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EARLY DIAGNOSIS AND PREVENTION OF HYPERTENSION IN YOUNG MILITARY PERSONNEL BASED ON STRESS TESTING AND BIOMARKERS.

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ABSTRACT Background. Arterial hypertension (AH) remains one of the leading modifiable risk factors for cardiovascular morbidity and premature mortality. The early development of hypertension in young military personnel represents a particular clinical and preventive challenge. Despite their young age, high level of physical activity, and mandatory medical selection, military personnel are exposed to a combination of specific risk factors, including acute and chronic psycho-emotional stress, night-duty schedules, sleep deprivation, circadian disruption, substantial physical exertion, extreme temperatures, irregular nutrition, and increased sympathoadrenal activity. Conventional office blood pressure (BP) measurement at rest does not always identify early abnormalities in circulatory regulation. Of particular importance are masked hypertension, increased BP variability, and an exaggerated pressor response to physical or psycho-emotional stress. Studies involving young military personnel have confirmed the clinical relevance of masked hypertension identified by ambulatory blood pressure monitoring (ABPM). Therefore, the integration of functional stress testing, ABPM, assessment of autonomic regulation, and laboratory biomarkers appears to be a promising approach.

Objective. To summarize current evidence on the pathophysiological mechanisms underlying the early development of hypertension in young military personnel and to determine the diagnostic and preventive value of stress testing, ambulatory blood pressure monitoring, indices of autonomic regulation, and neuroendocrine, inflammatory, metabolic, and vascular biomarkers.

Materials and Methods. A narrative review of the scientific literature was conducted using publications indexed in PubMed/MEDLINE and other international scientific databases. Studies addressing arterial hypertension, masked hypertension, blood pressure variability, military and occupational stress, cardiovascular reactivity, ambulatory blood pressure monitoring, physical and psycho-emotional stress testing, heart rate variability, cortisol, dehydroepiandrosterone sulfate, catecholamines, inflammatory and metabolic markers in young adults and military personnel were analyzed.

Results. The available literature indicates that the development of hypertension in young military personnel may begin long before a persistent elevation in office BP becomes evident. Potential early manifestations include an exaggerated pressor response to stress, increased BP variability, insufficient nocturnal BP reduction, masked hypertension, increased sympathetic activity, and altered heart rate variability.

Promising biomarkers include cortisol, the cortisol/DHEAS ratio, catecholamines, uric acid, lipid and carbohydrate metabolism indices, high-sensitivity C-reactive protein, and pro-inflammatory cytokines. A multimodal model integrating clinical risk factors, ABPM, standardized stress testing, HRV, and a panel of readily available biomarkers appears to be the most promising approach.

Conclusion. Early diagnosis of hypertension in young military personnel should shift from isolated assessment of office BP toward comprehensive evaluation of cardiovascular reactivity and individual risk. The combination of ABPM, functional stress tests, HRV, and biomarkers may

facilitate the detection of a preclinical hypertensive phenotype and support the development of personalized preventive strategies.

Keywords: arterial hypertension; military personnel; stress; stress testing; masked hypertension; ambulatory blood pressure monitoring; blood pressure variability; cortisol; DHEAS; biomarkers; heart rate variability; prevention.

INTRODUCTION

Arterial hypertension has traditionally been regarded as a disease predominantly affecting middle-aged and older individuals. However, contemporary epidemiological data indicate that the pathophysiological prerequisites for future hypertension may develop much earlier, during young adulthood, when most individuals have no pronounced clinical symptoms or structural target-organ damage.

This issue is particularly relevant to military personnel. Military occupational activity is characterized by a combination of factors capable of substantially altering cardiovascular regulation.

- chronic psycho-emotional stress;
- sudden intense stress exposure;
- prolonged and night-duty shifts;
- restricted sleep duration;
- circadian rhythm disruption;
- substantial physical workload;
- the need for rapid decision-making;
- high personal responsibility;
- extreme climatic conditions;
- noise exposure;
- irregular nutrition;
- limited recovery periods.

Unlike conventional cardiovascular risk factors, the effects of these exposures are often initially functional and may become evident only under conditions of stress.

Thus, a young servicemember may have normal BP during a routine medical examination but demonstrate an abnormal pressor response during duty, physical exertion, or psycho-emotional stress.

One of the major diagnostic challenges is masked hypertension, defined as normal office BP in the presence of elevated out-of-office BP.

