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EXEMPEL





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Comparison of loop diuretics; intravenous bolus injection versus continuous infusion in hospitalized patients with moderate to severe Congestive Heart Failure

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Background

Loop diuretics plays a key role in treatment of individuals with acute decompensated congestive heart failure (CHF). This treatment is frequently used to decrease fluid accumulation in hospitalized patients with decompensated CHF. NT-proBNP is the standard biomarker of wall strain, overload and to determine the severity of CHF. However the strategy behind how the physician decide what route of administration of loop diuretics, intravenous bolus injection (IV), or as a continuous infusion (CI), is not known.

We aimed to study benefits and outcome depending on the mode of loop diuretics as overload treatment of severe CHF.



Methods

Forty subjects in total, twenty (8 male, 12 female) in each group, diagnosed with severe CHF, were included consecutively at Emergency and Internal Medicine Clinic, during 2018.

All were treated with loop diuretics under the hospital stay as IV or CI. The patients' mean age were 85 vs. 80 years. Pared t-test was used for statistics, p-value of <0.05 was considered as significant.

Results

The use of CI was more frequent in patients with higher **NT-proBNP** (15901 ± 2977 vs. 9640 ± 2153 ng/L; $p < 0.05$) and lower blood pressure ($p < 0.05$) as compared to IV administration. There was no difference in estimated glomerular filtration rate (e-GFR). Patients treated with CI had 40 % all cause mortality rate compared with the IV group 10 % followed for a 3 months period. Five patients died as inpatient in the CI group and one in the IV group, after discharge.

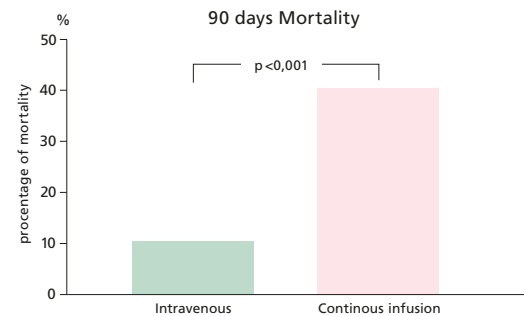
Discussion

The use of CI was preferred in this study of advanced stage of acute severe CHF patients but the rationale behind it is not known. Moreover the CI group had significantly higher NT-proBNP levels and lower blood pressure, compared to the IV group, which may explain the higher mortality rate. Further research is needed.

Subjects characteristics

Parameters	Diuretics IV	Diuretics CI	p-value
Age (year)	84±7	80±11	NS
Gender M/F	8/12	8/12	
Weight admission (kg)	73±17	72±16	NS
Weight discharge (kg)	74±18	70±14	NS
NYHA-class	III: 10 IV:10	III: 5 IV:15	NS
NT-proBNP (ng/L) admission	9640±2153	15901±2977	<0.05
NT-proBNP (ng/L) discharge	7380±1729	12536±2436	<0.05
Systolic Blood Pressure (mmHg) (SBP)	140±30	116±11	<0.05
Diastolic Blood Pressure (mmHg) (DBP)	82±15	73±11	<0.05
Ejection Fraction (%)	40	30	<0.05
EKG QRS (ms)	126±31	131±36	NS
e-GFR (mL/min/1.73m ²) admission	40±13	36±15	NS
e-GFR (mL/min/1.73m ²) discharge	40±13	35±16	NS
Loop diuretics mean daily dose (mg/day)	46	149	<0.05
30 days readmission rate	25 %	30 %	
Mortality rate	10 %	40 %	<0.05

The table illustrates the differences between CHF subjects treated with loop diuretic, intravenous bolus injection (IV) or continuous infusion (CI). Data are given as mean ±SD. For comparison, paired student t-test was used. Significance difference p-value of <0.05 was considered as significant.



Conclusions

- CI group had significantly lower blood pressure
- CI group had significantly higher NT-ProBNP
- CI group had significantly higher mortality rate

CAVEAT: We see no clear reason for choosing infusion of loop diuretics in severe CHF.

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Utgå alltid från de mallar som finns i Bild- och Mediebanken för att få korrekt placering.



Relationship status and serum levels of testosterone: A study on middle-aged healthy men from the general population

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Introduction

The present study aims to investigate the association between relationship status and serum levels of testosterone based on data from 118 healthy men from the general population.

