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Abstracts

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Fall des Jahres 2012

F01

Pleurales Rezidiv eines typischen pulmonalen Karzinoids 9 Jahre nach Operation

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Im Dezember 2011 erfolgt die ambulante Vorstellung des 74-jährigen Patienten, welcher vom niedergelassenen Pneumologen wegen linksseitiger pleuraler Raumforderungen mit der Verdachtsdiagnose Pleuramesotheliom zugewiesen wird.

Er befindet sich zu diesem Zeitpunkt in kardio-pulmonal kompensiertem Zustand, bei altersentsprechender körperlicher Belastbarkeit. Ein jahrzehntelanger Nikotinabusus mit berechneten 40 Packungsjahren ist seit 15 Jahren beendet. Er war über 50 Jahre in einer Zimmerei beschäftigt, eine Asbestexposition ist nicht erfragbar. Anamnestisch auffällig ist allerdings ein Zustand nach Lingularesektion wegen typischem Karzinoid im Jahr 2002 in einem zentralen Krankenhaus. Klinische Hinweise auf hormonelle/neuroendokrine Aktivitäten bestehen beim Erstkontakt nicht.

Im Routinelabor zeigen sich außer einer mäßigen Leukozytose keine wesentlichen Auffälligkeiten. Lungenfunktionell ergeben sich keine Hinweise für Obstruktion bzw. Restriktion, die Ruheblutgase liefern einen ausgeglichenen Befund. Die Tumormarker liegen, außer einer marginalen NSE-Erhöhung (16,6 ng/ml) allesamt im Normbereich. In der CT-Thorax finden sich linksseitig mehrere pleuraständige Tumore sowie ein Pleuraerguss. Das im Rahmen des Stagings durchgeführte DOPA-PET zeigt eine diffuse fleckige Speicherung über die gesamte linke Pleura. Das Vorliegen zerebraler Metastasen kann MR-tomographisch ausgeschlossen werden.

Zur Gewinnung einer repräsentativen Histologie erfolgt der Entschluss zur Thorakoskopie, bei der ausreichend Gewebeproben gewonnen werden können. Die feingewebliche Aufarbeitung liefert als Ergebnis ein typisches Karzinoid. In Zusammenschau der vorliegenden Befunde kann die Diagnose „Pleurales Rezidiv eines typischen pulmonalen Karzinoids" – 9 Jahre nach Lingularesektion aufgrund eines typischen Karzinoids – gestellt werden.

In der Folge wird eine palliative Chemotherapie mit Cisplatin/Etoposid verabreicht. Im Restaging nach 4 Zyklen zeigt sich bildgebend eine „stable disease".

F02

Unklare Raumforderung im vorderen oberen Mediastinum

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Kasuistik: Im vorliegenden Fall wurde ein 70-jähriger Mann aufgrund von zunehmenden Kreuzschmerzen in der neurologischen Notaufnahme vorstellig. An Vorerkrankungen war eine Refluxösophagitis mit St.p. Fundoplicatio 2005 sowie ein 10 Jahre zurückliegender Nikotinabusus mit 15 PY zu erheben. Bei der Aufnahme war der Patient respiratorisch vollkommen beschwerdefrei. Im Labor fielen eine Thrombopenie sowie stark erhöhte Leber- und Entzündungsparameter auf. Von Seiten der Neurologie wurde zur weiteren Abklärung ein MR der Wirbelsäule veranlasst. Dieses zeigte eine Tumorinfiltration der unteren BWS und oberen LWS mit mehreren pathologischen Frakturen. Daraufhin wurde im Rahmen der Tumorsuche ein CT des Thorax und des Abdomens durchgeführt. Der Radiologe beschrieb eine regressiv veränderte Raumforderung im vorderen oberen Mediastinum mit Perikardinfiltration sowie einen Rundherd im linken Oberlappen. Der Abdomenbefund war unauffällig. Die anschließend durchgeführte Skelettszintigraphie zeigte multipelste pathologische Speicherungen in nahezu allen Skelettabschnitten. Bei radiologischen Verdacht auf ein aggressiv wachsendes Lymphom wurde eine Beckenkammbiopsie durchgeführt. Diese erbrachte keinen Hinweis auf eine hämatologische Grunderkrankung.

In der Zwischenzeit kam es beim Patienten zu einer raschen Verschlechterung des Allgemeinzustandes und zur Entwicklung einer ausgeprägten Panzytopenie, sodass von der geplanten thorakoskopischen Lungenbiopsie Abstand genommen werden musste. Stattdessen wurde eine transthorakale Stanzbiopsie durchgeführt.

Im ersten histopathologischen Befund wurden als Differentialdiagnosen ein spindelzelliges Karzinom, ein epitheloides Sarkom und ein malignes Synovialom angeführt. Durch weitere immunhistochemische Untersuchungen konnte schließlich die Diagnose histiozytäres Sarkom gestellt werden. Dieser beim Menschen nur als Rarität vorkommende Tumor hat im fortgeschritten Stadium aufgrund seines schlechten Ansprechens auf Chemo- und Strahlentherapie eine infauste Prognose.

Auch unserem Patienten konnte, aufgrund der ausgeprägten Knochenmarkskarzinose und der konsekutiven Panzytopenie, nur noch eine symptomatische Therapie zur Erhaltung der Lebensqualität angeboten werden. Der Patient verstarb 2 Wochen nach Diagnosestellung.

F03

Lymphoide interstitielle Pneumonie (LIP) bei variablem Immundefektsyndrom (CVID)

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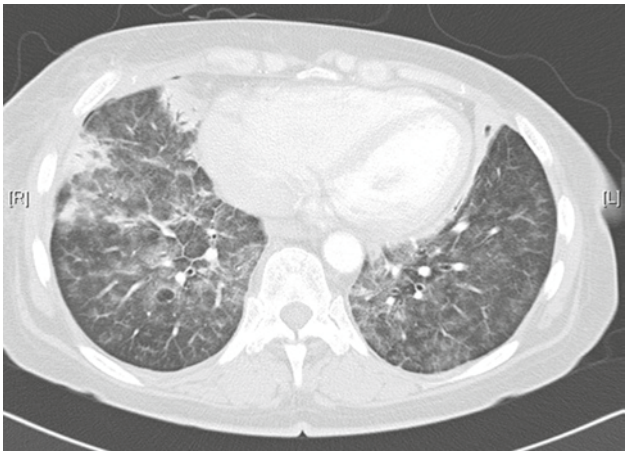
Grundlagen: Lymphoide interstitielle Pneumonie (LIP) ist eine seltene Erkrankung, die meist mit Autoimmunerkrankungen und Dysproteinämien assoziiert ist.

Kasuistik: Im Oktober 2009 wurde bei einer 51-jährigen Frau, die über seit 12 Monaten rezidivierende Fieberattacken klagte, die



Diagnose eines variablen Immundefektsyndroms (CVID) gestellt. In der CT-Thorax fanden sich bilaterale pulmonale Infiltrate und bronchoskopisch eine inflammierte bronchiale Mukosa sowie purulentes Sekret. Die Patientin erhielt Antibiotika, eine Immunglobulin-Substitution und war asymptomatisch bis Jänner 2012, als sie wegen Fieber und Müdigkeit erneut stationär aufgenommen wurde. Im CT-Thorax zeigten sich progrediente Verdichtungen in den basalen Lungenanteilen. Trotz umgehender Therapie mit Breitband-Antibiotika entwickelte die Patienten ein respiratorisches Versagen und benötigte mechanisch Beatmung und letztendlich eine extrakorporale Membranoxygenierung (ECMO). Fünf Tage nach Aufnahme wurde eine chirurgischen Lungenbiopsie durchgeführt. Die Histologie zeigte das Bild einer LIP mit diffuser interstitieller Infiltration von T-Lymphozyten, Plasmazellen und Histiozyten. Unter Therapie mit Prednisolon (1 mg/kg) kam es zu einer raschen klinischen und radiologischen Besserung. Nach 4 Wochen konnte die Patientin entlassen werden und ist seither mit einer Steroid-Erhaltungsdosis von 0,25 mg/kg stabil.

Schlussfolgerungen: Bei bilateralen Milchglas-Verschattungen in Patienten mit CVID sollte an eine LIP gedacht werden. Die chirurgische Lungenbiopsie ist zur Sicherung der Diagnose essentiell. Die Therapie basiert primär auf Kortikosteroiden, auf die diese Patienten exzellent ansprach.

F04

Polyglobulie- Kontrolle an der hämatologischen Ambulanz?

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Kasuistik: Ein 41-jähriger Mann wurde wegen einer auffälligen Polyglobulie (Hb 18,6 g/dl) in unserer Ambulanz vorstellig. 2 Wochen zuvor erlitt er einen Kleinhirninfarkt, er wurde lysiert, im Rahmen der internistischen Durchuntersuchung konnte im TEE ein winziges persistierendes Foramen ovale, ohne Shunt-Hinweis und ohne therapeutische Konsequenz dargestellt werden. Er war neurologisch rasch rehabilitiert, bezüglich der Polyglobulie wurde die Begutachtung an einer hämatologischen Ambulanz empfohlen.

In den Routineuntersuchungen bei uns wurde ein unauffälliges Thoraxröntgen befundet, die ventilatorische Lungenfunktionsprüfung ergab altersentsprechende statische und dynamische Lungenvolumina. Auffällig war jedoch eine ausgeprägte Hypoxämie bei geringer alveolärer Hyperventilation.

Kurzatmig oder in seiner Leistungsfähigkeit eingeschränkt, sei er nie gewesen (durch die kompensatorische Polyglobulie lag der Sauerstoffgehalt des Blutes im Normbereich). Schon als Jugendlicher habe er aber immer wieder „Black-Outs“ und Schwindel bemerkt.

Aufgrund der deutlich eingeschränkten Blutgase wurden differentialdiagnostisch eine Diffusionsstörung und, trotz einer im Wesentlichen unauffälligen Echokardiographie, ein Rechts-Links-Shunt in Erwägung gezogen.

Zur Differenzierung dessen wurde eine Blutgasanalyse unter Atmung von reinem Sauerstoff durchgeführt. Es kam zu einem unzureichenden Anstieg des pO2 (von 58 auf 108 mmHg), somit bestand der hochgradige Verdacht auf einen Rechts-Links-Shunt (RLS).