Studies in young National Guard personnel have demonstrated the clinical significance of this phenomenon and highlighted the need for ambulatory blood pressure monitoring.

This raises a fundamental question:

Can future hypertension be detected before persistent elevation of office BP develops?

Current concepts of early diagnosis suggest that this may be possible through simultaneous assessment of the following sequence:

stressor → physiological response → recovery → biochemical response → 24-hour BP profile**.**

CARDIOVASCULAR RISK CHARACTERISTICS IN YOUNG MILITARY PERSONNEL

Young military personnel represent a specific population.

On the one hand, occupational medical selection excludes many individuals with severe chronic diseases. On the other hand, military service generates a unique cardiovascular risk profile.

This creates the well-known “healthy soldier effect”, whereby favorable health indicators at the beginning of service do not necessarily guarantee persistently low cardiovascular risk over time.

A large study involving young military personnel demonstrated an association between psychological stress and long-term blood pressure variability.

The cumulative effect of multiple stressors appears to be particularly important.

night duty → sleep deprivation → sympathetic activation → increased heart rate → endothelial dysfunction → increased vascular resistance → elevated blood pressure.

When emotional stress is present simultaneously, activation of the hypothalamic-pituitary-adrenal axis also occurs.

Therefore, occupational cardiovascular risk in military personnel should be considered as the result of interactions among:

genetic predisposition × traditional risk factors × physical workload × psycho-emotional stress × sleep disturbances × autonomic regulation.

3. STRESS-INDUCED ARTERIAL HYPERTENSION

Stress is a physiological mechanism that enables adaptation to external threats.

Short-term activation of the stress response enhances functional performance and adaptation.

However, chronic or excessive activation may become pathophysiologically relevant.

The principal systems involved in the stress response include:

1. sympathetic nervous system;
2. hypothalamic-pituitary-adrenal axis;
3. renin-angiotensin-aldosterone system;
4. endothelial regulatory mechanisms;
5. immune-inflammatory pathways.

Military conditions create a setting in which these mechanisms may be activated repeatedly.

Initially, BP elevation may be entirely situational.

However, repeated pressor responses may lead to impaired baroreflex sensitivity and increased baseline vascular tone.

repeated stress → repeated hypertensive response → incomplete recovery → increased basal vascular tone → labile hypertension → sustained hypertension.

Sympathetic Nervous System

One of the central mechanisms of stress-induced hypertension is sympathetic hyperactivity.

Stress exposure increases catecholamine secretion.

Norepinephrine activates vascular α1-adrenergic receptors, leading to vasoconstriction.

Epinephrine, acting predominantly through β1-adrenergic receptors, increases:

- heart rate;
- myocardial contractility;
- cardiac output.

Blood pressure = cardiac output × total peripheral vascular resistance.

In chronic sympathetic hyperactivity, both components may increase.

Sympathetic renal stimulation is also important because it promotes renin release and sodium retention.

HYPOTHALAMIC-PITUITARY-ADRENAL AXIS

Another key component of the stress response is the hypothalamic-pituitary-adrenal (HPA) axis.

stress → corticotropin-releasing hormone (CRH) → adrenocorticotropic hormone (ACTH) → cortisol.

Cortisol is essential for normal stress adaptation.

However, chronically elevated cortisol levels or disruption of its circadian secretion may contribute to:

- insulin resistance;
- visceral adiposity;
- sodium retention;
- increased vascular sensitivity to catecholamines;
- endothelial dysfunction;
- sleep disturbances.

Therefore, cortisol measurement is of particular interest in military populations.

ROLE OF DHEAS

Dehydroepiandrosterone sulfate (DHEAS) is another adrenal hormone.

A potentially informative marker is not only the absolute cortisol concentration but also the:

cortisol/DHEAS ratio.

This index may reflect the balance between catabolic stress responses and potentially protective or adaptive mechanisms.

Studies in male veterans have demonstrated associations of cortisol and the cortisol/DHEAS ratio with hypertension.

Therefore, this parameter warrants further investigation in young active-duty military personnel.

RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM

Sympathetic activation closely interacts with the renin-angiotensin-aldosterone system (RAAS).

Increased renin secretion leads to increased formation of angiotensin II.