Method

Testosterone levels & biomarkers of systemic inflammation and subclinical atherosclerosis were measured. Data was also gathered on age, BMI, waist-to-hip ratio, relationship status, number of children, smoking, and alcohol consumption. Men were classified into two groups according to the relationship status, paired (married; living together but is not married; living apart together but is not married), and unpaired (divorced, separated) men. Statistical analyses were done using Mann-Whitney U test, Fisher exact test, Spearman's rank correlation coefficient test, and adjusted multivariate regression analysis model. P-values below 0.05 considered statistically significant.

Results

The mean (SD) age of men was 55 ± 4.0 years. Paired men had a significantly higher number of children as compared to unpaired men (2.0 child vs. 1.0 child, p = 0.04). The same trend was found regarding the consumption of wine (54 cl/week vs. 27 cl/week; p = 0.01) and ethanol (12 cl/week vs. 8.0 cl/week; p = 0.02), respectively. Serum testosterone levels were significantly lower in paired men when compared to unpaired men (14 nmol/l vs. 19 nmol/l, p = 0.01). On the other hand, age, BMI, waist-to-hip ratio, smoking, and biomarkers of subclinical systemic inflammation & subclinical atherosclerosis did not differ significantly between groups (p > 0.05) (Table I). No significant correlations between testosterone levels and the number of children, consumption of wine, and consumption of ethanol were found (p > 0.05) (Figure 1; a, b, and c). In a multivariate regression analysis model adjusted for the age of subjects; BMI; waist-to-hip ratio, smoking; alcohol consumption, a significant negative association between relationship status and testosterone levels was still found (β = -0.05; 95 % CI = -8.00, -2.00; p = 0.003) (Data not shown).

Conclusions

Our results contribute to the growing body of literature suggesting that paired men are associated with lower serum testosterone levels, while unpaired men are associated with higher serum testosterone levels. Additional researchs are needed to elucidate any causal relationships.

Table I:

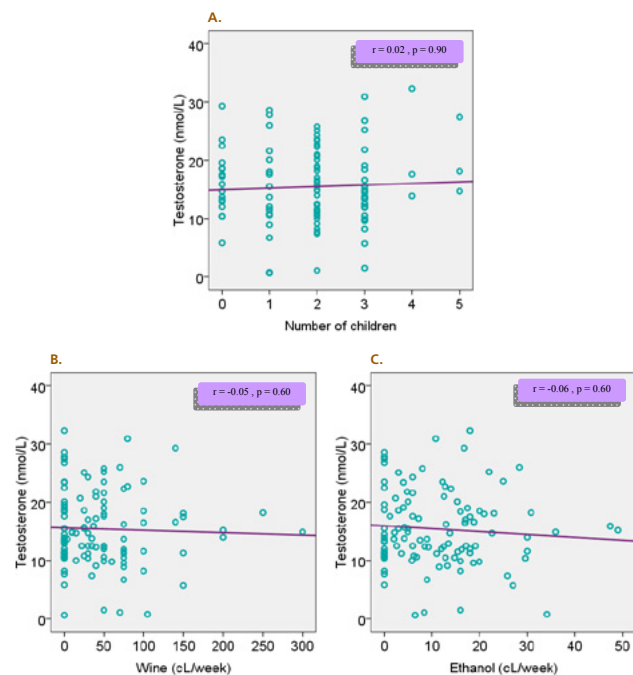
The demographic and biochemical markers according to the relationship status obtained from 118 middle-aged healthy men from the general population.

Variables	Relationship status		p
	Paired n = 94	Unpaired n = 24	
Age (years)	55 (±3.0)	56 (±4.0)	0.20
BMI (kg/cm ²)	27 (±3.0)	26 (±4.0)	0.50
Waist-to-hip ratio	1.0 (±0.1)	1.0 (±0.1)	0.30
Number of children	2.0 (±1.0)	1.0 (±1.0)	0.04
Smoking*			
Never	52 (55%)	9.0 (37%)	0.20
Past/current	42 (45%)	15 (63%)	
Alcohol consumption			
Beer (cl/week)	50 (±76)	27 (±59)	0.08
Wine (cl/week)	54 (±57)	27 (±45)	0.01
Spirits (cl/week)	8.0 (±12)	9.0 (±16)	0.30
Ethanol (cl/week)	12 (±10)	8.0 (±10)	0.02
Biochemical markers:			
Testosterone (nmol/l)	14 (±6.0)	19 (±8.0)	0.01
ApoA (g/l)	1.4 (±0.2)	1.3 (±0.2)	0.10
ApoB (g/l)	1.1 (±0.3)	1.0 (±0.2)	0.60
ApoB-to-ApoA ratio	0.8 (±0.2)	0.8 (±0.2)	0.70
CRP (mg/l)	2.7 (±7.0)	1.5 (±1.7)	0.60
Fibrinogen (g/l)	2.5 (±0.70)	2.6 (±0.6)	0.40

