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Pulmonary Circulation and Exercise: Friends or Foes?

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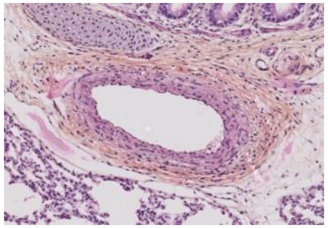
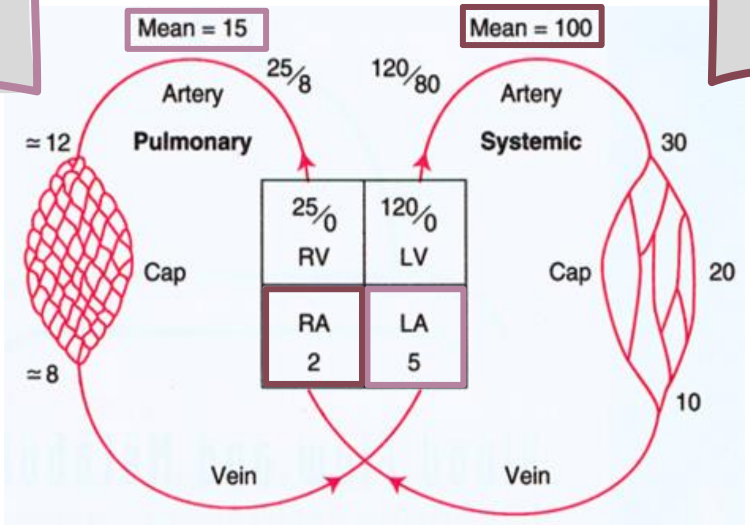
PLAN

- Introduction
- High-Altitude
- Highlanders
- Moderate altitude
- Normoxia
- Athletes
- Perspectives

PULMONARY VS. SYSTEMIC CIRCULATION

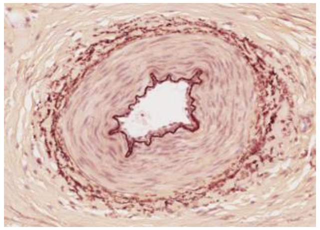
PULMONARY CIRCULATION





- Gaz exchange
- *shorter* and wider circulation:
  => lower flow rate
- **thin** artery walls and
  few smooth muscle fibers
- PVR = (PAP-LAP)/Q
  ~ 1,6 mmHg

SYSTEMIC CIRCULATION

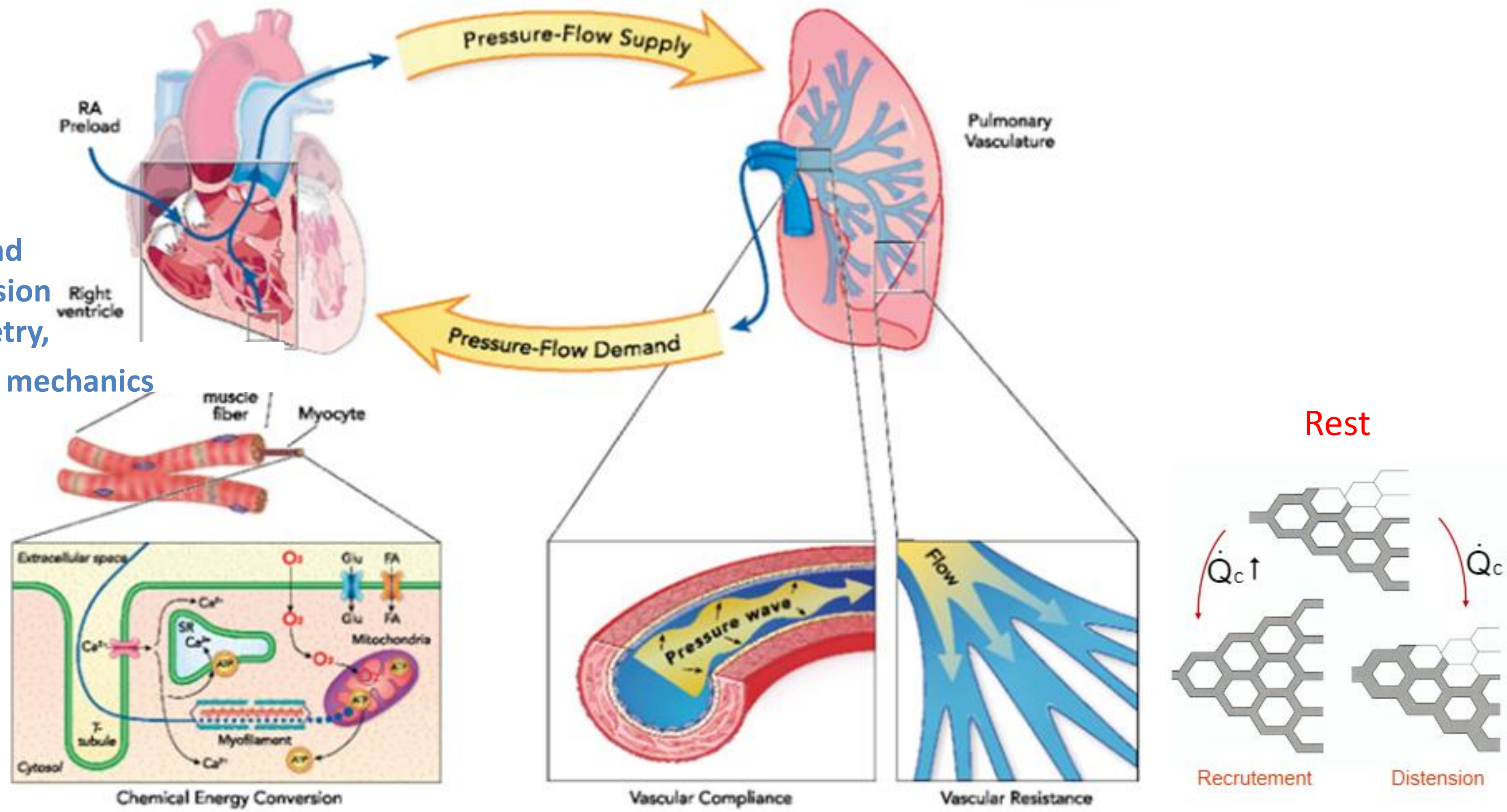


- Transport
- Wide and multi-organ
- **thick** artery walls and **many** smooth muscle fibers
- SVR = (SAP – RAP)/Q
  ~16,5 mmHg

RIGHT VENTRICLE-PULMONARY CIRCULATION UNIT

Determinant of RV afterload

- -RV pre-load
- -RV dimension and geometry,
- - myocytes mechanics



High compliant wall and Low resistance

Distensible arteries, accommodating the entire Q with low increase in pressure

Tabima et al. Physiology 2017

REGULATORY DETERMINANTS

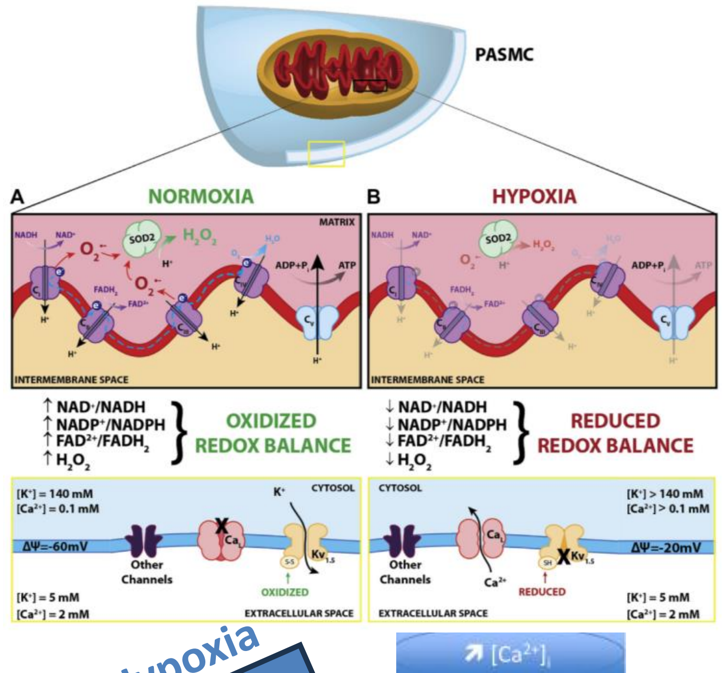
SYSTEMIC CIRCULATION

- autonomic nervous system (baroreflex, …)
- metabolic demand
- temperature
- hormonal signals

PULMONARY CIRCULATION

- **hypoxia**
- exercise
- acid/base balance and CO_2 levels
- alveolar & intrapleural pressures
- autonomic nervous system
- NO, Endothelin, Prostacyclin
- Inflammatory Mediators

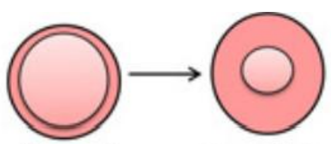
HYPOXIC PULMONARY VASOCONSTRICTION

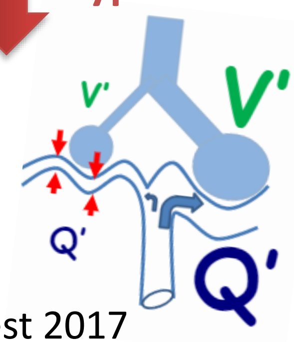


Chronic Hypoxia

Rho kinase activation
HIF activation
Sensibilisation of Ca++

Acute Hypoxia





SMC contraction strenghtening
Pulmonary vascular remodeling
Pulmonary Hypertension

Ridoux et al. 2019

Dunham-Snary H et al. Chest 2017

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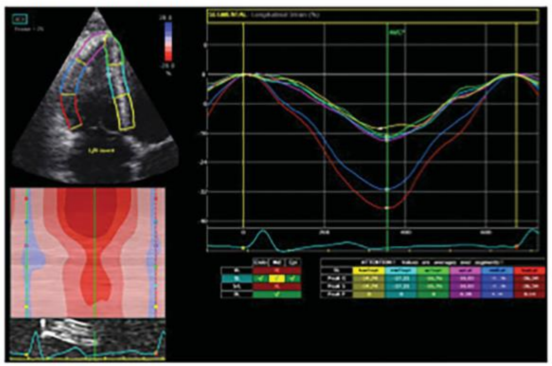
Right ventricular dyssynchrony during hypoxic breathing but not during exercise in healthy subjects: a speckle tracking echocardiography study

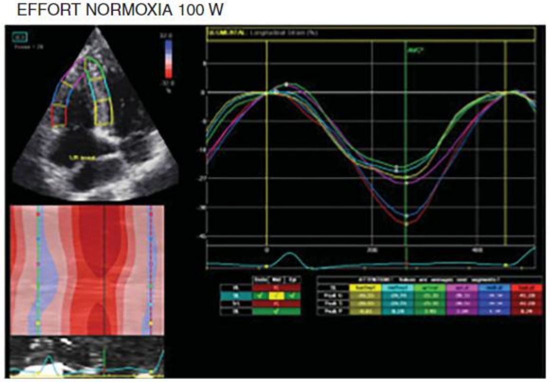
Right ventricular speckle tracking:
(SD of strain-time curves of 4 RV segments)
17 healthy subjects
- Normoxic aerobic exercise
- Acute hypoxia FiO2: 0.12

BASELINE REST NORMOXIA



mPAP 14 mmHg
PVR 1.3 WU
RV-SD4 7 ms

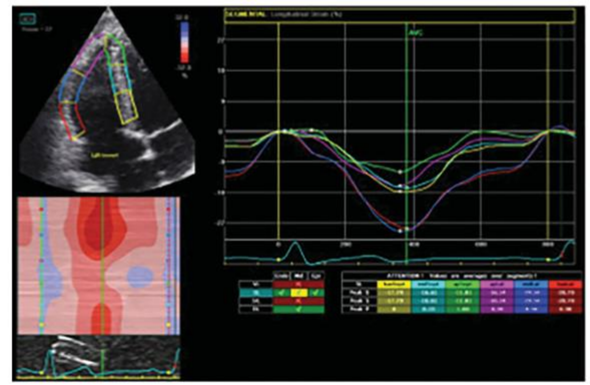
EFFORT NORMOXIA 100 W



mPAP 26 mmHg
PVR 1.31 WU
RV-SD4 6 ms

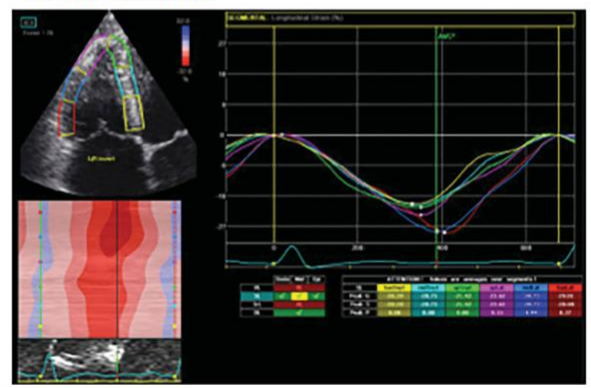
Reduction of PVR

BASELINE REST NORMOXIA



mPAP 11 mmHg
PVR 1.02 WU
RV-SD4 10 ms

REST HYPOXIA 45 MIN



mPAP 18 mmHg
PVR 1.58 WU
RV-SD4 30 ms

Increase of PVR

Hypoxic exposure, not exercise, is associated with a marked regional inhomogeneity of RV contraction
HPV? Hypoxia?

