Hematocrit and hematocrit viscosity ratio during exercise in athletes: Even closer to predicted optimal values?

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Abstract. The hemorheological theory of optimal hematocrit suggests that the best value of hematocrit (hct) should be that which results in the highest value of the hematocrit/viscosity (h/η) ratio. Trained athletes compared to sedentary subjects have a lower hct, but a higher h/η, and endurance training reduces the discrepancy between the actual hct and the «ideal» hct that can be predicted with a theoretical curve of h/η *vs* hct constructed with Quemada's model. In this study we investigated what becomes this homeostasis of h/η and hct during acute exercise in 19 athletes performing a 25 min exercise test. VO_{2max} is negatively correlated to resting hct and positively correlated to discrepancy between actual and ideal resting hct which is correlated to the maximal rise in hct during exercise. Predicted and actual values of the h/η were fairly correlated ($r = 0.970$ $p < 0.001$) but the actual value was lower at rest and this discrepancy vanished at 25 min exercise. Exercise-induced decrease in discrepancy between actual and theoretical h/η was negatively correlated with the score of overtraining. All these findings suggest that h/η is a regulated parameter and that its model-predicted «optimal» values yield a «theoretical optimal» hct which is close to the actual value and even closer when athletes are well trained. In addition, acute exercise sets h/η closer from its predicted ideal value and this adaptation is impaired when athletes quote elevated scores on the overtraining questionnaire.

Keywords: Blood viscosity, hematocrit, exercise, erythrocyte deformability, hematocrit/viscosity ratio

List of symbols

hct	hematocrit
RBC	red blood cell
SEM	standard error on the mean

1. Introduction

Hematocrit is most often acutely increased by exercise and lowered by exercise training, so that it has been repeatedly reported to be negatively correlated to aerobic working capacity [4].

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However, the issue of hct in exercise physiology is much more complex since a moderate increase in hct in physiological conditions induces vasodilation and thus improves blood flow [20], while a small decrease (approximately –10%) of hct induced by isovolumic hemodilution with homologous plasma in hamsters leads to an increase in blood pressure [21]. In addition there are training protocols that do not decrease hct and rather increase it [16].

The idea that there is an optimal hct is an old one [26] but it has recently gained an impressive support with studies on transgenic mice [25] showing that exercise performance describes a bell-shaped curve as a function of hct. Interestingly, this bell-shaped curve has been hypothesized on a theoretical basis since more than 30 years by hemorheologists [6, 27] and is explained by the biphasic effect of hct on h/η. Below optimal hct, any increase in hct increases h/η and thus (theoretically) O_2 supply to tissues, but above this optimal value, any further increase has the opposite effect and decreases h/η and O_2 supply.

It has become clear over the last years that h/η is not only a theoretical concept but a clinically relevant parameter that can predict vascular events [28] and is associated to tissue ischemia [29].

Therefore it is interesting to try to predict the optimal hct with hemorheological models that take into account this concept of h/η, and to compare its value to the actual one in various physiological and pathological conditions. An attractive procedure for this is to use the very classical Quemada's equation to reconstruct from actual viscosity factors the curve of h/η and to detect the hct corresponding to the top of this curve.

In a previous study we reported that endurance training tends to reduce the discrepancy between the actual hct and the «ideal» hct that can be predicted with a theoretical curve of h/η *vs* hct constructed with Quemada's model using actual viscosity parameters. We hypothesized that training involved «viscoregulatory» mechanisms that actually aim at maintaining an optimal h/η and that optimal hct is only a reflect of this homeostasis of h/η.

A raise in hct is the most classical hemorheological effect of exercise. It is due to fluid shifts and splenocontraction. To what extent this rise in hct during exercise modifies the homeostasis of h/η is not known. It can be hypothesized that resting hct in athletes is set at a level which allows to cope with exercise-induced increase in hct, but there is until now no clear evidence of this.

Therefore, in this study we investigated in another sample of athletes with various levels of aerobic capacity whether this discrepancy between the predicted "optimal" values of h/η and hct and the actual ones were related to fitness and what they became when hct increases during exercise.

2. Subjects and methods

2.1. Study subjects

We studied 19 male recreational and professional athletes (soccer, volleyball; age: 17–33 years; %fat: 6–12%; VO_{2max}: 41–61 ml/min/kg). Characteristics of subjects are given on Table 1. VO_{2max} ranged between 77% and 180% of the predicted theoretical value, so that this sample displays a wide rage of aerobic capacities.

Exercise test was done according to the protocol of Raynaud et al. [18] which is standardized for the exploration of metabolic and hormonal adaptation to exercise. This test consists of a progressive increase over 10 min in order to reach 85% of the maximal theoretical heart rate which is maintained over 15 min. In this test heart rate was monitored but not oxygen consumption. Blood samples are drawn at 10 and 25 min of exercise.

VO_{2max} was evaluated during this test according to Astrand's nomogram [1, 2], assuming the relationship between oxygen consumption (VO_2) in l/min and power output (P) in watts established by

Table 1
Clinical characteristics of the study subjects (mean + SEM)

Age (years)	21.74 ± 1.08
Weight (kg)	77.96 ± 1.72
Height (cm)	184.34 ± 2.29
Body mass index (kg/m^2)	22.96 ± 0.39
Fat mass (% total weight)	8.94 ± 0.39
Overtraining score SFMES	10.64 ± 1.61
VO_2max (ml/min/kg)	48.54 ± 2.72

Astrand and Ryhming $VO_2 = 0.1+0.938xP$ with a correction for age $f = 1.21–(9.1 \times 10^{-3}$ x age). This classical approach developed in physically fit college students has a reported accuracy of approximately 10%, which has been recently confirmed by Cink & Thomas [7]. It has been recently found to be valid for recreationally active males and females [5]. Note that in untrained sedentary subjects [19] it has been shown to yiel a 26.5% systematic underestimation of VO_{2max}.

