Lipoprotein(a), marker of statin's treatment resistance?

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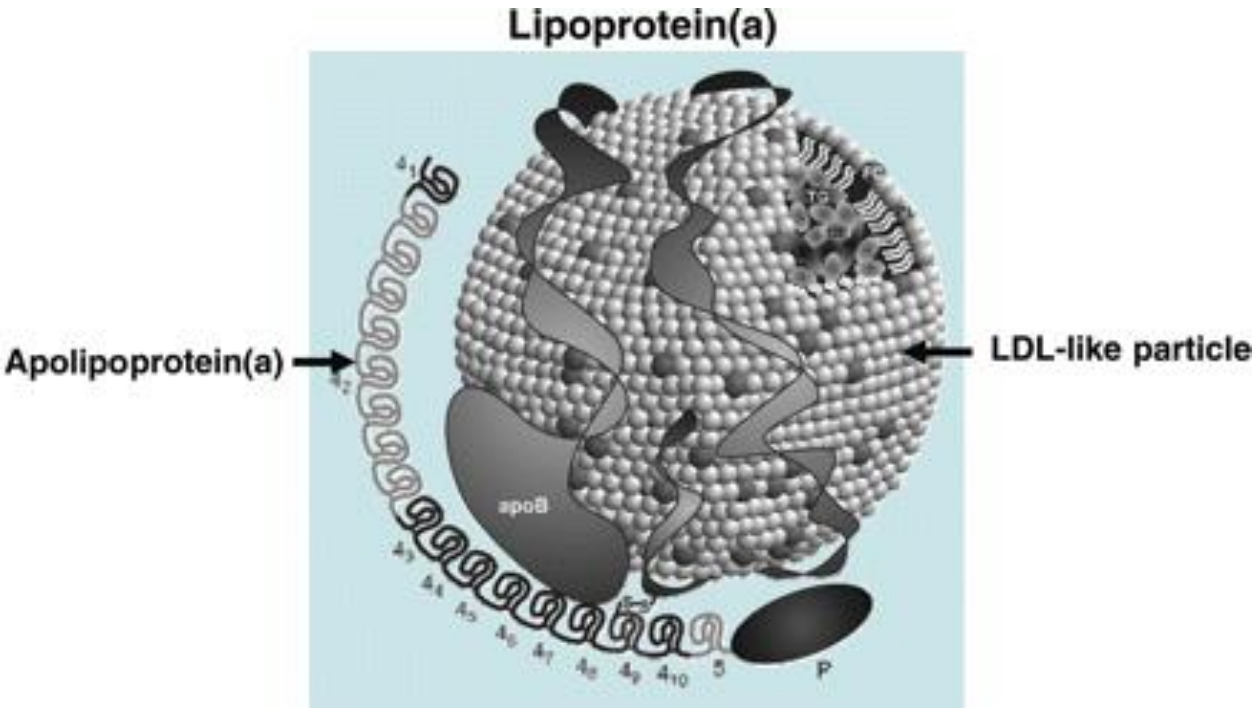
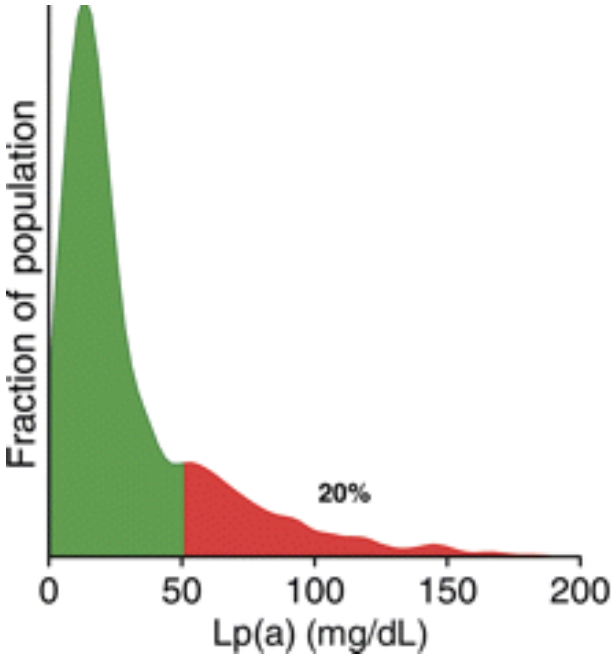
GROUPE JOLIMONT

1° What is Lp(a) ?