Data are mean (±SD) or n (%). BMI = body mass index. ApoA = Apolipoprotein A. ApoB = Apolipoprotein B. ApoB-to-ApoA ratio = Apolipoprotein B-to-Apolipoprotein A ratio. CRP = C-reactive protein. Statistical analyses were done using Mann-Whitney U test. *Statistical analyses were done using Fisher exact test. P-values below 0.05 considered statistically significant.

Figure 1.

Correlations between serum levels of testosterone and (A) number of children, (B) consumption of wine, and (C) consumption of ethanol obtained from 118 middle-aged healthy men from the general population.





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Aged garlic extract improves the microcirculation: A double-blind placebo controlled study

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Background

Laser Doppler Velocimetry (LDV) is a non-invasive method of estimating tissue perfusion. LDV provides a continuous record of the microvascular blood flow, and is therefore an excellent method to measure microvascular blood flow changes and microvascular perfusion. In patients with heart disease microvascular tissue perfusion has shown to be impaired even when global haemodynamic or signs of hypoperfusion are absent. Prior studies implies that Aged Garlic Extract (AGE) has a positive effects on vascular elasticity and endothelial function. This study aimed to assess the effect of long-term treatment with AGE on tissue perfusion.

Methods

A total of 122 patients with Framingham Risk Score ≥ 10 were randomized in a double-blind manner to placebo or treatment with 2400mg AGE daily for a period of 1 year and monitored externally. Microcirculation was measured using LDV at 0 and 12 months. The measurements was made on the forearm before and during reperfusion after a partially induced ischemia by compression using 250mmHg for 3 minute. The difference in LDV perfusion units between measurements was considered a proxy of microcirculation.

Results

A repeated measures ANOVA with a Greenhouse-Geisser correction determined that mean perfusion differed statistically significantly between time points ($F(1, 120) = 5.95$, $P < 0.016$).

Conclusions

The present study demonstrates that 12 months of AGE supplement improves the microcirculation measured by LDV compared to the placebo group. Increasing the microvascular blood flow might be due to an increased angiogenesis and vascular neovascularization but also by potentially affecting vascular tone and endothelial function.

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Figure 1

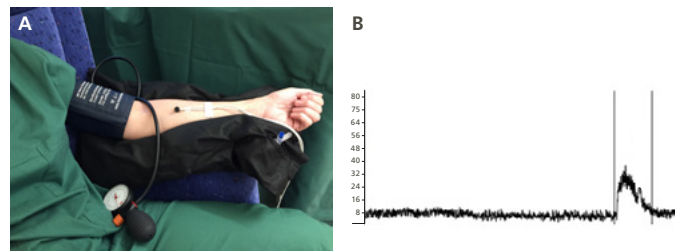
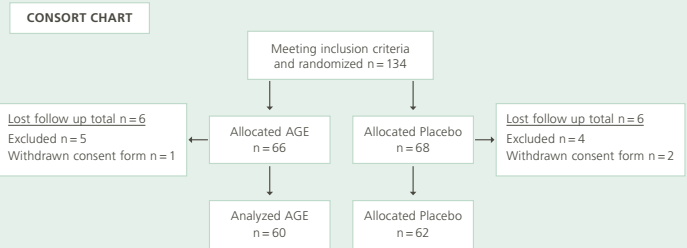


Figure 1 A shows a clinical setup with laser Doppler velocimetry (LDV). The measurements was made on the forearm before and during reperfusion after a partially induced ischemia by compression using 250mmHg for 3 minute.

Figure 1 B shows an example of an output data file from the LDV. The difference in LDV perfusion units between measurements was considered a proxy of microcirculation.

