On the potential increase of the oxidative stress status in patients with abdominal aortic aneurysm (Redox Report 17: 139-144, 2012)

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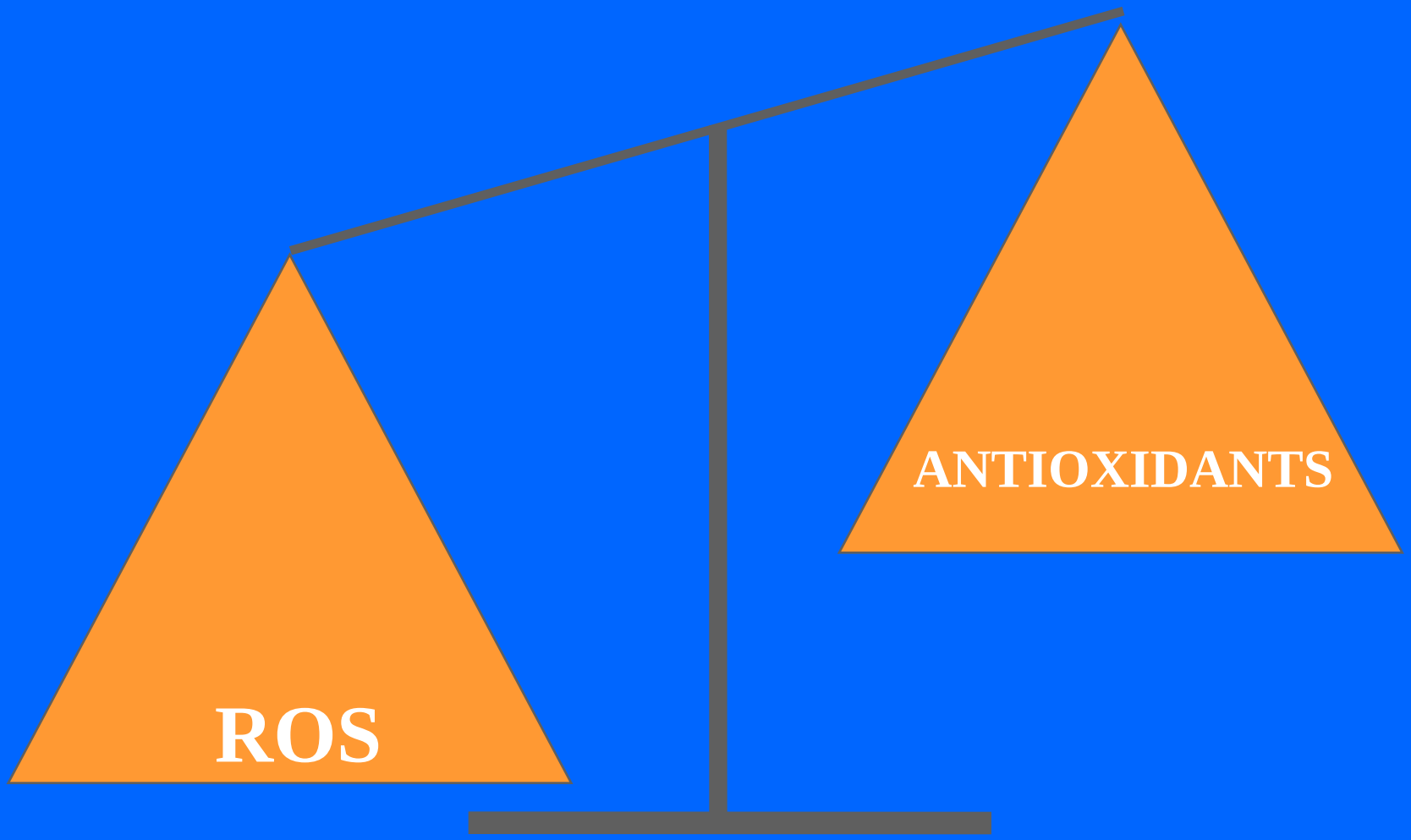
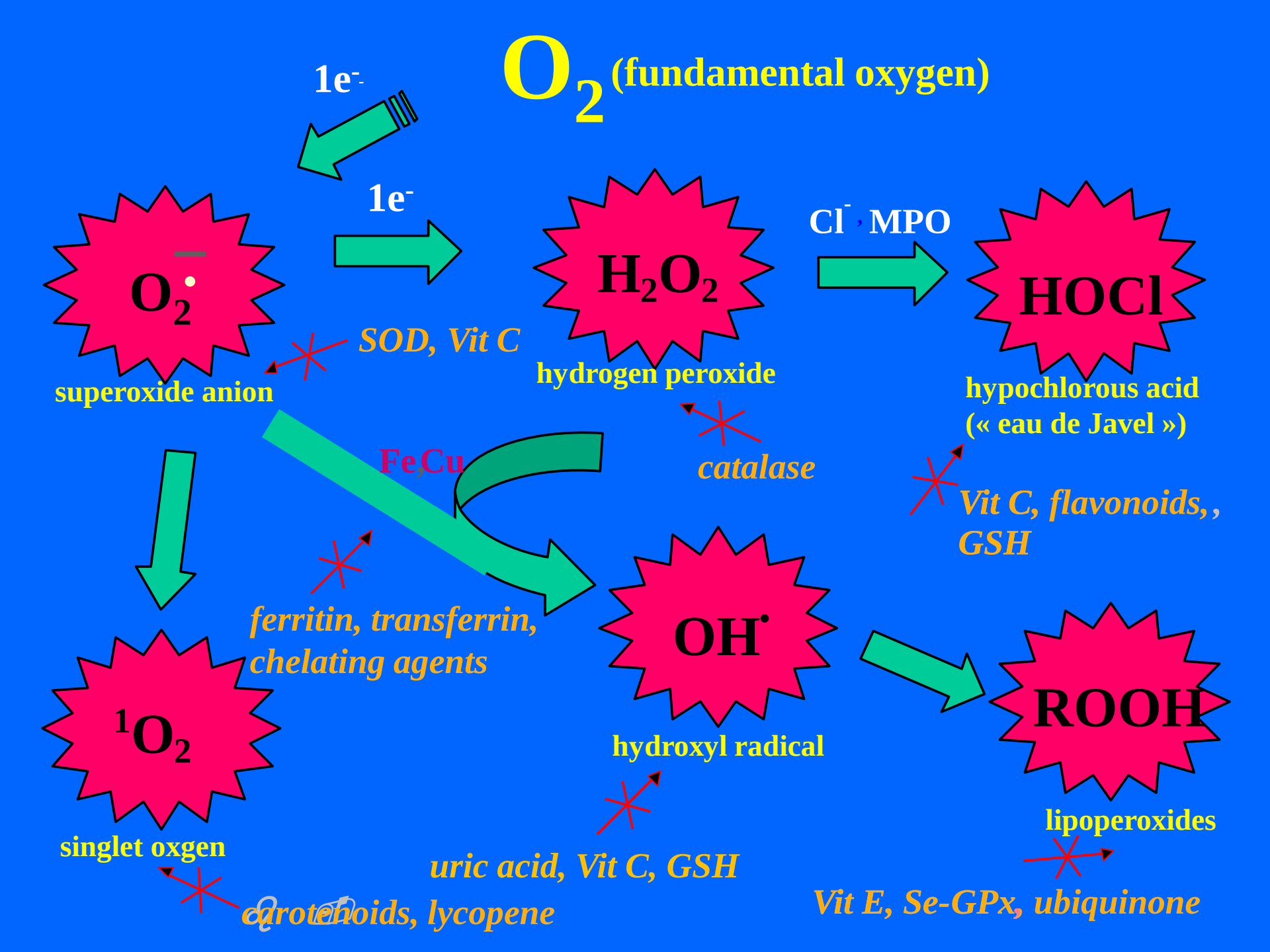
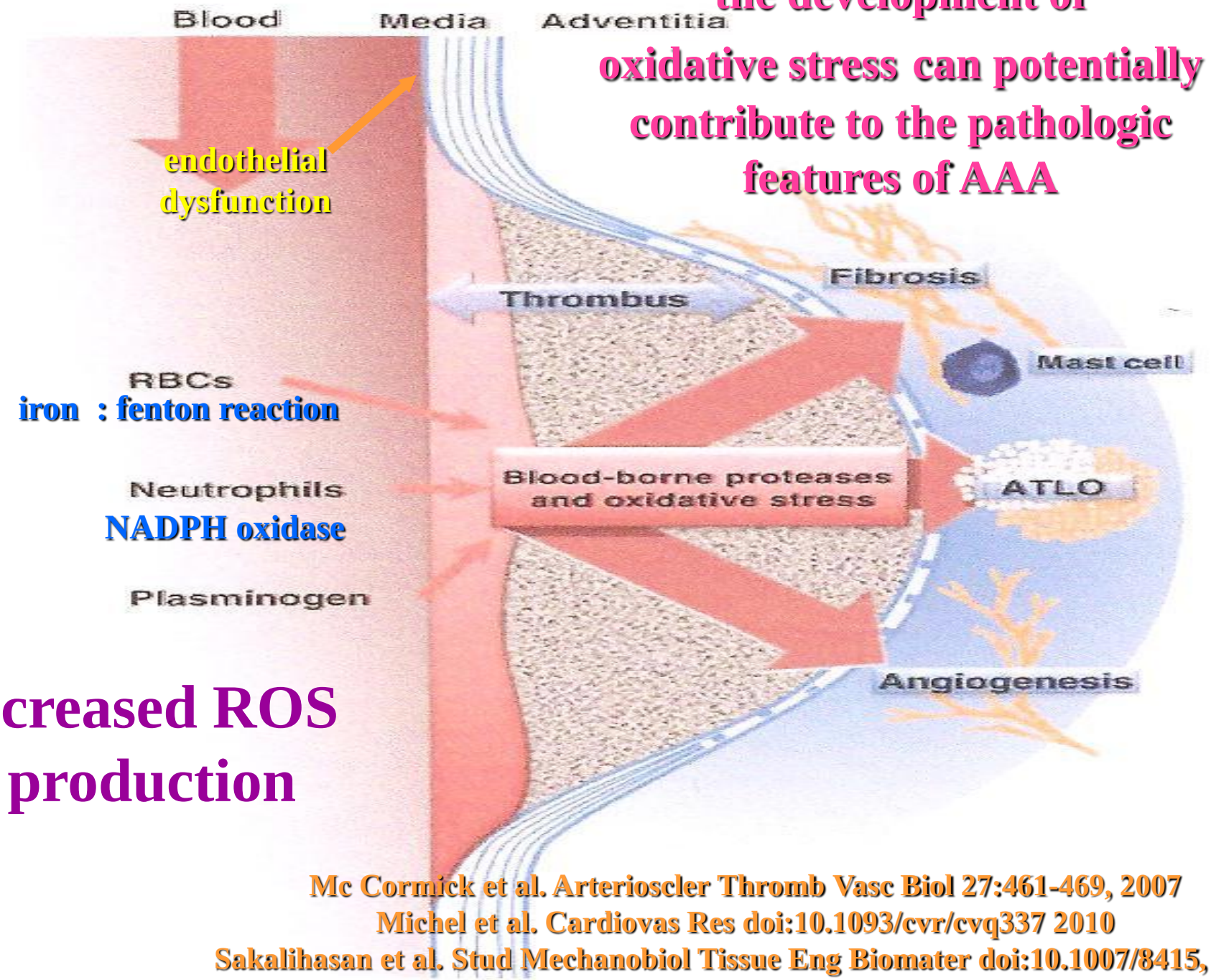
OXIDATIVE STRESS (OS)



