



Association of PCSK9 with biochemical markers of atherosclerosis at the population level

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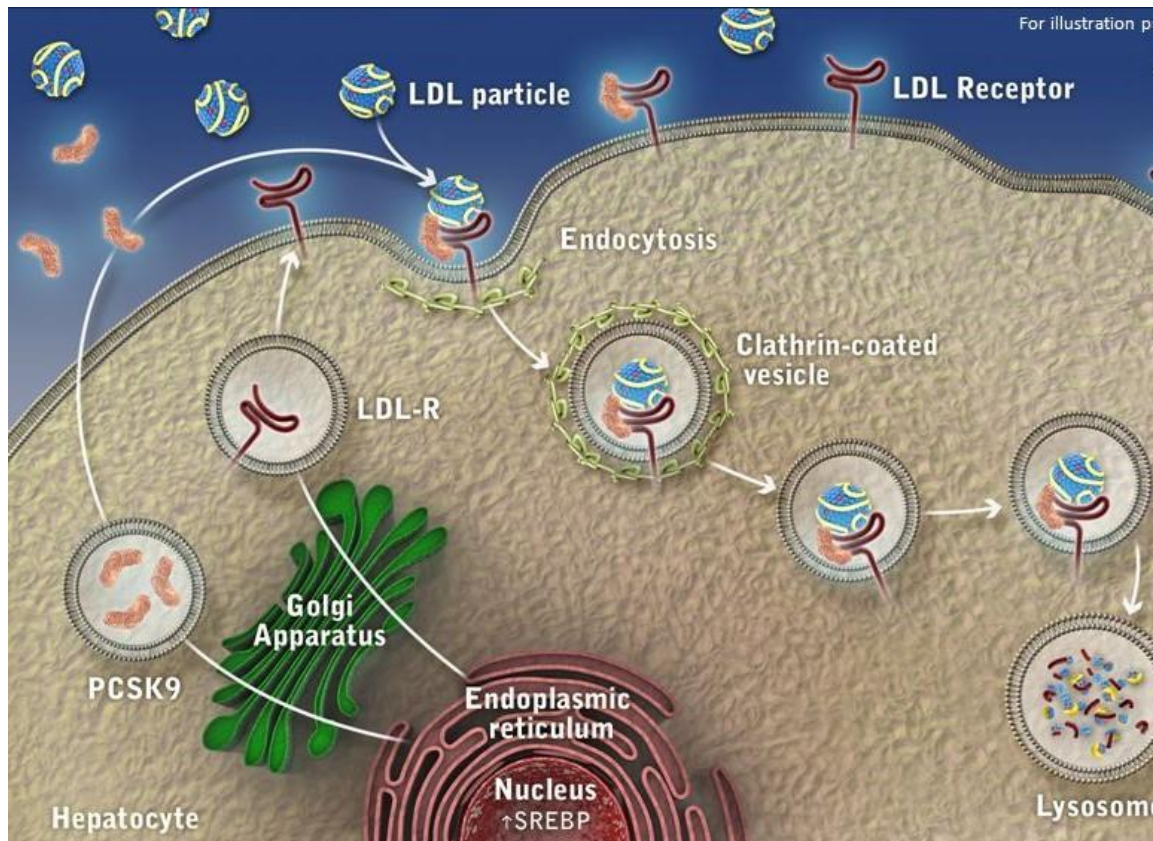
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Relevance

LDL - low density lipoprotein cholesterol

LDL-R - low density lipoprotein cholesterol receptor

PCSK9 - proprotein convertase subtilisin/kexin type 9



Inhibition

- ↓ LDL-C on 55-72%
- ↓ KV risk factors
- ↓ mortality

Polymorphisms

- mutation gain function
- autosomal dominant familial hypercholesterolemia



PCSK9

- proprotein convertase subtilisin/kexin type 9

Insulin resistance?

Carcinogenesis?

BP?

Glucose?

