The influence of cardiac and hematological parameters on the maximal oxygen uptake in healthy and athletic male adults

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Abstract

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Purpose:
The maximal oxygen uptake (VO_{2max}) and therefore the endurance performance seem to be dependent on cardiac and hematological parameters. The aim of this study is the direct measurement of, if possible, all parameters that could influence the VO_{2max} and to interrelate them with each other. Here, the focus is on the parameters blood volume (BV), total hemoglobin mass (tHb-mass) and the cardiac output per minute. So far, these parameters have rarely been measured directly.

Methods:
30 healthy and athletic male adults were examined. On one day, sociodemographic and anthropometric data were collected followed by a stress test (cycle ergometer – semi-recumbent) with ergo-spirometry, impedance cardiography and lactate diagnostics. On a second day, tHb-mass and BV were determined with a modified carbon monoxide rebreathing method.

Results:
A multiple linear regression (stepwise selection, backward elimination) was carried out. The parameters stroke $volume_{max,}$ (SV_{max}), heart $rate_{max}$ (HR_{max}) and arterio-venous oxygen difference ($avDO_2$) seemed to be best (r^2 = .948) to determine VO_{2max}. Regarding the absolute parameters, a high correlation between VO_{2max} and the maximum performance existed (r = .722), but VO_{2max} did not correlate with either the maximum cardiac output (r = .322), the maximum stroke volume (r = .286), the maximum heart rate (r = .207), the BV (r = .160), the arterio-venous oxygen difference (r = .198) or the tHb-mass (r = .346). Moderately significant correlations existed between VO_{2max} by body weight and the cardiac output by body weight (r=.484) and between the maximum stroke volume by body weight (r=.373) and the hemoglobin mass by body weight (r=.386). The BV and the VO_{2max} did not correlate with each other. Interindividual comparisons showed differences in the cardiac and hematological parameters of subjects with the same performance.

Conclusions:
References mention high correlations between the cardiac $output_{max}$, the SV_{max}, the BV and the tHb-mass, but these could not be demonstrated in a homogenous study population. With the summation of all the single influences, however, the dependence of $VO2_{max}$ on cardiac and hematological parameters could be shown. The interindividual comparisons showed that some of the subjects adjusted other parameters more to compensate deficits in cardiac and hematological parameters.

Key words:
Endurance performance, hemoglobin mass, cardiac output, oxygen uptake, body composition,

Introduction:

Hill and Lupton (1923) [1] have already assumed that hematological and cardiac parameters significantly limit the maximum oxygen uptake capacity (VO_{2max}) in healthy people. This has been confirmed by later researches of various authors [cf. 2, 3, 4, 5, 6]. After their examinations, Cerretelli and Di Prampero (1987) [7] have assumed that the limited oxygen uptake capacity depends to 70 - 85 % on the cardiac output only. Their assumption has been reinforced by examinations from Astrand, Rodahl, Dahl and Stromme (2003) that have proved a strong correlation between the cardiac output and the VO_{2max}.
However, it is still unclear how strong the single parameters limit the VO_{2max} and, especially, if diverse parameters may limit the VO_{2max} in different people. Also it has not yet been investigated sufficiently whether deficits such as a low cardiac output could be compensated by, e.g., a very high total hemoglobin mass (tHb-mass). The correlation of cardiac and hematological

parameters in connection with VO_{2max} has already been part of many researches. The problem, however, has consisted either in the little amount of examples or in the fact that parameters such as the tHb-mass have not been measured directly but only indirectly, measuring the hematocrit (Hct) or hemoglobin concentration (cHb), what may lead to wrong estimations [cf. 9].