Pezzuto et al. Experimental Physiol 2018

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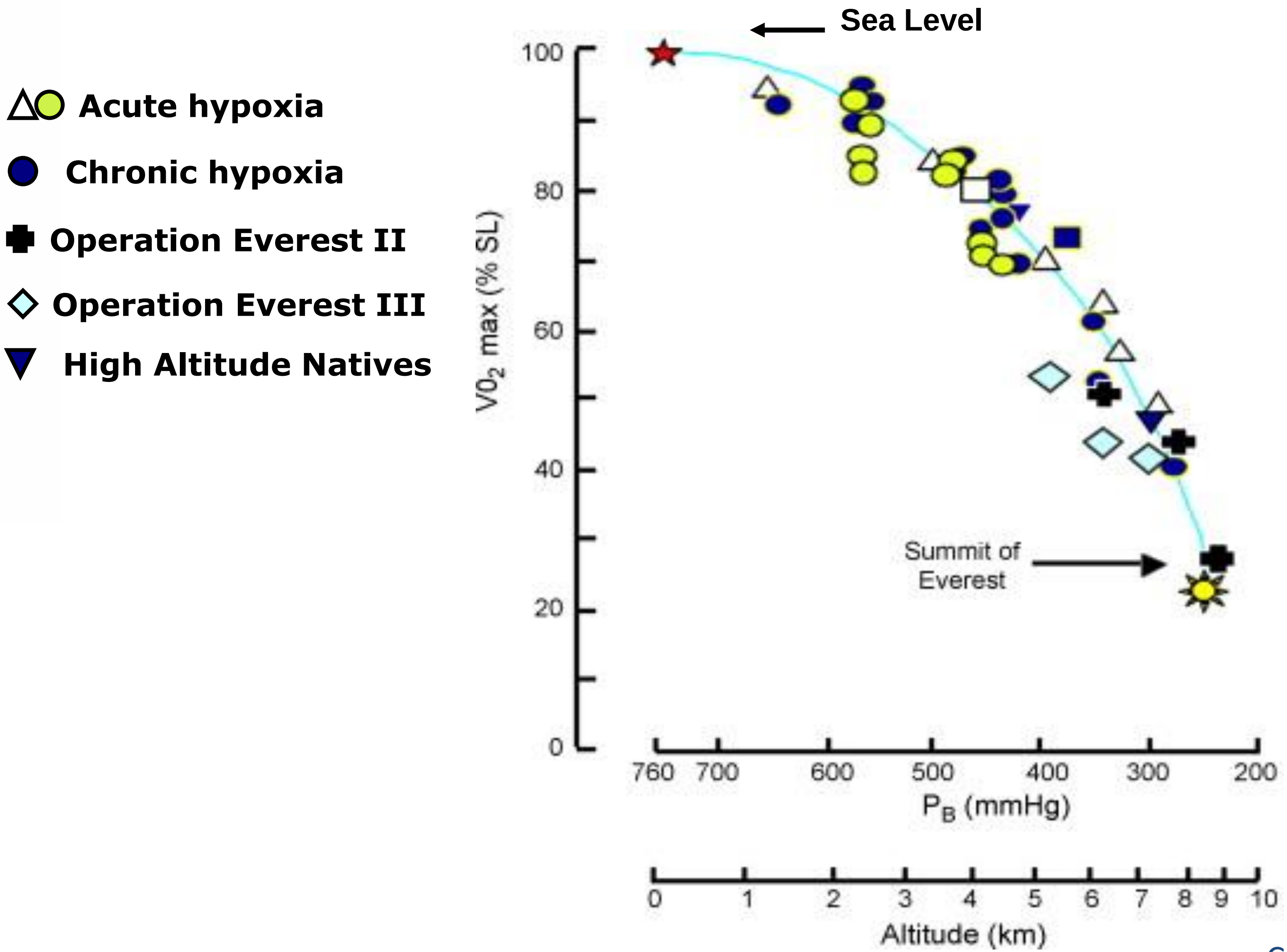
VO_2max paradox



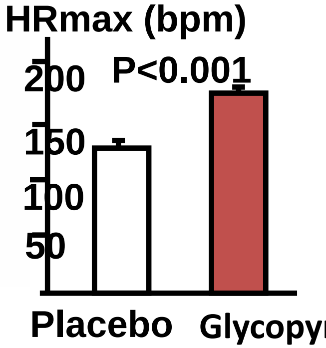
Cerretelli 1980

Fick Principle

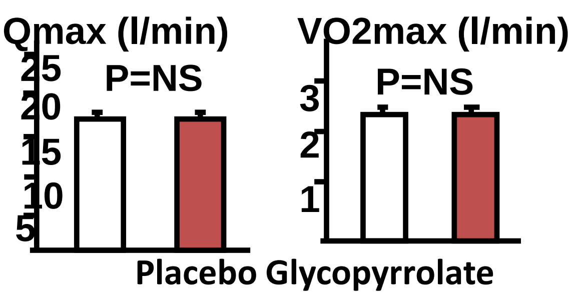
$$VO_2max = Q\ max \times (C_aO_2 - C_vO_2)max$$

At 5300m, VO_2max reduction: 1/3 Qmax limitation + 2/3: CaO_2max reduction

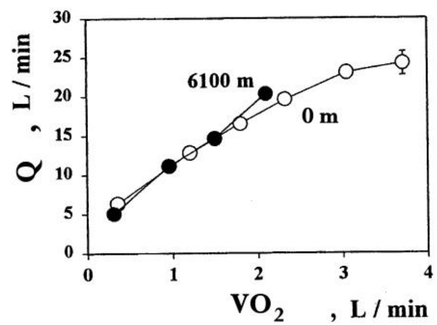
HRmax



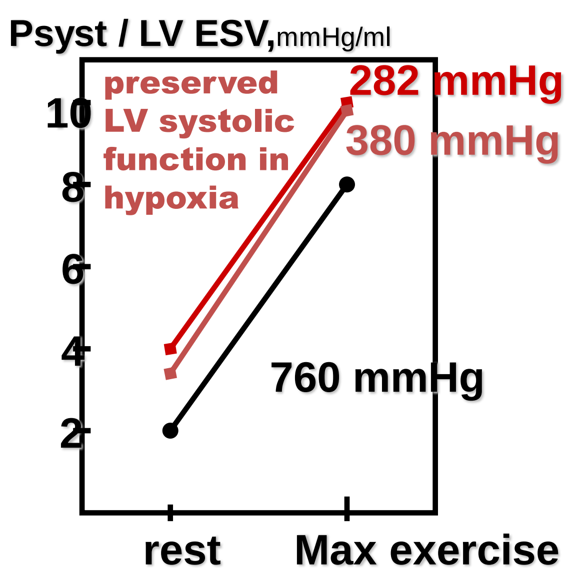
restoration by para-sympathetic blocage does not increase Qmax or VO_2max



Boushel et al. *Circulation* 2001

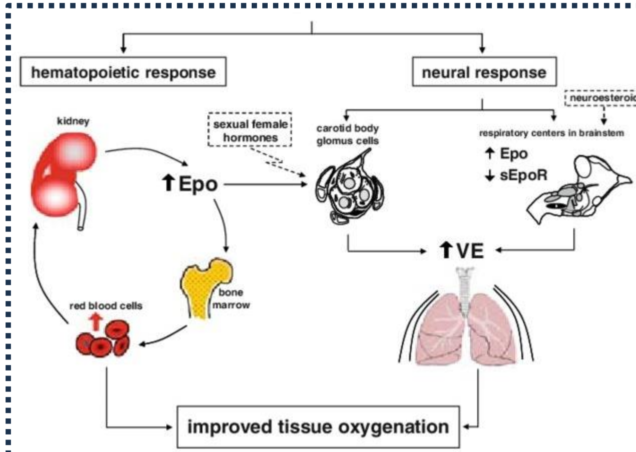


SVmax



Suarez et al. *Am J Cardiol* 1987

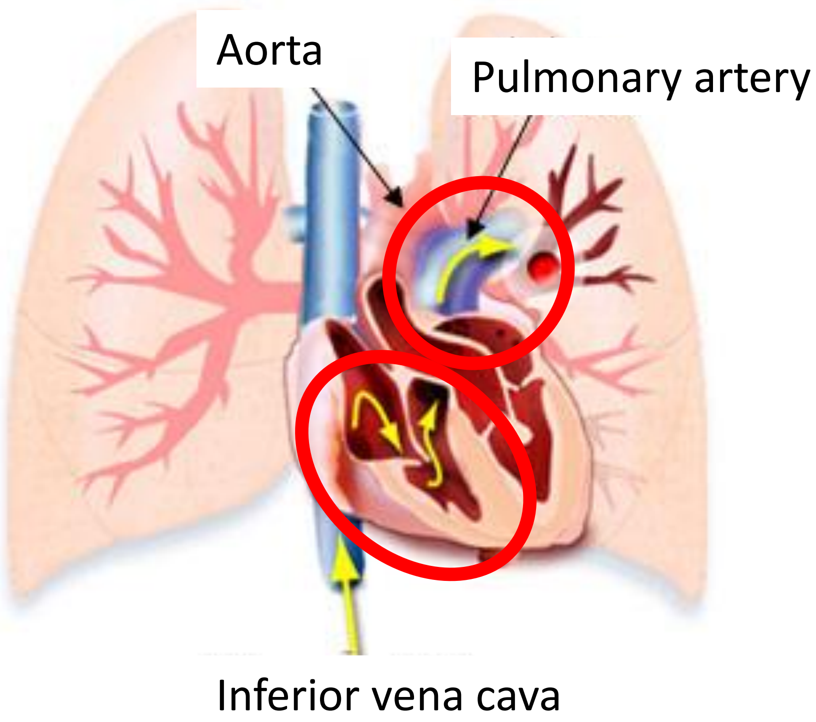
Calbet et coll. Am J Physiol. 2003



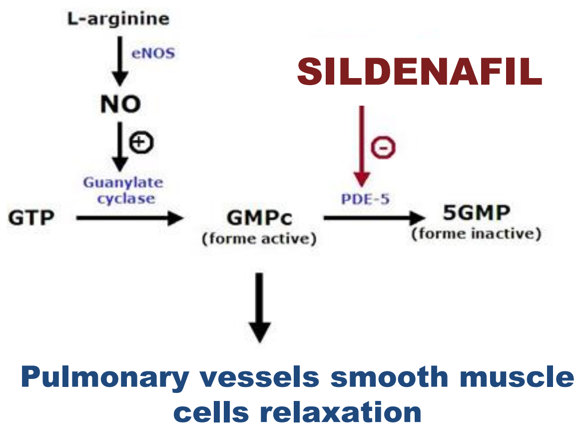
↓CaO_2 with altitude but is normalised through acclimatisation to an altitude of ~5000 m

Gassmann and Soliz 2009

Increased Pap during high-altitude exposure limits exercise capacity, by increasing RV afterload/work and limiting maximal cardiac output



Pulmonary vasodilation increases exercise capacity probably by reducing right ventricle afterload and increase maximal cardiac output in hypoxia

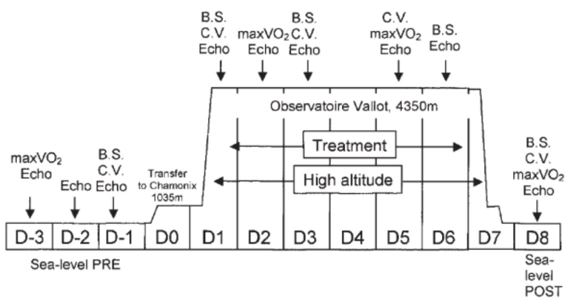


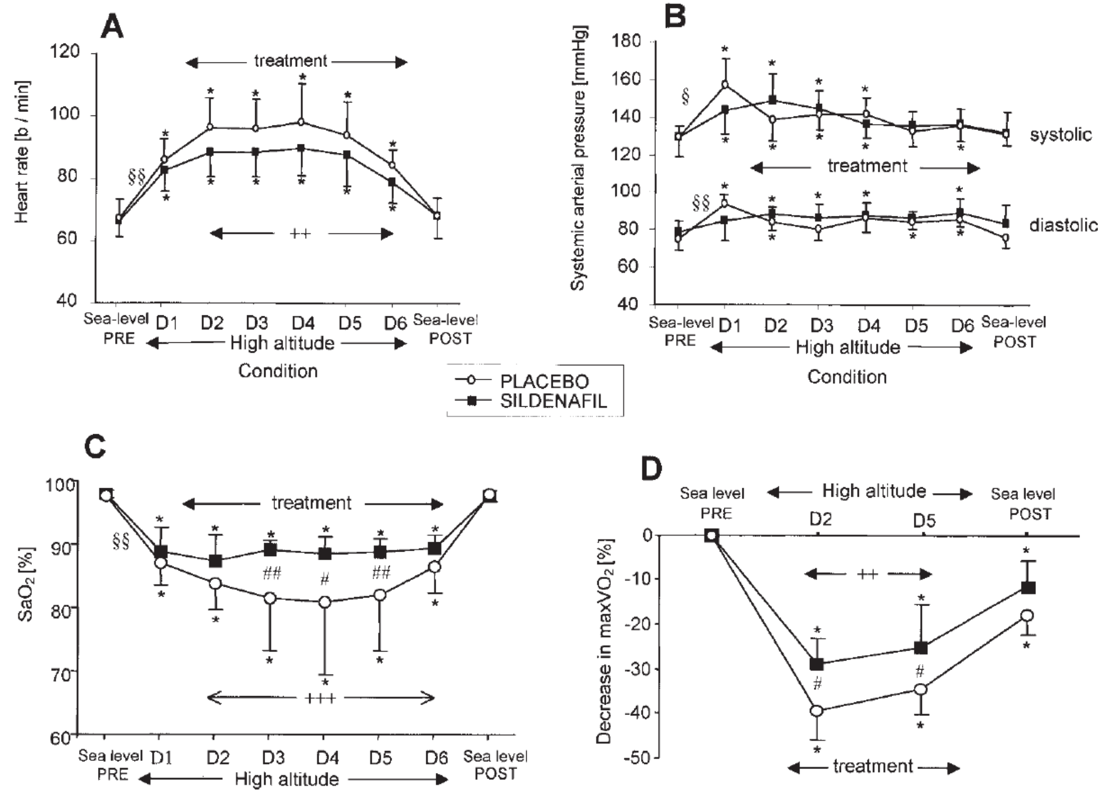
	NORMOXIA	**ACUTE HYPOXIA** (FiO_2: 0,10)		**CHRONIC HYPOXIA** (5240m)	
	baseline	**placebo**	**sildenafil**	**placebo**	**sildenafil**
sPap peak, mmHg	**25**	**43**	**36****	**34**	**28***
Load max, W	**263**	**131**	**173****	**171**	**190***
SaO_2 peak, %	**98**	**61**	**67****	**72**	**71**

Ghofrani et al. Ann.Intern.Med, 2004

Sildenafil Inhibits Altitude-induced Hypoxemia and Pulmonary Hypertension

Jean-Paul Richalet, Pierre Gratadour, Paul Robach, Isabelle Pham, Michèle Déchaux, Aude Joncquiert-Latarjet, Pascal Mollard, Julien Brugniaux, and Jérémy Cornolo





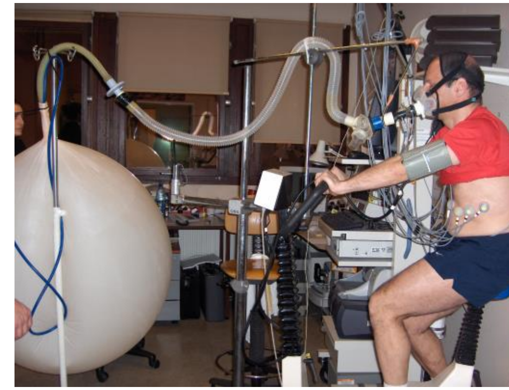
Richalet et al. Am J Resp Crit Care 2005

Effects of Sildenafil on Exercise Capacity in Hypoxic Normal Subjects

VITALIE FAORO,[1] MICHEL LAMOTTE,[2] GAEL DEBOECK,[1]
ADRIANA PAVELESCU,[2] SANDRINE HUEZ,[2] HERVÉ GUENARD,[3]
JEAN-BENOÎT MARTINOT,[4] and ROBERT NAEIJE[1]

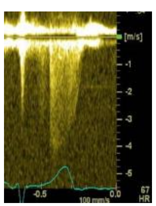
14 healthy subjects
1h after 50mg sildenafil/placebo
double-blind, cross-over