imbalance between oxidants (reactive oxygen species or ROS derived from oxygen) and antioxidants in favour of the oxidants, leading to a disruption of redox signalling and/or molecular damage.


O_2 (fundamental oxygen)
1e-
1e-
$O_2^{\bullet -}$
superoxide anion
SOD, Vit C
H_2O_2
hydrogen peroxide
catalase
Cl^-, MPO
HOCl
hypochlorous acid
(« eau de Javel »)
Vit C, flavonoids, , GSH
Fe,Cu
ferritin, transferrin, chelating agents
$OH^{\bullet}$
hydroxyl radical
uric acid, Vit C, GSH
ROOH
lipoperoxides
Vit E, Se-GPx, ubiquinone
$^1O_2$
singlet oxgen
carotenoids, lycopene

the development of oxidative stress can potentially contribute to the pathologic features of AAA



increased ROS production

Mc Cormick et al. Arterioscler Thromb Vasc Biol 27:461-469, 2007
Michel et al. Cardiovas Res doi:10.1093/cvr/cvq337 2010
Sakalihasan et al. Stud Mechanobiol Tissue Eng Biomater doi:10.1007/8415, 2010

could the local OS in AAA tissues be detected in the systemic circulation of the patients ?

only a few number of studies available

Sakalihasan et al

Ann N.Y. Acad Sci 1996; 800:278-282.

first report of decreased vitamin E level in AAA

Martinez – Pinna R et al,

Arterioscler Thromb Vasc Biol 2011; 31:935-943.

peroxiredoxin-1 as a novel biomarker of AAA.

variable	Control group (n = 18; 67 years)	AAA patients (n = 27; 70 years)
Gender		
Men	12	23
Women	6	4
Smoking		
No	14	17
Yes	3	10
Fruit and vegetables	3.5 servings	3.76 servings
Diabetes		
No	16	24
Yes	1	3
Medication		
statins		
No	14	9
yes	3	18

fasted for at least 12 hours before blood sampling

not allowed to drink fruit juice and to perform physical activity

not under antioxidant medication

blood immediately centrifuged after sampling and plasma or serum kept at – 80°C until analysis

investigated blood OS biomarkers

1° antioxidants

vitamin C

α and γ - tocopherol (vitamin E)

β- carotene

reduced glutathione /oxidized glutathione

ubiquinone (CoQ10)

glutathione peroxidase (GPx)

thiol proteins

2° trace elements

Se, Cu, Zn, ratio Cu/Zn

Cu : prooxidant (« Fenton like reaction »)