Die hausinterne Kardiologie empfahl eine MRT des Herzens, ein extrapulmonaler Shunt konnte ausgeschlossen werden (ein ASD oder eine Fehleinmündung der Lungenvenen kamen nicht zur Darstellung), auffällig waren jedoch 2 große, intrapulmonale AV-Malformationen im rechten Unterlappen mit einem resultierenden Shunt, das errechnete Shuntvolumen betrug 22 %.

In einer weiterführend veranlassten neurosonographischen Untersuchung (Bubble-Test) konnte ebenfalls eine Umgehung des Lungenkreislaufes nachgewiesen werden.

Eine der beiden AV-Malformationen konnte von den interventionellen Radiologen embolisiert werden, die zweite war aus technischen Gründen nicht zu okkludieren, weshalb an der Thoraxchirurgie des AKH Wien eine extraanatonmische Segmentresektion des rechten Unterlappens erfolgte.

Nach operativer Sanierung konnte weder funktionell noch in der Bildgebung ein hämodynamisch wirksamer Shunt nachgewisen werden.

Schlussfolgerungen: Bei unserem Patienten führte der RLS einerseits zu paradoxen Embolien, andererseits zu einer ausgeprägten Hypoxämie mit konsekutiver Polyglobulie. Eine unauffällige Echokardiographie schließt einen RLS nicht aus.

F05

Multiple pulmonale Rundherde – der Pathologe hat immer recht?

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Anamnese: Eine 28-jährige Patientin suchte wegen rezidivierender respiratorischer Infekte und trockenem Reizhusten im Jänner 2011 den Hausarzt auf. Im Thoraxröntgen zeigten sich beidseits kleinfleckige Verdichtungen. Bei Verdacht auf atypische Pneumonie wurde eine Therapie mit Moxifloxacin eingeleitet und bei fehlender Besserung eine HR-CT des Thorax veranlasst. Daraufhin wurde die Patientin zur bronchoskopischen Abklärung an unserer Abteilung vorstellig.

CT-Thorax: Vermehrung des lymphatischen Gewebes beidseits. Zentrales atypisches Infiltrat sowie multiple, subpleurale Rundherde mit Betonung der Mittel- und Obergeschoße.

Status und Befunde: Der physikalische Status war altersentsprechend. Ruhe- und Belastungsblutgase sowie Bodyplethysmographie inklusive CO-Diffusion waren unauffällig. Laborchemisch waren sämtliche Routineparameter im Normbereich, sIL-2R und ACE

nicht erhöht, pathologischen Autoantikörper nicht nachweisbar, der Quantiferon-TB-Gold-Test war negativ.

Bronchoskopie: Makroskopisch zeigten sich keine Auffälligkeiten, die mikrobiologischen Befunde, ZN-Färbung und auch PCR auf mykobakterielle DNA erbrachten keinen pathologischen Befund, sodass vom klinischen und radiologischen Bild die Verdachtsdiagnose einer Sarkoidose bestand. Nach Ausschluss einer weiteren Organmitbeteiligung wurde keine Therapie eingeleitet. Überraschenderweise wurden in der Zytologie der BAL säurefeste Stäbchen nachgewiesen und vom Pathologen eindeutig als Tuberkulose interpretiert. Eine antituberkulöse 4-fach Therapie wurde eingeleitet.

Verlauf: Nach 3-monatiger Therapie bestand der trockene Husten weiter, die Infiltrate blieben unverändert. Zwischenzeitlich langte ein negativer TB-Kultur-Befund ein. Die spezifische Therapie wurde abgesetzt. Eine Rebronchoskopie erbrachte hinsichtlich einer Mykobakteriose unauffällige Befunde. Bei regelmäßigen Kontrollen präsentierte sich die Patientin beschwerdefrei und blieb funktionell unauffällig. Im Jänner 2012 erfolgte wegen radiologischer Progredienz eine weitere Abklärung mittels VATS. Die Histologie ergab eine nekrotisierende Sarkoidgranulomatose mit Beteiligung der Pleura visceralis.

Diagnose: Die NSG ist eine seltene Form einer nodulären Sarkoidose mit granulomatöser Vaskulitis und der Besonderheit des Vorhandenseins infarktartiger Nekrosen. Deshalb wurde diese Erkrankung lange Zeit als Mischform einer Sarkoidose und Wegener Granulomatose gesehen. Eine Therapie mit systemischen Glucocorticoiden wird von der Patientin derzeit abgelehnt, es erfolgen engmaschige Kontrollen.

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F06

Aphasie und Cephalea nach Lungentransplantation

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Anamnese: Eine 36-jährige Patientin wurde vom Allgemeinmediziner wegen Pansinusitis unter laufender immunsuppressiver Therapie eingewiesen. Anamnestisch Cephalea seit mehreren Wochen, rezent seit 3 Tagen Sprachstörung, Müdigkeit, Abgeschlagenheit und Fieber. 4/2010 bilaterale Lungentransplantation bei CF im AKH Wien. CMV Status D+/R−. Postoperativ Induktion mit Campath. CFRDM mit laufender Insulintherapie.

Status: Deutlich reduzierter Allgemeinzustand, stark verwaschene Sprache und Wortfindungsstörung, kein Meningismus.

Labor: Mäßiggradig erhöhte Entzündungsparameter.

Thorax-Röntgen: Verschattung im rechten laterobasalen Unterfeld.

Therapie: Empirische Therapie mit Rocephin, Vfend und Cymevene.

Neurologischer Status: Diskrete Dysarthrophonie und Gangataxie.

Mrt Cerebrum: Kein richtungsweisender Befund. Für ein mögliches Posteriores reversibles Encephalopathiesyndrom radiologisch kein Hinweis. Im MRT sichtbar als multiple cortico-subcorticale T2 gewichtete hyperintense Signale occipital und parietal. PRES tritt bei Eklampsie, Hypercalcämie, hypertensiver Krise sowie unter laufender immunsuppressiver Therapie nach Organtransplantation auf.

Liquorpunktion: Zellzahl und Gesamteiweiß waren deutlich erhöht, die Glukose erniedrigt.

Mikrobiologie: Keine CMV Infektion, der Erregernachweis erfolgte mittels Antigennachweis und Kultur aus dem Liquor. Es handelte sich um den hefeähnlichen bekapselten Pilz Cryptococcus neoformans. Die Kryptokokkose ist eine opportunistische Infektion, die bei Patienten mit massiver Immunschwäche auftritt. Die Infektion erfolgt durch Inhalation sporenhaltiger Stäube in die Lunge und anschließender hämatogener Streuung bevorzugt in das ZNS. Eine Kryptokokkose ist für immunsupprimierte Menschen immer lebensbedrohlich und verläuft unbehandelt meist letal. Bei Organtransplantrecipienten tritt in 2,8 % eine Kryptococceninfektion auf. Die mediane Zeit bis zur Erkankung beträgt 21 Monate nach Transplantation.

Therapie: Modifikation auf Ancotil und Ambisome bis in den rezidivierenden Liquorpunktionen kein Erreger mehr nachweisbar war. Eine Konsolidierungsphase mit Diflucan wurde bei Entlassung eingeleitet. Nach etwa 8 Wochen folgte die Erhaltungstherapie. Eine Kryptokokkenmeningoencephalitis war ursächlich für die neurologische Symptomatik, diese besserte sich rasch nach Kombinationstherapie mit Flucytosin und Amphotericin B.

Zwischenzeitlich war die Patientin aufgrund einer Pneumokokkensepsis und akutem Nierenversagen in intensivmedizinischer Behandlung. Bis dato ist die Patientin in ausgezeichnetem Allgemeinzustand ohne Zeichen einer neurologischen Symptomatik.

F07

Better late than never – eine überraschende Erstdiagnose

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Kasuistik: Ein 19-jähriger Mann wurde zur Abklärung einer nativradiologisch diagnostizierten beidseitigen, Oberlappen-betonten reticulo-nodulären Strukturvermehrung bei seit 2 Monaten bestehendem produktiven Husten mit gelblich Auswurf stationär aufgenommen.

Im Status fielen Uhrglasnägel und ein leptosomaler Habitus auf. Anamnestisch erwähnenswert sind rezidivierende Antibiotikaeinnahmen bei wiederkehrenden Halsentzündungen seit der Kindheit. Die Blutgasanalyse bei Raumluft zeigte eine respiratorische Partialinsuffizienz (pO2 v. 65 mmHg).

Das Infektscreening ergab bei negativen Entzündungsparametern eine Sputumbesiedelung mit Pseudomonas aeruginosa. Die Spirometrie erbrachte eine Obstruktion der kleinen Atemwege („small airway disease“).

In der Thorax-Computertomographie konnten beidseitige Oberlappen-betonte Bronchiektasien, zudem deutliche Sekretretention mit Bronchialwandverdickungen sowie ein mikronoduläres zentrilobuläres Verdichtungsmuster gesehen werden.

Nach Antibiogramm-gerechter Therapie mit Piperacillin/Tazobactam sowie einer intensiven Atemphysiotherapie konnte eine Symptombesserung erzielt werden.

Endobronchial bestätigte sich eine chronisch entzündliche Bronchialschleimhaut mit ausgeprägten beidseitigen Bronchiektasien.

Differentialdiagnostisch wurden nun eine primäre Ziliendyskinesie (PCD), aber auch eine Cystische Fibrose (CF) in Erwägung gezogen.

Mittels Elektronenmikroskop konnte eine ziliäre Funktionsstörung ausgeschlossen werden. Zeitgleich wurde mittels hoch-positiven Schweißtest eine CF diagnostiziert, und der Patient an die Erwachsenen-CF-Ambulanz des Krankenhaus Hietzing überwiesen. Die dort veranlasste genetische Untersuchung ergab den am häufigsten (80 %) vorkommenden Genstatus DEL 508 homozygot. Weiters wurde eine exokrine Pankreasinsuffizienz, eine hepatale Steatose sowie extrem niedrige Spiegel aller fettlöslichen Vitamine nachgewiesen. Ein CF-related Diabetes mellitus (CFRDM) sowie eine sekundäre Osteoporose konnten ausgeschlossen werden. Trotz intravenöser pseudomonaswirksamer Kombinationsantibiose in CF-Dosierung gelang keine Eradikation, sodass eine inhalative antibiotische Dauertherapie mit Tobramycin im On/Off-Schema eingeleitet wurde. Zudem erfolgte eine entsprechende Enzym- und Vitaminsubstitution. Bei regelmäßigen Kontrollen konnten gleichermaßen wieder normale Blutgasanalysen, eine normale ventilatorische Leistungsbreite, sowie eine ausgezeichnete subjektive Leistungsfähigkeit erhoben werden.