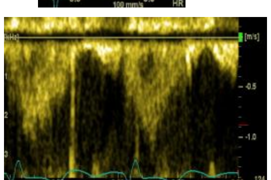
CPET and Stress-Echo
in 6 conditions =>



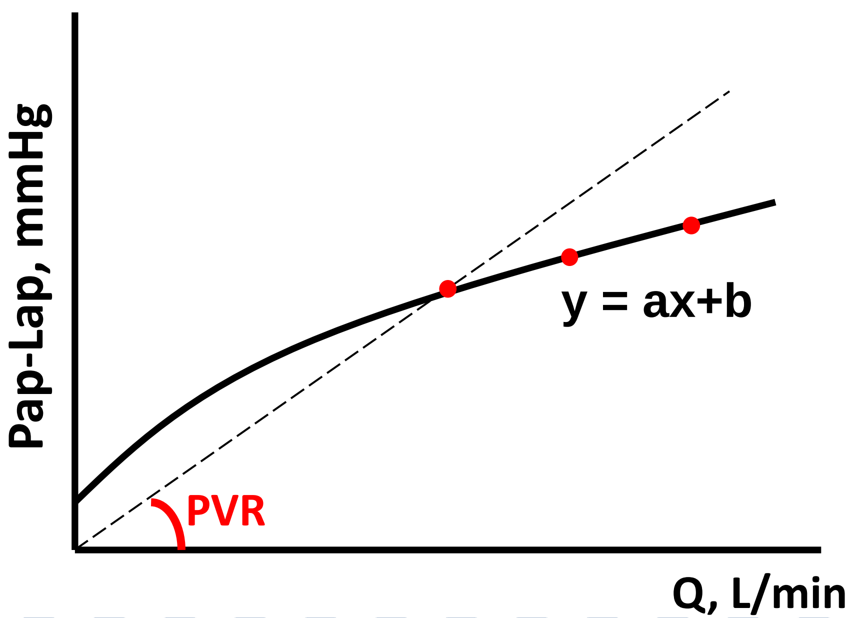
Normoxia + 1h normobaric hypoxia (FiO2:0.10)

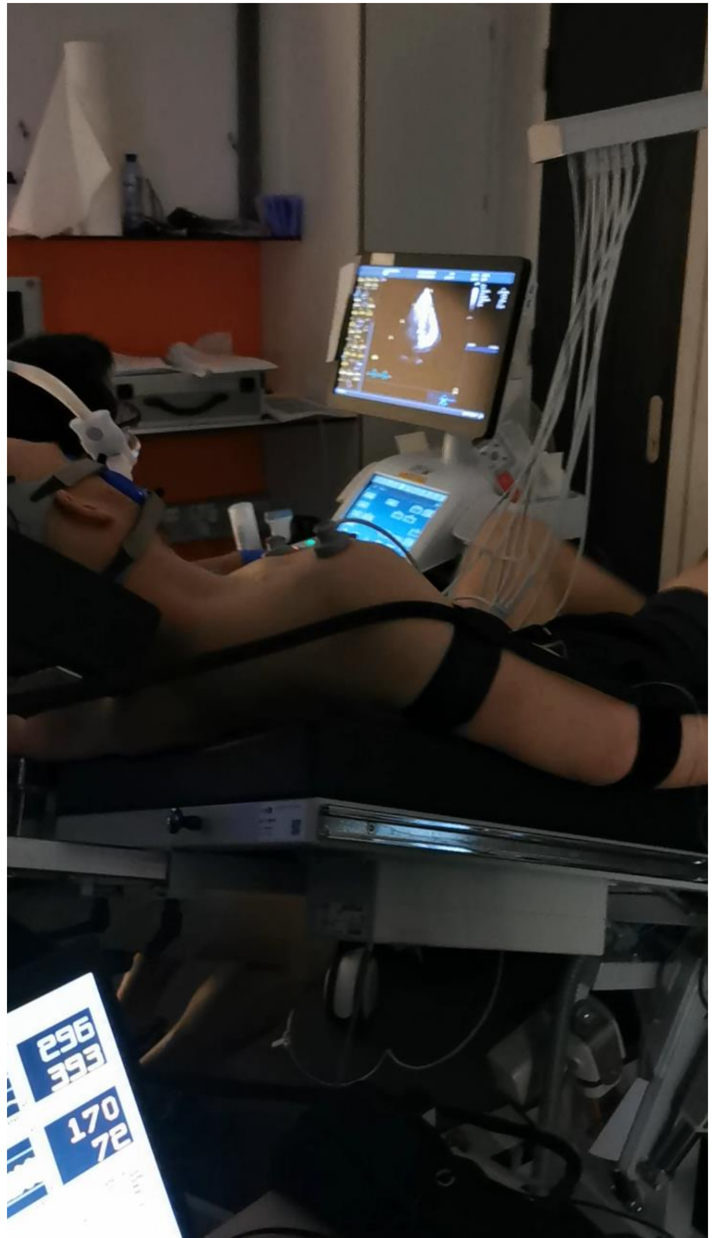
Chronic Hypoxia
After acclimatation
5000m, Chimborazo, Equator



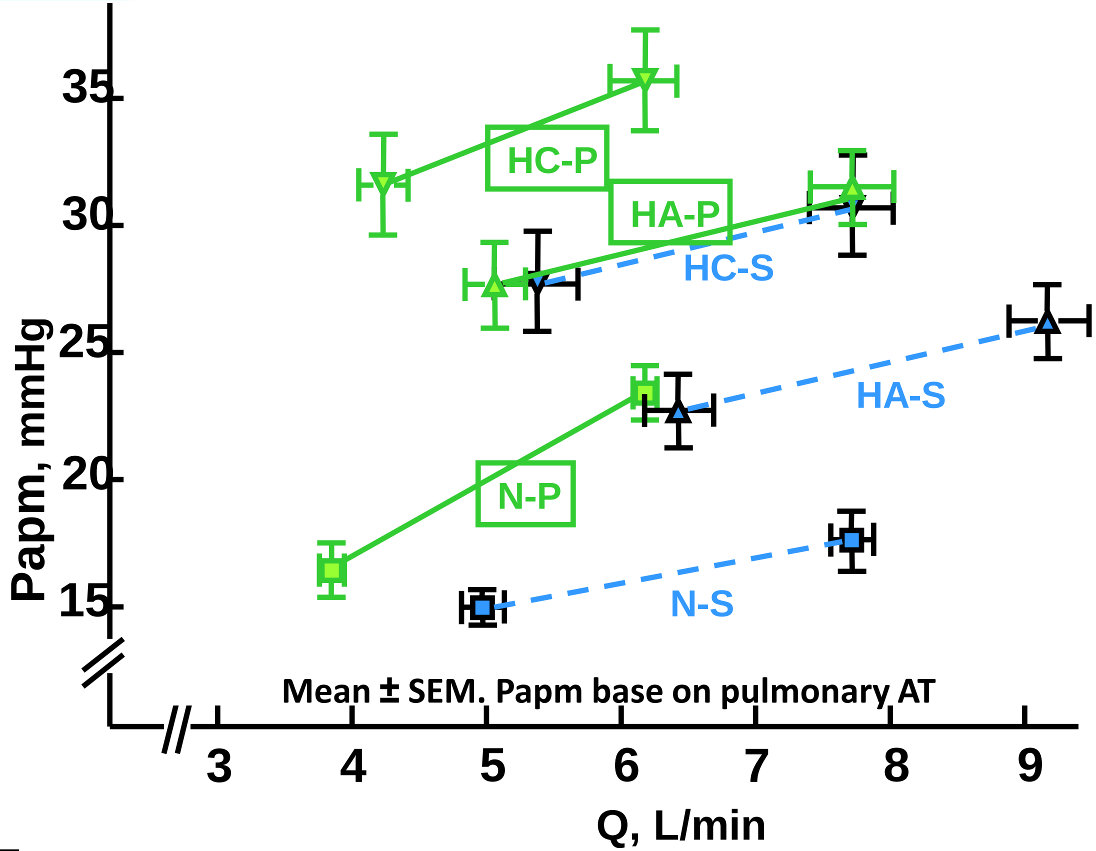


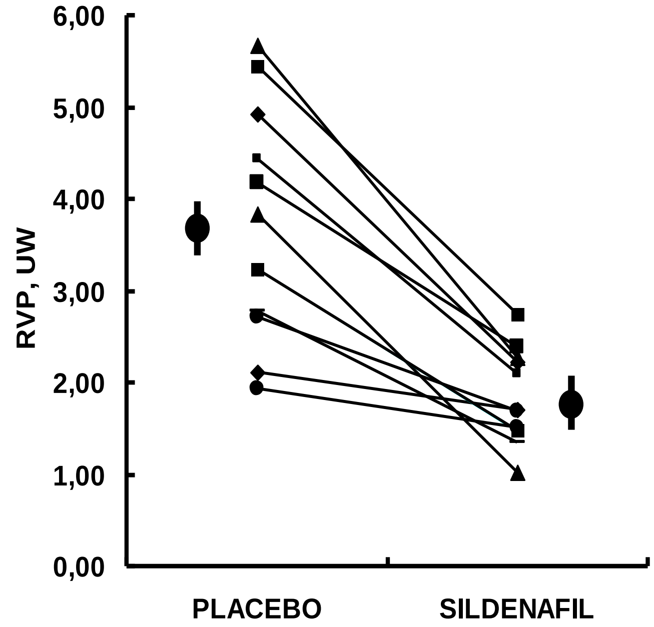
mPAP and LAP at increasing Q

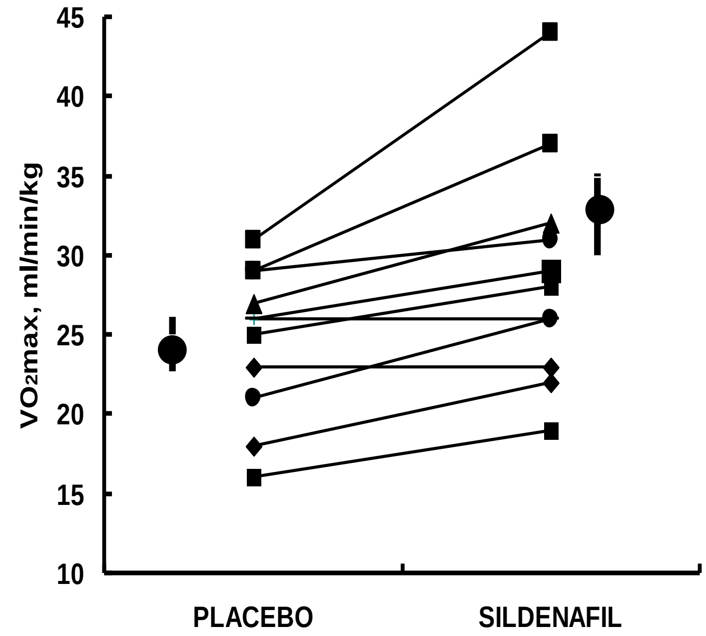



296
393
170
72

Results







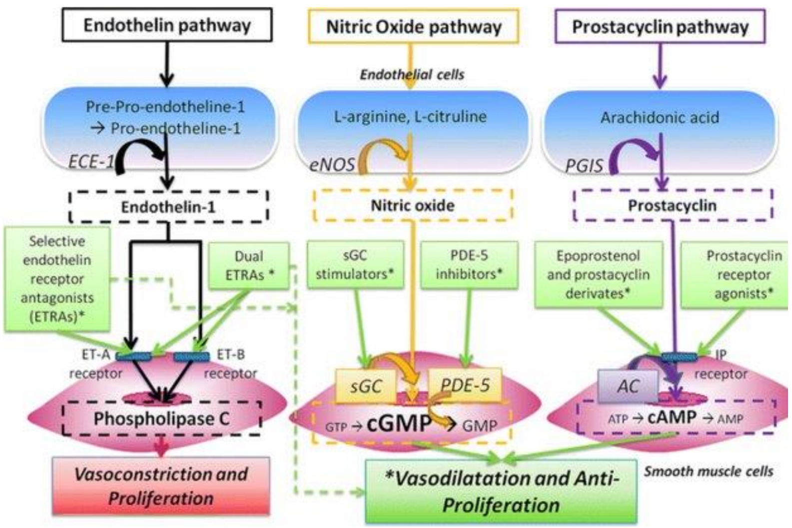
□ N- Normoxia
Δ HA - Hypoxie acute normobaric
∇ HC - Hypoxia chronic hypobaric

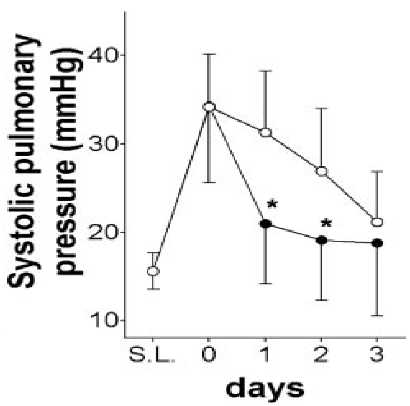
P - placebo
S - sildenafil

Sildenafil: limit the hypoxic decrease in VO_2max
Increased O_2 delivery or hemodynamic effect?

Other pharmacological agents ?

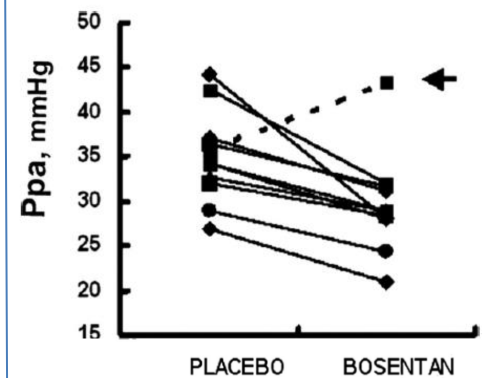
Bosentan, a non-selective endothelin receptor antagonist, inhibits HPV

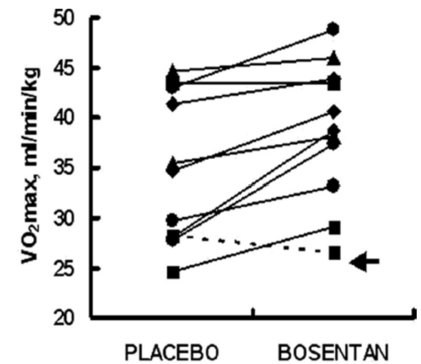


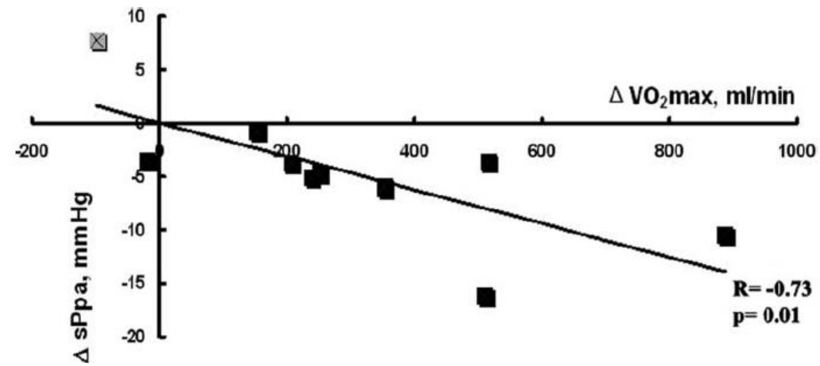


Modesti et coll. *Circulation* 2006

11 healthy subjects
Bosentan (2x62,5mg/24h et 4x125mg/48h)
Cross-over double-blind
Normoxia vs acute hypoxia (FiO2: 0.12)







Moderate hypoxic pulmonary hypertension partially contributes to decreased VO_2max at high altitude