In 2005, Schmidt and Prommer made it possible to routinely determine the tHb-mass with their optimized CO-rebreathing method [cf. 10], allowing an exact measurement of this parameter in bigger groups. This paper describes the direct measurement of all relevant cardiac and hematological parameters that have a limiting influence on VO_{2max}. The parameters were correlated with each other and it was examined whether interindividual differences exist. The cardiac output is primarily expected to limit the VO_{2max} what is why important knowledge for a better training control in the area of endurance training may be gathered by focusing on the exact determination of the blood volume (BV), the tHb-mass and the stroke volume (SV). The exact determination of performance limiting factors of a person may help to determine the amount and the area in which adjustment reserves are available.

Methods

Study Group:

In total, 36 subjects were examined, however, six of them could not be considered because of technical defects, wrong measurements or a missing stress test. The remaining 30 participants were active men at the age of 20-28 years who regularly exercise (3-15h per week) (see tab. 1). All subjects participated voluntarily on the study. They give were written informed consent after they were informed about the study and the risks.

Table 1 basic characteristics of the study participants

	Male (n = 30)
Age (years)*	23.7 ± 2.26
Height (cm)*	180 ± 6
Weight (kg)*	76.9 ± 8.5
BMI (kg/m²)*	23.8 ± 2.0
Lean body mass (kg)*	63.7 ± 5.7

* Mean value and standard deviation in the study group

Procedure:

All examinations took place in the sports medical ambulance of the University of Leipzig. After informing the subjects about possible risks, they had to fill out a questionnaire with questions about sociodemographic data (name and age), general lifestyle (physical activity, alcohol and cigarette consumption) and known diseases and allergies. A lung function test („easy-on-PC", ndd Medizintechnik AG, Switzerland), a body fat measurement („impedance analyser STA/BIA", Akern, Italy) and a stress test were made on the examination day *„performance diagnostics"*. On day two, *„blood volume determination"*, BV, tHb-mass and cHb were determined. The order of the examination days was randomized, but one followed the other always the day after. Any influence of the blood volume determination on the stress test can be excluded by the low half-life of COHb [10, 12]. Due to the fact that the regeneration time takes until the next day, it can also be excluded that the stress test has any influence on the blood volume determination. With the short time between the tests, no big changes can be assumed, especially concerning the tHb-mass.

On the **examination day „performance diagnostics",** a lung function test, body fat measurement and an electrocardiography („cardiax", mesamed GmbH, Germany) were made, followed by a stress test at rest, provided that no exclusion criteria existed after the pre-examinations. Exclusion criteria primarily included cardiovascular diseases (CHD, angina pectoris, cardiac arrhytmia, myocardial failure, disturbances of conduction) and pulmonary diseases (bronchial asthma, chronic obstructive bronchitis, pulmonary fibrosis, tuberculosis, pulmonary edema and pneumonia) but also every infectious disease within the last two weeks before the examination.

During the stress test the resistance was gradually increased starting with 50 watt and increasing it every minute by 15 watt until the highest values were reached. Afterwards, the stress was reduced to 25 % of the maximum performance (P_{max}). Before the test and during every third minute of it, the heart rate, the systolic (RRsys) and diastolic (RRdia) blood pressures, the subjective stress feeling and the oxygen saturation (S_aO_2) were measured as well as capillary blood samples were taken for determining lactate (Lac, device: „Super GL", Dr. Müller Gerätebau, Germany). Measurements were also made during minute one, three and five of the cool-down time. The electrocardiography (measured parameter: heart rate HR, device: „cardiax", Mesa Medizintechnik GmbH Germany), the data of the spirometry (measured parameters: VO_{2max}, minute ventilation V_E, respiratory exchange ratio RER; device: „K4B2", cosmed, Italy) and the impedance cardiography (measured parameters: stroke volume (SV), ejektion fraction (EF), cardiac output; device: „physioflow", Manatec Biomedical, France) were recorded continuously during the whole test. $avDO_2$ was calculated with the formula $avDO_2 = VO_{2max}$ / cardiac $output_{max}$.

The determination of the tHb-mass was scheduled for the **examination day „blood volume determination"** [12].

