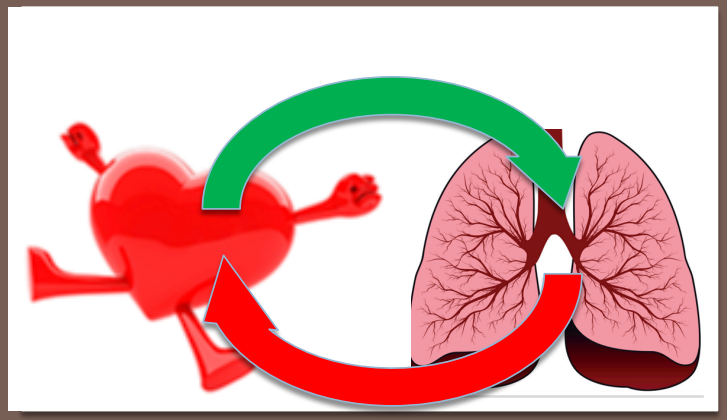
CARDIOPULMONALE INTERAKTION

AUS DER SICHT DES PNEUMOLOGEN

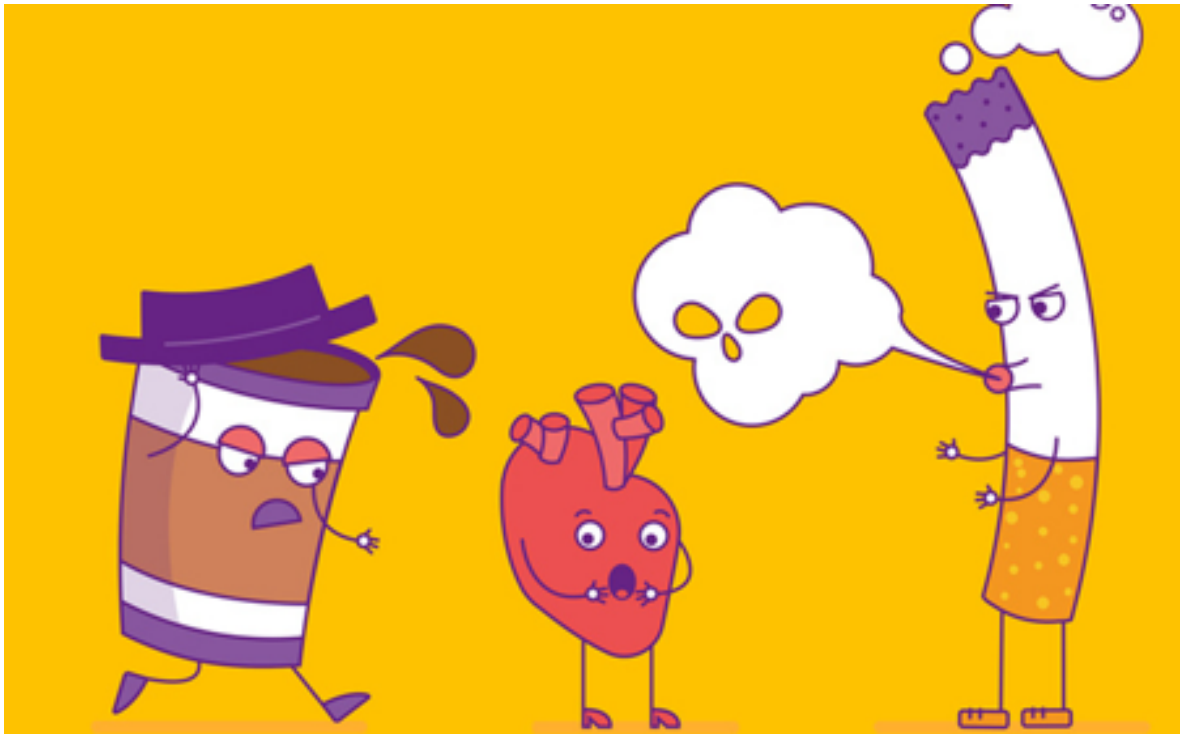
19.02.2020 TRAUNSTEIN

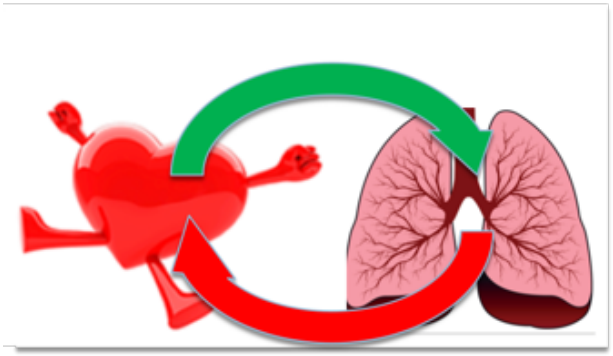


KLINIKEN SÜDOSTBAYERN

Dr. Christian Geltner, MSc MBA
Kreisklinikum Bad Reichenhall – Abteilung für Pneumologie

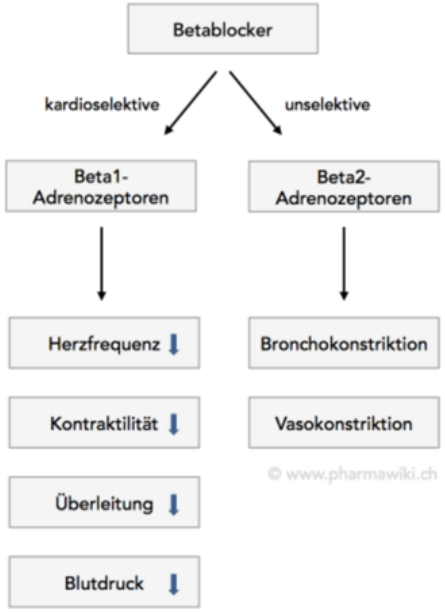
Gemeinsames Problem



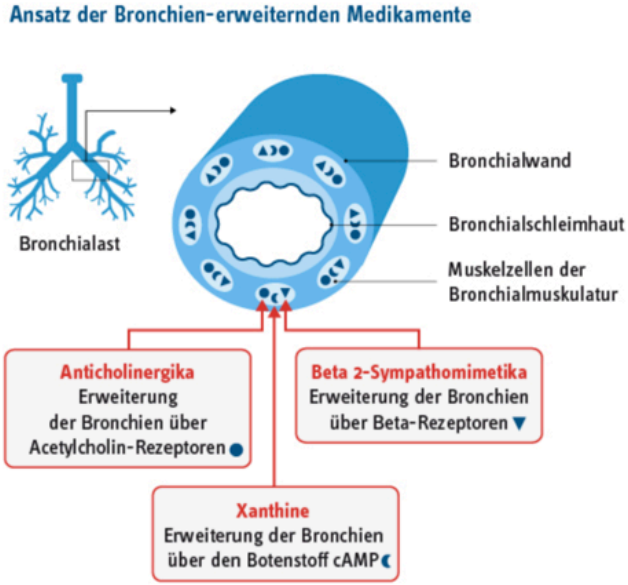


ACE HEMMER, BETABLOCKER, SARTANE

β–Blocker und Asthma



Herz	Beta 1: positiv chronotrop + inotrop + dromotrop + bathmotrop
Blutgefäße	Alpha 1: Vasokonstriktion peripher für Blutdruckanstieg Beta 2 : Vasodilatation bei niedriger Dosis (Abschwellung Schleimhäute)
Bronchialmuskulatur	Beta 2: Relaxation, Sekretion
Glatte Muskulatur	Beta 2: Tonussenkung, ruhigstellung von Uterus für Tokolyse

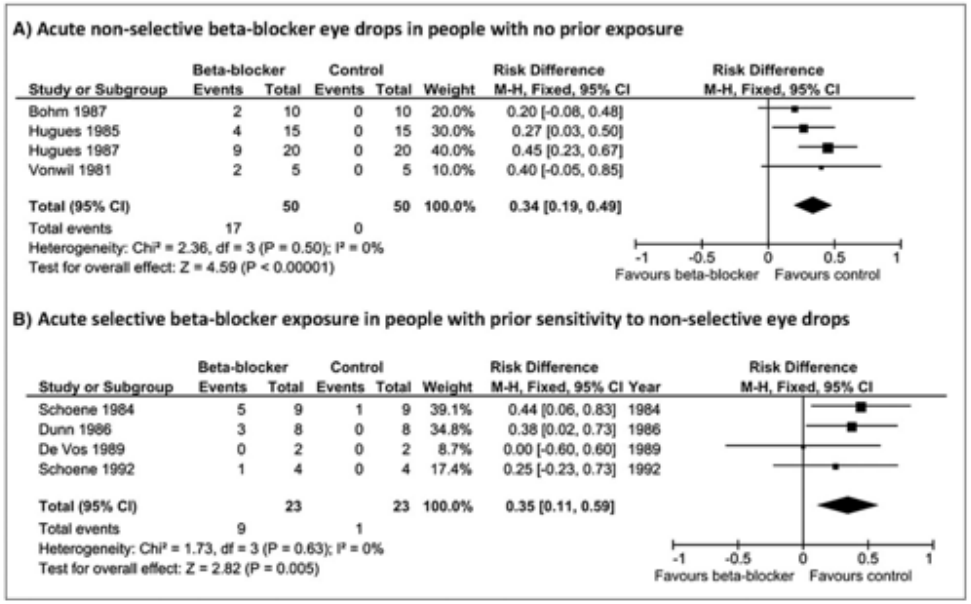


Bei Asthma KI, relativ?

- Bei Asthmapatienten ist das Risiko einer Verschlechterung der Lungenfunktion durch Betablocker höher als bei COPD-Patienten.
- In vielen Fachinformationen von Betablockern wird bronchiale Hyperreagibilität bei Asthma als Kontraindikation aufgeführt.
- Diese Einstufung basiert auf kleinen Fallserien der 1980er- und 1990er-Jahre mit initial sehr hohen Dosierungen der Betablocker bei jungen Patienten mit schwergradigem Asthma (»BMC Medicine« 2017, DOI: 10.1186/s12916-017-0781-0).

Gefahr: Augentropfen!

- Betablocker aus Augentropfen werden zu circa 80 Prozent absorbiert, unterliegen keinem First-Pass-Effekt und weisen eine schnelle systemische Resorption auf.
- Diese ist vergleichbar mit einer intravenösen Gabe in Bezug auf die Blockade von β_2-Rezeptoren und kardiopulmonalen Effekten.
- Es können also systemisch wirksame Plasmakonzentrationen mit der Gefahr eines Bronchospasmus erreicht werden.
- Eine Metaanalyse zeigte, dass eine akute Exposition mit nicht kardioselektiven, topischen Betablockern bei einem von drei Patienten zu einem Abfall der Einsekundenkapazität (FEV_1) von ≥ 20 Prozent führte



Morales ea, Br J Clin Pharmacol (2016) 82 814–822

Asthma im Alter

- 6-10% aller Erwachsenen >65a
- Je älter desto untypischer sind die Symptome
  - nächtlicher Husten
  - Begleiterkankungen (Herzinsuffizenz,
  - typische Symptome wie Wheezing, Atemnot, Thoraxschmerz sind oft anderen Erkrankungen zugeordnet
  - Lungenfunktion schwierig zu interpretieren (Reversibilität entscheidend, FEV1>80% häufig

- Allergien häufig, wenn Asthma-onset früh
- Komedikation ist häufig und häufig problematisch (Betablocker, ACE-Hemmer, COX2-Hemmer)

COPD oder Asthma

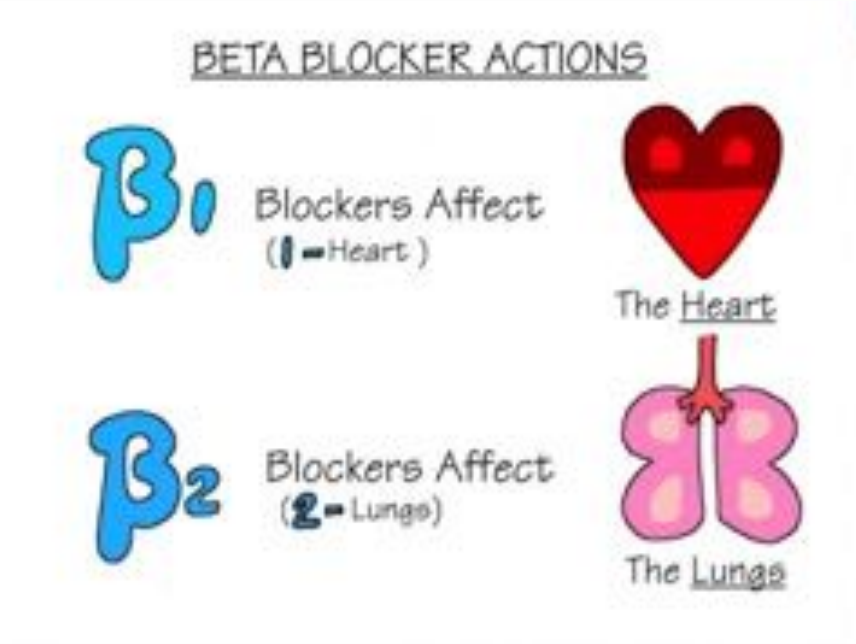
- Fehldiagnose COPD ?
  Patienten mit Asthma >65a (SARA Studie, Chest 2003)
  - 50% der älteren Raucher haben richtige COPD Diagnose
  - 20% falsche COPD Diagnose
  - 30% der Asthmatiker haben keine Diagnose
- COPD als Codiagnose bei langjährigen Asthma möglich –
  Asthma COPD Overlap (ACO)