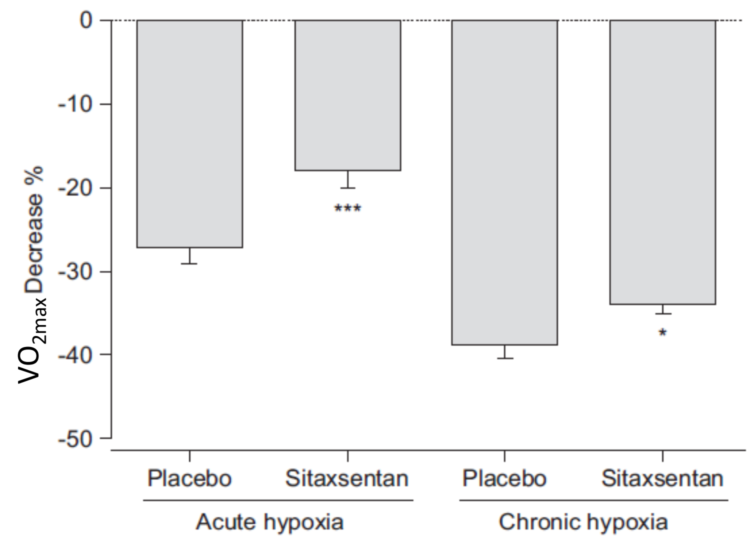
Faoro et al. Chest 2009

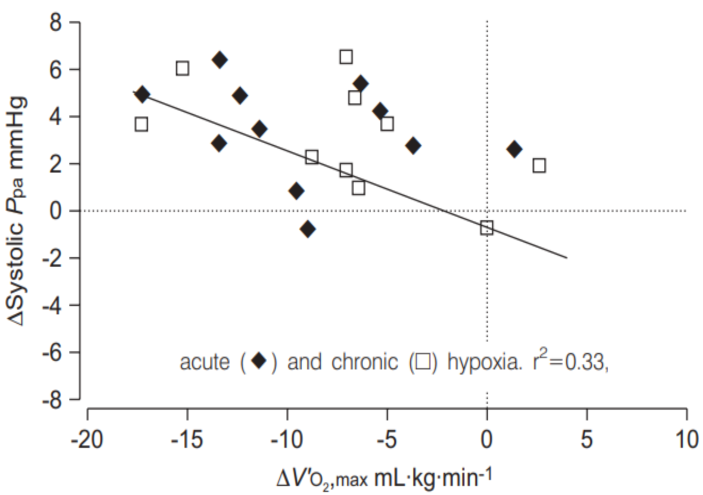
Pulmonary artery pressure limits exercise capacity at high altitude

R. Naeije*, S. Huez#, M. Lamotte#, K. Retailleau¶, S. Neupane+, D. Abramowicz§ and V. Faoro*

Pyramid hut, 5050m, Nepal

22 healthy subjects
Sitaxentan (100mg/day during 7 days) vs placebo (double-blind)
Cross over in acute hypoxia (FIO2:0.12)
Randomized in chronic hypoxia

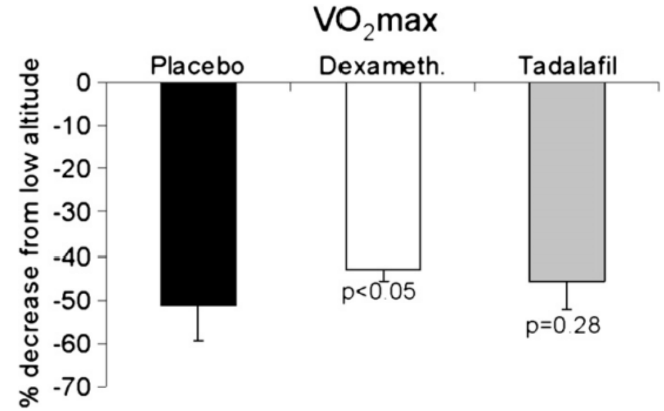




pulmonary vasodilation has positive effect on aerobic capacity, but this is particularly true in acute hypoxic condition whith reduced effect in chronic hypoxia.

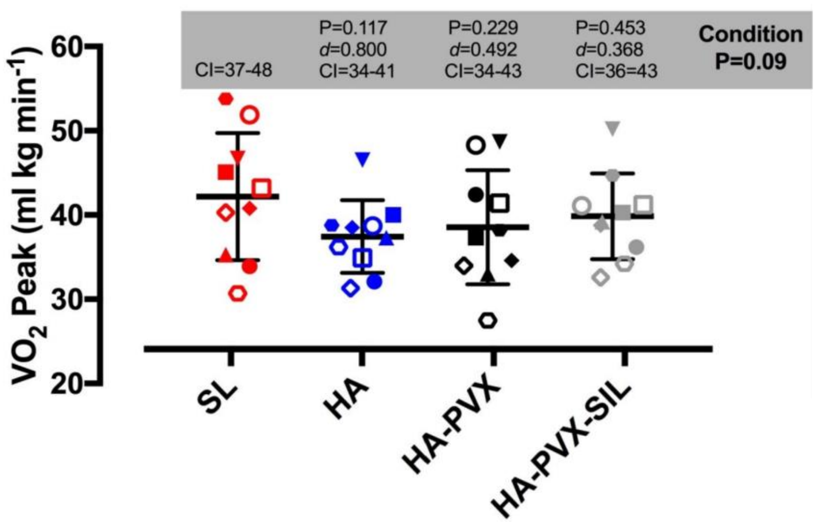
Naeije et al. Eur Respir J 2010

Still under debate…



- **Effect with Dexamethazone in HAPE-suceptible subjects**
- **Numerous confounding factors (Side effects? Acetazolamide?, Environment, …)**
- **Controvesial data …**
- **No pure pharmacological VPH inhibitor (ΔSpO2?)**

38 healthy subjects => Sea level and 5-10 days 3800m



Stembridge et al. J Physiol 2019

J Appl Physiol 112: 20–25, 2012.
First published October 6, 2011; doi:10.1152/japplphysiol.00670.2011.

Improvement in lung diffusion by endothelin A receptor blockade at high altitude

Claire de Bisschop,[1] Jean-Benoit Martinot,[2] Gil Leurquin-Sterk,[3] Vitalie Faoro,[3] Hervé Guénard,[4]

	Sitaxsentan (n = 11)			
	Baseline		After 7 Days	
	Rest	30 min PE	Rest	30 min PE
DL_{CO}, ml·min^{-1}·mmHg^{-1}	36 ± 3	35 ± 2	36 ± 2	38 ± 3
DL_{NO}, ml·min^{-1}·mmHg^{-1}	155 ± 12	145 ± 11*	168 ± 11#	156 ± 11*#
Dm, ml·min^{-1}·mmHg^{-1}	79 ± 6	74 ± 6*	85 ± 6#	79 ± 5*#
Vc, ml	100 ± 10	102 ± 9	97 ± 8	111 ± 10

Fischer et al. Am J Respir Crit Care Med 2009

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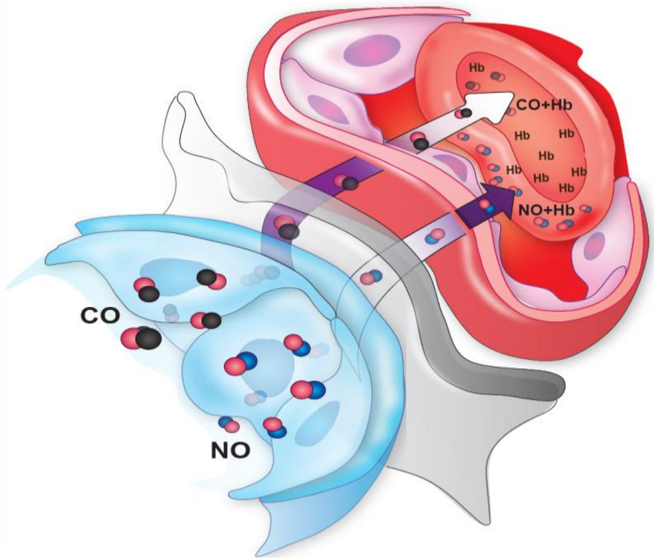
Membrane and Capillary component of diffusion capacity



Single breath method : D_L of 2 gases, NO and CO

Quantification of capillary blood volume (Vc) and membrane component (Dm) to diffusing capacity

$$1/D_{LNO} = 1/D_{mNO} + 1/\theta Vc$$

$$1/D_{LCO} = 1/D_{mCO} + 1/\theta Vc$$

D_{LNO} essentially dependant on membrane resistance

↓D_{LNO} / D_{LCO}

indicates more increase in Vc compared to Dm

$$\frac{1}{D_L} = \frac{1}{D_m} + \frac{1}{\theta . Vc}$$

Roughton et Forster *JAP* 1957

Guénard et al *JAP* 1987

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Highlanders

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Tibetans

- ↑ diffusion capacity
- ↑ VE
- ↓ Hb
- ↓ SaO_2
- ↓ Pap

Andeans

- ↓ VE
- ↑ Hb
- ↑ Pap
- ↑ SaO_2

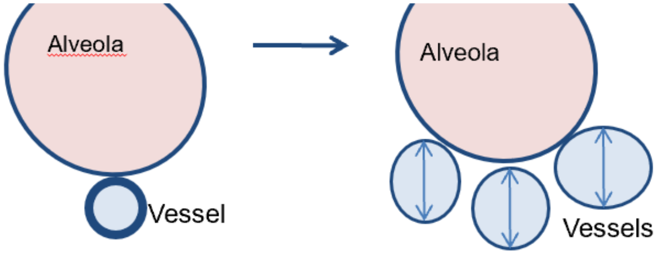
(↓ VE, ↑ Hb, ↑ Pap: Especially in CMS)

Different phenotypes

Andeans

Variable	All		
	Value	% SL pred.	*P*-value
$PcapO_2$ (mmHg)	63 ± 11	–	NS
TL_{COcor} ($mL.min^{-1}$ $mmHg^{-1}$)	50 ± 14	159 ± 35	0.004
TL_{NO} ($mL.min^{-1}$ $mmHg^{-1}$)	180 ± 53	119 ± 75	0.02
Dm_{CO} ($mL.min^{-1}$ $mmHg^{-1}$)	92 ± 27	119 ± 75	0.02
Vc_{cor} (ml)	180 ± 54	191 ± 49	0.001
VA (L)	6.6 ± 1.3	110 ± 20	NS
TL_{NO}/TL_{COcor}	3.6 ± 0.3	–	0.038

- high diffusing capacity:
probably reflecting pulmonary capillary distension but also explained by an increased amount of vessel



-- hypoxia-induced angiogenesis?

de Bisschop et al. 2010

Pulmonary circulation and gas exchange at exercise in Sherpas at high altitude

Vitalie Faoro,[1] Sandrine Huez,[2] Rebecca Vanderpool,[3] Herman Groepenhoff,[4] Claire de Bisschop,[5] Jean-Benoît Martinot,[6] Michel Lamotte,[2] Adriana Pavelescu,[3] Hervé Guénard,[7] and Robert Naeije[1,3]

13 healthy Sherpas
vs 13 acclimatized lowlanders
Altitude: 5050m, Pyramid Hut

Faoro et al. JAP 2014

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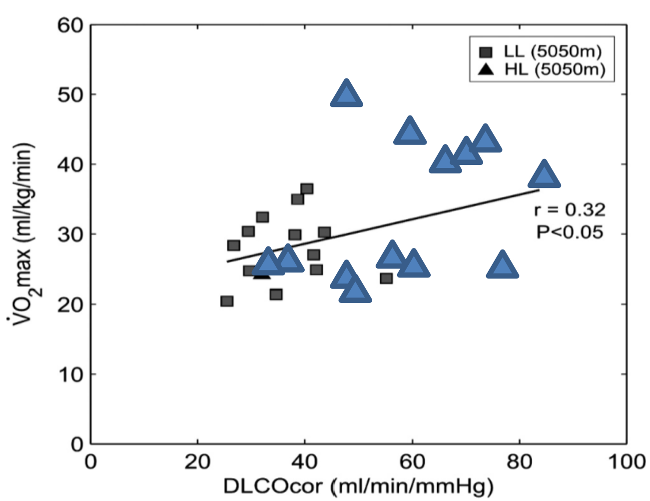
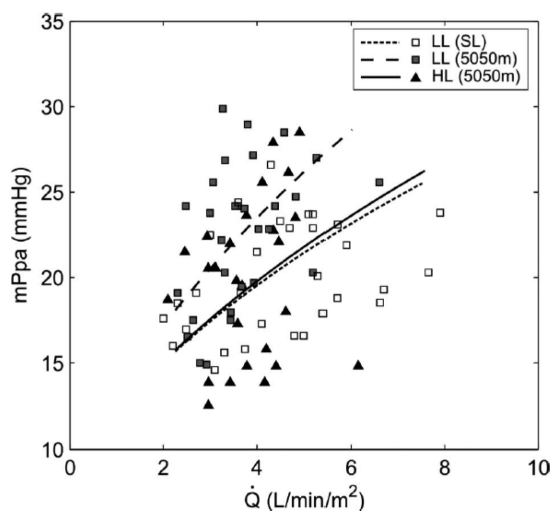
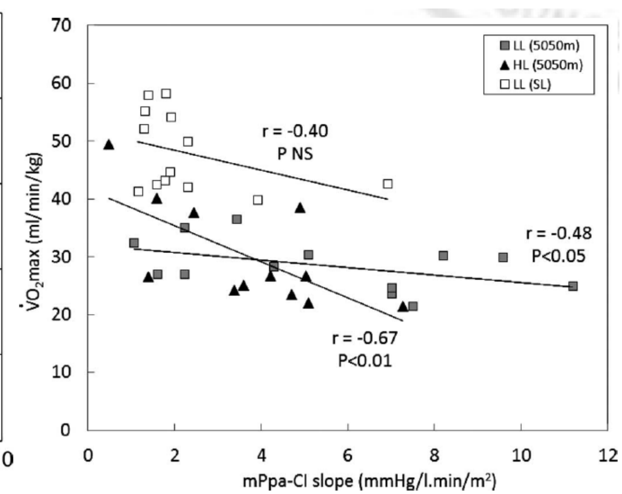
Pulmonary circulation and gas exchange at exercise in Sherpas at high altitude

Vitalie Faoro,[1] Sandrine Huez,[2] Rebecca Vanderpool,[3] Herman Groepenhoff,[4] Claire de Bisschop,[5] Jean-Benoît Martinot,[6] Michel Lamotte,[2] Adriana Pavelescu,[3] Hervé Guénard,[7] and Robert Naeije[1,3]

	Lowlanders (0 m)	Lowlanders (5,050 m)	Highlanders (5,050 m)
VA, liters	6.3 ± 0.4	6.6 ± 0.3*	7.4 ± 0.6
DL_{NO}, ml·min^{-1}·mmHg^{-1}	148 ± 11	153 ± 9	226 ± 18§
$DL_{CO\ cor}$, ml·min^{-1}·mmHg^{-1}	33 ± 2	37 ± 2†	61 ± 4§
DL_{NO}/DL_{CO}	4.5 ± 0.1	4.2 ± 0.1‡	3.7 ± 0.1§
P_{CO_2}, mmHg	109 ± 4	47 ± 1†	54 ± 1§







Sherpas: high gas exchange, decreased ventilatory response at exercise.
Lower RV afterload with little HPV and polycytemia

Faoro et al. JAP 2014

Inter-ethnic comparison

	Lowlanders 0m	Lowlanders 4350-5050m	Sherpas 5050m	Quechuas 4350m
Hb, g/dl	13.9± 0.3	15.1± 0.3	15.9 ± 0.3	17.6 ± 0.5°°°
SaO_2, %	98± 1	86 ± 1	86 ± 1	90 ± 1°*
mBP, mmHg	101±3	89±3	100±3$	98±3°
DL_{NO}, $ml.min^{-1}.mmHg^{-1}$	148±11	153±9	226±18###	204±11###°
$DL_{CO}cor$, $ml.min^{-1}.mmHg^{-1}$	33±2	37±2**	61±4###	55±3###°°
DL_{NO}/DL_{CO}	4.5±0.1	4.2±0.1***	3.7±0.1###	3.7±0.1###

