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www.worldheart.org

World Heart Federation er en internasjonal ikke-statlig organisasjon med base i Genève, Sveits. Organisasjonen arbeider for global bekjempelse av og kontroll av kardiovaskulær sykdom (CVD) og mottar medlemskapsavgifter fra kardiologiske selskaper og hjerteforeninger i mer enn 100 land. Verdenskongressen (WCC) med rådgivningsgrupper og tverrkontinentale nettverksforbindelser danner ryggraden i organisasjonen som fokuserer på "the burden of CVD" og har som mål å øve helsepolitisk innflytelse og utvikle helseprogrammer i økonomiske middelsjiktsland med prosjekter som har et kostnadsnivå som lar seg implementere i disse landene.

Organisasjonen utgår fra "International Council of Cardiology" som ble opprettet etter initiativ av Ignacio Chavez og Paul Dudley White. Den første "International Congress of Cardiology" ble holdt i Paris i 1950 og den neste i Washington i 1954. WCC blir nå arrangert med 2 års mellomrom – forrige gang i Barcelona i 2006 (XVth WCC) i samarbeid med ESC.

80 % av dødsfall forårsaket av kardiovaskulær sykdom forekommer i lav- og middelinntektsland. Organisasjonens nye motto "From Patients to Populations" ble introdusert ved årets kongress. Det er preventiv medisin som står i fokus, ettersom røking og abdominal fedme er i ferd med å ta av i de fattige landene.

Valentin Fuster gav et glimrende foredrag "Ignacio Chavez Lecture" om nødvendige helsetiltak rettet mot den eksplosive utviklingen av overvekt, diabetes og nyresvikt sett fra ulike profesjoners synsvinkel. I velstandsland bruker den enkelte 10-14 % av sin inntekt til helsefremmende tiltak, mens tilsvarende helsetjenester i de fattige landene ville koste den enkelte 60-80 % av inntekten. Behandling av kronisk sykdom er blitt en global helsepolitisk utfordring. I 2020 forventer man en 250 % økning av dødeligheten av kardiovaskulær sykdom i Brasil og 200 % økning i Kina mot 50-60 % økning i de rike landene. Vi bruker enorme summer på behandling av kroniske sykdommer og den økende hyppigheten av kardiovaskulær sykdom vil komme til å sprenge budsjettrammene. Fuster fokuserte innledningsvis på diagnostikk av latent diabetes og latent nyresvikt og fremhevet at dette var reversible prosesser, vesentlig knyttet til det metabolske syndrom og til røking. Han ønsket også en omprioritering i favør av mer forskning som ledd i flere forebyggende tiltak.

Universitetet i Bergen og Helse Vest har valgt ernæring som et eget satsingsområde. De to store universitetssykehusene i Helse Vest, Haukeland- og Stavanger Universitetssjukehus, hadde sendt inn flere abstrakter og var rimelig godt representert ved kongressen. Stavanger Universitetssjukehus har sammen med Universitetet i Bergen valgt å satse på Latin-Amerika og har etablert et eget frittstående kardiologisk institutt tilknyttet Universidad Catolica de Salta i det nordvestlige hjørnet av Argentina. Herfra ble det presentert fire abstrakter basert på relasjonen mellom omega-3-innholdet i cellemembraner og sirkulerende lipider. Stavanger- og Haukelandsgruppen hadde for øvrig flere presentasjoner basert på arbeider utført lokalt, med utgangspunkt i risikomarkører for det akutte koronare syndrom, hjertestansproblematikk og homocysteinhypotesen (WENBIT), sistnevnte er kort referert av Ottar Nygård. Det var ellers få abstrakter fra andre norske sykehus og totalt sett var den norske kontingenten liten.

Dennis W.T. Nilsen
Stedlig redaktør

WCC Buenos Aires, Argentina 2008. Haukeland Universitetssykehus.

Fra Hjerteavdelingen Haukeland Universitetssykehus deltok PhD-stipendiater, forskerlinjestudenter og leger med til sammen 10 abstrakter som alle var knyttet til kliniske studier eller dyrestudier der invasive metoder var sentrale. Blant de åtte abstraktene fra kliniske studier var syv presentasjoner basert på data fra Bergen Coronary Angiography Cohort (BECAC) [Pedersen, Pedersen, Svingen] og Western Norway B-vitamin Intervention Trial (WENBIT) [Bleie, Bleie, Blix, Løland], mens ett abstrakt fokuserte på den prognostiske nytteverdien av CK-MB-målinger etter elektiv hjertekirurgi [Vikenes]. De to abstraktene fra dyrestudier (gris) presenterte data på effekten av hjertepumpen Impella og væskebehandling på organperfusjon ved hjertestans [Tuseth] og av den syntetiske fettsyren TTA mot konstriktiv remodellering og neointimahyperplasi etter ballongskade når fettsyren ble gitt lokalt mot åreveggen fra ballongkateter [Pettersen].

Ottar Kjell Nygård
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Norske abstrakter på WCC

Identification of patients who benefit from implantable cardioverter defibrillators (ICD) by combining the genotypes for angiotensinogen (AGT), angiotensin-converting enzyme (ACE) and angiotensin II type1 receptor (AT1R).

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Introduction

The renin-angiotensinogen (RAS) system plays a critical role in blood pressure and tissue flow regulation and is activated by stepwise cleavage of angiotensinogen (AGT). Renin cleaves AGT to angiotensin I. Angiotensin I is cleaved by angiotensin I-concerting enzyme (ACE) to angiotensin II. The next step is binding of angiotensin II to the angiotensin II type 1 (AT1) receptor. Transient change of myocardium by ischemia is one arrhythmogenic mechanism. A “weak point” in the RAS-AT1 system may therefore “pave the way” for serious arrhythmias. Blood pressure regulating genes (AGT, ACE and AT1R) were selected as potential “weak points”. A variant in the angiotensinogen gene; the M235T has been associated with high plasma levels of AGT. In addition, a homozygous deletion in the ACE-gene, ACE-DD, has been associated with higher circulating plasma ACE levels than for ACE-II genotype carriers. A variant in the AT1 receptor gene (A1166C) has been identified to associate with complications of cardiovascular disease. The objective of the study was to examine whether the ACE II/DD, AGT M235T and AT1R (A1166C) variants, reflect risk of arrhythmias in patients with ICD.

Methods

44 patients were recruited, 40 with coronary heart disease and 4 with cardiomyopathy. Mean age 65yr±8 and ejection fraction (EF) 29±10. All patients had primary ICD implantation (Vitality DR®), except for one with change of device. Indication for ICD: Survivor of sudden cardiac death: 13, ventricular tachycardia (VT): 17, old myocardial infarction with EF<30% and non-sustained-VT: 14. Beta-blockers were used by 39, ACE-inhibitors by 21, angiotensin receptor blockers by 18 and amiodarone by 5. At follow-up at week 1,12,24,36 and 48, VF/VT events were present when 8 of 10 ventricular beats had a RR-interval ≤ 353 ms (≤400ms in 3) recorded. The follow-up time was 1 yr for 30 patients, 3-9 months for 14.

Results

At last follow-up, occurrence of one or more episodes of VF/VT was recorded in 14 patients, while 30 patients had no arrhythmias or non-sustained VT (N). A significant difference (p=0.01) in the

ACE-genotypes between VF/VT and N was found, but no significant differences between the ATIR-genes and AGT-genes. By considering the effect of each genotype, significance was only found for ID and II (Table 1).