- Composed of 30-40% of cholesterol (LDL-like).
- No reuptake possible with LDL receptors
- Variability of ApoA via Kringles IV-2 (amino-acids), genetically determined.

Modified from Koschinsky and Marcovina,
in Nordestgaard et al., Eur Heart J (2010), 31

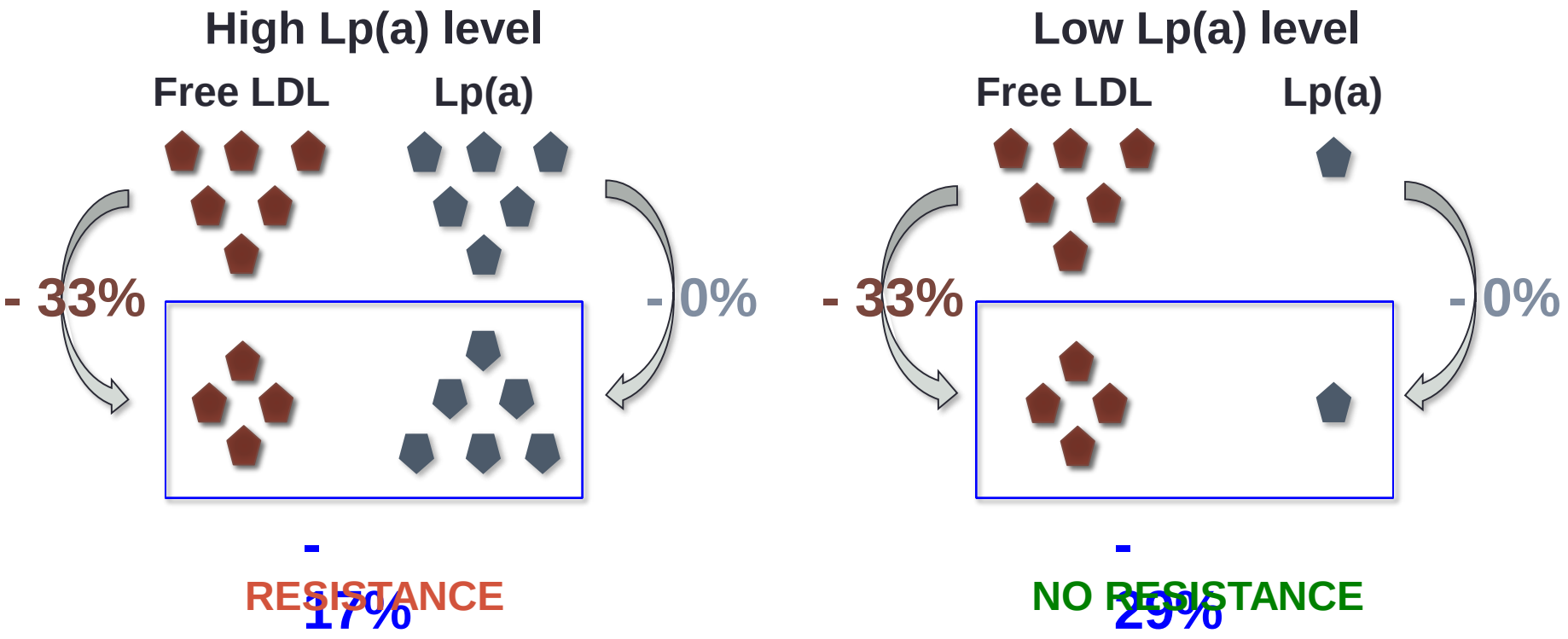
2° Why is Lp(a) so harmfull?