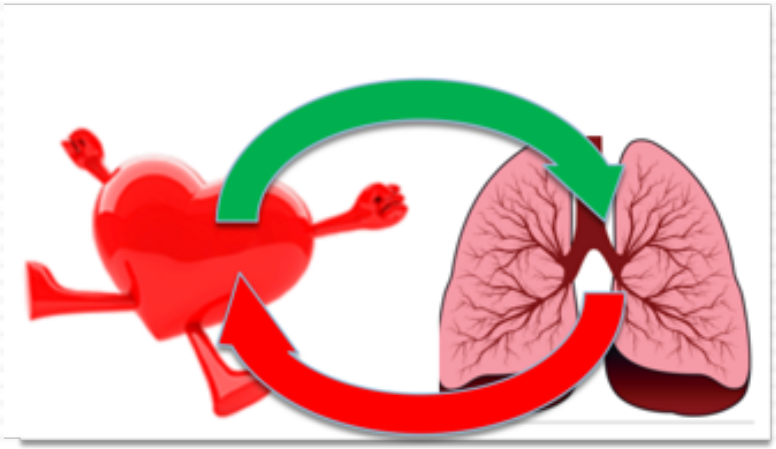
- Gründe für Fehldiagnose:
  - Altersdyspnoe
  - Sensorische Missempfindung
  - Aktivitätslimitierung
  - soziale Isolation
  - Depression
  - Ärztliche Meinung:
    Asthma ist keine Erkrankung des Alters
  - Komorbidität
- DD
  - COPD
  - Herzinsuffizienz
  - Bronchiektasien
  - Aspiration
  - Hyperventilation/Panik

Betablocker und Asthma

- Kontraindikation in den meisten Präparaten
- Sehr vorsichtige Gabe, nur hoch-selektiv
- Cave: Augentropfen

BETABLOCKER und COPD

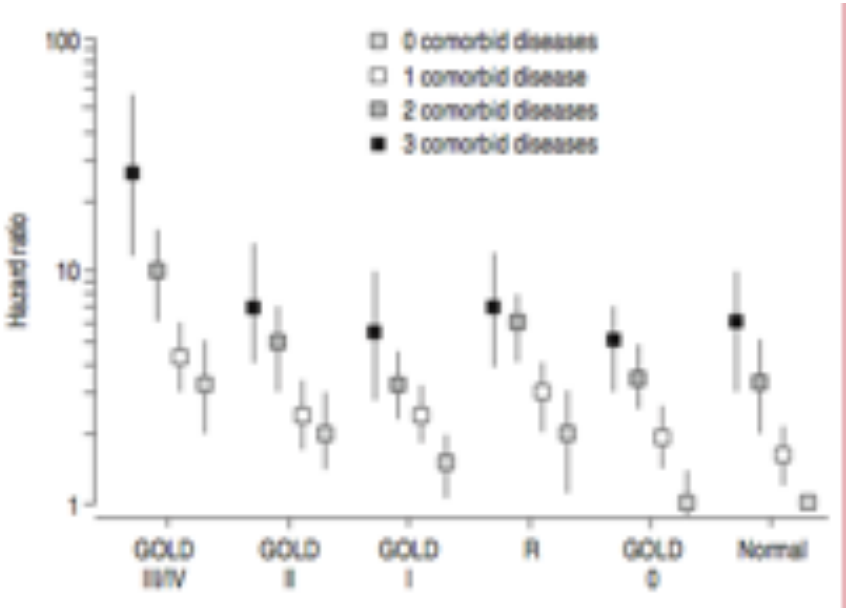




Woran sterben COPD Patienten?

Todesursachen bei COPD (TORCH Studie)

System	Subjects %
Cardiovascular	26
Congestive heart failure	3
Myocardial infarction	3
Stroke	4
Sudden death	16
Respiratory	35
COPD	27
Pneumonia	8
Other	<1
Cancer	21
Lung	14
Other	7
Other cause	10
Unknown cause	8



McGarvey ea, Thorax 2007
Shambu, Eur Respir Monogr 2013

HF und COPD

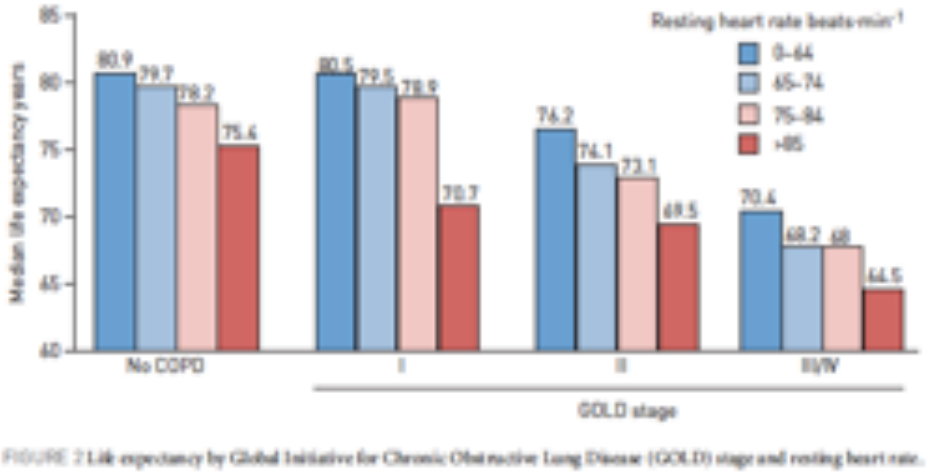
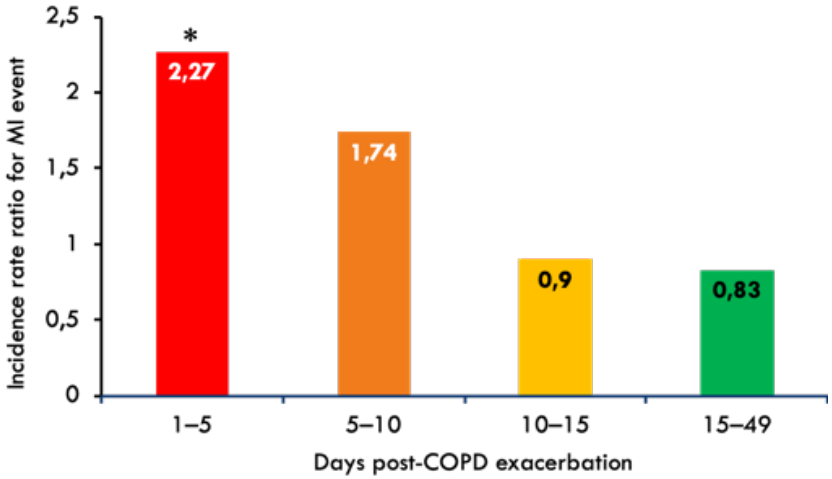


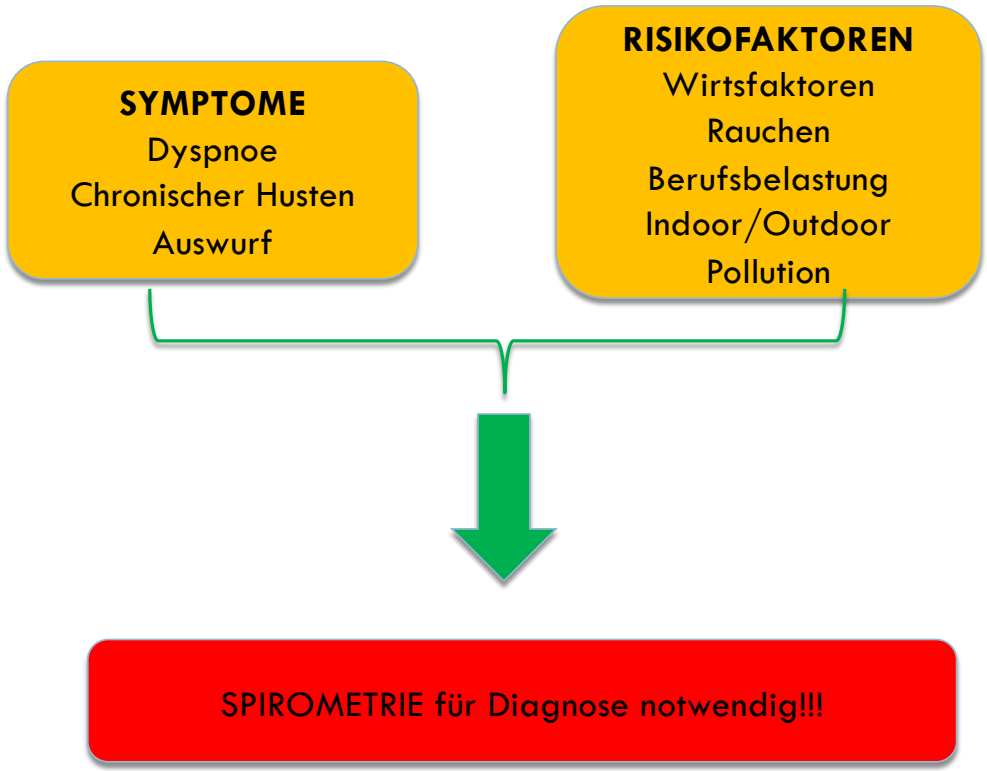
FIGURE 2 Life expectancy by Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage and resting heart rate.

Jensen, ERJ 2013, 42:341



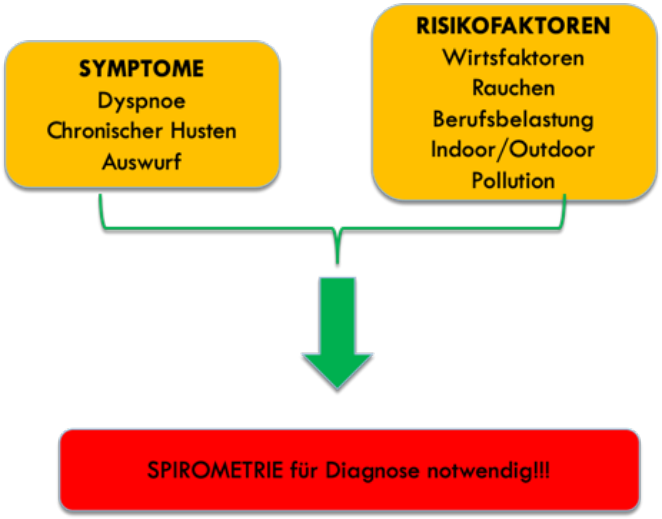
Donaldson GC, et al. *Chest* **2010**;137:1091-97.