Table 1. Distribution of genotypes according to VF/VT

	Yes	No	p
AC	5	13	ns
CC	0	3	ns
AA	9	14	ns
M/M	6	7	ns
MT	7	16	ns
TT	1	7	ns
DD	4	9	ns
ID	2	16	.023
II	8	5	.009

Conclusion: The ACE II genotype is linked to a significantly increased risk of VF/VT in patients with ICD. If the result is confirmed by similar studies, the finding will be of great importance for better identification of patients who benefit from ICD.

Comparison of the omega-3 index in the acute coronary syndromes in a beef-eating population in Argentina as compared to a fish-eating population in Norway.

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Background: The omega-3 index comprises eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in red blood cells, expressed as percent of total fatty acids (FA's). A threshold level of the omega-3 index may be of significance for risk evaluation in the acute coronary syndromes (ACS). In order to investigate the range and distribution of the omega-3 index across ACS populations with diets either poor or rich in n-3 FA's, we compared the quartile distribution of this index in a beef eating inland population in Argentina with a coastal population in Norway, respectively.

Methods: We included 190 Argentinean (Salta, Argentina) (mean age 64.2y, males 66.8%) and 398 Norwegian patients (Stavanger, Norway) (mean age 71.9y, males 65.1%) hospitalized with chest pain and a documented ACS, (troponin-T (TnT) > 0.01).

Results: Median (percentile 25-75) omega-3 index in the Argentinean population was 2.85 (1.47-4.10) compared to 6.53 (5.45-8.04) in the Norwegian coastal population. Table 1 shows the quartile distribution of the omega-3 index. Within each age quartile, the quartiles of EPA and DHA (and hence the omega-3 index) were higher, but the arachidonic:omega-3 ratio was lower for the Norwegian compared to the Argentinean population.

Conclusion: The highest quartile level of the omega-3 index in the Argentinean ACS population was similar to that of the lowest quartile of the Norwegian ACS population. As the Norwegian population may be generally protected by a background diet rich in n-3 FA's, a threshold level of the omega-3 index might be sought in populations like that in Argentina with a relatively low omega-3 index.

Table 1

Omega-3 index	Mean	95% CI; Lower bound	95% CI; Upper bound
Norway Q1	4.31	4.14	4.47
Q2	5.66	5.59	5.72
Q3	7.00	6.91	7.09
Q4	9.42	9.12	9.72
Total	6.86	6.66	7.07
Argentina Q1	0.84	0.74	0.95
Q2	2.06	1.95	2.18
Q3	3.58	3.47	3.69
Q4	5.09	4.83	5.35
Total	2.89	2.65	3.13

Activated Factor XII and B-type natriuretic peptide, but not C-reactive protein, are independent predictors of mortality following admission with suspected myocardial infarction.

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Background: The study aim was to assess the utility of activated Factor XII type A (XIIaA), B-type natriuretic peptide (BNP) and highly sensitive C-reactive protein (hsCRP) in multivariate analysis

models predicting all-cause mortality in patients admitted with chest pain.

Methods: Multivariate analysis of all cause mortality in 871 patients admitted with suspected MI was performed using the Cox Proportional Hazard Ratio. Data input into the model included XIIaA, BNP and CRP as well conventional risk factors for mortality such as age, smoking, previous history of coronary heart disease (CHD), hypertension, diabetes mellitus, left ventricular function (EF), troponin T (TnT) and se-creatinine.

Results: Of 871 patients, 386 had a TnT concentration [TnT]>0.05 ng/mL at admission whilst 485 had a [TnT]≤0.05ng/mL. 66 % of the latter group had known pre-existing CHD. 138 patients died within 24 months. Hazard ratios associated with XIIaA, BNP and CRP are shown in the table. Both XIIaA and BNP are independent predictors for all-cause mortality in the group containing all patients, BNP is an independent predictor for all cause mortality in patients who had confirmed MI (TnT>0.05ng/mL) at admission, whereas XIIaA is an independent predictor for all cause mortality in patients with low or absent TnT release at admission. In contrast, hsCRP was not an independent predictor of all-cause mortality in the studied population.

Conclusion: XIIaA and BNP provide independent and complementary information on all-cause mortality risk following admission with suspected MI. XIIaA is particularly useful in predicting mortality in patients who did not have MI at admission, whereas BNP is effective in predicting mortality in patients with confirmed MI.

Activated Factor XII type a is an independent predictor of cardiovascular outcome in coronary patients admitted with troponin T negative chest pain

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Background: Activated Factor XII (XIIa) is a predictor of recurrent coronary ischemic events in patients following a myocardial infarction (MI). Recently, novel in-vivo types of XIIa have been described. We assessed the relation between admission levels of activated factor XII type A (XIIaA) and a combined endpoint of recurrent troponin T (TnT) positive events (TnT >0.05 ng/mL and an MI typical pattern of gradual rise and fall in TnT) and cardiac mortality in a large, consecutive cohort of patients admitted with chest pain.

Methods: Blood samples for XIIaA determination were obtained immediately following admission in 871 patients admitted with chest pain and suspected acute coronary syndrome (ACS). Plasma XIIaA concentrations were determined by ELISA at admission. Cardiovascular outcome within each quartile of XIIaA was compared at 6 months follow-up.

Results: At index hospitalization, 386 (44.3%) patients had a peak TnT concentration exceeding 0.05 ng/mL and 485 (55.6%) had a peak TnT concentration of 0.05ng/mL or below. Of the latter group, 66% had known pre-existing coronary heart disease (CHD). After a follow-up period of 6 months, 67 patients had suffered from a recurrent TnT positive event and 52 patients had died from a cardiac reason. Whilst XIIaA levels were not related to increased risk for cardiovascular outcome in the group of patients with TnT>0.05ng/mL at admission, XIIaA predicted 6 months cardiovascular outcome for patients with absent or low TnT at admission. This risk prediction was particularly pronounced in the subgroup of patients with pre-existing CHD. The unadjusted odds ratios (OR) for quartile 4 versus quartile 1 for the combined endpoint of cardiac death or TnT positive events for the different subgroups are displayed in table 1. In a multivariate logistic regression model, XIIaA added prognostic information for cardiovascular outcome after adjustment for age, sex, peak TnT, BNP, CRP, creatinine, history of CHD or heart failure, NYHA class, hypertension, diabetes mellitus, smoking history, ejection fraction (EF), administration of clopidogrel, thrombolysis or statin prior to admission and angiography following admission.(table 1).

Conclusion: XIIaA is a powerful and independ-

		All patients	TnT >0.05 ng/mL at admission	TnT ≤0.05 ng/mL at admission
Cox Proportional Hazard Ratio (95% CI)	XIIaA	2.30** (1.37-3.86)	N.S.	3.75** (1.63-8.63)
	BNP	5.47** (2.11-14.19)	4.34* (1.36-13.83)	N.S.
	hs-CRP	N.S.	N.S.	N.S.

**: p<0.05; **: p<0.01; N.S. = Not significant.*

Table 1: ORs comparing patients with XIIaA in Q4 with patients in Q1 for the combined endpoint of cardiac death or a recurrent TnT positive event 6 months following admission for chest pain.

	Univariate analysis, OR (95% CI; p)	Multivariate analysis, logistic regression; OR (95% CI; p)
TnT >0.05ng/mL) (n=386)	1.03 (0.47-2.24; ns)	--
TnT ≤0.05 ng/mL (n=485)	5.85 (1.65-20.79; p<0.01)	5.44 (1.43-20.67; p<0.05)
TnT≤0.05 ng/mL pre existing CHD (n=318)	4.00 (1.24-12.88; p<0.05)	3.76 (1.06-13.28; p<0.05)

CI: confidence interval; ns: not significant

ent indicator of 6 months cardiovascular outcome in CHD patients admitted with chest pain with low or absent TnT release and provides prognostic information above and beyond conventional risk factors.

