

Model Construction for Safety Thresholds in Bloodletting Therapy: An Exploration of Precision Medicine Based on Multimodal Physiological Parameter Monitoring

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ABSTRACT

Objective: To establish a quantitative system for the safety thresholds of bloodletting therapy based on modern physiology, biophysics, and mathematical modeling, providing scientific and individualized operational standards for traditional bloodletting therapy and promoting the modernization transformation of traditional Chinese external treatments. **Methods:** Using principles of fluid dynamics, hemodynamics, cybernetics, and systems biology, the mathematical relationships between blood pressure, hemoglobin, heart rate, blood oxygen saturation, and blood loss were derived to establish a multiparameter comprehensive safety threshold model; infrared thermography technology was integrated to construct a local stasis assessment system, forming a “local-systemic” dual-layer safety monitoring framework. **Results:** A comprehensive model was constructed, including quantitative assessment of local stasis $v_{local} = \alpha_{local} \cdot K \cdot A \cdot \Delta T$ and systemic physiological safety monitoring ($V_{safe, total}$), proposing an individualized bloodletting volume calculation formula $V = \min(V_{local}, V_{safe, total}, 10mL)$. This model introduces a Traditional Chinese Medicine (TCM) syndrome differentiation correction coefficient, achieving an organic integration of the traditional principle “reduce excess” with modern physiology. **Conclusion:** The mathematical-physical model established in this study provides a quantifiable, reproducible, and verifiable scientific basis for the safe implementation of bloodletting therapy, marking an important transition from “empirical medicine” to “precision medicine,” with demonstrative significance for the modernization of TCM.

Keywords: Bloodletting Therapy; Safety Threshold; Mathematical Model; Hemodynamics; Precision Medicine; Integration of Traditional Chinese and Western Medicine; Infrared Thermography

Abbreviations: TCM: Traditional Chinese Medicine; LBNP: Lower Body Negative Pressure; CRM: Compensatory Reserve Measurement; IgG: Immunoglobulin G; MAP: Mean Arterial Pressure; CO: Cardiac Output; TPR: Total Peripheral Resistance; HR: Heart Rate; SV: Stroke Volume; EDV: End-Diastolic Volume; SBP: Systolic Pressure; DBP: Diastolic Pressure; MCFP: Mean Circulatory Filling Pressure; PRA: Right Atrial Pressure; Hb: Hemoglobin

Introduction

Research Background and Significance

Bloodletting Therapy is one of the oldest therapeutic methods in the history of human medicine, with applications traceable to ancient Egypt and Greece around 1500 BC [1]. In China, the “Huangdi Neijing Ling Shu” clearly states the therapeutic principle “remove the congested and stagnant,” laying the theoretical foundation for blood-

letting therapy [2]. However, with the development of modern medicine, due to the lack of quantitative standards and safety guarantees, bloodletting therapy has gradually been marginalized, limited to therapeutic phlebotomy for a few specific diseases (such as polycythemia vera) [3]. In recent years, with the rise of systems biology, mathematical modeling technology, and precision medicine, the modernization transformation of traditional medicine has encountered a historic opportunity. As an important component of TCM external therapies,

bloodletting therapy has unique efficacy in promoting blood circulation and removing stasis, dredging meridians and activating collaterals, clearing heat and purging fire, etc. However, its safety issues have always been the key bottleneck limiting its clinical promotion [4]. Traditional operations mostly rely on the physician's personal experience, lacking objective physiological monitoring indicators and quantitative operational standards, leading to unstable efficacy and potential risks. This study aims to use modern physiology, biophysics, and mathematical modeling methods to establish a safety threshold mathematical model based on core physiological indicators such as blood pressure, hemoglobin, heart rate, and blood oxygen saturation, and to integrate infrared thermography technology to achieve quantitative assessment of local stasis, constructing a "local-systemic" dual-layer safety monitoring system, providing scientific, individualized, and standardized operational norms for bloodletting therapy.

Current Research Status at Home and Abroad

Research Progress in Hemodynamic Mathematical Models

Hemodynamic mathematical modeling began with the Windkessel model proposed by Stephen Hales in 1733. This model treats large arteries as an elastic chamber, describing the formation mechanism of the blood pressure waveform [5]. In 1899, Otto Frank developed it into a mathematical model, laying the foundation for cardiovascular system modeling [6]. In the 1960s, Guyton et al. established the famous circulatory physiology model, proposing the theory that the intersection of the venous return curve and the cardiac function curve determines cardiac output, providing an important framework for understanding the compensation mechanism of blood loss [7]. In recent years, important progress has been made in the mathematical modeling of hemorrhagic shock. Hirshberg, et al. [8] proposed a simplified hemorrhagic shock model capable of describing the temporal evolution of blood pressure, heart rate, and cardiac output after blood loss [8]. This model achieves a good balance between simplicity and clinical relevance and is widely used in combat casualty care and emergency medicine research [9]. Cecconi, et al. [10] published an international consensus on circulatory shock and hemodynamic monitoring, emphasizing the important role of mathematical models in guiding fluid resuscitation [10]. In the study of blood loss tolerance, the Lower Body Negative Pressure (LBNP) model has become the gold standard for simulating hemorrhagic shock [11]. This model induces central hypovolemia through lower limb negative pressure suction, allowing the study of the human body's compensatory response to blood loss under safe and controllable conditions. This difference is closely related to autonomic nervous regulation ability, baroreceptor sensitivity, and cerebrovascular autoregulation function [12].

Compensatory Reserve Measurement (CRM) and Early Warning

Traditional vital signs (blood pressure, heart rate) often remain normal in the early stages of blood loss, not showing significant

changes until compensatory mechanisms are exhausted, leading to delayed diagnosis [13]. To address this issue, the U.S. Army Institute of Surgical Research developed Compensatory Reserve Measurement (CRM) technology, quantifying the body's compensatory capacity for hypovolemia by analyzing arterial waveform morphological features

[14]. CRM is defined as $CRM = 1 - \frac{BLV}{(BLV - HDD)}$, where BLV is blood loss volume, and BLVHDD is the blood loss volume required to reach hemodynamic decompensation [15]. Studies show that CRM can predict the occurrence of hemorrhagic shock 30-60 minutes before traditional vital signs become abnormal, providing a time window for early intervention [16]. Latimer et al. (2023) validation study in pre-hospital trauma patients showed that CRM<0.4 has high specificity for predicting hemorrhagic shock [15].

Modern Research on Bloodletting Therapy

Modern research has revealed the mechanism of action of bloodletting therapy from multiple perspectives. At the microcirculation level, bloodletting can improve local hemorheological status, reduce platelet aggregation rate and plasma viscosity, and promote vascular endothelial repair [17]. At the immunomodulation level, bloodletting can stimulate local and systemic immune responses, increase immunoglobulin G (IgG) content, and regulate lymphocyte subset levels [18]. At the neurohumoral regulation level, stimulating specific acupoints can regulate the autonomic nervous system through neural reflexes, releasing endogenous analgesic substances [19]. In terms of clinical application, Meta-analysis shows that bloodletting therapy for gouty arthritis is superior to conventional Western medicine treatment in terms of total effective rate (RR=1.15, 95% CI: 1.10-1.21), reduction in blood uric acid (SMD=-1.54), and pain score (SMD=-0.77), with fewer adverse reactions [20]. In the treatment of psoriasis vulgaris, combined bloodletting can improve clinical effective rate (RR=1.15), reduce PASI score (MD=-0.96), and decrease recurrence rate (RR=0.41) [21].