Diagnosekriterien COPD –
GOLD 2017



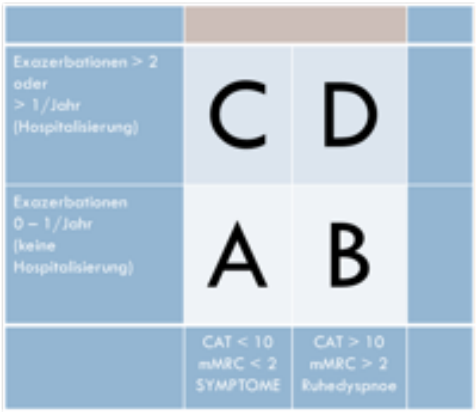
Evaluierung/Graduierung der COPD

GOLD 2017

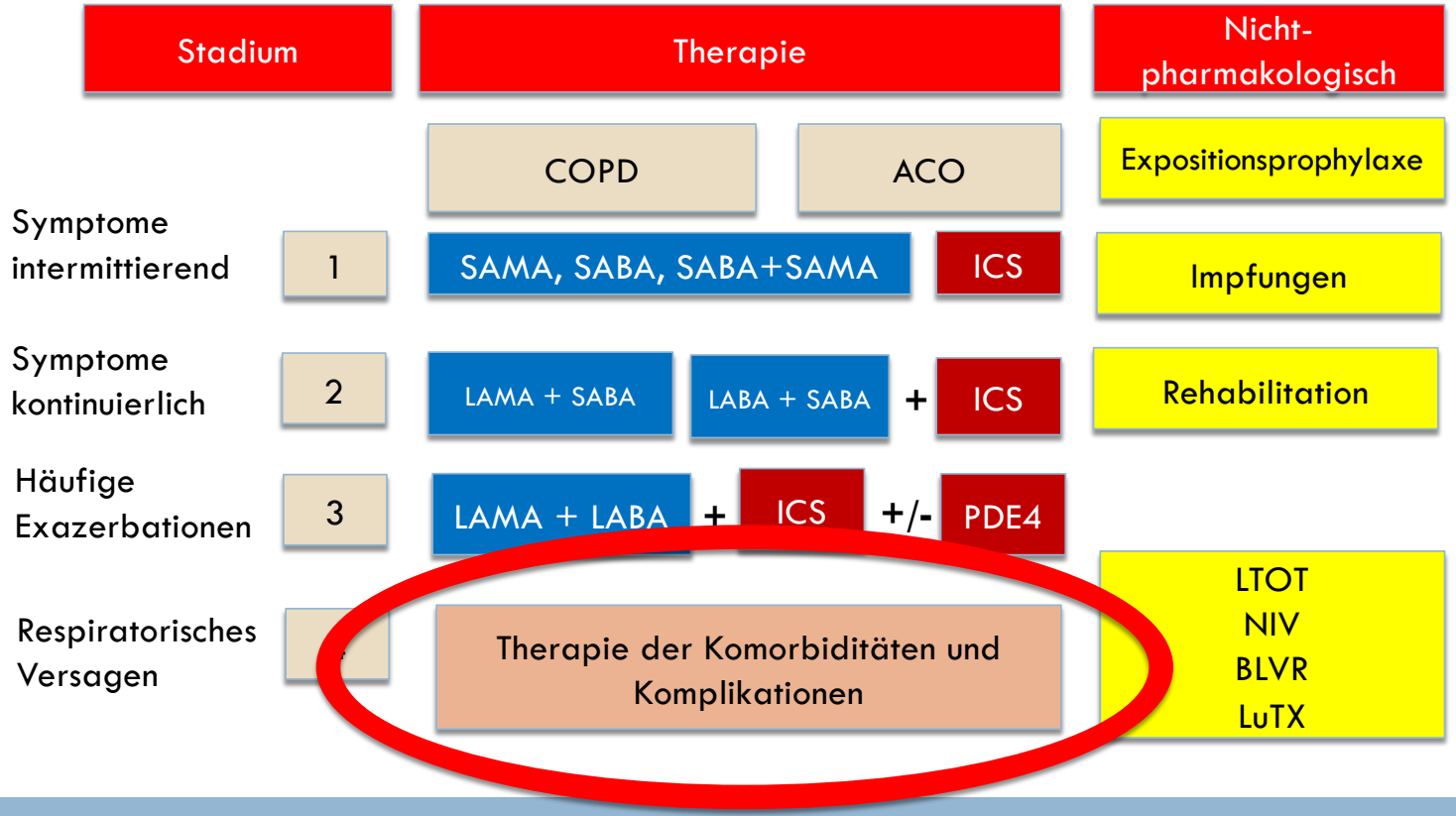


FEV1/FVC < 70%

	FEV1 predicted
GOLD 1	> 80%
GOLD 2	50 - 79%
GOLD 3	30 - 49%
GOLD 4	< 30%



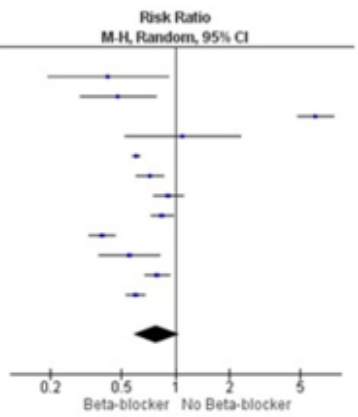
Behandlung der stabilen COPD – deutsche Empfehlungen



Betablocker gut für COPD

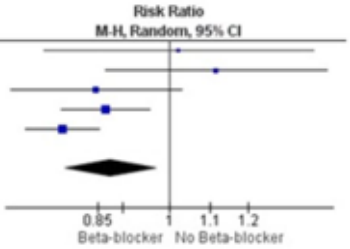
Study or Subgroup	Beta-blocker Events	Total	No Beta-blocker Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Andell 2015	0	4086	0	772		Not estimable
Angeloni 2013	8	104	19	104	5.7%	0.42 [0.19, 0.92]
Au 2004	16	257	222	1709	7.5%	0.48 [0.29, 0.78]
Bhatt 2016	119	474	123	2990	8.8%	6.10 [4.84, 7.70]
Dransfield 2008	8	142	35	683	5.9%	1.10 [0.52, 2.32]
Gottlieb 1998	1550	9228	9059	32586	9.3%	0.60 [0.58, 0.63]
Hawkins 2009	162	643	215	615	9.1%	0.72 [0.61, 0.86]
Mentz 2013	199	506	93	216	9.0%	0.91 [0.76, 1.10]
Rutten 2010	181	665	506	1565	9.1%	0.84 [0.73, 0.97]
Rutten 2013	149	1460	795	3033	9.1%	0.39 [0.33, 0.46]
Staszewsky 2007	24	140	151	488	8.1%	0.55 [0.38, 0.82]
Stefan 2012	197	10070	620	25012	9.1%	0.79 [0.67, 0.92]
Van Gestel 2006	184	462	532	803	9.2%	0.60 [0.53, 0.68]
Total (95% CI)		**28237**		**70576**	**100.0%**	**0.79 [0.58, 1.06]**
Total events	2797		12370			

Heterogeneity: Tau² = 0.25; Chi² = 441.86, df = 11 (P < 0.00001); I² = 98%
Test for overall effect: Z = 1.57 (P = 0.12)



Study or Subgroup	Beta-blocker Events	Total	No Beta-blocker Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Angeloni 2013	46	104	45	104	9.3%	1.02 [0.75, 1.39]
Au 2004	55	257	328	1709	12.4%	1.12 [0.87, 1.44]
Bhatt 2016	92	474	685	2990	17.2%	0.85 [0.70, 1.03]
Rutten 2010	284	665	772	1565	29.3%	0.87 [0.78, 0.96]
Stefan 2012	654	10070	2071	25012	31.8%	0.78 [0.72, 0.85]
Total (95% CI)		**11570**		**31380**	**100.0%**	**0.88 [0.79, 0.98]**
Total events	1131		3901			

Heterogeneity: Tau² = 0.01; Chi² = 9.40, df = 4 (P = 0.05); I² = 57%
Test for overall effect: Z = 2.42 (P = 0.02)



Metaanalyse - Villalobos, ERJ 2018

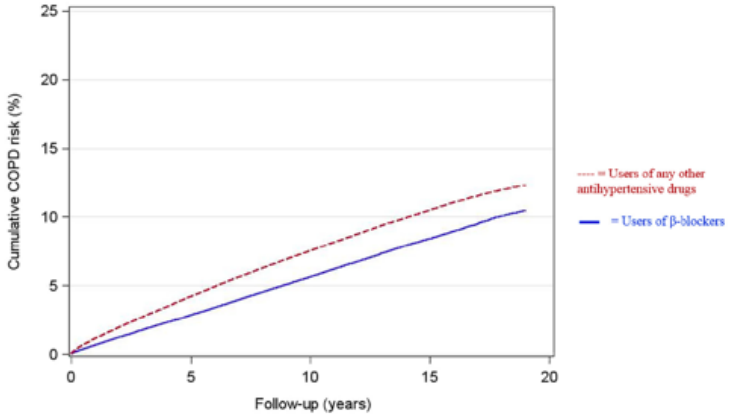


Fig. 1. Cumulative risk of COPD hospitalizations.

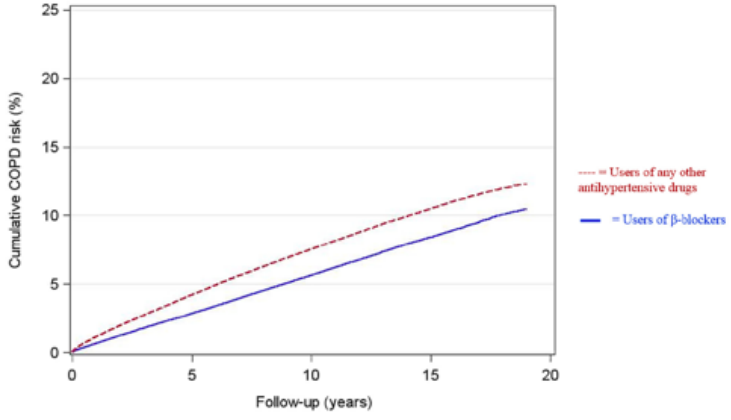
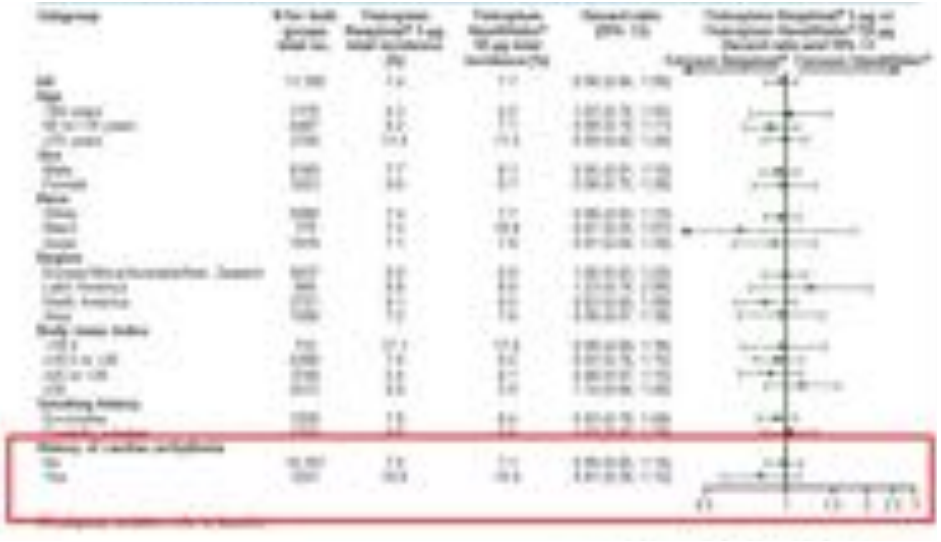


Fig. 1. Cumulative risk of COPD hospitalizations.

A.O. Nielsen et al. / EClinicalMedicine 7 (2019) 21–26

LAMA und Kardiovaskuläres Risiko



Wise RA, et al. *N Engl J Med 2013*

Kardiovaskuläre und respiratorische Ereignisse (>1%, Inzidenz pro 100 Patientenjahre)

	Tiotropium n=2986	Control n=3006	Risk Ratio	95% CI
SOC kardiovaskulär	3.56	4.21	0.84	0.73, 0.98*
Angina pectoris	0.51	0.36	1.44	0.91, 2.26
Vorhofflimmern	0.74	0.77	0.95	0.68, 1.33
Herzinsuffizienz	0.29	0.48	0.59	0.37, 0.96*
Koronare Herzkrankheit	0.21	0.37	0.58	0.33, 1.01
Myokardinfarkt	0.69	0.97	0.71	0.52, 0.99*
SOC respiratorisch**	11.32	13.47	0.84	0.77, 0.92*
Bronchitis	0.37	0.31	1.20	0.73, 1.98
COPD-Exazerbation	8.19	9.70	0.84	0.76, 0.94*
Dyspnoe	0.38	0.62	0.61	0.40, 0.94*
Pneumonie	3.28	3.46	0.95	0.81, 1.11
Resp. Insuffizienz	0.90	1.31	0.69	0.52, 0.92*

