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Gestational Endotheliopathy as Trigger Disorder of Haemodynamics Pregnancy Supply

Dmytro Konkov, George Belkania, Levon Dilenyan, Victor Rud, Liana Puchalska, Alina Piskun and Larisa Klimas

Abstract

The idea for this study is based on endothelial-dependent adaptation of hemodynamic circulation in pregnancy. The optimization of the circulatory component of the cardiovascular system (CVS) during pregnancy via blood pressure (BP), especially in physiological pregnancy (PhP), is accompanied by a clear overall increase in systolic characteristics of the pumping function of the heart. This orientation in cardiac output (CO) is unambiguously manifested throughout all three trimesters as with PhP—in a prone and standing position in total according to 24 characteristics out of 24 ($P < 0.01$), while for gestational endotheliopathy (PaP)—by 18 out of 24 ($P < 0.05$) clear restructuring of the dynamic organization of the circulatory state according to the anthropophysiological ratio to the hyperkinetic state according to CO in a standing position (type III) was noted with all blood pressure (BP) regimes. If the manifestation of type III under hypotonic, normotonic, and hypertonic regimes in BP was 8, 12, and 6%, respectively, then in the case of PhP, it was 21, 36, and 50%, respectively ($P < 0.01$), and for PaP, it was 48, 66, and 76% ($P < 0.01$). Hemodynamically identified heart failure (HF) syndrome, as the earliest preclinical circulatory endothelial-dependent form, is examined as a trigger of formation of perinatal pathology corresponding to preeclampsia.

Keywords: pregnancy, gestational endotheliopathy, perinatal pathology, cardiovascular system, circulation, pumping function of heart, cardiac output, cardiac index, heart failure

1. Introduction

In early gestational age, the decidua has been extensively studied to define the spiral artery remodeling process that occurs during pregnancy. The remodeling results from a complex interaction between maternal decidual immune cells in the uterine wall and invasive trophoblasts. During remodeling the arterial muscular layer is replaced by fibrinoid material, and the arterial diameter increases 4–12-fold [1, 2]. The process of optimal trophoblast invasion is often defective in preeclampsia, particularly in early-onset preeclampsia, affecting the endothelium (gestational endotheliopathy) but not the interstitial invasion pathway; the remodeling of

myometrial spiral artery segments is particularly affected. However, defective remodeling is also seen in other cases of perinatal pathology and even rarely in normal pregnancy. The resulting abnormal uteroplacental flow is associated with placental oxidative stress, probably from ischemia reperfusion injury of the placenta. It is not known why some woman with gestational endotheliopathy develop preeclampsia, while others do not [3–6].

It is important to understand that all organism mechanisms providing pregnancy depend, foremost, on the hemodynamic system and the priority role of the perfusion complex (volume–tube–pump–pressure–blood flow)—pumping function of heart. More research assures that preeclampsia is examined not so much as the first event in subsequent development for women with cardiovascular diseases [7], but rather as a special circulatory state due to not insufficient, in our view, but tense adaptation of the CVS [8–10] in women, as straight-walking creatures, in pregnancy. However, a faithful a faithful parcel in determination of relations reason–result determines the necessity of establishment of certain factor or terms, according to which such adaptations show up in the CVS in pregnancy, and also determination of hemodynamic structure of perfusion mechanisms lying in and defining the orientation of this adaptation at physiological and pathological pregnancy. Such synergy substantially impacts tension of adjusting of blood circulation on a gravitational factor, especially in the upright position. In turn, antigravity tension of the CVS affects the blood circulation of pregnant women, which is critical for maintenance and development of fetoplacental circulation of blood. The real influence of formed biophysical terms related to pregnancy shows up from the second half of pregnancy, on circulation of blood and in the lying position [10–12].

Some studies have shown an association that displays growth of circulatory tension and gestational endotheliopathy of typology alteration of dynamic organization of CVS with growth of hyperkinetic state of circulation of blood in position straight standing–type III of antropophysiological correlation (upright/lying, %), minute volume of blood (MVB), system resistance of arterial vessels, especially on circulatory responsible regions (abdominal and pelvic circulation of blood), often combining with the ischemic state, together with the increase of hemodynamically identified [13, 14] circulatory syndromes of heart failure (HF). Obtained data suggest that antigravity tension of the CVS is a circulatory basis for both early and late preeclampsia. It is thus necessary to mean that blood pressure (BP) in pregnant, to that attention is brought over its determination of the state of preeclampsia, is the external display (a result, but not reason) of adaptation changes of all difficult complex of maternal circulation of blood, especially its basic mechanisms of perfusion, in the hemodynamic fetoplacental complex and, actually, organism of pregnant. Orthostatic proteinuria, which in preeclampsia is associated with arterial high BP, reflects tension of kidney link in the adaptation of the CVS to the gravitational factor of circulation of blood and out of pregnancy [15, 16].

The aim of this study is antropophysiological analysis of the circulatory state of the CVS in PhP and pregnancy with gestational endotheliopathy as a trigger, in the development of hemodynamic supply disorder in pregnancy and perinatal pathology (PaP).

2. Materials and methods

The study was performed at the National Pirogov Memorial Medical University, Vinnytsya, Ukraine, under budget grant No. 0121 U109141. Observational clinical studies were undertaken on 114 women with physiological pregnancy (PhP) and 131 pregnant women with perinatal pathology (PaP). The former group consisted of 23 women in their first trimester, 38 women in their second trimester, and 55

women in their third trimester, whereas the latter group consisted of 20 women in their first trimester, 36 women in their second trimester, and 75 women in their third trimester. A control group was formed by 115 healthy nonpregnant women. General age of pregnant women was 17–36 years ($n = 245$); only four pregnant women were older than 30 years.

We enrolled pregnant women with gestational endotheliopathy, who were diagnosed when microalbuminuria was more than 5.0 mg/mmol (screening test) and endothelium-dependent vasodilation was less than 10% (approving test).

Multicentral description of “hemodynamic model” of the examined conditions (not pregnant and pregnant women) was made basis on antropophysiological research [6] of the circulatory state of the CVS, using the diagnostic system ANTROPOS-CAVASCREEN [17], which is an innovative diagnostic complex for analyzing the performance of various blood circulation sections using noninvasive methods (thoracal and regional tetrapolar rheography, electrocardiography, BP measurement, electrometrial features of skin).

According to basic criteria and syndromal analysis of multicentral complex of hemodynamic characteristics [18–21] of the “hemodynamic model” of providing of pregnancy [22] was held special antropophysiological analysis of showing up (part in % on a selection) of the different modes is conducted on middle blood pressure (BPm)—hypo-, normo- and hypertensive on positions of body upright and lying. For determining raised and lowered BPm, we used general normative descriptions of systolic BP (<140 and > 90 mmHg) and diastolic BP (<90 and > 60 mmHg). According to our special diagnostic scale, [23] group normative descriptions for BPm = BPd + 0.32*(BPs-BPd) in the lying position were well associated with the accepted diagnostic criteria; for women up to age 35 years, BPm was 79–105 mmHg. In standing position, there have been used connected to antropophysiological characteristics correlations of BPm to its criteria in position lying (in %), that allowed to identify the adaptive orientation of adjusting on the mode of BP in position upright, in that influence of gravitational (hydrostatical) factor of circulation of blood maximally impact circulatory state of the CVS. According to used criterion and by syndromal analysis [24, 25], criteria of raised and lowered BP were identified, as well as normotensive state.