Before beginning with the determination of the BV, an earlobe was stimulated with the ointment Finalgon® (Boehringer Ingelheim Pharma GmbH & Co. KG, Germany) for better blood circulation. After a short application time, Finalgon® was removed and at least two blood samples were taken from the earlobe of each subject using glass capillaries coated with Heparin that were analysed in an Oxymeter (OSM80, Radiometer

GmbH, Denmark). Wrong values caused by the withdrawal or the device were avoided by continuing the trial only when two consecutive values showed a difference of max. 0.1 %. After connecting the subject with the mouthpiece (filter for bacteria and viruses) to the breathing system, the participants were asked to exhale completely into the spirometer and to hold the breath for a short time. During the time of holding the breath, the individual carbon monoxide dose (CO) of 1 ml CO per kg body mass was initiated using a glass syringe (Fortuna, Poulten & Graf GmbH, Germany). To support the CO diffusion (cf. Schmidt et al. 2005) the subjects were asked to hold the breath for 10 seconds after inhaling. Then the subjects breathed for 15 minutes in a closed breathing system (Wenoll-System, EMS GmbH, Germany). O_2 was continuously substituted into the breathing system and CO_2 got bound by an absorber. The O_2- and CO-concentration in the system was determined every minute by a CO-O_2 sensor (Prototyp, ACEOS GmbH; CO-220 Fluke GmbH, Germany).

At the end of the rebreathing phase, the subjects were asked to exhale completely into the breathing system. A flowmeter (Easy-on-PC, ndd AG) determined the exact expiration volume (V_{exp}). The whole volume of the system was calculated by the summation of the individual residual volume (RV) of the study participants (determined from reference values for lung volumes in Stocks et al. 1995 [13]), the measured V_{exp} and the rest volume of the breathing system (tube volume + absorber volume). The amount of CO that was not absorbed ($CO_{Rest;}$) could be calculated by checking the CO-concentration in the total volume (Wenoll-System, rebreathing bag).

The tHb-mass was calculated afterwards [11, 12], whereby the steady-state-concentration minus the COHb-concentration at rest determine the ΔCOHb [12].

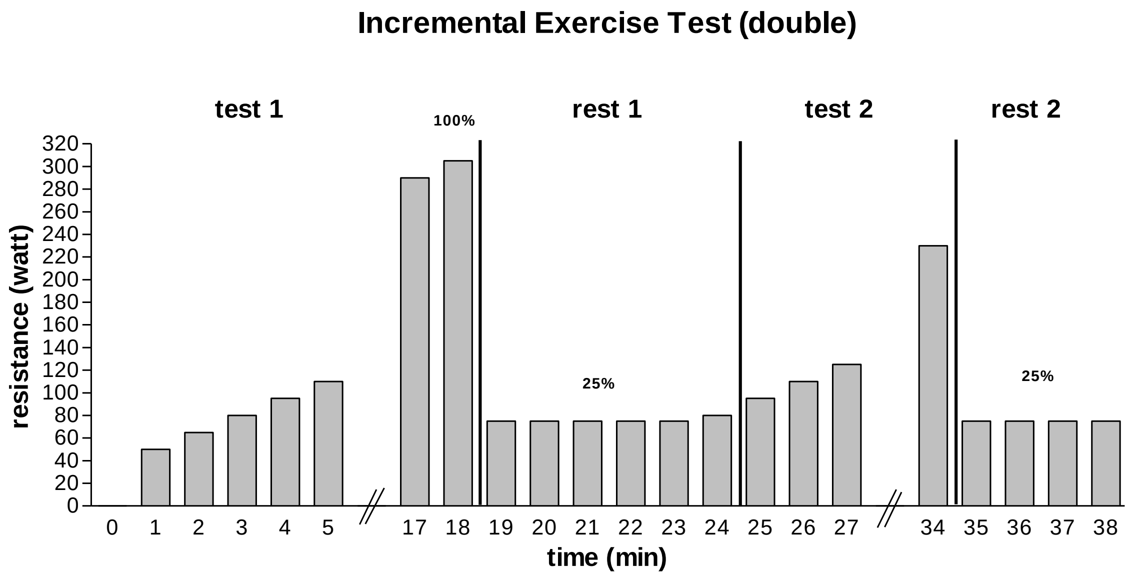

Figure 1: Test Procedure

Statistics:

Mean value and standard deviation were used for descriptive statistics. Tables and graphics were created with Excel 2010 (Microsoft Corp., USA) and the statistical evaluation was made with SPSS Statistics 20 (IBM Corp., USA). The control of the normal distribution with the Kolmogorov-Smirnov-test revealed that only the parameters P_{max}, EF, SaO_2 and the cigarette- and alcohol consumption were distributed normally. This is the reason why the correlations for the individual consideration of the parameters were calculated according to Spearmen [cf. 14] and evaluated according to its correlations.

A significance level of $\alpha < 0.05$ was determined for controlling the significance.

A multiple linear regression („backward elimination") was performed to develop a probable forecast model of connections with the VO_{2max} using the various measured parameters.

Results

Table 2 shows the absolute results of the stress test. The reached P_{max} amounted to 308 ± 25 watt on average. This corresponds to a relative performance of 4.1 watt per kg BM in the study group. The VO_{2max} amounted to 4152 ml/min on average, corresponding to a relative VO_{2max} of 54 ml/min/kg. The cardiac output amounted to 23.3 l/min on average during maximum exertion.

Table 2 overall exercise results

	Rest	Max
P (watts)*	0 ± 0	308.5 ± 25
HR (bpm)*	68.8 ± 11.7	187.6 ± 8.9
RRsys (mmHg)*	123 ± 15	219 ± 28
RRdia (mmHg)*	79 ± 11	74 ± 16
Lac (mmol/l)*	1.0 ± 0.3	9.7 ± 2.4
VE (l/min)*	12.6 ± 4.4	139.5 ± 18.2
VO2 (ml/min) *	427 ± 103	4152 ± 346
SV (ml) *	91 ± 12	125 ± 17
Cardiac output (l/min) *	7.0 ± 1.4	23.3 ± 3.3
CI (l/m²) *	3.6 ± 0.7	11.9 ± 1.7
$avDO_{2max}$ (ml/dl) *	6.3 ± 1.3	18.1 ± 2.7

* Mean value and standard deviation in the study group

Table 3 shows that the determined tHb-mass in the study group amounted to 1100 ± 140 g. The blood volume determination showed a result of 7107 ± 1000 ml. Strong interindividual differences in the tHb-mass and BV became clear.

Table 3 overall hematological results

	Absolute	Relative to body mass
cHb (mmol/l)*	10.2 ± 0.7	-
tHb-mass*	1100 ± 140	14.4 ± 1.5 g/kg
BV*	7107 ± 1000	93 ± 10 ml/kg

* Mean value and standard deviation in the study group

Multiple linear regression

A multiple linear regression (backward elimination) of the absolute maximum values, with VO_{2max} as dependent variable and the parameters EF_{max}, tHb-mass, BV, tHb, Lac_{max}, VE_{max}, $SaO2_{max}$, $avDO2_{max}$, HF_{max}, and SV_{max} as independent variables, was carried out. After excluding the parameters EF_{max}, tHb-mass, BV, Lac_{max}, VE_{max} SaO_{2max} and tHb, model 8 showed a significance of p = .000 for the parameters $avDO2_{max}$, HF_{max} and SV_{max} with an adjusted r^2 = .888 and a „standard error" = 122.

In a second multiple regression, also with backward elimination, all weight dependent parameters of the initial regression analysis (tHb-mass, BV, SV_{max}) were relativized by the body weight. The VO_{2max}/BM was included as dependent variable. After the exclusion of Lac_{max}, tHb, EF_{max}, VE_{max}, BV/BM, tHb-mass/BM and SaO_{2max}, model 8 showed a significance of p = .000 for the parameters $avDO2_{max}$, HR_{max} and SV_{max}/BM with an adjusted r^2=.948 and a „standard error" = 1.486.