Schlussfolgerungen: In Österreich wurde das flächendeckende Neugeborenenscreening für CF erst 1997 eingeführt. Zudem wurden rezidivierende respiratorische Infekte vom Kinder- und Hausarzt als alleinige Halsentzündungen verkannt und die mangelnde Gewichtsentwicklung bei wiederkehrenden Diarrhoen nicht entsprechend beachtet. Bei klinischem Verdacht sollte man daher auch im Erwachsenenalter eine entsprechende Abklärung durchführen.

F08

NSTEMI, PE, Alveolitis, Verwirrung – viele Puzzlesteine, hätten Sie es gewusst?

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Ein 1938 geborener männlicher Patient wird aufgrund zunehmender Dyspnoe mit höhergradiger respiratorischen Partialinsuffizienz an unserer pulmologischen Abteilung zur weiteren Diagnostik stationär aufgenommen. In der rezenten Voranamnese des Patienten ist eine KHK mit Sanierung einer LAD-Stenose und postinterventioneller NSTEMI-Symptomatik erhebbar. Weiters wurde eine Pulmonalembolie auswärts diagnostiziert. Aufgrund dieser Ereignisse ist der Patient sowohl mit einer dualen Thrombozytenaggregationshemmung als auch mit Phenprocoumon vorbehandelt. Die dadurch bedingte Gerinnungshemmung macht es unmöglich, eine in der Computertomographie des Thorax suspizierte Alveolitis bioptisch abzuklären.

Es wird aufgrund der ausgeprägten respiratorischen Symptomatik mit Hypoxämie bei einer höhergradigen Diffusionsstörung eine Corticosteroidtherapie verabreicht, worunter es zu einer klinischen und radiologischen Besserung kommt.

Nach zweiwöchigem Intervall wird der Patient jedoch aufgrund einer Verschlechterung des Allgemeinzustandes mit neu aufgetretener neurologischer Symptomatik (Verwirrtheit und Polyurie) wiederaufgenommen. Ein Insultgeschehen kann radiologisch ausgeschlossen werden. Leider kann die progressive Verschlechterung des Allgemeinzustandes nicht aufgehalten werden und der Patient verstirbt. Die pathologische Befundung fügt die Puzzlesteine der multiplen Erkrankungen zusammen.

F09

COPD … oder was sonst?

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Ein 53-jähriger Patient kommt zu uns zur geplanten Bronchoskopie. Bezüglich der Beschwerdesymptomatik bestehen seit 2004 zunehmende Belastungsdyspnoe, wie zum Beispiel beim Stiegensteigen, mit der Erschöpfungsdauer von 1/2 min. Zusätzlich vermehrte Schleimbildung sowie Rasseln im Kehlkopfbereich, stressabhängige Verschlechterung des Hustenreizes tagsüber. Beruflich ist unser Patient als Bauleiter tätig.

Den Alkoholkonsum hatte er bereits vor einigen Jahren völlig eingestellt, Z. n. chronischem Nikotinabusus vom 14.–21. Lebensjahr. Ansonsten besteht gesunde Ernährung bei gleichbleibendem Gewicht.

In der Vorgeschichte sind seit der Kindheit rezidivierende Bronchitiden sowie in den letzten Jahren ein vermehrtes Auftreten von Bronchopneumonien zu erheben.

Die Lungenfunktion zeigt eine hochgradig obstruktive Ventilationsstörung, wie bei COPD III bei einem FEV1 von 1,48 l und einem Sollwert von 3,84 l (38,6 %). Der Tiffeneau-Index liegt bei 46,88 %, deutlicher Knick in der Fluss-Volumen-Kurve.

Im mitgebrachten CT-Thorax zeigt sich eine hochgradige Ausweitung von Trachea und Bronchien mit irregulärer Wandverdickung und einem maximalen Trachealdurchmesser unmittelbar vor der Bifurkation von 5,6 cm mit zystischer Dilatation sämtlicher Bronchien im Ober-, Mittel- und Unterlappen bds., multiplen Bronchiektasien mit Schleimimpaktierung und nachgeschalteter Minderbelüftung. Weiters findet sich ein paraseptal betontes, zum Teil bullöses Lungenemphysem.

In der CO-Diffusion zeigt sich eine Einschränkung auf 62,8 % aufgrund eines Mangels an Sauerstoffaustauschfläche im Rahmen des Lungenemphysems. Histologisch konnte die Erkrankung aufgrund der chronischen Entzündung im Knorpelgewebe nicht bestätigt, jedoch auch nicht ausgeschlossen werden, klinisch und funktionell entspricht die Erkrankung einem klassischen Mounier-Kuhn-Syndrom. Dieses Syndrom ist gekennzeichnet durch eine seltene deformierende Anomalie der Atemwege mit Instabilität der zentralen Bronchialanteile. Die Erkrankung ist nicht heilbar und verläuft progredient.

Da der Patient beruflich sehr belastet ist und während seiner Tätigkeit unterschiedlichsten Infektionsquellen ausgesetzt ist, wurde unsererseits ein Pensionsansuchen gestellt. Die medikamentöse Therapie besteht aus Spiriva 1 × 1, physikalischer Therapie mit dem RS-Cornet. Die Empfehlung zur Pneumokokken- und Influenzaschutzimpfung wurde von unserer Seite ausgesprochen.

F10

Therapieherausforderung im Schlaflabor

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Die Kasuistik berichtet über einen jungen Patienten mit Meningomyelocele und einer resp. Globalinsuffizienz als Grunderkrankung.

Anamnese und Diagnose eines schweren OSAS im Schlaflabor sowie Therapie von CPAP bis BIPAP, mit übergreifender Nachsorge im Schlaflabor und RCU.

F11

Aller guten Dinge sind drei

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Ein 71-jähriger Patient präsentiert sich 2009 an unserer Klinik mit seit mehreren Wochen bestehendem Husten, Fieber, Gewichtsverlust sowie Abgeschlagenheit. Bis auf eine Hyperthyreose sowie ein Glaukom waren keine wesentlichen Vorerkrankungen bekannt. Im CT-Thorax zeigten sich Veränderungen passend zu einer Sarkoidose IV. Eine anschließende Bronchoskopie war inkonklusiv, jedoch wurde, basierend auf den CT-Befund, eine Therapie mit Glukokortikoiden durchgeführt, welche jedoch nicht erfolgreich war.

Eine 2. Biopsie war wieder inkonklusiv, jedoch wurden die Veränderungen hier eher zu einer Tuberkulose als zu einer Sarkoidose passend beschrieben.

Trotz fehlendem TBC-Nachweis wurde ein antituberkulöser Therapieversuch gestartet, welcher ebenfalls nicht erfolgreich war.

Ein weiteres CT-Thorax sowie ein 3. Biopsieversuch mittels VATS konnten schließlich ein MALT-Lymphom der Lunge nachweisen.

Nach entsprechender Chemotherapie konnte eine deutliche Größenregredienz des MALT-Lymphoms nachgewiesen werden sowie ein Sistieren der Symptomatik.

F12

Lungentransplantation bei medikamentös induzierter Lungenfibrose nach Herztransplantation

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Grundlagen: Eine Vielzahl von Medikamenten mit potentiell toxischen Nebenwirkungen auf den Respirationstrakt sind bekannt. Zytotoxische Substanzen wie Methotrexat oder Bleomycin und andere Pharmaka wie Amiodaron oder diverse Antibiotika werden am häufigsten als Ursache für eine medikamentös induzierte interstitielle Lungenerkrankungen genannt.

Kasuistik: Wir berichten den Fall eines 64-jährigen Patienten, der im Oktober 2010 wegen dilatativer Kardiomypathie mit terminaler Herzinsuffizienz eine orthotopen Herztransplantation erhielt. Zu diesem Zeitpunkt bestand radiologisch bereits der Verdacht auf eine Amiodaron-induzierte Lungenfibrose mit funktionell reduzierten Werten: VC 3,49 l (73 %), FEV1 3,28 l (86 %), MEF50 6,52 l (135 %) und TLC 5,88 l (84 %). Der postoperative Verlauf gestaltete sich von kardialer Seite komplikationslos, allerdings war der Patient respiratorisch stark limitiert. Der Weaningprozess gestaltete sich aufgrund einer Lobärpneumonie protrahiert. Auch auf der Normalstation fiel bei geringsten Belastungen die Sauerstoffsättigung auf bis zu 87 %. Die Lungenfunktion 2 Monate nach HTX ergab eine restriktiven Ventilationsstörung mit VC 1,33 l (37,9 %), FEV1 1,29 l (34,3 %), MEF50 3,3 l (71,2 %), TLC 2,76 (39,4 %), PaO2 52,8 % und PaCO2 38,7 %.

Zur Histologiegewinnung wurde nach inkonklusiver Bronchoskopie eine offene Lungenbiopsie durchgeführt, welche das Vorliegen einer Lungenfibrose vom UIP-Typ ergab.

Die Kontroll-Echokardiographien zeigten durchwegs eine gute rechts-und linksventrikuläre Funktion, allerdings verschlechterte sich der respiratorische Zustand des Patienten zunehmend, sodass er „high urgent" zur Lungentransplantation gelistet werden musste. Ein größen- und blutgruppenkompatibles Spenderorgan wurde verfügbar, und eine bilaterale Lungentransplantation mit veno-arterieller ECMO-Unterstützung durchgeführt. Die ECMO konnte am Ende der Operation bei hämodynamisch und respiratorisch stabilen Verhältnissen wieder explantiert werden. Die Ischämiezeit der rechten Lunge betrug 340 min und links 460 min.

Am 19. postoperativen Tag kann der Patient auf die Normalstation verlegt und nach weiteren 23 Tagen aus dem Krankenhaus entlassen werden.

Schlussfolgerungen: Entgegen der allgemeinen Erwartung, dass eine Fibrose unter immunsuppressiver Therapie ein geringes Risiko für Progression hat, zeigte sich in diesem Fall eine dramatische Entwicklung nach der Herztransplantation. Deshalb sollte eine Lungenfibrose vor einer HTX genau abgeklärt werden und engmaschige postoperative Kontrollen durchgeführt werden.

F13

Pulmonale Osteoporose?

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Anamnese: 40-jähriger männlicher Patient mit rezidivierenden Pneumonien vom 4. Lebensmonat bis zum 5. Lebensjahr, wobei als Säugling auch eine Behandlung im Sauerstoffzelt notwendig war. Seither bestehen eine geistige Retardierung und eine leicht progrediente Belastungsdyspnoe, die primär auf Übergewicht zurückgeführt wurde.