With the examined modes for BP was analyzed expression of circulatory syndromes of HF at them hemodynamically identified by diagnostic algorithm worked out by us [26], as a system estimation of pumping function of heart (PFH) in the circulatory state of the CVS. PFH additionally was estimated by trimester measuring of cardiac output (CO, ml) and cardiac index on body weight (CI, ml/kg) separately in standing and lying positions. By antropophysiological ratio of CO upright/lying (APR, %) typological description of dynamic organization of the circulatory state of the CVS was made [27]. The last was presented by three types of blood circulation: type I or hypokinetic state, with the decrease of BP in standing position (93% and less) comparing to it's size in a prone position; type II or eukinetic state, with BP of 94-106% from standing to lying position; and type III or hyperkinetic state, with increase of BP up to 107% or more in the upright position.

For the integral estimation of the analyzed condition of the CVS we additionally used system characteristics, including syndrome of greater biological age (aging, age-related depreciation) and syndrome of hemodynamic risk [5, 17] on the index of hemodynamic non-optimality (IHU > 30%), as well as regional and system estimation of syndrome of resistance (vasoconstrictions) of the arterial vessels of the head, lungs, stomach, pelvis, femur, and calf [13, 14], and increases of the systolic post-loading (post+) on the left (LV) and right (RV) ventricles of the heart.

For statistical description of obtained data methods of variation and non-parametric analysis were used with Microsoft Excel 2010. Evaluation was performed by variations of criteria of student, non-parametric to the criteria of signs and rule

of specificity of predominating of bigger part of a selection or compared sub-groups (part) in selections of “control-pregnant” and “physiological pregnancy vs pathological pregnancy” [28] with the accepted level of probability no less than 95%.

3. Results and discussion

Data on mBP for nonpregnant (control) and pregnant women were analyzed on general and actual selections on the BP mode. General selections were formed on correlation of BP “upright or lying.” Decreased BP “upright or lying” is hypotonic mode (“-” marks), increased BP “upright or lying” is hypertensive mode (it marks “+”), and accordance of BP to normative limits “lying and upright” is the normotonic state (“0” marks). The actual modes were formed on the real combination of the modes for BP upright/lying with corresponding marks (-0+/-0+) (see **Figures 1** and **2**). It should be noted that in the normotonic mode—general (“0”) and to the variants actual (0/-+) normative description of changes of BP upright there is however a primary increase of pressure, pressure orientation in adjusting of CVS in position upright.

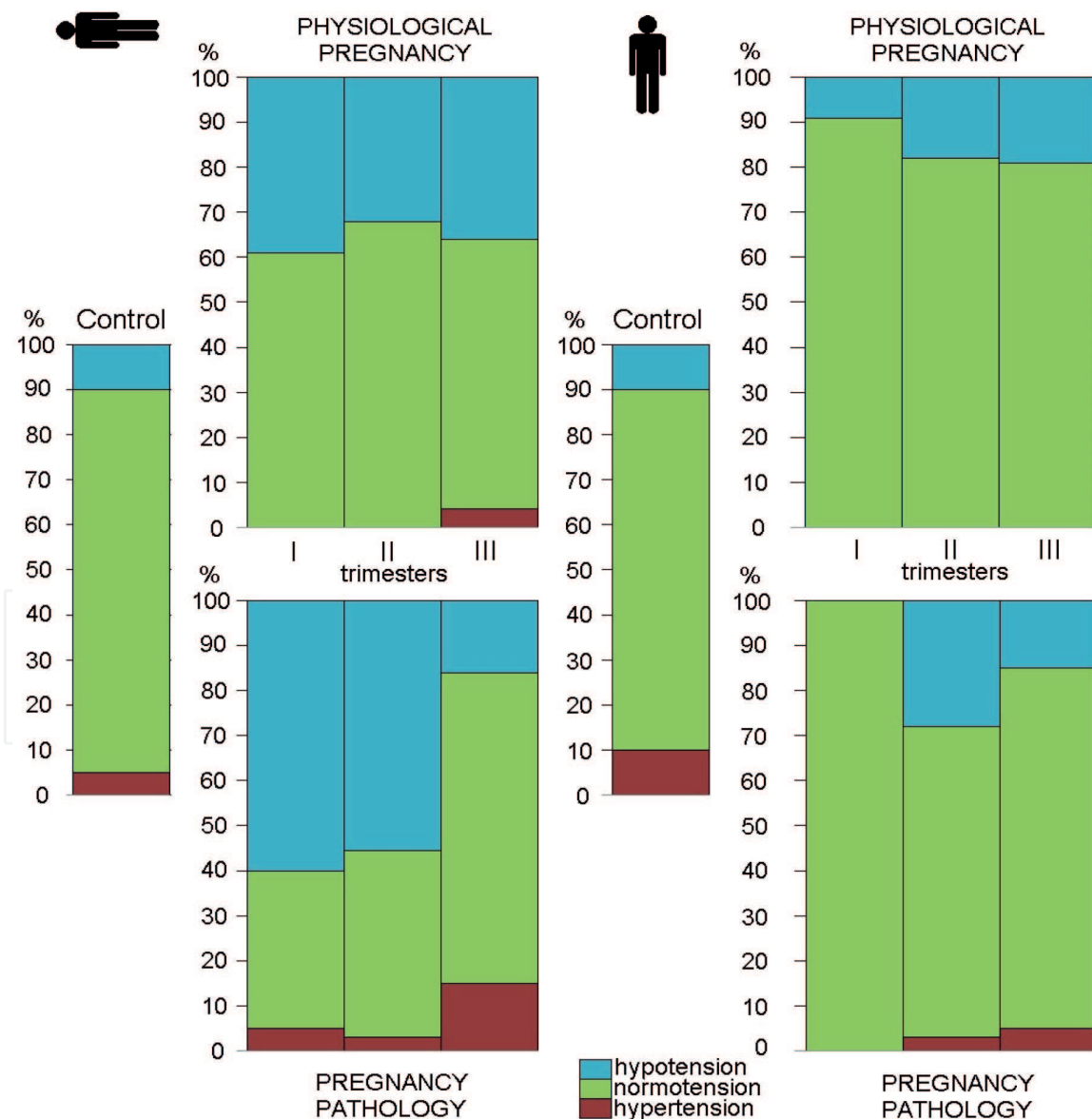


Figure 1. Distribution of stake of people (in %) with the general modes of cardiovascular system according to BP (normotonic—Upright and lying, high blood pressure and hypotension—Upright or lying) for women of reproductive age (control) and in the first, second, and third trimesters of PhP and PaP.