Effect of cardiac arrest induced by cardioverter defibrillator (ICD) testing on ischemia modified albumin (IMA).

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Introduction

Ischemia modified albumin (IMA) is a biomarker of cardiac ischemia. IMA rises within minutes of the onset and remains elevated for several hours after cessation of ischemia. It is an early marker to help in ruling out patients with an acute coronary syndrome. IMA also detects transient myocardial ischemia following direct current cardioversion and in patients undergoing percutaneous coronary intervention (PCI). After implantation of an implantable cardioverter defibrillator (ICD), ventricular fibrillation is induced in order to test the ICD. The duration of asystole is at least 15- 20 seconds before cardioversion by the device, and in the present study we sought to evaluate the effects of induced cardiac arrest on the serum levels of IMA.

Methods

We studied 32 patients with coronary heart disease (CHD), mean age 65yr±9 and ejection fraction (EF) 30±10. All patients had primary ICD implantation. Serum for determination of IMA1 was harvested in the morning on the day of ICD implantation, IMA2 was sampled within 2 hours after implantation and IMA3 at 8PM the day of implantation. The samples from all patients were frozen within 2 hours at -70 ° C and stored for a mean of 307 days, range 39-641, until analysis. Serum IMA was measured by the albumin cobalt binding test (ACB®).

Results

IMA (n:30) increased 6.8 % from a mean of 106.2 ±16,5 U/ml in IMA1 to 113,4 ±12,6 U/ml in IMA2, p<0,05. IMA (n:32) increased 5,2 % from a mean of 106.8 ±16,5 U/ml in IMA1 to 113,4 ±12,6 U/ml in IMA3, p<0.05. For comparison, other publications have shown that the increase in IMA after cardioversion of atrial fibrillation is in the range of 3.3% - 29%, and after inducing chest pain during percutaneous intervention, it increases from 10.1% to 39.3%. The patients were divided into two categories by the median value of age and EF. There were significant differences (p<0.05) in the increase between IMA1 and IMA2 but not IMA3 for age<66 (yearlow) and age ≥66 (yearhigh). The IMA values for the two age group were significantly (p<0.05) different. For EF≤26 (EF-low), there were no significant differences between IMA1 and IMA2 or IMA3, but for EF≥27 (EF-high) there were significant (p<0.05) differences for these IMA-values.

Conclusion

After cardiac arrest for at least 15-20 seconds, there is a small, but significant increase in IMA. Older people with CHD have higher resting IMA, but experience a similar increase in IMA after cardiac arrest. It is speculated that coronary flow may be a prerequisite for the increase in IMA and that measurement of IMA after sudden cardiac arrest may have prognostic implications.

Intracardiac Electrocardiographic (EGM) Morphology Changes In Patients With Implantable Cardioverter Defibrillator (ICD).

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Introduction

The purpose of this work is to investigate if there are changes in the EGM of patients with ICD, and if these changes have any relation to appropriate ICD therapy.

Methods

We studied 32 patients, 30 with coronary heart disease and 2 with cardiomyopathy, mean age 64yr±8 and ejection fraction (EF) 31±10. All patients had primary ICD implantation (Vitality DR®), except one with change of device. Indication for ICD: Survivors of sudden cardiac arrest:9, ventricular tachycardia (VT):9, old myocardial infarction with EF<30 and non-sustained-VT:14. Follow-up time was 24 weeks for 27 patients and 4-12 for 5, respectively. VT and ventricular-fibrillation (VF) zone (VTVF) ≤ 352 ms.

Three minutes of EGM, sampling rate 200 Hz, was recorded at follow-up at week 1, 4, 12 and 24.

We compared characteristics in beat shape diversity of normal beats to study changes in the EGM. Normal beats were extracted according to the highest beat similarity, first within each recording and second within the complete recording series. First, all QRS complexes and P waves were detected using a variable threshold for isolating the desired peaks. For each beat, b(i) (i=1, ..., N), the correlation coefficient, Rij, and root mean square sample deviation, RMSij, to all other beats, b(j), were calculated. All beats satisfying the beat similarity criterion Rij ≥0.95 and RMSij>0.3 were allocated to the same group, g(k), as b (i). This procedure was repeated for b(i+1). If b already belonged to a group, g(k), all beats satisfying the similarity criterion were merged into g(k). Otherwise, b (i+1), would be the originator of a new group, g (k+1). A series of groups, G(week1), G(week4), ..., G(week24), were determined. Beat shape diversity was characterised by beat correlation, number of groups and the variations in the PR intervals.

Results

During the observation period EGM changes were indicated by correlation < 0.95 in 7 (20%), group >5 in 14 (44%) and standard deviation of PR interval (SD-PR) >1 in 15 (47%), see Table 1. By crosstabulation of these data with registration of whether patients had any VTVF events during follow up, using a Chi-Square test, there were no significant differences.

Table 1

	VTVF:	Yes	No	Total	p'
EGM	Corr.<.95	2	5	7	
	Corr.≥.95	7	18	25	
	Total:	9	23	32	ns
Group	>5	5	9	14	
	≤5	4	14	18	
	Total:	9	23	32	ns
SD-PR	>1	5	10	15	
	≤1	4	13	17	
	Total:	9	23	32	ns

**Fisher's Exact Test*

Conclusion

During the observation period, EGM changes were indicated by high number of ecg beat shape groups and variation in AV conduction changes in 44-47 % of the cases, but with no significant differences between patients with and without VTVF.

The relationship between serum lipids and quartiles of the omega-3 index in a beef eating population in Argentina as compared to a fish eating ACS population in Norway.

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Background: Serum lipids consisting of total cholesterol, HDL-cholesterol and triglycerides reflect the background diet. We chose to evaluate these lipid fractions in a beef eating population in inland Argentina as compared to a coastal population in Norway. All study subjects presented with an acute coronary syndrome (ACS). We related serum lipids to the quartiles of the omega-3 index comprising eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in red blood cells, expressed as percent of total fatty acids.

Methods: Only non-statin treated ACS patients with a similar median increase in troponin-T were included; 160 (mean age 64.1, males 65.6%) from Salta, Argentina, and 330 (mean age 72.1, males 62.4%) from Norway. Blood samples were drawn immediately after admission.

Results: Median (percentile 25-75) of omega-3 index in the Argentineans was 2.85 (1.47-4.10) as compared to 6.53 (5.45-8.04) in the Norwegians. The distribution of the lipid fractions within the quartiles of the omega-3 index is illustrated in Table 1.

