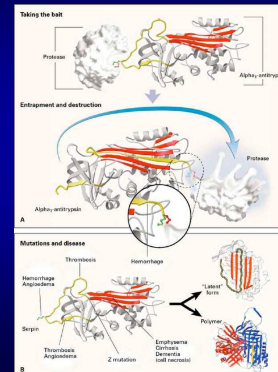


CHOPN s deficitem α -1 AT

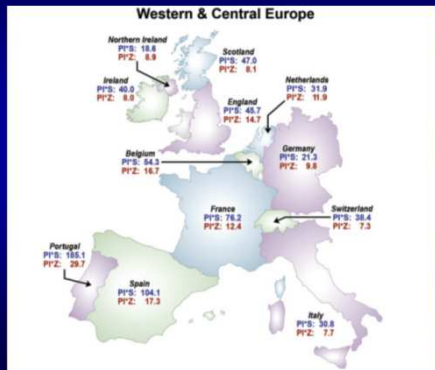
j. chlumský
Pneumologická klinika 1.LF UK a
Thomayerovy nemocnice, Praha



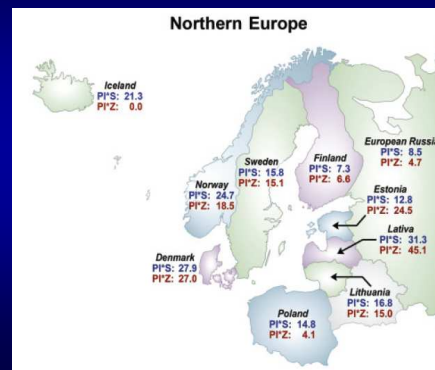
Defektní AAT



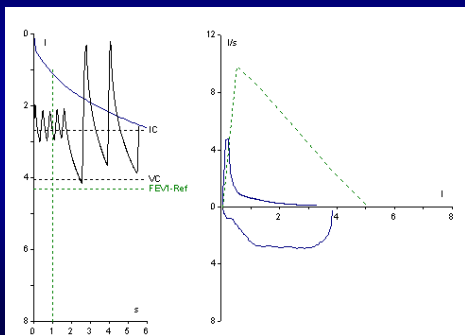
Prevalence alel Z a S



Prevalence alel Z a S

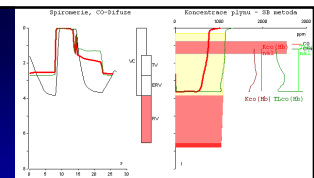


Klinická prezentace CHOPN s AATD



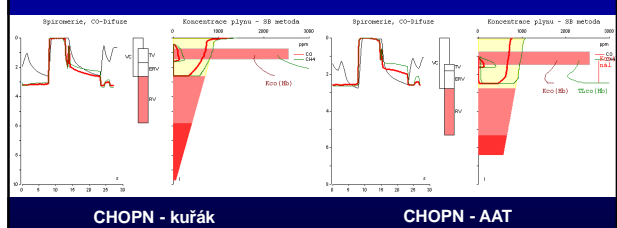
TL_{CO}

normální

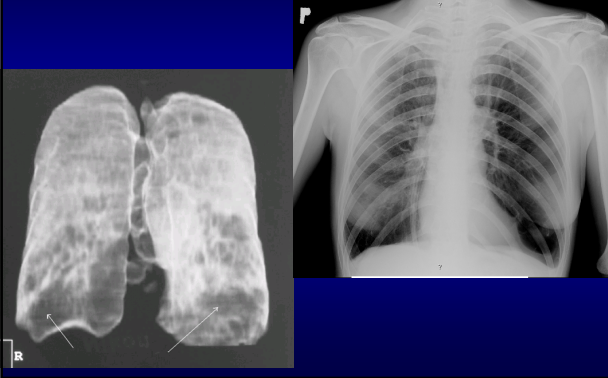


CHOPN - kuřák

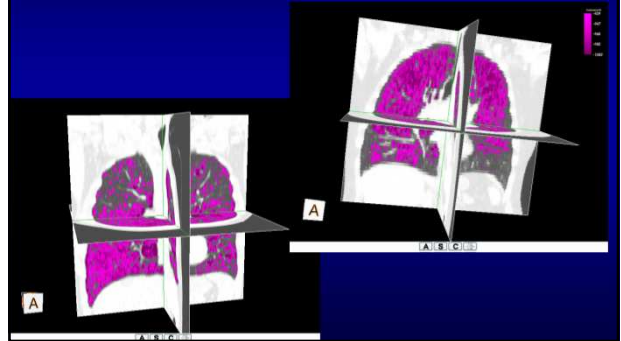
CHOPN - AAT



Klinická prezentace CHOPN s AATD



CT denzitometrie



CT denzitometrie

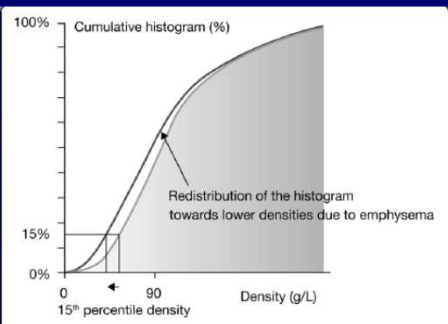
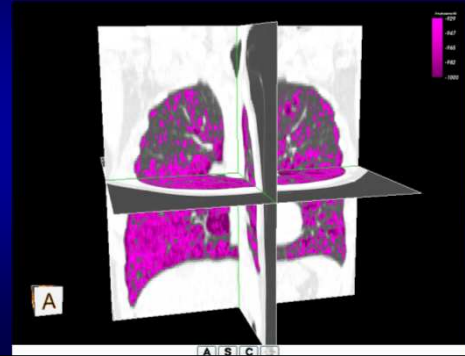