It is necessary to mean that in position upright taking into account expression of the hypertensive state totally with a normative increase of BP the stake of the states of CVS of pressor orientation for women arrives at 90–92%, demonstrating actuality of the tense of pressor adjustment in adaptation of CVS to the gravitational

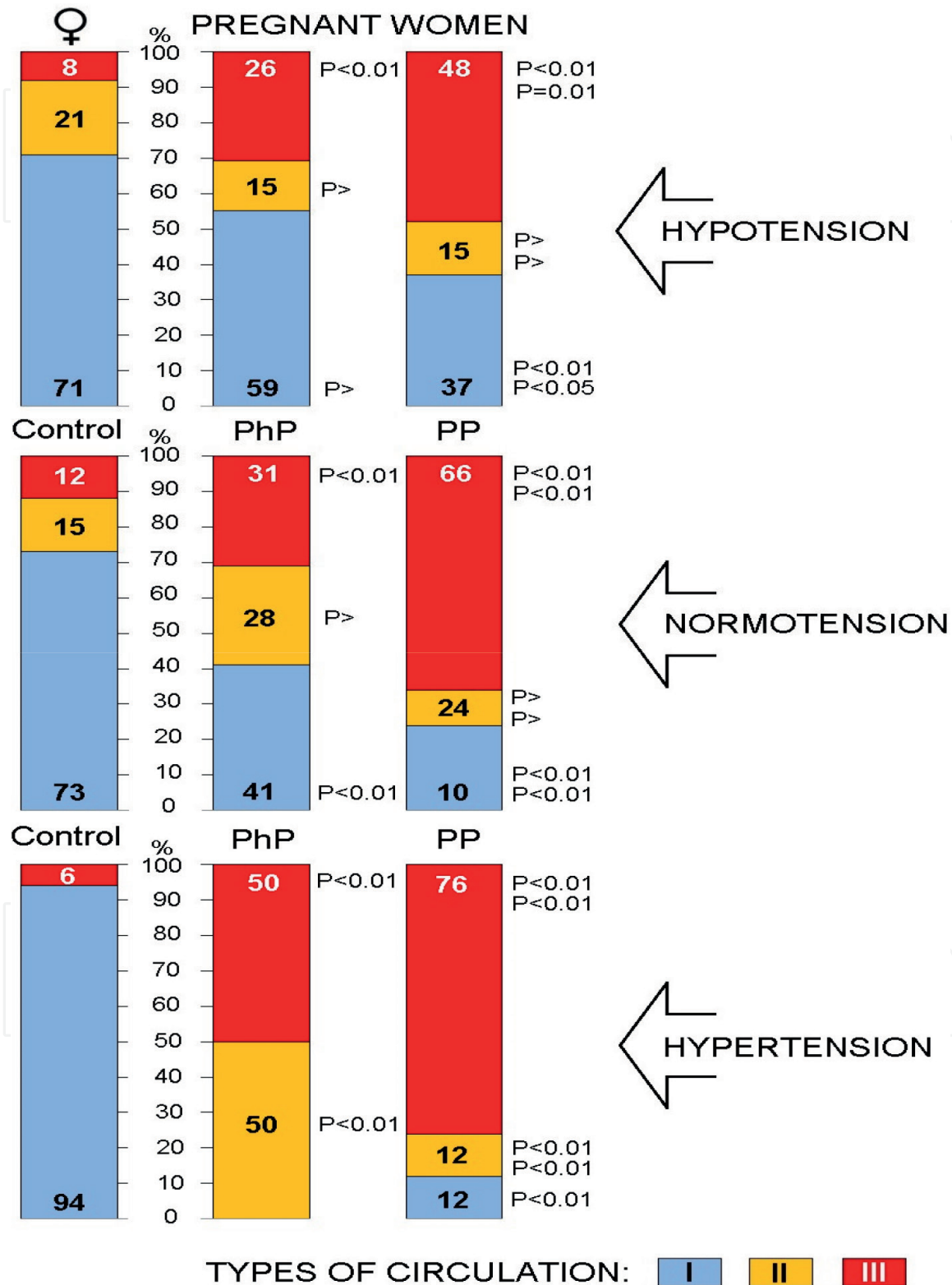


Figure 2. Distribution of types of circulation (numbers on a diagram are a stake in % on a selection) in antropophysiological ratio of cardiac output (CO) upright/lying—Hypokinetic (I), eukinetic (II), and hyperkinetic (III) at the general modes of BP (hypotension, normotension, hypertension) of the circulatory state of CVS for nonpregnant women (control), PhP, and PaP. Authenticity of distinction (D) on the types of circulation is brought between control and PhP, by control and PaP (first row), and between PhP and PaP (second row).

(hydrostatical) factor of circulation of blood for a human as straight-walking creature. There is a background to examine it as physiological basis of forming of the hypertensive state [3, 4], including, for pregnant.

Figure 3 shows the subsequent dynamics of this setting for pregnancy in the first and second trimesters of PhP. It shows a clear reduction of the hypertensive states to their absence in the lying position, and it is especially shown in the upright position up to the third trimester. Such dynamics at PhP demonstrate optimization of the circulatory state of the CVS, at least on the mode of BP especially it's important for maturing of pregnancy in terms of straight-walking (sitting, upright, at walking). Clear growth of expression of hypotonic states is thus marked in the lying position, with 10% for nonpregnant women (control group) to the first (39%) and the second trimesters - 32% ($P < 0.01$).

Figure 1 shows less expressed marked orientation in distribution of the modes for BP in the upright position determined at PaP. The hypertensive state is absent only in the first trimester. It appears in the second and third trimesters, though at lower levels (3–5%; $P \leq 0.05$) compared to nonpregnant women (10%). For PaP, the hypertensive states are present in the lying position during all three trimesters, increasing three times (from 5% for nonpregnant women to 15% in PaP; $P < 0.05$).