Tabel 1									
	Total cholesterol			HDL-cholesterol			Triglycerides		
Omega-3 index quartile	Mean	95%CI; Lower bound	95%CI; Upper bound	Mean	95%CI; Lower bound	95%CI; Upper bound	Mean	95%CI; ¨Lower bound	95%CI; Upper bound
Norway Q1	5.67	5.44	5.91	1.27	1.19	1.35	1.73	1.47	2.00
Q2	5.60	5.30	5.90	1.40	1.31	1.49	1.66	1.31	2.00
Q3	5.69	5.43	5.95	1.32	1.21	1.42	1.74	1.53	1.95
Q4	5.71	5.48	5.94	1.44	1.34	1.54	1.50	1.23	1.77
Total	5.67	5.54	5.79	1.35	1.31	1.40	1.66	1.52	1.80
Argentina Q1	4.82	4.45	5.19	0.95	0.86	1.05	2.33	1.82	2.84
Q2	5.29	4.87	5.71	1.04	0.93	1.15	2.38	1.56	3.20
Q3	4.88	4.41	5.34	0.91	0.79	1.04	2.14	1.72	2.55
Q4	4.63	4.28	4.99	1.01	0.89	1.13	1.67	1.40	1.94
Total	4.91	4.71	5.11	0.98	0.92	1.03	2.14	1.87	2.40

Conclusion: We found significant lower HDL levels and higher triglycerides in the Argentineans, but the atherogenic impact of these changes may be balanced by the lower total cholesterol as compared to the Norwegians. The highest quartile of omega-3 index in the Norwegian population contained significantly higher HDL-cholesterol as compared to the lowest within-country quartile (p =0.011), and a similar but opposite trend for triglycerides was noted in the Argentineans (p=0.09), suggesting that the level of these lipid fractions is related to the cellular content of n-3 FA's.

The relationship between BNP and HSCRP and quartiles of the omega-3 index in a beef eating ACS population in Argentina as compared to a coastal ACS population in Norway.

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Background: B-type natriuretic peptide (BNP) is a counter-regulatory peptide hormone predominantly synthesized in the ventricular myocardium. This marker of neurohormonal activation and inflammation plays a pivotal role across the spectrum of ACS. C-reactive protein (CRP) is an acute-phase reactant that is produced in response to acute injury, infection or other inflammation stimuli. It is a marker for underlying systemic inflammation and plays an important role in the initiation and propagation of atherosclerosis and ultimately to plaque rupture and the ensuing thrombotic complication. We have investigated whether these two markers measured immediately after admission for an acute coronary syndrome (ACS) differ by quartiles of the omega-3 index [percentage of eicosapentaenoic acid (EPA) and docosahexaenoic acid acid (DHA) of total fatty acids (FA`s) in red blood cells] in two ACS populations with diets either poor or rich in omega-3 FA's.

Methods: We included 190 Argentinean patients (Salta, Argentina) (mean age 64.1y, males 65.6%) and 398 Norwegian patients (Stavanger, Norway) (mean age 72.1y, males 62.4%) hospitalized with chest pain and a documented ACS as defined by a troponin-T (TnT) >0.01. Blood samples were

Table 1						
	BNP			hsCRP		
Omega-3 index quartile	Mean	95%CI; Lower bound	95%CI; Upper bound	Mean	95%CI; Lower bound	95%CI; Upper bound
Norway Q1	273.18	183.17	363.20	18.40	8.99	27.80
Q2	400.63	281.00	520.27	19.59	11.47	27.71
Q3	473.52	333.75	613.30	28.24	18.00	38.48
Q4	358.34	266.92	449.76	25.10	10.55	39.65
Total	385.58	327.91	443.25	23.34	17.70	28.98
Argentina Q1	246.69	135.82	357.57	30.06	12.75	47.37
Q2	259.63	166.51	352.76	20.86	4.36	37.37
Q3	361.91	190.63	533.18	16.61	6.40	26.81
Q4	399.49	217.62	581.37	19.33	7.79	30.88
Total	316.87	246.11	387.62	21.68	14.73	28.63

drawn immediately after admission in both populations.

Results: Median (percentile 25-75) omega-3 index in the Argentinean population was 2.85 (1.47-4.10) as compared to 6.53 (5.45-8.04) in the Norwegian coastal population. The distribution of BNP and high sensitive CRP (hsCRP) through the quartiles of the omega-3 index in the two populations is shown in Table 1.

Table 1

	Total Cholesterol			HDL-Cholesterol			Triglycerides		
Omega-3 index quartile	Mean	95%CI; Lower bound	95%CI; Upper bound	Mean	95%CI; Lower bound	95%CI; Upper bound	Mean	95%CI; Lower bound	95%CI; Upper bound
Argentina Q1	5.08	4.51	5.65	0.96	0.87	1.04	2.57	1.98	3.16
Q2	4.91	4.61	5.21	1.05	0.97	1.13	2.01	1.69	2.34
Q3	5.22	4.82	5.62	0.92	0.82	1.02	2.84	2.12	3.57
Q4	4.75	4.48	5.03	1.03	0.93	1.12	1.67	1.44	1.89
Total	4.99	4.79	5.19	0.99	0.94	1.03	2.28	2.02	2.54

Conclusion: There were no significant differences in BNP and hsCRP within and between country quartiles of the omega-3 index.

Serum triglycerides may reflect the content of cellular omega-3 fatty acids in CHD populations with a low intake of fish.

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Background: Early studies of Greenland Eskimos who consumed a diet rich in n-3 fatty acids (FAs) emphasized that population's lower coronary mortality as compared with Danish controls. Moreover, several prospective epidemiologic studies have reported significant associations between fish intake and a lower risk of coronary heart disease (CHD), but there seems to be a lack of a dose-response relation. In the US Physicians Health Study (JAMA 1998;279:23–8) there was a continuous relationship between blood n-3 FAs and risk for sudden death up to one fish meal per week. N-3 FAs lower triglycerides and elevated fasting triglycerides may be an independent risk factor for CAD. In this study we investigated whether serum triglycerides in a beef eating population with low dietary intake of n-3 FAs may be associated with the omega-3 index [the sum of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in red blood cells, expressed as percent of total FAs].

Methods: We included 229 non-statin treated chest pain patients from Salta, Argentina (mean age 63.4, males 63.3%), consecutively admitted with verified CHD, with and without a troponin-T release. Blood samples were drawn immediately after admission. We performed one way ANOVA of serum lipids across quartiles of the omega-3 index.

Results: The median omega-3 index was 2.15% (P25 = 1.19, P75 = 3.89). There was no significant association between total cholesterol or HDL cholesterol levels and omega-3 index (each $p > 0.05$). Triglycerides in Q4 were 1.67 mmol/L (CI 1.44-1.89) as compared to 2.57 mmol/L (CI 1.98-3.16) in Q1 ($p = 0.006$). The p value for Scheffé's analysis of contrast for Q4 versus Q1 was 0.012 and for Q4 versus Q1-Q3 was 0.007 (see Table 1).

In conclusion, in a CHD population with a very low dietary intake of fish products, serum triglycerides were lowest in those patients with the highest omega-3 index, suggesting that a threshold level of the omega-3 index for a triglyceride lowering (and possibly CHD protective) effect might be sought in low fish eating populations like that in Argentina.

Effects of resistance stress on cardiac biochemical markers in power lifters

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Background: The aim of this investigation was to assess short-term effects of sub maximal resistance stress on serum levels of cardiac markers in a group of healthy power lifters.

Methods: 20 male elite power lifters were enrolled in the study. All participants performed a

standardized exercise program exerting resistance stress including a short warm-up period, followed by exercising «bench press», «dead lift» and «squat» with 5 sets of 2 repetitions respectively. The lifters were encouraged to exercise with 80% of one repetition maximum weight in each set. None of the subjects performed additional training 24 hours prior to or during the investigation.

Venous blood samples for the determination of creatine kinase catalytic activity (CK total), CK isoenzyme MB catalytic activity (CKMBact), mass concentration of CK isoenzyme MB (CKMB mass), myoglobin and cardiac troponin T (cTnT) were obtained prior and 8 hours following exercise.

Results: Baseline levels of cTnT were beneath the 0.01 µ g/l detection limit of the assay in all subjects. Following exercise, no increase in cTnT levels over the detection limit was observed.