2010 wurde er zur Abklärung einer als Zufallsbefund entdeckten unklaren interstitiellen Lungenerkrankung mit entsprechender lungenfunktioneller Pathologie vorstellig. Nach VATS mit Wedge-Resection ergab die Histologie eine „diffuse pulmonale Ossifikation" mit ausgeprägten Anteilen interstitiellen reifen metaplastischen Lamellenknochens, zum Teil mit Verzweigungen, zum Teil mit fettreichem Knochenmark.

Nach Ausschluss einer sekundären Form einer pulmonalen Ossifikation konnten wir letztendlich eine „idiopathische pulmonale Ossifikation" diagnostizieren.

Befunde: CT-Thorax 4/2010: deutliche interstitielle Strukturvermehrung mit Fibrosierung, vergrößerte mediastinale Lymphknoten. CT-Thorax 9/2010: Rezente Pulmonalembolie bds. CT-Thorax 1/2011: kein Hinweis auf Pulmonalembolie. CT-Thorax August 2011: Im Vergleich zu 4/2010 Regredienz der streifig-retikulären Verdichtungen. Lungenfunktionsverlauf bei restriktiver Ventilationsstörung,

Ruhe-/Belastungshypoxämie und Diffusionsstörung: VC von 2,22 auf 2,77 l; FEV 1 von 1,67 auf 2,13 l; TLC von 3,51 auf 4,51 l; DLCO von 44 auf 64 mmol/min/kPA.

Verlauf: Nach Diagnosestellung wurde in Ermangelung klarer Evidenz-basierter Therapieempfehlungen ein Cortisonversuch gestartet. Als Komplikation trat nach Wochen eine Pulmonalembolie bds. mit begleitender schwerer pulmonaler Hypertonie und Hypoxämie auf. Beide Komplikationen bildeten sich vollständig zurück, die Cortisontherapie wurde unter OAK weitergeführt.

In den folgenden Kontrollen kam es zu einer Besserung der Lungenfunktionsparameter (VC max, FEV 1, TLC und DLCO), der Blutgase und auch der CT-Morphologie, wobei sich die Oxygenierung nach Beendigung der sechsmonatigen Aprednisolontherapie jedoch wieder verschlechterte. Seitdem läuft eine Erhaltungstherapie mit 5 mg. Der Patient ist bei stabilen Lungenfunktionsparametern bis auf eine Belastungsdyspnoe ab 75 Watt beschwerdefrei.

Schlussfolgerungen: Bei der diffusen pulmonalen Ossifikation handelt es sich um eine seltene Erkrankung unbekannter Pathogenese mit meist asymptomatischem Verlauf. Es gibt sowohl eine idiopathische – ca. 30 Fallberichte in der Literatur beschrieben – als auch eine sekundäre Form. Bei unserem Patienten führte der Therapieversuch mit systemischem Cortison zu einer deutlichen radiologischen und funktionellen Besserung. Als Komplikation der Therapie ist allerdings eine – vollständig reversible – Pulmonalembolie mit begleitender PH aufgetreten. Eine niedrig dosierte Erhaltungstherapie ist derzeit weiter erforderlich.

F14

Alveolar Duct Smooth Muscle Hyperplasia – Hyperplasie der Alveolargangsmuskulatur

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Kasuistik: Eine adipöse Raucherin, geboren 17.6.1952, präsentiert sich 01/2004 mit einer dichten Oberlappenpneumonie links, IgM-positiver Mykoplasma pneumoniae-Serologie und einer akuten Verschlechterung ihrer COPD mit asthmoider Komponente. Unter antibiotisch-antiobstruktiver Therapie völlige Remission.

Neuerdings Komplettverschattung des linken Oberlappens (LiOL) 06/2009. Zwischenzeitlich Manifestation einer eosinophilen Inflammation ohne Atopie als Pansinusitis. Die Atemfunktion hat sich zwischenzeitlich beträchtlich verschlechtert.

	2004–2009
FEV1	2,580–1,380 L
VC	3,630–2,750 L
FEV1 %VC	71,2–50,4 %
MEF50	2,310–0,770 L/s
Rtot	0,29–0,53 kPa/L/s
TLCO	9,33–5,78 mmol/min/kPa

2005 Gastric banding mit nachfolgender Fettschürzen-OP wegen Gewichtszunahme auf 112 kg (BMI 36,2). Als Langzeitkomplikation kommt es zu einer hernienartigen Ösophagusdilatation mit Retention von Speiseresten und einer Ösophagitis.

Tumorabklärung ohne nachweisbare Metastasierung, aber in einer bronchoskopischen Nadelaspiration aus dem proximal stenosierten linken Unterlappenbronchus Gewinnung einer Zytologie, hoch verdächtig auf ein großzelliges Bronchialkarzinom. Im 17-FDG-PET-CT zeigte der konsolidierte linke Oberlappen eine inhomogene, aber nur gering metabole Aktivität. Im Schädel-MR fand sich bis auf eine chronische Rhino-Sinusitis keine Abnormität.

Nach Optimierung der Atemsituation erfolgte eine LiOL-Komplett- sowie Unterlappen-bronchus-Sleevere-sektion.

Postoperativ traten keine chirurgischen Komplikationen auf, dagegen eine Besserung der Atemfunktion im Sinne einer Volumsreduktion bei COPD. Die Histologie zeigte einen tumorfreien Resektionsrand, jedoch eine ausgeprägte Hyperplasie der glatten Muskulatur der Alveolargänge, die von einer inhomogenen unspezifischen Inflammation durchsetzt war.

Schlussfolgerungen: Das Vorkommen einer Alveolar duct smooth muscle hyperplasia liegt unter 1/1,000.000. Man nimmt als Ätiologie eine reaktive eher als eine neoplastische Proliferation von Fibromyoblasten an. Uns ist kein Zusammenhang mit einer Mykoplasmeninfektion, auch keine Kausalität mit einem chronischen Zigarettenkonsum bekannt. Eine rezidivierende Aspiration bei liegendem Magenband scheint möglich, aber als Ursache unwahrscheinlich, da die LiOL-Konsolidation erstmals 2004 vor dem bariatrischen Eingriff aufgetreten war.

Poster

Die mit * markierten Poster wurden in einem anonymisierten Reviewerverfahren als beste Poster ausgewählt.

P01

Evidence of impaired spontaneous baroreceptor sensitivity in patients with COPD as a potential link to cardiovascular morbidity and mortality*

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Background: Recent studies suggest reduced cardiac filling pressures in patients with COPD due to hyperinflation. A reduction in cardiac preload may result in unloading of baroreceptors. We thus investigated spontaneous baroreceptor sensitivity, an independent predictor of cardiovascular morbidity and mortality, in patients with COPD and controls.

Methods: 33 patients with severe airflow obstruction but free from clinical cardiovascular disease (age 64 ± 7 yrs, BMI 23 ± 4 kg/sqm, FEV1 27 ± 7 %, TLC 140 ± 19 %) and 12 age, gender, and body-weight matched controls without airflow obstruction were studied. Spontaneous baroreceptor activity was measured using the sequence method during resting conditions. The baroreceptor effectiveness index was calculated from the total number of baroreceptor sequences divided by the total number of systolic blood pressure ramps.

Results: The mean slope of spontaneous baroreceptor sequences (7.0 ± 4.7 msec/mmHg vs. 13.5 ± 6.4 msec/mmHg, $p < 0.01$) and the baroreceptor effectiveness index (71 ± 54 vs. 103 ± 34, $p < 0.05$) were significantly lower in patients with COPD than controls. There was a significant inverse relationship between the slope of baroreceptor sensitivity ($r = -0.302$, $p < 0.05$) and baroreceptor effectiveness index ($r = -0.391$, $p < 0.01$) with RV/TLC ratio. There were no such associations with airflow obstruction.

Conclusions: Our findings indicate a link between hyperinflation and baroreceptor function in patients with COPD.

P02

Mortality of COPD exacerbations in Austria – a report from the ERS COPD Audit

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Background: Chronic Obstructive Pulmonary Disease (COPD) is currently the fourth leading cause of death worldwide. Acute COPD exacerbations are known to negatively impact patients' prognosis and mortality. However, no studies are available investigating hospital mortality rate of patients admitted due to acute COPD exacerbations (AECOPD) in Austria.

Objectives: Therefore, the aim of our study was to analyze, besides patients length of hospital stay and 90 days readmission rate, patients hospital mortality rate after admission for acute COPD exacerbation throughout Austria compared to European peers.

Methods: In total 14.996 European and 823 Austrian patients with AECOPD were included in the ERS COPD Audit, a prospective observational study performed in 421 hospitals from 13 European countries. Patients' lung function was analyzed as well as length of stay, 90 days readmission rate, and hospital mortality rate were recorded.

Results: Patients' baseline characteristics with respect to lung function and GOLD stage were comparable between Austrian and European peers. Median length of stay was significantly higher in Austria compared to Europe [11.2 ± 9 days vs. 9.4 ± 9 days, respectively; $p < 0.001$). Hospital readmission rate within 90 days was 40 % in Austria vs. 35 % in Europe $p < 0.05$). Overall mortality rate was 10 % in Austria and 10.8 % in Europe ($p =$ n. s.). Furthermore, hospital mortality rate was similar in Austria and Europe 4.1 and 5.0 %, respectively; $p =$ n. s.) as well as 90 days mortality rate (6.1 % in Austria, 6.2 % in Europe, respectively; $p =$ n. s.). When looking at gender related differences, female overall mortality rate was higher in both, Austria and Europe (10.4 vs.9.7 %; $p =$ n. s. and 12 vs. 10.3 %, respectively; $p < 0.05$) compared to male.

Conclusions: In Austrian COPD exacerbations, length of stay and 90 days hospital re-admission rate was higher compared to European peers. Furthermore, mortality rate is high and gender related differences in mortality rate were observed in both, female Austrian and European patients.

P03

Characteristics and treatment of COPD exacerbations in Austria – a report from the ERS COPD Audit

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Background: Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of morbidity and mortality worldwide and a major burden of resources in healthcare. Exacerbations and co-morbidities contribute to the overall severity in the individual patient. However, evidence is growing that patient care, including (none)-pharmacological treatment of patients admitted to hospital due to an acute COPD exacerbation (AECOPD), varies between different hospitals and may be not consistent with current guidelines.

Objectives: Therefore, the aim of our study was to evaluate patients baseline characteristics as well as (none)-pharmacological treatment at time of hospital admission due to an AECOPD throughout Austria.