Figure 2



CONSORT statement (consolidated standards of reporting trials) flow chart. Showing demographics and baseline clinical information of the study cohort.

Figure 3

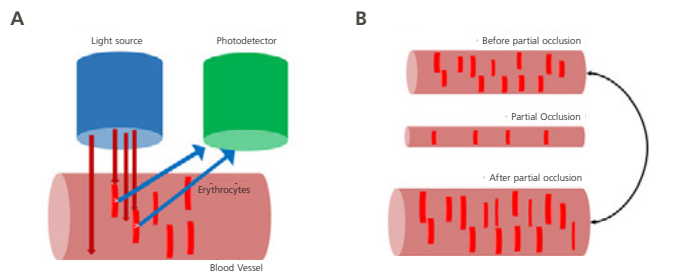


Figure 3 A shows a schematic of the laser Doppler velocimetry technique. Light impinging on blood cells in motion undergoes a change in wavelength (Doppler shift) while light impinging on static objects remains unchanged. The information is collected by a returning fibre, converted into an electronic signal, and analysed.

Figure 3 B shows how the magnitude and frequency distributions of the changes are directly related to the number and velocity of red blood cells. Before and after a partial occlusion.

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The effect of aged garlic extract on the atherosclerotic process – a double blind placebo-controlled trial

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Background

Aged garlic extract (AGE) has shown positive effects on inflammatory biomarkers and cholesterol-lowering effects in a non-European population.

Objective

To evaluate whether AGE can influence coronary artery calcification (CAC) in a European population, and also to create an algorithm, the AGE Algorithm, using a cross industry standard process for data mining (CRISP-DM) to predict individual outcome of AGE.

Methods

A total of 104 patients with a Framingham risk score ≥ 10 , were randomised after CT scan, in a double-blind manner to placebo or AGE (2400mg daily) for 1 year. Blood pressure and biomarkers were measured every 3 months. CAC score was defined again after 1 year. The AGE Algorithm was created to predict CAC progression and blood pressure.

Results

A logistic regression analysis showed an OR of 2.95 (1.05 - 8.27) for CAC progression, blood glucose OR 3.1 (1.09 - 8.85) and IL-6 OR 2.56 (1.00 - 6.53) with all $p < 0.05$ in favour of the AGE group. A significant decrease in systolic blood pressure between 0 months, 148 ± 19 mmHg, and 12 months, 140 ± 15 mmHg ($p = 0.027$) in favour of the AGE group was also observed. At a selected probability cut-off value of 0.5, the accuracy score for CAC progression was 80%, with precision score of 79% and recall score of 83%. Similar results predicting blood pressure were also obtained.

Conclusions

The AGE Algorithm predicted with 80% precision which patient will have a significantly reduced CAC progression using AGE supplement and could predict with a 74% precision which patient will have a significant lowering of blood pressure using the AGE supplement. The present study concludes that AGE inhibits CAC progression and lowers IL-6, glucose levels and blood pressure.

Figure legends



CONSORT 2010 Flow Diagram

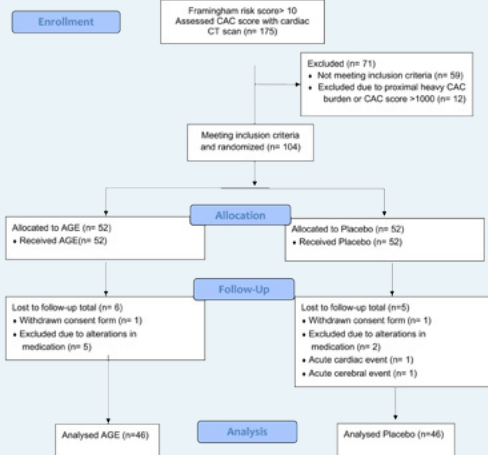


Figure 1. CONSORT statement (consolidated standards of reporting trials) flow chart. Showing demographics and baseline clinical information of the study cohort. Aged garlic extract (AGE), coronary artery calcification (CAC).

Table 1: Using multivariable methods, logistic regression, two proof of concept predictive models were developed and validated using leave-one-out cross validation (LOOCV), one for CAC progression and one for systolic blood pressure. Each model was trained and tested 46 times, resulting in all patients belonging to the training sample 45 times and the test sample once.