Zn : inhibition of Cu prooxidant effect

investigated OS parameters

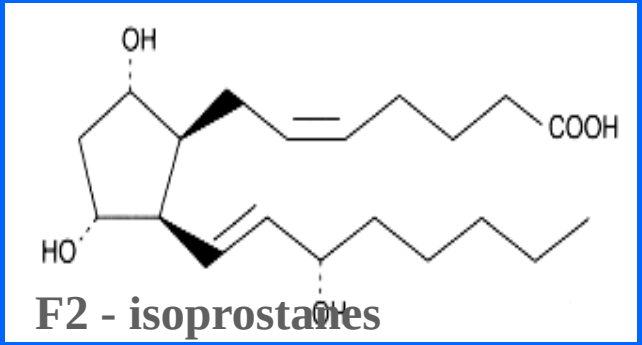
3° markers of oxidative damages to lipids

lipid peroxides (not MDA or TBAR's)

oxidized LDL (ox-LDL)

antibodies against ox-LDL

isoprostanes *(gold standard)*



F2 - isoprostanes

4° marker of neutrophils activation

myeloperoxidase (MPO)

Variable	control group (n = 18)	AAA patients (n = 27)	P value
vitamin C (µg/mL)	10.9 ± 3.85	8.43 ± 2.98	0.035
α - tocopherol (µg/mL)	14.5 ± 3.34	12.1 ± 3.01	0.021
γ - tocopherol (µg/mL)	0.81 ± 0.38	0.80 ± 0.43	0.97
β - carotene (mg/L)	0.29 ± 0.17	0.16 ± 0.14	0.032
thiol proteins (µM)	311 ± 38	328 ± 44.7	0.19
ubiquinone (mg/L)	0.84 ± 0.32	0.64 ± 0.22	0.037
copper (mg/L)	0.88 ± 0.12	0.90 ± 0.28	0.78
zinc (mg/L)	0.79 ± 0.14	0.69 ± 0.13	0.022
copper/zinc ratio	1.14 ± 0.21	1.33 ± 0.40	0.093
selenium (µg/L)	92.7 ± 16.4	77.8 ± 20.3	0.022

after adjustment for smoking and diet

Variable	control group (n = 18)	AAA patients (n = 27)	P value
lipid peroxides (µM)	520 ± 228	570 ± 331	0.79
oxidized LDL (ng/mL)	756 ± 964	231 ± 231	0.019
antibodies against oxidized LDL (UI/L)	263 ± 283	208 ± 240	0.42
isoprostanes (ng/mL)	1.01 ± 0.66	1.40 ± 0.77	0.18
total glutathione (µM)	852 ± 203	943 ± 175	0.1
oxidized glutathione (µM)	1.01 ± 0.67	4.73 ± 11.8	0.17
glutathione peroxidase (UI/g Hb)	51.5 ± 9.97	51.3 ± 10.9	0.93
myeloperoxidase (ng/mL)	22.0 ± 24.4	51.4 ± 83.8	0.11

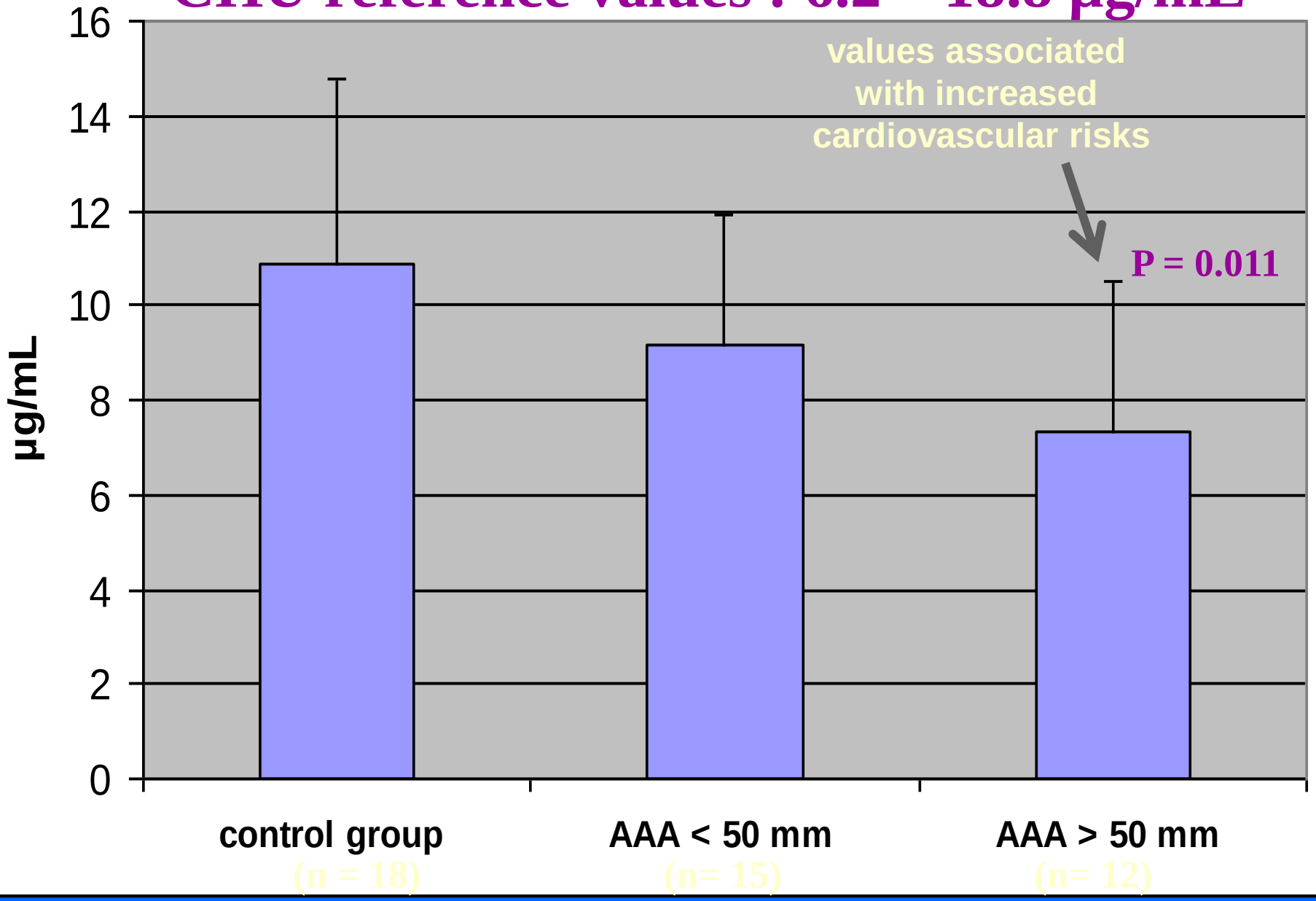
after adjustment for smoking and diet

is there a relationship between the alteration of OS status and the aneurysm diameter ?