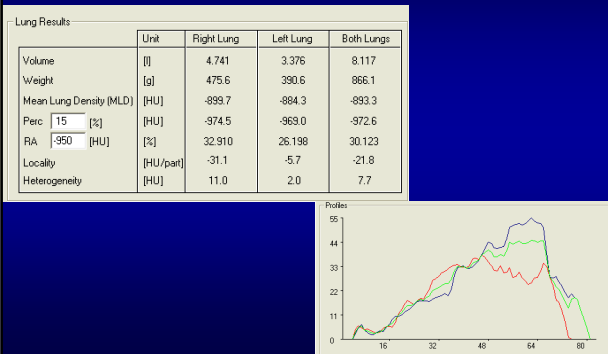


Figure 2 Measurement of progression of emphysema.

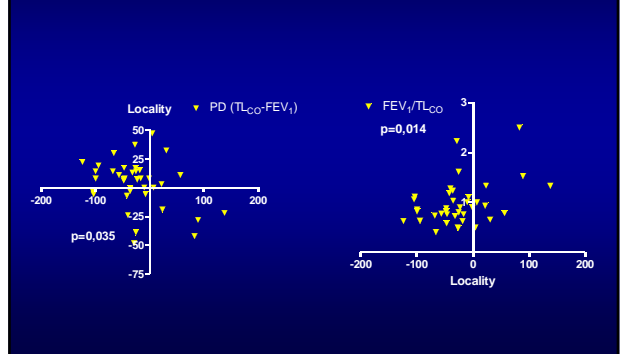
CT denzitometrie



CT denzitometrie



Predilekce emfyzemu



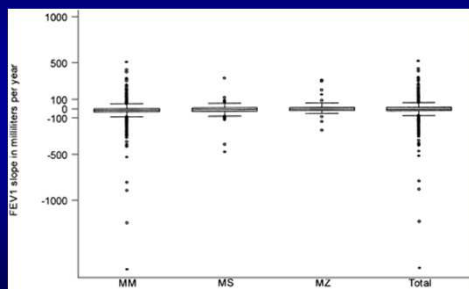
Screening

- 1) CHOPN s převahou emfyzému u pacientů mladších 65 let věku
- 2) CHOPN s převahou emfyzému u pacientů bez expozice rizikovým faktorům (kuřácká anamnéza < 20 balíčků cigaret)
- 3) CHOPN s převahou emfyzému s predilekcí v oblasti dolních laloků plic
- 4) Bronchiektázie nezjištěné etiologie (při vyloučení cystické fibrózy, primární ciliární diskineze, dysgamaglobulinemie, apod.)
- 5) Jinak neobjasněné jaterní onemocnění
- 6) Nekrotizující panikulitida
- 7) Rodinná anamnéza kteréhokoliv onemocnění uvedeného výše

