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The Wugeng China Initiative: A Muscle-centric Microcirculation Paradigm for Eliminating Lethal Stroke, Dementia, and Heart Attack – Operationalizing "Treating Pre-disease" Through the 4s Muscle Maintenance Model

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Defining Wugeng China: The Disruptive Health Objective

"Wugeng" (无梗)—literally meaning "free of obstruction/infarction for stroke and dementia" represents a transformative national health goal for China: the annual elimination or near-zero incidence of lethal stroke, dementia, and heart attack through systematic preservation of the muscle-vascular-brain axis. These three conditions collectively account for over 70% of cardiovascular-cerebrovascular mortality in China [1].

The COVID-19 pandemic has amplified this urgency. SARS-CoV-2 infects host cells via ACE2 receptors abundantly expressed on vascular endothelium, causing direct endothelial injury and persistent dysfunction in long COVID affecting ~400 million globally [2–4]. The Wugeng China framework addresses this through an innovative 4S (Systemic, Standardized, Sustainable, Scalable) automobile maintenance model:

The 4s core principle

In the future, over 90% of people will be expected to achieve health through 4S, with less than 10% requiring medical intervention in China. People need annual maintenance when healthy, like automobile maintenance, one service cannot last years.

The Core Hypothesis: The Muscle-Vascular-Brain Axis

We propose that progressive microcirculatory endothelial dysfunction (MED) driven by sarcopenia (age-related muscle loss), myokine deficiency, and accelerated by COVID-19-induced ACE2 downregulation represents the universal pre-disease state underlying lethal stroke, dementia, and heart attack.

Skeletal muscle as the microcirculatory engine

Skeletal muscle comprises around 40% of body mass and houses the body's largest microvascular bed, functioning as a critical endocrine organ secreting 600+ myokines that regulate systemic vascular function [5,6]. Key myokines include:

Myokine	Function	Wugeng Relevance
Irisin (FNDC5)	Enhances endothelial function via AMPK-eNOS; crosses blood-brain barrier; promotes neurogenesis [7–9]	Prevents post-stroke cognitive dysfunction; improves cerebral microcirculation
IL-6	Induces VEGF, promotes angiogenesis, regulates inflammation [5,6,10]	Enhances muscle capillarization; supports cardiac and cerebral collateral circulation
FGF21	Protects against mitochondrial dysfunction, improves insulin sensitivity, acts as mitokine [11–13]	Metabolic protection, vascular anti-aging, stress adaptation
BDNF	Brain-derived neurotrophic factor; enhances synaptic plasticity, neurogenesis [9]	Cognitive protection, neurovascular coupling

Sarcopenia-microcirculatory decline

Age-related muscle loss reduces microcirculatory reserve by:

- **Capillary rarefaction**: Reduced muscle VEGF/angiopoietin signaling decreases systemic microvascular density [14]
- **Myokine deficiency**: Loss of irisin, IL-6, and FGF21 impairs endothelial protection and angiogenesis [5,7,11]
- **Endothelial dysfunction**: Reduced IGF-1 signaling in aging muscle disrupts muscle-endothelial crosstalk, accelerating microvascular senescence [15]

Post-COVID amplification

SARS-CoV-2 infection accelerates attrition through ACE2 downregulation, reduced NO bioavailability, and persistent pro-thrombotic endothelial phenotype [2–4].

Dual-strategy approach

We further propose that "Activating Blood Circulation to Remove Stasis" (活血化瘀, Huó Xuè Huà Yū) package that we practice synergizes with muscle-targeted interventions by improving muscle perfusion, enhancing myokine delivery, and addressing hemorheological disturbances whenever necessary [16–18].

The Scientific Foundation: Microcirculatory Deterioration and Sarcopenia

The annual attrition law

Microcirculatory density declines ~1% annually after age 30, driven by sarcopenia-related myokine deficiency and capillary rarefaction [14,19]. Without annual 4S maintenance, this crosses the Wugeng Threshold (30% residual function), triggering stroke, dementia, or myocardial infarction [14,19].