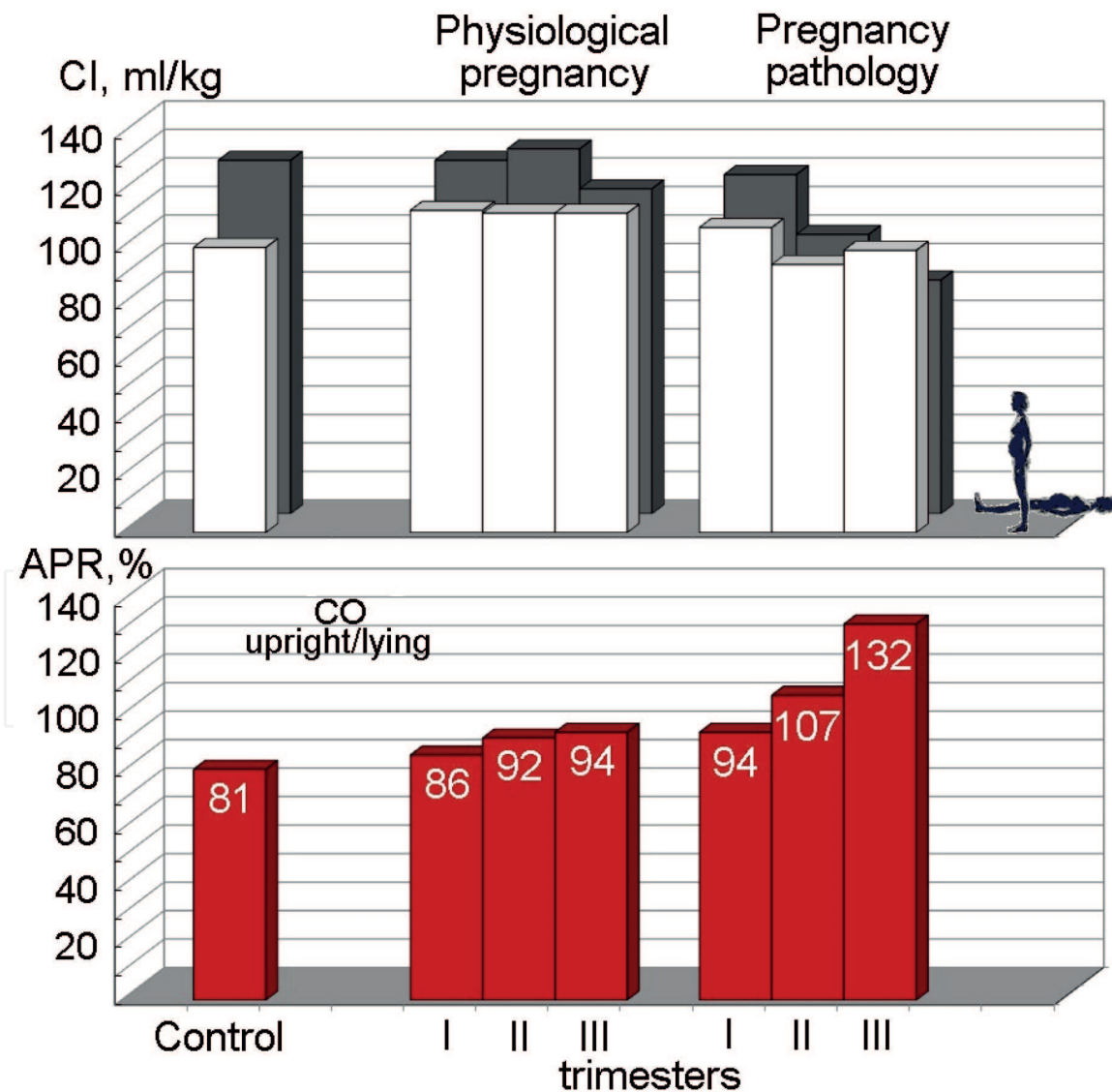


Figure 3. Dynamics of the hemodynamic providing of physiological pregnancy (PhP) and pathological pregnancy (PP) on a cardiac index (CI = CO/kg body weight) in the lying and upright positions (marked by figures) and on antropophysiological correlation (APR = CO upright/lying, in %)—Index of typology alteration of dynamic organization of the CVS.

It should be noted, that according to optimization of the state of the CVS on the mode of BP for pregnant raising of systolic function of heart, especially clearly expressed at physiological pregnancy, was marked. **Table 1** presents the data on MBV, on positions lying SI and APF and upright in the first, second, and third trimesters of pregnancy. For analysis, we used an average ($X \pm m_x$) and non-parametric statistical descriptions of hemodynamic parameters: median (Me) and percentile range. The k -value of percentile was determined with 95% probability

Status	Bodyweight	CO, ml		APR, %	CI, ml/kg	
		Lying	Standing		Lying	Standing
Nonpregnant women						
Women (of even-aged control group) $n = 114$	58	7164	5668	81	124	700
	51–56	5240–9255	4620–6974	64–100	88–157	79–123
	59 ± 1	7225 ± 222	5779 ± 186	84 ± 3	126 ± 3	100 ± 3
Physiological pregnancy (PhP)						
First trimester $n = 23$	65	8282	7018	86	124	113
	59–70	6204–15,581	6332–9323	70–123	78–181	73–144
	64 ± 1	9896 ± 585	7485 ± 211	91 ± 4	133 ± 9	116 ± 7
Increase of systolic descriptions—in 17 out of 20 ($P < 0.07$)						
Second trimester $n = 38$	62	7996	6788	92	128	112
	50–67	5837–11,130	5033–9408	79–109	77–175	81–150
	60 ± 1	7996 ± 344	6885 ± 229	94 ± 3	127 ± 6	114 ± 4
Increase of systolic descriptions—in 19 out of 20 ($P < 0.01$)						
Third trimester $n = 53$	71	9534	6640	94	114	103
	63–79	5264–10,528	5101–9536	86–103	77–146	78–145
	71 ± 1	7443 ± 242	7444 ± 225	112 ± 4	102 ± 4	108 ± 5
Increase of systolic descriptions—in 16 out of 20 ($P = 0.01$)						
Perinatal pathological with gestational endotheliopathy (PaP)						
First trimester $n = 20$	57	7754	7789	94	119	107
	49–62	5841–9297	4491–14,578	71–146	87–149	67–203
	56 ± 1	7840 ± 406	8809 ± 803	103 ± 8	125 ± 9	131 ± 14
Increase of systolic descriptions—in 14 out of 20 ($P = 0.05$)						
Second trimester $n = 36$	61	8019	7741	107	98	94
	56–69	5507–9428	6454–9817	84–135	64–157	65–160
	62 ± 1	7286 ± 419	7800 ± 480	106 ± 10	106 ± 9	110 ± 9
Increase of systolic descriptions—in 14 out of 20 ($P = 0.05$)						
Third trimester $n = 75$	68	5774	8305	132	82	99
	64–74	4075–6900	3615–9570	95–159	53–105	49–147
	69 ± 1	5730 ± 196	7128 ± 279	127 ± 5	84 ± 5	102 ± 4
Increase of systolic descriptions—in 9 out of 20 ($P >$)						
Statistical parameters of selection: the first row of digital data is a median (Me) of selection, second row is a percentile range (k_0 – k_1) with 95% probability ($P \leq 0.05$), and the third row is an average by the c error of middle ($X \pm m_x$).						

Table 1. Cardiac output for nonpregnant women in control group and for pregnant women (first, second, and third trimesters).

($P \leq 0.05$) taking into account a sample size, percentile with $k \geq 0$ was determined as the lower limit of the percentile range, and $k \geq 1$ was determined as the higher limit. For convenience, shorthand signs will be used for -lower ($k0$) and overhead ($k1$) percentile.

MVB (minute volume of blood), APR (antropophysiological correlation), and CI (cardiac index) are homogeneous hemodynamic indexes and therefore they are taken for systole descriptions (parameters) of the hemodynamic providing of pregnancy on the pumping function of heart. A non-standard approach was used to estimate the differences of these descriptions in nonpregnant women (CG) and between PhP and PaP. Each one, of the estimated hemodynamic parameters (MBV, APF, and SI), as marked higher, on one or another condition (trimester, lying, upright) used, four descriptions, that is driven in **Figure 1** in order of their placement— $Me, k0-k1, X$.

Analyzing of the dynamics generally in all trimesters, was conducted by three hemodynamic criteria – MBV, CI (in a prone and standing position) and APR, in every separate trimester; a total number makes 20 descriptions. In comparison with a control group, and also PP and PaP, on non-parametric criteria; the amount of the descriptions is taken to the account with unidirectional difference (anymore, less than, absent).