only a few number of studies available

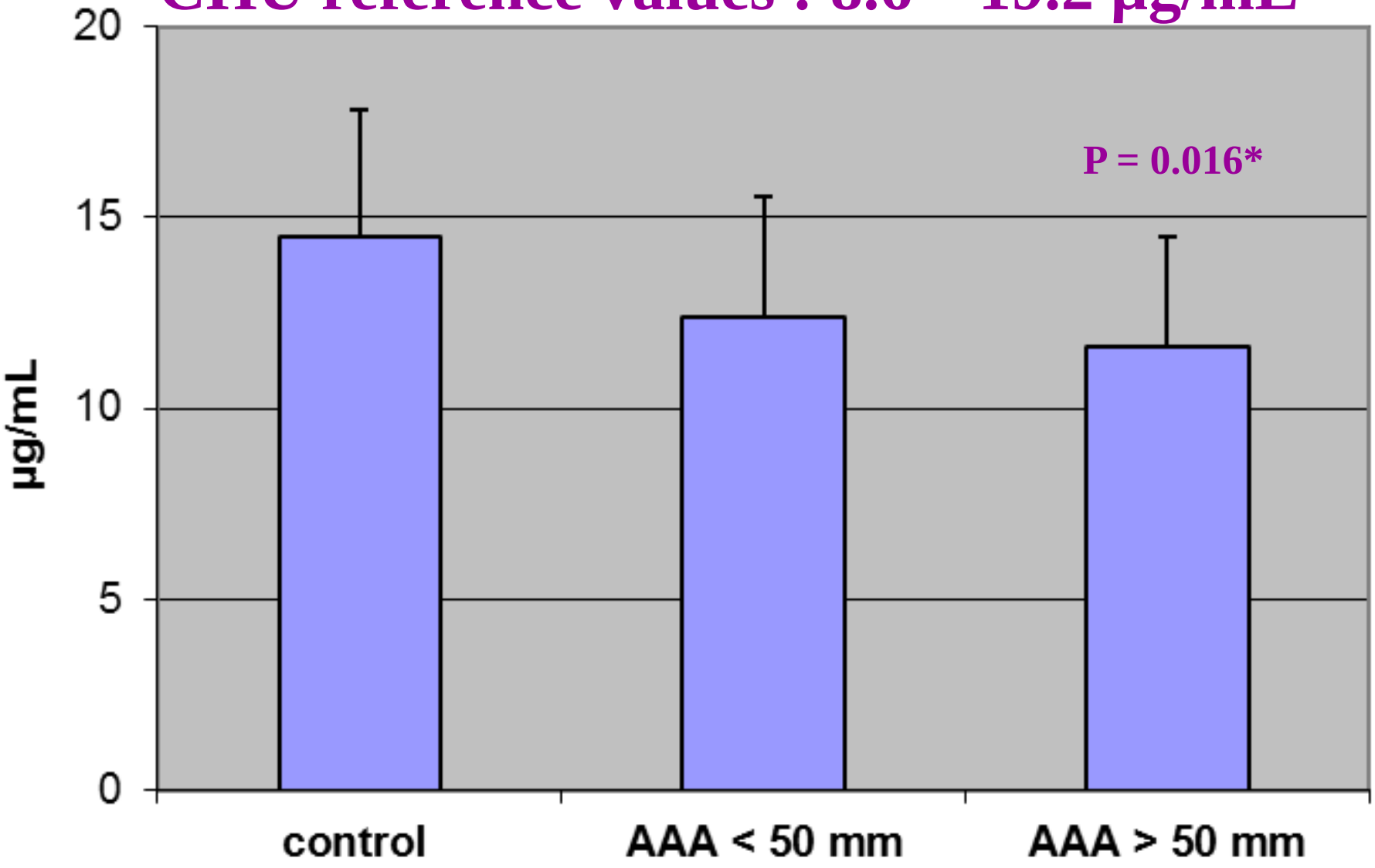
vitamin C

CHU reference values : 6.2 – 18.8 µg/mL



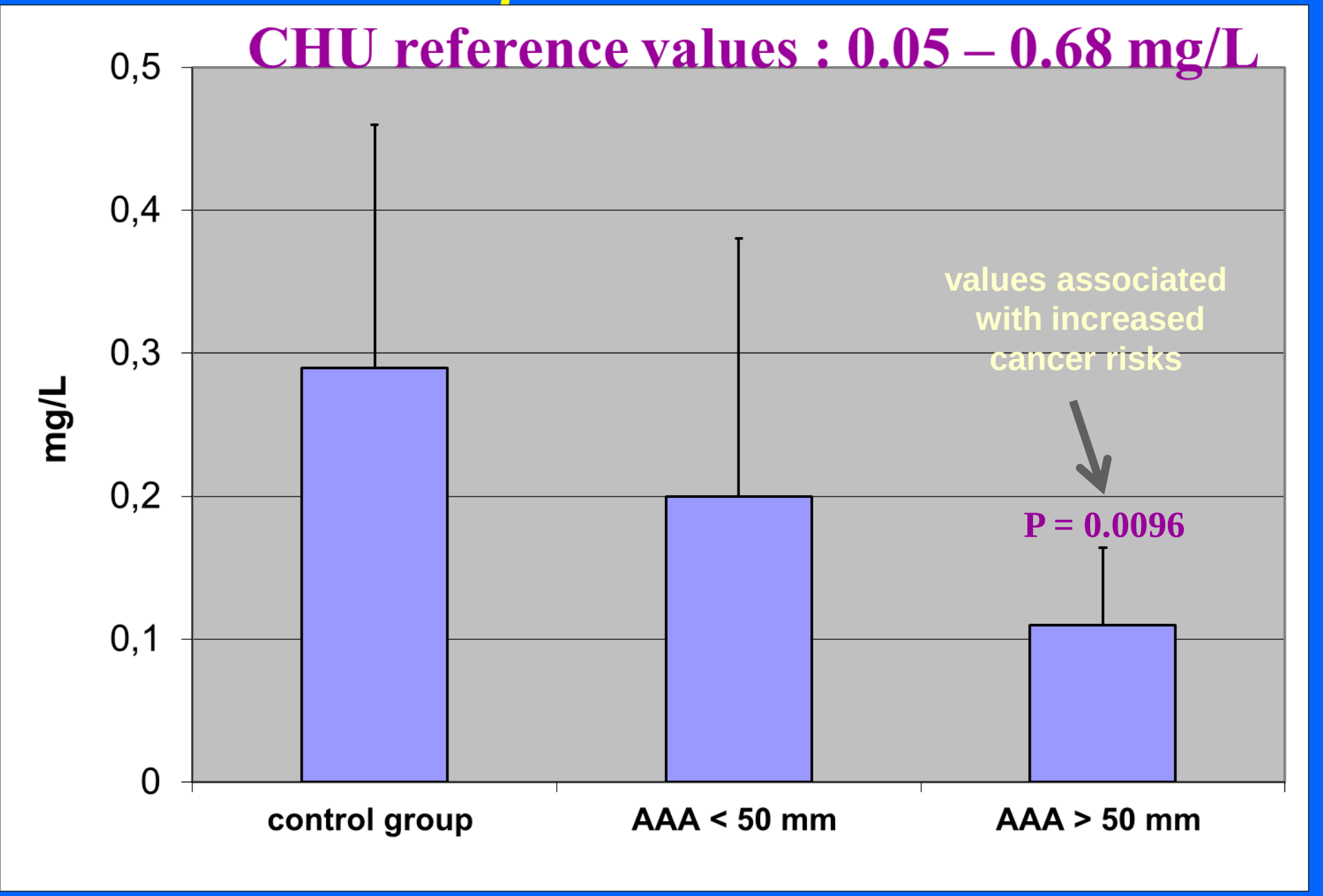
vitamin E (α – tocopherol)