However, existing studies generally suffer from insufficient standardization of bloodletting volume. Literature-reported bloodletting volumes range from 0.1 mL to 200 mL, with most relying on the practitioner's experience and lacking physiological-based quantitative standards [22]. A study found through data mining that 0-10 mL or 0-15 drops is the most commonly used bloodletting volume, but the overall distribution is scattered, with no clear concentration trend [23]. This lack of standardization not only affects efficacy reproducibility but also poses safety risks.

Application of Infrared Thermography in TCM Diagnosis

Infrared thermography technology provides an objective quantitative tool for TCM "observation diagnosis" by detecting body surface temperature distribution. Research shows that infrared thermography can accurately capture the body surface temperature characteristics of TCM syndrome patterns, such as the significant specificity of temperature distribution in patients with Chaihu Guizhi Ganjiang

Decoction syndrome [24]. In the study of meridians and acupoints, infrared thermography can display temperature abnormalities along meridian pathways, providing visual evidence for the theory “where the meridian passes, it governs” [25]. In stasis assessment, infrared thermography can quantify the local temperature difference (ΔT) and abnormal area (A), reflecting the degree of microcirculation impairment [26]. The thermographic stasis $indexI_{therm} = \frac{(A \cdot \Delta T)}{(A \cdot 0 \cdot \Delta T - 0)}$ is positively correlated with the degree of local blood flow reduction, providing an objective basis for bloodletting site selection and dosage determination [27].

Research Objectives and Innovations

The main objective of this study is to establish a safety threshold system for bloodletting therapy based on mathematical-physical models, achieving the following innovations:

1. Theoretical Innovation: Integrating fluid dynamics, hemodynamics with TCM “Qi and Blood theory,” constructing a mathematical model of “stasis-blood loss-compensation,” providing a modern physiological interpretation of the “reduce excess” principle.

2. Methodological Innovation: Integrating multiparameter monitoring of blood pressure, hemoglobin, heart rate, blood oxygen, etc., establishing an individualized safety threshold calculation formula; introducing infrared thermography technology to achieve quantitative assessment of local stasis.

3. Application Innovation: Proposing a dual-constraint model of “local demand-systemic safety,” formulating hierarchical and graded bloodletting operation standards, providing quantifiable and reproducible operational standards for clinical practice.

Blood Pressure Formation Mechanism and Mathematical Model of Blood Loss Hazard Threshold

Physical-Physiological Basis of Blood Pressure Formation

The Fluid Dynamic Nature of Blood Pressure

Blood pressure is the lateral pressure exerted by blood flow on the vessel wall, and its physical essence conforms to the basic laws of fluid dynamics. According to Pascal's principle and Newton's law of fluid dynamics, blood pressure can be expressed as:

$$P = \frac{F}{S} = \frac{\rho \cdot v^2}{2} + \rho \cdot g \cdot h + R \cdot Q$$
 Where F is the force exerted by blood on the vessel wall, S is the vessel wall area, ρ is blood density, v is blood flow velocity, g is gravitational acceleration, h is liquid column height, R is vascular resistance, and Q is blood flow [28].

In the cardiovascular system, the formation of blood pressure requires three basic conditions: a closed circulatory pipeline system (cardiovascular system), a driving pump (heart), and a resistive pipe network (vascular system). According to the fluid dynamics analogy of Ohm's law, mean arterial pressure (MAP) is jointly determined by cardiac output (CO) and total peripheral resistance (TPR):

$$MAP = CO \times TPR$$

Cardiac output is further expressed as the product of heart rate (HR) and stroke volume (SV):

$$CO = HR \times SV$$

Frank-Starling Mechanism and Cardiac Pump Function

Stroke volume is determined by cardiac preload, afterload, and myocardial contractility. The Frank-Starling law describes the relationship between initial myocardial fiber length and contractile force:

$$SV = SV_{\max} \times (1 - e^{-kEDV})$$

Or simplified to a linear relationship:

$$SV = k \cdot (EDV - V_0)$$

where EDV is end-diastolic volume, directly related to blood volume; V_0 is the theoretical zero volume; and k is the myocardial compliance coefficient [29,30].

Recent multiscale modeling studies have revealed that the Frank-Starling mechanism involves complex interactions between cellular length-dependent activation, ventricular geometry, and cardiovascular system dynamics [31]. This multiscale nature explains why simple linear approximations are valid only within physiological ranges.

The Elastic Cavity Model of Blood Pressure (Windkessel Model)

Model Construction and Differential Equations

The Windkessel model treats large arteries as an elastic chamber, describing the dynamic changes of the blood pressure waveform. The basic assumption of this model is: the compliance (C) of the arterial system stores blood during cardiac ejection and releases it during diastole, maintaining continuous blood flow [32].

The model's differential equation is:

$$\frac{dP}{dt} = \frac{Q_{in} - \frac{P}{R}}{C} \text{ where:}$$

- P=arterial blood pressure (mmHg)
- Q_{in} =instantaneous ventricular ejection volume (mL/min)
- R=peripheral resistance (mmHg·min/mL)
- C=arterial compliance (mL/mmHg), defined as $C = \frac{dV}{dP}$

The solution to this equation gives the quantitative relationship between systolic pressure (SBP), diastolic pressure (DBP), and stroke volume, resistance, and compliance:

$$P(t) = P_{diastolic} \cdot e^{-\frac{t}{RC}} + \frac{SV}{C} \cdot \left(1 - e^{-\frac{t}{RC}}\right)$$
 The time constant $\tau = R \cdot C$ determines the decay rate of the pressure waveform, approximately 1.0-1.5 seconds in normal adults [33].

Physiological Significance of Arterial Compliance

Arterial compliance reflects the elastic reservoir function of the arterial system and is closely related to age, blood pressure, and vascular wall structure. With age, arterial wall collagen fibers increase, elastic fibers break, leading to decreased compliance (arteriosclerosis), increased systolic pressure and decreased diastolic pressure, and widened pulse pressure [34]. In the state of blood loss, changes in arterial compliance affect the buffering capacity of blood pressure. During hypovolemia, vascular smooth muscle contracts, compliance decreases, blood pressure fluctuation amplitude increases, which enhances stimulation to baroreceptors, triggering compensatory responses [35].

Guyton's Venous Return Theory and the Blood Volume-Blood Pressure Relationship

Venous Return Curve and Cardiac Function Curve

The core view of Guyton's theory is: in a steady state, venous return must equal cardiac output. Therefore, the actual blood pressure and cardiac output can be determined by the intersection of the venous return curve and the cardiac function curve [36].

Venous return formula:

$$\text{Venous return} = \frac{MCFP - PRA}{R_{VR}}$$

where:

MCFP (Mean Circulatory Filling Pressure) = mean systemic filling pressure

PRA = right atrial pressure

RVR = venous return resistance

MCFP is proportional to blood volume (BV):

$$MCFP = \frac{BV - V_{unstressed}}{C_{venous}}$$
 where $V_{unstressed}$ is the unstressed volume (approximately 70% of total blood volume), and C_{venous} is venous compliance (approximately 20 times arterial compliance) [37].

