


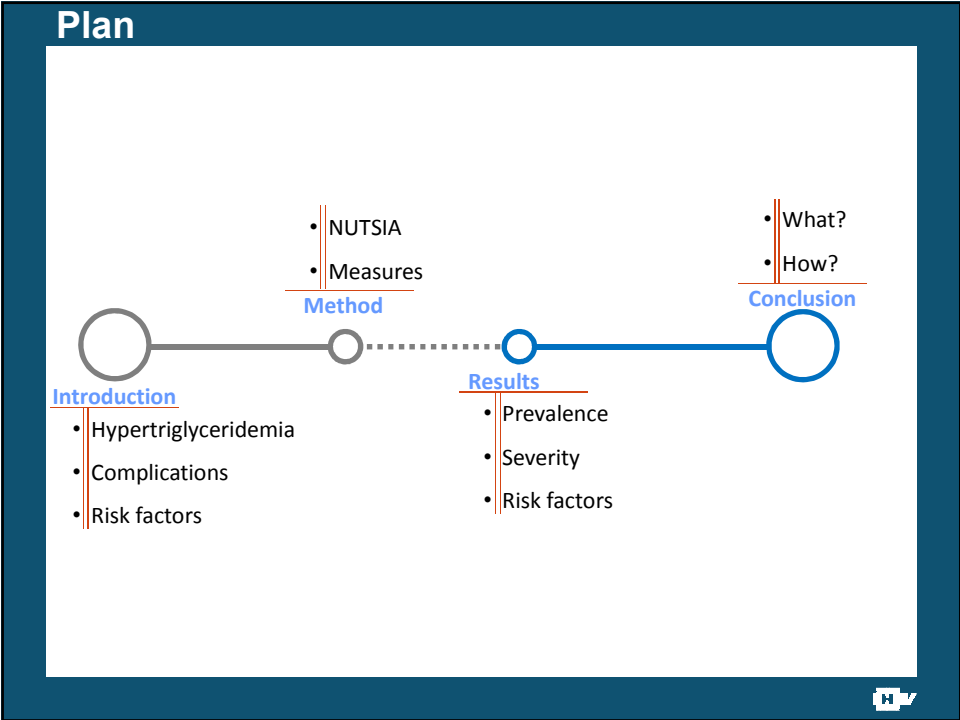
8th PhD Day
School of Pharmacy Geneva-Lausanne

Hypertriglyceridemia: an unexpected metabolic side effect of propofol sedation in critical illness

31th May 2013



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Introduction – Hypertriglyceridemia¹

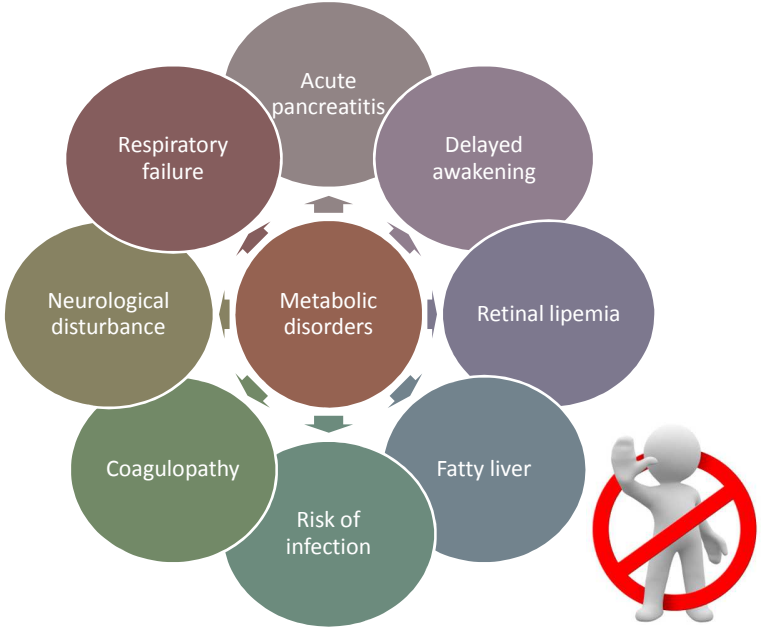
Lipid profile



¹Gibbons RJ et Al. J Am Coll Cardiol. 2003 Jan 1;41(1):159-68.