Biomarker?

Inflammation?

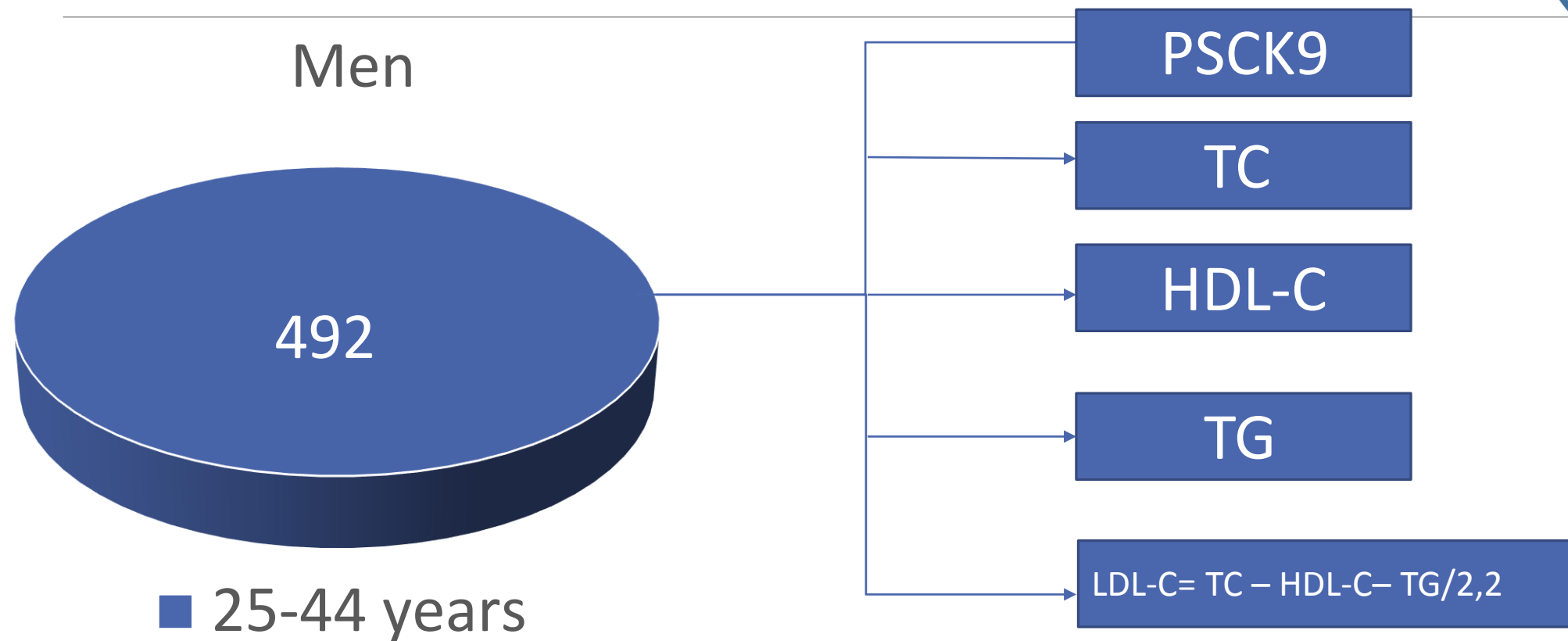
Forecast?



Purpose of the study

To estimate the level of proprotein convertase subtilisin/kexin type 9 (PCSK9) in the population group of young men in Novosibirsk and the relationship of this protein with the lipid parameters.