The specific questionnaire for detection of overtraining in athletes, developed in France by the French Society of Exercise and Sports Medicine (SFMES), was also employed [3, 12, 15]. This score which is also validated on a modified form in children [30] indicates the heaviness of training and when its score is >20 it indicates that an individual is at least on the edge of overtraining [14].

2.2. Bioelectrical impedance measurements

Prior to the exercise-test, subjects' body composition was assessed with bioimpedance analysis with a six terminal impedance plethismograph BIACORPUS RX 4000, (SoAGIL DEVELOPPEMENT, 8 avenue Jean-Jaurès 92130 Issy-les-Moulineaux, France) with data analysis with the software Body-Comp 8.4. This device measures total resistance of the body to an alternative electric current of 50 kHz [9]. Body fat mass, fat-free mass were calculated in each segment of the body according to manufacturer's database-derived disclosed equations, and total water with published equations using the classical cylindric model and Hanai's mixture theory [10].

2.3. Hemorheological in vitro measurements

Blood samples for hemorheological measurements (7 ml) were drawn with potassium EDTA as the anticoagulant in a vacuum tube (Vacutainer). Viscometric measurements were done at very high shear rate (1000 s^{-1}) with a falling ball viscometer (MT 90 Medicatest, F-86280 Saint Benoit). The coefficient of variation of this method ranges between 0.6 and 0.8%. We measured with this device apparent viscosity of whole blood at native hct, plasma viscosity, and blood viscosity at corrected hct (45%) according to the equation of Quemada [17].

$$\eta = \eta_p(1 - 1/2\, k\, \phi)^{-2} \tag{1}$$

– where ϕ is hematocrit, η_p is plasma viscosity, and $k(\gamma)$ is a shear-dependent parameter quantifying the contribution of erythrocyte rheological properties to whole blood viscosity.
– At the high shear rate used here $k(\gamma)$ is representative of red cell rigidity (*i.e.*, the lower $k(\gamma)$), the higher is erythrocyte deformability).

With this equation it is possible to standardize η for hct 45% after calculating k:

$$k = 2 \cdot (1 - \eta\, r^{-0.5}) \cdot \phi^{-1} \tag{2}$$

This value of k is reintroduced in equation (1) with ϕ set at 0.45. Dintenfass's 'Tk' index [6] was also calculated as an index of red cell rigidity.

RBC aggregation was assessed with the Myrenne aggregometer [23] which gives two indices of RBC aggregation: "M" (aggregation during stasis after shearing at 600 s^{-1}) and "M1" (facilitated aggregation at low shear rate after shearing at 600 s^{-1}). Hematocrit was measured with microcentrifuge.

2.4. *Prediction of the theoretical optimal hematocrit and hematocrit viscosity ratio*

The curve of theoretical optimal h/η plotted *vs* hct was reconstructed with Quemada's equation presented above. The equation of h/η as a function of h was thus:

$$h/\eta = h/[\eta_p\,(1 - 1/2\ k\ \phi)^{-2}] \tag{3}$$

The hct corresponding to the top of this curve was considered as the "theoretical optimal hematocrit". The highest value of h/η (the top of the curve) was considered as the optimal h/η.

2.5. *Statistics*

Values are presented as mean $\pm$ standard error of the mean (SEM). Normality of samples was checked with the Kolmogorov-Smirnov test. After verification of normality, we used ANOVA followed by *post-hoc* Student's *t* test for paired samples. Correlations were assessed with Pearson's procedure (least square fitting). A value of $p < 0.05$ was considered as significant.

3. Results

The graded 25 min exercise test was performed with drawings at 0, 10 and 25 min, i.e. at 10%, 48% and 76% VO_{2max}. Table 2 shows the main hemorheologic changes during this exercise test.

It can be seen that whole blood viscosity at both native ($p < 0.01$) and corrected hct ($p < 0.05$) increases during exercise, due to a rise in hct ($p < 0.02$) and plasma viscosity ($p < 0.02$) while RBC rigidity is not significantly changed in this study.

Table 2

Hemorheologic changes during exercise. It can be seen that whole blood viscosity at both native and actual hematocrit increase during exercise, due to a rise in hematocrit, plasma viscosity. In this sample changes in RBC rigidity index are not significant

	Rest	Time 10 min	Time 25 min	Overall comparison (ANOVA) exercise effect
Actual hct (%)	44.63 ± 0.53	45.97 ± 0.61	46.05 ± 0.86	$p < 0.02$
Whole blood viscosity at hct corrected 45% (mPa.s)	3.37 ± 0.10	3.41 ± 0.10	3.69 ± 0.21	$p < 0.05$
Whole blood viscosity at actual hct (mPa.s)	3.36 ± 0.10	3.62 ± 0.10	3.65 ± 0.08	$p < 0.01$
Plasma viscosity (mPa.s)	1.40 ± 0.01	1.43 ± 0.01	1.47 ± 0.03	$p < 0.02$
'k' index (Quemada)	1.58 ± 0.05	1.63 ± 0.05	1.60 ± 0.04	NS
Theoretical maximal h/η	13.65 ± 0.43	12.95 ± 0.45	12.88 ± 0.32	$p < 0.05$
Actual h/η	13.48 ± 0.44	12.74 ± 0.46	12.86 ± 0.35	$p < 0.05$
Theoretical optimal hct (%)	42.89 ± 1.48	41.33 ± 1.55	42.58 ± 1.08	NS

*$p < 0.05$ *vs* baseline.