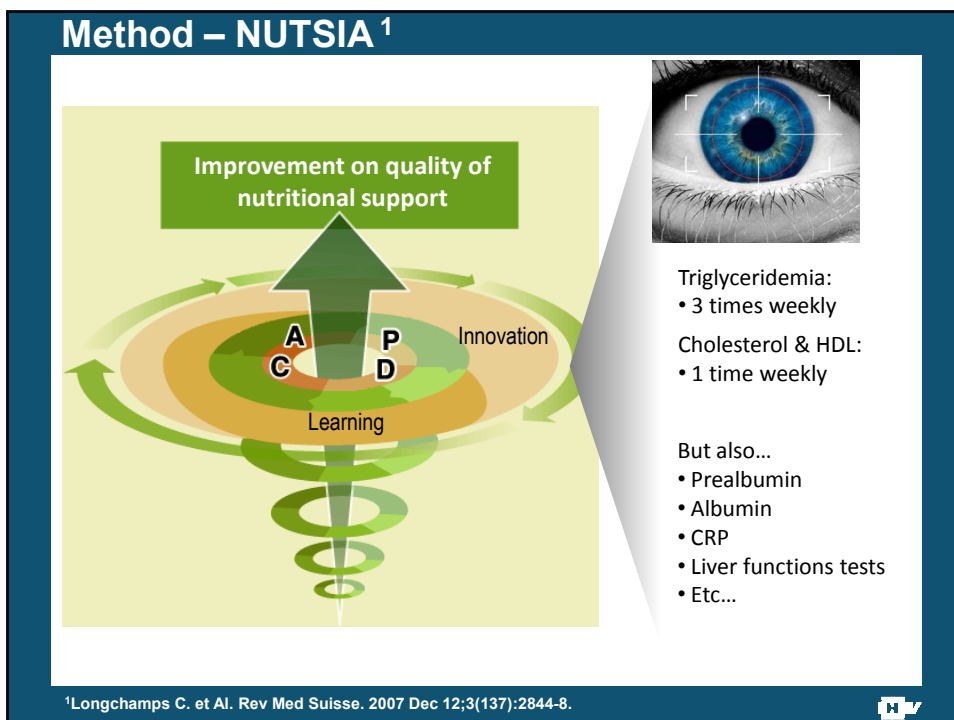
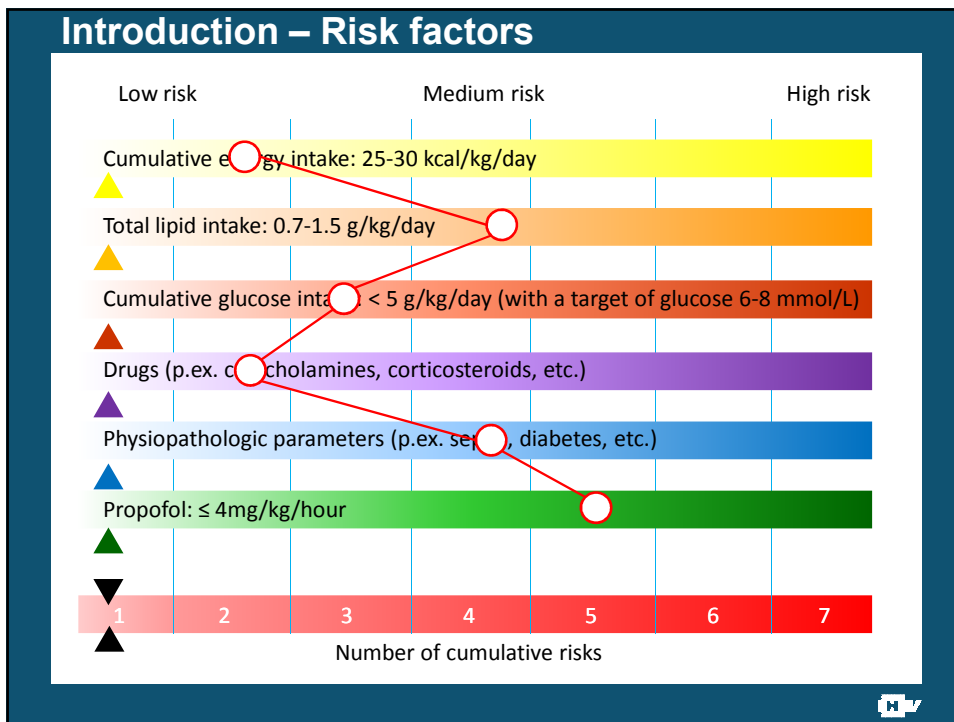