Impact of Blood Loss on Venous Return

Acute blood loss leads to a reduction in blood volume ΔBV , and MCFP decreases accordingly:

$$\Delta MCFP = -\frac{\Delta BV}{C_{venous}}$$

The venous return curve shifts left and downward, and the intersection with the cardiac function curve moves down, leading to a decrease in cardiac output and blood pressure. However, the body maintains stable blood pressure through a series of compensatory mechanisms (increased heart rate, peripheral vasoconstriction, venous constriction mobilizing unstressed volume) until blood loss exceeds the compensatory limit [38].

Mechanism of Blood Loss's Impact on Blood Pressure and Mathematical Modeling

Immediate Effects and Compensatory Responses

The process of blood pressure change caused by acute blood loss ΔBV can be divided into two stages:

Immediate effects (seconds to minutes after blood loss):

Direct reduction in blood volume, decreased venous return, leading to:

$$\Delta P_{msf} = -\frac{\Delta BV}{C_{venous}}$$

$$\Delta SV \approx -k \cdot \Delta P_{msf} = k \cdot \frac{\Delta BV}{C_{venous}}$$

$$\Delta CO \approx HR \cdot \Delta SV = HR \cdot k \cdot \frac{\Delta BV}{C_{venous}}$$

Without considering compensation, the blood pressure drop is:

$$\Delta MAP \approx \Delta CO \cdot TPR = HR \cdot k \cdot TPR \cdot \frac{\Delta BV}{C_{venous}}$$

Compensatory responses (minutes to hours after blood loss):

1. Increased heart rate: via baroreceptor reflex, sympathetic excitation, vagal inhibition

$$\Delta HR = \alpha \cdot \frac{\Delta BV}{BV} \cdot HR_0$$

2. Increased peripheral resistance: arteriole constriction maintains blood pressure

$$\Delta TPR = \beta \cdot \frac{\Delta BV}{BV} \cdot TPR_0$$

3. Venous constriction: mobilization of unstressed volume increases venous return

$$\Delta V_{mobilized} = \gamma \cdot \Delta BV$$

The compensated blood pressure change can be approximated as:

$$\Delta MAP = [HR_0(1 + \alpha f) \cdot SV_0(1 - kf) \cdot TPR_0(1 + \beta f)] - HR_0 \cdot SV_0 \cdot TPR_0$$

where $f = \Delta BV / BV$ is the blood loss proportion. Ignoring higher-order terms (f^2 and above):

$$\Delta MAP \approx MAP_0 \cdot [(\alpha + \beta) - k] \cdot f$$

Compensation Limit and Decompensation Threshold

When compensatory mechanisms saturate, blood pressure begins to drop sharply. Let the maximum heart rate increase coefficient be $\alpha_{\max}$, and the maximum peripheral resistance increase coefficient be $\beta_{\max}$. Then the critical blood loss proportion f_c satisfies:

$$(\alpha_{\max} + \beta_{\max}) - k = 0$$

For healthy adults, typically $f_c \approx 0.15 \sim 0.20$, meaning decompensation occurs when 15-20% of blood volume is lost [39]. This is highly consistent with the Advanced Trauma Life Support (ATLS) classification standard for Class II hemorrhagic shock (blood loss 15-30%, heart rate 100-120 bpm, blood pressure begins to drop) [40].

Mathematical Formula for Blood Pressure Hazard Threshold Based on Blood Loss Volume

Definition of Basic Hazard Threshold

The blood pressure hazard threshold is defined as: the minimum blood loss volume that, when reached, renders the body's compensatory capacity unable to maintain blood pressure within a safe range (e.g., MAP drop exceeding 20% or systolic blood pressure <90mmHg).

Let the initial blood pressure be P_0 , and the allowable maximum blood pressure drop proportion be θ (usually 0.2). Then the critical blood loss volume V_{crit} satisfies:

$$P_0 - \Delta P(V_{\text{crit}}) \geq (1 - \theta) P_0 \text{ That is:}$$

$$\Delta P(V_{\text{crit}}) \leq \theta P_0 \text{ Substituting}$$

$$\Delta P = P_0 \cdot K \cdot \frac{V_{\text{crit}}}{BV} \text{ BV gives:}$$

$V_{\text{crit}} = \frac{\theta \cdot BV}{K}$ Where K is the comprehensive compensation coefficient, reflecting the proportion of blood pressure drop per unit blood loss, determined by the compensation efficiency of heart rate, peripheral resistance, and stroke volume.

Corrected Model Considering Chronic Disease Status

Patients with chronic diseases have reduced compensatory capacity, requiring the introduction of a compensation retention coefficient α ($0 < \alpha \leq 1$):

$V_{\text{crit}} = \alpha \cdot \frac{\theta \cdot BV}{K_0}$ Where K_0 is the comprehensive compensation coefficient for healthy individuals.

Based on clinical observation and physiological data, the blood loss volume at which blood pressure begins to drop significantly (MAP drop >10%) in healthy adults is approximately 15% of blood volume, i.e.:

$$V_{\text{crit, healthy}} = 0.15 \times BV$$

Considering individual differences and chronic disease factors, the clinically practical formula is:

$$(V_{\text{crit}} = 0.15 \times BV \times \alpha \times \beta) \text{ where:}$$

BV=blood volume (L), BV=body weight (kg) $\times c$, c male 0.075, female 0.065

α =chronic disease compensation coefficient (healthy 1.0, mild disease 0.8, moderate disease 0.6, severe disease 0.4)

β =age correction coefficient (<60 years 1.0, 60-75 years 0.9, >75 years 0.8)

Formula for Estimating Blood Loss Volume Based on Magnitude of Blood Pressure Drop

If the blood pressure drop ΔP is known, the blood loss volume can be estimated:

$$V_{\text{loss}} = BV \times \frac{\Delta P}{P} \times \frac{1}{K}$$

where k is the blood pressure-blood loss proportionality coefficient, approximately 0.15-0.20 for healthy individuals.

Based on therapeutic bloodletting, clinically using the absence of significant blood pulsation as a reference, the allowable blood volume loss after blood pressure drops of 10%, 5%, and 1% is calculated respectively:

Blood loss (mL) = blood loss proportion $\times$ blood volume (L) $\times 1000$

Safe bloodletting volume per kg body weight:

• Male:

10% BP drop $\rightarrow 11.25 \text{ mL/kg}$

5% BP drop $\rightarrow 5.625 \text{ mL/kg}$

1% BP drop $\rightarrow 1.125 \text{ mL/kg}$

• Female:

10% BP drop $\rightarrow 9.75 \text{ mL/kg}$

5% BP drop $\rightarrow 4.875 \text{ mL/kg}$

1% BP drop $\rightarrow 0.975 \text{ mL/kg}$

Clinical Common Standard

Male, 70kg

Blood volume =70×0.075=5.25 L

BP drop 10%→15%×5.25 L=787.5 mL(decompensation critical)

BP drop 5%→7.5%×5.25 L=393.75 mL(safe therapeutic)

BP drop 1%→1.5%×5.25 L=78.75 mL(very safe)

Female, 70kg

Blood volume =70×0.065=4.55L

BP drop 10%→15%×4.55L=682.5mL

BP drop 5%→7.5%×4.55L=341.25mL

BP drop 1%→1.5%×4.55L=68.25mL

Conclusion

Taking a 70kg adult as an example:

BP drop 10% → allowable bloodletting approx. 788mL (male)/683mL (female) (decompensation critical)

BP drop 5% → allowable bloodletting approx. 394mL (male)/341mL (female) (clinically safe therapeutic range)

BP drop 1% → allowable bloodletting approx. 79mL (male)/68mL (female) (minimal fluctuation, very safe)

Mathematical Model of Hemoglobin Dynamic Changes and Blood Loss Threshold

Physiological Functions and Physicochemical Characteristics of Hemoglobin

Molecular Mechanism of Oxygen Transport

Hemoglobin (Hb) is the metalloprotein in red blood cells responsible for oxygen transport. Each Hb molecule contains four heme groups and can reversibly bind four oxygen molecules. The oxygenation process has a synergistic effect, manifesting positive cooperativity: after the first oxygen molecule binds, Hb conformation changes, promoting the binding of subsequent oxygen molecules [41].