Individual correlations of VO_{2max} with the absolute maximum measurement values

Table 4 below shows the correlation analyses of the individual, absolutely determined parameters and the VO_{2max}. A high correlation existed between the reached maximum performance and the VO_{2max}. Small but not significant connections with the VO_{2max} existed only in the cardiac output and the maximum tHb. All further parameters showed no statistically relevant correlations with the VO_{2max}.

Table 4: correlation between VO_2max and cardiac and hematological parameters

r (spearman)	VO_{2max} (ml/min)	p
P_{max} (W)	.722	.000
Cardiac $output_{max}$ (l/min)	.322	.083 (ns)
SV_{max} (ml/)	.286	.126 (ns)
HF_{max} (/min)	.207	.271 (ns)
$avDO_{2max}$ (ml/100 ml)	.198	.298 (ns)
BV (ml)	.160	.398 (ns)
tHbmass (g)	.346	.061 (ns)
cHb (mmol/l)	.140	.460 (ns)

Individual correlations of VO_{2max}/BM with the maximum measurement values relativized by the body weight

The correlation analyses of the individual parameters and VO_{2max}/BM are shown in table 5. Between the reached maximum performance per kg bodyweight and the VO_{2max} per kg bodyweight a very high connection existed. Mean and significant correlations with VO_{2max}/BM clearly existed in the maximum cardiac output per kg BM, the maximum SV/BM and the tHb-mass/BM. BV, relativized with BM, showed no statistically relevant connection with VO_{2max}/BM.

Table 5: correlation between VO_2max/BM and relative cardiac and hematological parameters

r (spearman)	VO_{2max}/BM (ml/kg/min)	p
P_{max}/BM (W/kg)	.894	.000
Cardiac $output_{max}$/BM (l/min/kg)	.484	.007
SV_{max}/BM (ml/kg)	.373	.042
BV/BM (ml/kg)	.162	.393 (ns)
tHbmass/BM (g/kg)	.386	.035

Figure 2 and 3 show the correlations of P_{max} and VO_{2max} (absolute Fig. 2, relative Fig. 3). A stronger correlation between VO_{2max} and P_{max} existed by relativizing them to the body mass.

Figure 4 and 5 show the correlation between the cardiac $output_{max}$ and the VO_{2max} (absolute Fig. 4, relative Fig. 5). In referring it to the body weight, a stronger connection became clear.

Figure 6 and 7 show a correlation between tHb-mass and VO_{2max} (absolute Fig. 6, relative Fig. 7). Concerning the strength of the correlation, no differences existed between the absolute and relative measurement values.