	Patient 1	Patient 2	...	Patient 44	Patient 45	Patient 46
Model 1	Train	Train	...	Train	Train	Test
Model 2	Train	Train	...	Train	Test	Train
Model 3	Train	Train	...	Test	Train	Train
...
Model 46	Test	Train	...	Train	Train	Train

Table 2: Patient demographics at baseline.

Variable	AGE		Placebo		P
	n = 47	%	n = 46	%	
Gender (male)	30	(65%)	31	(66%)	0.94
Hypertension	37	(80%)	41	(87%)	0.38
Hypercholesterolaemia	24	(52%)	32	(68%)	0.12
Diabetes mellitus	5	(11%)	12	(26%)	0.07
Current smoker	5	(11%)	3	(6%)	0.57
Family history of CVD	33	(72%)	25	(53%)	0.09

Table 3: Measurements at baseline, 0 months in absolute values. Coronary artery calcification (CAC), C reactive protein (CRP), High-density lipoprotein (HDL), Low-density lipoprotein (LDL).

Variable	AGE		Placebo		P
	n = 46	SD	n = 47	SD	
Framingham risk score	23	(7)	21	(7)	0.27
Age (years)	63	(6)	64	(6)	0.95
BMI	27.6	(3.7)	30.0	(4.6)	0.01
CAC	207.3	(237.7)	121.0	(178)	0.05
CRP (mg/L)	2.2	(3.6)	2.2	(3.5)	0.97
Triglycerides (mmol/L)	1.4	(0.7)	1.6	(1.2)	0.21
Cholesterol (mmol/L)	5.2	(1.3)	4.6	(1)	0.03
HDL (mmol/L)	1.6	(0.5)	1.4	(0.4)	0.07
LDL (mmol/L)	3.4	(1.1)	2.9	(0.9)	0.01
IL-6 (ng/L)	4.5	(3.7)	4.4	(2.3)	0.83
ApoB/ApoA	0.7	(0.2)	0.7	(0.2)	0.30
Homocysteine (µmol/L)	13.4	(3.8)	13.2	(3.6)	0.76
Glucose (mmol/L)	6.3	(1.2)	6.6	(1.3)	0.43

Interleukin -6 (IL-6), Apolipoprotein A and B (ApoB/ApoA).

Table 4: Results of a logistic regression with a median split. Coronary artery calcification (CAC), C reactive protein (CRP), High-density lipoprotein (HDL), Low-density lipoprotein (LDL), Interleukin -6 (IL-6), Apolipoprotein A and B (ApoB/ApoA).

Variable	AGE vs. Placebo		P
	Adjusted OR	(95%-CI)	
CAC	2.95	(1.05-8.27)	0.040
Glucose (mmol/L)	3.1	(1.09-8.85)	0.034
IL-6 (ng/L)	2.56	(1.0-6.53)	0.049
Cholesterol (mmol/L)	0.57	(0.23-1.43)	0.228
LDL (mmol/L)	0.62	(0.24-1.58)	0.317
Triglyceride (mmol/L)	1.59	(0.6-4.16)	0.349
HDL (mmol/L)	1.43	(0.55-3.76)	0.463
Homocysteine (µmol/L)	1.18	(0.47-2.96)	0.724
ApoB/ApoA	0.9	(0.34-2.39)	0.840
CRP (mg/L)	1.45	(0.56-3.77)	0.447
Glucose (mmol/L)	6.3	(1.2)	0.43

Table 5: Systolic blood pressure for the AGE and placebo group, at 0 and 12 months.

Variable	0 months		12 months		P
	Mean	(SD)	Mean	(SD)	
AGE (n = 46)	148	(19)	140	(15)	0.027
Systolic blood pressure					
Placebo (n = 47)	142	(29)	142	(14)	0.996
Systolic blood pressure					

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Thyroid blood flow doppler as new activity parameter in Graves' thyrotoxicosis

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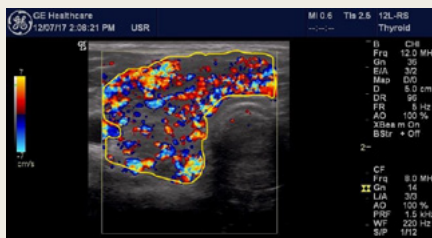
Objective

TSH receptor antibodies (TRAb) are currently used as the major activity parameter for Graves' disease (GD), both in early and later treatment phase as well as when patients are suggested to stop anti-thyroid drugs (ATD) treatment.