Methods: Data from 823 hospitalised patients with AECOPD from 26 Austrian hospitals were analysed from the Austrian ERS COPD Audit, a prospective, observational, multi-centred study. Collected data included: lung function (FEV_1; forced expiratory volume in the first second), GOLD stage, blood gas analyses, smoking status, self-reported co-morbidities as well as applied (none)-pharmacological treatment during admission.

Results: Results of the Austrian ERS COPD Audit on patients' baseline data as well as on recorded (none)-pharmacological treatments are shown in Tab. 1.

Table 1. Patients' characteristics and applied (none)-pharmacological treatment

Patient characteristics ($n=823$)	Median
Age, years	69
Male gender (%)	59
Spirometry available (%)	66
FEV_1, % pred.	40
GOLD stage, %, I, II, III, IV	21, 14, 37, 28
Acidotic pH (<7.35) (%)	13
Smoking status (%)	
Never smoker	14
Former smoker	56
Current smoker	31
Co-morbidities	
Cardiovascular diseases	43
Type II diabetes	24
Applied treatment	
Systemic corticosteroids (%)	87
Antibiotics (%)	54
Theophyllin i.v (%)	41
Non invasive ventilation (%)	10
Invasive ventilation (%)	2

Conclusions: Interestingly, severity of disease was not different with respect to admission frequency. Furthermore, cardiovascular and metabolic co-morbidities are commonly present. Last, when looking at (none)-pharmacological treatment striking differences were found compared to current guidelines.

P04

Efficacy and safety of ciclesonide in the treatment of patients with persistent allergic or non-allergic asthma – results of an Austrian non-interventional study

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Aim: To evaluate the efficacy and safety profile of ciclesonide (CIC) in the treatment of persistent allergic or non-allergic asthma in a real-life setting in Austria.

Methods: 307 patients suffering from persistent asthma of any severity grade (42 % treatment-naive) were enrolled in this non-interventional study (NIS). 50.8 % thereof were female, the mean age was 45.7 years (age range 15–92). After prescription of CIC (most frequently 160 µg/d) patients were observed for 3 months. At study start 85 % were prescribed concomitant medication, primarily short-acting β2-agonists. Efficacy was evaluated by FEV1, Asthma Control

Questionnaire (ACQ), Asthma Quality of Life- (AQLQ[S]), asthma symptoms, physical activity limitations and use of rescue medication.

Results: Mean FEV_1 % increased by 0.3 L from 2.60 ± 0.87 to 2.89 ± 0.86 L, mean FEV_1 % predicted increased from 75.1 ± 15.4 to 83.7 ± 14.9 %. At the end of the observation period, the percentage of patients with daily symptoms had declined from 33.2 % to 3.9 %, nighttime symptoms from 21.8 % to 5.2 %, physical activity limitations from 73.9 % to 24.4 %, and rescue medication usage from 70.0 to 29.3 %. The mean total ACQ score was 2.32 ± 1.14 at baseline and 1.08 ± 0.88 at study end. The number of patients with well-controlled asthma (ACQ-score < 1) increased considerably from 11.0 % to 52.2 %. Accordingly, clinically important mean improvements were observed in the total self-assessed AQLQ(S) score. A low incidence of adverse drug reactions (ADR) was observed (4 ADRs in 3/307 patients).

Conclusions: This NIS in patients with persistent asthma confirmed the efficacy and safety of CIC in routine clinical care showing improvements in symptom control, lung function, and quality of life. CIC was well tolerated in this heterogeneous patient population.

P05

Pulmonary thromboembolism associated with thrombophilia mimicking bronchial asthma – case report

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Background: Submassive pulmonary thromboembolism (PTE) is manifested mostly by respiratory symptomatology occasionally mimicking bronchial asthma, while cardiovascular symptoms are suggesting diagnosis of massive PTE.

Case Report: Patient, 63 years old, was examined at Emergency Center due to unconsciousness. Neurological and endocranial CT examinations excluded disease of central nervous system. ECG showed sinus rhythm, normogram. Due to dyspnoea and suspected exacerbation of asthma, patient was admitted to Clinic for pulmonary diseases. At admission, patient was tachypnoic, with normal breathing sound. Left leg was swollen with varices and few ulcus lesions on lower leg. Blood gas analysis showed normoxemia, hypocapnia and alkalosis (PaO_2 10.3 kPa; $PaCO_2$ 3.9 kPa; pH 7.54). Chest X-ray findings were normal. ECG showed sinus rhythm, turned heart axis to left, negative T3. Value of D-dimer was 478 µg/L (normal level < 160 µg/L). In past, patient was treated as asthma since he was 35 years old. He was hospitalized in age of 62 due to sever exacerbation of asthma. From age of 20, he had recurrent thrombosis of left leg. Though patient was treated as asthma, clinical appearance was pointing out to PTE, so anticoagulant treatment was started. Diagnosis was supported by MSCT- recent bilateral subsegmental PTE was verified. Haemostasis analysis was performed. Antitrombin III was 58 %. Spyrogram revealed normal ventilation and histamine test was negative. Latest MSCT showed no signs of PTE. Patient doesn't have respiratory symptoms any more.

Conclusions: In patients with clinical feature of uncontrolled asthma and history of deep vein thrombosis of lower extremities since youth, it is necessary to think of PTE and thrombophilia.

P06

Socio-demographical, psychological and health related factors regarding smoking habit – results of a questionnaire applied to a romanian population

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Rationale: There are multiple factors interfering with will of smoking and succes of cessation. For better results of counceling we should find out wich are these factors.

Methods: We studied the impact of socio-demographical, psychological and health-related factors on smoking habits of romanian former and active smokers using 2 questionnaires regarding socio-demographic data, motivation, preparation for quitting, health status, determinant factors for tobacco consumption.

Results: 240 persons interviewed: 83 women/157 men, mean age 47 ± 16.2 years; 124 active smokers (53.7 % carry cardiovascular disease-CVD, 42.6 % respiratory disease-RD, 3.7 % both diseases), 116 former smokers (32.9 % CVD, RD 44.3, 22.8 % both). Most of the respondents are belonging to urban (88.3 %), are married (62.9 %), have higher education (41.3 %). From all smokers, 57.2 % are at the stage precontemplation, only 32.2 % are in the preparation and action stage. Comparing smokers with ex-smokers, smoking cessation is defficient in catheogies: women ($p = 0.02$), single persons ($p = 0.0237$), urban habitat ($p = 0.007$), educated persons ($p = 0.015$). Among ill patients, smoking cessation is more frequent on patients with RD then CVD ($p = 0.0038$). Smoking is associated with a rate of 66.6 % with coffee and with alcohol at a rate of 16.6 %. Withdrawal by its own will is invoked by 96.2 % of persons; constipation, weight gain, withdrawal symptoms and stress are the main fears associated with cessation.

Conclusions: All these obtained results will help us to adopt individualised approach for counceling smokers. The actual results of these new strategies will be evaluated in a future study.

P07

Resistant versus controlled hypertension in a population with obstructive sleep apnea syndrome – the need of higher CPAP pressure among patients with resistant HT

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Rationale: RHT is common in obese patients, refractoriness among these patients is frequently caused by OSA. A previous study conducted in our clinic showed that patients with RHT had higher CPAP failure rate.

Method: After exclusion criteria (central/mixed SAS, obesity-hypoventilation/overlap syndrome, obstructive/restrictive respiratory dysfunction, CPAP failure) applied to 214 patients with sleep apnea syndrome and HT, we studied 34 patients with controlled HT and RHT (demographics, anthropometrics, symptoms, comorbidities, sleep study's: Chi test, T-test, Pearson). The 2 groups were similar in terms of smoking habit and antihypertensive treatment.

Results: Controlled HT-27 patients (79.4 %): 19 men (70.4 %), 8 women (29.6 %); RHT – 7 patients (20.6 %): 4 men (57.1 %), 3 women (42.9 %). RHT patients were younger (49.6 ± 8.8 vs 58.4 ± 12.1 years, $p < 0.04$), morbidly obese (45.5 % vs 7.4 %, $p < 0.01$), had higher Epworth score (12.6 ± 5.1 vs 8.6 ± 4.2, $p < 0.005$) and more comorbidities (ischemic heart disease: 33.3 vs 7.6 %, $p < 0.02$, dyslipidemia: 83.3 % vs 28.6 %, $p < 0.02$). Also RHT patients needed higher pressure to correct respiratory events (11.7 ± 1.2 vs 8.9 ± 1.7 cm H_2O), even if they had mild OSA in a higher rate (57.1 vs 22.2 %, $p < 0.05$). There was no linear dependence between BMI and CPAP pressure, variables after CPAP(AHI, minimum SaO_2) and BP values (Pearson, p = n. s.).

Conclusions: After CPAP failure exclusion, patients with OSA and RHT still need higher CPAP values, which does not correlate with obesity. RHT patients will cost more the health system due to their cardiovascular comorbidities, young age and sleepiness. Further studies have to elucidate the need of higher CPAP pressures in RTH patients.

P08

Activation of notch receptors stimulates migration in human neutrophils

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Background: Activation of the Notch pathway is believed to play a key role in the development of the immune system. Recently, Notch was found to confer antigen presenting cell function on mast cells, induce histamine release in human basophils and regulate migration and survival of eosinophils. Additionally, Notch-2 expression was detected in G-CSF-induced granulocytes originating from the 32D murine progenitor cells. These biological functions suggest an involvement in inflammatory processes, also. Until now, nothing is known on the role of Notch activation regarding neutrophil migration and superoxide anion release.

Methods: Human neutrophils were isolated from venous blood of healthy donors after discontinuous density gradient centrifugation on Percoll by dextran sedimentation and hypotonic lysis of contaminating erythrocytes using dextran. Neutrophil chemotaxis was tested using the leading front assay in a modified Boyden microchemotaxis chamber (5 µm pore-sized filters). Respiratory burst activity was detected fluorometrically.

Results: To explore the functionality of Notch in neutrophils, migration towards different concentrations of the Notch ligand Jagged-1 [5 µg/ml to 1 ng/ml] was evaluated. After 25 min cellulose nitrate filters were then dehydrated, fixed and stained and migration depth was analysed by microscopy. Jagged-1 significantly stimulated migration between 5 µg and 10 ng/ml, the maximal effect was observed at 100 ng/ml ($p < 0.0001$). To show specificity of the observed effect, neutrophils were preincubated with the specific gamma secretase inhibitor DAPT [10^{-4} M] which completely abolished the effect of Jagged-1 [100 ng/ml] ($p < 0.01$). Furthermore, Jagged-1 was unable to directly stimulate superoxide anion release. However, preincubation of cells with Jagged-1 further increased superoxide release stimulated by PMA [10^{-6} M].