The oxygen dissociation curve is S-shaped, mathematically described by the Hill equation:

$$Y = \frac{P^n}{P^n + P_0^n}$$

where:

- Y=oxygen saturation (0-1)
- P=oxygen partial pressure (mmHg)
- P₀ =half-saturation oxygen partial pressure (normally approx. 26.6mmHg)
- n = Hill coefficient (approx. 2.7-3.0, reflecting cooperative effect strength)

Recent studies have shown that modified Hill equations with Lorentz or Gauss distributions provide better approximations to experimental oxyhemoglobin dissociation curves, with coefficients of determination (*r*²) exceeding 0.9999 [42].

Carbon Dioxide Transport and Blood Buffering

Hb transports about 20% of CO₂ in the form of carbamino-hemoglobin, while binding H⁺ through imidazole groups, maintaining blood pH stability. Hb's isoelectric point is approximately 6.8; at physiological pH (7.4) it is weakly alkaline and can accept H⁺, making it an important blood buffer pair [43].

Physicochemical Parameters of Hemoglobin

(Table 1).

Table 1.

Parameter	Value	Unit
Molecular Weight	64,450	Da
Normal Concentration (Male)	130-175	g/L
Normal Concentration (Female)	120-160	g/L
Oxygen Binding Capacity	1.34	mL O ₂ /g Hb
Normal Arterial Oxygen Content (CaO ₂)	16-22	mL/dL

Key Factors Affecting Hemoglobin Concentration

“Container-Flow” System Model

Hemoglobin concentration is the result of dynamic equilibrium, influenced by multiple factors: production, destruction, loss, and fluid volume regulation. From a systems theory perspective, it can be viewed as a state variable of a “container-flow” system:

$$\frac{dM}{dt} = G - D - L$$

where:

M = Hb ×BV=total hemoglobin mass (g)

G=generation rate (g/day)

D = physiological destruction rate (g/day)

L = blood loss rate (g/day)

In steady state ($\frac{dm}{dt} = 0$), G=D+L, and Hb concentration is determined by blood volume:

$$Hb = \frac{M}{BV} = \int \frac{(G - D - L)dt}{BV}$$

Principle of Hemodilution After Acute Blood Loss

Assuming acute blood loss volume is *V*_{loss} (L), pre-bleeding blood volume is BV, and hemoglobin concentration is *Hb*₀. At the moment of blood loss, the lost blood has the same composition as the whole body's blood, so the lost hemoglobin mass is *Hb*₀ × *V*_{loss}.

At this time, the remaining hemoglobin mass in the body is *Hb*₀ × (*BV* − *V*_{loss}), and blood volume is also reduced to *BV* − *V*_{loss}, so the immediate hemoglobin concentration remains unchanged:

$$Hb = \frac{Hb_0(BV - V_{loss})}{BV - V_{loss}} = Hb_0$$

However, the body subsequently restores blood volume to the initial level BV through capillary refill (tissue fluid entering vessels at approx. 1 mL/kg/h), iatrogenic fluid replacement, and renal sodium and water retention mechanisms. When blood volume is restored to the initial level BV, the hemoglobin mass remains $Hb_0(BV - V_{loss})$, so the new hemoglobin concentration is:

$$Hb_1 = \frac{Hb_0(BV - V_{loss})}{BV} = Hb_0 \left(1 - \frac{V_{loss}}{BV} \right)$$

Linear Relationship Between Blood Loss Volume and Hemoglobin Drop

Define hemoglobin drop $\Delta Hb = Hb_0 - Hb_1$ then:

$$\Delta Hb = Hb_0 \cdot \frac{V_{loss}}{BV}$$

That is, the hemoglobin drop is proportional to the blood loss volume, with the proportionality coefficient being $\frac{Hb_0}{BV}$.

Conversely, given a target drop ΔHb , the required blood loss volume is:

$$V_{loss} = BV \cdot \frac{\Delta Hb}{Hb_0}$$

Definition of Blood Loss Hazard Threshold Based on Hemoglobin

Physiological Basis of Tissue Oxygen Delivery

Hemoglobin drop leads to a decrease in arterial oxygen content (CaO_2):

$$CaO_2 = 1.34 \times Hb \times SaO_2 + 0.003 \times PaO_2 \approx 1.34 \times Hb \times SaO_2$$

Tissue oxygen delivery (DO_2) is the product of cardiac output (CO) and CaO_2 :

$$DO_2 = CO \times 1.34 \times Hb \times SaO_2$$

When Hb decreases, if CO cannot increase accordingly, DO_2 decreases. Healthy individuals can compensate by increasing CO (increased heart rate, increased stroke volume) and oxygen extraction ratio (O_2ER), but there is a limit [44].

It is generally believed that when DO_2 drops below 50% of baseline at rest, tissue hypoxia may occur. The critical Hb value corresponding to this depends on the CO compensation capacity.

Threshold Reference from Clinical Transfusion Guidelines

Clinical transfusion guidelines often use absolute Hb thresholds:

- a. General patients: consider transfusion at $Hb < 70$ g/L

- b. Cardiovascular disease patients: consider transfusion at $Hb < 80-100$ g/L
- c. Elderly: thresholds appropriately raised

These thresholds are based on evidence from large-scale clinical trials (e.g., TRICC trial), balancing transfusion risks and anemia risks [45].

Mathematical Definition of Blood Loss Hazard Threshold

Define the hazard threshold as: the minimum blood loss volume leading to Hb dropping to a certain critical value Hb_{crit} :

$$V_{crit} = \alpha \cdot BV \cdot \frac{Hb_0 - Hb_{crit}}{Hb_0}$$

Where Hb_{crit} needs to be set individually based on patient condition:

- Healthy adult: $Hb_{crit} = 70$ g/L
- Coronary heart disease patient: $Hb_{crit} = 90$ g/L
- Elderly: $Hb_{crit} = 80$ g/L

Correction Factor Considering Individual Differences

Introduce a chronic disease index α ($0 < \alpha \leq 1$) reflecting the patient's reduced tolerance to anemia:

$$V_{crit} = \alpha \cdot \beta \cdot BV \cdot \frac{Hb_0 - Hb_{crit}}{Hb_0}$$

Clinical hazard thresholds cannot serve as safety thresholds for therapeutic bloodletting therapy. Clinically, the allowable bloodletting volume corresponding to each 1g/L~10g/L drop in Hb from the original concentration needs to be calculated, forming a quantitative change list to aid clinical analysis. From $\Delta Hb = Hb_0 \cdot \frac{V_{loss}}{BV}$, the calculation formula is derived:

$$V_{loss} = BV \cdot \frac{\Delta Hb}{Hb_0}$$

- V_{loss} : bloodletting volume (L)
- BV: total blood volume (L)
- ΔHb : hemoglobin drop value (g/L)
- Hb_0 : initial Hb (g/L)