Optimization of the circulatory state of the CVS during pregnancy accompanied by the clear increase of systolic descriptions on the pumping function of heart and shows up on all three trimesters, especially at PP (**Table 1**). On MBV such orientation simply shows up during all three trimesters as at PhP—lying and upright totally for 24 descriptions from 24 ($P < 0.01$) and at PaP—also for 18 from 24 ($P < 0.05$). However at development of pregnancy substantially, that the pumping function of heart provided increasing pregnant body and fetus weight, therefore the calculation of SI is oriented not to the surface of body of pregnant, but on its weight. Consideration of SI demonstrates clear weakness of systolic possibilities of the heart during PhP—in position lying on all 12 from 12 descriptions of SI lower as compared to nonpregnant, and for 11 from 12 descriptions lower as compared to PaP (see a **Table 1**). Unlike PhP at PaP the clear and increasing decline of SI was marked during all pregnancy (**Figure 3**), as compared to both nonpregnant women and PhP.

Unlike position of body lying—upright SI increases for 10 from 12 characteristics (totally for three trimesters) at PP ($P < 0.05$), while at PaP—only for 7 from 12 ($P >$). At this SI at PaP in position upright was for less comparing to PP—for 9 descriptions from 12 ($P < 0.05$). Should be noted clear change during pregnancy of correlation MBV upright/lying (in %) on the index of APF, which is the typological reflection of dynamic organization of the circulator state of CVS and demonstrated at pregnancy in position upright hyperkinetic alteration of pumping function of heart and circulatory state of the CVS. Thus, both on PhP and PaP—for 12 descriptions of APF from 12 ($P = 0.01$). However most expressed such alteration is in PaP, that totally during all three trimesters marked for 12 from 12 descriptions of APF ($P < 0.01$).

It should be noted that such alteration of typological structure of the circulator state of the CVS at pregnancy was marked at all general modes of BP (**Figure 2**). It's evident, that as compared to nonpregnant, stake of type III (in %) at PhP and PaP for increases at all three modes of BP ($P < 0.01$).

Thus at PaP it is greater comparing to PhP ($P < 0.01$), arriving at normotonic and hypertensive modes of BP of level of specific description on a selection—accordingly 66 and 76%. It is necessary to underline that both these modes of BP, unlike the hypotonic mode, are the reflection of pressor adjusting of the CVS. From the data presented on **Figure 4**, its evident, that at these modes of BP pressor

orientation lowers representative hypokinetic state of the CVS (type I) with a decline MBV in position upright—to 10–12%.

It is necessary to mean that hemodynamic adaptation at pregnancy that was accompanied by increasing antigravity tension of CVS and that shows up in forming of the hyperkinetic state of MVB in position upright, from one side, directionally on the hemodynamic providing, increase of pumping function of heart; and, from another side, limits functional abilities of the CVS in type III.

In the conditions of such tension extreme depreciation of heart is real. Thus, there can be both the real clinical state developing during pregnancy (dystrophy, cardiomyopathy, ischemia, etc.) and hidden from standard diagnostic determination not clinically, and the hemodynamically identified transitory heart failure (tHF), as most early form of display of this state. Earlier we showed such possibility,

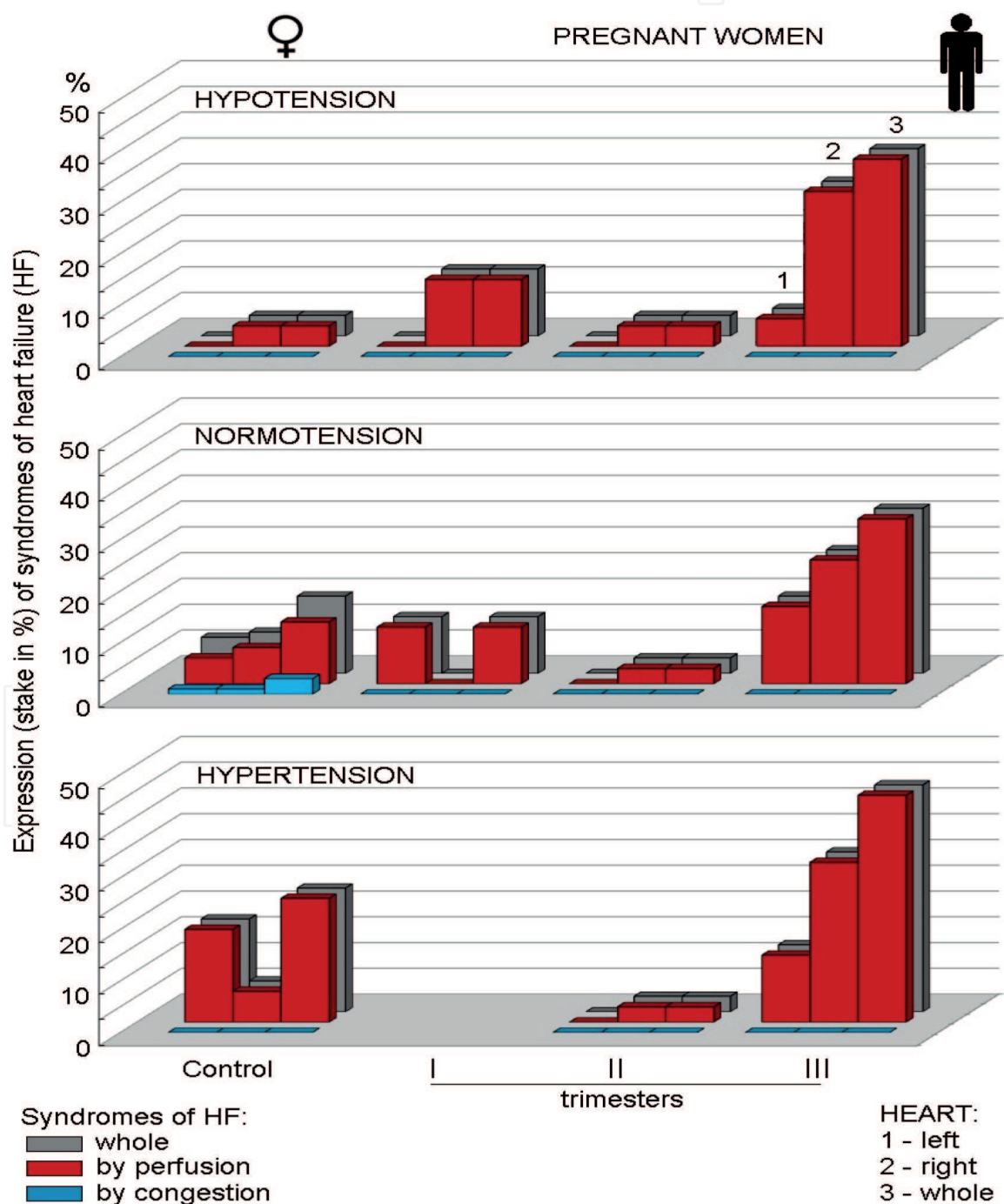


Figure 4. Expression (stake in %) of syndromes of transitory heart failure (tHF) at the general modes of BP for women of reproductive age (control) and in the first, second, and third trimesters of pregnancy in the upright position.

including, in pregnancy [29], and also clear association of most expressive hemodynamic syndromes of insufficiency of circulation of blood is shown, including HF, exactly at type III of the circulatory state of CVS [30].