Prognóza

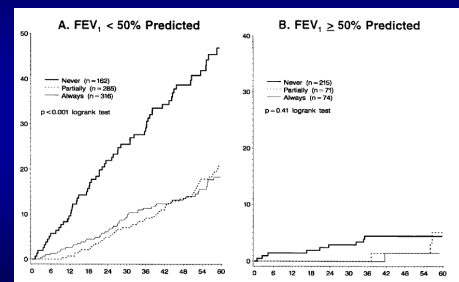
Reference	n	Ever Smokers (%)	Months of Follow-up*	FEV ₁ Slope (ml/yr) [†]		
				Overall	Never Smokers	Current Smokers
Rauk, 1983 (135) [‡]	30	97	62 (36)	111 (102)		
Rauk, 1983 (135) [‡]	41	83	74 (47)	104 (94)		
Janus, 1985 (140)	21	67	72 (10) [§]	80 (38) [§]	61 (43) [§]	316 (80) [§]
Hutchison, 1987 (139)	82			66 (55)	44 (36)	67 (46)
Wu, 1988 (145)	80	58	71	61 (100)	81 (70)	61 (170)
Seersholm, 1995 (142)	161	89		86 (107)	52 (80)	132 (105)
Seersholm et al., 1997 [‡] (143)	97	100	70 (41)		75 (60) (95% CI, 63-87)	
NHLBI, 1998 (134)	927	79	52 (12-86) [§]	56 (4) [§]	67 (95% CI, 56-78)	55 (95% CI, 46-63)
Pitulainen, 1999 (141)	608	65	66 (12-372) [§]	48 (79)	47 (95% CI, 41-53)	70 (95% CI, 58-82)
Djukan, 1999 (137)	56	100	36**			59 (12) [§]
Wencker, 2001 (144)	96	88	48 (28)	49 (61)		
Dawkins, 2009 (136)	101	82	36**	50 (7)		
Djukan, 2009 (138)	77	90	24**	23 (10) [§]		
Tenehi, 2009 (146)	40	79	42	37 (12) [§]	41 (22,47)	

Rychlost poklesu FEV₁



G.E.Silva et al, Chest 2003

Mortalita NHLBI registr



AATD Registry Study Group, AJRCCM 1998

Efektivita suplementace A-1-AT

Table 1 Studies on clinical efficacy of augmentation therapy

Reference	Date	Design	Outcome measures	Main results
Seersholm et al ⁶	1997	Observational cohort, concurrent controls	FEV ₁ decline	In patients with FEV ₁ 31-45% augmentation slowed decline of FEV ₁ by 21 ml/year
NHLBI Registry ⁷	1998	Observational cohort, concurrent controls	FEV ₁ decline and survival	In patients with FEV ₁ 35-49% augmentation slowed decline of FEV ₁ by 27 ml/year. Risk ratio for death with augmentation 0.64 compared with non-recipients
Dirksen et al ⁸	1999	Randomised controlled trial	FEV ₁ decline lung density (CT)	Loss of lung tissue 2.6 g/l/year with placebo and 1.5 g/l/year with augmentation
Gottlieb et al ⁹	2000	Descriptive	Urinary desmosine	Augmentation did not reduce the rate of elastin degradation
Lieberman ¹¹	2000	Observational (web based survey)	Frequency of lung infections	Number of lung infections per year decreased from 3-5 before augmentation to 0-1 after augmentation
Wencker et al ⁶	2001	Observational (before-after)	FEV ₁ decline	Rates of FEV ₁ decline before and after augmentation 49.2 and 34.2 ml/year, respectively
Stockley et al ¹²	2002	Descriptive	Sputum inflammatory markers	Augmentation reduced sputum leukotriene B ₄

Efektivita suplementace AAT

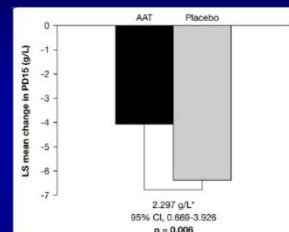


Figure 3 Progression of emphysema in AAT-treated versus placebo-treated subjects (modified ITT). *Estimated treatment difference between mean changes in unadjusted 15th percentile lung density from baseline. AAT, alpha-1 antitrypsin; LS, least squares; PD15: 15th percentile lung density.

