	0.505	-26.80832, 18.35339
IL-6	3.349	-0.22	0.833	-8.651885, 7.184829
IL-10	2.412	3.21	0.085	-2.639147, 18.11923
TNF-α	3.656	0.55	0.622	-9.629142, 13.6397
CRP	0.279	-1.54	0.263	-1.630322, 0.7699717

Table 3. Egger test results for ultra-low temperature exposure and inflammatory factor levels.

The results of publication bias analysis

The results of Egger test showed that there was no significant publication bias in the studies on the effects of WBC on the levels of inflammatory factors (Table 3).

Discussion

This study was based on a randomized controlled trial (RCT) to systematically evaluate the effect of whole-body cryotherapy (WBC) on the inflammatory response in humans. Inflammation has been proved involved in almost all diseases[4,35–37]. The levels of inflammatory factors regulate the inflammatory process[10]. It is important to reduce the levels of proinflammatory factors[38] and increase the levels of anti-inflammatory factors[39] to control the inflammatory response. Some studies have shown that WBC can reduce inflammation[23], reduce muscle soreness in athletes[17], and reduce fat mass and body fat percentage in obese individuals[40]. However, WBC has also been found to have negative effects on muscle function, soreness, and many blood parameters[26,41]. It is important to systemically assess the effect of whole-body cryotherapy on the inflammatory response in humans based on RCT. In this study, a total of 11 RCTs in 11articles were included.

IL-1β, a member of the IL-1 family, is the central mediator of innate immunity and inflammation in human's body, with local and systemic effects[42]. IL-1β has pro-inflammatory activity, which can trigger and enhance the inflammatory response in the body[43,44]. The results of meta-analysis showed that level of IL-1β in serum of people exposed to WBC was lower than that in control group, which means exposure to WBC may reduce inflammation by reducing the level of proinflammatory factor IL-1β. We also found that athletes exposed to WBC were more likely to benefit from this than the general population.

IL-6 can induce B cell differentiation and antibody production[45], and induce T cell activation, proliferation and differentiation[46], participate in the body's immune response, and is the initiator of inflammatory response[47]. IL-6 has become a key node in some cytokine storm syndromes (CSS)[48]. Originally described as B-cell differentiation factor 2 (BSF-2)[38] and macrophage and granulocyte inducer factor 2 (MGI-2), IL-6 has significant pro-inflammatory and pyrogen properties[49]. The results of meta-analysis showed that there was no significant difference in the level of IL-6 in serum of people exposed to WBC with that in control group. This might be due to the presence of small studies in the study population. Interventions with IL-6 have had limited effect in some cases, suggesting that we need to better understand the biological function of these cytokines in different inflammatory states. When designing for a specific disease, such as rheumatoid arthritis, the more appropriate regimen should be chosen.

IL-10 can reduce antigen presentation by down-regulating the expression of major histocompatibility complex classII on the surface of monocytes[50]. Down-regulated T lymphocyte activity, inhibited the activation, migration and adhesion of inflammatory cells[51]. At the same time, IL-10 can inhibit the synthesis and release of inflammatory factors[52]. The results of meta-analysis showed that level of IL-10 in serum of people exposed to WBC was higher than that in control group, which means exposure to WBC may reduce inflammation by increasing the level of anti-inflammatory factor IL-10. The results of subgroup analysis also showed that obese people exposed to WBC were more likely to benefit from this than athletes. It might be that athletes are in better physical condition and have a better ability to adapt and regulate different inflammatory responses in the body.

TNF-α is the earliest and most important inflammatory mediator in the inflammatory response process[53]. It can activate neutrophils and lymphocytes[54], increase the permeability of vascular endothelial cells[55], regulate metabolic activity in other tissues[56], and promote the synthesis and release of other cytokines[57]. The results of meta-analysis showed that there was no significant difference in the level of TNF-α in serum of people exposed to WBC with that in control group. This might be due to the insufficient number of included studies. It is suggested that WBC reduce inflammation may not by reducing the level of TNF-a. This difference is important in clinical practice, especially when choosing biomarkers and treatment options.

The overall quality of the 11 studies is high, and the Sensitivity analysis showed that the results were stable. Furthermore, the results of Egger test showed that there was no significant publication bias in the studies on the effects of WBC on the levels of inflammatory factors. All of these proved our study can provide an accurate evidence about the effect of WBC on inflammation. However, the number of included studies was small, and some of the included studies had small sample sizes and limitations. More randomised controlled trials with larger sample sizes should be conducted to complement existing studies.

In conclusion, systemical meta-analysis about the effect of whole-body cryotherapy on the inflammatory response in humans based on RCT showed that exposure to WBC may reduce inflammation by reducing the level of proinflammatory factor IL-1β and increasing the level of anti-inflammatory factor IL-10. Athletes and obese people were more likely to benefit from WBC. WBC can be used to clinically suppress the inflammatory response and reduce its negative effects.

Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [Jun He], [Xinyu Zhang] and [Zhili Ge]. The first draft of the manuscript was written by [Jun He] and [Xinyu Zhang], and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to J.H. or J.C.

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