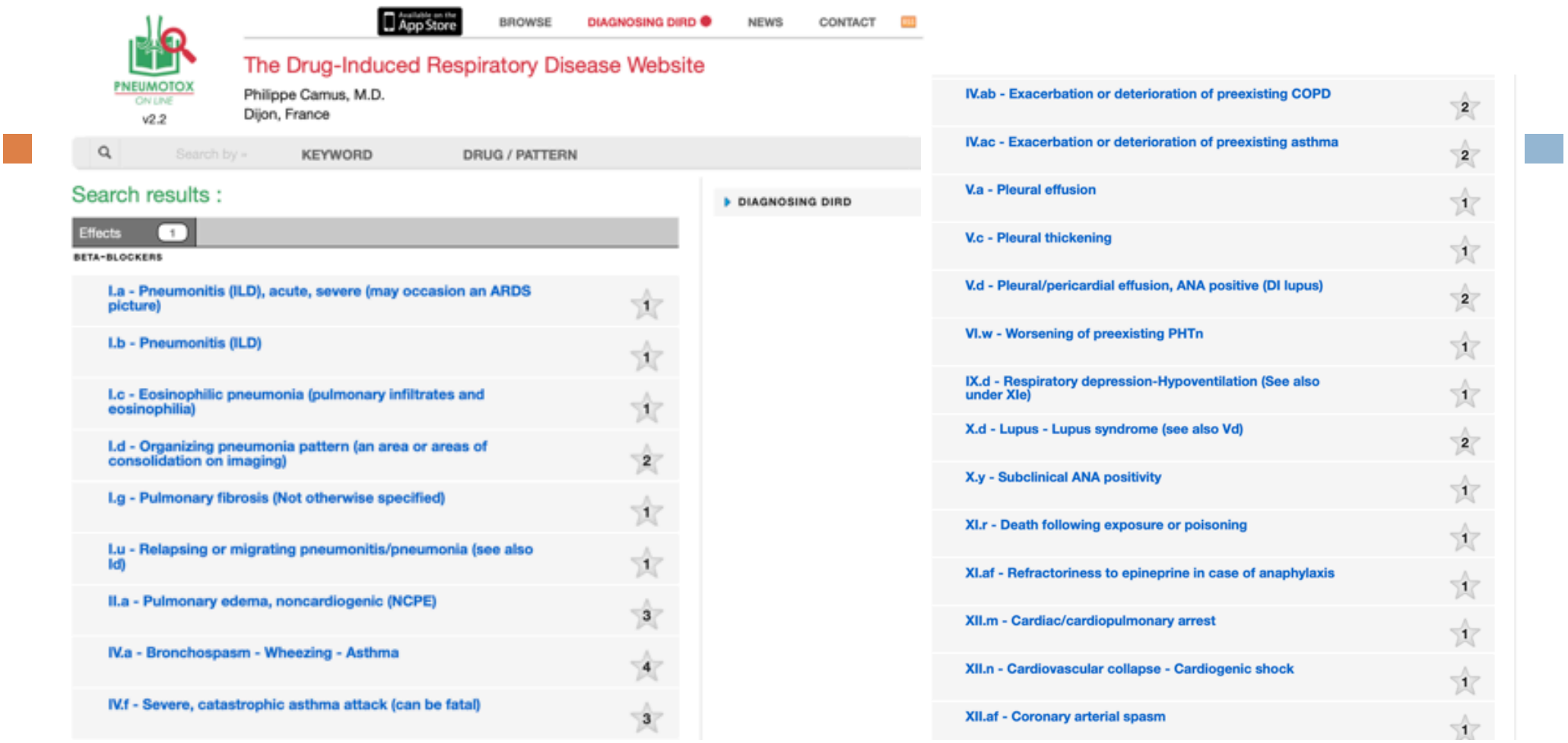
*p<0.05
**exkl. Malignome

NEJM 2008;359:1543-54

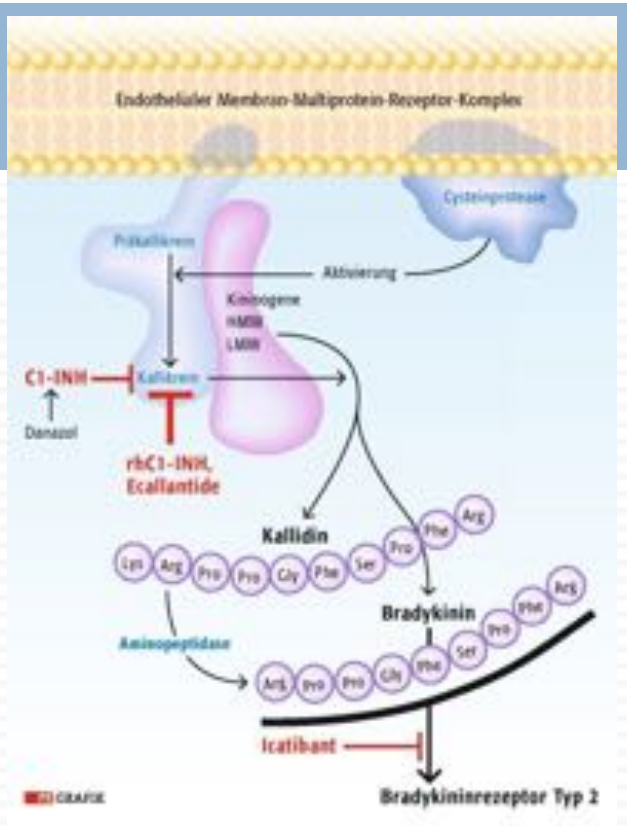
- Zwei Metaanalysen kamen zu dem Ergebnis, dass der Einsatz von kardio-selektiven Betablockern bei Patienten mit COPD aufgrund des geringen Risikos für Bronchospasmen möglich ist (Cochrane Database of Systematic Reviews 2005, DOI: 10.1002/14651858.CD003566.pub2; »Respiratory Medicine« 2003, DOI: 10.1016/S0954-6111(03)00168-9).
- Als eine von vielen Leitlinien bewertet die europäische Leitlinie zu Herzinsuffizienz Betablocker daher als nicht kontraindiziert bei COPD, favorisiert allerdings den Einsatz kardioselektiver Betablocker. Es mehren sich zudem Hinweise, dass der Einsatz von Betablockern bei Patienten mit COPD nach Myokardinfarkt beziehungsweise bei Herzinsuffizienz, aber auch allgemein sogar mit einer besseren Überlebenswahrscheinlichkeit verbunden ist.
- Zudem gibt es Anhaltspunkte, dass es bei Anwendung von Betablockern zu weniger Exazerbationen kommt.

Betablocker und COPD

- Keine KI zur Gabe von β_1-selektiven Blockern in der COPD
- Kardiale Komorbiditäten sind zu behandeln nach den Leitlinien unabhängig von der COPD (gilt für Betablocker, ACE Hemmer, ARB Blocker, Statine, NOACs, etc.) – GOLD Leitlinien
- Cardioprotektiver Effekt ist wichtig
- Vorteil in der Exazerbation (?)
- Langwirksame Betamimetika sind save, gilt nicht für **kurzwirksame**
- LAMA (Tiotropium) haben keinen negativen Effekt auf die kardiale Begleiterkrankungen


PNEUMOTOX ON LINE v2.2
Available on the App Store
BROWSE
DIAGNOSING DIRD
NEWS
CONTACT
The Drug-Induced Respiratory Disease Website
Philippe Camus, M.D.
Dijon, France
Search by :
KEYWORD
DRUG / PATTERN
Search results :
Effects 1
BETA-BLOCKERS
I.a - Pneumonitis (ILD), acute, severe (may occasion an ARDS picture) 1
I.b - Pneumonitis (ILD) 1
I.c - Eosinophilic pneumonia (pulmonary infiltrates and eosinophilia) 1
I.d - Organizing pneumonia pattern (an area or areas of consolidation on imaging) 2
I.g - Pulmonary fibrosis (Not otherwise specified) 1
I.u - Relapsing or migrating pneumonitis/pneumonia (see also Id) 1
II.a - Pulmonary edema, noncardiogenic (NCPE) 3
IV.a - Bronchospasm - Wheezing - Asthma 4
IV.f - Severe, catastrophic asthma attack (can be fatal) 3
DIAGNOSING DIRD
IV.ab - Exacerbation or deterioration of preexisting COPD 2
IV.ac - Exacerbation or deterioration of preexisting asthma 2
V.a - Pleural effusion 1
V.c - Pleural thickening 1
V.d - Pleural/pericardial effusion, ANA positive (DI lupus) 2
VI.w - Worsening of preexisting PHTn 1
IX.d - Respiratory depression-Hypoventilation (See also under XIe) 1
X.d - Lupus - Lupus syndrome (see also Vd) 2
X.y - Subclinical ANA positivity 1
XI.r - Death following exposure or poisoning 1
XI.af - Refractoriness to epineprine in case of anaphylaxis 1
XII.m - Cardiac/cardiopulmonary arrest 1
XII.n - Cardiovascular collapse - Cardiogenic shock 1
XII.af - Coronary arterial spasm 1

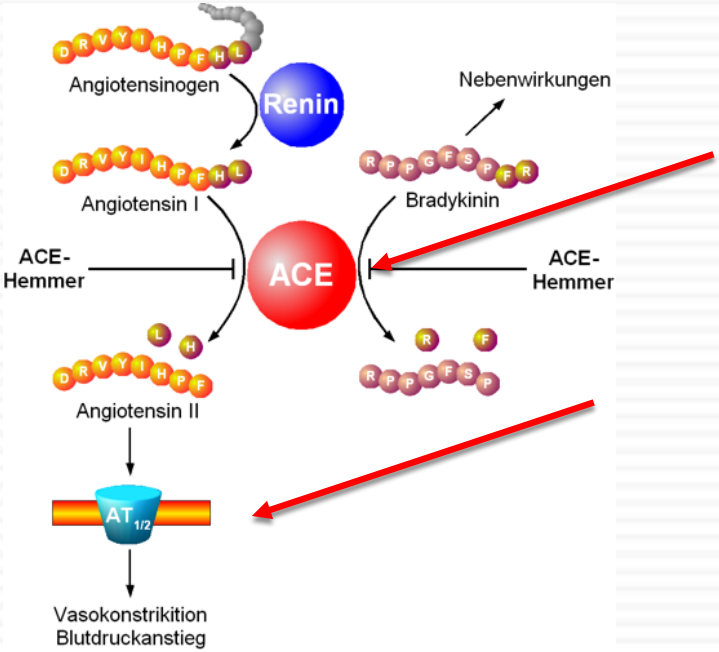
ACE Hemmer HUSTEN



ACE Hemmer und Lunge

- Husten durch PGE_2 und Substanz P ausgelöst
- Ca. 15% (- 50% in asiatischen Studien) der behandelten Patienten
- Absetzen löst Problematik ohne Langzeitkomplikationen
- Viele haben Hyperreagibles Bronchialsystem als Frühform des Asthma bronchiale
  (Br Med J (Clin Res Ed). 1988 Jan 9; 296(6615): 86–88.)
- Auch Entwicklung eines klassischen Asthmas möglich
- Geninduktion wahrscheinlich Gen Insertions/Deletions-Polymorphismus
  (Li YF et al, Angiotensin-Converting Enzyme (ACE) Gene Insertion/Deletion Polymorphism and ACE Inhibitor-Related Cough: A Meta-Analysis, PLOS 2012)

ARBs – Sartane und Lunge



ARBs – gut für die Lunge?

Eur J Pharmacol. 2019 Jun 5;852:25-33. doi: 10.1016/j.ejphar.2019.02.035. Epub 2019 Feb 21.

Suppressive effects of type I angiotensin receptor antagonists, candesartan and irbesartan on allergic asthma.

Kim MJ[1], Im DS[2].

Author information

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Abstract

The effects of candesartan and irbesartan, antagonists of the type I angiotensin II receptor, were investigated on allergic asthma. The antigen-induced degranulation was measured by evaluating β-hexosaminidase activity in vitro. Additionally, a murine ovalbumin-induced allergic asthma model was used to test the in vivo efficacy. It was observed that while candesartan inhibited the antigen-induced degranulation in rat RBL-2H3 mast cells, irbesartan did not. Administration of candesartan and irbesartan decreased the number of immune cells in the bronchoalveolar lavage fluid and reduced the expression of Th2 (IL-4, IL-5, and IL-13) and Th1 cytokines (IL-2 and IFN-γ) in the lung tissues of mice with ovalbumin-induced allergic asthma. Histological studies revealed that both antagonists reduced inflammation and mucin production in the lungs. Therefore, these findings provide evidence that candesartan and irbesartan could have potential applications as anti-allergic agents.

KEYWORDS: Angiotensin II receptor; Anti-allergic; Anti-asthmatic; Candesartan; Degranulation; Irbesartan; Mast cell

PMID: 30797786 DOI: 10.1016/j.ejphar.2019.02.035

Candesartan

Last update 11/04/2012

VIII - Central-large-upper airway (incl pharyngeal-nasal) involvement

VIII.a Angioedema (may cause UAO, asphyxia and death)

PNEUMOTOX ON LINE v2.2

Available on the App Store BROWSE DIAGNOSING DIRD

The Drug-Induced Respiratory Disease Website

Philippe Camus, M.D.
Dijon, France

LIPIDSENKER - STATINE

Statine - Toxizität seit langem bekannt

Statin-induced fibrotic nonspecific interstitial pneumonia

S. Lantuejoul*, E. Brambilla*, C. Brambilla#, G. Devouassoux#

Statin-induced fibrotic nonspecific interstitial pneumonia. S. Lantuejoul, E. Brambilla, C. Brambilla, G. Devouassoux. ©ERS Journals Ltd 2002.