Angiotensin II:

- causes vasoconstriction;
- stimulates aldosterone secretion;
- promotes sodium retention;
- enhances sympathetic activity;
- promotes oxidative stress;
- stimulates vascular remodeling.

Thus, a positive feedback loop may develop between stress, sympathetic activation, and the RAAS.

ENDOTHELIAL DYSFUNCTION

Normal endothelial function plays a fundamental role in the regulation of vascular tone.

Nitric oxide (NO) is one of the principal endogenous vasodilators.

Chronic stress, sleep disturbance, inflammation, and oxidative stress may reduce NO bioavailability.

vasodilators ↓ / vasoconstrictors ↑

Potential biomarkers of endothelial dysfunction include:

- endothelin-1;
- NO metabolites;
- asymmetric dimethylarginine (ADMA);
- adhesion molecules.

However, their use in large-scale military screening is currently limited by cost and insufficient standardization.

SYSTEMIC INFLAMMATION

In recent years, hypertension has increasingly been viewed not only as a hemodynamic disorder but also as a condition associated with chronic low-grade inflammation.

Military-related stress may be accompanied by alterations in:

- interleukin-6 (IL-6);
- tumor necrosis factor-alpha (TNF-α);
- C-reactive protein (CRP);
- other immune mediators.

Studies of intensive military training have demonstrated changes in cortisol and inflammatory biomarkers.

IL-6 is of particular interest because it may integrate the effects of:

stress + physical exertion + inflammation + vascular dysfunction.

However, IL-6 concentrations measured immediately after intense physical activity should be interpreted cautiously, because skeletal muscle itself is an important source of IL-6.

OXIDATIVE STRESS

Increased sympathetic activity and angiotensin II signaling enhance the production of reactive oxygen species.

Oxidative stress:

- reduces NO bioavailability;
- damages the vascular endothelium;
- increases arterial stiffness;
- enhances inflammation;
- promotes vascular remodeling.

Potential research biomarkers include:

- malondialdehyde;
- 8-hydroxy-2′-deoxyguanosine (8-OHdG);
- total antioxidant capacity;
- superoxide dismutase.

At present, their role in population-wide screening remains primarily investigational.

SLEEP DISTURBANCE AS A RISK FACTOR FOR HYPERTENSION

Sleep plays a fundamental role in cardiovascular recovery.

Military personnel are frequently exposed to:

- reduced sleep duration;
- night-duty shifts;
- sleep fragmentation;
- circadian desynchronization.

Sleep deprivation may increase sympathetic activity and reduce parasympathetic control.

Under normal conditions, BP decreases by approximately 10–20% during sleep.

Sleep disturbances may lead to a non-dipping blood pressure pattern.

This may represent one of the earliest signs of impaired BP regulation.

For this reason, ABPM may be particularly informative in military personnel working night shifts.

MASKED ARTERIAL HYPERTENSION

Masked hypertension is one of the most important diagnostic challenges.

It is characterized by:

normal office BP + elevated out-of-office BP.

In military personnel, such a profile may occur because routine examinations are typically performed in a calm clinical environment.

During actual military duty, additional factors are present, including:

- stress;
- physical exertion;
- sleep deprivation;
- caffeine intake;
- noise;
- high responsibility.

Studies involving young National Guard personnel support the use of ABPM for detecting masked hypertension.

AMBULATORY BLOOD PRESSURE MONITORING

ABPM should be regarded as a central component of the proposed early-detection strategy.

It provides information on:

- 24-hour mean BP;
- daytime BP;
- nighttime BP;
- BP variability;
- morning BP surge;
- dipping status;
- overall hypertensive load.

For military personnel, it is essential that monitoring be performed during a typical working day.

Otherwise, the diagnostic value of the examination may be reduced.

non-duty day ↔ duty day.

BLOOD PRESSURE VARIABILITY

Mean BP is not the only indicator of cardiovascular risk.

In young individuals, increased BP variability may be an early manifestation of cardiovascular dysregulation.

Potential causes include:

- sympathetic hyperactivity;
- impaired baroreflex sensitivity;
- emotional lability;
- sleep disturbances;
- smoking;
- stimulant use;
- metabolic abnormalities.

Studies involving young military personnel have demonstrated an association between psychological stress and long-term BP variability.

Therefore, blood pressure variability may be regarded as an intermediate phenotype linking stress exposure with sustained hypertension.

BIOMARKERS OF EARLY RISK

There is currently no single universal biomarker capable of predicting future hypertension.