CHU reference values : 8.6 – 19.2 µg/mL



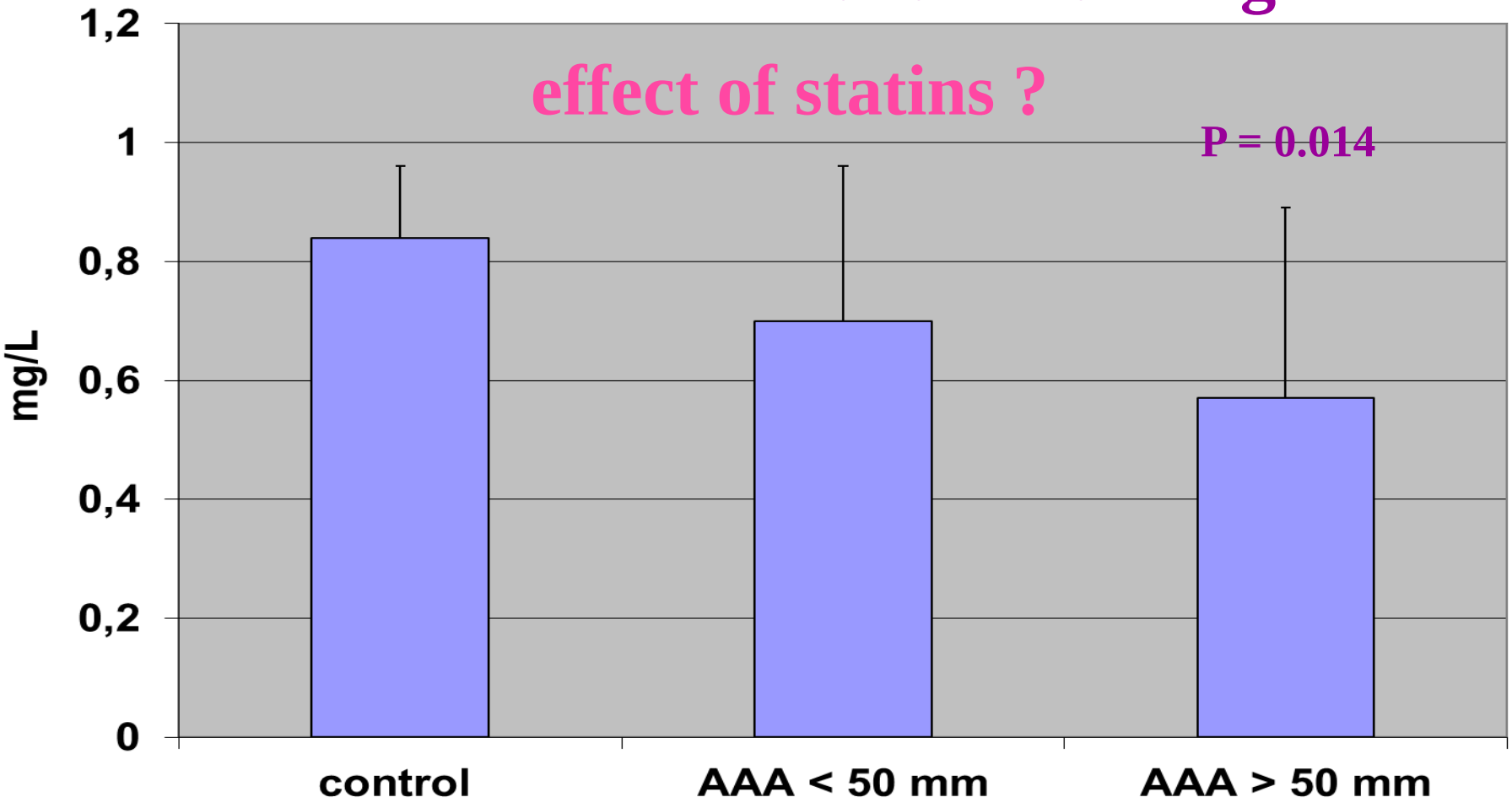
* not significant after standardization to cholesterol

β- carotene


CHU reference values : 0.05 – 0.68 mg/L
0,5
0,4
0,3
0,2
0,1
0
mg/L
values associated with increased cancer risks
P = 0.0096
control group
AAA < 50 mm
AAA > 50 mm

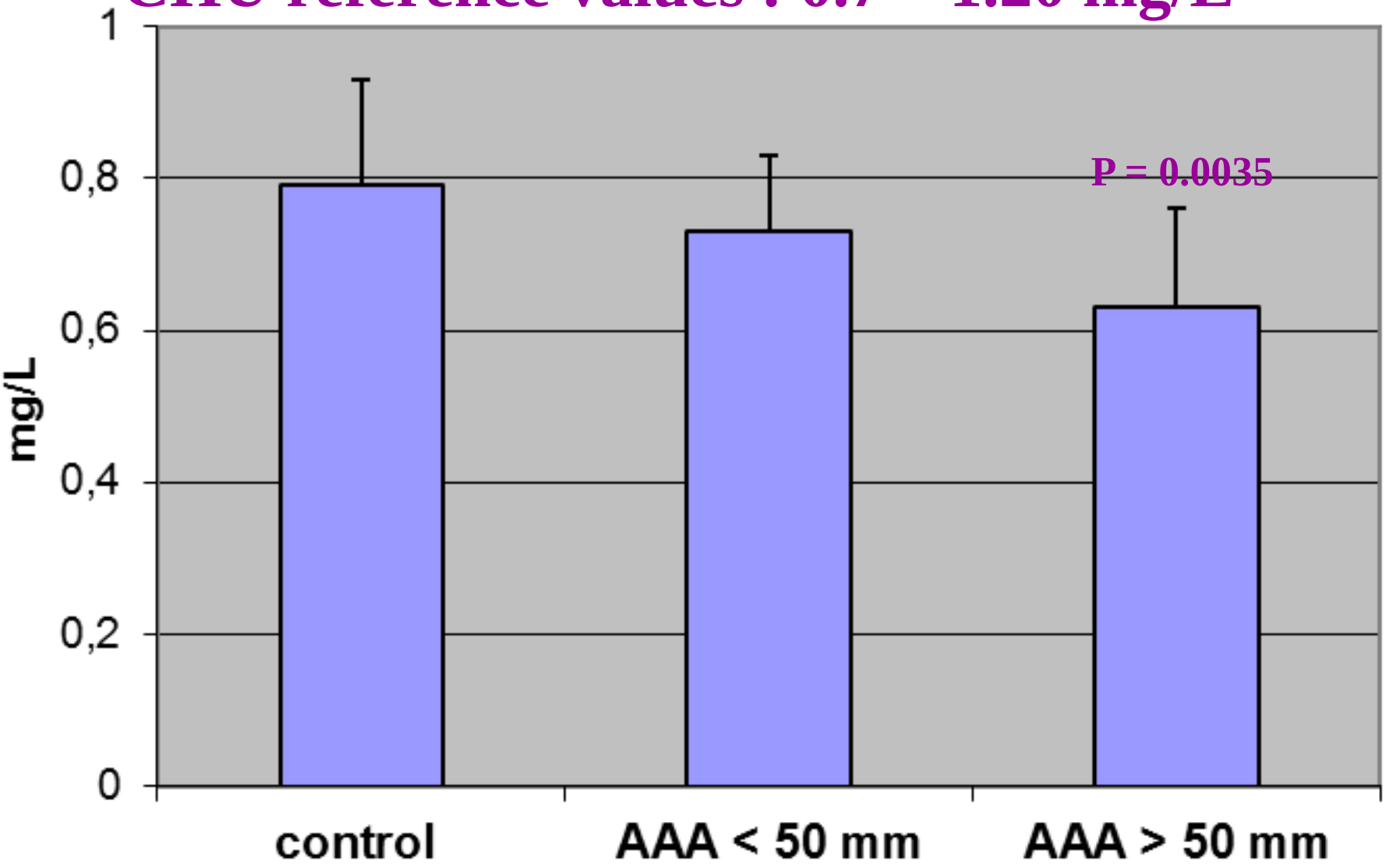
ubiquinone or CoQ10 (implicated in energy production)