ABSTRACT: Statins inhibit the 3-hydroxy-3-methylglutaryl coenzyme A reductase, reduce the serum level of low-density lipoprotein cholesterol, and are extensively prescribed to prevent cardiovascular mortality and morbidity. Few systemic adverse effects, such as pseudopolymyositis, lupus-like syndromes, and anecdotal hypersensitivity pneumonitis, have been reported.

A simvastatin-induced diffuse interstitial pneumonia associated with a nonspecific interstitial pneumonia pattern at histological analysis is repoted here. Ultrastructural analysis showed a diffuse cytoplasmic accumulation of intralysosomial lamellar inclusions in type II pneumonocytes, histiocytes and endothelial cells, suggesting a shared pathogenesis with amphiphilic drug-induced toxic lung injury. Because statins are increasingly prescribed, statin-induced interstitial lung disorders may be more frequently observed and early recognition will be required.

Eur Respir J 2002; 19: 577–580.

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Keywords: Hypersensitivity, nonspecific interstitial pneumonia, phospholipidosis, statins, toxic

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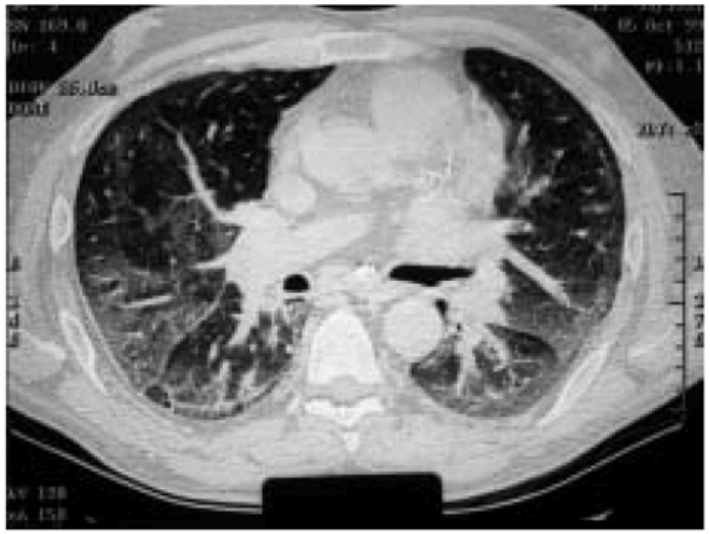


Fig. 1.– Lung computed tomography scan showing bilateral interstitial infiltrates with ground-glass opacities predominating in the lower lobes.

Lu et al. Respiratory Research (2019) 20:17
https://doi.org/10.1186/s12931-019-0984-3

Respiratory Research

REVIEW Open Access

Effectiveness of long-term using statins in COPD – a network meta-analysis

Yongbin Lu[1], Ruixia Chang[2*], Jia Yao[1], Xinni Xu[1], Yongjun Teng[1] and Ning Cheng[3*]

Abstract

Objectives: To evaluate the effectiveness of long-term treatment of statins for chronic obstructive pulmonary disease (COPD), and to answer which one is better.

Methods: General meta-analysis was performed to produce polled estimates of the effect of mortality, inflammatory factors, and lung function index in COPD patients by the search of PubMed, Web of Science, Embase, and China National Knowledge Infrastructure for eligible studies. A network meta-analysis was performed to synthetically compare the effectiveness of using different statins in COPD patients.

Results: General meta-analysis showed that using statins reduced the risk of all-cause mortality, heart disease-related mortality and COPD acute exacerbation (AECOPD) in COPD patients, the RR (95% CI) were 0.72 (0.63,0.84), 0.72 (0.53,0.98) and 0.84 (0.79,0.89), respectively. And using statins reduced C-reactive protein (CRP) and pulmonary hypertension (PH) in COPD patients, the SMD (95% CI) were − 0.62 (− 0.52,-0.72) and − 0.71 (− 0.85,-0.57), respectively. Network meta-analysis showed that Fluvastatin (97.7%), Atorvastatin (68.0%) and Rosuvastatin (49.3%) had higher cumulative probability than other statins in reducing CRP in COPD patients. Fluvastatin (76.0%) and Atorvastatin (75.4%) had higher cumulative probability than other satins in reducing PH in COPD patients.

Conclusions: Using statins can reduce the risk of mortality, the level of CRP and PH in COPD patients. In addition, Fluvastatin and Atorvastatin are more effective in reducing CRP and PH in COPD patients.

Keywords: Statins, Mortality, CRP, PH, Network meta-analysis

Bronchiektasien

CHRONISCHE BRONCHIALE INFEKTION
Langzeit AB-Therapie
Eradikation von Besiedlungen
Antibiotische Therapie der Exazerbation

STRUKTURELLE LUNGENERKRANKUNG
Langzeit Bronchodilatation
Chirurgie
Pulmonale Rehabilitation

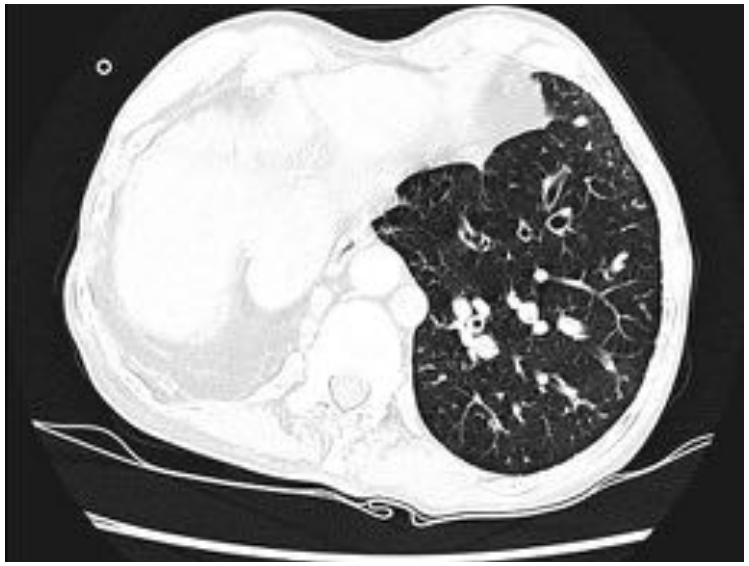
ENTZÜNDUNG
Antientzündliche Therapie

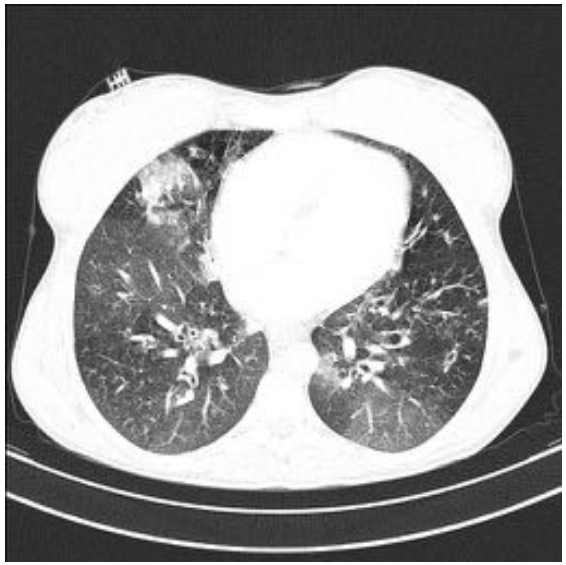
GESTÖRTE MUKOZILIÄRE CLEARANCE
Mukoaktive Behandlung
Airway Clearance

Nach: Polverino, ERJ 2017

Eradikationstherapie

- Nur bei de novo Besiedlung/Infektion mit *p. aeruginosa*





Anti-inflammatorische Therapie

- Keine Statine ! (Polverino et al. ERS/ATS guideline for managemnt of adult bronchiectasis, 2017)

There are no large trials of anti-inflammatory therapies in bronchiectasis and the existing studies show minimal and, in most cases, no clinically significant benefits. The increased frequency of adverse events, particularly with statins, justifies a recommendation against their use.

- Inhalative Steroide bei Bronchiektasien werden nicht empfohlen wegen Pneumonierisiko
- Bei Asthma und COPD soll die Präsenz von BE nicht über JA/NEIN zur Steroidempfehlung entscheiden

Statins

5

(A.k.a. HMG-CoA reductase inhibitors). Convincing cases reports of ILD contrast with the lack of epidemiological evidence (PMID 17223772, 23299962). Cerivastatin was recalled/discontinued worldwide in 2001, due to an excess rate of rhabdomyolysis, a complication common to statins and other lipid-lowering agents

Last update 16/10/2017

:

I - Interstitial/parenchymal lung disease

I.a	Pneumonitis (ILD), acute, severe (may occasion an ARDS picture)	2
I.b	Pneumonitis (ILD)	2
I.d	Organizing pneumonia pattern (an area or areas of consolidation on imaging)	2
I.f	Acute fibrinous organizing pneumonia (AFOP)	1
I.g	Pulmonary fibrosis (Not otherwise specified)	1
I.u	Relapsing or migrating pneumonitis/pneumonia (see also Id)	-
I.x	Pleuroparenchymal fibroelastosis (PPFE)	-
I.ar	The association of ILD and myositis	1

IV - Airway involvement

IV.d	Cough (lone)	2

V - Pleural and/or pericardial involvement

V.a	Pleural effusion	1
V.b	Eosinophilic pleural effusion	1
V.d	Pleural/pericardial effusion, ANA positive (DI lupus)	1

VIII - Central-large-upper airway (incl pharyngeal-nasal) involvement

VIII.a	Angioedema (may cause UAO, asphyxia and death)	1

IX - Neuromuscular / CNS involvement - Disordered breathing during sleep

IX.a	Diaphragm/inspiratory muscle weakness/paralysis (w/wo ARF)	1
IX.ac	Myositis of the respiratory muscles (May lead to respiratory muscle paralysis)	1

X - Systemic/Distant conditions, syndromes and reactions

X.d	Lupus - Lupus syndrome (see also Vd)	1
X.j	Myopathy-Myositis-Polymyositis (see also under Xba)	2
X.ba	Rhabdomyolysis (see also under Xj)	3

XI - Miscellaneous

XI.b	Chest pain (acute or subacute), lone or prominent	1

XII - Cardiovascular involvement / toxicity

XII.ab	Pericardial fat necrosis	-

XV - Pathology

XV.c	Path: Organizing pneumonia (OP/BOOP) pattern (see also Id)	1
XV.d	Path: Acute fibrinous organizing pneumonia (AFOP-pattern) (see also If)	1
XV.o	Path: Endogenous lipoid pneumonia (phospholipidosis)	1
XV.ap	Path: Pleuroparenchymal fibrosis/fibroelastosis (PPFE)	-

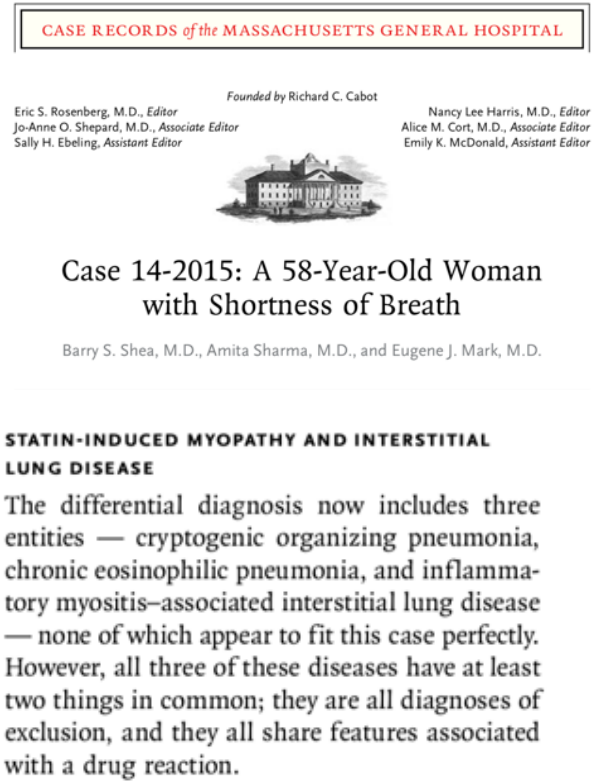
PNEUMOTOX ON LINE v2.2

Available on the App Store BROWSE DIAGNOSING DIRD

The Drug-Induced Respiratory Disease Website

Philippe Camus, M.D.
Dijon, France

Fall löst Diskussion aus



CASE RECORDS *of the* MASSACHUSETTS GENERAL HOSPITAL

Founded by Richard C. Cabot

Eric S. Rosenberg, M.D., *Editor*
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Nancy Lee Harris, M.D., *Editor*
Alice M. Cort, M.D., *Associate Editor*
Emily K. McDonald, *Assistant Editor*

Case 14-2015: A 58-Year-Old Woman with Shortness of Breath

Barry S. Shea, M.D., Amita Sharma, M.D., and Eugene J. Mark, M.D.