- Independant cardiovascular risk factor, independant of LDL-c.
- High level is associated with strokes and MI risk.
- Mechanistic hypothesis :
  - Cholesterol as LDLc.
  - Pro-inflammatory : recruitment of inflammatory cells, and binding of pro-inflammatory phospholipids.
  - Pro-thrombotic : kringles structure like in plasminogen.

3° The concept of pseudo-resistance

1. Statins increases LDL receptors.
2. No reuptake of Lp(a) by LDL receptors.
3. Statins doesn't reduce the Lp(a) level.

Statin A : expected reduction of 33%



Kostner and al. 1989. *Circulation.* **80**: 1313-1310.

Aim of the study

Does it exist a pseudo-resistance to statins in the patients with a high level of Lp(a)?

Methods

- **Retrospective study**.
- **Inclusion criteria** :
  - All the patients with a dosage of Lp(a) in Jolimont Hospital during the years 2015-2016.
  - Extract randomly an equal number of patients with very high (Lp(a) >100 mg/dL) versus low (Lp(a) < 50 mg/dL)
- **Exclusion criteria :**
  - Not treated patients (intolerance, no treatment needed).
  - No value of LDLc found before OR after the treatment (e.g. no follow up).

Cohort characteristics

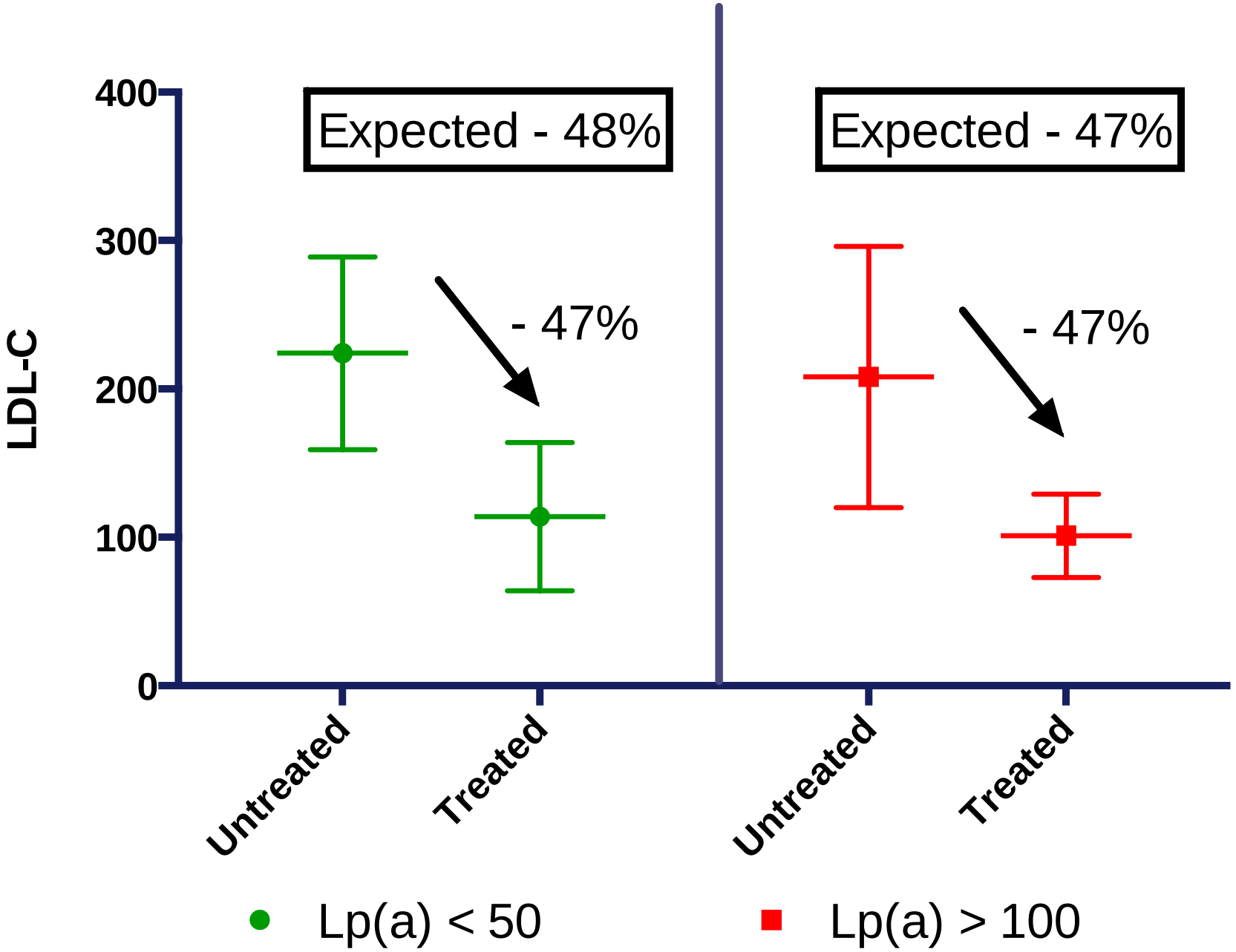
Characteristics	Lp(a) < 50mg/dL (N = 34)	Lp(a) > 100mg/dL (N = 27)
Age - yr	52 +/- 16	53 +/- 15
Male sex – No (%)	16 (47)	9 (33)
Body mass index – kg/m²	27 +/- 8,4	27,3 +/- 5
Cardiovascular risk factors – No (%)		
Current or recent smoking History of smoking	5 (15) 4 (12)	0 (0) 3 (11)
Hypertension	16 (47)	10 (37)
Diabetes	6 (18)	6 (22)
History of acute coronary syndrome Ischemic cardiopathy (PCI or CABG)	2 (6) 4 (12)	0 (0) 2 (7)
Familial history (ACS, Stroke)	15 (44)	13 (48)
Familial hypercholesterolemia – No (%)	12 (35)	8 (30)

