Cardiovascular Health and Pulse Dynamics: Lessons from Eastern Medicine

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ABSTRACT

Context: Vascular health is important for the optimal functioning of human body. The aging process and the correlated status of silent inflammation influence vascular function, which can be assessed by measuring arterial stiffness through pulse wave velocity. Pulse wave analysis by feeling several pulses in the radial arteries is the major diagnostic means in Traditional Tibetan medicine, which since ancient times links pulse characteristics to disease states such as chronic inflammation. In Tibetan Medicine chronic or silent inflammation is known as the concept called hidden fever. Herbal compounds have been developed to reduce the effects of inflammation on vascular (dys-) function. The Tibetan multi compound formula Padma 28 has been shown effective in different conditions associated with silent inflammation and chronic inflammatory processes. It has numerous anti-inflammatory, anti-oxidative and cell-protecting activities, suggesting a multi-target mode of action.

Aims: To monitor and assess the vascular health status possibly using a portable device with finger electrocardiogram and photoplethysmograph sensors measuring the pulse wave velocity. Results: Two different subjects equipped with finger photoplethysmogram and electrocardiograms were recorded while performing mental stress tasks and slow breathing. Pulse wave velocity dynamic across the protocol showed increase during stress and decrease during slow breathing in most subjects.

Conclusions: The aging and vessels inflammation processes are proposed to be assessed by pulse wave velocity measurements using a finger-based sensor. Slow deep breathing is a potential means to control the inflammation mostly in vessels together with ad-hoc multi-compound Tibetan medicine formula such as Padma 28.

Keywords
Pulse wave analysis, Inflammation, Vascular health, Tibetan Medicine.

The clinical and prognostic significance of arterial vascular stiffness

Almost all currently known cardiovascular risk factors are associated with atherosclerotic and structural changes in the arteries. A common denominator of these changes is an increased inflammatory state and many chronic inflammatory diseases have been recognized as risk factors [1,2]. In addition, chronic, low-level inflammatory processes are identified as leading cause for the degenerative and pathological processes of advancing age (inflammaging) [2-4].

In the arteries, the aging process in combination with other factors such as hypertension leads to increased stiffness of the vascular walls of the large elastic arteries. In addition to intima-hyperplasia, the elastic fibers of the media of the central arteries of the elastic type (aorta) are getting thinner. Degraded fibers are replaced by collagen, which is about 500 times less elastic. Especially the age-related loss of elastin may be of importance in the observed changes in diameter. In young people, the elastic fibers (elastin) of the vessels are stretched by 10% with each heartbeat. This mechanical stress (approx. 300 million strains in 10 years) leads to material fatigue. With older age, the elastin content decreases, elastin fibers elongate and lose some of the elastic recoil properties [5]. Consequently, arteries rely more on the stiffer collagen in the arterial wall and become somewhat larger.

This increases vascular stiffness, which causes increased pulse wave reflections that in turn lead to pathological changes in the heart such as increased post load, left heart hypertrophy, ischemia,
and heart failure. It also affects the microcirculation of the brain contributing to subcortical encephalopathy, dementia, and insult. Furthermore, the kidneys are affected, and albuminuria and renal insufficiency is promoted [6]. In an evaluation of the Framingham study a relationship between blood pressure and arterial stiffness could be established over a 7-year period in 1,759 participants. Increased vascular stiffness is significantly associated with the future incidence of hypertonic blood pressure levels. Arterial vascular stiffness is thus an independent marker of vascular health and prognostic for cardiovascular risk [7].

Various non-pharmacological measures have been shown to improve vascular stiffness, among others salt reduction, weight loss, physical training and smoking cessation. In addition, favorable effects have been described for hormone replacement therapy, fish oil and alpha-linoleic acid [6]. Since most factors that contribute to arterial stiffness have a chronic inflammatory background it is not surprising, that all such measures rely on their inherent anti-inflammatory and anti-oxidative effects.