STATIN-INDUCED MYOPATHY AND INTERSTITIAL LUNG DISEASE

The differential diagnosis now includes three entities — cryptogenic organizing pneumonia, chronic eosinophilic pneumonia, and inflammatory myositis–associated interstitial lung disease — none of which appear to fit this case perfectly. However, all three of these diseases have at least two things in common; they are all diagnoses of exclusion, and they all share features associated with a drug reaction.

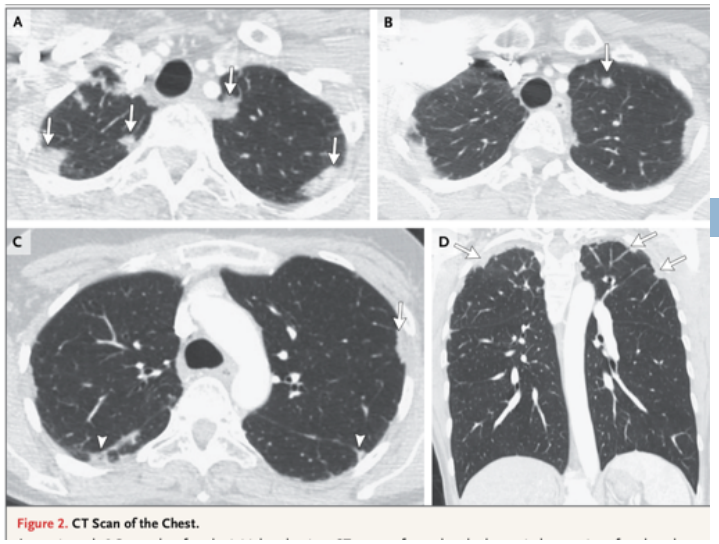


Figure 2. CT Scan of the Chest.

- HMG CoA Reduktase Hemmer bewirken unspezifische toxische Alveolitis (diffuse parenchymal lung disease - DPLD)
- Bilder sind mehrdeutig:
  - Akute fibrinöse organisierende Pneumonie
  - COP
  - Eosinophile Pneumonie
  - Rheumatoide-assoziierte Lungenerkrankung (IPAF)
  - Auslöser von Lupus-Syndrom mit ANA+
  - PPFE – Pleuroparenchymale Fibroelastose

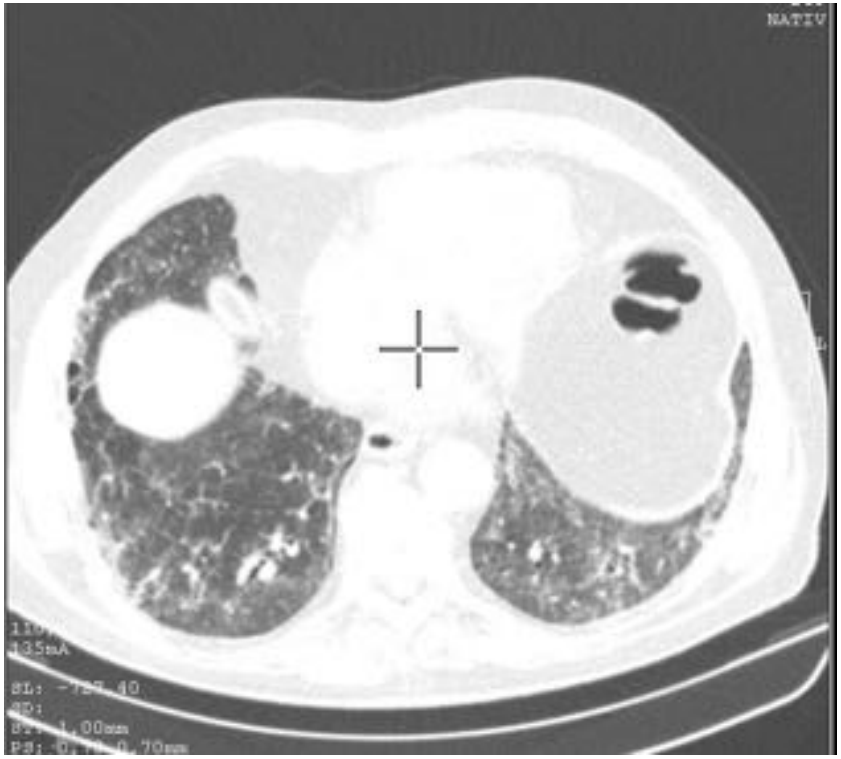
N Engl J Med 372;18 nejm.org April 30, 2015

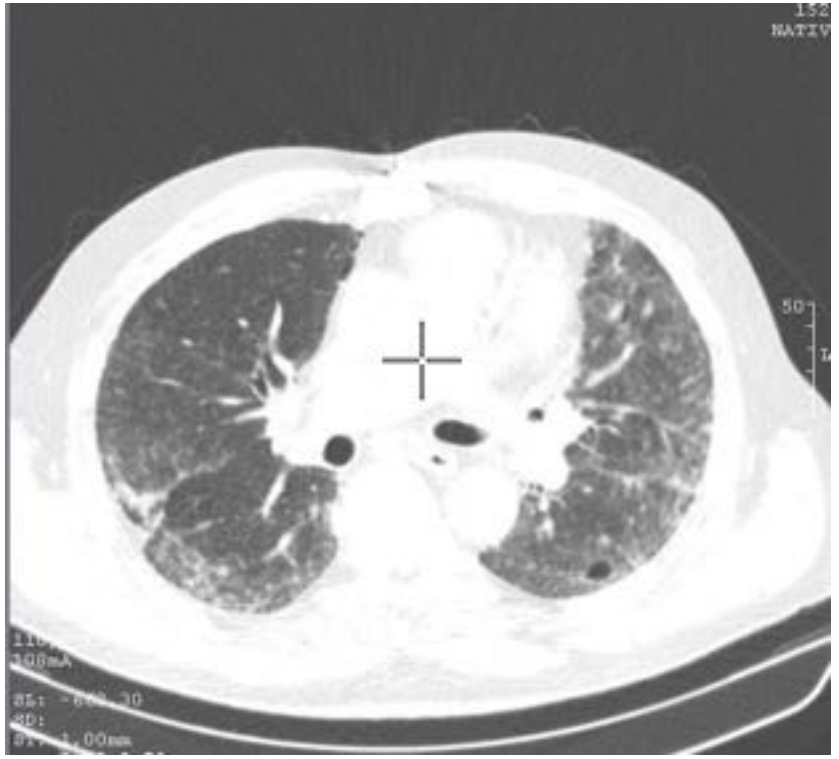
Häufigste Bilder

- Akute fibrinöse organisierende Pneumonie (AFOP)
- Cryptogen organisierende Pneumonie (COP)
- Eosinophile Pneumonie (AEP, CEP)
- Flüchtige Infiltrate (eosinophil)
- NSIP-artige Fibrosen
- Rheumatoide-assoziierte Lungenerkrankung (IPAF)
- Auslöser von Lupus-Syndrom mit ANA+
- PPFE – Pleuroparenchymale Fibroelastose

- Histologische Zeichen von toxischen Alveolitiden
- Eosinophilie im Gewebe (+BAL)
- Gemischte lympho/granulozytäre Infiltrate

Fall 1





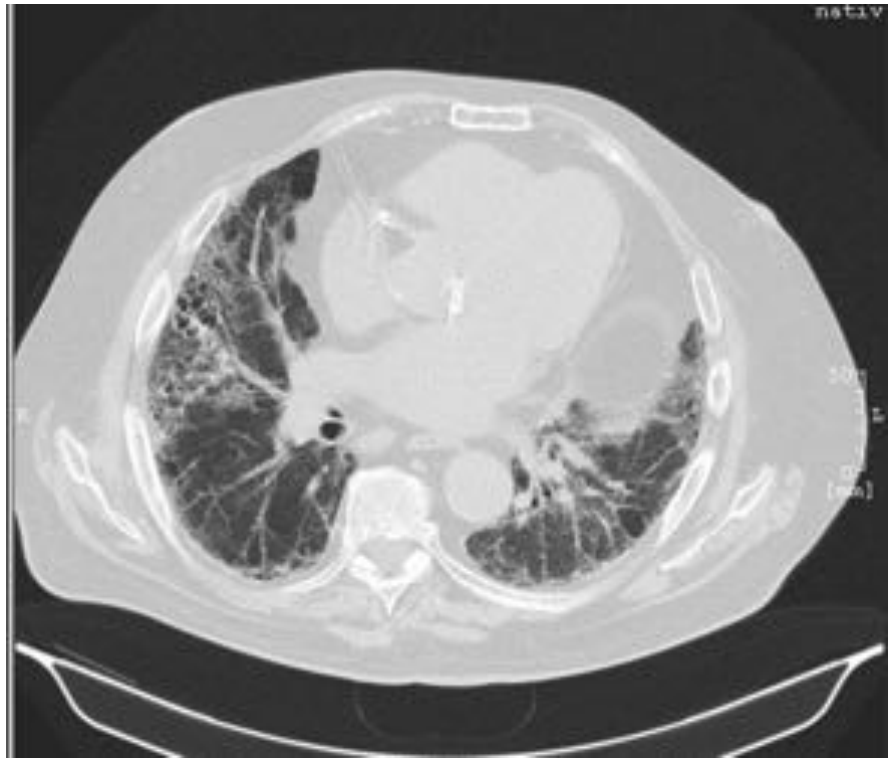
Patient, 80a, m,

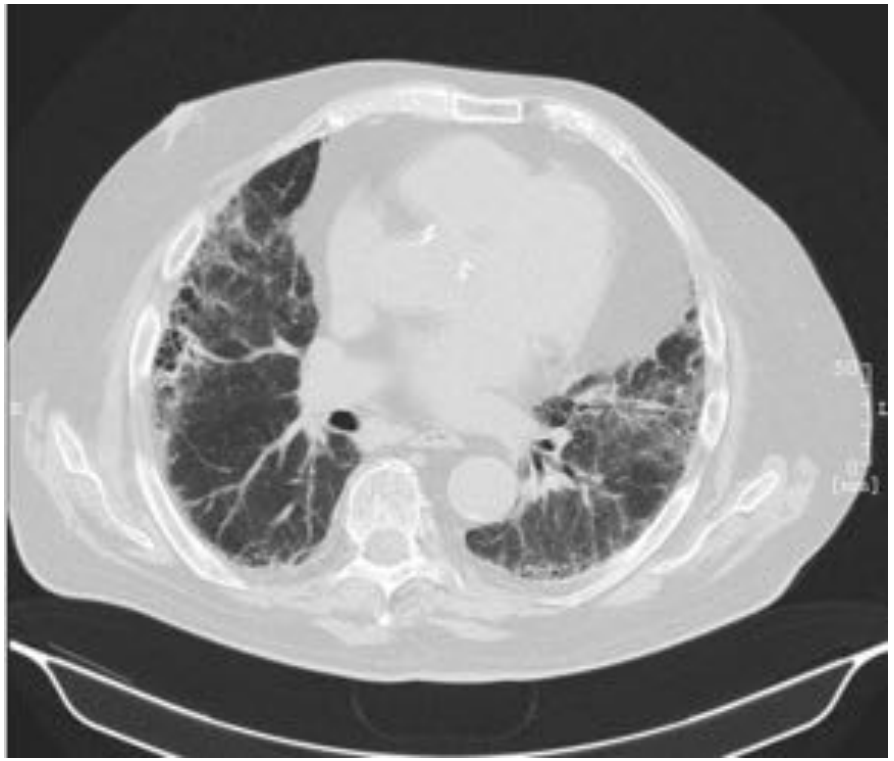
- BAL: Eosinophil
- TBB: mögliche toxische Reaktion
- TBCB: NSIP artiges Bild
- Auslöser denkbar:
  Atorvastatin
  Apixaban
  Kontrastmittel nach CAG
- Oder doch idiopathisch?

Medikamentenanamnese:

Wirkstoff /Stärke	Häusliche Vormedikation / Medikation bei Aufnahme mo.	mi.	ab.	na.	**Medikation bei Entlassung** mo.	mi.	ab.	na.	Veränderungen zur Vormedikation - Erläuterungen
Ramipril 2,5 mg	1	0	0		**1**	**0**	**0**		
Bisoprolol 2,5 mg	1	0	0		**1**	**0**	**0**		
Lyrica 25 mg	1	0	1		**1**	**0**	**1**		
Atorvastatin 40 mg	0	0	1		**0**	**0**	**1**		
ACC 600 mg	1	0	0		**1**	**0**	**0**		Für 2 Wochen bB
Prednisolon 50 mg					**1**	**0**	**0**		**Bis Mo., den 19.11.2018** dann wöchentlich reduzieren um 10 mg bzw. Empfehlung nach Erhalt der ausstehenden Ergebnisse, auch Absetzen möglich, falls nur Einblutung unter NOAK am wahrscheinlichsten ist
Eliquis									Pausiert
Clexane 0,4 ml s.c.					**1**	**0**	**1**		Absetzen Clexane und Wiederaufnahme Eliquis z.B. 2 x 2,5 mg wird bei Befundbesprechung nächste Woche diskutiert werden!
ASS 100 mg					**0**	**1**	**0**		Bis zur Klärung, wann Eliquis wieder verordnet werden kann

Fall 2: Älterer Herr, unklare Lungenfibrose





- Histo: eher NSIP-artig, medikamentös toxisch möglich
- Keine EAA, ANA, Rheuma oder andere Ursache
- Medikamente?