*: $P < 0.05$; Sherpa *vs* Quechua at high altitude

$: $P < 0.05$, £££: $P < 0.001$; Sherpa vs Lowlanders at 4350 m

°: $P < 0.05$, °°°: $P < 0.001$; Quechua vs Lowlanders at 5050m

ULB

Pap-Q relationships corrected for Hb

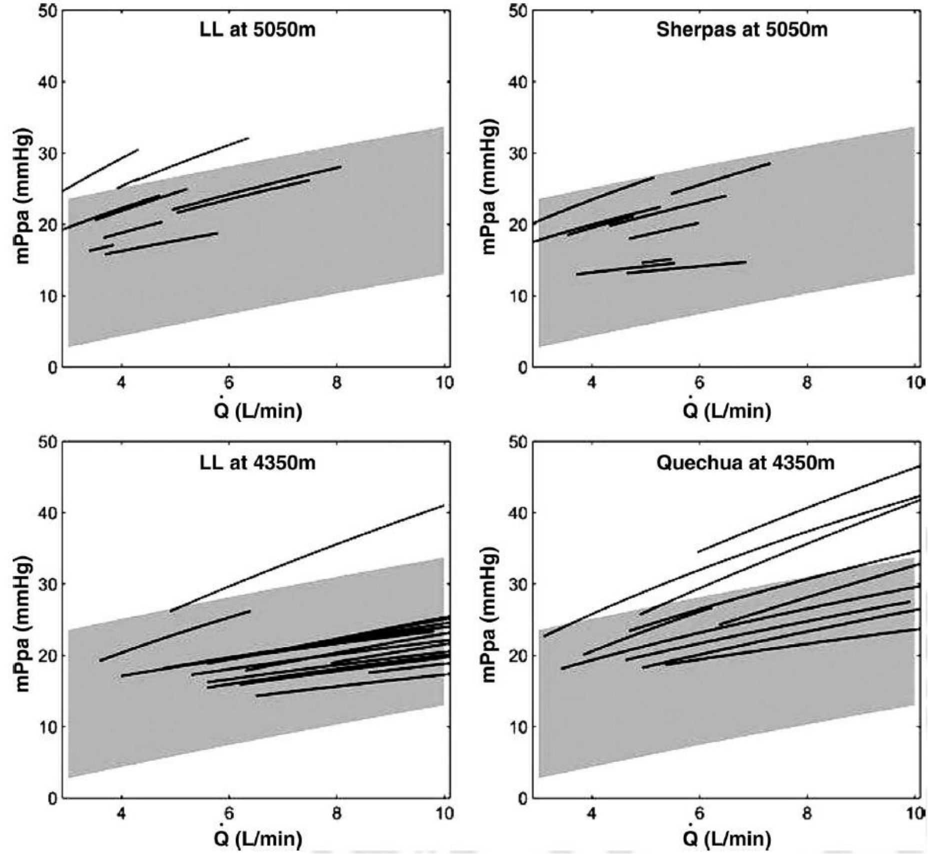
Lowlanders 4350-5050m	Sherpas 5050m	Quechuas 4350m
5.2 ± 0.3	4.3 ± 0.5[££]	4.4 ± 0.3[£]

Relative PVR at a hematocit of 45% according to the exponential relationship between resistance and hematocrit

$$R_0(45\%) = R_0 \frac{1}{\exp(2(\varphi - 0.45))}$$

φ: hematocrit level

Linehan et al. JAP 1992



Exercise capacity

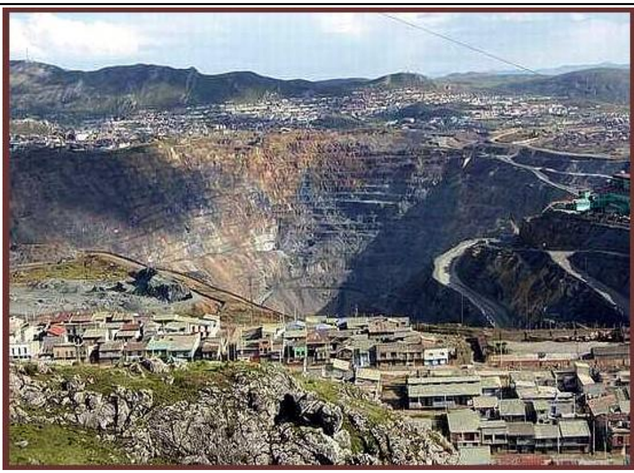
	Lowlander 0m	Lowlander 5050m	Sherpas 5050m	Quechuas 4350m
VO_2max, ml.kg^{-1}.min^{-1}	44±2	28±1***	32±3	32±2
HR max, bpm	186±3	162±4***	170±4	160 ± 4°
SaO_2max, %	93±1	78±2***	81±3	88 ± 1##°°
RER max	1.24±0.03	1.20±0.03	1.30±0.03#	1.13±0.01#°°
$V_E$max, l/min	114±7	128±9*	114±12	106 ± 8
V_E/VCO_2at AT	26±1	49±2***	44±1##	38±1###°°

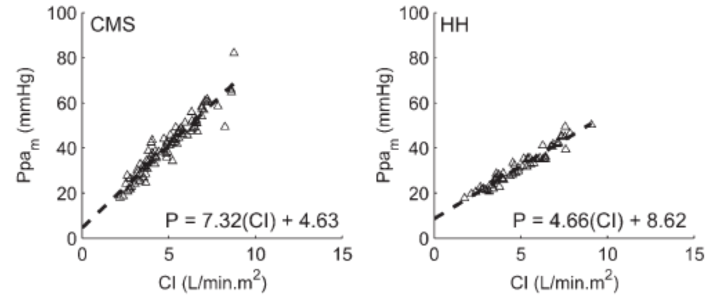
*: Lowlanders at SL vs HA
#: Highlanders vs Lowlanders
°: Quechua vs Sherpa

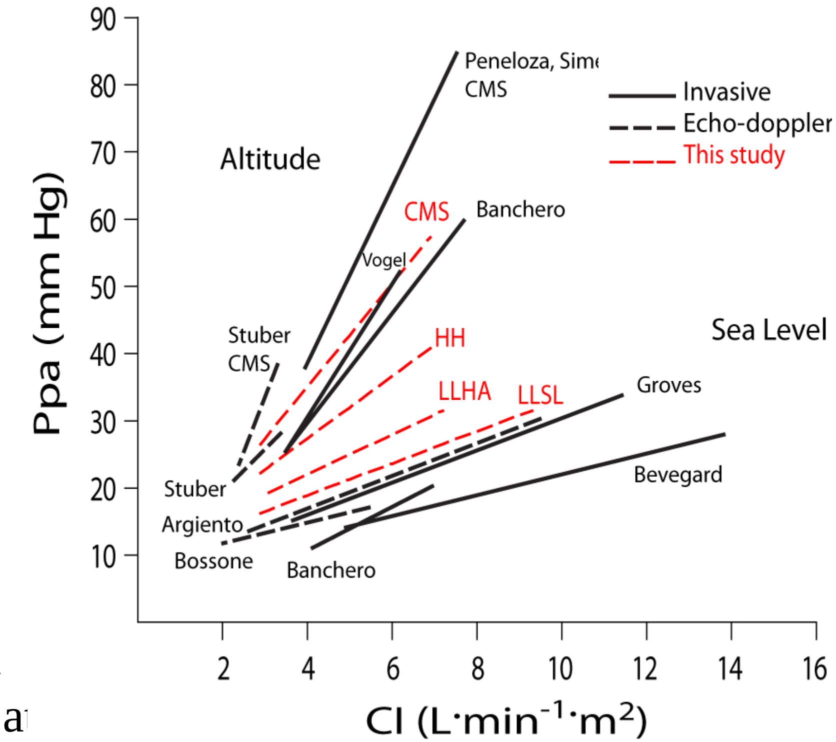
"VO2 paradox": unremarkable aerobic exercise capacities contrasting with superior field performance of Andean or Tibetan natives at high altitudes.

Chronic Mountain Sickness

13 CMH patients, [Hb]: 24±1 g/dl
15 Healthy Highlanders, [Hb]: 18±1 g/dl
15 Lowlanders at SL, [Hb]: 15±1 g/dl
4359m Cerro de Pasco, Peru







Groepenhoff et al. Chest 2012

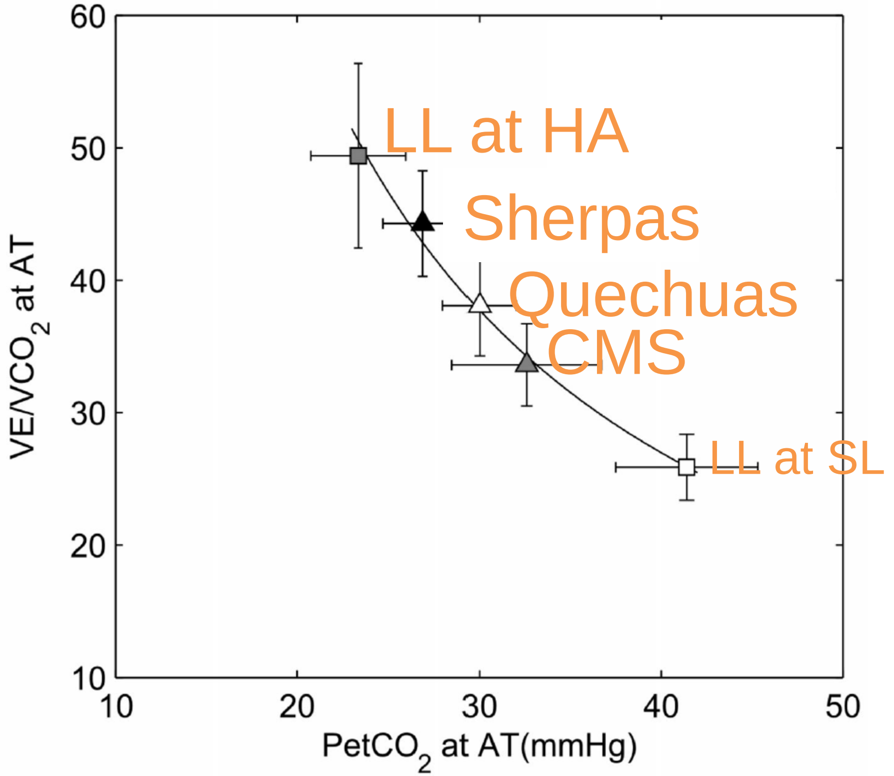
Both diffusion capacity components increased similarly in highlanders with or without CMS at

(However, Hb dependent values were increased by 15%)

Decreased chemosenstivity

Measure	Patients With CMS	Highlanders
Power, W	137 ± 7[a]	119 ± 9[a]
Power, % reference	81 ± 4	92 ± 8
$\dot{V}O_2$, % reference	102 ± 6	117 ± 13
$\dot{V}O_2$, mL/min/kg	32 ± 1	32 ± 2
RER	1.13 ± 0.02	1.13 ± 0.01
$\dot{V}E/\dot{V}CO_2$ slope	32 ± 1[a,c]	36 ± 1[a]
$\dot{V}E$, L/min	105 ± 8[a]	106 ± 8 [a]
$\dot{V}E$/MVV, %	70 ± 5	73 ± 6
HR, beat/min	145 ± 5[a,c]	160 ± 4
HR, % reference	87 ± 3	93 ± 2
O_2 pulse, mL/beat	16 ± 1[c]	12 ± 1[a]
O_2 pulse, % reference	80 ± 3	77 ± 5
SpO_2, %	82 ± 1[c]	88 ± 1[a]
CaO_2, mL/dL	26 ± 1[a,c]	21 ± 1[a]
SBP, mm Hg	153 ± 6	148 ± 4
DBP, mm Hg	85 ± 3	83 ± 2

[a] $P < .05$ vs lowlanders at altitude.
[b] $P < .01$ vs lowlanders at sea level.
[c] $P < .05$ vs highlanders.



More severe depression of chemosensitivity in CMS.
In keeping with the notion of a continuum of ventilatory responses from health to CMS

Groepenhoff H, CHEST 2011

PLAN

- ✓ Introduction
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- ✓ Highlanders
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- ○ Perspectives

Pulmonary Vascular Function and Aerobic Exercise Capacity at Moderate Altitude

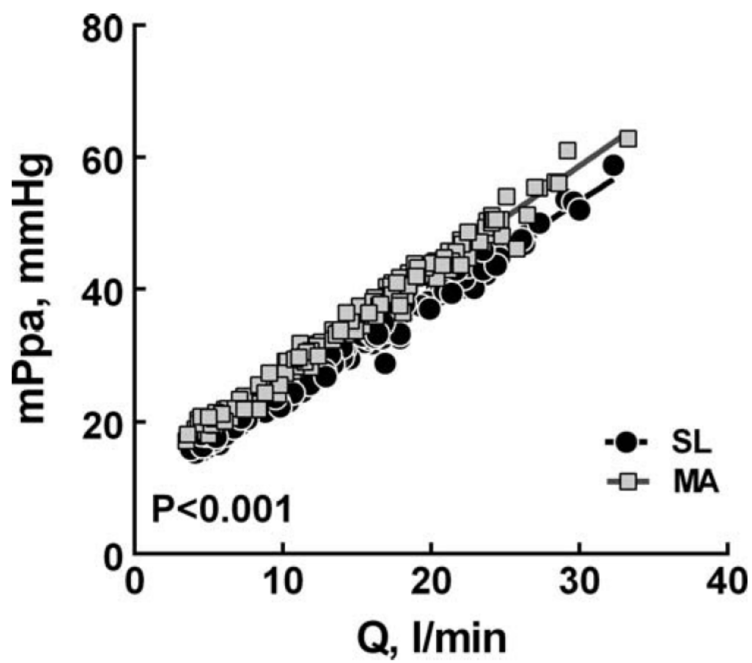
VITALIE FAORO[1], GAEL DEBOECK[1,2], MARCO VICENZI[1,2,3], ANNE-FLEUR GASTON[4], BAMODI SIMAGA[1], GRÉGORY DOUCENDE[4], ILONA HAPKOVA[4], EMMA ROCA[5], ENRIC SUBIRATS[5,6], FABIENNE DURAND[4],

