

Effect of Intermittent Apheresis on LDL cholesterol is Underestimated by the Kroon formula.

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1.) Background

To compare the constant effect of PCSK9 inhibitors with intermittent effect of lipid apheresis, the time-averaged LDL-C concentration ($C_{average}$) should be estimated.

$$C_{average} = C_{min} + 0.73 * (C_{max} + C_{min})$$

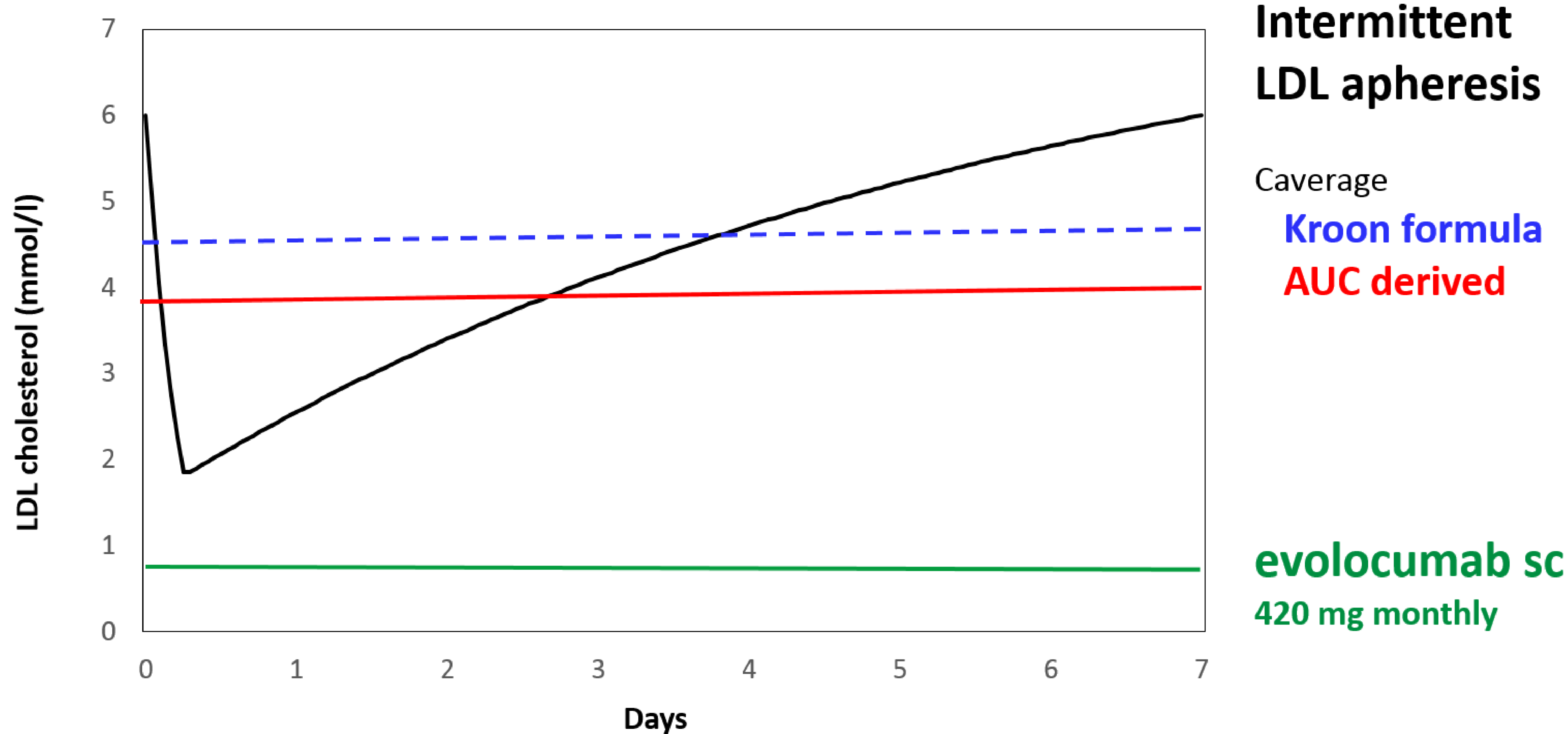
The **Kroon formula** with an arbitrary coefficient of 0.73 has been proposed for this purpose [1].

2.) Methods

Both, elimination during time of lipid apheresis (t_{elim}) and the proliferation during the time interval after the procedure (t_{prolif}) the **AUC derived** average concentration can be estimated [2].

$$C_{average} = (AUC_{elim} + AUC_{prolif}) / (t_{elim} + t_{prolif})$$

We have measured and compared the LDL-C in 20 patient under treatment on average for 9 years with 5 different apheresis procedures, namely HELP, DSA, DALI, IMAL and MDF [2].



Intermittent LDL apheresis

Coverage

Kroon formula

AUC derived

 evolocumab sc
 420 mg monthly

Figure 1: Effect of intermittent lipid apheresis is underestimated by the Kroon formula. With evolocumab LDL constantly is decreased to 0.78 mmol/l = 30 mg/dl [3]

LDL-cholesterin (mmol/l)						Mean
	HELP	DSA	DALI	IMAL	MDF	
Cmax	5.6	4.55	4.89	7.76	4.17	5.39
Cmin	2.06	1.28	1.6	2.63	1.66	1.85
-delta %	-63 %	-72 %	-67 %	-66 %	-60 %	-66 %
C average						
Kroon formula	4.64	3.67	4.00	6.37	3.49	4.44
AUC-derived C	4.08	3.03	3.83	5.59	3.26	3.96

Table 1: LDL concentrations in 20 patients during 9 year treatment with 5 different apheresis modalities [2]

3.) Results

The LDL-C concentration was reduced by 66 % during the procedures and the AUC-derived average LDL-C concentration 11 % less than estimated by the Kroon formula (Table 1).

4.) Conclusions

- Apheresis efficacy might be underestimated by the arbitrary Kroon formula when compared to the AUC-derived average LDL-C concentration (Figure 1).
- With intermittent LDL apheresis even the minimum LDL-C levels (C_{min}) are still above the range constantly achieved by the new PCSK9 inhibitors (Figure 1).

References

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- 3) Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD, Murphy SA, Kuder JF, Wang H, Liu T, Wasserman SM, Sever PS, Pedersen TR; FOURIER Steering Group. Epub ahead of print

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