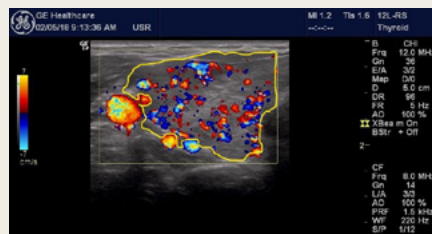
Aim: define a unit for the quantification of thyroid blood flow by measuring color doppler pixels in the region of interest and to use this unit as an estimation of disease activity in patients with GD treated with ATD.

Methods

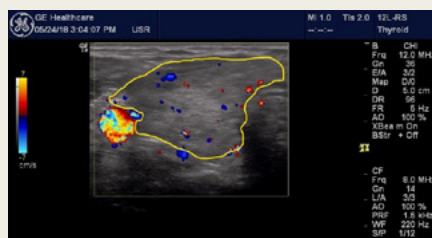
Patients with GD treated with ATD (n=14 plus one excluded late responder) were followed with regular visits and analysis of TSH, thyroid hormones, TRAb and thyroid-peroxidase antibodies (anti-TPO). Thyroid color doppler was performed in the largest cross-sectional area and three separate pictures were saved from both lobes. The margins of the largest cross-sectional thyroid areas were outlined and the number of red and blue pixels, which indicate blood flow, was calculated as a percentage of total pixels in the region of interest by a specifically designed program.



Picture 1. Doppler ultrasound of the right thyroid lobe before the beginning of treatment with ATD. Patient JO.



Picture 2. Doppler ultrasound after 3 months' treatment.



Picture 3. Doppler ultrasound after 6 months' treatment.

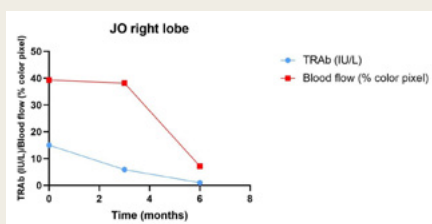


Figure 1. Kinetics of TRAb and blood flow in the right lobe.

Results

The mean values of TRAb and percentage of color pixels are presented in Figure 2. Thyroid blood flow color doppler decreased in parallel with TRAb. However, the kinetics differed and in most cases blood flow doppler signal showed a continuous decrease, although TRAb had already reached a stable low titer. The decrease in blood flow doppler signal was similar in both lobes and it was statistically significant over time.

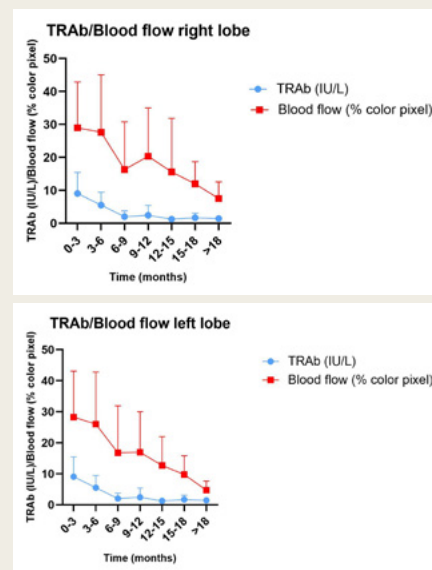


Figure 2. Development of TRAb and blood flow over time.

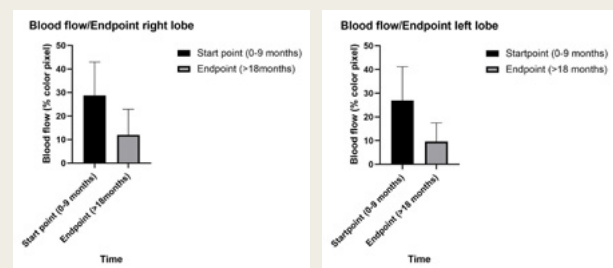


Figure 3. Comparison of percentage of color pixels between the startpoint (0-9 months) and the endpoint (>18 months) of treatment. P-value < 0.05.