Materials and methods



Clinical characteristics of the group

	M ± SD	Me (25%;75%)
Age, years	35,98 ± 5,86	35,86 (31,17;41,08)
BMI	26,65 ± 4,95	26,49 (23,16;29,48)
TC, mmol\l	5,11 ± 1,02	5,06 (4,39;5,73)
LDL-C, mmol\l	3,27 ± 0,88	3,21 (2,62;3,83)
HDL-C, mmol\l	1,21 ± 0,28	1,16 (1,03;1,37)
TG, mmol\l	1,40 ± 0,98	1,10 (0,77;1,69)
Glucose	5,91 ± 0,84	5,83 (5,52; 6,24)
BP, mmHg	126,13 ± 13,4/ 82,91 ± 9,93	124,50 (117,00;133,50)/ 82,00 (76,00;89,50)
Smoked 56% (277 people)		

A histogram of the distribution of PCSK9 protein levels in the study group

Intermediate PCSK9:

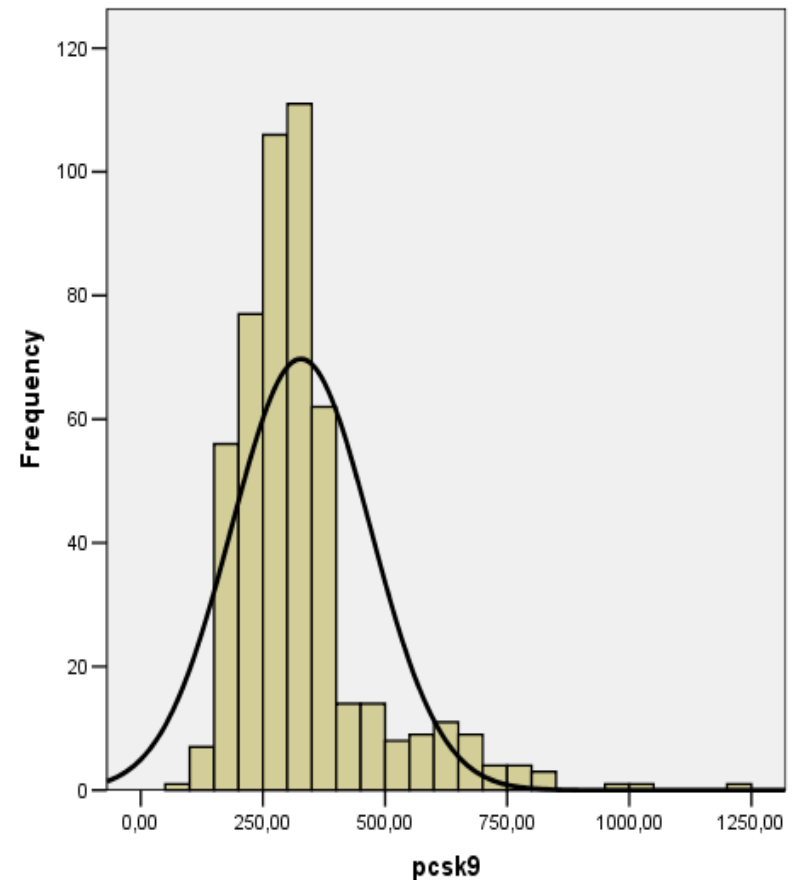
M - 325.9 ± 141.97 ng / ml

Me - 300.19 (240.20; 361.80) ng / ml

High variability:

minimum 20.90 ng / ml

maximum 1249.04 ng / ml



The distribution of PCSK9 in pairs of independent samples that differ in terms of cholesterol, LDL, HDL, TG, and age.