Introduction – Complications¹



¹Marik PE. Crit Care Clin. 2006 Jan;22(1):151-9





Method – Measures

Inclusion

- ICU stay \geq 4 days

Exclusion

- **One determination of TG**
- Oral feeding

Calculation of delta-TG

Lowest TG value

Highest TG value

Dynamic measure

Time	Triglycerides (mmol/L)
D1	1.5
D3	1
D5	1.2
D8	3

TG: Triglyceridemia

Method – Measures

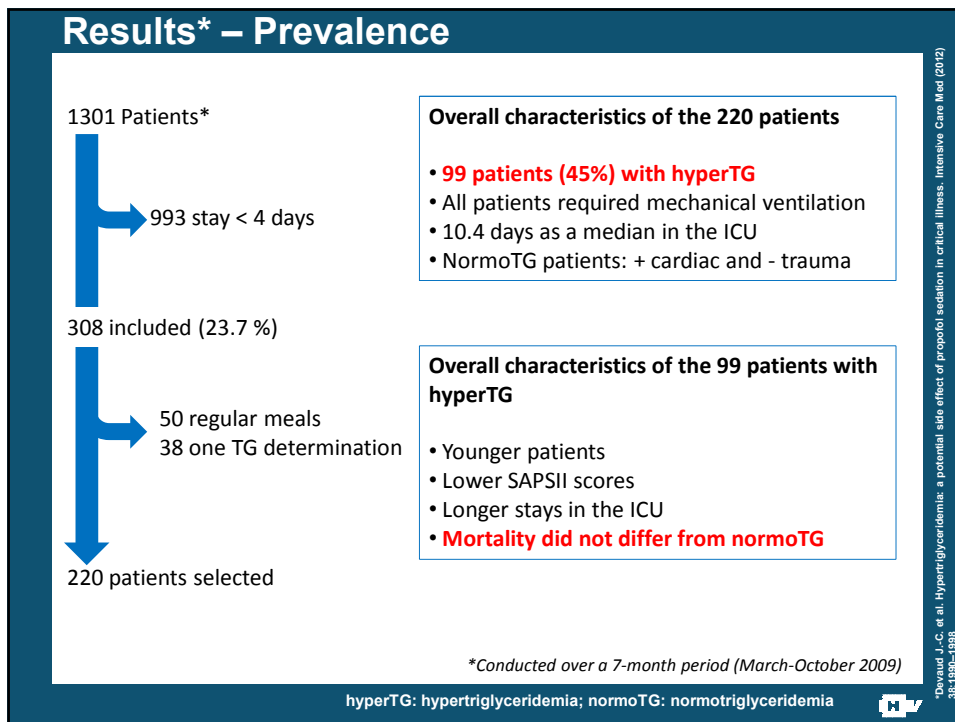
Patient data

- Age
- Admission weight
- BMI
- Type of admission
- Diagnosis
- Mortality (ICU + Hosp)
- Recorded medications