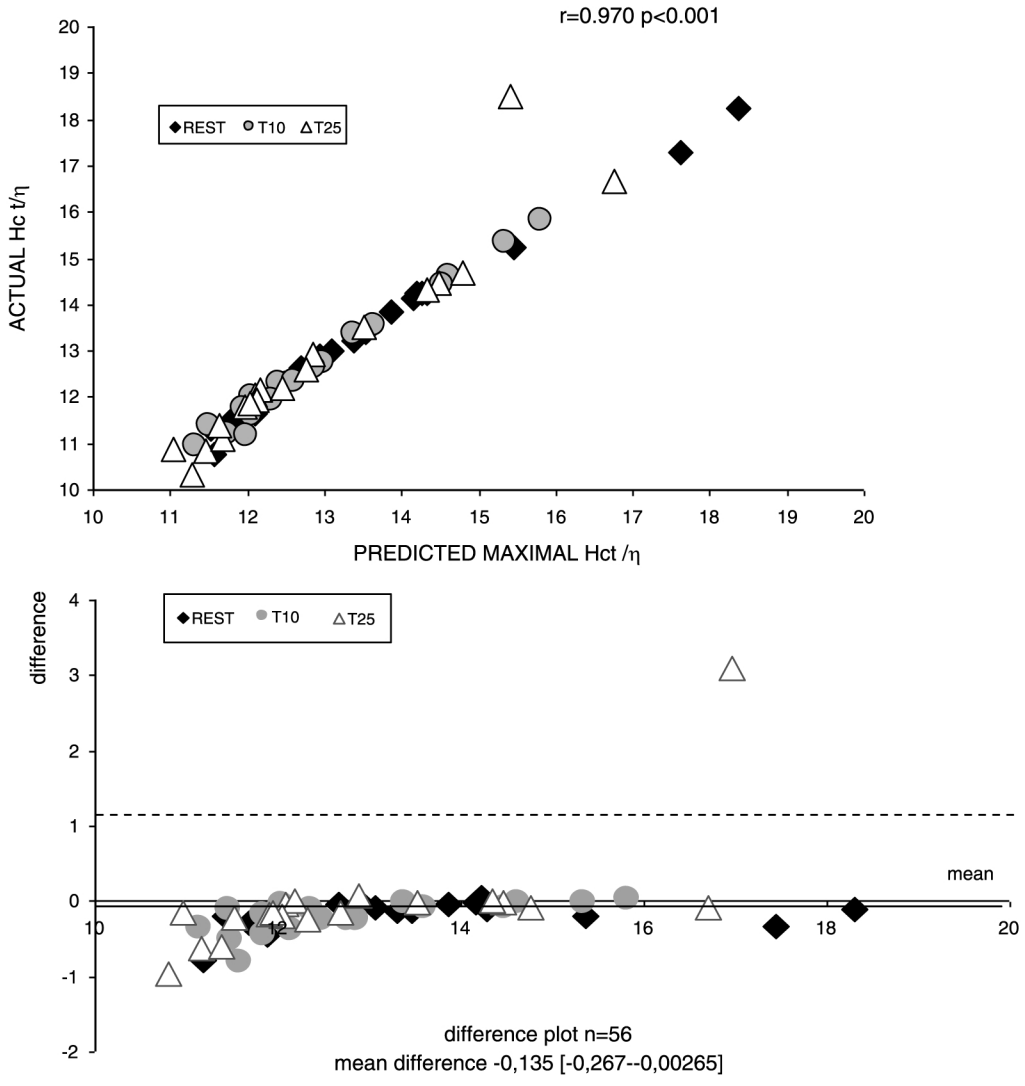

Fig. 1. Upper pannel: Correlation between the h/η ratio predicted with the model and the actual h/η. Lower pannel: Bland-Altman plot showing the agreement between the h/η ratio predicted with the model and the actual h/η. On the whole the agreement between theoretical and optimal is very strong. However one point at T25 has a h/η markedly higher than predicted.

Figure 1 shows that here is a fair agreement between theoretical and optimal values of h/η. Predicted and actual values of the h/η were fairly correlated ($r = 0.970, p < 0.001$) but the actual value was slightly lower at rest (1.26, $p < 0.01$) and at 10 min exercise (–1.68, $p < 0.001$) and this discrepancy vanished at 25 min exercise.

However, as seen on Fig. 2, agreement is less close between optimal hct predicted with the model and the actual hct.

It can be seen that on the average actual hct is slightly higher than the predicted optimal hct. Figure 3 shows reconstructed curves of the theoretical optimal h/η plotted *vs* actual hct in the subjects at rest and at exercise, showing that the theoretical optimal h/η tends to be higher at rest than during exercise ($p < 0.01$). On Fig. 4 it can be seen that exercise decreases the discrepancy between theoretical and actual h/η ratio but increases the discrepancy between theoretical and actual hct.