Conclusions: Herewith, we could show for the first time that the Jagged-1/Notch signalling pathway is affecting human neutrophil functions such as superoxide anion release and cell migration in vitro.

P09

VO_2 equations revised: is the use of assumed oxygen consumption acceptable?

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Background: LaFarge/Miettinen's formula for the assumption of oxygen consumption (VO_2) is one of the most used in hemodynamic calculations. Considering the importance of VO_2 for the calculation of hemodynamics needed for disease evaluation (e.g. pulmonary hypertension), the need for an acceptable agreement between assumed and measured VO_2 becomes obvious. A well known variation of the original formula is the one by Bergstra. In both equations, age, sex and BSA are factors determining the VO_2, plus the heart rate (HR) in the original formula.

We compared directly measured VO_2 with values calculated by both the LaFarge/Miettinen and the Bergstra equations.

Methods and results: VO_2 of 122 volunteers (20–65 y) was directly measured by the Innocor™ (Innovision). VO_2 was then recalculated by both the equations. Directly measured VO_2 (VO_2^{INN}) was 363 ± 84 ml/min in males, 224 ± 52 ml/min in females. VO_2 calculated by Bergstra was 298 ± 24 ml/min in males, and 233 ± 24 ml/min in females. VO_2 by LaFarge/Miettinen was 258 ± 24 ml/min in males, 182 ± 21 ml/min in females. Direct comparison of VO_2^{INN} with calculated VO_2 showed significant differences between all the methods. Factors found to be influencing the VO_2 in our cohort included sex, HR and BSA whereas age seemed to have no effects. Significant correlations were found between VO_2 and hemoglobin, oxygen saturation (SpO_2), fitness level and systolic blood pressure.

Conclusions: Comparison of directly measured VO_2 values with assumed data obtained by both the LaFarge/Miettinen and Bergstra equations showed that none of the formula is satisfying in terms of agreement with measured data. Based on this result we assume that the use of the mentioned oxygen consumption equations may result in major bias of hemodynamic parameters and we urge that resulting data should therefore be interpreted critically.

P10

Carboxyhemoglobin levels in medical intensive care patients: a retrospective, observational study

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Introduction: Critical illness leads to increased endogenous production of carbon monoxide (CO) due to the induction of the stress-response enzyme, heme oxygenase-1 (HO-1). There is evidence for the cytoprotective and anti-inflammatory effects of CO based on animal studies. In critically ill patients after cardiothoracic surgery, low minimum and high maximum carboxyhemoglobin (COHb) levels were shown to be associated with increased mortality, which suggests that there is an ‚optimal range' for HO-1 activity. Our study aimed to test whether this relationship between COHb and outcome exists in non-surgical ICU patients.

Methods: We conducted a retrospective, observational study in a medical ICU at a university hospital in Vienna, Austria involving 868 critically ill patients. No interventions were undertaken. Arterial COHb was measured on admission and during the course of treatment in the ICU. The association between arterial COHb levels and ICU mortality was evaluated using bivariate tests and a logistic regression model.

Results: Minimum COHb levels were slightly lower in non-survivors compared to survivors (0.9 %, 0.7 to 1.2 % versus 1.2 %, 0.9 to 1.5 %; $P=0.0001$), and the average COHb levels were marginally lower in non-survivors compared to survivors (1.5 %, 1.2 to 1.8 % versus 1.6 %, 1.4 to 1.9 %, $P=0.003$). The multivariate logistic regression analysis revealed that the association between a low minimum COHb level and increased mortality was independent of the severity of illness and the type of organ failure.

Conclusions: Critically ill patients surviving the admission to a medical ICU had slightly higher minimum and marginally higher average COHb levels when compared to non-survivors. Even though the observed differences are statistically significant, the minute margins would not qualify COHb as a predictive marker for ICU mortality.

P11

Long term follow-up of patients treated with endobronchial one-way valves for persistent bronchopleural fistulas

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Rationale: Patients with bronchopleural fistulas (BPF) are at an increased risk of morbidity and mortality. Endoscopic one-way valve implantation may be a minimally invasive treatment alternative for patients with BPF.

Objectives: To assess efficacy and long term follow-up associated with valve therapy for BPF.

Methods: 18 patients with persistent (>7days) post-surgical or spontaneous peripheral bronchopleural fistula and continuous air leakage were studied. Endoscopic balloon occlusion technique together with real-time air leakage flow using digital chest tube monitoring were used to identify the source of BPF and predict the response to treatment. Endobronchial (Pulmonx) or intrabronchial (Spiration) one-way valves were implanted at the segmental or subsegmental level as appropriate.

Results: The source of BPF was endoscopically identified in 13 patients who underwent valve therapy within the same session. Air leakage flow was reduced from 870 ± 551 to 76 ± 69 ml/min after valve implantation. There were no periprocedural complications. Mean duration of chest tube drainage was 20 ± 8 days before and 8 ± 5 days after valve treatment ($p<0.01$). 10 patients (76 %) were considered responders with no requirement for further treatment. Patients who did not qualify for valve treatment ($n=5$) underwent surgical treatment or long-term chest tube drainage with a significantly longer hospital stay compared with valved patients ($p<0.05$). There were no late complications in valve treated patients with a mean follow-up of 6 months.

Conclusions: The implantation of endobronchial one-way valves may be a valuabe treatment option in selected patients with BPF.

P12

Target lobar volume reduction and COPD outcome measures after endobronchial one-way valve (EBV) therapy*

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Background: We hypothesized that lobar volume reduction associated with EBV therapy may be linked to improved integrated health outcome measures, such as the BODE index, in the emphysematous type of COPD.

Methods: Data from 416 patients (62 % male, age 63 ± 7 yrs, body-mass-index 24 ± 4 kg/m^2) with advanced emphysema and hyperinflation, who were randomized to EBV ($n=284$) or conservative therapy ($n=132$) were analyzed. Pulmonary function, exercise capacity, dyspnea scores, and CT analysis of lobar volume reduction of the treated lobe were assessed before and 6 months after EBV therapy.

Results: Of patients randomized to the treatment group, 49 (17 %) showed >50 % target lobar volume reduction, 57 (20 %) demonstrated TLVR between 20 and 50 %, and 178 patients (63 %) <20 % TLVR at 6 months post intervention ($p<0.01$). Patients with TLVR >50 % demonstrated greater improvements in lung function parameters, exercise capacity (6-MWT), quality of life (SGRQ) and dyspnea score (mMRC). Consequently, delta BODE index at 6 months was significantly ($p<0.001$) higher in patients with TLVR >50 % (delta BODE 1.4 ± 1.8) compared with the other groups (delta BODE 0.2 ± 1.3, and 0.1 ± 1.3 points in patients with <50 % TLVR >20 %, and TLVR <20 %, respectively). Logistic regression analysis identified target lobar volume reduction as the strongest independent predictor of improved BODE index scores from baseline to 6 months.

Conclusions: The extent of lobar volume reduction predicts improvement in BODE index and health outcomes associated with bronchoscopic lung volume reduction using one-way valves.

P13

Phenotypical characterization of circulating endothelial progenitor cells in pulmonary hypertension

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Background: The role of circulating endothelial progenitor cells (EPCs) in pulmonary hypertension (PH) patients is unknown. In this pilot study we established a nine-colour staining assay for the Fluorescent Activated Cell Sorting (FACS) to characterize the circulating EPCs in PH patients as compared to healthy controls.

Methods: Peripheral and central venous blood was taken from PH patients and healthy controls. Mononuclear blood cells were isolated by means of density gradient centrifugation. The cells were simultaneously stained with fluorescent conjugated antibodies against the cell surface markers c-kit, CXCR2, VEGFR2, CD34, CD14, CD31, CD133, CD16, and CD45. EPCs were defined as CD34+ CD133+ VEGFR2+ cells. Appropriate isotype controls were used to set the specific gates.

Results: $N = 10$ PH patients ($n = 4$ idiopathic, $n = 3$ chronic thromboembolic, $n = 3$ left heart disease), mean pulmonary artery pressure: 42 ± 14 mmHg, pulmonary vascular resistance: 539 ± 290 dyn·s/cm^5) and $n = 10$ healthy controls were included. No spectral overlap occurred during the nine-colour staining assessment. Fixation neither affected the cell count nor the fluorescence intensities of conjugates. Circulating EPCs counted from peripheral and central blood revealed no significant differences. All cells were CD45+, suggesting their hematopoietic origin. CD34+ cells were significantly decreased in PH patients as compared to controls (0.3 vs. 1.8 % of the mononuclear gate, $p < 0.005$). EPCs were significantly lower in PH patients vs. control (2 vs. 44 % of CD34+ CD133+ cells, $p < 0.0001$).

Conclusions: These preliminary results suggest that multi-colour FACS is suitable for EPC quantification and characterization. Further studies are necessary to define distinct circulating EPCs as markers of PH.

P14

Implementing a respiratory care unit (RCU) in a major general hospital: the first year in review

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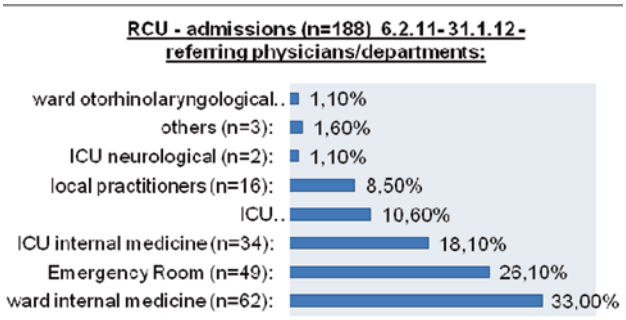
Background: Respiratory care units (RCUs) mostly provide an intermediate level of care between the intensive care unit (ICU) and the general ward for patients with single organ respiratory failure. The advantages of RCUs are linked to economic reasons and to better utilisation of the ICU. In February 2011 a 4-bed RCU was opened at the respiratory medicine department of the University Hospital Graz.

Objectives: To assess characteristics, weaning success, outcome of admitted patients and resources gained for ICUs.

Methods: The data of patients admitted to RCU between Feb 11 und Jan 12 were retrospectively analysed.