Laboratory data

- ALAT
- ASAT
- Albumin
- Amylase
- Direct bilirubin
- Creatinine
- γ -GT
- Glycemia
- Lipase
- Alkaline phosphatase
- Procalcitonin
- CRP
- Thromboplastin time
- Urea

Triglycerides, cholesterol, and HDL-cholesterol were analyzed as independent variables



Results – Severity

Variables	All (n=220)	NormoTG (n=121)	HyperTG (n=99)	p-Value
Peak triglycerides (mmol/L)	1.9 [1.4 ; 2.9]	1.5 [1.1 ; 1.7]	3 [2.6 ; 3.9]	<0.001
Reference TG (mmol/L)	1.2 [0.8 ; 1.7]	0.9 [0.7 ; 1.2]	1.7 [1.35 ; 2.3]	<0.001
Delta TG (ref-peak) (mmol/L)	0.7 [0.4 ; 1.3]	0.5 [0.3 ; 0.6]	1.3 [0.9 ; 1.9]	<0.001
Time in ICU before peak (days)	7 [4 ; 9]	7 [4 ; 9]	7 [4.8 ; 9]	NS
HDL-Cholesterol (mmol/L)	0.6 [0.3 ; 0.9]	0.8 [0.5 ; 1.1]	0.4 [0.2 ; 0.7]	<0.05
Total Cholesterol (mmol/L)	3.5 [2.6 ; 4.2]	3.3 [2.5 ; 4]	3.7 [2.7 ; 4.7]	NS

Results presented as median [interquartile range]

hyperTG patients have higher reference TG values (but within normal values)

Delta TG is higher in the hyperTG group

hyperTG: hypertriglyceridemia; normoTG: normotriglyceridemia

Results – Risk factors

Peak triglyceride concentration correlated with...

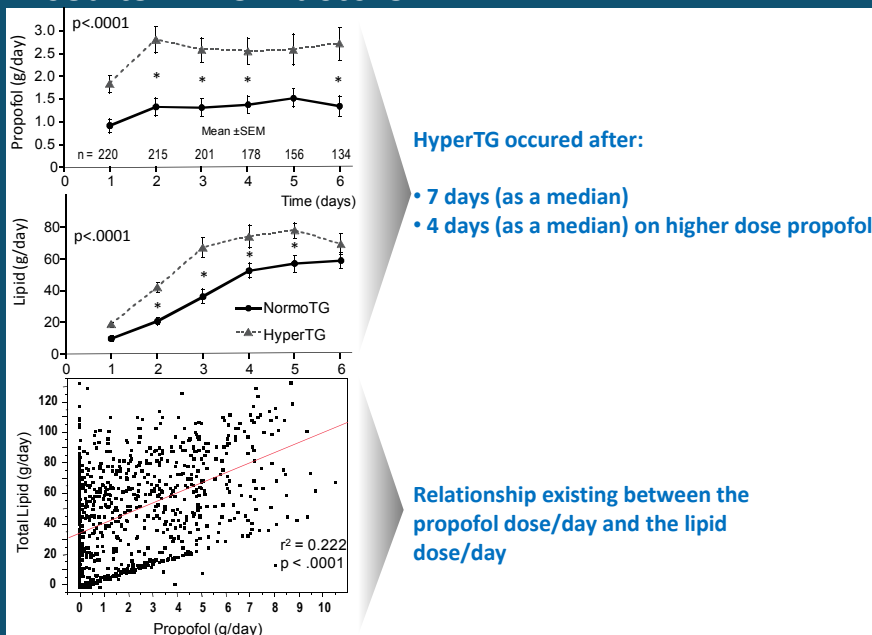
Parameter term	Pearson's coefficient (r ²)	p-Value
Propofol (mg/kg/hour)	0.28	<0.001
Lipids from propofol (g/kg/j)	0.26	<0.001
CRP (mg/L)	0.19	0.004
Total lipid intake (g/kg/day)	0.14	0.024
Cumulative glucose intake (g/day)	0.12	NS
(g/kg/day)	0.11	NS
Cumulative energy intake (kcal/kg/day)	0.09	NS
LCT + MCT parenteral lipids (g/kg/day)	0.07	NS
Total LCT intake (g/kg/j)	0.04	NS
LCT + MCT enteral lipids (g/kg/day)	0.04	NS
Insuline dose (UI/24h)	0.02	NS