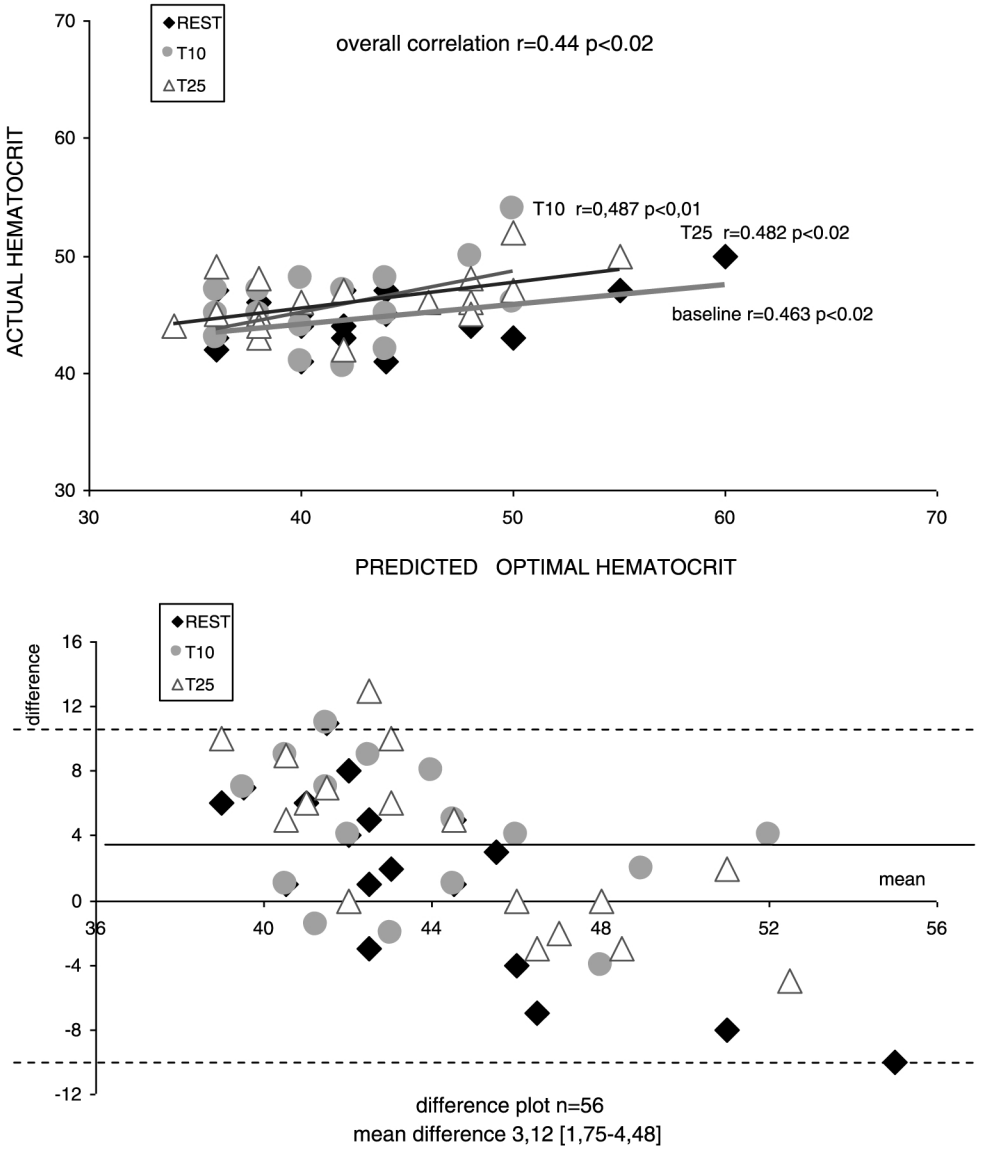

Fig. 2. Upper pannel: Correlation between optimal hematocrit predicted with the model and the actual hematocrit. Lower pannel: Bland-Altman plot showing the agreement between optimal hematocrit predicted with the model and the actual hematocrit. On the average actual hematocrit is slightly higher than the predicted optimal hematocrit.

Correlations among the various viscosity factors and VO_{2max} were looked for, and the only one which appeared significant in this sample was the correlation with hct (see Fig. 5). VO_{2max} was negatively correlated with native but not optimal hct and was positively correlated with the discrepancy between them. This means that in the less fit subjects hct is higher than optimal and in the fitter ones this difference vanishes with some values of actual hct slightly lower than optimal.

Figure 6 shows the correlations between the discrepancy (theoretical *vs* actual hct during exercise) and the hct response to exercise. Both the maximal value during exercise and the maximal rise in hct during exercise are correlated to this discrepancy. This means that when actual hct is higher than optimal, it predicts also a greater increase in hct during exercise and a higher hct during exercise.

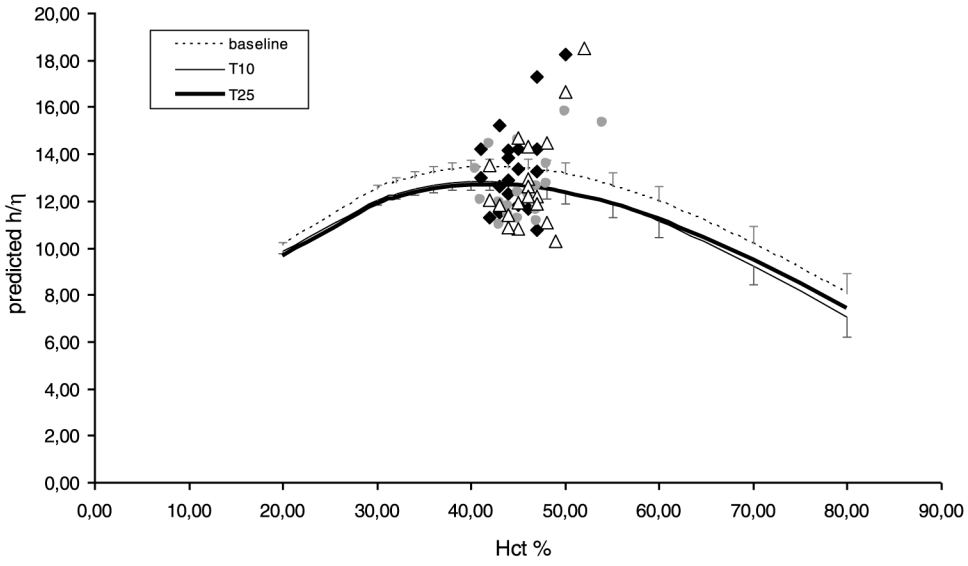

Fig. 3. Comparison between reconstructed curve of the theoretical optimal h/η plotted *vs* actual hematocrit in the subjects at rest and at exercise, showing that the theoretical optimal h/η is higher at rest and decreases during exercise ($p < 0.01$) due to the rise in plasma viscosity and/or red cell rigidity.