CHU reference values : 0.3 – 1.39 mg/L



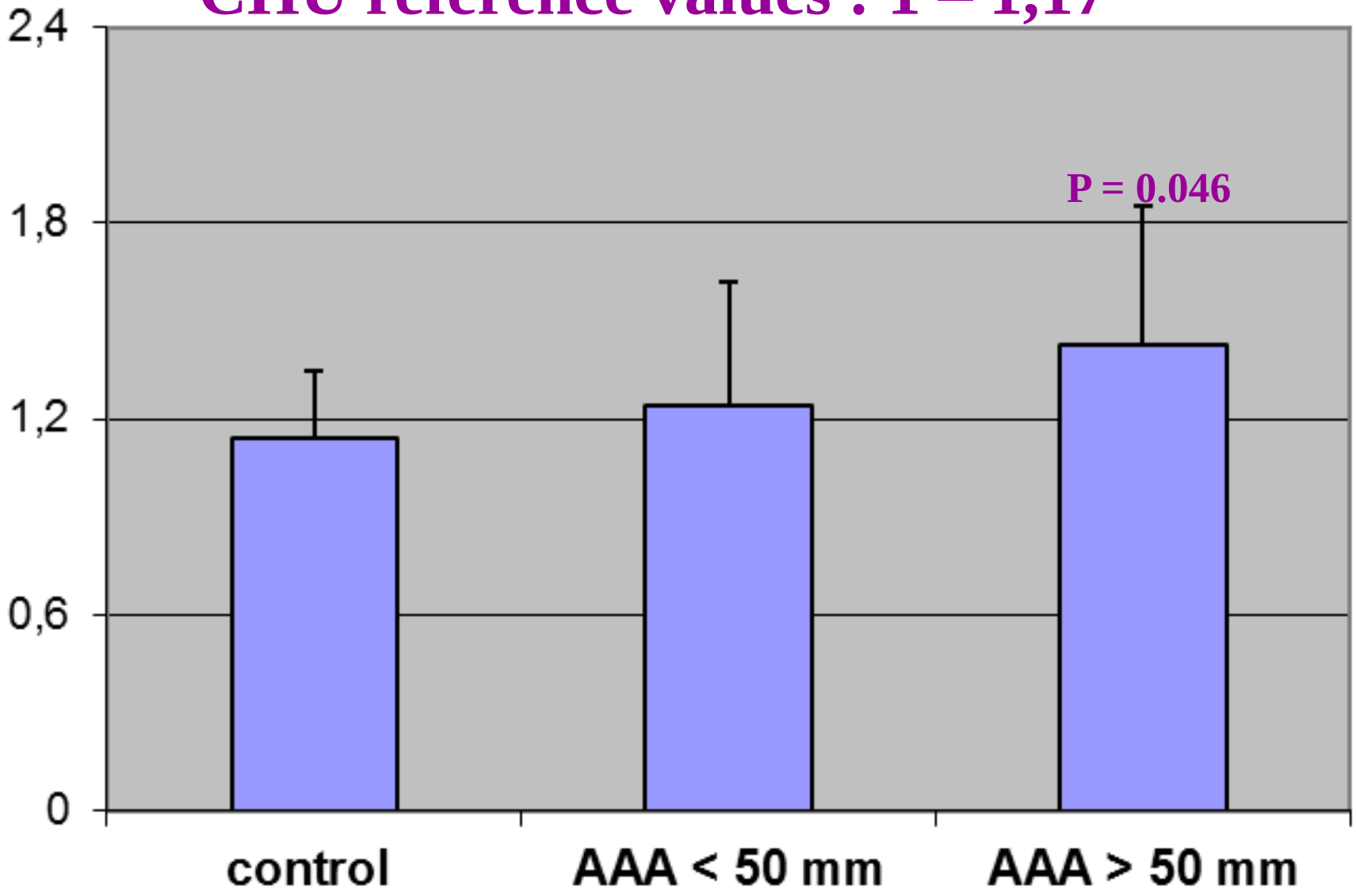
zinc

CHU reference values : 0.7 – 1.20 mg/L

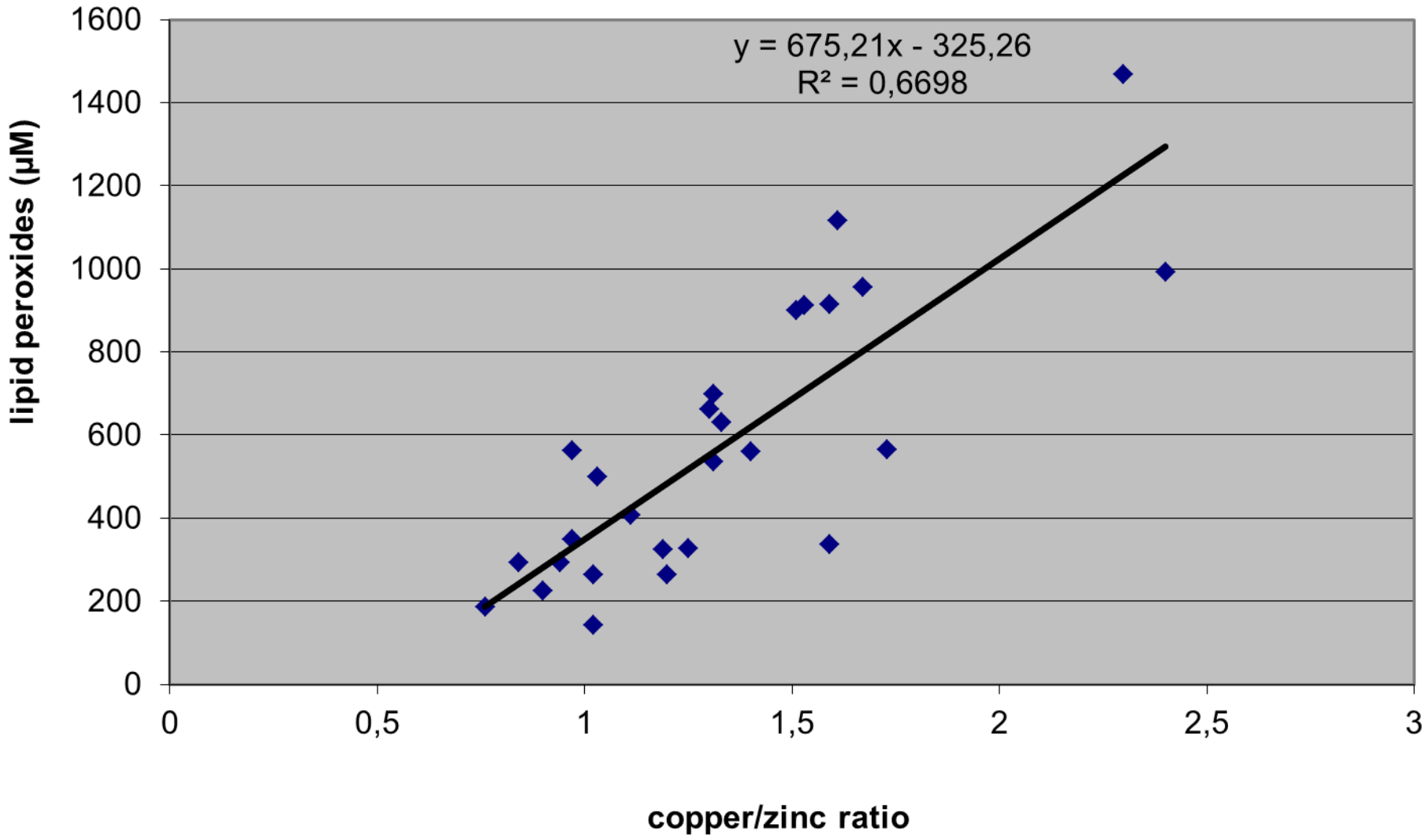


copper/ zinc (prooxidant marker)