Clinical Common Standard

Male: $BV = 0.075 \times \text{body weight (kg)}$

Female: $BV = 0.065 \times \text{body weight (kg)}$

Most commonly used: 70kg adult

Assume initial $Hb = 140$ g/L (mid-range for healthy adults)

Male, 70kg

Blood volume $BV=70 \times 0.075=5.25L$

Initial $Hb_0=140$ g/L

Hb drop per 1~10 g/L → corresponding bloodletting volume (mL)

1. Hb↓1 g/L → 37.5 mL
2. Hb↓2 g/L → 75 mL
3. Hb ↓3 g/L → 112.5 mL
4. Hb ↓4 g/L → 150 mL
5. Hb ↓5 g/L → 187.5 mL
6. Hb ↓6 g/L → 225 mL
7. Hb ↓7 g/L → 262.5 mL
8. Hb ↓8 g/L → 300 mL
9. Hb ↓9 g/L → 337.5 mL
10. Hb ↓10 g/L → 375 mL

Female, 70kg

Blood volume $BV=70 \times 0.065=4.55L$

Initial $Hb_0=140$ g/L

Hb drop per 1~10 g/L → corresponding bloodletting volume (mL)

1. Hb ↓1 g/L → 32.5 mL
2. Hb ↓2 g/L → 65 mL
3. Hb ↓3 g/L → 97.5 mL
4. Hb ↓4 g/L → 130 mL
5. Hb ↓5 g/L → 162.5 mL
6. Hb ↓6 g/L → 195 mL
7. Hb ↓7 g/L → 227.5 mL
8. Hb ↓8 g/L → 260 mL
9. Hb ↓9 g/L → 292.5 mL
10. Hb ↓10 g/L → 325 mL

- **Conclusion:** According to the hemodilution model after acute blood loss, taking a 70kg healthy adult with initial $Hb_0=140$ g/L as an example:
- In therapeutic bloodletting, for each 1g/L drop in Hb, a male can let approx. 37.5mL, female approx. 32.5mL.
- A 5g/L Hb drop corresponds to a safe bloodletting volume of approx. 188mL (male)/163mL (female).
- A 10 g/LHb drop corresponds to a bloodletting volume of approx. 375 mL(male)/ 325 mL(female).

This quantitative relationship can serve as a clinical basis for the individualized and precise application of therapeutic bloodletting, completely avoiding shock hazard thresholds, and is only used for safe, controllable, small-dose bloodletting.

Mathematical Model of Heart Rate Compensatory Response and Blood Loss Safety Threshold

Physiological Function and Regulatory Mechanism of Heart Rate

Core Role of Heart Rate

Heart Rate (HR) is the most fundamental dynamic parameter of the cardiovascular system. Its core functions include:

1. Determining cardiac output: $CO=HR \times SV$; when stroke volume is relatively stable, HR is the primary means of regulating CO.
2. Reflecting autonomic nervous balance: HR is regulated dually by sympathetic nerves (accelerating) and vagus nerves (decelerating).
3. Compensatory response indicator: In circulatory volume changes, increased HR is the earliest compensatory mechanism to appear [46].

Cybernetic Model of Heart Rate Regulation

From a cybernetics perspective, HR can be seen as an output variable influenced by multiple factors:

$$HR = HR_0 + \Delta HR_{symp} - \Delta HR_{para} + \Delta HR_{humoral}$$

Where:

HR_0 =intrinsic inherent frequency (approx. 100 bpm, but inhibited by vagus to 60-80 bpm)

- ΔHR_{symp} =heart rate increase caused by sympathetic excitation
- ΔHR_{para} =heart rate decrease caused by vagal excitation
- $\Delta HR_{humoral}$ =regulation by humoral factors (adrenaline, thyroid hormone)

Linear Relationship Model Between Blood Loss and Heart Rate

Baroreceptor Reflex Mechanism

Blood loss leads to reduced effective circulating blood volume, affecting heart rate through the following pathways:

1. Baroreceptor reflex: Arterial blood pressure drops, afferent impulses from carotid sinus and aortic arch baroreceptors decrease, vagal inhibition, sympathetic excitation, heart rate increases.
2. Volume receptor reflex: Atrial and venous system volume re-

ceptors sense decreased venous return, reflexively increasing heart rate.

3. Chemoreceptor reflex: Severe blood loss causes tissue hypoxia, peripheral chemoreceptors are excited, further increasing heart rate [47].

Mathematical Relationship Derivation

Within the compensatory range, the heart rate increase is approximately linearly related to the blood loss proportion. Let the blood loss proportion be $f = \frac{V_{loss}}{BV}$, then:

$$\Delta HR = k \cdot HR_0 \cdot f$$

Where k is the proportionality coefficient, reflecting individual sensitivity of heart rate response to blood loss. For healthy adults, k is approximately 1.0-1.5 (i.e., 1% blood volume loss leads to approx. 1%-1.5% heart rate increase).

This linear relationship originates from the following physiological logic chain:

Blood pressure drop $\Delta MAP \propto f \rightarrow$ baroreceptor afferent frequency change $\Delta freq \propto \Delta MAP \rightarrow$ sympathetic output change $\Delta symp \propto \Delta freq \rightarrow$ heart rate change $\Delta HR \propto \Delta symp$, therefore $\Delta HR \propto f$

Safety Bloodletting Volume Formula Based on Stable Heart Rate

Safety Threshold Definition

In therapeutic programs, if heart rate is required to remain stable (i.e., no significant increase), the blood loss volume must be controlled within the range before heart rate begins to increase significantly. Clinically, the fluctuation range of heart rate at rest is approx. ± 5 to 20 bpm. Define the safety upper limit as a heart rate increase not exceeding $\Delta HR_{safe} = 5$ to 20 bpm.

Formula Derivation

From the linear relationship $\Delta HR = k \cdot HR_0 \cdot \frac{V_{loss}}{BV}$, set $\Delta HR \leq \Delta HR_{safe}$, giving:

$$V_{loss} \leq BV \cdot \frac{\Delta HR_{safe}}{k \cdot HR_0}$$

Considering the impact of chronic disease on overall compensatory capacity, introduce correction coefficients α and β . Then the safe bloodletting volume is:

$$V_{safe,HR} = \alpha \cdot \beta \cdot BV \cdot \frac{\Delta HR_{safe}}{k \cdot HR_0}$$

Parameter description:

BV: blood volume (L)

- HR_0 : baseline heart rate (bpm)
- k: heart rate response coefficient (healthy 1.0-1.2, beta-blocker users 0.5-0.8, heart failure patients 0.5)
- α : chronic disease compensation retention coefficient (healthy 1.0, mild 0.8, moderate 0.6, severe 0.4)
- β : age correction coefficient (<60 years 1.0, 60-75 years 0.9, >75 years 0.8)
- ΔHR_{safe} : allowable upper limit of heart rate increase (recommended 5 bpm)

Using 70 kg healthy male as unified calculation parameters, derive bloodletting volumes corresponding to heart rate changes of 1%, 5%, 10%, 15%, 20%:

- Gender: male
- Weight: 70 kg
- $BV = 70 \times 0.075 = 5.25L$
- Baseline heart rate: $HR_0 = 70$ bpm
- Healthy individual: $k = 1.0$; $\alpha = 1.0$, $\beta = 1.0$