Medikamente

Wirkstoff /Stärke	Häusliche Vormedikation / Medikation bei Aufnahme mo. mi. ab. na.	**Medikation bei Entlassung**	Veränderungen zur Vormedikation - Erläuterungen
Prednisolon 30 mg		**1-0-0**	
Vigantoletten 1000 IE		**1-0-0**	
Pantozol 20 mg		**1-0-0**	
Metoprolol 95 mg		**1-0-1**	
HCT 12,5 mg		**1-0-0**	
Candesartan 16 mg		**1-0-0**	
ASS 100 mg		**1-0-0**	
Amlodipin 5 mg		**0-0-1**	
Simvastatin 30 mg		**0-0-1**	
Metformin 1000 mg		**1-0-1 1/2**	
Lantus		**0-0-0-18 IE**	um 21:00 Uhr
Actrapid nach Plan			
LOT (bestellt)			4 Liter/min. in Ruhe 6 Liter/min. unter Belastung

Interstitielle Lungenerkrankungen

Chest. 2008 Oct;134(4):824-30. doi: 10.1378/chest.08-0943. Epub 2008 Aug 8.

Statins and interstitial lung disease: a systematic review of the literature and of food and drug administration adverse event reports.

Fernández AB[1], Karas RH, Alsheikh-Ali AA, Thompson PD.

Author information

1 Section of Cardiovascular Medicine, Yale University School of Medicine, New Haven, CT, USA.

CONCLUSIONS: Statin-induced ILD is a possible newly recognized side effect of statin therapy. The mechanism of lung injury is not defined. The current review provides novel information from the FDA-AER that supports a possible, although unusual, pulmonary class effect of statins.

data. Given the paucity of information, all case reports and case series in English and French were included. All adverse event reports from the FDA-AER database in which a statin was listed as causative suspect were included.

RESULTS: The literature search using PubMed yielded eight articles describing a total of 14 case reports of ILD in association with statin use. The FDA-AER system database contained 162 cases of reported statin-induced ILD as of June 2007. For every 10,000 reports of a statin-associated adverse event, approximately 1 to 40 reports were for ILD.

CONCLUSIONS: Statin-induced ILD is a possible newly recognized side effect of statin therapy. The mechanism of lung injury is not defined. The current review provides novel information from the FDA-AER that supports a possible, although unusual, pulmonary class effect of statins.

Zusammenfassung: ILD und Statine

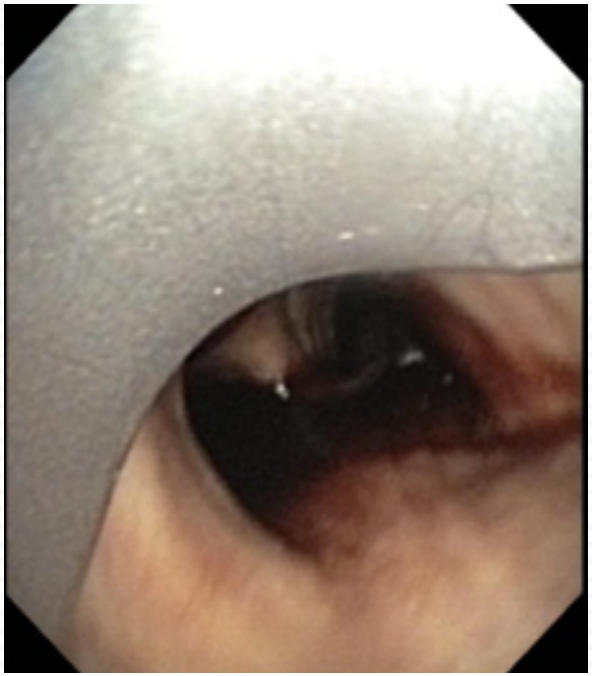
- Statine als Auslöser von medikamentösen toxischen Reaktion bekannt
- Kombinationen mit anderen Toxinen möglich (Amniodaron, NOACs, Antirheumatika, Antineoplastika, etc.)
- Im Zweifelsfall absetzen oder ersetzen
- Bilder radiologisch und histologisch sehr unterschiedlich

Reaktionsmuster der Lunge auf toxische Substanzen

- Bronchospasmus
- Angioödem
- Nicht-cardiales Lungenödem (NCPE)
- Eosinophile Infiltrate (AEP, CEP)
- Interstitielle Lungenerkrankungen (COP, NSIP, AFOP, IPAF, ARDS, PPFE, Lipidpneumonie)
- Pleuraergüsse (PE, EPE, ANA+-PE)

ANTIKOAGULANTIEN und Co.

IATROGENE BLUTUNG



Anamnese

- Menge:
  Hämoptysen bis 200ml/24h
  oder 100ml akut
  Massiver Hämoptoe >200ml/24h oder >150ml akut (entspricht anatomischem Totraum)
- angloamerikanisch: hempotysis
- Farbe
- Verlauf

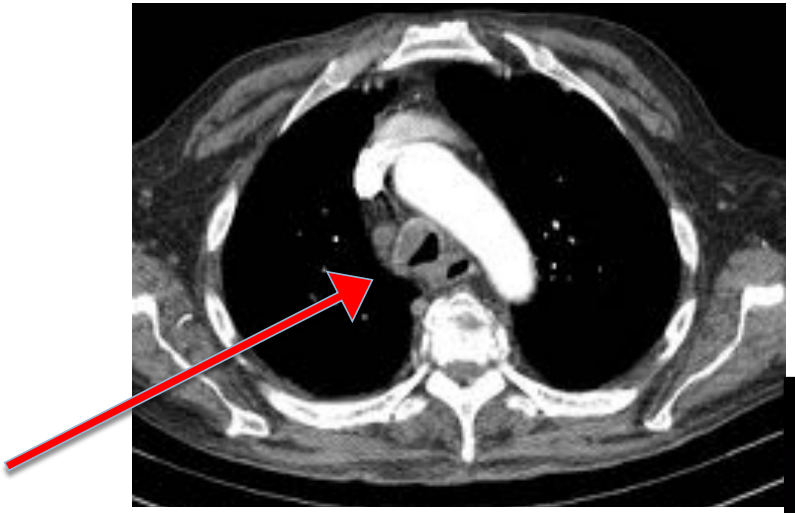
Häufigkeit

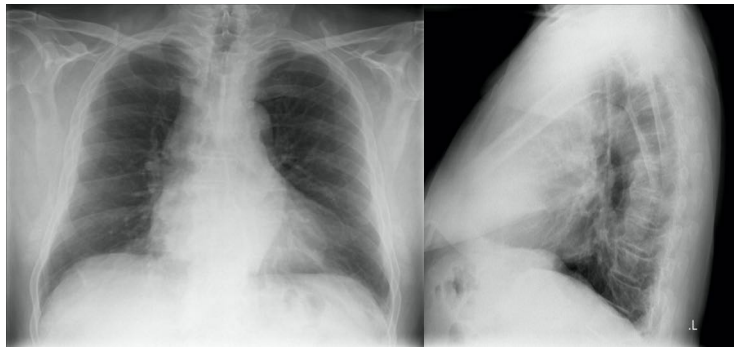
- weltweit: Tuberkulose
- bei uns:

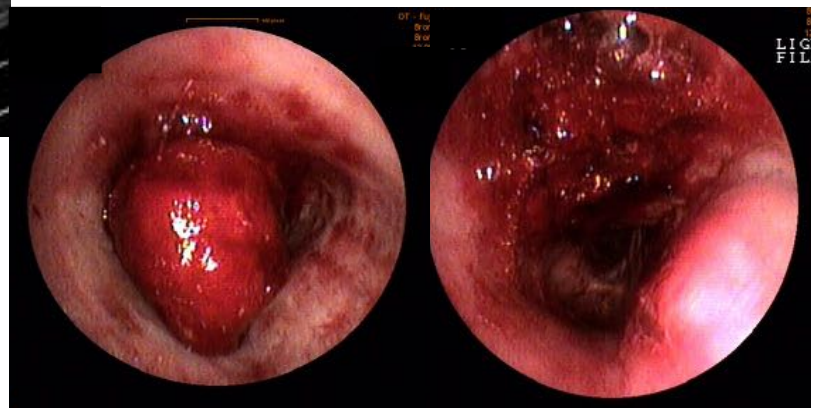
  IATROGEN

  Bronchuskarzinome
  Bronchiektasien
  Tuberkulosen
  Aspergillome
  ARDS
  Diffuse alveolare Hämorrhagien

Blutender Trachealtumor – Fall SJ







Iatrogene Blutung – Bronchologe ist schuld (?)

- TBB
- Zentrale Biopsie
- Rekanalisation, Tumorabtragung
- Fremdkörperentfernung

VORTEILE

- Patient bereits intubiert
- Blutungsquelle bekannt

RISIKOREDUKTION

- ASS ist keine KI
- Gerinnung: INR <1,5 (PT > 50%) als Ziel
- Zielläsion
- CT, EBUS

Was geht unter AK/TAGH/NOAC/dual oder triple

Substanz	Angriffspunkt	Hauptanwendungsgebiete
Acetylsalicyl-säure	thrombozytäre COX-1-, TxA2-Synthese	• Sekundärprophylaxe arterieller ischämischer kardio- und zerebrovaskulärer Erkrankungen
ADP-Rezeptor-Antagonisten	thrombozytärer ADP($P2Y_{12}$)-Rezeptor	• duale Aggregationshemmung bei PTCA und ACS (kombiniert mit ASS) • PAVK • alternativ zu ASS zur Sekundärprophylaxe kardiovaskulärer Erkrankungen
GP-IIb/IIIa-Antagonisten	thrombozytärer GP-IIb/IIIa-Rezeptor	• drohender Myokardinfarkt bei instabiler AP • PTCA mit hohem Risiko
Dipyridamol	thrombozytäre Adenosinaufnahme, PDE, z. T. ungeklärt	• Sekundärprophylaxe nach CVI und TIA (in Kombination mit ASS)

Was geht unter AK/TAGH/NOAC/dual oder triple

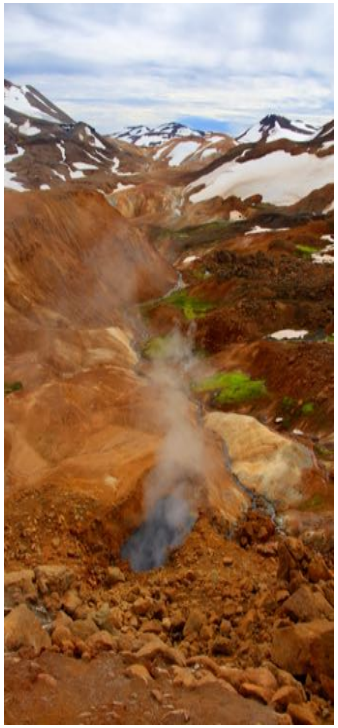
Intervention	ASS	NOAC	VKA	TAGH	Clopido + NOAC	Clopido + NOAC + ASS	Thrombopenie
Absetzzeit	7 d	2 d	pT >60	7d	7d	7d	> 80000
Bronchoskopie	YES	YES	YES	YES	Cave	Cave	YES
BAL	YES	YES	YES	YES	YES	YES	YES
TBB	YES	NO	NO	NO	NO	NO	Cave
EBUS-TBNA	YES	YES	YES	YES	NO	NO	Cave
TBCB	NO	NO	NO	NO	NO	NO	NO
Ventile	YES	NO	NO	NO	NO	NO	NO
Coils	Cave	NO	NO	NO	NO	NO	NO
Pleurapunktion	YES	YES	YES	YES	Cave	Cave	Cave
Drainage	YES	Cave	NO	Cave	NO	NO	NO
TTP CT oder US	YES	NO	NO	NO	NO	NO	NO