Sepsis was highly significantly associated with this metabolic alteration

LCT: Long chain triglycerides; MCT: Medium chain triglycerides



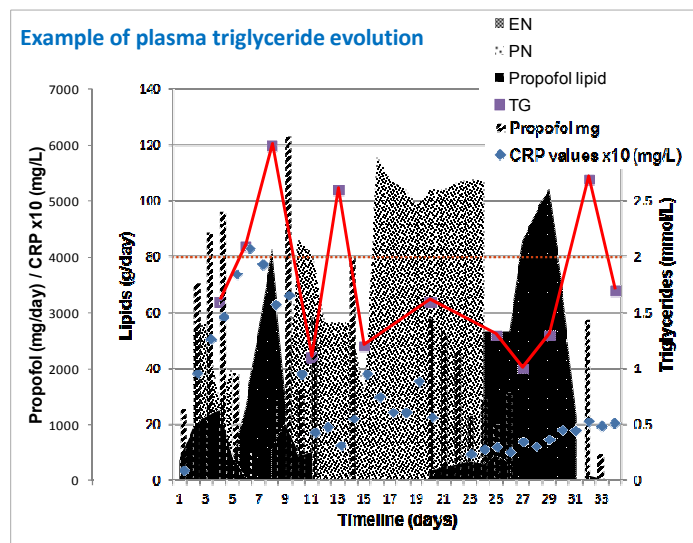
Results – Risk factors



hyperTG: hypertriglyceridemia; normoTG: normotriglyceridemia



Results – Risk factors



The observed changes in TG levels were not a unified process, but the conjunction of infection and high-dose propofol was a frequent pattern

EN: enteral nutrition; PN: parenteral nutrition



Results – Risk factors

Propofol intake

- 144 patients (65.5%)
- Received before peak TG value: 0.04 to 5.83 mg/IBW/h
- Median dose associated with hyperTG: 2.04 mg/kg/h



The magnitude of the TG increase (deltaTG) was influenced by

- The cumulated dose of propofol before the peak ($r^2=0.038$, $p=0.0037$)
- The propofol dose (mg/kg/h) ($r^2=0.061$, $p=0.0002$)

But less by

- the number of days on propofol before the peak ($r^2=0.020$, $p=0.034$)
- The lipid dose ($r^2=0.027$, $p=0.013$)

Total cholesterol and HDL-cholesterol levels were unaffected by the propofol dose

TG: triglyceridemia



Conclusion – What?

Nonsignificant risk factors....

Pathologies and drugs

- Except sepsis and propofol, nothing significant in this study

Nutrition

- No hyperalimentionation observed in this study (lipid or glucose)

Finally hypertriglyceridemia observed....

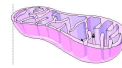
Infection

- Impact of the acute-phase response on the lipid metabolism



Propofol

- Lipid associated with propofol?
- Action on the mitochondria?



Conclusion – How?

Cumulative doses control

MetaVision Suite
Version 5.46.38 (Hotfix 29)

200 mg/h of propofol intake during 24 hours corresponding to a lipid intake of

- 24g with 2% propofol
 - 48g with 1% propofol
- } This corresponds to ¼ to ½ of the recommended daily lipids intake

Patients monitoring

Infection + propofol

- TG monitoring at least 2-3 times weekly



TG: Triglyceridemia



What's Next?

Where are the costs?



PHARMACOECONOMY
of propofol



END 2013



MIDDLE 2014