Endothelial-to-mesenchymal transition (EndMT)

EndMT represents the fundamental mechanism wherein endothelial cells transform into mesenchymal cells [20]:

- **Stroke**: Cerebral microvascular EndMT reduces collateral circulation [20, 21].
- **Dementia**: Hippocampal microvascular EndMT causes chronic hypoperfusion; irisin deficiency impairs neurogenesis [22].
- **Heart attack**: Coronary microcirculatory EndMT precipitates plaque instability; FGF21 deficiency impairs cardiac protection [11,20].

Microcirculatory Environment Cleansing: Dual-Strategy Implementation

Defining microcirculatory environment cleansing (微血管环境清理)

Pathological Accumulation	Muscle-Centric Mechanism	TCM Syndrome
Capillary rarefaction	Reduced myokine (VEGF, angiopoietin) signaling	**Blood Stasis (瘀血)**
Myokine deficiency	Sarcopenia, physical inactivity	**Qi Stagnation (气滞)**
Microthrombosis	Post-COVID ACE2 downregulation, NETs formation [4]	**Blood Stasis (瘀血)**
Oxidative stress	Mitochondrial dysfunction, reduced FGF21 [11]	**Phlegm-Dampness (痰湿)**

Strategy A: Muscle-targeted MVAR (modern precision medicine)

Primary interventions

- **Myokine-enhancing exercise**: Resistance training to increase muscle capillarization by 20-40% and boost irisin/FGF21 secretion [5,7,11].

- **ACE2 pathway restoration**: Counter COVID-induced downregulation [2,3].
- **TGF-β modulation**: Suppress EndMT to preserve muscle-vascular coupling [20].
- **Glycocalyx regeneration**: Sulodexide for endothelial barrier repair [23].

Strategy B: TCM Huó Xuè Huà Yū (活血化瘀) package mechanisms

- **Huó Xuè (Activating Blood)**: Improves muscle capillary perfusion, enhancing myokine delivery to brain and heart [16–18].
- **Huà Yū (Resolving Stasis)**: Fibrinolytic activation, anti-thrombotic effects, addressing post-COVID microthrombosis [16–18].

Evidence base

- **Meta-analysis (Chen *et al.*, 2018)**: the RCTs (n>1,500) demonstrated Huoxue Huayu therapy reduced in-stent restenosis by 43% (RR=0.57) [16,17].
- **Systematic review (Gao *et al.*, 2025)**: the RCTs (n>3000) confirmed TCM formulas improved microcirculation (D-dimer, fibrinogen, endothelin) [18].
- **Xuefu Zhuyu Tang**: Improves hemorheology, enhances muscle pump efficiency [24–26].

The Wugeng Muscle-Vascular Reserve Index (WMVRI)

So far, we formalize the 4S maintenance schedule through the AI-aided articulate Wugeng Muscle-Vascular Reserve Index (WMVRI):

WMVRI Score	Status	Primary Strategy	TCM Integration	Population Target
>0.7 (70%)	**Green**	Annual myokine-focused exercise	Wellness Qi regulation (optional)	Around 85% of population
0.3–0.7	**Yellow**	Resistance training + Huó Xuè Huà Yū	Primary therapy for muscle perfusion	12% at-risk population
<0.3 (30%)	**Red**	Emergency intervention + myokine replacement	Adjunctive TCM	3% require hospital care

Post-COVID adjustment

LC patients automatically classified as Yellow Status for 12 months.

4s station service integration

***4s station core services**:*

1. **Screening**: Annual DEXA muscle mass, serum irisin/FGF21, capillary imaging, sarcopenia index, post-COVID ACE2 autoantibodies.
2. **Muscle index**: Personalized exercise (irisin-boosting HIIT, resistance training for capillarization), myokine modulation.
3. **TCM evaluation**: Constitution identification; **Huó Xuè Huà Yū** package for Status muscle-perfusion optimization.
4. **Integrated monitoring**: tracking with muscle strength, gait speed, hemorheology.