Accordingly, a panel-based approach appears to be the most promising strategy.

Table 1. Potential Biomarkers

Category	Biomarker	Potential Significance
HPA axis	Cortisol	Stress burden
HPA axis	DHEAS	Adaptive reserve
Index	Cortisol/DHEAS ratio	Stress–adaptation balance
Sympathetic nervous system	Norepinephrine	Sympathetic activity
Sympathetic nervous system	Epinephrine	Acute stress response
Stress	Salivary α-amylase	Non-invasive marker of sympathetic nervous system activity
Inflammation	hs-CRP	Low-grade inflammation
Inflammation	IL-6	Inflammatory and stress response
Inflammation	TNF-α	Inflammatory activity
Metabolism	Uric acid	Vascular/metabolic risk
Metabolism	Glucose	Carbohydrate metabolism
Metabolism	Insulin	Insulin resistance
Metabolism	HOMA-IR	Early metabolic risk
Lipids	TG/HDL-C ratio	Atherogenic and metabolic profile
Endothelium	Endothelin-1	Vasoconstriction
Endothelium	ADMA	Reduced NO bioavailability
Myocardium	NT-proBNP	Hemodynamic stress

23. CORTISOL AS AN ACCESSIBLE STRESS BIOMARKER

Cortisol has several advantages:

- strong biological rationale;
- extensive scientific evidence;
- broad laboratory availability;
- potential for measurement in saliva.

However, interpretation requires careful standardization.

The following factors should be considered:

- time of day;
- food intake;

- caffeine;
- physical activity;
- sleep duration;
- smoking;
- medications.

A single random measurement has limited diagnostic value.
A more informative approach may include assessment of:
baseline level + response to stress + recovery.

METABOLIC PARAMETERS

Even in physically active military personnel, assessment should include:

- body mass index;
- waist circumference;
- fasting glucose;
- HbA1c;
- triglycerides;
- HDL cholesterol;
- LDL cholesterol;
- uric acid.

Metabolic risk may amplify the cardiovascular effects of occupational stress.
Therefore, it is more appropriate to consider the interaction:
stress × metabolic phenotype.

COMPARISON OF DIAGNOSTIC METHODS

Table 2. Methods for Early Identification of a Hypertensive Phenotype

Method	Advantage	Limitation	Practical Value
Office BP	Simplicity	May miss masked hypertension	High
Home BP monitoring	Repeated measurements	Depends on adherence and technique	High
ABPM	24-hour BP profile	Cost	Very high
Handgrip test	Simple	Limited specificity	Moderate/high
Cold pressor test	Assesses sympathetic reactivity	Discomfort	Research-oriented
Orthostatic test	Assesses autonomic regulation	Protocol-dependent	High
Treadmill test	Physiological exercise stress	Requires equipment	High
Mental stress test	Simulates psycho-emotional stress	Standardization challenges	Promising

HRV	Assesses autonomic balance	Sensitive to external influences	High
Cortisol	Reflects HPA-axis activity	Circadian variation	High
α-Amylase	Non-invasive	Limited standardization	Promising
hs-CRP	Widely available	Non-specific	High
IL-6	Pathophysiological relevance	Cost	Research-oriented

WHY A SINGLE STRESS TEST IS INSUFFICIENT

In a classic study involving young hypertensive men, BP responses to individual stress tests did not fully reflect 24-hour BP variability or the degree of cardiovascular involvement.

This represents an important methodological consideration.

Therefore, a single stress test should not be used as an independent diagnostic criterion for hypertension.

Its diagnostic value increases when combined with:

- ABPM;
- HRV;
- biomarkers;
- traditional risk factors.

A POTENTIAL MODEL FOR INDIVIDUAL RISK ASSESSMENT

A promising research direction is the development of an integrated risk index.

Military Hypertension Risk Score = clinical risk + BP phenotype + stress reactivity + autonomic dysfunction + biomarkers.

Block A — Traditional Risk Factors

- family history of hypertension;
- BMI;
- waist circumference;
- smoking;
- metabolic abnormalities.

Block B — Occupational Factors

- duration of military service;
- number of night-duty shifts;
- sleep duration;
- perceived stress.

Block C — Hemodynamic Parameters

- office BP;
- ABPM;
- BP variability;
- dipping status.