In contrast, CK total levels increased from 195 (131-586) to 345 (236-314) U/l, CKMBact from 12 (8-17) to 14 (12-19) U/l , CKMBmass from 3.1 (1.9-4.1) to 4.6 (3.4-6.1) µ g/l and myoglobin from 45.0 (41.8-54.9) to 92 (61-183) µ g/l from pre to post-exercise values (median and 25- and 75% percentiles, $p< 0.01$ for all parameters) respectively. The ratio of CKMB to CK did not increase over 0.03 in any of the samples.

Conclusions: Increases in CK, CKMB and myoglobin in this study are most likely originated in skeletal muscle. Our results suggest that short-term resistance stress does not cause myocardial damage in hearts of healthy, well trained subjects.

Table. Least Squares Mean % Changes in Lipids from Baseline to Wk 12.

Treatment Group	LDL-C	TG‡	HDL-C	non-HDL-C	apo B
ERN/LRPT	-17.0	-21.6	23.4	-18.1	-17.1
SIMVA 20 mg	-34.7	-13.4	4.2	-31.2	-25.9
SIMVA 40 mg	-38.2	-15.1	6.8	-34.6	-30.2
Pooled SIMVA	-37.20	-14.7	6.0	-33.4	-28.8
ERN/LRPT + SIMVA 20 mg	-45.7**§	-30.9** §	27.7* §	-43.9** §	-39.8**§
ERN/LRPT + SIMVA 40 mg	-48.9** §	-33.6** §	27.4* §	-46.7** §	-41.5**§
Pooled ERN/LRPT + SIMVA	-47.9** †	-33.3** †	27.5*†	-45.8**†	-41.0**†

*LDL-C=low-density lipoprotein cholesterol; TG=triglycerides; HDL-C=high-density lipoprotein cholesterol; apo B=apolipoprotein B. ‡Median % change; **p<0.001 vs. ERN/LRPT; * p<0.050 vs. ERN/LRPT; †p<0.001 vs. pooled SIMVA; §p<0.001 vs. corresponding dose of SIMVA*

Lipid-altering efficacy and safety profile of co-administered extended release niacin/laropiprant and simvastatin in patients with dyslipidemia

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Objectives: A tablet containing 1 g of extended-release niacin and 20 mg of the DP_1-selective antagonist laropiprant (ERN/LRPT) reduces flushing while preserving ERN's efficacy. This randomized, double-blind, Phase III, 12-wk study assessed the efficacy/safety of ERN/LRPT coadministered with simvastatin (ERN/LRPT+SIMVA) in pts with primary hypercholesterolemia or mixed hyperlipidemia.

Methods: After a 6- to 8-wk washout and a 4-wk diet/placebo run-in, 1398 dyslipidemic pts were randomized equally to: ERN/LRPT 1g/20 mg, SIMVA (10, 20, or 40 mg), or ERN/LRPT 1 g/20 mg+SIMVA (10, 20, or 40 mg) once-daily for 4 wks. At Wk 5, treatment doses were doubled in all groups except SIMVA 40 mg (unchanged) and ERN/LRPT 1 g/20 mg+SIMVA 40mg (switched to ERN/LRPT 2 g/40 mg+SIMVA 40 mg). The primary endpoint was mean % change from baseline to Wk 12 in LDL-2 for ERN/LRPT vs. ERN/LRPT + SIMVA (pooled across SIMVA doses).

Results: ERN/LRPT+SIMVA (pooled across doses) significantly improved key lipid parameters compared with ERN/LRPT and pooled SIMVA (Table). At the individual doses, ERN/LRPT+SIMVA produced significant improvements in lipids compared to SIMVA alone. Coadministration of ERN/LRPT+SIMVA was generally well-tolerated with a safety profile similar to ERN/LRPT. The incidences of consecutive LFTs >3x ULN were 0.5%, 1.0%, and 0.3% for ERN/LRPT, pooled SIMVA, and pooled ERN/LRPT+SIMVA. One pt taking ERN/LRPT (0.5%) had CK >10x ULN without muscle symptoms.

Conclusions: Coadministration of ERN/LRPT and SIMVA effectively improved the overall lipid profile and was generally well-tolerated in pts with dyslipidemia.

Percutaneous Left Ventricular Assist in Ischemic Cardiac Arrest

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Context Ischemic cardiac arrest represents a challenge for optimal emergency revascularization therapy. A percutaneous left ventricular assist device (LVAD) may be beneficial.

Objective To determine the effect of a percutaneous LVAD during cardiac arrest without simultaneous chest compressions, and assess effects of intensified volume loading.

Design 16 pigs randomized to either conventional or intensive fluid with LVAD support during ventricular fibrillation (VF).

Setting Acute experimental trial with pigs under general anesthesia.

Subjects Farm pigs of both sexes.

Interventions After randomization for fluid infusion, VF was induced by balloon occlusion of the proximal left anterior descending artery. LVAD and fluid was started after VF had been induced.

Measurements Brain, kidney, myocardial tissue perfusion, and cardiac index were measured with the microsphere injection technique at baseline, 3 and 15 minutes. Additional hemodynamic monitoring continued until 30 minutes.

Main results Mean cardiac index at 3 minutes of VF was 1.2 L.min/m2 (29% of baseline, $P<0.05$). Mean perfusion at 3 minutes was 65% in the brain and 74% in the myocardium compared to baseline($P\leq 0.05$=NS), then remained unchanged during the initial 15 minutes. At 30 minutes LVAD function was sustained in 11/16 animals (8/8 intensified fluid vs. 3/8 conventional fluid) and was associated with intensified fluid loading ($P<0.001$).

Conclusions During VF a percutaneous LVAD may sustain vital organ perfusion. Intensified fluid loading was associated with prolonged LVAD performance. A potential clinical role of the device during cardiac arrest and coronary revascularization has yet to be established.

Locally delivered Tetradecylthioacetic acid (TTA) reduces inflammation and collagen formation after coronary balloon injury in a porcine model

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Background. The sulfur containing Tetradecylthioacetic acid (TTA) is anti-inflammatory agent. TTA has been shown to reduce negative remodelling after balloon angioplasty injury following a single bolus local delivery. We tested if local drug delivery of TTA inhibits vascular inflammation, cell proliferation, and collagen deposition as possible mechanisms for counteracting constrictive remodelling and neointimal formation.

Methods. Thirty four domestic pigs undergoing percutaneous balloon injury were randomly assigned in separate experiments to either TTA (9 mM solution) or placebo delivered via a local drug delivery balloon. The pigs were sacrificed after four weeks. In 18 pigs one treated artery was perfusion fixed with formaldehyde, the other was immediately frozen in liquid nitrogen. Collagen density was assessed by histomorphometric analysis using picrosirius red staining, figure1. Inflammatory markers and lipid fractions were assessed in the vessel wall. In 16 pigs, cell proliferation was measured by immunohistochemistry using antibodies against bromodeoxyuridine (BrdU), whereas antibodies against α-actin were used for detection of smooth muscle cells and myofibroblasts. In 6 non-randomised pigs, cytokines were measured in normal segments and at 1, 3, and 5 days after balloon injury and delivery of TTA.

Results. Collagen particle count was lower after TTA compared to placebo, 177±11 n/area versus 225±13 n/area ($p=0.007$), figure 2. IL 2 concentra-

tion was also reduced compared to placebo 1.6 pg/ml (1.4-1.6) versus 1.7 pg/ml (1.6-5.3), (p=0.01), with a similar trend for IL 6 (p=0.07), figure 3. The anti-inflammatory index was increased after TTA, 46.28±12.06 versus 34.66±4.54 (p=0.025). There were no differences between TTA and placebo with regard to the expression of BrdU (30±3µm2 versus 29±3µm2, p=NS) and α-actin (136±16 n/area versus 101±10 n/area, p=NS), figure 4. There was no rise in inflammatory markers during the first 5 days after TTA administration.