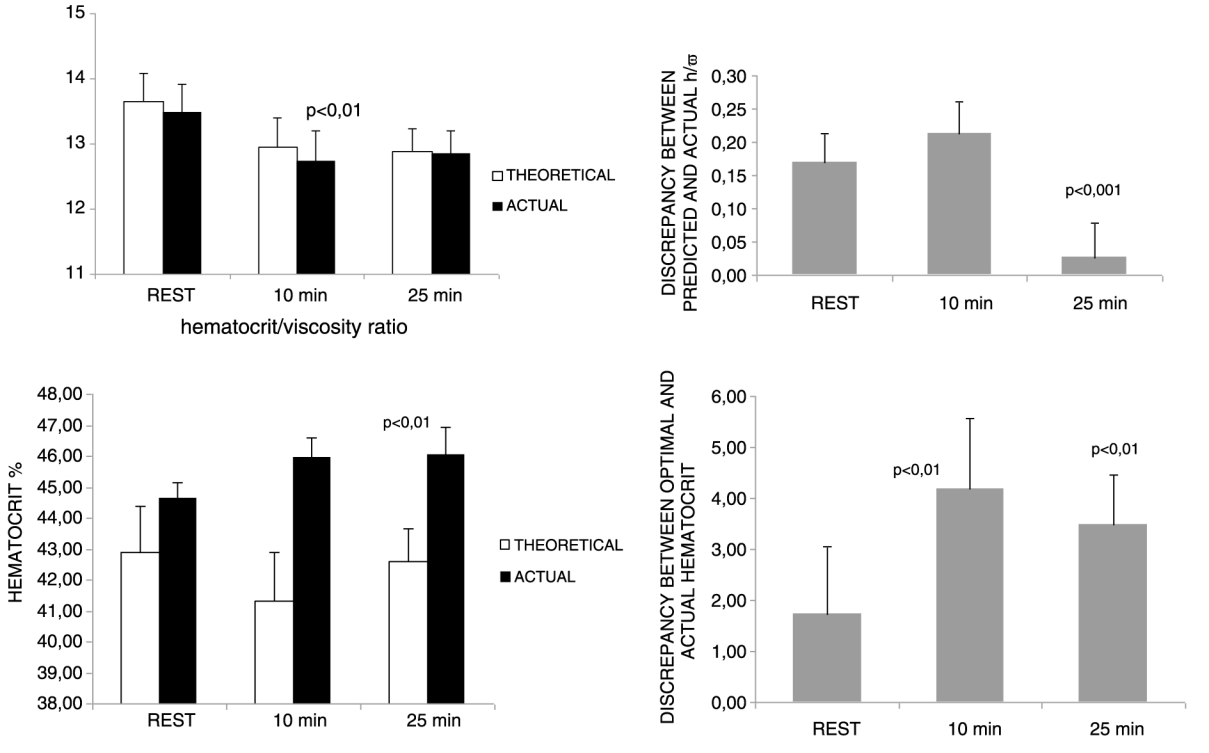

Fig. 4. Evolution of both theoretical values and actual values (left) and of the discrepancy between them (right) for hematocrit/viscosity ratio (upper pannel) and hematocrit. Exercise has initially (at T10) no effect on the discrepancy between theoretical and actual hematocrit/viscosity ratio but then decreases it, while it increases the discrepancy between theoretical and actual hematocrit.