Cohort treatments

Characteristics	Lp(a) < 50mg/dL (N = 34)	Lp(a) > 100mg/dL (N = 27)
« Strong statins »	16 (47)	11 (40)
« Moderate statins »	14 (41)	12 (44)
« Low statins »	2 (5)	4 (15)
Ezetrol	13 (38)	6 (22)

Results

Characteristics	Lp(a) < 50mg/dL (N = 34)	Lp(a) > 100mg/dL (N = 27)
Lp(a) – mg/dl	16 +/- 13	162 +/- 40
Cholesterol – mg/dl		
Before treatment	308 +/- 70	312 +/- 101
After treatment	197 +/- 54	194 +/- 65
HDLc – mg/dl		
Before treatment	55 +/- 16	56 +/- 14
After treatment	55 +/- 14	56 +/- 16
LDLc – mg/dl		
Before treatment	224 +/- 65	223 +/- 108
After treatment	114 +/- 50	115 +/- 69
Triglycerides – mg/dl	166 +/- 79	164 +/- 91
Before treatment	138 +/- 102	114 +/- 60
After treatment		


400
300
200
100
0
LDL-C
Expected - 48%
Expected - 47%
- 47%
- 47%
Untreated
Treated
Untreated
Treated
Lp(a) < 50
Lp(a) > 100

Limitations of the study

- Retrospective study.
- Not blinded?
- Low number of patient with a very very high level (>300mg/dL) of Lp(a) group BUT…
- Cohort with high level of LDLc (familial hypercholesterolemia).

Conclusion

In a real clinical setting, the present study doesn’t show an evidence of pseudo-resistance to statins in patients with high level of Lp(a).

Thanks for your attention

"I'd better warn you - I've high cholesterol!"