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Conclusion. Local delivery of TTA reduced the local inflammatory response after coronary overstretch injury for at least 4 weeks and was associated with significant inhibition of collagen accumulation, but had no effect on cell proliferation.

Long Time Prognostic Value of CK-MB Mass in Low-Risk Patients with Stable Angina Scheduled for Cardiac Surgery

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Background: Long time prognostic value (> 5 years) of elevated cardiac biomarkers in low risk patients after routine cardiac surgery is still not clear. Many previous studies have included high risk, unstable patients. The follow up time has often been relatively short with a low number of prospective blood samples. In this study, we have determined the prognostic value of high versus low CK-MB mass values after elective heart surgery.

Methods: 230 consecutive patients were included in the final analysis. Using a cut off value of 5 times UNL, 100 patients had peak CK-MB mass values ≥ 25 µg/L (high), 130 patients < 25 µg/L (low). Patients with high/low CK-MB were comparable regarding age and common risk factors. In the low CK-MB group, there was a preponderance of males and aortic cross clamp time was significantly shorter (43 vs 60 minutes, P< 0.001). None of the patients developed new Q-waves on ECG. Blood samples were prospectively drawn just before and at 5 time intervals after surgery up to around 60 hours. Patients with elevated CK-MB values at baseline, as well as patients suffering an acute coronary syndrome < 1 month earlier, were not included. The median follow up time was 95 months.

Results: Mean peak value of CK-MB was 15.8 µg/L vs 46.4 µg/L in low/high CK-MB groups, respectively. Long aortic cross clamp time predicted higher peak CK-MB values. In a Kaplan-Meier plot, all cause mortality and readmission for acute coronary syndromes were more frequent in patients with high CK-MB (30.0% vs 17.9%, P=0.022). Similar figures for death alone were 83.1% vs 74.0%, P= 0.088. In a multivariate logistic regression analysis, high CK-MB and EF were the only variables independently related to worsened event-free survival.

Table 1. Event free survival (freedom of all cause mortality in brackets) during long time follow up (median of 95 months)

	CK-MB <25µg/L	CK-MB ≥25µg/L	P-value	Mean follow up (months)
All patients (n=230)	83.1 * (83.1)	70.0 * (74.0)	0.022 (0.088)	84.8
Bypass surgery (n=174)	83.8 (83.8)	73.0 (77.8)	0.099 (0.314)	86.6
Valve surgery (n=42)	73.3 (73.3)	70..4 (70.4)	0.860 (0.968)	78.3
CABG + Valve (n=14)	100.0 (100.0)	50.0 (50.0)	0.109 (0.109)	83.1

** percentages*

Conclusions: During a median of nearly 8 years of follow up after elective cardiac surgery, there was a significantly higher number of deaths and readmissions for ACS in stable, low risk patients with peak CK-MB values ≥5 times UNL compared to patients with CK-MB <5 times UNL. In the CABG subgroup this was true also for target vessel revascularisation.

290 Homocysteine lowering B-vitamin therapy and in-stent restenosis. A WENBIT sub study

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Background: Studies on B-vitamin supplementation to prevent restenosis after percutaneus coronary intervention (PCI) have been conflicting. We studied whether homocysteine lowering with B-vitamins has beneficial effects on restenosis after coronary stenting.

Methods: The Western Norway B-vitamin Intervention Trial (WENBIT) is a secondary prevention study conducted in a population without mandatory folic acid fortification of foods. Using two-by-two factorial design, participants were assigned to four groups receiving daily oral treatment with folic acid (0.8 mg)/vitamin B12 (0.4 mg)/vitamin B6 (40 mg), folic acid/vitamin B12, vitamin B6 alone or placebo. The current study is a pre-described substudy (WENBIT-PCI) on patients who had coronary bare metal stent placement for de novo stenosis in a native vessel. Among 456 eligible participants, 365 were re-examined with quantitative coronary angiograms (QCA) of 509 lesions at 6–12 months after PCI to assess possible in-stent restenosis. In 209 of these subjects, additional intravascular ultrasound (IVUS) was performed in a total of 265 stent treated segments. The primary endpoints were the continuous variables of minimum luminal diameter (MLD), percentage diameter stenosis (DS) and in-segment restenosis (_50% diameter stenosis as a binary variable) assessed by QCA. Endpoints assessed by IVUS were minimum luminal area (MLA) and percent neointimal hyperplasia volume (NIHV). **Results:** At baseline, mean (SD) age was 64 (10.3) years (82% men), serum cholesterol 5.0 (1.4) mmol/L, creatinine 74 (13) _mol/L, folate 12.8 (18.2) nmol/L and plasma total homocysteine 10.4 (5.5) _mol/L (p_ns between treatment groups). Reference diameter of the examined segments was 3.0 (0.56) mm, MLD 2.7 (0.49) mm and DS 11.2 (8.4) %, with no significant difference between treatment groups (p_0.2). Follow-up QCA of all segments showed MLD 1.9 (0.76) mm and DS 30.0 (23.3) %, a significant change compared to baseline (both p_0.001). No effect on these parameters were seen according to treatment by folic acid/vitamin B12 or vitamin B6 (p_0.15 by repeated measure ANOVA). During follow-up, in-stent restenosis occurred in 17.9 % of segments with no difference between groups (p_0.9). In lesions measured by IVUS at follow-up, MLA was 4.53 (1.11) mm2 in patients treated with folic acid/vitamin B12 and 4.42 (1.38) mm2 in patients not treated with folic acid (p_0.5). In the same patients, NIHV was 20.0 (8.9) % and 18.9 (9.1) %, respectively (p_0.4). Likewise, treatment with vitamin B6 showed no effect on MLA or NIHV at follow-up compared to no vitamin B6 (p_0.2). **Conclusion:** Among patients treated with bare metal coronary stents, homocysteine lowering therapy with folic acid/vitamin B12 or treatment with vitamin B6, show no effect on in-stent restenosis evaluated by angiography and IVUS.

370 Homocysteine lowering B-vitamin therapy improves coronary flow in patients with stable coronary artery disease, a WENBIT substudy

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Purpose. We examined the effects of B-vitamin therapy on coronary flow and endothelial function in patients with established coronary artery disease (CAD). **Methods.** Forty patients with CAD recruited into the Western Norway B-Vitamin Intervention Trial (WENBIT), were randomly assigned to daily oral treatment with 0.8 mg folic acid and 0.4 mg vitamin B12 or placebo, and 40 mg vitamin B6 or placebo, using a 2x2 factorial design. All patients were treated with statins for at

least two months prior to inclusion. At baseline, and after 9 and 24 months of treatment, epicardial coronary dilatation and coronary blood flow (CBF) were assessed by coronary angiography and doppler flow-wire measurements during intracoronary saline infusion (CBF-basal), incremental (0.72 _g/min, 7.2 _g/min and 36.0 _g/min) doses of acetylcholine and 2.4 mg/min adenosine (CBF-adn). **Results.** At baseline, mean (SD) age was 57.8 (9.0) years (eight females), serum LDL-cholesterol 2.9 (0.7) mmol/L, creatinine 88 (9.9) _mol/L, folate 12.2 (6.5) nmol/L and plasma total homocysteine 10.7 (2.9) _mol/L (p_0.4 between treatment groups). We found a significant increase in CBF-basal (p_0.02) and CBF-adn (p_0.05) in those subjects receiving folic acid/vitamin B12 compared to placebo or vitamin B6 alone (difference in trends during 24 months). Folic acid/vitamin B12 or vitamin B6 treatment did not change endothelial-dependent response following acetylcholine infusion or flow-dependent proximal dilatation in response to adenosine-induced maximal hyperemia (p_0.45). **Conclusion.** Treatment with a combination of folic acid and vitamin B12 improved basal CBF and adenosine-induced maximal CBF. Our data suggests a beneficial effect of folic acid/ vitamin B12 on coronary arteries in patients with stable CAD.