**Silent inflammation - the Eastern concept of hidden fever**

The mechanisms underlying age-associated vascular dysfunction are largely connected to increased vascular oxidative stress and inflammation, specifically chronic, low-level inflammation. An increase of such a chronic inflammatory state is associated with aging. This process that is called inflammaging is caused by cellular and immune senescence and is accompanied by a senescence-associated secretory phenotype (SASP), characterized by an increase in pro-inflammatory cytokines, growth factors, proteases, and chemokines among others. Studies in older humans have found increased levels of inflammatory proteins, such as pro-inflammatory nuclear factor-kB and cytokines (e.g. IL-6, TNF-α, MCP-1) [8-10]. Inflammaging not only promotes the aging processes in general but plays a causative role in age-related diseases such as atherosclerosis, Alzheimer's disease, diabetes mellitus, periodontal disease and cancer [4,10]. Regarding the vascular system Inflammaging is associated with increased endothelial cell oxidative stress and markers of inflammation, both of which are related to the age-related impairment in endothelial function [11,12].

In contrast to the acute inflammation the classic cardinal signs of inflammation (redness, swelling, pain, function laesa) are missing in the chronic low-level inflammatory state described above. It can therefore not be recognized through the clinical symptoms but only on the basis of blood markers such as inflammatory mediators. Since these overt signs are missing the condition is called 'silent inflammation'. From this description an analogy can be drawn to the term 'hidden fever', that is known in the traditional systems of Eastern medicine, especially Tibetan Medicine.

In the context of Tibetan Medicine health is seen as a dynamic and personal equilibrium of three principles: Lung, Tripa and Beken, each of which has specific characteristics, e.g. regarding thermal properties and function in the body (Table 1). Tibetan Medicine recognizes several types of fever, among these e.g. 'unripened fever', 'acute fever' and so called 'hidden fever' [13,14]. Hidden fever is a multi-layered condition and, while phenotypically it may present as a 'cold' disorder, underlying it is of a hot nature (in Tibetan terms a Tripa-disease, most often combined with Lung- and/or Beken-disturbances). In the treatment additionally to specific dietary recommendations herbal medicines are recommended with the aim to balance the three principles, specifically to reduce the Tripa principle.

One herbal formula that is traditionally used specifically in hidden fever is the formula Gabur 25 (camphor 25), which is available as an authorized medicine in different European countries under the names of e.g. Padma 28 or Padma Circosan [13,14].

<table>
<thead>
<tr>
<th>Dynamic principle</th>
<th>Lung</th>
<th>Tripa</th>
<th>Beken</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common English translation</td>
<td>Wind</td>
<td>Bile</td>
<td>Phlegm</td>
</tr>
<tr>
<td>Corresponding elements</td>
<td>Air</td>
<td>fire</td>
<td>water, earth</td>
</tr>
<tr>
<td>Thermic properties</td>
<td>Cool</td>
<td>hot</td>
<td>cold</td>
</tr>
<tr>
<td>Characteristics</td>
<td>moving, life sustaining</td>
<td>motivating, catabolic</td>
<td>stabilizing, anabolic</td>
</tr>
<tr>
<td>Functions in the body</td>
<td>mind, fantasy, movement, blood flow, excretion</td>
<td>body temperature, digestion, vision, sense of purpose</td>
<td>structure, physical and emotional stability, bodily fluids, sleep, joints</td>
</tr>
</tbody>
</table>

**Table 1:** The three dynamic principles responsible for all physical and mental functions in the human organism and their specific characteristics.

**The anti-inflammatory properties of the Tibetan formula Padma 28**

The formulation Padma 28 has been approved as a medicine in Switzerland since 1977 for the use in symptoms of circulatory disorders. During this long time a great number of scientific studies have been performed on the medicinal product. Over 30 clinical studies show an efficacy of Padma 28 in several chronic inflammatory disorders, mainly cardiovascular diseases and specifically peripheral arterial occlusive disease (PAOD), which is caused by atherosclerosis [15,16]. Besides the clinical research numerous experimental studies demonstrated different mechanisms of action demonstrating a multi-target mode of action with a pleiotropic activity signature. Specifically, several anti-inflammatory and anti-oxidative mechanisms could be detected, many of which are relevant in the pathogenesis of chronic inflammatory diseases such as atherosclerosis and diabetes mellitus [17,18]. Among other anti-inflammatory and protective effects Padma 28 has been shown to reduce the formation of advanced glycation end-products (AGE) and advanced oxidative protein products (AOPP), which play a pivotal role in the development of diabetic complications such as accelerated vessel aging [19].

Recent studies have suggested that the age-related increase in AGE in the arterial wall may also contribute to vascular dysfunction [20].
AGEs represent the end-product of a non-enzymatic reaction with sugar derivates that lead to irreversible crosslinks with proteins. In the arterial wall, AGEs can bind to collagen, leading to changes in the mechanical properties of the vascular wall [21].