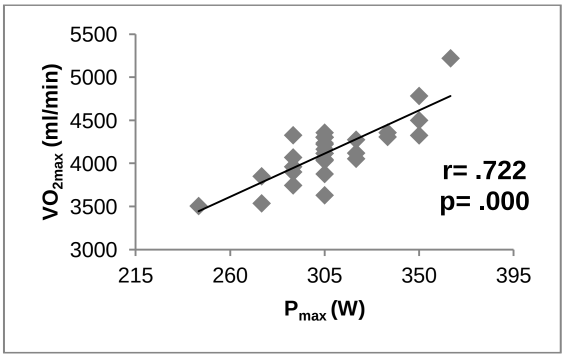

Fig. 2: correlation between VO_{2max} and P_{max}

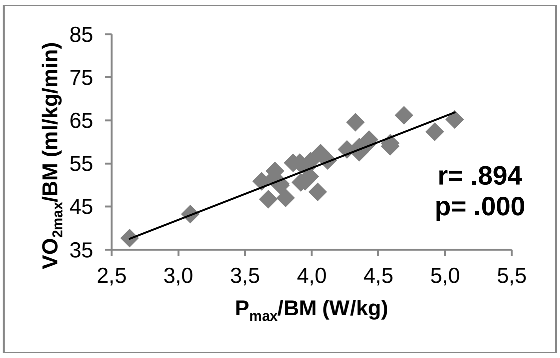

Fig. 3: correlation between VO_{2max}/BM and P_{max}/BM

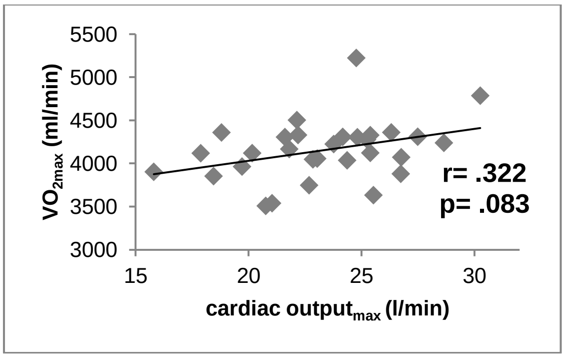

Fig. 4: correlation between VO_{2max} and cardiac $output_{max}$

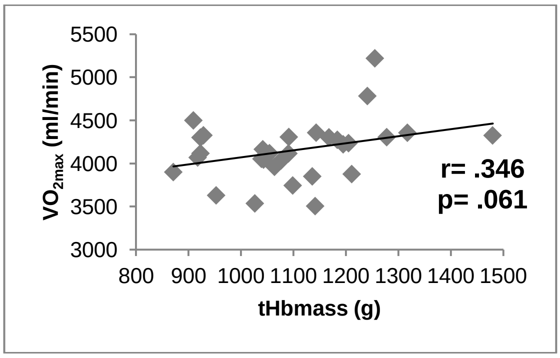

Fig. 6: correlation between VO_{2max} and tHb-mass

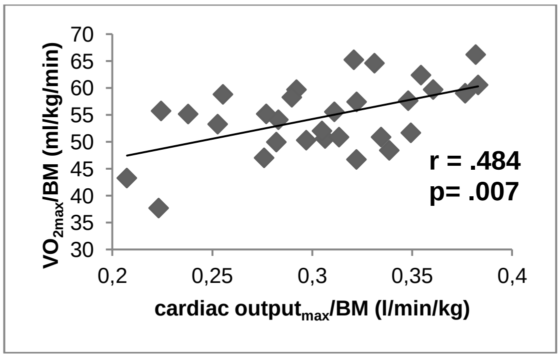

Fig. 5: correlation between VO_{2max}/BM and cardiac $output_{max}$/BM

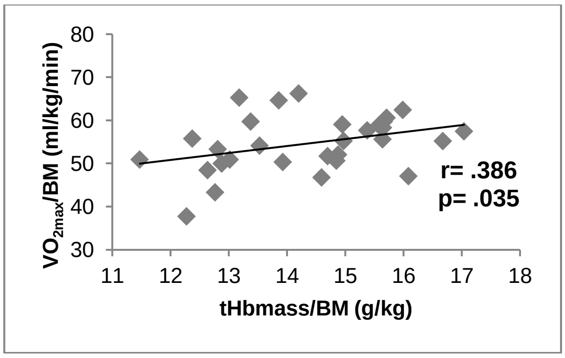

Fig. 7: correlation between VO_{2max}/BM and tHb-mass/BM

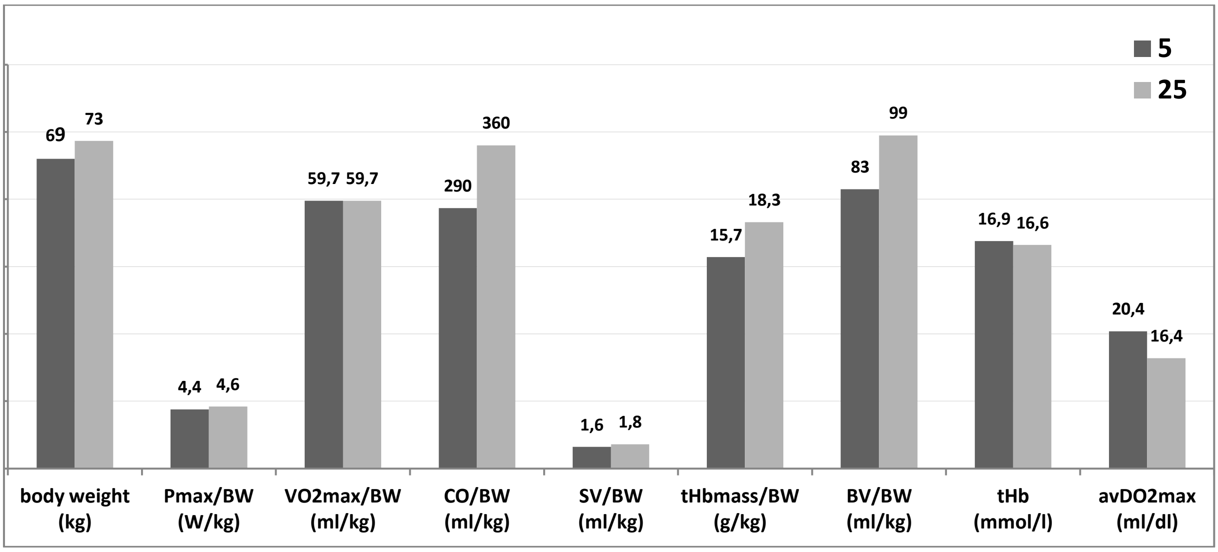

Fig. 8: individual comparison of subject 5 and 25

Figure 8 compares the measurement parameters of two subjects. The relative VO_{2max} was the same (each 59.7 ml/min/kg) but the cardiac $output_{max}$/BM of subject 5 amounted to 290 ml/kg while subject 25 presented a value of 360 ml/kg. The tHb-mass of subject 5 amounted to 15.7 g/kg BM and in subject 25 to 18.3 g/kg BM. Subject 5 reached an $avDO_2$ of 20.4 ml/dl and subject 25 one of 16.4 ml/dl.

Discussion

Overall, the study group of the present paper was utterly homogenous and presented a performance above-average. Having a bodyweight of 77 (±8.5) kg on average, the subjects reached a performance of 4.1 (±0.5) W/kg. With about 37 %, this lies over the nominal output of 3 W/kg for people under 30 years [15].
The single correlation analyses of VO_{2max} as dependent variable and the cardiac and hematological measurement values as independent variables partially showed no or only little to mean connections. All parameters showed stronger and partially significant correlations with VO_{2max} after being relativized to the bodyweight (cf. table 4 and 5; fig. 2-7).
The correlation model calculated with the multiple linear regression analysis shows an extremely strong totalized influence of the single measurement parameters on the VO_{2max}. As was expected according to the principle of Fick, the forecast model with the parameters SV_{max}, HF_{max} and $avDO_{2max}$ shows the strongest directed correlation with VO_{2max}.