Heart rate change proportion: $\frac{\Delta HR}{HR_0} = 1\%, 5\%, 10\%, 15\%, 20\%$, i.e.:

$$\frac{\Delta HR}{HR_0} \times (0.01, 0.05, 0.10, 0.15, 0.20)$$

From formula $V_{loss} = \frac{BV \cdot \Delta HR}{k \cdot HR_0}$, simplified calculation results:

1. Heart rate increase 1% $\rightarrow$ bloodletting volume 52.5 mL
2. Heart rate increase 5% $\rightarrow$ 262.5 mL
3. Heart rate increase 10% $\rightarrow$ 525 mL
4. Heart rate increase 15% $\rightarrow$ 787.5 mL
5. Heart rate increase 20% $\rightarrow$ 1050 mL

Clinical recommendations:

1. The proportion of heart rate increase and bloodletting volume are in a perfect linear relationship, consistent with the "unified multi-model" academic logic.
2. Clinical therapeutic bloodletting is recommended to be controlled at heart rate increase $\leq 1-5\%$, corresponding to bloodletting ≤ 262.5 mL (70kg male). This range is safe, with no significant palpitations, no significant blood pulsation, and no over-compensation; parameters can also be adjusted based on baseline Hb concentration.

Blood Loss Threshold Model for Blood Oxygen Saturation

Physiological Significance and Influencing Factors of Blood Oxygen Saturation

Basis of Tissue Oxygen Supply

Blood oxygen saturation (SpO_2 or SaO_2) is the percentage of oxygenated hemoglobin to total hemoglobin in the blood, a core indicator reflecting the body's oxygenation state. Arterial oxygen content and oxygen delivery are respectively:

$$CaO_2 = 1.34 \times Hb \times SaO_2$$

$$DO_2 = CO \times 1.34 \times Hb \times SaO_2$$

Impact of Acute Blood Loss on SpO_2

Acute blood loss has a weak direct effect on SpO_2 , but can affect it indirectly through the following pathways:

1. Decreased cardiac output $\rightarrow$ reduced pulmonary blood flow $\rightarrow$ ventilation/perfusion mismatch $\rightarrow$ SpO_2 drop (only occurs in severe blood loss)
2. Tissue hypoxia $\rightarrow$ chemoreceptor excitation $\rightarrow$ deepened and accelerated respiration $\rightarrow$ may cause a brief rise in SpO_2 (if lung function is normal)

Therefore, SpO_2 is insensitive to blood loss and is usually a late indicator [48].

Mathematical Relationship Between Blood Oxygen Saturation and Blood Loss Volume

Empirical Linear Model

Establish an empirical linear model:

$$\Delta SpO_2 = \alpha \cdot k_{SpO_2} \cdot SpO_{2,0} \cdot \frac{V_{loss}}{BV}$$

Where K_{SpO_2} is very small in healthy individuals (0.01-0.05), meaning a 10% blood volume loss results in a 0.1%-0.5% drop in SpO_2 . In patients with chronic diseases (e.g., COPD), K_{SpO_2} can be 0.1-0.2.

Safety and Hazard Threshold Formulas

Safety threshold $\Delta SpO_{2,safe} = 0.01$

$$V_{safe, SpO_2} = \alpha \cdot BV \cdot \frac{\Delta SpO_{2,safe}}{k_{SpO_2} \cdot SpO_{2,0}}$$

Hazard threshold ($\Delta SpO_{2,crit} = 0.05$):

$$V_{crit, SpO_2} = \alpha \cdot BV \cdot \frac{\Delta SpO_{2,crit}}{k_{SpO_2} \cdot SpO_{2,0}}$$

For healthy individuals, the safety threshold can exceed 50% of blood volume, indicating that SpO_2 is extremely insensitive to blood loss and is usually not a limiting factor. However, for patients with respiratory system diseases, close monitoring is required [49].

Multiparameter Comprehensive Safety Threshold Model

Physiological Basis and Integration Concept

The human body's tolerance to blood loss is determined by multiple physiological systems. The characteristics of each indicator are as follows:

- Blood pressure: reflects circulatory volume status
- Heart rate: reflects autonomic nervous compensatory response
- Hemoglobin: reflects oxygen delivery capacity
- Blood oxygen saturation: reflects pulmonary gas exchange function

Quantitative relationships exist between changes in these indicators and blood loss volume, but their sensitivity and time windows differ. Heart rate changes earliest (seconds to minutes), blood pressure changes next (minutes to tens of minutes), hemoglobin changes later (hours to tens of hours), and blood oxygen saturation changes latest (in severe blood loss) [50].

Therefore, the comprehensive safety threshold should take the minimum value of each indicator's threshold, following the principle of "the most sensitive indicator determines the risk."

Summary of Safety Threshold Formulas for Each Indicator

(Table 2).

Table 2.

Indicator	Safety Threshold Formula	Sensitivity Coefficient	Applicable Population
Blood Pressure	$V_{BP,safe} = 0.07 \times BV \times \alpha \times \beta$	High	All populations
Heart Rate	$V_{HR,safe} = \alpha \times \beta \times BV \times \frac{5}{k \times HR_0}$	Highest	Non-beta blocker users
Hemoglobin	$V_{Hb,safe} = \alpha \times \beta \times BV \times \frac{10}{Hb_0}$	Medium	Strict for anemic patients
Blood Oxygen Saturation	$V_{spO_2,safe} = \alpha \times BV \times \frac{0.01}{k_{spO_2} \cdot spO_{2,0}}$	Low	Respiratory system diseases

Comprehensive Safety Threshold Formula

$V_{safe} = \min(V_{BP,safe}, V_{HR,safe}, V_{Hb,safe}, V_{SpO_2,safe})$

Applicable rule: For healthy individuals, usually $V_{HR,safe}$ or $V_{BP,safe}$ is the limiting factor; for chronic disease patients, $V_{Hb,safe}$ may be more stringent.

Comprehensive Mathematical Formula Based on Blood Pressure and Heart Rate Changes as Early Rapid Detection Parameters

Blood pressure and heart rate are the most sensitive monitoring indicators for early blood loss. Combining them to build an early rapid detection comprehensive formula for real-time monitoring and immediate assessment during bloodletting:

$$V_{safe,early} = \min\left(0.07 \times BV \times \alpha \times \beta, \alpha \times \beta \times BV \times \frac{5}{k \times HR_0}\right)$$

Comprehensive Mathematical Formula Based on Blood Pressure, Heart Rate, and Hemoglobin as Post-Treatment Monitoring Parameters

Hemoglobin is the core indicator of oxygen delivery capacity in the long term after bloodletting. Combined with the short-term compensatory indicators of blood pressure and heart rate, a post-treatment monitoring comprehensive formula is constructed for efficacy assessment and subsequent treatment planning after bloodletting:

$$V_{safe,post} = \min\left(0.07 \times BV \times \alpha \times \beta, \alpha \times \beta \times BV \times \frac{5}{k \times HR_0}, \alpha \times \beta \times BV \times \frac{10}{Hb_0}\right)$$

Local Bloodletting Volume Formula Based on Thermography and Integration with TCM Syndrome Differentiation

Physical Model of Local Stasis

Pathophysiological Nature of Stasis

TCM believes “stasis” (blood stasis) is a pathological state caused by obstructed Qi and blood flow, with blood accumulating locally. Modern research shows the essence of stasis is microcirculation disorder, manifested as:

- Abnormal constriction or dilation of arterioles
- Slowed or stagnant capillary blood flow velocity
- Abnormal hemorheology (increased viscosity, enhanced aggregation)
- Tissue hypoxia and metabolic waste accumulation [51].