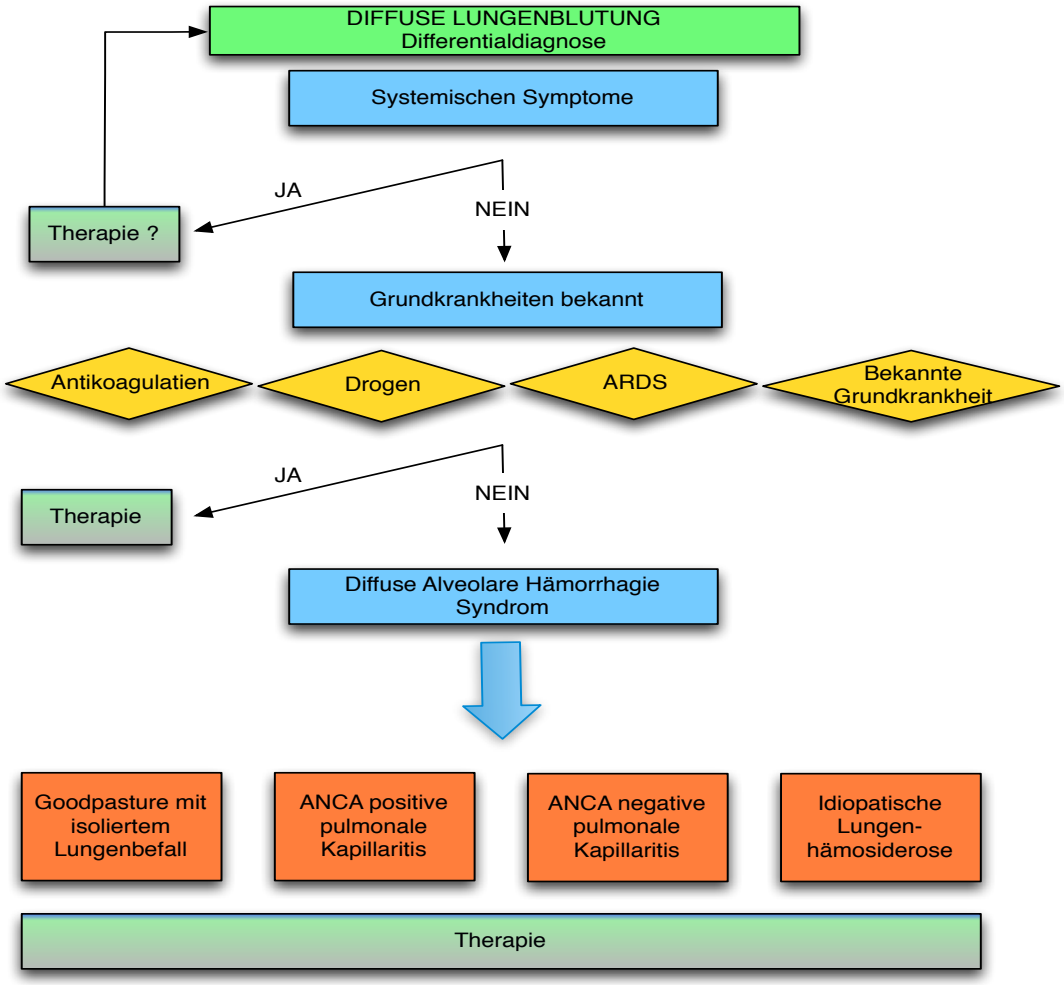
Iatrogene Blutung – Kardiologe (Internist) ist schuld (?)

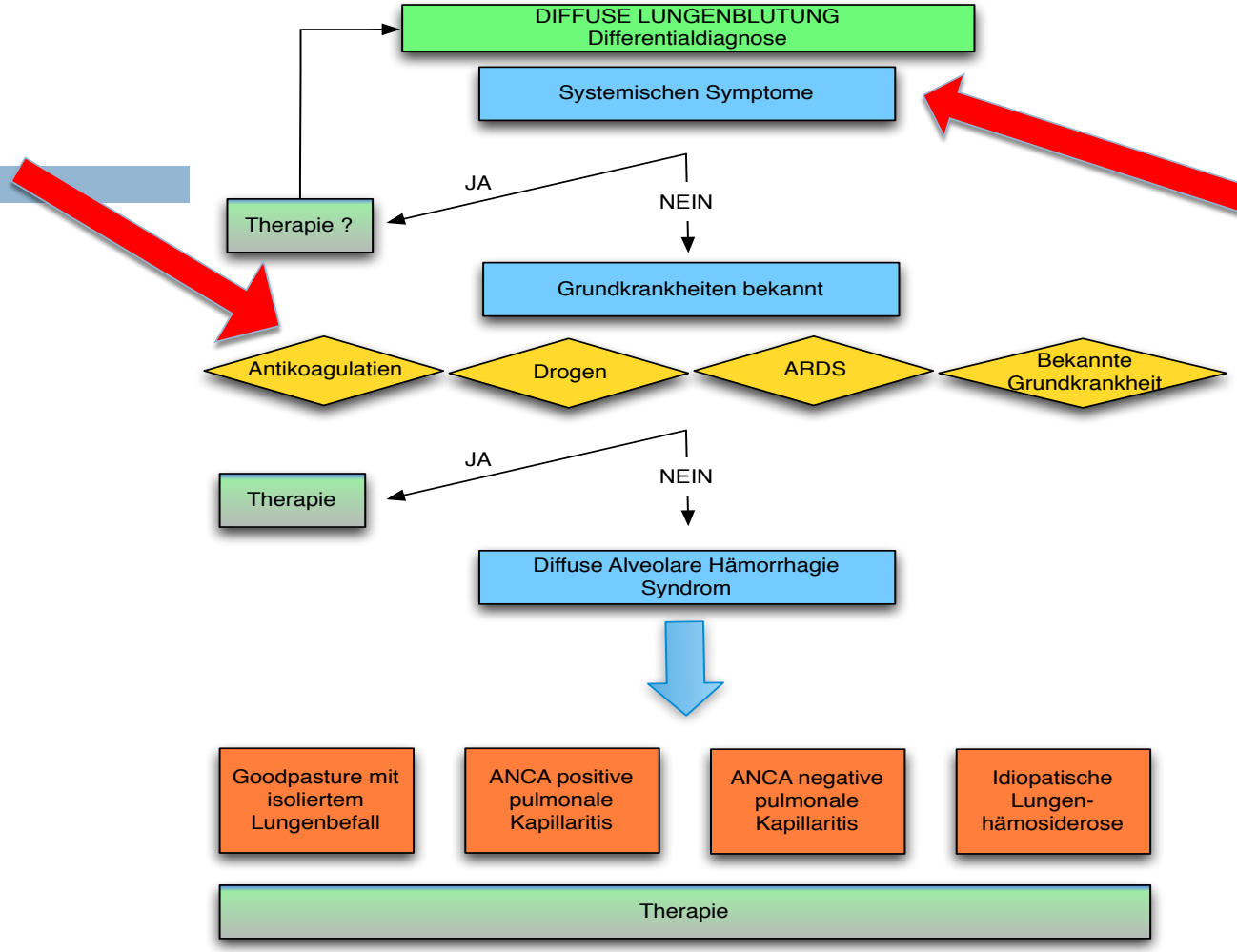
- Therapeutische Antikoagulation ist häufigste Ursache für diffuse Blutungen
- ASS ist keine KI für PE/TBB/TBNA
- Clopidogrel u.ä abgesetzt werden

ANTAGONISIEREN !

- Normalisierung der Gerinnung bei lebensbedrohlichen Blutungen




DIFFUSE LUNGENBLUTUNG
Differentialdiagnose
Systemischen Symptome
JA
NEIN
Therapie ?
Grundkrankheiten bekannt
Antikoagulatien
Drogen
ARDS
Bekannte Grundkrankheit
JA
NEIN
Therapie
Diffuse Alveolare Hämorrhagie Syndrom
Goodpasture mit isoliertem Lungenbefall
ANCA positive pulmonale Kapillaritis
ANCA negative pulmonale Kapillaritis
Idiopatische Lungen-hämosiderose
Therapie


DIFFUSE LUNGENBLUTUNG
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ANCA positive pulmonale Kapillaritis
ANCA negative pulmonale Kapillaritis
Idiopatische Lungen-hämosiderose
Therapie

Interstitielle Lungenerkrankungen – schon wieder?

J Stroke Cerebrovasc Dis. 2016 Jul;25(7):1767-1769. doi: 10.1016/j.jstrokecerebrovasdis.2016.03.036. Epub 2016 Apr 15.

Development of Interstitial Lung Disease after Initiation of Apixaban Anticoagulation Therapy.

Tomari S[1], Homma K[2], Noguchi T[3], Aiba T[3], Matsuki T[2], Suzuki R[2], Koga M[2], Takigami M[3], Tagawa H[4], Hashimoto T[4], Toyoda K[2].

Author information

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3 Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Center, Suita, Osaka, Japan.
4 Department of Respiratory Medicine, Saiseikai Senri Hospital, Suita, Osaka, Japan.

Abstract

BACKGROUND: Nonvitamin K antagonist oral anticoagulants may cause interstitial lung disease (ILD) similar to that seen for other cardiovascular drugs. The aim of this study was to determine trends and medical conditions associated with ILD in patients taking apixaban.

METHODS: A single-center observational survey conducted between February 2013 and May 2015 examined patients who developed ILD after initiation of apixaban administration.

RESULTS: Chest computed tomography showed that 4 (~.45%) out of approximately 870 apixaban users developed ILD. All patients were elderly Japanese men with decreased creatinine clearance who had nonvalvular atrial fibrillation. Three of the four were confirmed smokers, whereas three had a history of lung disease. Dyspnea occurred during the initial week after starting apixaban administration in 3 patients and at 90 days in 1 patient. All patients underwent methylprednisolone pulse therapy, with three requiring mechanical ventilation. Although 2 patients recovered, the other two died of respiratory failure.

CONCLUSIONS: Development of ILD during anticoagulation with apixaban is not rare. When apixaban is administered in elderly high-risk patients, subjects need to be carefully monitored for respiratory symptoms. As drug-induced ILD is often reported in Japan, further studies that clarify if these types of cases are common in countries other than Japan will also need to be undertaken.

Anticoagulants, direct oral (anti-thrombin, -IIa, -Xa) - NOAC 2

See under specific drugs. Initially called 'new' antocoagulants: e.g. anti-IIa: dabigatran. Anti-Xa: rivaroxaban, apixaban. Management, reversing agents and antidotes see under PMID 27330657. Montitoring of DOAC activity at PMID 27637548. Antidotes at PMID 26872887

Last update 10/12/2018

I - Interstitial/parenchymal lung disease

I.a	Pneumonitis (ILD), acute, severe (may occasion an ARDS picture)	1
I.b	Pneumonitis (ILD)	3

II - Pulmonary edema - Acute lung injury - ARDS

II.b	ARDS - Acute lung injury	1

III - Pulmonary/alveolar hemorrhage

III.a	Alveolar hemorrhage, diffuse (DAH)	1
III.c	Hemoptysis	-
III.k	Epistaxis	2
III.m	Coagulopathy	2

V - Pleural and/or pericardial involvement

V.e	Hemothorax - Serosanguineous pleural effusion	1
V.n	Hemopericardium - Bloody pericardial effusion	1

IX - Neuromuscular / CNS involvement - Disordered breathing during sleep

IX.x	Thoracic epidural or spinal hematoma	1

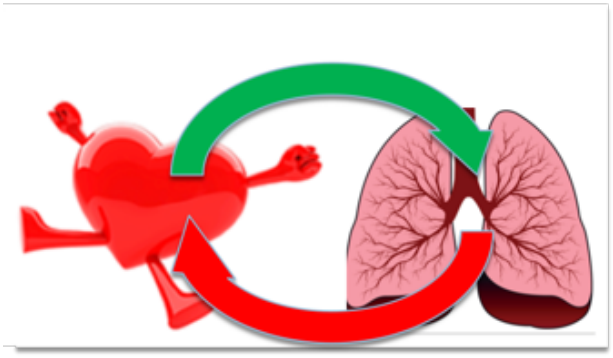
PNEUMOTOX ON LINE v2.2

Available on the App Store BROWSE DIAGNOSING DIRD

The Drug-Induced Respiratory Disease Website

Philippe Camus, M.D.
Dijon, France


DETOX YOUR LUNGS




52. Bad Reichenhaller Kolloquium
SAVE THE DATE
Pulmonale Infektiologie –
von guten und bösen Erregern
Chancen und Möglichkeiten in Prävention und Therapie
19.–20. Juni
2020
Tagungspräsident
Prof. Dr. med. Tobias Welte
Wissenschaftliche Leitung
Prof. Dr. med. Andreas Rembert Koczulla
Dr. med. Christian Geltner, MSc MBA
Initiator
Bad Reichenhaller Forschungsinstitut
für Krankheiten der Atmungsorgane e.V.
www.kolloquium-br.de

DANKE für die Aufmerksamkeit

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KLINIKEN SÜDOSTBAYERN