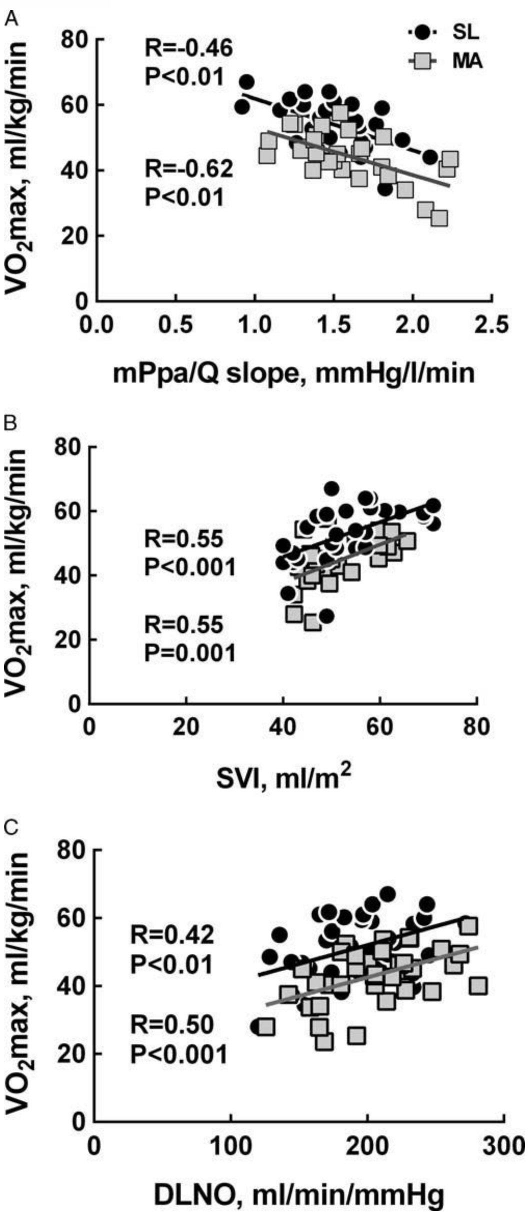
38 healthy and fit subjects
Sea level
2250m, Masella, Spain
ECHO, DIFFUSION, CPET

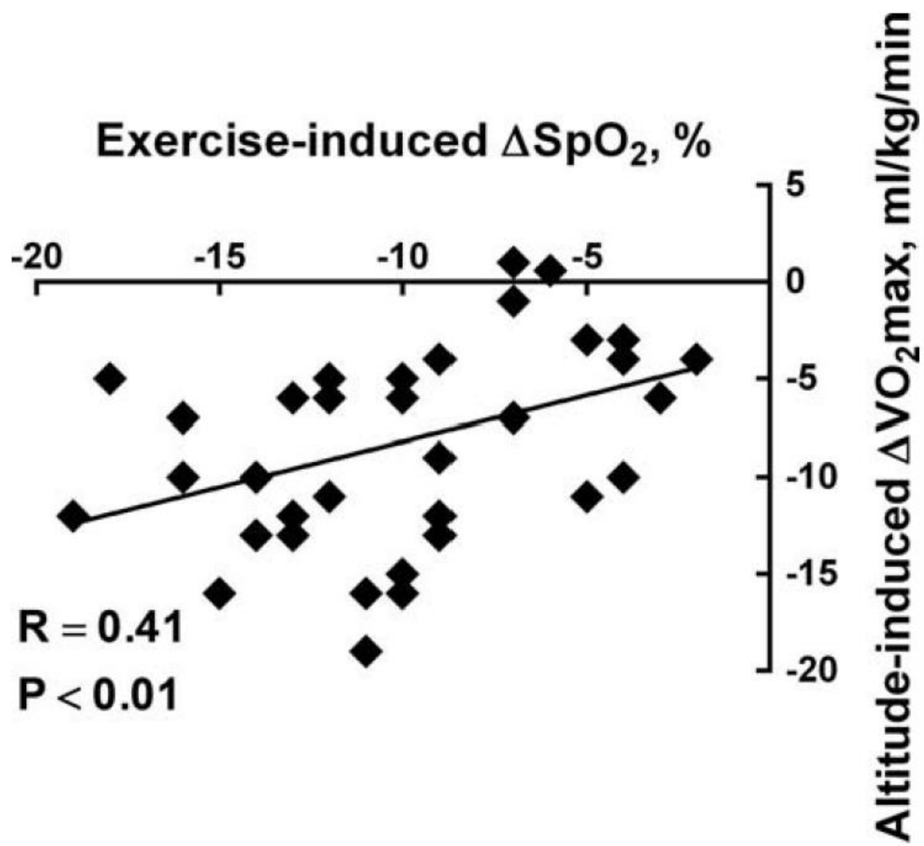
TABLE 1. Cardiopulmonary exercise testing at sea level and at 2250 m (N = 38).

	Sea Level	Moderate Altitude
Rest		
HR, bpm	61 ± 10	58 ± 6
SpO_2, %	99 ± 1	95 ± 2***
CaO_2, mL·dL^{-1}	19.1 ± 1.6	18.6 ± 1.7***
Mean BP, mm Hg	85 ± 10	88 ± 10
Pet CO_2, mm Hg	38 ± 2	36 ± 2***
Maximal exercise		
Mean BP, mm Hg	114 ± 16	117 ± 16
W, W	351 ± 69	317 ± 70***
$\dot{V}O_{2max}$, mL·min^{-1}·kg^{-1}	51 ± 9	43 ± 8***
HR, bpm	176 ± 10	171 ± 9**
$\dot{V}_E$, L·min^{-1}	136 ± 32	134 ± 36
Pet CO_2, mm Hg	36 ± 3	33 ± 3***
RER	1.18 ± 0.09	1.27 ± 0.12***
SpO_2, %	95 ± 3	85 ± 5***
O_2 pulse, mL per beat	22 ± 5	19 ± 5***
$\dot{V}_E/\dot{V}CO_2$ at AT	28 ± 3	30 ± 3***
$\dot{V}O_2$ at AT, % $\dot{V}O_{2max}$	68 ± 8	66 ± 8

SpO_2, arterial oxygen saturation; CaO_2, arterial O_2 content; W, maximum workload; $\dot{V}O_{2max}$, maximum O_2 uptake; $\dot{V}_E$, ventilation; SpO_2, pulse oximetry O_2 saturation; $\dot{V}CO_2$: CO_2 output.
**$P < 0.01$, moderate altitude vs sea level.
***$P < 0.001$, moderate altitude vs sea level.







Aerobic exercise capacity at sea level as well as at moderate altitude is modulated by **pulmonary vascular reserve**, but essentially determined by O_2 delivery to the tissues at moderate altitude more than at sea level.

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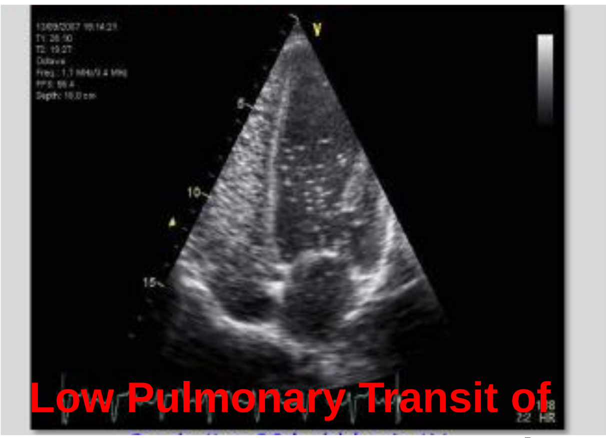
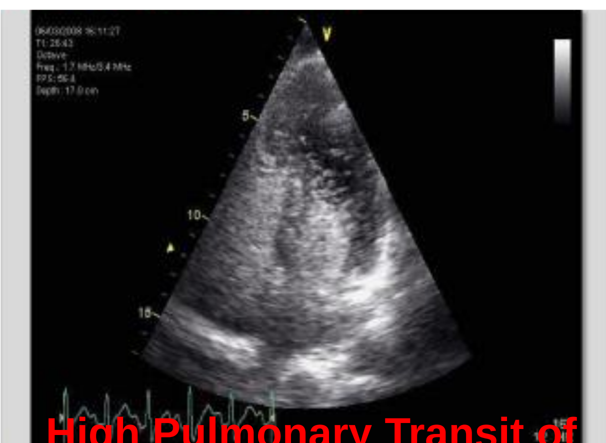
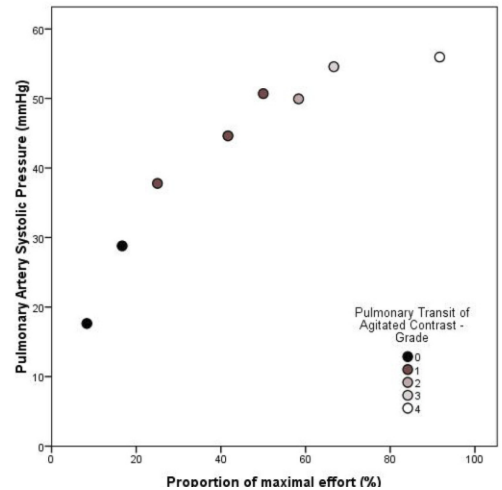
Does pulmonary circulation limits exercise capacity at sea level?



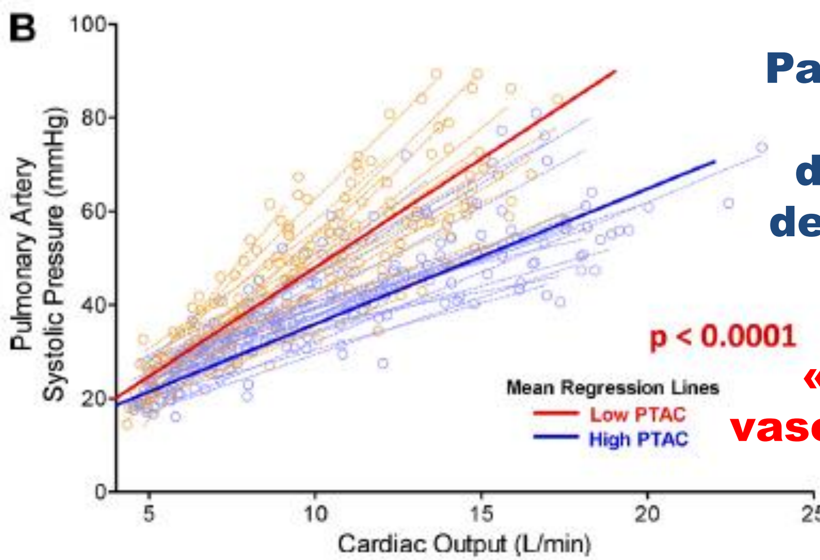
Low Pulmonary Transit of Agitated Contrast (PTAC)



High Pulmonary Transit of Agitated Contrast (PTAC)



Positive PTAC probably reflects pulmonary arteriolar and capillary distension => participation of decrease PVR at exercise



p < 0.0001

Participation of capillary distension to decreased PVR

Theory of « pulmonary vascular reserve »

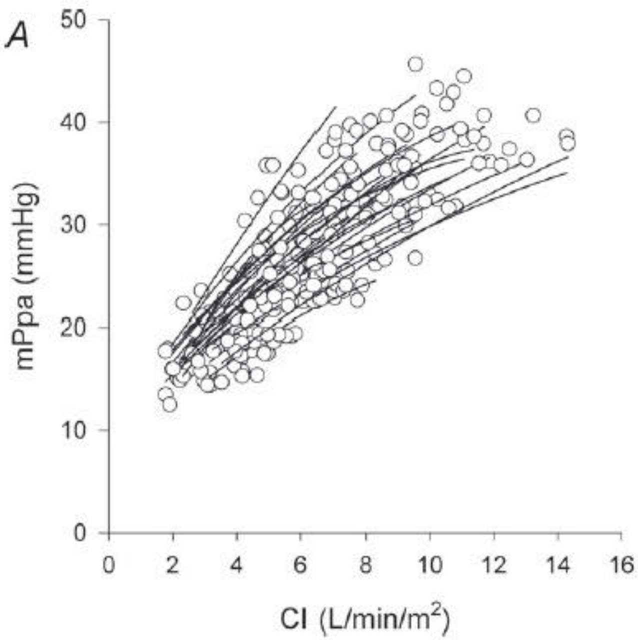
La Gerche et al. JAP, 2010

Pulmonary vascular distensibility predicts aerobic capacity in healthy individuals

Sophie Lalande, Patrick Yerly, Vitalie Faoro and Robert Naeije

In healthy individuals, higher maximal aerobic capacity is associated with greater pulmonary vascular distensibility and lower pulmonary vascular resistance

24 healthy subjects



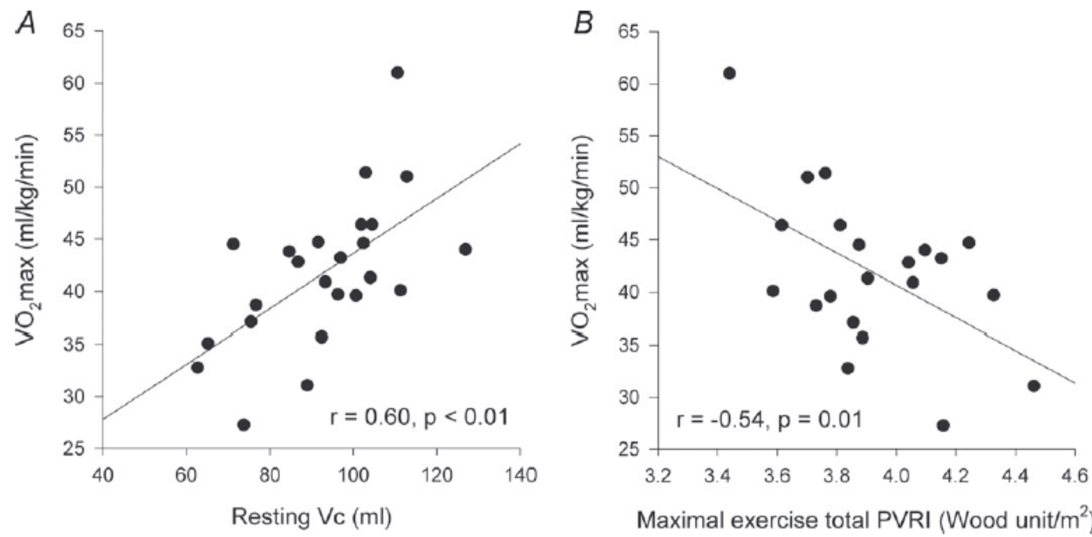


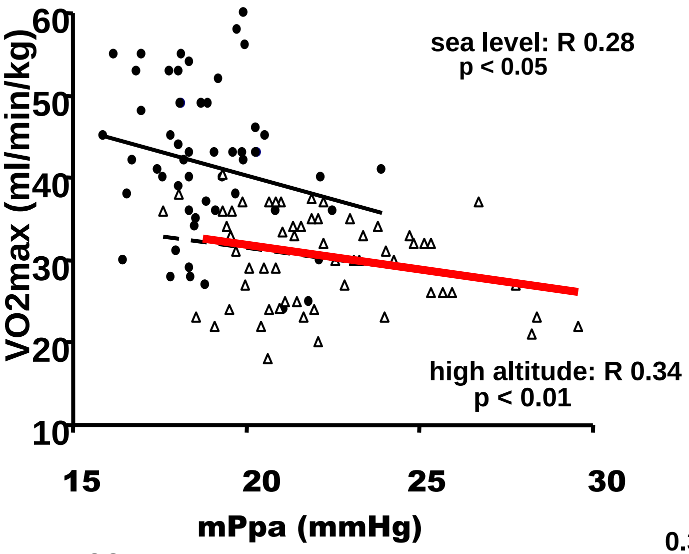
Figure 4. Relationships between maximal aerobic capacity ($\dot{V}_{O_2max}$) and its independent predictors resting values of pulmonary capillary blood volume (V_c) (*A*) and maximal exercise values of total pulmonary vascular resistance index (PVRI) (*B*)