**Pulse wave dynamics to assess the vessel age**

The biomedical and pharmacological mechanisms of action of Padma 28 and their relevance for the vascular function reflected in the pulse wave properties according to the traditional diagnosis allow the link to modern analytical methods and interpretation of pulse wave characteristics. Pulse wave velocity (PWV) indicates the speed at which the pressure pulse propagates through the arteries [22,23]. The stiffer the artery, the higher the PWV. PWV also increases towards the periphery. Due to this simple correlation the PWV is a direct measure of arterial vessel stiffness and increased PWV has been proven a strong cardiovascular risk factor; a PWV value of greater than 10 m/s is a strong predictor of cardiovascular mortality and morbidity [6]. Increased PWV is also a predictor of mortality in the elderly, in patients with terminal renal insufficiency, diabetes mellitus, hypertension as well as in a broad population with "normal" intermediate cardiovascular risk [7,24-31].

Cardiovascular damage can be quantified using PWV measurement, whereby PWV functions as a global, integrative risk marker. Besides being a cardiovascular risk factor increased PWV is also causative in the formation of cardiovascular diseases and complicates the course of an existing underlying disease [32].

Because of the close relationship between blood pressure and vascular stiffness, changes in PWV and augmentation index should always be interpreted in context with a simultaneous decrease in blood pressure. The shape and speed of the pulse wave depend to a significant extent on the vessel stiffness [33]. From the heart, the vascular tree (funnel effect) tapers into the periphery, causing an increase in blood pressure amplitude, called blood pressure amplification. Systolic blood pressure should therefore always be lower centrally than in the periphery. With vascular stiffening, the funnel effect is more pronounced and thus at the same time the central blood pressure increases. Thus, PWV measurement allows a direct assessment of the artery and as an additional parameter is superior to the risk assessment solely based on classical factors such as blood pressure, age or cholesterol levels.

PWV can also be interpreted as an indicator of the biological vessel age [33]. To compare to norm curves valid standard values are required, which may differ for each measuring device. From Figure 1, we can draw the following example, if an aortal PWV of 7 m/s was e.g. measured in a 60 year old, then the comparison against a norm curve would result in a biological vascular age of 70 years. This patient would therefore clearly have pre-aged arterial vascular system but may not (yet) have manifest end organ damage. Experience shows that the confrontation of this vividly described pre-ageing is very well understood by patients [6]. Vessel stiffness measurement is particularly important as a very sensitive tool in preventive medicine. In addition, it is used for risk stratification and thus may influence advice to patients with classical cardiovascular risk factors or diseases such as hypertension or diabetes mellitus. There are few non-pharmacological means to reduce arterial stiffness and thus potentially improve vascular condition and reduce the effect of the inflammatory process. Among these is a deep slow breathing technique which has been shown to improve autonomic function in type-1 diabetes and also increase baroreflex sensitivity [34]. Device guided slow breathing (RESPeRATE ©, Newark, USA) has been used to reduce blood pressure and sympathetic activity [35], both of which are linked to vascular health. The archetypal example of Figure 1 would be to measure a PWV of 5 m/s which would result in a younger vascular age of 50 years.

**Figure 1:** (a) PWV measured with Vic order or Phase Contrast MRI and its correlation to chronological age in healthy subjects [51]. (b) Two examples of higher and lower Pulse Wave Velocity of a person of chronological age of 60 years.
PWV as a surrogate marker of arterial stiffness has been shown to be correlated to inflammatory processes and noteworthy to endothelial dysfunction and atherosclerosis [36-41].