CHU reference values : 1 – 1,17

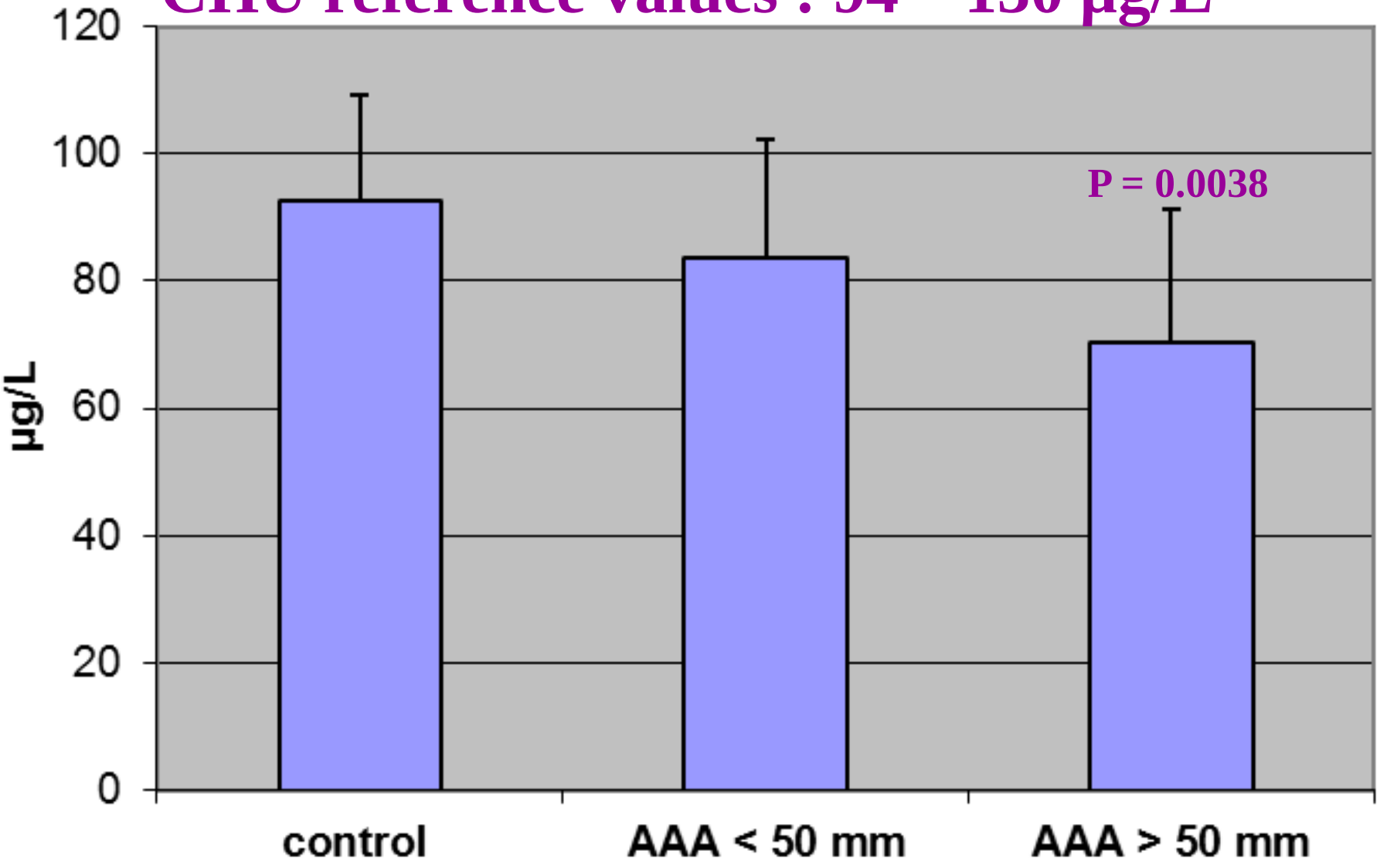


relationship between Cu/Zn ratio and blood lipid peroxides in AAA patients

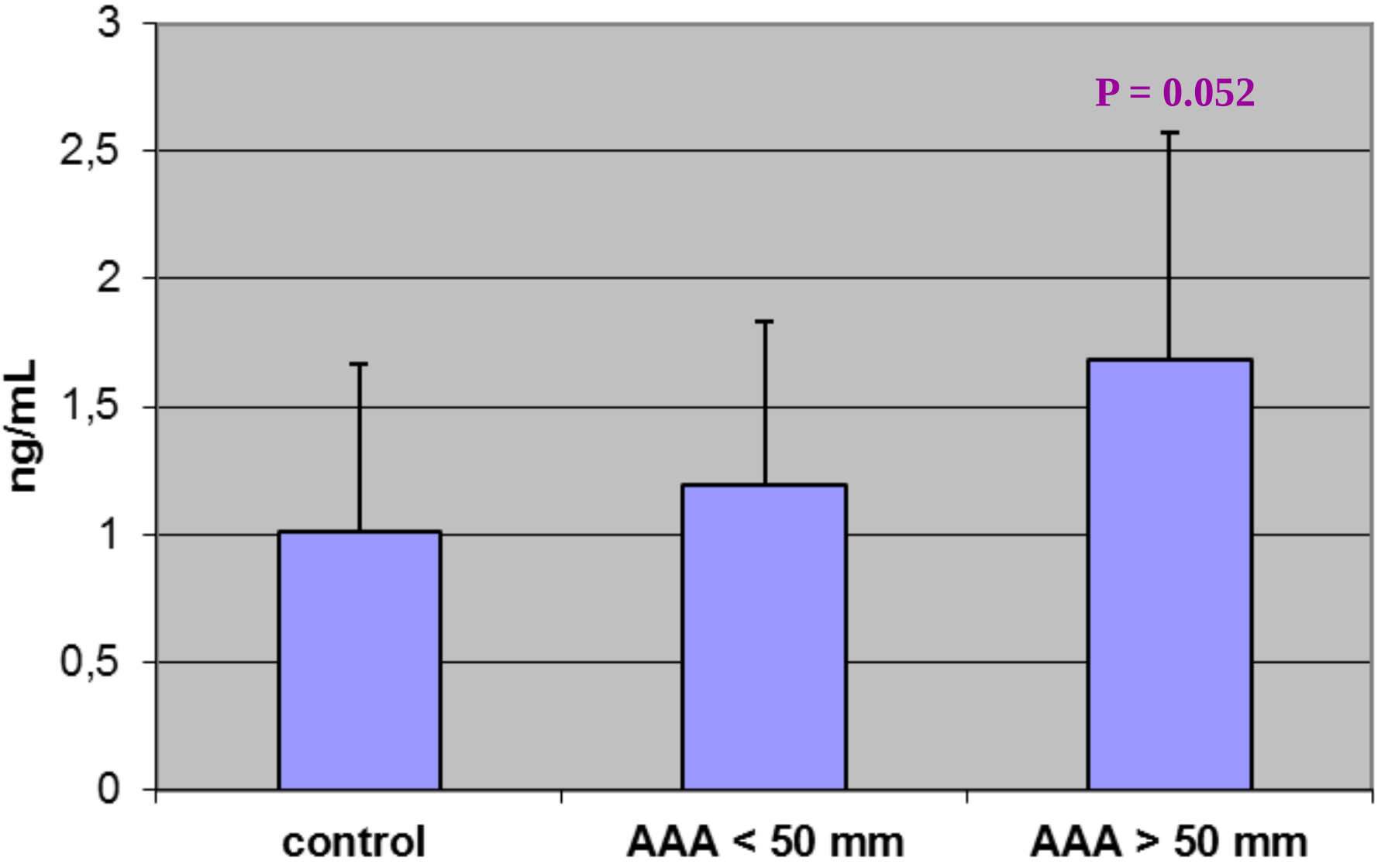


selenium

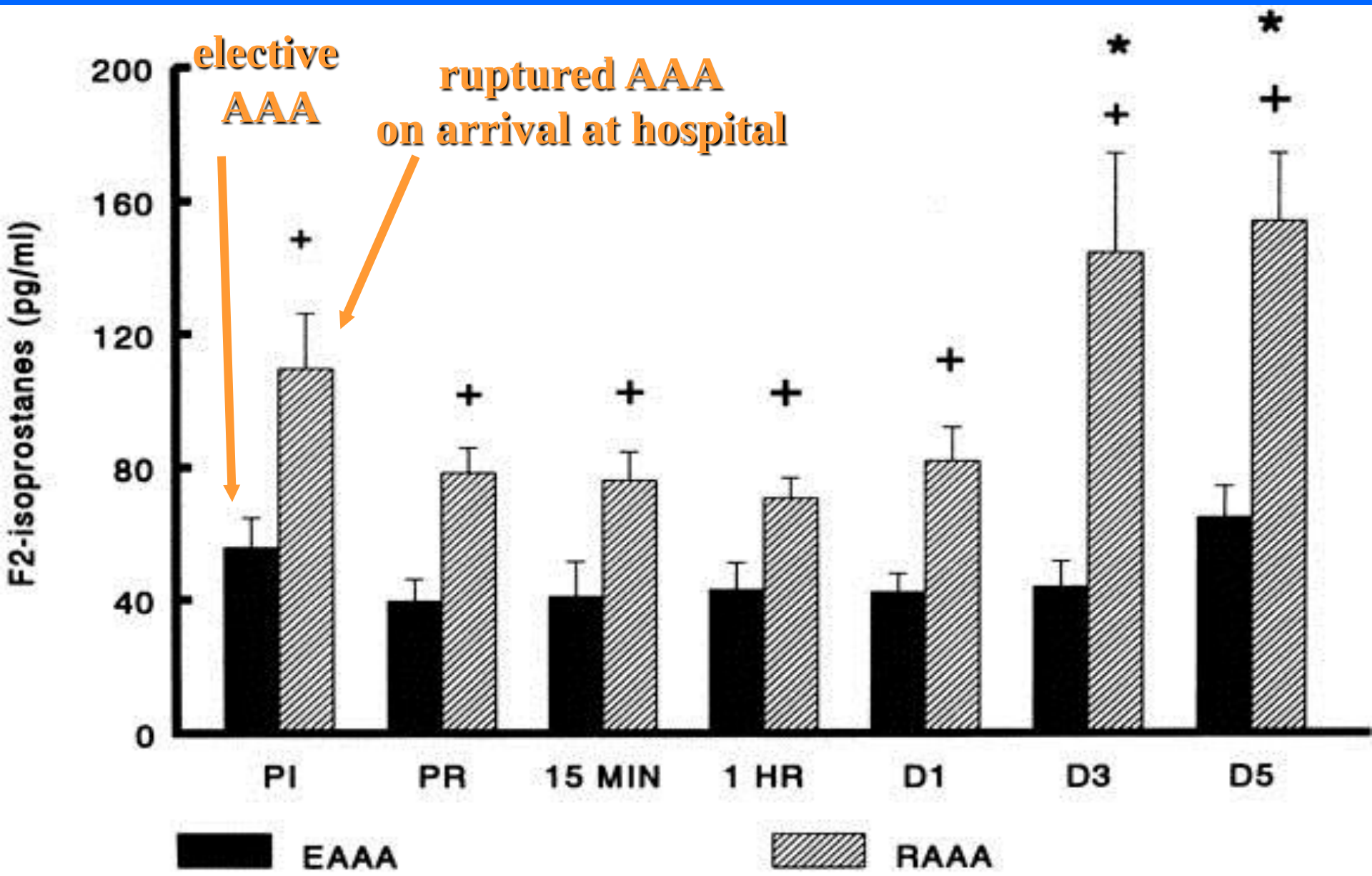
CHU reference values : 94 – 130 µg/L



isoprostanes



Lindsay et al. J Vas Surg 30:219-228, 1999



correlation between aneurysm diameter and OS parameters

variable	correlation coefficient	P value
vitamin C (µg/mL)	-0.45	0.01
β - carotene (mg/L)	-0.41	0.01
zinc (mg/L)	-0.57	0.01
copper/zinc ratio	0.43	0.01
selenium (µg/mL)*	-0.44*	0.01

no correlation for the other investigated parameters

*** Witkowska et al. Biol Trace Element Res 114:31-40, 2006**
r=-0.382

conclusions (I)

1° when compared to control group, the blood concentration of some important actors (vitamin C, β- carotene, selenium, zinc, ubiquinone) implicated in the antioxidant network **is significantly reduced in AAA patients**

2° the antioxidant network is more affected in patients having a AAA size > 50 mm than those with an AAA size < 50 mm

conclusions (II)

3° there is a significant negative correlation between these parameters and the AAA size

→ monitoring of these biomarkers to identify AAA prone to rupture ?

→ more patients to be studied

4° more attention must be given to the measurement of isoprostanes as a specific marker of lipid peroxidation, a process involved in the aneurysm development.

conclusions (III)

5 ° the weakening of the antioxidant defences may suggest that an antioxidant therapy could be beneficial to AAA patients.

- in angiotensin II-infused apolipoprotein E-deficient mice, vitamin E inhibits AAA formation
(Gavrilla et al. 2005)

- in a rat model, vitamin E reduces 8-isoprostane content and aortic macrophage infiltration in AAA tissues
(Nakahashi et al. 2002)

conclusions (III)

5 ° the weakening of the antioxidant defences may suggest that an antioxidant therapy could be beneficial to AAA patients.

- by contrast, in a controlled trial, vitamin E or β-carotene supplementation did not have a preventive effect for large sized AAAs among male smokers.

(Törnwall et al. 2001)