Relationship Between Thermographic Parameters and Stasis Degree

Infrared thermography can quantify local microcirculation status. Core parameters are:

- Abnormal temperature area A (cm²): reflects the spatial extent of stasis
- Average temperature difference ΔT(°C) compared to the contralateral or surrounding normal tissue: reflects the degree of microcirculation disorder

Studies show that the temperature difference ΔT is positively correlated with the degree of local blood perfusion abnormality. The thermographic stasis index is defined as:

$$I_{therm} = \frac{A \cdot \Delta T}{A_0 \cdot \Delta T}$$

Where $A_0 = 50\text{ cm}^2$, $\Delta T_0 = 1.0^\circ\text{C}$ represent moderate stasis [52].

Equivalent Volume Estimation of Stagnant Blood

Assuming the stasis area in subcutaneous tissue approximates a uniform-thickness thin layer with physical thickness h (cm), obtainable via ultrasound measurement or anatomical site empirical values. Since not all tissue in the stasis area is blood, the actual blood volume fraction participating in stasis is ϕ (usually 0.3-0.5). The equivalent volume of stagnant blood is:

$$V_{statis} = \phi \cdot h \cdot A$$

Derivation of Local Bloodletting Volume Formula

Bloodletting Coefficient K per Unit Area-Temperature Difference

Introduce the unit area-temperature difference bloodletting coefficient

K ($\text{mL} \cdot \text{cm}^{-2} \cdot ^\circ\text{C}^{-1}$), defined as:

$$K = \beta \cdot h_{eff}$$

where:

- β = drainage proportion coefficient (mild stasis 0.1, moderate 0.2, severe 0.3)
- $h_{eff} = \phi \cdot h$ = stasis equivalent thickness (cm)

Physical meaning of K : the blood volume (mL) that needs to be let out per unit stasis area (1cm^2) and per unit temperature difference (1°C).

Common site K value reference (based on anatomical thickness and volume fraction estimation): (Table 3).

TCM Syndrome Differentiation Correction Coefficient α_{local}

TCM emphasizes treatment based on syndrome differentiation. The nature of stasis and therapeutic response differ among syndrome patterns. Therefore, introduce the TCM Syndrome Differentiation Correction Coefficient α_{local} to achieve individualized local bloodletting volume adjustment. Specific values are as follows: (Table 4).

Table 3.

Site	Physical Thickness Range (cm)	Stasis Volume Fraction	Equivalent Thickness h (cm)	K value ($\beta = 0.2$)
Waist/Back	0.6-1.0	0.4-0.5	0.24-0.50	0.048-0.100
Limbs	0.3-0.5	0.3-0.4	0.09-0.20	0.018-0.040
Head/Face	0.2-0.3	0.3-0.4	0.06-0.12	0.012-0.024

Table 4.

Syndrome Pattern	Core Pathogenesis	Adjustment Coefficient α_{local}	Explanation
Cold Congealing Blood Stasis	Cold pathogen constricting, blood flow congealing	0.8	Cold nature congeals, small amount of bloodletting can warm and unblock
Qi Stagnation Blood Stasis	Qi mechanism stagnation, blood flow unsmooth	1.0	Standard pattern, use conventional amount
Heat Toxin Blood Stasis	Heat congesting blood stasis, local redness and swelling	1.2	Heat exuberance causing flesh rot, can appropriately let more
Phlegm-Dampness Blood Stasis	Dampness and stasis congealing, sticky and difficult to remove	0.9	Dampness is sticky, requires fractional small amounts
Qi Deficiency Blood Stasis	Qi deficiency unable to move blood	0.6	Healthy Qi insufficient, strictly limit amount
Yin Deficiency Blood Stasis	Yin fluid insufficient, blood flow sluggish	0.7	Yin and blood deficient, cautiously prevent injuring Yin

Local Bloodletting Volume Formula

Combining the TCM Syndrome Differentiation Correction Coefficient, unit area-temperature difference bloodletting coefficient, and stasis area and temperature difference detected by infrared thermography, derive the core local bloodletting volume formula:

$$V_{local} = \alpha \cdot K \cdot A \cdot \Delta T$$

This formula achieves the integration of TCM syndrome differentiation with modern thermographic quantification technology, precisely matching the bloodletting demand to the local stasis degree.

Integration of Systemic Safety Threshold

Bloodletting therapy must balance local stasis clearance with systemic physiological homeostasis. Therefore, on the basis of local bloodletting volume, systemic indicators such as blood pressure, heart rate, and hemoglobin are integrated to construct the systemic safety threshold formula, ensuring no significant abnormality in systemic physiological state during bloodletting:

$$V_{safe, total} = \alpha_{systemic} \cdot \beta_{age} \cdot BV \cdot \min \left(0.07, \frac{5}{k \cdot HR_0}, \frac{\Delta Hb_{safe}}{Hb_0} \right)$$

where:

$\alpha_{systemic}$: systemic chronic disease compensation coefficient (same as blood pressure model, healthy 1.0, mild disease 0.8, moderate 0.6, severe 0.4);

β_{age} : age correction coefficient (<60 years 1.0, 60-75 years 0.9, >75 years 0.8);

ΔHb_{safe} : safe hemoglobin drop value, clinically recommended ≤ 10 g/L.

Final Comprehensive Bloodletting Volume Formula

The actual bloodletting volume for a single bloodletting treatment must take the minimum of local stasis demand, systemic physiological safety, and also set an absolute upper limit of 10 mL (based on the conventional safe dose for clinical bloodletting). Finally, the individualized comprehensive bloodletting volume formula is obtained:

Clinical supplementary principle: If local demand exceeds the systemic safety threshold, treatment should be divided into sessions, each not exceeding , with treatment intervals of 3-7 days, until infrared thermography shows significant improvement in local stasis.

Model Validation, Clinical Application, and Discussion

Comparative Validation with Classic Literature and Clinical Data

The safety threshold model for bloodletting therapy constructed in this study, through comparative validation with classic physiological theories and clinical diagnostic and treatment norms, confirms the model's scientificity and rationality.

Comparison with Guyton Physiology

Guyton's classic circulatory physiology textbook states: 10% blood volume loss, blood pressure can be maintained; 20% blood loss, blood pressure begins to drop; 30% blood loss, shock occurs [53].

The blood pressure hazard threshold for healthy adults derived in this model, (15% blood volume), and safety threshold (7% blood volume), are highly consistent with Guy-

ton's theory. Moreover, the model provides refined classification of bloodletting volume into safe-critical-hazardous, better fitting clinical treatment needs.

Comparison with Blood Donation Medicine

Clinical voluntary blood donation standards are 400-500 mL per donation (approx. 8%-10% of a healthy adult's blood volume). Most donors show no significant blood pressure or heart rate fluctuation; a few experience dizziness and other mild discomfort. This dose falls within the safety threshold range (7% BV) of this model.

Simultaneously, hemoglobin typically drops 10-15 g/L after donation, consistent with the prediction of the linear relationship between hemoglobin drop and blood loss volume in this model [54].

Comparison with Therapeutic Phlebotomy

Clinical therapeutic phlebotomy for polycythemia vera is usually 300-500 mL per session, with intervals ranging from days to weeks, targeting hematocrit (Hct) <45% [55].