Conclusion

We developed a new method for quantifying thyroid blood flow doppler and demonstrated that both blood flow doppler and TRAb are activity parameters with different kinetics in Graves' disease treated with anti-thyroid drugs.

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Effekt av intravenöst givet K-vitamin till kritiskt sjuka patienter med spontant förlängd protrombintid

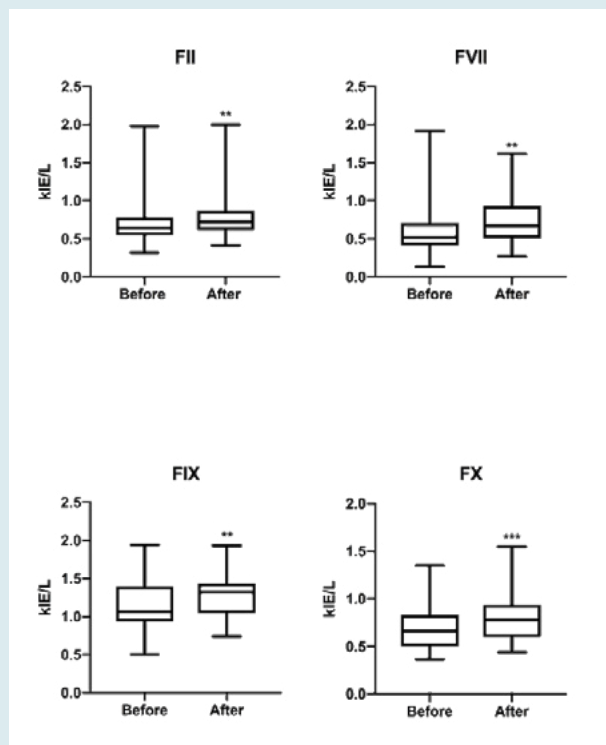
DOLORE MAGNA, LOREM IPSUM, DOLOR SIT AMET, CONSECTETUR ADIPISCING

Slutsats

Studien demonstrerar att protrombintid (PT) och aktivitet av K-vitaminberoende koagulationsfaktorer hos kritiskt sjuka patienter med spontanförlängda PT-värden har förstärkts 24 timmar efter Konakion.

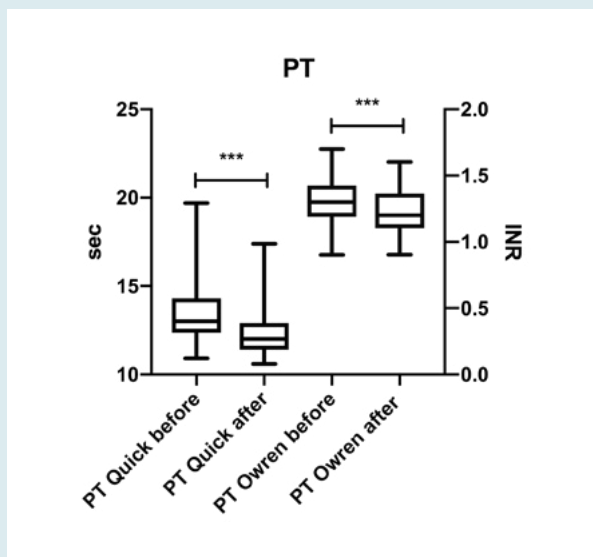
Introduktion

Tidigare studier indikerar att K-vitaminbrist är vanligt hos kritiskt sjuka patienter. Spontan koagulopati är vanligt förekommande i denna patientgrupp och kan ibland korrigeras med K-vitamin. K-vitamin krävs för att aktivera protein involverade i koagulation, arterio-skleros och benmetabolism. Syftet med den aktuella studien var att undersöka effekten av intravenöst givet K-vitamin på rutinmässiga och avancerade koagulationsanalyser.



Metod

Kritiskt sjuka patienter med lätt förlängd protrombintid (PT(på svenska PK))–Owren(PK-INR) >1,2 inkluderades konsekutivt på kontorstid. Rutinkoagulationsstatus (PT–Owren, PT-Quick), aktivitet av faktor (F) II, FVII, FIX, FX och koncentration av protein C och S, trombingeneration(TGA) samt tromboelastometri(ROTEM ExTEM), mättes före och 24 timmar (h) efter att 10 mg K-vitamin (Konakion)givits intravenöst (iv). Exklusionskriterier: pågående waran-eller NOAC-behandling, hepatocellulär cancer, leverresektion <6 månader, känd koagulopati eller behandling med Konakion <36 h.