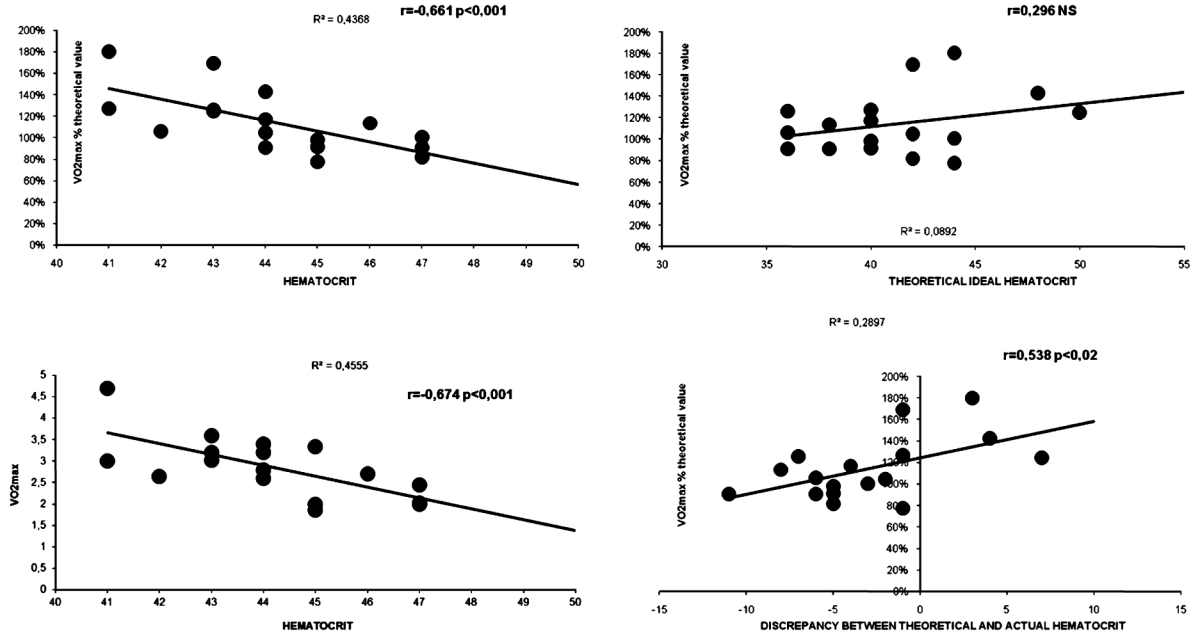

Fig. 5. Correlations between VO_{2max} and hematocrit, showing that aerobic capacity is negatively correlated to actual but not theoretical hematocrit and that the discrepancy between actual and optimal is correlated to aerobic capacity, *i.e.* in the less fit subjects hematocrit is higher than optimal and in the fitter ones this difference vanishes with some values of actual hematocrit slightly lower than optimal. Discrepancy is presented as optimal minus actual hematocrit, *i.e.* the more it is negative the more actual is higher than optimal.

There was also a negative correlation between changes in plasma viscosity and changes in RBC rigidity at exercise at T10 ($r = –0.566$, $p < 0.02$) and at T25 ($r = –0.495$, $p < 0.01$).

4. Discussion

This study shows that in a sample of athletes the prediction of h/η ratio and ideal hct with Quemada's equation yields values well correlated to the actual measured values. However hct exhibits discrepancies with the theoretical "optimal" values and these discrepancies are proportional to exercise-induced hct increase, and lower in the fitter athletes.

The old concept of ideal hct, and its hemorheological definition with the top of the curve of h/η ratio is now supported by a large body of experimental and clinical evidence [29].

Experimentally in transgenic mice the relationship between hct and VO_{2max} describes a bell-shaped curve parallel to that of h/η [25].

In preceding studies we showed that actual hct is always lower than the predicted value in either athletes or sedentary subjects, but that the discrepancy is around 13-14% (i.e. 6-7% in units of hct) in sedentary subjects and of 1–5% or less (i.e. 0.5–2% in units of hct) in athletes. Apparently the more the athletes are trained the lower the discrepancy. The same is true for the ratio h/η which is closely correlated to its theoretical optimal value (and slightly lower) in fit athletes while in sedentary individuals it is 2–6% higher. In this sample the same tendency is observed.

There is however a large overlap in values of hct and h/η among sedentary and trained subjects so that it is difficult on the basis of these measurements to define if an individual is trained or not [16]. By contrast various reports indicate that aerobic training (in contrast to resistance training) is associated with a hemorheological profile that promotes both oxygen transport and delivery [24], and