Thus it should be noted that at any modes of BP expression of hemodynamically identified HF for pregnant and nonpregnant women exactly in position upright—maximal antigravity tension of CVS, as compared to position lying, certainly higher (**Figure 5**).

So, if nonpregnant in control group in position lying in hypotonic, normotonic and hypertensive mode of expression of HF (stake in %) made about 0, 3 and 0%, then in position upright it increased in all three modes, accordingly to 4% ($P < 0.05$), 15% ($P < 0.01$) and 24% ($P < 0.05$). In general, but even more distinctly marked correlations on primary expression of tHF in position upright determined for pregnant. Thus, clearly growing from I to III trimester (**Figure 5**). It should be noted that all trimesters did not have any fundamental distinctions of expression of HF. An exception was made only by the hypertensive mode, which made expression of HF (50%) in II trimester, comparing to III trimester (44%).

Out of antigravity tension of CVS in lying position certain features showed up on different general modes of BP. So, at normotonic general orientation is traced—from the clear display of optimization of the circulatory state of CVS in I trimester with absence of CH to the increase of its expression in III trimester to 7% ($P = 0.05$). Absence of tHF in position lying for pregnant of “general” hypertensive mode and in II and in III trimesters attracts attention.

Another feature in position upright and lying of the circulatory state of CVS on the analyzable “general” modes of BP is differentiation of display of tHF on a right and left heart, and also on basic circulatory syndromes—on the syndrome of decline of arterial perfusion and syndrome of venous stagnation and insufficiency. From data presented in **Figure 4**, clearly evident, what for nonpregnant and pregnant (totally PhP and PaP) in position upright shows up mainly HF on a perfusion type, growing from the hypotonic mode to normotonic and, especially increasing at the hypertensive mode.

When it comes to pregnant, her real increase of expression of tHF in position upright in I trimester marked at the hypotonic state (**Figure 4**). On the whole dynamics on expression of HF in I and II trimesters of pregnancy reflects to the noted optimization of the circulatory state of CVS. Especially distinctly it shows up on II trimester, that is reflected in the low level of expression of HF. Substantial feature of the circulatory state of CVS at pregnancy in position upright is a primary display of right-heart tHF of perfusion type—on **Figure 4** practically on all positions, except pregnant with the normotonic mode. It's a sign that antigravity tension of CVS for pregnant in position upright the weakest links a right heart, consequently, pulmonary hemodynamics. As a result—growing pressure in the pulmonary artery and increased post-tension on the right ventricle.

Especially meaningful is the increase of expression of tHF in position upright determined in III trimester of pregnancy, including, and mainly on a right heart. Exactly on this stage of development of pregnancy the well-known physical terms, related to the increase of the sizes of uterus and fetus, maximally strengthen their synergistic influence on adjusting of circulation of blood on a gravitational (hydrostatic) factor and corresponding antigravity tension of CVS, directed of hemodynamic providing of pregnancy and actually organism of pregnant. It is necessary to remember, that dualism is real in this biologically important adaptation—not all, that is positive for the hemodynamic providing of fetoplacental complex, is positive for pregnant women. Actually, solving such dualism determines success of physiological development of pregnancy or pathological consequences during or afterwards.

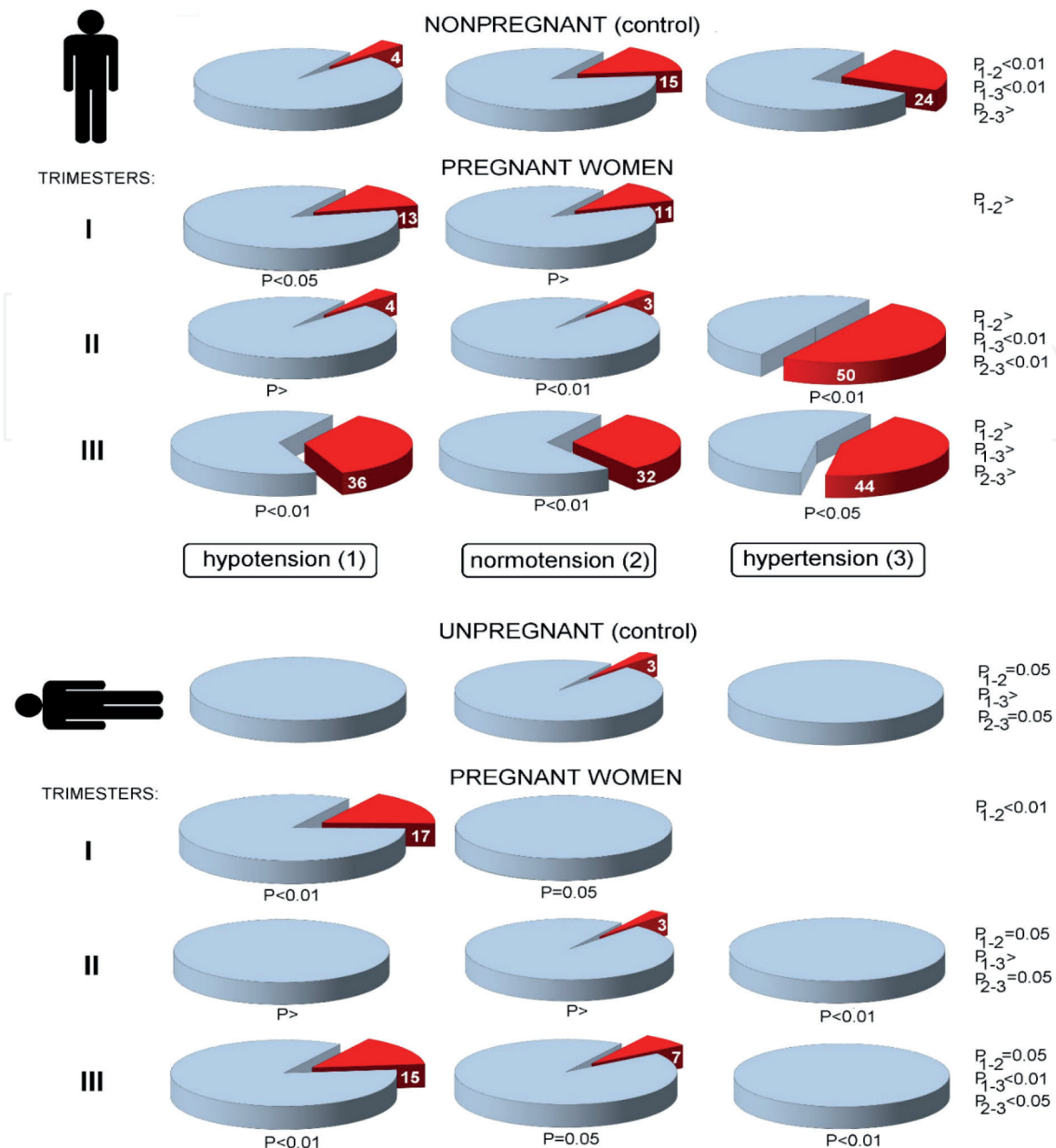


Figure 5. General expression (stake in %) of syndromes of HF (total of left and right heart) for healthy nonpregnant women (control group) and on the general group of pregnant (total of PhP and PaP) at the “general” modes of the state of CVS for BP (hypotension, normotension, high blood pressure) in the upright and lying positions (marked by figures).