M - arithmetic mean

SD - standard deviation

Me – median

25%; 75% - interquartile range

TC - total cholesterol

TG – triglycerides

HDL-C - high density lipoprotein cholesterol

LDL-C - low density lipoprotein cholesterol

		PCSK9 (ng/ml)			
Risk factors		Number of people in a subgroup	M ± SD	Me (25%;75%)	p
TC	< 5 (mmol/l)	238	315,72 ± 142,31	291,02 (221,13; 354,97)	0,048
	≥ 5 (mmol/l)	254	335,38 ± 141,28	308,86 (252,52;368,46)	
LDL-C	< 3 (mmol/l)	196	316,10 ± 140,95	288,09 (219,80;355,72)	0,041
	≥ 3 (mmol/l)	295	332,86 ± 142,47	309,39 (251,80;365,93)	
HDL-C	> 1,03 (mmol/l)	378	326,66 ± 144,51	297,89 (237,43;363,32)	0,52
	≤ 1,03 (mmol/l)	114	323,25 ± 133,79	309,96 (250,29;356,67)	
TG	< 1,7 (mmol/l)	370	324,09 ± 144,50	298,08 (240,11;356,87)	0,37
	≥ 1,7 (mmol/l)	122	331,27 ± 134,46	307,67 (243,99;372,71)	
Age	< 35 (years)	224	324,08 ± 133,90	303,70 (238,68;361,77)	0,010
	≥ 35 (years)	268	327,37 ± 148,62	298,44 (245,26;361,86)	



Spearman correlation analysis

TC	$r = 0,115, p = 0,01$
LDL-C	$r = 0,091, p = 0,04$
Glucose	$r = 0,122, p = 0,007$
Smoke	$r = 0,115, p = 0,010$

Multiple Linear Regression Analysis of the Relationship of Risk Factors with PCSK9

• B - regression coefficient, SE - standard error of the coefficient, BMI - body mass index, TC - total cholesterol, SBP - systolic blood pressure

Options	B (SE)	p
Age	0,264 (1,138)	0,82
SBP	0,410 (0,522)	0,43
BMI	-1,693 (1,424)	0,24
TC	15,196 (6,603)	0,02
Smoking (no smoking/ smoking)	18,492 (12,897)	0,15

PCSK9 level, ng / ml

Real study	325,9 ± 141,97; 300,19 (240,20; 361,80)
Population study of men 44-73 years old	131,1 ± 4,2 нг/мл; 119,8
Relatives of persons with FC, A.N. Meshkov (n = 29)	193,83 (166,44 -220,29)
DallasHeartStudy (population)	450
PPID Nanjing Study (population)	68,29 ± 28,73
	103,9 (82,5 – 130,2)
Chernogubova et al study (population)	83,1 (67,0 – 103,0)
	77,1 (61,9 – 95,3)
	93,6 (72,8 – 121,5)
PLIC (populatione)	280,8 ± 198

Familial hypercholesterolemia

Russian research program for the diagnosis and treatment of patients with familial hypercholesterolemia, individuals with a level of TC ≥ 7.5 mmol/l and / or LDL-C ≥ 4.9 mmol/l	382 ± 148; 359 (289–448)
Popova et al., Persons with familial hypercholesterolemia, according to Dutch and British criteria	428,8 (334,5; 634) и 426,0 (372,4; 681,8)
Patients with FC, A.N. Meshkov	258,77 (221,67 - 299,17)

Discussions

Higher than other population studies.

Population specificity.

Discussions



- Wide variability of the indicator was also observed in DallasHeartStudy (from 33 to 2988 ng / ml).
- The left-shift distribution was observed in the PPID Nanjing Study, a study by A. Popova. et al. Right - at DallasHeartStudy.

Discussions



- Correlations between PCSK9 and TC, LDL-C: consistent with data from Lakoski S.G. (2009), Cui Q. (2010), Chernogubova E. (2012), Tibolla G. (2014), Ragino Yu.I. (2017), Mayne J. (2013)/
- Correlations between PCSK9 and TG were not obtained, although they were found in some studies.
- A higher level of PCSK9 with higher TC and LDL-C is supported by studies by Yu.I. Ragino et al., I.J. Mayne et al.

Conclusion

This study is the only one in Russia that gives an information about the levels of PCSK9 protein, the nature of its distribution, the relationship with lipid parameters in the population of young men and are of interest, since these indicators are population-specific.

The level of PCSK9 in the male population of Novosibirsk was higher than in the majority of population studies. Found correlation with TC and LDL-C is compatible with those in the various world population-based studies.

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