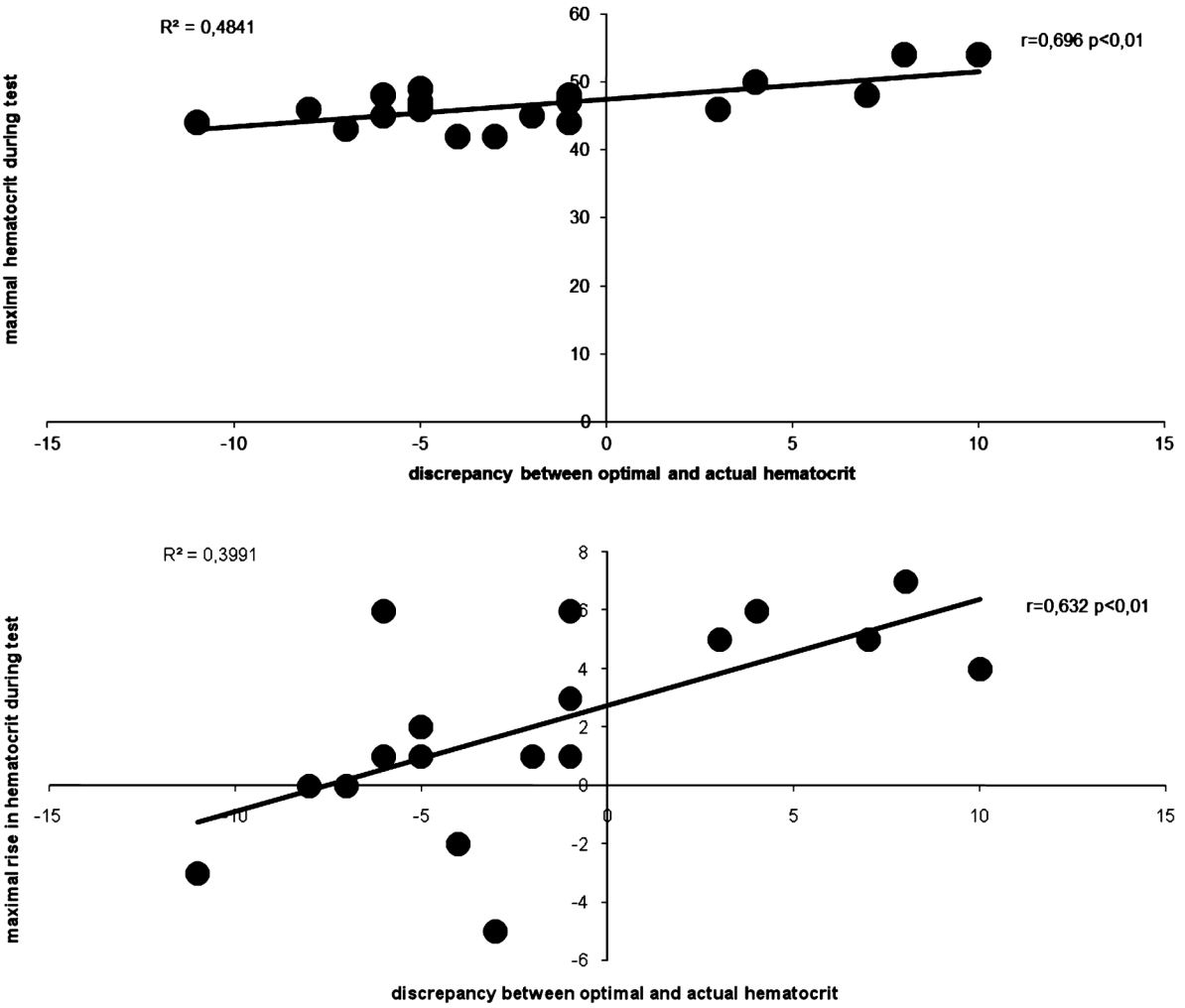

Fig. 6. Correlations between the discrepancy between theoretical and actual hematocrit during exercise and hematocrit maximal value during exercise (upper pannel) and the maximal rise in hematocrit during exercise (lower pannel). Discrepancy is presented as optimal minus actual hematocrit, *i.e.* the more it is negative the more actual is higher than optimal. This figure shows that when actual hematocrit is higher than optimal, it predicts also a greater increase in hematocrit during exercise and a higher hematocrit during exercise.

accordingly it is commonly observed that aerobic training increases h/η despite the decrease in hct it induces [8, 22].

It is clear that the regulation of hct is a complex issue. First of all, there are huge differences among hct values found in various territories of circulation [13] and hct undergoes in these various tissues drammatic modifications in situations such as exercise [11]. Presumably, during exercise, a rise in hct in muscular vessels is an important mechanism, and the parallel rise in systemic hct is less important for muscle performance. However, our findings support the concept that systemic hct, which is quite similar in veins and arteries, is set close to its "ideal" value. In fact, it is interesting to notice that the agreement between theoretical and actual values is almost 3-fold closer for h/η than hct, suggesting that h/η (or O_2 delivery that it is assumed to represent) is the regulated value rather than hct, and that this homeostasis seems to be more efficient in trained subjects.

On the whole, our study suggests that hct needs to increase during exercise in order to allow an increase in muscular microvascular hct, but regulatory mechanisms prevent systemic hct to increase

above its optimal value and to decrease blood flow. The discrepancy between optimal and actual hct represents this reserve allowing systemic hct to increase. In sedentary people this gap between optimal and actual hct allows the possibility to increase hct by 6-7% (in units of hct). In endurance athletes such as those studied here, physiological adaptations make this systemic hct response less necessary and thus the gap is lower (0.5–2% in units of hct) allowing systemic hct to be set even closer from the ideal value. This regulation of hct is underlied by a regulation of h/η explaining that h/η is set more closely to its ideal value as predicted by a hemorheologic model. Presumably, a regulatory loop involving erythropoietin and triggered by both PO_2 and viscosity plays a central role in this homeostasis.

Whether the picture is the same in other sports, for example resistance sports, remains to be studied.

5. Conclusions

Therefore, on the whole, we show in this study that endurance trained athletes have a value of hct and h/η closer to the optimal value predicted by a hemorheologic model based on Quemada's equation. This is likely to be due to the fact that the gap between theoretical and actual values represents a physiological reserve allowing systemic hct to increase during exercise without trespassing the ideal value, avoiding this hct response to impair oxygen delivery to tissues. In endurance-trained athletes this protective reserve seems to be less necessary. Other studies are needed in order to ascertain whether this is a general mechanism or an adaptation which is different among sports.

Acknowledgments

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References

[1] P.O. Astrand and I. Ryhming, A nomogram for calculation of aerobic capacity (physical fitness) from pulse rate during sub-maximal work, *Journal of Applied Physiology* **7**(2) (1954), 218–221.

[2] P.O. Astrand, K. Rodahl, H.A. Dahl and S.B. Strømme, Textbook of Work Physiology Physiological Bases of Exercise. Champaign, IL, U.S.: Human Kinetics, 2003, pp. 273.

[3] J.-F. Brun, C. Boegner and C. Fédou, Hyperthyroïdie chez un sportif: Aux frontières du surentraînement, *Science et Sports* **29**(2) (2014), 95–100.

[4] J.-F. Brun, E. Varlet-Marie, P. Connes and I. Aloulou, Hemorheological alterations related to training and overtraining, *Biorheology* **47**(2) (2010), 95–115.

[5] T. Chambers, M. Seymour and A. Grewing, Validating the Âstrand-rhyming submaximal protocol for VO2max prediction in recreationally active individuals, *International Journal of Exercise Science Conference Proceedings* **11**(2) (2014), Article 9.

[6] S. Chien, Present state of blood rheology. In: K. Messmer and H. Schmid-Schonbein (Eds) Hemodilution. Theoretical Basis and Clinical Application, Karger, Basel, 1972, pp. 1–45.

[7] R.E. Cink and T.R. Thomas, Validity of the Astrand-Ryhming nomogram for predicting maximal oxygen intake, *Britisch Journal of Sports Medicine* **15** (1981), 182–185.

[8] M. Diaw, S. Diop, F.Y.W. Soubaiga, M. Seck, B.F. Faye, M.N. Niang, A. Samb and P. Connes, Blood viscosity is lower in trained than in sedentary sickle cell trait carriers, *Clinical Hemorheology and Microcirculation* **61**(1) (2015), 23–29.