Phase I: Green status maintenance (ages 20–30)

- **Muscle Target**: Maintain lean mass >90th percentile; serum irisin >15 ng/mL.
- **Exercise**: Combined aerobic + resistance to maximize myokine diversity [5,7].
- **Post-COVID**: 6-month enhanced monitoring.
- **TCM option**: Preventive Qi and Blood regulation.

Phase II: Yellow status restoration (ages 30–50, including all post-covid)

- **Muscle Target**: Reverse early sarcopenia; restore capillary density.
- **Exercise**: High-load resistance training (3×/week) to increase muscle capillarization by 25% [14].
- **TCM Primary**: **Huó Xuè Huà Yū therapy** (Xuefu Zhuyu Tang) for muscle microcirculation and myokine transport [16–18].

Phase III: Red status intervention (ages 50+, severe lc, advanced sarcopenia)

- **Interventions**: Myokine replacement (irisin analogs), intensive exercise rehabilitation.
- **TCM Adjunct**: Intensive muscle perfusion support, and beyond.

Implementation Through Muscle-Vascular Microphysiological Systems

The FDA Modernization Act 2.0 and NIH PAR-25-198 enable regulatory-qualified testing [27–29]. However, in near future, Wugeng Muscle-Vascular Digital Twins will need to integrate:

- **Muscle fiber-ECM-vascular units:** Patient-derived myocytes with endothelial co-culture to test myokine secretion.
- **Sarcopenia modeling**: Age-related muscle atrophy MPS to optimize MVAR protocols [30].
- **Post-COVID modeling**: ACE2-downregulated vasculature to test EER strategies [31].
- **TCM validation**: Huó Xuè Huà Yū compound testing for muscle perfusion enhancement.

Societal Implementation: Scaling the Muscle-Centric 4s Network

Infrastructure:

Towards 10 thousand nationwide Wugeng 4S Muscle Stations

Workforce:

- **Exercise myokine specialists**: Certified in irisin-boosting protocols, sarcopenia assessment, resistance training prescription.
- **Modern EER specialists**: Post-COVID cardiovascular rehabilitation, ACE2 pathway expertise.
- **TCM muscle practitioners**: Huó Xuè Huà Yū for muscle-perfusion optimization.

Computed economic model:

- **Green Status**: ¥500/year (muscle maintenance, exercise prescription).
- **Yellow Status (including all LC)**: ¥1,000/year (resistance training + Huó Xuè Huà Yū therapy + myokine monitoring).
- **Red Status**: Intensive intervention (vs. stroke/dementia/LC costs: ¥100,000–600,000).

Testable Predictions

1. **90/10 prediction**: Expect Annual 4S muscle maintenance achieves >90% Green/Yellow Status with <10% medical intervention in China.
2. **Sarcopenia reversal**: estimate that 12-week resistance training restores muscle capillarization and reduces arterial stiffness, preventing progression to Red Status [14].
3. **Myokine efficacy**: Theoretically Irisin-boosting exercise increases cerebral microcirculatory density by 15-20%, delaying dementia onset by 5-10 years [7,9]
4. **TCM-muscle synergy**: Yellow Status patients receiving resistance training + Huó Xuè Huà Yū show 30% faster WMVRI improvement than exercise alone (enhanced muscle perfusion → increased myokine delivery).

Conclusion

The Wugeng China initiative establishes skeletal muscle as the command center of microcirculatory health, expecting to integrate modern myokine science (irisin, FGF21, IL-6, resistance training) with TCM Huó Xuè Huà Yū (muscle perfusion optimization). By targeting sarcopenia reversal, myokine signaling restoration, and post-COVID endothelial repair, we may create a resilient dual-strategy framework.

The 4S model treats muscle as the "engine" requiring annual maintenance with 90% achieving health through muscle preservation, <10% requiring medical intervention in China. This muscle-centric approach honors both biomedical rigor and cultural medical heritage in the service of a singular goal: so far, what successfully hundreds of cases have been treated successfully is a promising signal towards a China free of lethal stroke, dementia, and heart attack.

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