Resultat

27 patienter inkluderades. En signifikant sänkning av PT–Owren och PT–Quick påvisades 24 h efter givet K-vitamin (p < 0.001). Aktiviteten av FII, FVII, FIX och FX ökade (p < 0.01, p < 0.01, p < 0.01, p < 0.001). Koncentrationen av protein C och S var oförändrad. Ingen skillnad demonstrerades i TGA eller ROTEM-analyserna CT, CFT, α -vinkel, LI60 och ML. En signifikant (p < 0.05) ökning av ROTEM–MCF påvisades troligtvis sekundär till en ökning i plasma-fibrinogen som i motsats till de K-vitaminberoende proteinerna är en akutfasreaktant.

Conclusions

Adopting a culturally sensitive lifestyle intervention approach in primary health care settings could be potentially beneficial for improving lifestyle habits and reducing the risk of T2D and poor mental health in this vulnerable immigrant population.

Aims

I) In residents of Malmö born in Iraq or Sweden, to study the prevalence & risk factors associated with poor mental health.

Background

T2D and poor mental health are two major public health concerns in Europe. Ethnicity is identified as a risk marker for both conditions. Middle-Eastern immigrants (MEI), the largest group of non European immigrants in Sweden are at increased risk for T2D. Physical activity not only prevents/delays onset of T2D but also shows favorable effects on mental health. However, the evidence related to the efficacy of such interventions in non-European immigrants is scarce.

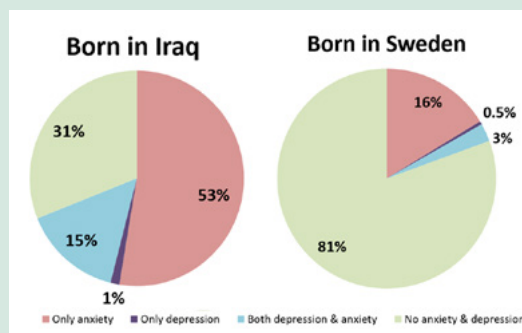
II) In MEI, to elaborate on the effects of a culturally adapted lifestyle intervention on lifestyle habits, cardio metabolic profile & mental health.

Methods

I) The MEDIM study (n=1889), a population based cross sectional study, conducted between 2010 and 2012. Iraqi born and Swedish born residents of Malmö (30–75 years) were randomly selected from the census register and invited to participate. Information on lifestyle, socio-demography and mental health (Hospital Anxiety and Depression Scale (HADS)) was provided through questionnaires.

II) The MEDIM intervention study, a randomised controlled trial, recruiting Iraqi immigrants at high risk of T2D, was conducted in 2015. High risk for T2D was defined as having a body mass

index (≥ 28 kg/m²) and/or waist circumference (≥ 80 cm in women, and ≥ 94 cm in men) and/or pre diabetes. Anthropometric measurements, oral glucose tolerance test and assessment of mental health using Montgomery Åsberg Depression Rating Scale (MADRS S) and HADS, was performed at the start, mid and end of the study. Physical activity data was collected using accelerometers. Linear mixed models and proportional odds model were assessed. The intervention comprised of seven gender specific group sessions including one cooking class, delivered over a period of four months and addressed lifestyle change.



Prevalence of anxiety and/or depression in participants born in Iraq (left) or Sweden (right).

Results

I) Compared to Swedes, anxiety was 3x and depression 5x as prevalent in Iraqi immigrants. Iraqis had 3x higher odds of anxiety/depression. Physical inactivity, economic insecurity, inability to trust people and smoking were associated with anxiety and depression in the Iraqis.

II) A reduction in body weight (0.4%/month) and LDL cholesterol levels (2.1%/month), as well as improvement in insulin sensitivity index

(10.9%/month), was observed in the intervention group (IG, n=50) compared to the control group (CG, n=46). An increase in number of hours/day spent in light intensity activities was observed in the IG vs. the CG. No significant changes in dietary intake were observed in the IG. The odds of scoring lower on MADRS S and HADS for depression at follow up vs. Baseline were higher in the IG compared to the CG.

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