Block D — Stress Reactivity

- ΔSBP;

- ΔDBP;
- ΔHR;
- recovery time.

Block E — Autonomic Regulation

- SDNN;
- RMSSD.

Block F — Biomarkers

- cortisol;
- DHEAS;
- uric acid;
- hs-CRP.

However, specific numerical scores should not be assigned theoretically. They must be derived from prospective cohort data using regression modeling and subsequently undergo external validation.

PREVENTION

The primary goal of early diagnosis is not simply to assign a diagnosis to a young individual but to prevent progression from functional cardiovascular hyperreactivity to sustained hypertension.

Preventive strategies should therefore be personalized.

PRACTICAL IMPLICATIONS FOR MILITARY MEDICINE

The proposed approach may help identify high-risk military personnel before clinically apparent hypertension develops.

This creates an opportunity to initiate preventive measures at an earlier stage.

From an organizational perspective, the most feasible strategy is a staged model:

low-cost population screening → functional assessment → ABPM → biomarker testing only in high-risk individuals.

Such an approach is likely to be more cost-effective than performing expensive laboratory investigations in all service members.

CONCLUSION

Early diagnosis of hypertension in young military personnel represents an important area of preventive cardiology and military medicine.

Conventional office BP measurements do not provide a complete assessment of cardiovascular risk because early regulatory abnormalities may become apparent only during physical or psycho-emotional stress.

The most important early phenotypes include:

- masked hypertension;
- increased blood pressure variability;
- exaggerated pressor response;
- non-dipping BP pattern;
- sympathetic hyperactivity;
- reduced heart rate variability.

The most promising strategy appears to be an integrated approach combining:

ABPM + stress testing + HRV + clinical risk factors + biomarkers.

Among biomarkers, cortisol, DHEAS and the cortisol/DHEAS ratio, uric acid, and hs-CRP may have particular practical value, whereas IL-6, TNF-α, salivary α-amylase, and markers of endothelial dysfunction may be especially useful in research protocols.

Future preventive strategies should focus not only on lowering already elevated BP but also on preventing the transition from functional stress-induced cardiovascular hyperreactivity to sustained hypertension.

Thus, the development of personalized risk models integrating clinical data, ABPM, autonomic indices, stress-test responses, and biomarkers may represent a new direction in the early prevention of cardiovascular disease among young military personnel.

REFERENCES

1. Olga V, Lucio M, Giuseppe G, Stefano M, Paolo P. Blood pressure response to stress tests does not reflect blood pressure variability and degree of cardiovascular involvement in young hypertensives. Int J Cardiol. 1995;48(3):303–310. doi:10.1016/0167-5273(94)02237-D.
2. Lin YP, Fan CH, Tsai KZ, Lin KH, Han CL, Lin GM. Psychological stress and long-term blood pressure variability of military young males: the cardiorespiratory fitness and hospitalization events in armed forces study. World J Cardiol. 2020;12:626–633.
3. Lin YK, Liu PY, Fan CH, Tsai KZ, Lin YP, Lee JM, Lee JT, Lin GM. Metabolic biomarkers and long-term blood pressure variability in military young male adults. World J Clin Cases. 2020;8(11):2246–2254.
4. Liu PY, Lin YK, Chen KW, Tsai KZ, Lin YP, Takimoto E, Lin GM. Association of liver transaminase levels and long-term blood pressure variability in military young males: the CHIEF study. Int J Environ Res Public Health. 2020;17:6094.
5. Lin GM, Li YH, Lee CJ, et al. Rationale and design of the cardiorespiratory fitness and hospitalization events in armed forces study in Eastern Taiwan. World J Cardiol. 2016;8:464–471.
6. Howard JT, Stewart IJ, Kolaja CA, et al. Hypertension in military veterans is associated with combat exposure and combat injury. J Hypertens. 2020;38:1293–1301.
7. Koval SM, Snihurska IO. Stress-induced arterial hypertension and arterial hypertension of wartime: contemporary challenges. Arterial Hypertension. 2015.
8. Kravchenko AM. Stress-induced arterial hypertension in military personnel. Ukrainian Journal of Cardiology. 2004;5:57–62.
9. Yaribeygi H, Panahi Y, Sahraei H, Johnston TP, Sahebkar A. The impact of stress on body function: a review. EXCLI J. 2017;16:1057–1072. doi:10.17179/excli2017-480.