Stockley, RA et al, Respir Research 2010

Indikace léčby

- a) CHOPN s FEV₁ v rozmezí 30-60% normy
- b) hladina AAT je pod 0,5 g/l (PiZZ, Pnull)
- c) jsou nekuřáky (s objektivní verifikací)

Jak je to u nás?

Situace v Centru

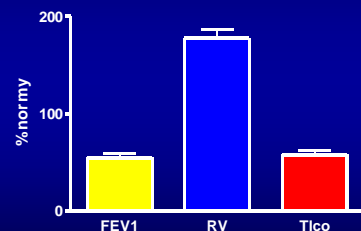
- Celkový počet PiZZ 52
- CHOPN k indikaci 24
- CHOPN pod limitem 12
- CHOPN nad limitem 7
- Bez postižení plicních funkcí 12

Suplementace podávána 24/16 pacientům
(celkem/nyní)

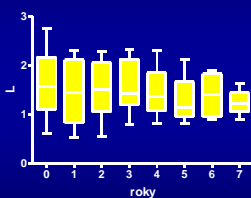
Studie RAPID 2 pacienti
Neléčeno 15 pacientů
LuTx/WL 5

Funkční charakteristika

Věk - 50,0 let
(25-69)
FEV₁ - 54,5%
(15-113%)

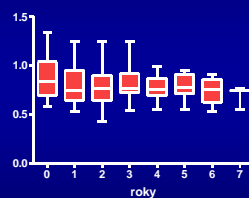


Progrese onemocnění (follow-up 1-7 let)



FEV₁

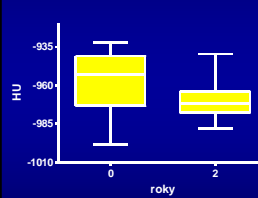
Průměrný pokles 93 ml/rok
medián 81 ml/rok (0-230ml)



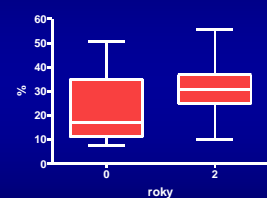
TL_{CO}

Průměrný pokles 0,027
mmol/kPa/L/min

Progrese onemocnění (follow-up 1-7 let)

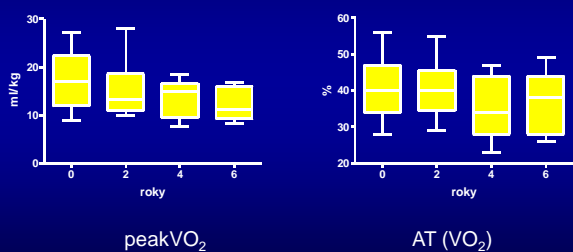


15 percentil



RA (-950 HU)

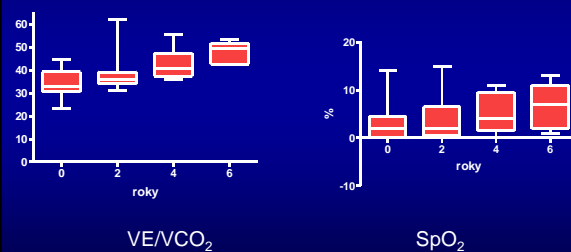
Progrese onemocnění (follow-up 1-7 let)



peakVO₂

AT (VO₂)

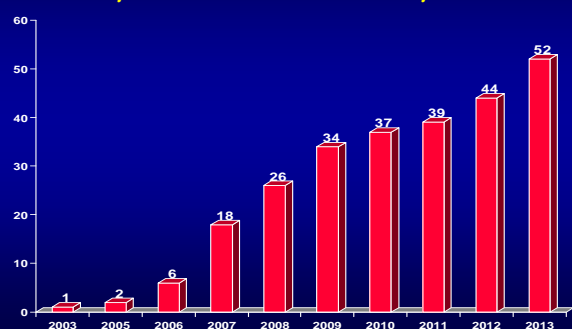
Progrese onemocnění (follow-up 1-7 let)



VE/VCO₂

SpO₂

Nárůst detekce - PiZZ odhad prevalence v ČR 400-500 pacientů !!!



Centrum pro AATD

Jediné centrum pro ČR

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E-mail: jan.chlumsky@ftn.cz