1012 The ratio of apolipoproteins ApoB/ApoA1 as a predictor of angiographic progression of atherosclerosis in patients with coronary artery disease

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Background Studies indicate that the ratio of circulating apolipoproteins ApoB to ApoA1 may correlate with subsequent risk of adverse cardiovascular events in patients with coronary artery disease (CAD). We have tested the effect of the levels of ApoB/ApoA1-ratio on the angiographic progression of CAD in patients undergoing conventional medical therapy including treatment with statins. **Methods** 348 patients (288 male, mean age 60 _ 10.2 years) undergoing percutaneous coronary intervention (PCI) at Haukeland University Hospital in 2001 to 2004 were screened for inclusion in our study. The coronary angiograms were evaluated at baseline, and at either scheduled follow-up (if applicable), or at acute hospitalization before scheduled control, but at least 90 days after baseline. Mean follow-up was 10.1 _ 2.6 months. Analysis was performed using quantitative coronary angiography (QCA) by two independent observers (inter-observer correlation coefficient _0.90), using contour-detecting computer software. Inclusion criteria were coronary artery segments with reference diameter of _ 2.0 mm and an untreated lesion with _ 30 % diameter stenosis (DS) at either baseline or follow-up. A total of 183 patients with 309 segments were included. Patients were treated with conventional medical therapy including statins (93%) and platelet inhibitors (98%). The end-point was angiographically assessed change in luminal obstruction, measured as change in minimum lumen diameter (MLD) or diameter stenosis (DS). **Results** At baseline we found mean (SD) serum creatinine 73.7 (12.0) _mol/L, ApoB 0.90 (0.24) g/L, ApoA1 1.29 (0.26) g/L and cholesterol 5.1 (1.7) mmol/L. Median (25th – 75th percentile) serum CRP was 2.0 (1.0 – 5.8) mg/L. Reference Diameter (RD) of study segments were mean (SD) 3.08 (0.75) mm, MLD 1.92 (0.55) mm and DS 37.6 (9.7) %. At follow-up we found a significant decrease in MLD from baseline (-0.17 (0.40) mm, p_0.001) and a more severe DS (42.0 % vs. 37.6 %, p_0.001). A linear regression analysis adjusting for age, sex, BMI, smoking, diabetes, hypertension, use of statins and platelet inhibitors, creatinine and ApoB/ApoA1-ratio showed that only CRP (p_0.039) correlated significantly with the progression of atherosclerosis, measured as change in DS. The ratio of ApoB/ApoA1 was not significantly (p_0,125) associated with CAD progression using the same model. **Conclusion** Our study indicates that the inflammatory marker CRP is a better predictor of CAD progression than ApoB/ApoA1-ratio in patients with established CAD treated with conventional medical therapy including statins.

The Effect of Homocysteine-lowering B-vitamin Intervention on Angiographic Coronary Artery Disease May Be Adverse - A WENBIT Sub-Study

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Background Total plasma homocysteine (tHcy) is an independent risk factor for Coronary Artery Disease (CAD). We tested the effect of tHcy-lowering therapy on the angiographic progression of CAD in a sub-study of the Western Norway B-vitamin Intervention Trial (WENBIT). **Methods** A total of 348 (288 male, mean age 60 _ 10.2 years) undergoing percutaneous coronary intervention at Haukeland University Hospital in 2001 through 2004 were screened for recruitment into this sub-study. Patients were randomized to daily oral treatment with a combination of 0.8 mg folic acid/0.4 mg vitamin B-12 or placebo, and with 40 mg vitamin B-6 or placebo, in a 2x2 factorial design. Coronary angiography was evaluated at baseline and at either scheduled follow-up or clinically indicated hospitalization _90 days from baseline (mean follow-up was 10.1 _ 2.6 months). 183 patients with a total of 309 untreated lesions with a reference diameter _ 2.0 mm and a diameter stenosis _ 30 % at either baseline or follow-up were included. Quantitative Coronary Angiography (QCA) was performed by two independent observers. Angiographic end-points were Minimum Lumen Diameter (MLD), Diameter Reduction (DR) and estimates of lesion plaque volume. All included segments were analyzed by both observers (Inter-observer Correlation Coefficient 0.90). **Results** At baseline mean (SD) plasma tHcy was 10.5 (7.0) _mol/L, serum folate 14.0 (24.7) nmol/L, cobalamin 467.6 (1333.5) pmol/L, creatinine 73.7 (12.0) _mol/L and cholesterol 5.1 (1.7) mmol/L. Median (25th – 75th percentile) serum CRP was 2.0 (1.0 – 5.8) mg/L. Reference Diameter (RD) of lesions was mean (SD) 3.08 (0.8) mm, MLD 1.92 (0.6) mm and DR 37.6 (9.7) %. At follow-up we found a significant decrease in MLD from baseline (-0.17 (0.4) mm, p_0.001) and a more severe DR (42 % vs. 37.6 %, p_0.001). Treatment with folate/B-12 reduced tHcy by 2.71 _mol/L (p_0.001), but had no effect (repeated measure ANOVA) on change in DR (p_0.16) or MLD (p_0.66), nor did treatment with vitamin B-6 (p_0.26 and p_0.07, respectively). A post-hoc analysis of lesions with diameter reduction _1 SD (defined as rapid progression) from baseline showed a significant relationship with the administration of folic acid. After adjustment for age, gender, BMI and baseline folate levels, lesions in patients treated with folic acid was associated with a more rapid CAD progression (odds ratio (95 % confidence interval) 1.87 (1.10 – 3.18, p_0,020)). **Conclusion** Among patients with established CAD, treatment with folic acid/B-12 or with vitamin B-6 has no beneficial effect on the progression of atherosclerosis measured with QCA. Our findings do however suggest that folic acid supplementation may promote a more rapid atherosclerotic progression observed in a small sub-group of patients.