Practically one level of expression of tHF in III trimester at all examined general modes of BP testifies to independent meaning fullness to the PFH and syndrome of tHF in expression of antigravity tension of CVS and as possible circulatory basis of insufficiency of hemodynamic adaptation in pregnancy. It gives certain grounds to suppose that it's not in the mode of BP, and in structural organization of the circulatory state of CVS, functional basis of that is made by the pumping function of heart, and actually the state of last. Actually certain mode is the result of such alteration. Thus the marker of tension of hemodynamic alteration is a transition on the cardiac output to the hyperkinetic state in position upright comparing to lying—to type III of dynamic organization of the circulatory state of CVS, and by the predictor of insufficiency of adaptation of CVS, including, at pregnancy—results of hemodynamically identified by antropophysiological diagnostic algorithm of circulatory syndromes of HF. Last, as the most early circulator form of HF of perfusion type on preclinical level is a trigger of forming of dynamic organization of the

circulatory state of CVS, corresponding to the hypertensive state, including, one in pregnancy.

Therefore, there is a clear association between tHF and dynamic alteration of the circulatory state of the CVS to the hyperkinetic condition (type III) in the upright position. On **Figure 6** at the same orientation of such alteration it is clearly determined higher stakes of type III, both for nonpregnant and for pregnant, exactly in a group with the syndromes of HF. During postnatal ontogenesis in the process of adaptation to the gravitational factor of circulation of blood, a transition to III to the type of dynamic organization of the circulator state of CVS was marked, that was accompanied by general growth on CVS and the blocks of circulation of blood of syndrome of the age-related depreciation (greater biological age) of the hemodynamically risky states, especially expressed at type III. Thus clearly grew expression of syndromes of HF. There are reasons to suppose that these two constituents

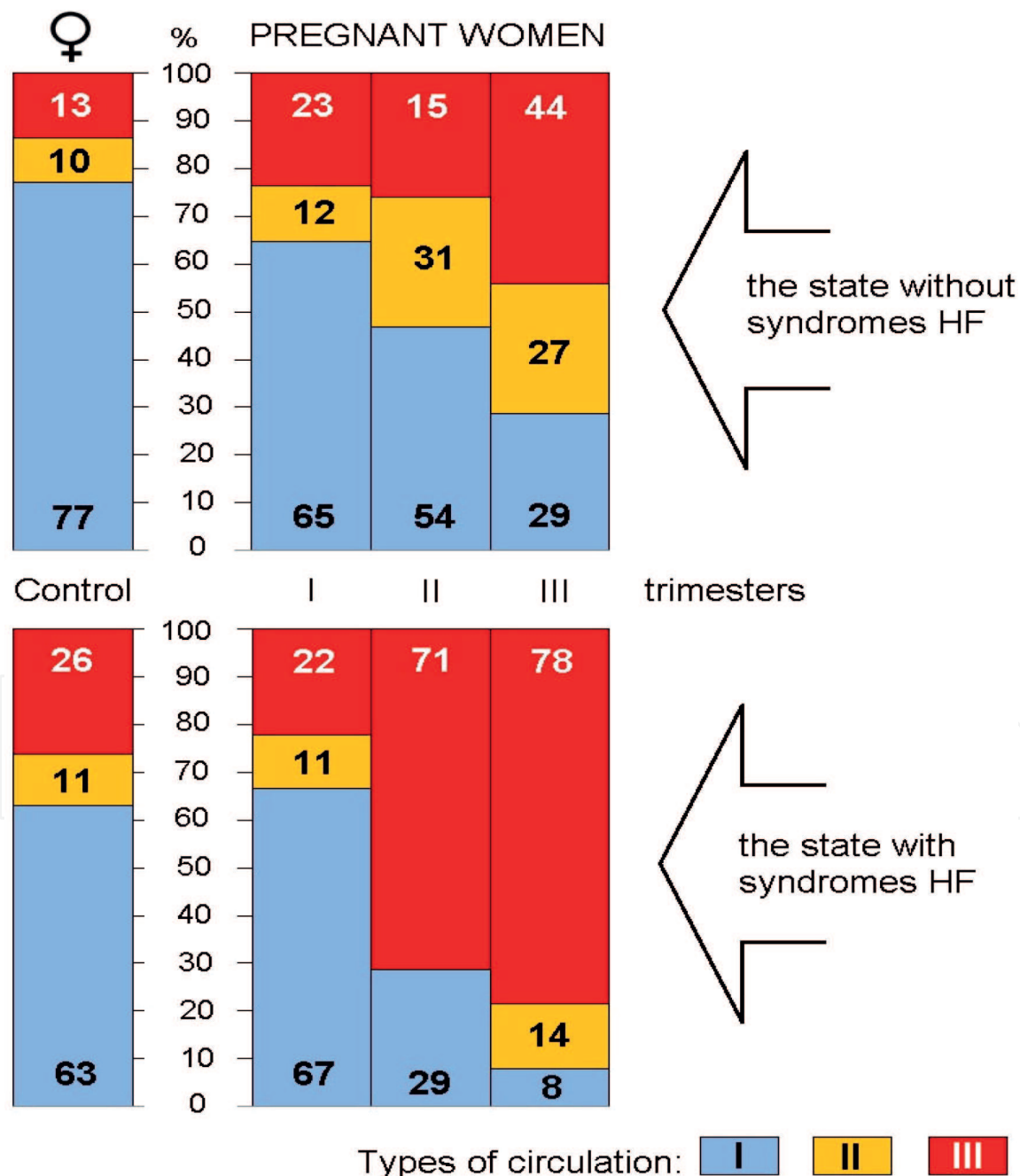


Figure 6. Distribution of types of circulation (stake in % on a diagram) of blood on antropophysiological correlation of minute volume of blood (MVB) upright/lying—Hypokinetic (I), eukinetic (II), and hyperkinetic (III) in nonpregnant (control) women and pregnant women on the states with and without syndromes of tHF.

(typology alteration and HF) induce the features of dynamic organization of CVS at one or another somatic state.

Besides a trigger function, tHF was, as marked higher, by the display of anti-gravity tension of CVS, leading to functional depreciation of CVS and to increase of hemodynamic risk, both on the general state of circulation of blood and on the basic circulatory blocks of CVS.

At overlook of dynamic organization of the circulatory condition of CVS it is necessary to remember the state of the capacity making adjusting of CVS on the gravitational (hydrostatical) factor of circulation of blood, which is present in position upright, including for pregnant, in system vasoconstriction of arterial vessels, especially shown in vascular regions below level of heart [31]. It is necessary to notice, that in diagnostic algorithm as a syndrome of resistance, the state when indexes of arterial impedance (vascular resistance) exceed a normative increase, is fixed. Mentioned on **Figure 7** data clearly demonstrate the value of the state of heart in this system adjusting to pressor orientation, especially in position upright. Both for nonpregnant and pregnant those who have hemodynamically identified tHF, as a rule, perfusion type, in position upright marked more expressed (red blocks), as compared to the states without tHF (green blocks), system vasoconstriction. By grey color marked blocks of circulation of blood, on which distinctions are absent.