Influence of cardiac parameters on VO_{2max}

Between the cardiac $output_{max}$, HF_{max} and SV_{max} only moderate, not significant correlations existed with the VO_{2max}. Relativizing the weight-dependent parameters ($VO2_{max}$, SV_{max}, cardiac $output_{max}$) to the bodyweight, mean significant correlations emerged. This does not correspond to the results of Astrand et al. (2003) [8]. The collective examined by Astrand et al. has been a far more heterogeneous collective. The sample of this trial was composed of an absolutely strong homogeneity concerning the training condition, age, gender and body mass what could have a negative influence on the significance level of the correlations because scatterings are more important due to the lower variety of the measurement values.
The fact that there are no or only little correlations between the cardiac $output_{max}$, HF_{max} as wells as SV_{max} and VO_{2max}, however, does not mean that these parameters are not important in persons of this training condition and also does not stand in contradiction with the current knowledge of many authors [cf. 2, 3, 4, 5, 7]. The multiple linear regression with backward elimination, including all parameters of the blood volume determination and the stress parameters during 100% of the relative performance, confirms this. The calculation showed a significance level of p = .000 for the parameters HF_{max}, SV_{max} and $avDO_{2max}$. The variance explanation amounted to $r^2 = .888$.
According to this, the mentioned parameters HR_{max}, SV_{max} and $avDO_{2max}$ are extremely important for VO_{2max} and therefore for the performance of the group.
The low correlation of the single parameters only means that the subjects with the highest SV, for example, does not need to have the highest VO_{2max}, too, and the subject with the smallest SV does not need to have the smallest VO_{2max}. The summation of the single effects of the cardiac parameters shows their importance for VO_{2max}.

Influence of hematological parameters on VO_{2max}

Between VO_{2max} and BV (absolute and relative) no correlation could be recognized. Even the tHb-mass only shows a mean correlation with the relative VO_{2max} after relating it to the body weight.
Against the here determined results, experimental studies in which the blood volume was reduced and enlarged unphysiological, [16, 17] showed a high correlation between the corpuscular BV and the VO_{2max}. Gledhill (1982) [21] has concluded by a meta-analysis that significant increases of the VO_{2max} could only be reached by a strong (unphysiological) increase of the hemoglobin mass.
Also Gore, Hahn, Burge and Telford (1997) [18] as well as Böning, Cristancho, Serrato, Reyes, Mora, Coy and Rojas (2004) [19] have found a connection between the VO_{2max} and the tHb-mass. Schmidt (1999) [20] also has determined a connection between the VO_{2max} and the BV.
Ahlgrim (2010) [22] has conducted examinations on a collective of 36 trained sportsmen that have showed, as well as our trial, that there is no important connection between the blood parameters and the VO_{2max}.
Ahlgrim has constituted the low connections between VO_{2max} and tHb-mass by the high correlations of the tHb-mass and their body composition [22]. Accordingly, subjects with higher LBM have statistically high absolute blood volumes and/or a high tHb-mass. This does not require a high aerobe performance capacity concerning the body weight. In an anthropometric homogeneous study collective as in this one, the correlation between tHb-mass and performance capacity may consecutively turn out as low. The importance of the tHb-mass for aerobe performance capacity is especially due to its ability of describing BV and cHb and therefore, on the one hand, influences the cardiac output hemodynamic and on the other hand determines the O_2 transport capacity per blood volume.

Comparison of the individual subjects

The interindividual comparisons clearly showed that some of the subjects, having the same maximum performance, generate the correlating oxygen uptake by peripheral or central factors that are developed differently. Deficits in central factors, which are expressed by a smaller cardiac output, are compensated and turned via the stronger extraction ($avDO_2$) of oxygen in the working muscle or a higher oxygen transport capacity (cHb, tHb-mass) in blood.

Conclusion

References mention high connections between the HZV_{max}, the SV_{max}, the BV as well as the tHb-mass and the VO_{2max}, however, these cannot be illustrated in a homogenous study group. In summation of the single influences, the dependence of VO_{2max} on the cardiac parameters was superficially proved.

The creation of reference values for hemodynamic and hematological parameters in competitive sportsmen and young competitive sportsmen could essentially improve the identification and classification of performance reserves of endurance athletes.

The specifically applied development of either central performance requirements such as the improvement of the cardiac output or the superficial increase of peripheral O_2-exhaustion should increase the individual maximum endurance performance in the high performance area. A complex performance diagnostic should include spirometry and the determination of lactate but also the determination of the hemodynamic cardiac output and the measurement of total hemoglobin.

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