This model calculates for a healthy individual ($Hb_0=150$ g/L, target $Hb=130$ g/L):

$$V = BV \times \frac{20}{150} = 0.133 \times BV$$

For a 70kg male ($BV=5.25L$), $V \approx 700mL$, divided into 2 sessions, 350 mL each, consistent with clinical practice, validating the model's clinical applicability.

Calculation Examples and Clinical Decision Support

To intuitively demonstrate the model's clinical application method, using a healthy adult and an elderly chronic disease patient as cases, the safe dose for a single bloodletting session is completely calculated, and clinical decision advice is given.

• Example 1: Healthy Adult Bloodletting

Patient info: 30-year-old male, 75kg, no underlying disease, local stasis in waist/back (infrared thermography: $A=50 \text{ cm}^2$, $\Delta T=1.2^\circ\text{C}$), TCM syndrome differentiation: Qi Stagnation Blood Stasis.

Basic parameters: $BV = 0.075 \times 75 = 5.63$, $HR_0 = 65bpm$, $Hb_0 = 150$ g/L, $k = 1.1$, $\alpha_{local}=1.0$, $K=0.064$ (mid-range K value for waist/back), $\alpha_{systemic}=1.0$, $\beta_{age}=1.0$.

Step-by-step calculation:

1. Local bloodletting volume: $V_{local} = 1.0 \times 0.064 \times 50 \times 1.2 = 3.84 \text{ mL}$

2. Systemic safety threshold:

$$V_{BP, safe} = 0.07 \times 5.63 \times 1.0 \times 1.0 = 394mL$$

$$V_{HR, safe} = 1.0 \times 1.0 \times 5.63 \times \frac{5}{1.1 \times 65} = 394mL$$

$$V_{Hb, safe} = 1.0 \times 1.0 \times 5.63 \times \frac{10}{150} = 375mL$$

$$V_{safe} = \min(394, 394, 375) = 375 \text{ mL}$$

Final bloodletting volume: $V = \min(3.84, 375, 10) = 3.84 \text{ mL}$.

Clinical decision: Select 2 stasis acupoints on the waist/back, let approx. 2mL per point. No need to monitor systemic vital signs; observe local bleeding post-procedure.

• **Example 2: Elderly Chronic Disease Patient Bloodletting**

Patient info: 70-year-old female, 60kg, coronary heart disease, hypertension (mild chronic disease compensation).

Basic parameters: $BV = 0.065 \times 60 = 3.9 \text{ L}$, $HR_0 = 72 \text{ bpm}$, $Hb_0 = 130 \text{ g/L}$, $k = 1.0$, $\alpha = 0.7$, $\beta = 0.9$.

Waist/back stasis: $A = 80 \text{ cm}^2$, $\Delta T = 1.5^\circ \text{C}$, Syndrome pattern: Qi Deficiency Blood Stasis ($\alpha_{local} = 0.6$)

Step-by-step calculation:

1. Local demand: $V_{local} = 0.6 \times 0.064 \times 80 \times 1.5 = 4.6$

2. Systemic safety threshold:

$$V_{BP, safe} = 0.07 \times 3.9 \times 0.7 \times 0.9 = 172 \text{ mL}$$

$$V_{HR, safe} = 0.7 \times 0.9 \times 3.9 \times \frac{5}{1.0 \times 72} = 171 \text{ mL}$$

$$V_{Hb, safe} = 0.7 \times 0.9 \times 3.9 \times \frac{10}{130} = 189 \text{ mL}$$

$$V_{safe, total} = \min(172, 171, 189) = 171 \text{ mL}$$

Final bloodletting volume: $V = \min(4.6, 171, 10) = 4.6 \text{ mL}$

Clinical decision: Select 2 Back-Shu points, let 2-3mL per point, strictly monitor vital signs.

Limitations of the Model and Future Research Directions

Although the safety threshold model for bloodletting therapy constructed in this study achieves “local-systemic” quantitative monitoring, it still has certain limitations. Subsequent improvements are needed from theoretical, methodological, and clinical dimensions.

“Incommensurability” of Theoretical Frameworks

TCM “stasis” and modern medicine “microcirculation disorder” have overlaps but are not equivalent. TCM emphasizes the dynamic “state” of Qi and blood flow, while Western medicine focuses on static “accumulation.” This model quantifies TCM “stasis” as thermographic parameters, potentially neglecting intangible stasis like Qi mechanism stagnation [56].

Limitations of Linear Assumptions

In reality, the relationship between stasis degree and bloodletting volume may be nonlinear: mild stasis may be cleared with a small amount, severe stasis may have a “threshold effect”—beyond a cer-

tain amount, efficacy no longer increases, instead damaging healthy Qi [57].

Individual Differences and Dynamic Changes

Model parameters (k , α , β) need calibration through clinical experience and cannot be precisely unified. Future research should conduct multicenter real-world studies, use machine learning for dynamic model optimization, and establish a “learning-type” clinical decision support system [58].

Lack of “Healthy Qi” Assessment

The model does not sufficiently incorporate TCM indicators of internal injury to healthy Qi like “Qi following blood loss” and “injuring Yin consuming fluids.” Future research should establish a “Healthy Qi” multidimensional scale (Qi deficiency, blood deficiency, Yin deficiency, Yang deficiency) to expand the safety threshold system.

Conclusion and Outlook

This study, based on principles of fluid dynamics, hemodynamics, cybernetics, and systems biology, constructed a multiparameter mathematical-physical model for the safety thresholds of bloodletting therapy. Main contributions include:

1. Established a mathematical model of the blood pressure-blood volume relationship, derived the hazard threshold formula $V_{crit} = 0.15 \times BV \times \alpha \times \beta$, highly consistent with Guyton physiology and ATLS shock classification.

2. Constructed a hemoglobin dynamic change model, proposed an individualized threshold based on oxygen delivery theory $V_{crit} = \alpha \cdot BV \cdot \frac{Hb_0 - Hb_{crit}}{Hb_0}$

3. Integrated compensatory indicators like heart rate and blood oxygen saturation, established a multiparameter comprehensive safety threshold system $V_{safe} = \min(V_{BP}, V_{HR}, V_{Hb}, V_{SpO_2})$

4. Innovatively introduced infrared thermography technology, proposed the local stasis quantification formula $V_{local} = \alpha_{local} \cdot K \cdot A \cdot \Delta T$, achieving objectification of TCM syndrome differentiation.

5. Constructed a “local-systemic” dual-layer safety monitoring model $V = \min(V_{local}, V_{safe, total}, 10 \text{ mL})$, providing quantifiable, reproducible, and verifiable scientific standards for bloodletting therapy.

This model marks an important transition of bloodletting therapy from “empirical medicine” to “precision medicine,” with demonstrative significance for the modernization of TCM external therapies. Future research should focus on: conducting large-scale multicenter clinical trials to validate model effectiveness; establishing a “Healthy Qi” assessment system to improve safety standards; developing intelligent decision support systems for dynamic optimization; exploring the modern biological essence of “stasis” to deepen theoretical understanding.

Author Contribution Statement

All authors participated in research design, mathematical derivation, literature analysis, and paper writing.

Conflict of Interest Statement

Authors declare no conflicts of interest.

Ethics Statement

This study is theoretical modeling research, not involving human trials, but the proposed formulas require clinical validation before application.

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