B6 vitamers and long term mortality in patients with stable angina

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Background and aim Previous studies demonstrate an association between vitamin B6 status, inflammation and cardiovascular disease (CVD). Low levels of vitamin B6 are observed in several conditions of chronic inflammation, probably reflecting increased consumption, rather than ineffective intake. Thus, inflammation may be the common link between vitamin B6 and atherosclerosis. Pyridoxal 5-phosphate (PLP), pyridoxal (PL) and the catabolite pyridoxic acid (PA) are the predominating B6 vitamers in the human body. The ratio PA / (PLP_PL), here denoted PAR, represents the fraction of catabolised vitamin B6. We have evaluated PAR as a predictor of mortality in stable angina patients, and studied its association to homocysteine (tHcy) and inflammation markers CRP and neopterin. **Methods** A total of 1039 consecutive patients (28% women) with suspected coronary artery disease (CAD) were examined

with diagnostic angiography in the period between January 2000 and June 2001. Their mean (SD) age was 61.5 (10.5) years. A total of 236 (22.7%) had no significant CAD, whereas 357 (34.4%) had triple vessel disease. Blood was sampled before angiography and immediately frozen at -80oC until analysis. **Results** Median levels (inter-quartile range) of the B6 vitamers were PLP 43.7 (30.5–61.6), PL 8.9 (7.2–12.0) and PA 21.5 (16.0 –31.1) nmol/L, PAR 0.43 (0.32– 0.59). Strong correlations (Spearman) were observed between PAR and age (r_0.28), extent of CAD (r_0.16), ejection fraction (r_-0.12), tHcy (r_0.26), creatinine (r_0.34), neopterin (r_0.34) and CRP (r_0.28) (all p _0.001). During a mean (SD) follow-up of 5.9 (1.3) years, 118 patients (11.4%) died. Relative risk (RR (95%CI)) of mortality was calculated trough the use of Cox regression analysis for trend over quartiles. In a model adjusting for gender and age, neither PLP, PL nor PA predicted mortality, whereas PAR was a strong determinant (RR 1.44 (1.20 –1.73)). After additional adjustment for creatinine, tHcy, hypertension, BMI, diabetes, current smoking, extent of CAD, baseline treatment (medication only, PCI, bypass surgery) and ejection fraction, PAR still predicted mortality (RR 1.28 (1.05–1.55)). However, when adding CRP and neopterin to the multivariate model, the PAR effect was no longer significant (RR 1.21(0.98 –1.48)). **Conclusion** The fraction of catabolised B6 vitamin, PAR, correlates with inflammation markers CRP and neopterin, and strongly predicts mortality in stable angina patients.

Mortality in stable angina patients

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Background and aim Inflammation is centrally involved in the pathogenesis of cardiovascular disease (CVD). CD4_ T lymphocytes within the atherosclerotic plaques mediate cellular (Th1) immune responses in which the macrophage activating cytokine interferon-gamma plays a crucial role. Interferon-gamma stimulates the production of neopterin and conversion of amino acid tryptophan to kynurenine in macrophages. Recent studies also suggest that macrophages increase their production of homocysteine, when stimulated. We have assessed neopterin, kynurenine, the kynurenine / tryptophan ratio (KTR), total homocysteine (tHcy) and CRP as predictors of mortality in patients with stable angina. **Methods** A total of 1039 consecutive patients with suspected coronary artery disease (CAD) were examined with coronary angiography between January 2000 and June 2001. Mean (SD) age at inclusion was 61.5 (10.5) years, and 291 (28.0%) of the patients were women. A total of 236 patients (22.7%) had no significant CAD, whereas 357 (34.4%) had triple vessel disease. Samples were taken before angiography and immediately frozen at -80o C until analysis. **Results** The following median (25th-75th percentile) levels were observed: neopterin 7.36 (5.92–9.53) nM, kynurenine 1.65 (1.33–2.04) _M, tryptophan 73.4 (64.3– 82.4) _M, KTR 22.4 (18.1–24.1). tHcy 10.3 (8.59 –12.5) _M, and CRP 1.95 (0.98 –3.74) mg/L. Significant bivariate correlations (Spearman) were found for tHcy with kynurenine (r_0.24), KTR (r_0.30), neopterin (r_0.35) and CRP (r_0.17) (all p _0.001). During a follow-up of mean (SD) 5.9 (1.3) years, 118 patients (11.4%) died. Results of Cox regression are presented as relative risk RR (95% CI) per quartile increment in the specified variable. In univariate analyses, tHcy (RR 1.78 (1.48 –2.14)), neopterin (RR 1.49 (1.26 –1.77)), KTR (RR 1.40 (1.18 –1.66)), kynurenine (RR 1.31(1.11–1.55)) and CRP (RR 1.35 (1.14 –1.59)), but not tryptophan, predicted mortality. After adjustment for age and gender, the effects of kynurenine and KTR were no longer significant (p _ 0.13). The risk estimates for tHcy (RR 1.50 (1.24 –1.82)), CRP (RR 1.32 (1.12–1.56)) and neopterin (RR 1.27 (1.06 –1.52)) were moderately attenuated. In multivariate analysis, we additionally adjusted for daily smoking, extent of CAD, ejection fraction and levels of creatinine, neopterin, tHcy and CRP. In this model, neopterin did no longer predict mortality (p_0.36). Only the risk estimates for tHcy (RR 1.34 (1.09 –1.64)) and CRP (RR 1.22 (1.03–1.45)) remained significant. **Conclusion** Among patients with stable angina, tHcy is a stronger predictor of mortality than the immune / inflammation markers KTR, neopterin and CRP.

Asymmetric and symmetric dimethylarginine are weaker predictors than homocysteine of long-term mortality in both men and women with stable angina

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Total homocysteine (tHcy) is an established marker of mortality in patients with cardiovascular disease. It has recently been claimed that asymmetric dimethylarginine (ADMA), a competitive inhibitor of the enzyme, nitric oxide synthase (NOS), may be a particular strong prognostic marker. Symmetric dimethylarginine (SDMA) may reflect impaired renal function and competitively inhibit trans-membrane transport of other arginines. We studied these arginines as predictors of long-term mortality in both men and women with stable angina. Between January 2000 and June 2001, a total of 1039 patients (291 (28.0%) women) with suspected coronary artery disease (CAD) were examined with diagnostic coronary angiography, and then followed for an average (SD) of 5.85 (1.25) years. Mean (SD) age was 61.5 (10.5) years. Women were significantly older than men, mean (SD) ages 63.4 (10.7) and 60.8 (10.3) years (p_0.001), respectively. Extent of CAD was scored as 0–3 according to the number of vascular territories affected by a stenosis of at least 50% of the vessel diameter. Among the patients, 235 (22.6%) had no significant CAD, whereas 357 (34.4%) had 3 vessel disease. Mean (SD) levels of analytes at baseline were tHcy 11.3 (5.0) _M, L-arginine 48.9 (11.1) _M, ADMA 0.75 (0.14) _M, SDMA 0.59 (0.19) _M and creatinine 80.0 (32.1) _M. tHcy (r_0.34), ADMA (r_0.28) and SDMA (r_0.68) were strongly related to creatinine, and tHcy showed significant associations with ADMA (r_0.20) and SDMA (r_ 0.38) (all p_0.001). A total of 118 patients (11.4%) died during follow-up. All Cox regression models are adjusted for gender and age, and results are represented as increase in risk (95% CI) per quartile increment in the specified variable. Mortality was significantly predicted by tHcy (RR 1.50 (1.24 –1.82)) and SDMA (RR 1.28 (1.06 –1.54)), but not by ADMA (RR 1.14 (0.96 –1.35)), L-arginine (RR 0.94 (0.80 –1.11)), creatinine (RR 1.19 (0.98 –1.44)), or ratios between various arginines (data not shown). In a model including tHcy, SDMA, creatinine, extent of CAD and treatment after angiography (medication only, PCI, bypass surgery, other surgery), tHcy (RR1.43 (1.17–1.75)), but not SDMA (RR 1.15 (0.92–1.44)), predicted survival. Adjustment for hypertension, diabetes, previous myocardial infarction, ApoA1, ApoB and CRP minimally attenuated these estimates, whereas additional adjustment for current smoking or ejection fraction somewhat weakened their effect; tHcy (RR 1.31 (1.06 –1.61)). In gender specific, multivariate models, both ADMA and SDMA failed to prove as significant markers for mortality, whereas tHcy remained significant (p_0.04). In conclusion, tHcy is a stronger predictor of long-term mortality than ADMA or SDMA in patients with stable angina, regardless of gender.