**PWV measurement**

Photoplethysmography (PPG) is an optical measurement technique used to monitor changes in the blood volume of a microvascular bed of tissues non-invasively and continuously. The waveform, i.e. the photoplethysmogram, has a widespread range of clinical applications. Since the signal morphology is like the arterial blood pressure waveform, the study of PPG became a potential non-invasive tool, especially in the assessment of the cardiovascular and autonomic function as well as mental state [42-46]. PWV is usually measured using two signals separated by some distance. If one uses two PPG signals, it has been shown that a distance of 12 mm is sufficient to estimate the PWV [47]. The smaller the distance the higher the accuracy and resolution of the sensor should be and the more noise sensitive the system is. Typically, an electrocardiogram (ECG) or a PPG is used as a first signal, and another PPG as a second signal [47,48]. The larger the distance between these two signals the more accurate and noise resistant the PWV estimation will be. For the measurement the person must be at rest without moving and must breathe calmly. Then, if the quality of the PPG signal is good the measurement over the period of a few heartbeats is sufficient [49]. Typical measurement duration is few breath cycles. Best PPG signal quality is obtained from the finger, the earlobe and temporal artery [44]. Radial artery is also a good location but hard to access due to the anatomical complexity of the tendons and bones. SATHeart has designed a specific sensor as shown in Figure 1 which includes synchronized ECG and finger PPG signals at high sampling rate. For the PWV measurement the person places a finger of each hand on each of the gold-plated ECG electrodes, which constitutes the PPG sensor.

**Typical examples of PWV dynamics**

We present two typical results of PWV estimation in a laboratory experiment (for details about the protocol see the freely available article [46]). Figure 3 shows the PWV as estimated with the SomnoTouch device (SOMNOmedics GmbH, Randersacker, Germany) with a two lead ECG and an infrared PPG sensor at one finger. Healthy subjects aged 29 (Figure 3 (a)) and 31 (Figure 3 (b)) were asked to perform two stress tests (Stroop word color tests). The RESPeRATE device was used to relax the subjects between the two stress tests. Figure 3 shows a clear difference in the average PWV in these two subjects which is partly linked to their chronological age, but which does not account for all of the difference according to Figure 1. Figure 3 shows how these two subjects’ reacts to stress and device guided breathing. While for the first subject (a), PWV reacts very dynamically; for the second subject (b), PWV reacts much mildly. There might be several factors influencing this difference: 1) the baroreflex sensitivity, 2) the vascular condition, 3) the state of mind. This point to the fact that arterial stiffness is a dynamic process which is controlled both centrally by the autonomic nervous system and locally by the endothelial function. Using the average PWV in Figure 3 during the baseline condition prior to the first stress test and the data from Figure 1, we deduce that subject (a) has a vascular age of 27 and subject (b) a vascular age of 27.
Arterial stiffness has been linked with the three principles of Asian medicine explained above whereby Lung (Ayurvedic Vata) pulse showed lower arterial stiffness than Tripa (Ayurvedic Pitta) and Beken (Ayurvedic Kapha) in normative subjects [50]. Lung pulse is felt distal from the heart and has the feeling of disappearing when pressed. Lung pulse for healthy people has small pulse amplitude (systolic – diastolic) which is called the force of the pulse in Tibetan and Ayurvedic medicine. All this information confirms the fact that Lung types of people have low arterial stiffness which means small PWV. People with Lung imbalance have however increased PWV due to the rigidification of the artery walls. Lung imbalance can be caused or promoted by atherosclerosis.

The Aging process leads to an increase of arterial stiffness as shown in Figure 1 and increased PWV. In Traditional Tibetan Medicine, it is well known that due to a naturally increasing Lung-principle with advancing age elderly people often develop Lung imbalance, which corresponds to a frequently higher PWV as compared to their normal vascular age curve.

**Conclusion**

The specific case of silent inflammation is discussed according to both Tibetan and Western medicine. The concept of ‘hidden fever’ can be linked to modern insights into inflamming and its relevance for arterial health and the biological vessel age, which represents a useful marker easily understood by patients.

Eastern medicine responds to ‘hidden fever’ with cooling i.e. anti-inflammatory herbal formulas, which can be used as preventive or therapeutic agents. The Eastern concepts also extend to reading of the pulse wave. Traditionally pulse reading is performed by skilled doctors, but the concept can be expanded into the modern age by using pulse measuring devices with advanced algorithms to extract more parameters and data, e.g. pulse wave velocity. Some aspects of the pulse wave velocity as a marker of arterial stiffness are derived and proved to be valid. A portable, handheld device measuring the finger electrocardiogram and photoplethysmogram is proposed to assess and monitor pulse wave velocity with good accuracy. For the measurement the user must be at rest. We have further showed some examples of the effect of mental stress and slow breathing on pulse wave velocity, showing the possibilities of using deep slow breathing techniques for improving vascular health. Further research is needed to validate this hypothesis.

**Conflict of interest**

HS and CV are employees of Padma AG, Switzerland. HS and PC are founders of SATHeart SA, Switzerland.

**References**


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