[9] M. Guiraudou, L. Maimoun, J.-M. Dumas, M. Julia, I. Raingeard and J.-F. Brun, Composition corporelle mesurée par impédancemétrie segmentaire (BIAS) et performance de sprint chez les rugbymen/Body composition measured by bioimpedance segmental (BIAS) analysis and sprint performance in rugby players, *Science & Sports* **30 [N°5]** (2015), 298–302.

[10] M.Y. Jaffrin and H. Morel, Body fluid volumes measurements by impedance: A review of bioimpedance spectroscopy (BIS) and bioimpedance analysis (BIA) methods, *Medical Engineering & Physics* **30**(10) (2008), 1257–1269.
[11] C.A. Kindig, T.E. Richardson and D.C. Poole, Skeletal muscle capillary hemodynamics from rest to contractions: Implications for oxygen transfer, *Journal of Applied Physiology* **92**(6) (2002), 2513–2520.
[12] P. Legros et le groupe "surentraînement", Le surentraînement: Diagnostic des manifestations psychocomportementales précoces, *Science & Sports* **8** (1993), 71–74.
[13] H.H. Lipowsky and S. Kovalcheck, The distribution of blood rheological parameters in the microvasculature of cat mesentery, *Circulation Research* **43**(5) (1978), 738–749.
[14] F. Maso, G. Lac and J.-F. Brun, Analysis and interpretation of SFMS questionnaire for the detection of early signs of overtraining: A multicentric study, *Science et Sports* **20** (2005), 12–20.
[15] F. Maso, G. Lac, E. Filaire, O. Michaux and A. Robert, Salivary testosterone and cortisol in rugby players: Correlation with psychological overtraining items, *British Journal of Sports Medicine* **38** (2004), 260–263.
[16] A. Pichon, P. Connes and P. Robach, Effects of acute and chronic hematocrit modulations on blood viscosity in endurance athletes, *Clinical Hemorheology and Microcirculation*.
[17] D. Quemada, Rheology of concentrated disperse systems. II. A model of non newtonian shear viscosity in steady flows, *Rheologyca Acta* **17** (1978), 632–642.
[18] E. Raynaud, J.-F. Monnier, J.-F. Brun, M. Solère and A. Orsetti, Biochimie et hormonologie de l'exercice submaximal; standardisation d'un test d'effort chez le sportif, *Science & Sports* **12** (1997), 72–74.
[19] L.B. Rowell, H.L. Taylor and Y. Wang, Limitations to prediction of maximal oxygen intake, *Journal of Applied Physiology* **19** (1964), 919–927.
[20] B.Y. Salazar Vázquez, P. Cabrales, A.G. Tsai, P.C. Johnson and M. Intaglietta, Lowering of blood pressure by increasing hematocrit with non–nitric oxide–scavenging red blood cells, *American Journal of Respiratory Cell and Molecular Biology* **38**(2) (2008), 135–142.
[21] B.Y. Salazar Vázquez, J. Martini, A.G. Tsai, P.C. Johnson, P. Cabrales and M. Intaglietta, The variability of blood pressure due to small changes of hematocrit, *American Journal of Physiology Heart and Circulatory Physiology* **299**(3) (2010), H863–H867.
[22] B. Sandor, A. Nagy, A. Toth, M. Rabai and B. Mezey, Effects of moderate aerobic exercise training on hemorheological and laboratory parameters in ischemic heart disease patients, *PLoS One* **9**(10) (2014), e110751.
[23] H. Schmid-Schönbein, E. Volger and H.J. Klose, Microrheology and light transmission of blood III: The velocity of red cell aggregate formation, *Pflugers Archiv European Journal of Physiology* **254** (1975), 299–317.
[24] M.M. Smith, A.R. Lucas, R.L. Hamlin, L. Robert and S.T. Devor, Associations among hemorheological factors and maximal oxygen consumption. Is there a role for blood viscosity in explaining athletic performance? *Clinical Hemorheology and Microcirculation* **60**(4) (2015), 347–362.
[25] B. Schuler, M. Arras, S. Keller, A. Rettich, C. Lundby, J. Vogel and M. Gassmann, Optimal hematocrit for maximal exercise performance in acute and chronic erythropoietin-treated mice, *Proceedings of the National Academy of Sciences USA* **107**(1) (2010), 419–423.
[26] H. Stark and S. Schuster, Comparison of various approaches to calculating the optimal hematocrit in vertebrate, *Journal of Applied Physiology* **113**(3) (2012), 355–367.
[27] J.F. Stoltz and M. Donner, New trends in clinical hemorheology: An introduction to the concept of the hemorheological profile, *Schweizerische medizinische Wochenschrift* (**Suppl 43**) (1991), 41–49.
[28] A. Toth, J. Papp, M. Rabai, P. Kenyeres, Z. Marton, G. Kesmarky, I. Juricskay, H.J. Meiselman and K. Toth, The role of hemorheological factors in cardiovascular medicine, *Clinical Hemorheology and Microcirculation* **56**(3) (2014), 197–204.
[29] X. Waltz, M-D Hardy-Dessources, N. Lemonne, D. Mougenel, M-L Lalanne-Mistrih, Y. Lamarre, V. Tarer, B. Tressières, M. Etienne-Julan, O. Hue and P. Connes, Is there a relationship between the hematocrit-to-viscosity ratio and microvascular oxygenation in brain and muscle? *Clinical Hemorheology and Microcirculation* **2** (2015), 37–43.
[30] L. Winkler, P. Thoreux and F.J. Lhuissier, Lien entre le score de fatigue de l'enfant sportif et la présence de blessures en section sportive scolaire, *Science & Sports* (2016). in press.