Optimization of the circulatory state of CVS during pregnancy by the regime of blood pressure, especially with FP, was accompanied by a clear overall increase in systolic characteristics of the PhP. This orientation in the cardiac minute volume (CMV, ml) unambiguously manifested itself during all three trimesters as with PhP—lying and standing in total according to 24 characteristics out of 24 ($P < 0.01$), while with gestational endotheliopathy—by 18 out of 24 ($P < 0.05$). If the manifestation of type III under hypotonic, normotonic, and hypertonic regimes in blood pressure was 8, 12, and 6%, respectively, then in case of PhP it was 21, 36, and 50%, respectively (for all P positions < 0.01) and for PaP, 48, 66, and 76% (for all positions $P < 0.01$). For gestational endotheliopathy in all modes of blood pressure, the representativeness of the hyperkinetic state in the e pumping function of

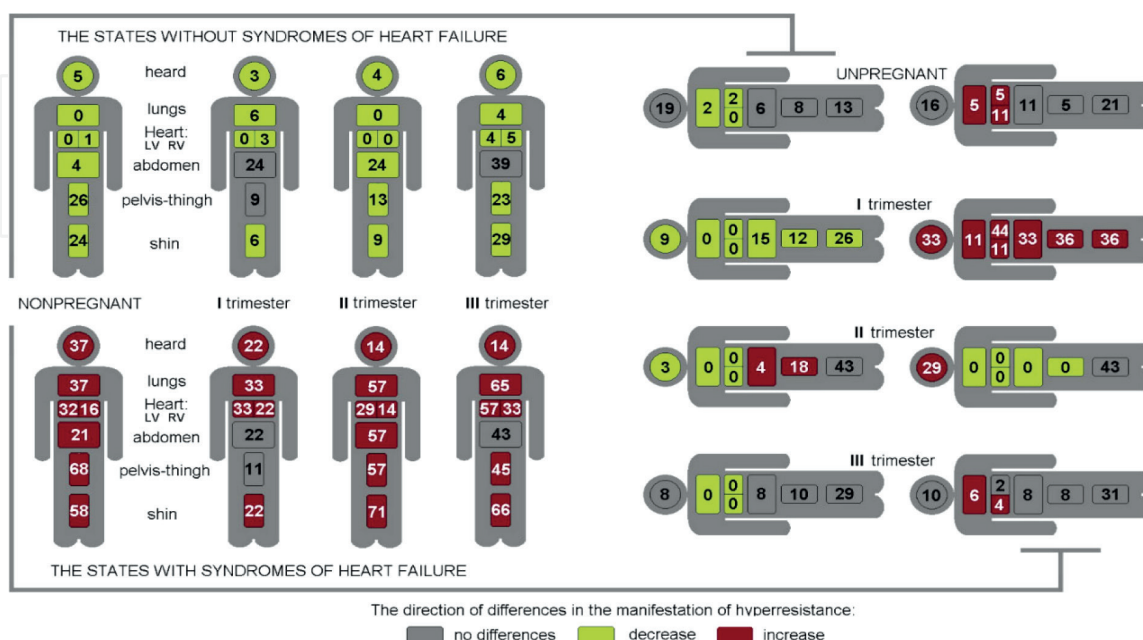


Figure 7. Antropophysiological (upright and lying positions) characteristics of differences of expression (stake in %) of syndromes of hyperresistance of arterial vessels for nonpregnant (control) women and pregnant women at comparison on groups with syndromes of HF and without.

the heart standing (type III) was significantly higher compared to PhP ($P < 0.01$). According to it, the marker of tension of hemodynamic alteration was a transition on the CMV to the hyperkinetic state in position from standing to lying—to type III of dynamic organization of the circulator state of CVS and system hyperresistance of arterial vessels, and by the predictor of insufficiency of adaptation of CVS was displayed mostly in the position upright by perfusion type, combining with circulatory syndromes limiting adaptive possibilities of arterial circulation.

For hemodynamic providing of pregnancy such system of vasoconstriction has a critical value, especially for circulatory blocks, directly responsible for hemodynamic providing of fetoplacental link—abdominal and pelvic circulation of blood. Placenta, volume of amniotic fluid, and self-weight of fetus in max decrease influence of gravitational (hydrostatical) pressure at straight-walking (sitting, upright, walking). However direct dependence of the hemodynamic providing of fetoplacental complex from maternal circulation of blood is saved, both from regional, especially abdominal and pelvic and the circulatory state of CVS in general and its central link—pumping function of heart [32].

Expression of autonomic “slipping out” of arterial vessels of abdominal and pelvic circulation from under system vasoconstriction, probably because of endothelium-depending humoral mechanism, determine phenomenon of optimization of the circulatory state of CVS at the beginning of pregnancy, especially expressed at PhP, and inhibition of pathological changes. And, vice versa, expressed vasoconstriction of abdominal and pelvic arterial vessels, along with hypoperfusion and decrease of pumping function of heart determine circulatory basis of PaP (in the first place preeclampsia). Therefore, estimating the circulatory state of CVS for pregnant, and nonpregnant, necessary to be oriented not on the mode of BP, but on condition of basic perfusion mechanisms a “volume of blood—pumping function of heart—vascular capacity—blood stream” and regulators of autonomic regional blood flow—endothelial function providing distribution of peripheral circulation of blood, and it explained that gestational endotheliopathy is the trigger component of disorder hemodynamics supply pregnancy and development of perinatal pathology. In fact, the state of perfusion mechanisms that form the basis of hemodynamic support of any somatic condition and especially pregnancy, taking into account the formation of a fetoplacental complex «above organism» and necessity of hemodynamic adaptation of CVS of pregnant as straight-walking creature, to formed exceptional organism situation not only in gestational feature, but also in aspect of adaptation.

4. Conclusions

1. The typological transition in the dynamic organization of the circulatory state of the CVS by CO to the hyperkinetic state in the standing relative to the lying position (type III) and the manifestation of systemic hyperresistance of arterial vessels reflects the tension of adaptation of the CVS during hemodynamic support of pregnancy.
2. The predictor of insufficiency of adaptation of the CVS during hemodynamic support of pregnancy, especially with PaP, is gestational endotheliopathy. Playing a role of a trigger, for manifestation of a hemodynamic syndrome of HF in a perfusion type, which is predominantly in a standing position, combined with circulatory syndromes that limit the adaptive capabilities of arterial circulation (hyperresistance, ischemia), which is especially relevant for abdominal and pelvic circulation.

3. Hemodynamically identified HF by perfusion type, as the earliest circulatory form at the preclinical level for gestational endotheliopathy, is considered a trigger for the formation of a dynamic organization of the circulatory state of the CVS corresponding to the hypertensive state, including during pregnancy (preeclampsia).

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Conflict of interest

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