Results: In the aforementioned period our RCU had 188 admissions. The reasons for admission were acute respiratory failure (56.9 %), chronic respiratory failure (19.1 %), prolonged weaning (13.3 %) and monitoring/NIV after bronchoscopy (10.6 %).



We mainly received patients from our internal medicine ward (33 %), ICUs (29.8 %) and the emergency room (26.1 %). The mean length of stay in the RCU was 6.6 days. RCU mortality was 3.7 %. 20 patients (80 %) were successfully weaned (mean duration 8.8 days). The RCU had a capacity utilization of 84.6 %. In total 1172 patient days could be gained for ICUs.

Conclusions: In its first year our RCU was successfully implemented in the hospital. Mortality was low and resources for ICUs were gained.

P15

RENEWING HEALTH – Telemonitoring of COPD (REgioNs of Europe WorkING Together for HEALTH)

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Background: Telemonitoring with feedback to the attending physicians and hospital is a modern method of treatment and prevention COPD exacerbations. This has not been evaluated systemically yet. Effectivity, safety and cost effectiveness in patients with COPD – Gold class III and IV should be evaluated.

Methods: Granted by an EU project (Grant EU 250487) for telemonitoring and prevention of COPD and diabetes, patients with COPD (Gold class III and IV) are included in a multicenter, randomized pilot-study trial for implementation of a lifelong telemonitoring system. The patients are included in different monitoring protocols in several european clusters. The Austrian patients are randomized to the intervention versus control group by 2:1. 300 patients in Austria were planned to be included.

Endpoints: Rate of hospitalisation, mortality, quality of life SF-36 and CAT, parameters of economical and IT outcome.

Intervention: Patients with COPD III and IV are randomized into 3 groups:

1. Web-based CAT-questionnaire/online-approach
2. automatically CAT-questionnaire/callcenter
3. online data transfer within the home nursing system

There is a daily evaluation of the CAT questionnaire and an automatically daily analysis. An alarming cut off level for CAT-questionnaire was defined by >8 points. Exceedance of this value is transmitted automatically to the attending physicians. Collected and calculated data are loaded into the hospital IT system every 30 days. Observational phase is one year after randomization. Study inclusion was closed by April 2012. An extension program for the patients is planned.

Preliminary results: In the 3 Austrians centers (Landeskrankenhaus Klagenfurt, Laas und Villach) 66 patients has been included finally. 13 were randomized in the web-portal-group, 27 call-center-group and none in the nurse-associated-monitoring-group. Meanwhile 4 patients have droped out already. 27 are providing the data daily.

The possibility of telemonitoring shows a high level of acceptance in the intervention group. We can present final results after one year period in March/April 2013.

P16

Neutrophil extracellular traps (NET's) formation in chronic obstructive pulmonary disease (COPD) airways inflammation

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Background: Chronic obstructive pulmonary disease (COPD) is an airway disease which is characterized by persistent and progressive airway inflammation and tissue infiltration of neutrophils. Persistent chronic inflammation together with the infiltration of neutrophils and bacterial challenge has been repeatedly shown to involve neutrophile extracellular trap formation (NET's).

Aims: The aim of this pilot study is to examine the formation of NETs in patients with chronic obstructive pulmonary disease and healthy smokers.

Study population, materials and methods: We examined the induced sputa of 14 outpatients, 14 hospitalized patients. The control group consists of healthy smokers. Sputum induction is performed according to the protocol of the ECLIPSE study.

Preeliminary-results: NET's are present in the majority of patients with COPD, whereas we couldn't find any NETs in smokers without pulmonary obstruction.

Conclusions: NET's are present in patients with COPD suggesting there is marked difference between inflammatory processes in COPD and healthy airways.

P17

Staging accuracy and 1 year follow up of surgical lung cancer treatment in Krems

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Background: This observation study should estimate the quality of staging and surgical treatment of lung cancer in our hospital.

Methods: Between March 2011–June 2011 we diagnosed 19 patients with lung cancer appropriate to surgical treatment. The staging was made with an usual diagnostic algorithm. In this study we compared the expected stage of disease with the pathological results after the surgical treatment. We used a questioner to analyse the 1 year follow up of this patients group.

Results: PET scan was used on 84 % of the cases. With the usual diagnostic algorithm we managed to find the preoperative diagnosis in 74 % of the patients. The histological diagnosis was accurate in 92 %, T and N descriptor were correct in 84 and 68 %.

Based on the postoperative pathological study we had to choose another treatment approach instead of the surgical treatment in only 1 case (5 %) – neoadjuvant chemotherapy in Stadium IIIB.

We found no perioprative mortality. One year after surgery there was a metastatic disease in 1 patient (5.26 %), this patient died despite radiotherapy. We estimated 5.26 % mortality in the first year after treatment. Most of the patients complained from pains and shortness of breath for a long time after the surgical treatment.

Conclusions: Using the common diagnostic algorithm with a PET scan showed a satisfactory staging of lung cancer before surgery. The postsurgical care of patients could be improved. The follow up is done continuously.

P18

EML4-ALK mutation in Austrian patients with NSCLC: a multicentre study

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Background: EML4 (echinoderm microtubule-associated protein-like 4) – ALK (anaplastic lymphoma kinase) fusion-type tyrosine kinase, an oncoprotein found in a subgroup of non-small-cell lung cancer (NSCLC) predicts the response to ALK inhibitors (e.g. Crizotinib®). In general, AML4-ALK mutation is found in 2–7 % of Caucasian patients with NSCLC and occurs more often in never and former smokers, adenocarcinomas, and younger, male patients (1). However, the frequency of EML4-ALK mutation in Austrian patients with NSCLC is unknown.

Aim: To evaluate the prevalence of EML4-ALK mutation in Austrian patients with NSCLC.

Methods: From September 2011 to March 2012 tumor tissue from bronchoscopy, CT- and ultrasound guided biopsies and surgical specimen with histological type of adenocarcinoma and NSCLC NOS (Not Otherwise Specified) excluding squamous cell carcinoma, large cell carcinoma and neuroendocrine carcinoma were analysed for EML4-ALK mutations from 4 hospitals in Austria with high expertise in the management of lung cancer. Mutation detection was performed with a two-step procedure. First an immunhistochemical staining was done (ALK confirm/Ventana®) and further on positive cases were tested by ALK FISH (dual colour breakapart FISH/Abbott Vysis®).

Results: In total 293 patients were analysed. EML4-ALK positive immunohistochemical staining was found in 15 patients (5.12 %). 9 of these patients (3.07 %) showed positive ALK FISH analysis.

Conclusions: Frequency of EML-ALK mutations in Austrian patients with NSCLC was similar to other Caucasian peers.

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P19

Recent trends in inhalation of antibiotics in cystic fibrosis patients

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Background: Cystic fibrosis (CF) causes recurrent and chronic pulmonary infections by various bacterial strains, in particular Pseudomonas aeruginosa. Treatment and prevention of these is based on antibiotics administered intravenously and by the inhaled route. Inhalation has the advantage of high local drug doses. Prerequisites are adequate delivery by inhalation devices resulting in sufficient pulmonary deposition and usability of the compound for inhalation (e. g. sufficient stability, no local toxicity). We performed a literature review on studies on inhalation of antibiotics.

Methods: Studies on inhalation of antibiotics in CF patients were analysed focusing on recent publications.

Results: Initial studies on inhalation of antibiotics were published more than 30 years and controlled studies were performed in the USA about 20 years ago. Typically, drugs were approved for oral or intravenous administration. In most studies tobramycin solution was administered by means of different nebulisers. Accordingly, required doses, volumes and number of daily inhalations differ strongly. Recently, a tobramycin dry powder inhaler (DPI) has been introduced in the market. Publications on colistin frequently describe nebulisation of liquids. However, a dry powder version has recently been approved. Administration of aztreonam solution by means of different nebulisers is also approved. Additionally, there are phase 2 and 3 studies on inhalation of levofloxacin (liquid), fosfomycin/tobramycin (liquid), amikacin (liposomes in fluid) and ciprofloxacin (aqueous liposomes, DPI). Other studies investigated e. g. gentamicin, doripenem, gallium compounds, lactoferrin and antimicrobial peptides.

Conclusions: Inhalation of antibiotics in CF patients is of increasing interest. Frequently treatment is based on distinct combinations of drug and nebuliser. Some methods are based on powder aerosols and DPI. Modern methods are characterised by shorter inhalation times and lower required doses and therefore improved usability. In consequence modern methods for inhalation of antibiotics may further improve life expectancy and quality of life of CF patients.

P20

Relevance of exhaled nitric oxide (eNO) in patients with chronic liver disease

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Background: For almost two decades it has been recognized that nitric oxide (NO) appears in the exhaled breath and several studies suggested that exhalatory NO (eNO) is associated with severity of cirrhosis. However, measurement of eNO was not standardized in these studies. Recently, assessment was standardized by the ATS/ERS recommendations (1), and there is a lack of data investigating eNO in patients with chronic liver disease according to these guidelines.

Aims: Aim of the study was to investigate the relation between eNO and severity of liver disease in patients with chronic liver disease and cirrhosis.

Methods: eNO was measured in 37 patients with chronic liver disease (20 with cirrhosis and 17 with chronic viral hepatitis METAVIR score F1–3) and related with respect to presence and absence of liver cirrhosis and severity of cirrhosis according to Child Pugh Score (CTP). Measurement of eNO was performed using a chemiluminescence analyzer (NO VARIO-Analysator by FILT, Germany).

Results: eNO was significantly increased in patients with cirrhosis (9.9 ppb ± 3) in contrast to patients with chronic viral hepatitis but without cirrhosis (8.1 ppb ± 2.7, $p \leq 0.05$). eNO did not differ significantly in different non cirrhotic fibrosis stages. Furthermore patients with mild liver disease (CTP A) had a significant lower level of eNO (9 ppb ± 2.8) than patients with advanced liver disease (CTP B and C) (15.1 ppb ± 6, $p \leq 0.05$).

Conclusions: eNO is significantly elevated in patients with cirrhosis in comparison to patients with chronic viral hepatitis without liver cirrhosis. Furthermore, eNO is higher in patients with advanced stages of cirrhosis.

Reference

1. ATS/ERS recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide, 2005. Am J Respir Crit Care Med. 2005;171:912–30.

P21

Osteoporosis in COPD patients

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Chronic obstructive pulmonary disease (COPD) is a complex disease with cough and dyspnea as initial symptoms. Several other symptoms may develop with disease progression and a lot of patients have comorbid diseases. In addition osteoporosis might develop as comorbid disease possibly due to systemic inflammation, smoking, lower body weight and impaired mobility. Unfortunately, osteoporosis is often undiagnosed in these patients although it may impair respiratory function, especially if the patient experiences vertebral compression and loss of height.