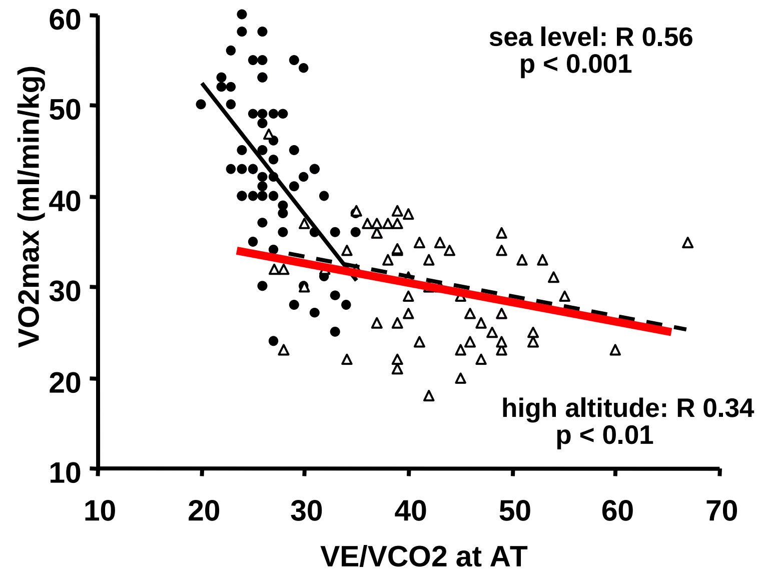
Lalande S et al. J Physiol, 2012

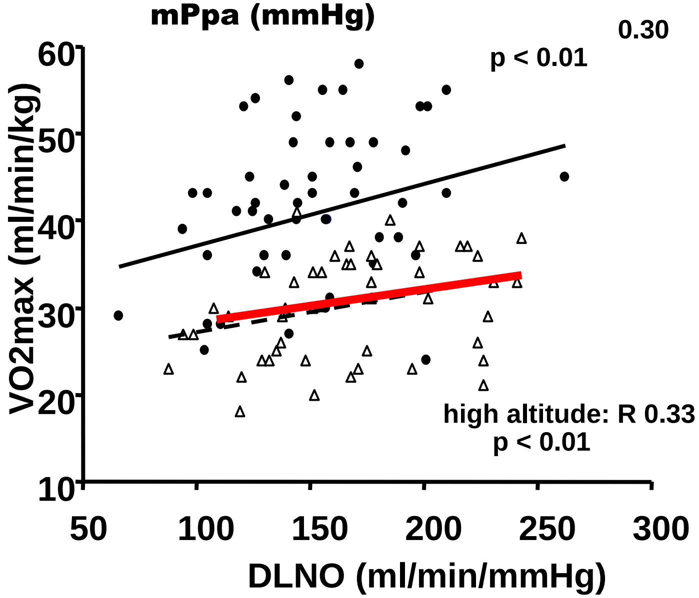
Pulmonary Vascular Reserve and Exercise Capacity at Sea Level and at High Altitude

64 healthy lowlanders
Sea level +
Altitude 4350 – 5050m

Independent predictors of aerobic capacity







At sea level and high altitude, a higher "pulmonary vascular reserve" allows for superior exercise capacity at lower ventilatory cost

Pavelescu et al. HAMB 2013

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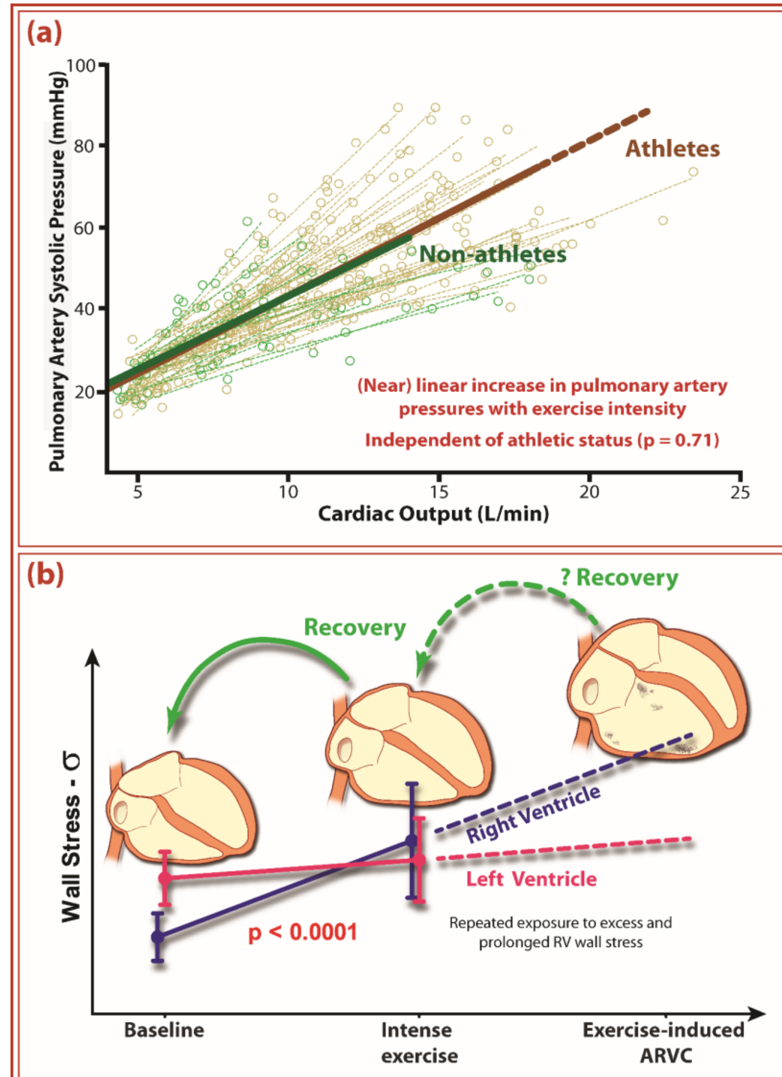
Athletic pulmonary circulation

Table 1. Right ventricular function and pumonary haemodynamics at rest and during exercise in healthy subjects versus athletes.

	Healthy		Athletes	
Parameters	Rest	Peak exercise	Rest	Peak exercise
RV function				
TAPSE (mm)	>16	⬆	–	⬆
RV ejection fraction (%)	>50	⬆	–/⇩	⬆
Pulmonary haemodynamics				
CO (L/min)	4–8	⬆	–/⇧	⬆⬆
PASP (mmHg)	<36	⬆	–/⇧	⬆⬆
RAP (mmHg)	3–5	⬆	–	⬆
mPAP (mmHg)	<25	⬆	–/⇧	⬆⬆
PVR (WU)	<3	⇩	–	⇩
PAWP (mmHg)	<15	–	–	⬆



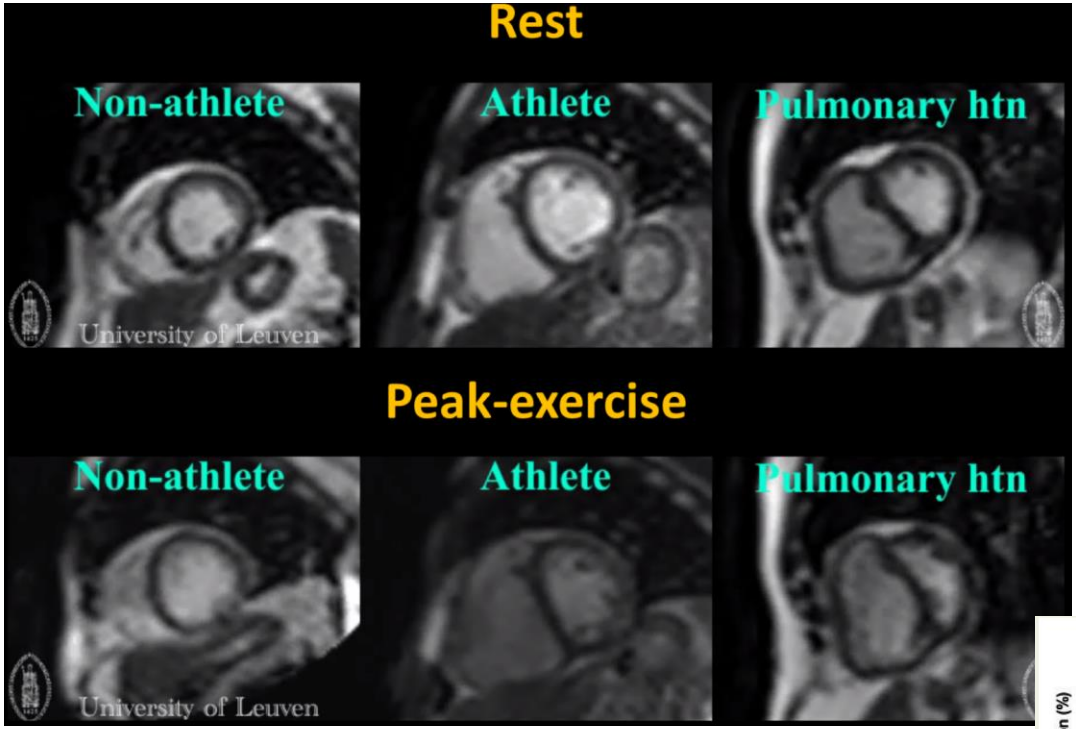
La Gerche A, Ferrara F, D'Andrea A, Bossone E. Pulmonary vascular remodelling in athletes: an anti-concept to be proved. Eur J Prev Cardiol. 2020

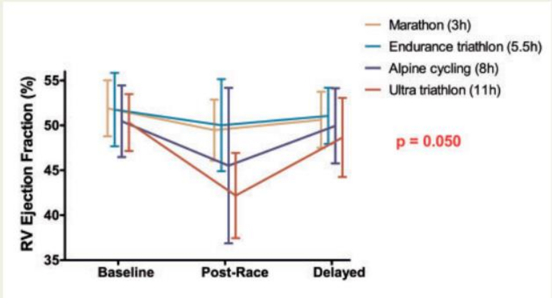
Claessen G, et al. JACC Cardiovasc Imaging 2016

ULB

Exercise and the right ventricle: a potential Achilles' heel

Andre La Gerche[1,2,3]*, Dhrubo J. Rakhit[1,4], and Guido Claessen[2]





Cardiac MRI during exercise: RV dilatation and diastolic i

La Gerche, Circ Cardiovasc Imag 2013; 6: 329-38

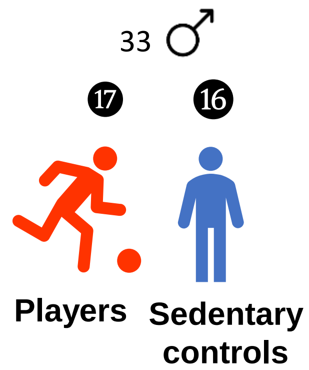
Repeated or high increase in RV afterload during high-intensity exercise may become a critical constraint

Increased RV load/afterload => RV dilation (+ delay in contraction) => septal shift toward LV => attenuate early diastolic filling of the LV => further increase LA pressures => **Arrhythmogenic RV cardiomyopathy?**

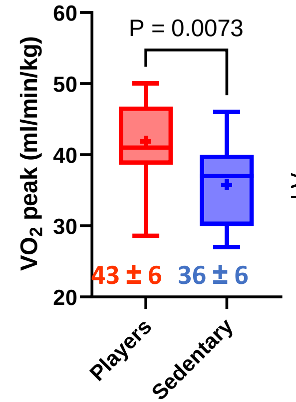
LaGerche, et al. Cardiovasc Research 2017

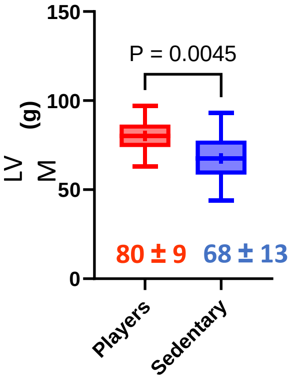
Increased pulmonary vascular distensibility

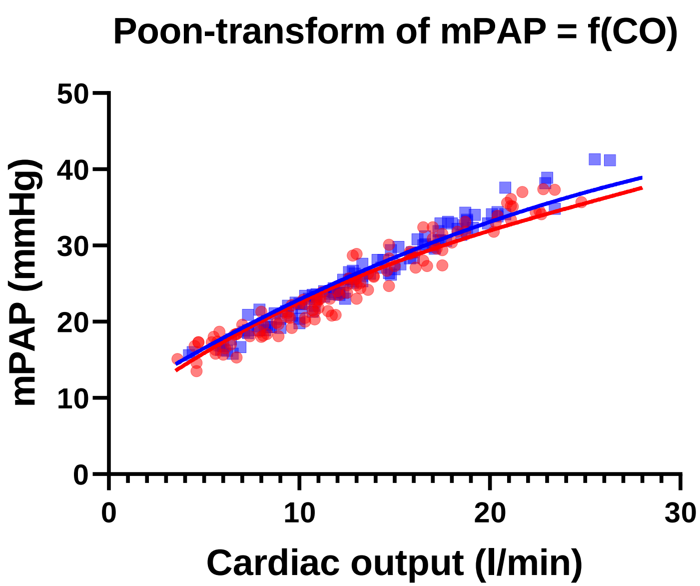
POPULATION

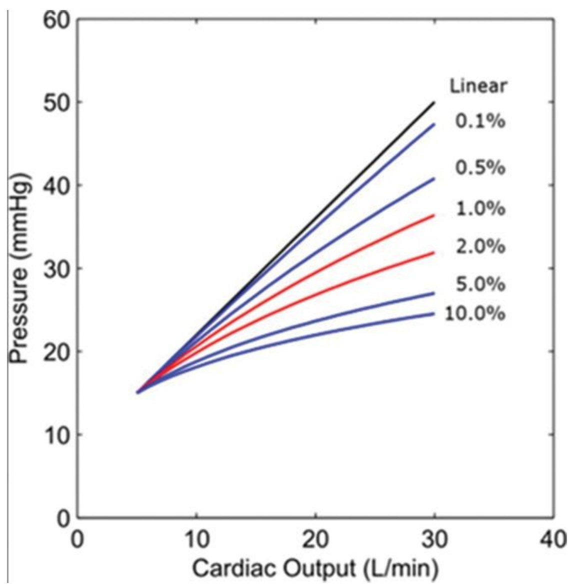


	PLAYERS	SEDENTARY
Height (cm)	181,5 ± 6,8	179,5 ± 7,4
Weight (kg)	77,2 ± 5,5	75,1 ± 9,7
Age (years)	24 ± 3	24 ± 3
BMI	23 ± 1	23 ± 3
BSA (m²)	1,98 ± 0,1	1,93 ± 0,15









Curvi-linear model:

$$Pa = \frac{[(1 + \alpha Pv)^5 + 5\alpha R_0 \dot{Q}]^{1/5} - 1}{\alpha}$$

Sedentary: R0 = 2.776 mmHg.min/l; α = 1.09%

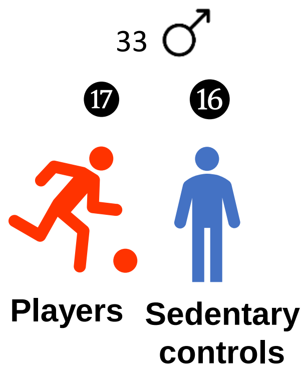
Players: R0 = 2.957 mmHg.min/l; α = 1.28%

Linehan JAP 1985

Carpentier M et al. 2023

Increased pulmonary vascular distensibility

POPULATION



	PLAYERS	SEDENTARY
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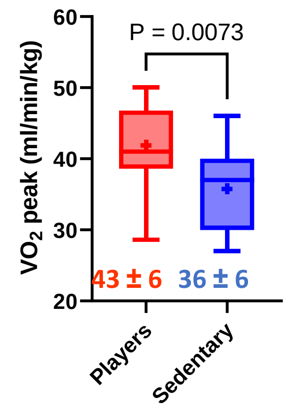
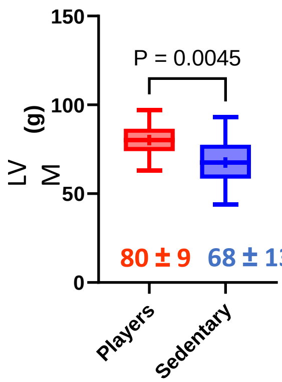
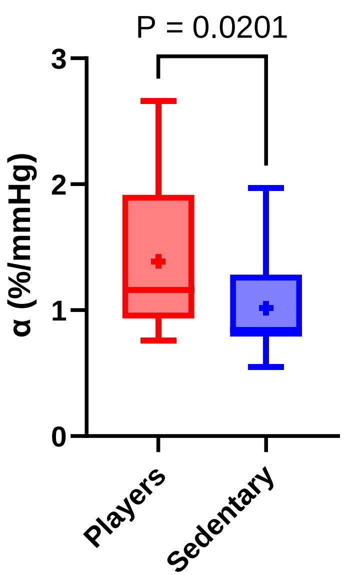
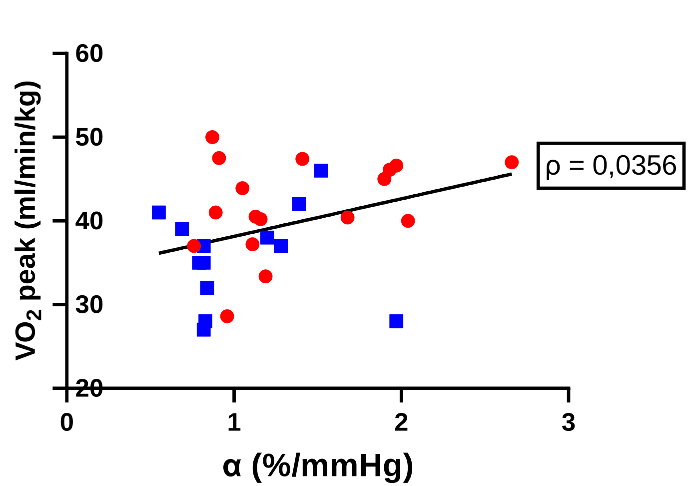
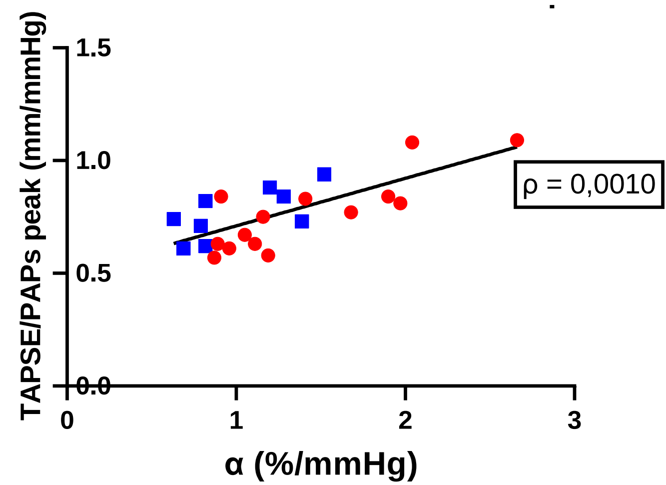
BSA (m²)	1,98 ± 0,1	1,93 ± 0,15











Higher α_{pulm} allows a better RV-arterial coupling at exercise which may be an advantage to reach higher aerobic capacity

Carpentier M et al. 2023

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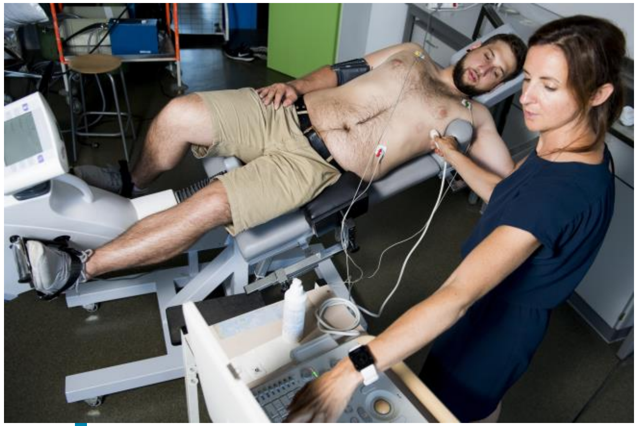
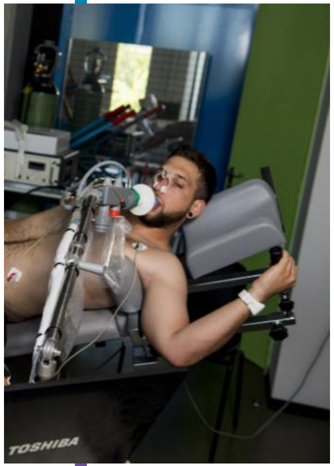
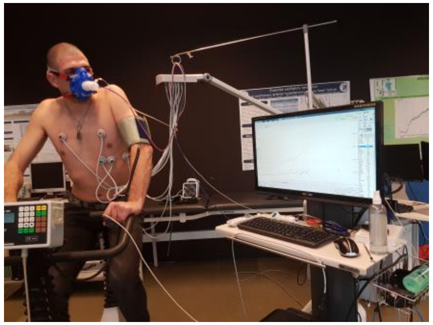
ONGOING PROJECTS



- Longitudinal effects of aerobic training (HIIT) on the RV-pulmonary vascular unit





- Effects of menstrual cycle and contraception on the cardio-vascular adaptation to exercise

- Migrated Sherpas to Belgium: first and second generation

CONCLUSION

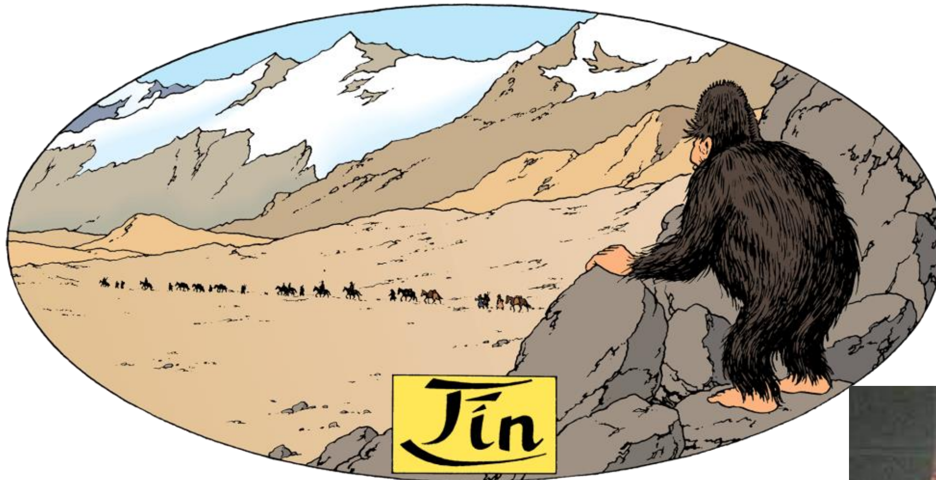
FIENDS

- Well **adapted** to moderate to intense physical exercise, without extreme elevation of Pap, thanks to its arteriolar **distensibility** and **recruitability**.
- HPV will lead to **moderate HP**
- Wide **pulmonary vascular reserve** contributes to higher aerobic capacity with better gaz exchange
- **Sherpas** have little HPV and large Vc
- Athletes have a higher pulmonary vascular **distensibility**

FOES

- Wide inter-subject **variability**
- Limits exercise capacity, particularly at **high-altitude**
- Suceptible subjects
- **Andeans** have higher PVR < increased in **CMH**
- But high **volume of training** at high Q may affect RV function

Thank you!



The team…

Pr Van De Born

Pr Moraine

Pr Naeije

Cyril Tordeur

Jérémy Rabineau

Paniz Balali

Elza Abdessater

Marine Carpentier

Bert Celie

Laboratory of Cardiorespiratory Exercise Physiology, FSM, ULB
Laboratory of Physics and Physiology – Dpt Cardiology, Erasme Hospital

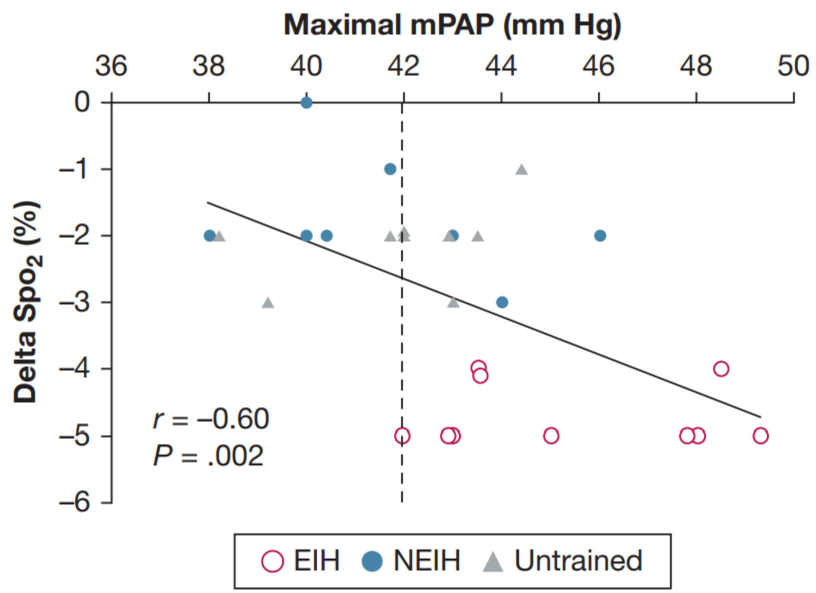


Figure 2 – *Correlation for mean mPAP with ΔSpo$_2$ during exercise. The solid line represents the linear regression of the present correlation (*r = *–0.60;* P = *.002). This graphic illustrates that an mPAP value exceeding a threshold of 42 mm Hg (long dashed line) at maximal exercise is reached in all athletes with arterial oxygen desaturation. mPAP = maximal pulmonary arterial pressure. See Figure 1 legend for expansion of other abbreviations.*

Training and PH

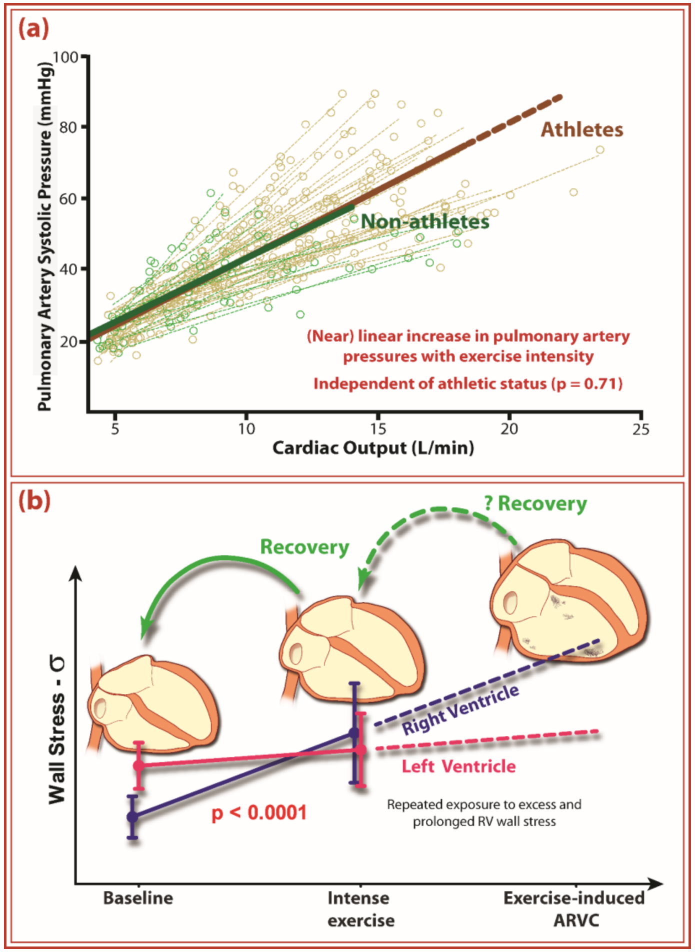
- Exercise-induced pulmonary vasoconstriction may occur in some patients with pulmonary hypertension (Kulik 1983).
- However, exercise in patients with pulmonary hypertension can lead to sharp increases in pulmonary artery pressure and a limitation of aerobic capacity (Naeije 2012).
- Aerobic exercise training has been shown to be effective in reducing fatigue and increasing physical activity in patients with pulmonary arterial hypertension (PAH) (Weinstein 2013).
- It may also have a beneficial effect on PAH by attenuating arterial pulmonary hypertension (Madonna 2016).
- Despite potential risks, exercise training has been found to improve exercise capacity, quality of life, muscle function, and pulmonary circulation in PAH patients (Vecchia 2018).
- The optimal intensity of aerobic exercise for improving exercise capacity and quality of life in PAH patients is still under investigation (Seo 2021).

Athletic pulmonary circulation remodeling

Table 1. Right ventricular function and pumonary haemodynamics at rest and during exercise in healthy subjects versus athletes.

Parameters	Healthy Rest	Healthy Peak exercise	Athletes Rest	Athletes Peak exercise
RV function				
TAPSE (mm)	>16	⬆	–	⬆
RV ejection fraction (%)	>50	⬆	–/⇩	⬆
Pulmonary haemodynamics				
CO (L/min)	4–8	⬆	–/⇧	⬆⬆
PASP (mmHg)	<36	⬆	–/⇧	⬆⬆
RAP (mmHg)	3–5	⬆	–	⬆
mPAP (mmHg)	<25	⬆	–/⇧	⬆⬆
PVR (WU)	<3	⇩	–	⇩
PAWP (mmHg)	<15	–	–	⬆

CO: cardiac output; mPAP: mean pulmonary artery pressure; PASP: pulmonary artery systolic pressure; PAWP: pulmonary artery wedge pressure; PVR: pulmonary vascular resistance; RAP: right atrial pressure; RV: right ventricular; TAPSE: tricuspid annular plane systolic exertion; WU: woods unit; –: similar to healthy subjects; arrows black: higher; arrows white: slightly higher or reduced.



Claessen G, La Gerche A, Voigt JU, et al. Accuracy of echocardiography to evaluate pulmonary vascular and RV function during exercise. JACC Cardiovasc Imaging 2016; 9: 532–543.

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CONCLUSIONS

FRIENDS

FOES

RECRUTEMENT and DISTENSION

High altitude dwellers and sojourners who are able to maintain a higher V
“pulmonary vascular reserve” defined as, a combination of low pulmona
resistance and high lung diffusing capacity.

Wide inter-individual variation

The aerobic exercise profile of life-long high altitude adaptation observed
Quechua includes a combination of:
- **markedly increased lung diffusion capacity**
- **decreased ventilatory response**

With, as difference;
- **higher hemoglobin in Quechua**