The aim of our study was to investigate the prevalence of osteoporosis and osteopoenia in symptomatic COPD patients. Twenty four outpatients from the respiratory unit with stable COPD were included (8 males and 16 females, mean age 66.6 years). No other cause of osteoporosis was present. All participants had sufficient daily intake of calcium and Vitamin D. Mean postbronchodilator forced expiratory volume in first second (FEV_1) was 47.8 % (2 patients in GOLD I stage, 8 patients in GOLD II stage, 11 patients in GOLD III stage, 3 patients in

GOLD IV stage). Bone mineral density (BMD) of lumbar spine and hip were measured with densitometer Hologic Discovery. The BMD was decreased in 20 patients (83 %), osteoporosis in 14 (58 %) patients, osteopenia in 6 (25 %), the thoracic vertebral compressive fracture was suspicious in 1 patient without symptoms related to fracture and X-ray revealed later.

Thus 83 % of the participants had osteoporosis or osteopenia but glucocorticoid use alone could not explain the increased prevalence of osteoporosis. The treatment for osteoporosis was indicated for a majority of these COPD patients in order to prevent further bone loss and to reduce future risk of osteoporotic fractures.

According to our results, it is necessary to screen osteoporosis in COPD patients and to find the individual risk for fracture and to initiate the prophylaxis or treatment for the osteoporosis.

P22

Inspiratory flow – decision criterion for the device? Switching from DPI to an extrafine pMDI causes changes in asthma control and reliever usage

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Background: The choice of the inhalation device influences lung deposition and asthma control in the treatment of asthma. Individual inspiratory flow limits the selection within the device-systems.

Methods: A prospective, multicenter, non-interventional study (NIS) was conducted in pulmonary and general practices all over Austria in 2011. Asthmatics treated with a pMDI fixcombination of extrafine 100 µg beclomethasone and 6 µg formoterol were monitored over twelve weeks regarding asthma control, symptom scores and tolerability. In the screening phase inspiratory flow was measured and a patient-check was performed to determine asthma control status. Pulmonary function, the number of asthma attacks as well as the severity of asthma symptoms and exacerbations were assessed.

Results: 213 patients (mean age 49 years, 51 % female) were analyzed. Asthma control and pulmonary function (PEF, FEV_1 and FVC) could be significantly improved while the exacerbation rate was significantly decreased. At baseline 67.8 % of patients switched from DPI to extrafine pMDI ($n=87$) showed an inspiratory flow below 60 l/min. In this subgroup a significant improvement towards well controlled asthma was observed in 72.4 % (vs. 2.3 % at baseline). Usage of reliever medication more than twice a week could be diminished from 79.3 to 17.2 % after twelve weeks of treatment with BDP/F extrafine. Additionally, the rate of weekly exacerbations in this subgroup significantly decreased from 14.9 to below 1 %. In the group of frequent exacerbators after receiving the study medication the rate of uncontrolled asthma could be significantly reduced to 8.3 % during the study. No adverse effects were reported.

Conclusions: The results of this NIS show that the pMDI extrafine BDP/F fixcombination enhances effectively patients' asthma control by decreasing asthma symptoms, reliever usage as well as exacerbations and it improves lung function parameters and patient reported outcomes. Patients with an inspiratory flow below 60 l/min may particularly benefit from this pMDI extrafine therapy.

P23

The influence of external resistors on airway resistance and FRC (the "resistance loop")

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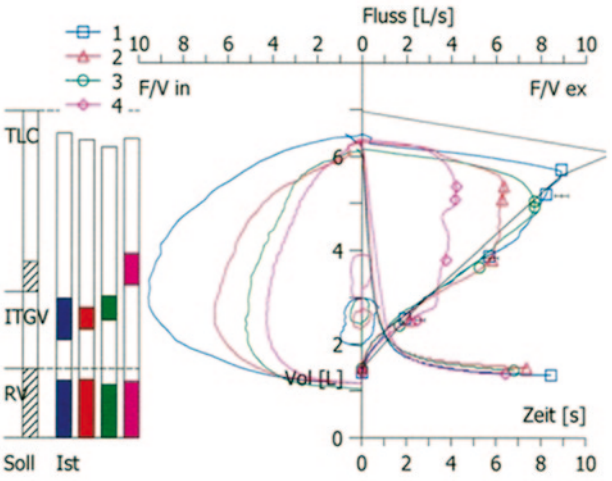
Background: External resistors impact differently on maximal inspiratory and expiratory flows due to diverging physiological mechanisms. We extended our studies exploring the influence of external resistors on intrathoracic gas volume (ITGV = FRC) and measurements of resistance®.

Methods: A Jaeger bodyplethysmograph and spirometry unit was used. Calibrated Hans Rudolph resistors of 0.3, 0.5, and 0,8 (series I) and 0.5, 1.0, and 2.0 kPa/L/s (series II) were interposed between mouth and pneumotachograph. 9 healthy individuals (4 F, 5M – age M ± 2 SD 33.9 ± 25.3 years) performed two series of resistance and ITGV-tests.



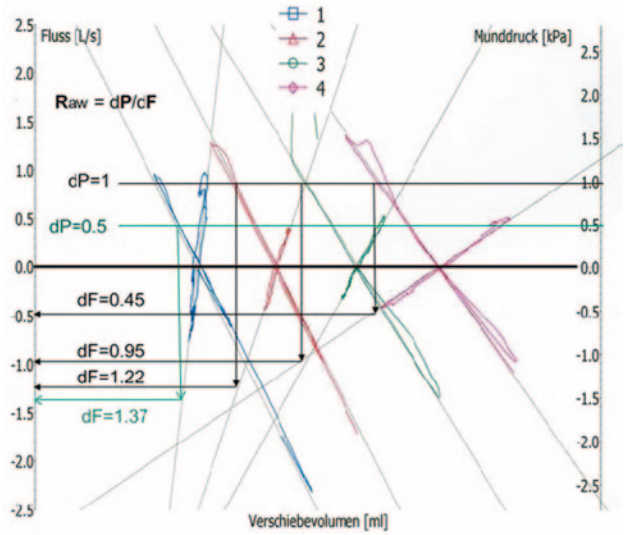
Impingement occurs on large airways first (the effect of **R**external 0.5, 1.0 and 2.0 kPa/L/s is shown in one subject aged 23)

Results: Applying external resistors, the means for **R**tot, **R**eff, **R**in and **R**ex are presented:

Rexternal	0.00	0.30	0.50	0.80	1.00	2.00
Rtot	0.162	0.398	0.561	0.753	0.984	1.898
Reff	0.114	0.341	0.514	0.710	0.942	1.847
Rin	0.138	0.383	0.463	0.688	0.924	1.692
Rex	0.167	0.436	0.602	0.821	1.072	1.957
*Rtot*expected	0.162	0.462	0.662	0.962	1.162	2.162

All **resistances** fall short to match Rexpected indicating a progressive drop of internal airway resistance and dilation of central airways. Given bronchodilation occurs, air velocity will drop potentially impairing cough. The alternative explanation might be an underestimation of dP and R.

FRC-ITGV measurements revealed a slight, but significant increase: ITGV%ref = 7.9519 × Rext + 105.3 with $r^2 = 0.8783$ – resembling either mild hyperinflation or an overestimation by the bodybox.



Not only do flow-volume-loops (unit = 1/time) turn clockwise with external resistances added, but also does the slope dP/dV ≈ 1/ITGV decrease indicating a gain in FRC. Raw (dP/dF) rises with flow limitation. Thus the specific resistance Raw × ITGV = time increases even more meaning that filling and empting of the lungs takes longer.

Conclusions: The unexpected rise of FRC contradicts the intention of deflation by PEP-devices. By calculation the internal resistance drops with external resistance added either causing bronchodilation and reduction of air velocity or underestimation of pressures (dP) with bodyplethysmography, resulting in an overestimation of FRC (≈ dV/dP).

In the graph above airway resistance can be deduced directly from the ratio dP/dF – either at dP = 1 or dP = 0.5 kPa. There congruent scaling of mouth pressure and flow becomes essential.

P24

The interpretation and clinical relevance of heart rate increase during the six-minute walk test in pulmonary hypertension

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Background: Six-minute walk test (6MWT) is an acknowledged prognostic marker in pulmonary hypertension (PH) and has been used as primary end-point in several clinical studies. It may be hypothesized that a clinical improvement may not only be characterized by an increased walking distance but also by changes in the Borg dyspnea score (BDS) and heart rate.

Methods: Patients with PH and subjects without PH but with abnormal exercise-induced pulmonary pressure increase were included. Each patient performed a regular 6MWT with „normal" effort, a test with „less than normal" effort, and a test with „more than normal" effort.

Results: 23 patients with PH ($n = 11$ pulmonary arterial hypertension, $n = 10$ chronic thromboembolic PH, $n = 2$ other PH; mean pulmonary arterial pressure [PAP]: 40 ± 12 mmHg) and 6 subjects with abnormal exercise-induced pulmonary pressure increase (resting mean PAP: 16 ± 4 mmHg) participated in the study. 6MWT were 482 ± 98, 447 ± 80 and 402 ± 82 m in the walks with „more than normal", „normal" and „less than normal" effort (472 ± 104 vs 437 ± 84 vs 392 ± 84 m in PH patients). The respective BDS and heart rate increase was 3.2 ± 1.5, 2.0 ± 1.2 and 0.7 ± 0.9, and 38 ± 16, 31 ± 14 and 23 ± 14 min^{-1} (3.0 ± 1.4, 2.0 ± 1.3 and 0.8 ± 0.9, and 40 ± 16 vs 34 ± 13 vs 23 ± 15 min^{-1} in PH patients). The difference in walk distance between the „less than normal" and the „more than normal" tests was associated with the difference in heart rate increase during the test ($p = 0.001$, $r = 0.61$ in all subjects; $p < 0.001$, $r = 0.76$ in PH patients). On average, an 80 m increase in 6MWT was associated with an additional 15 min^{-1} heart rate increase. Interestingly, between the BDS and 6MWT there was no significant correlation.

Conclusions: According to our pilot study, heart rate may be suitable to assess the effort level of subjects and may be incorporated to improve the accuracy of 6MWT in the follow-up of PH patients.

P25

Routine non-invasive parameters in the practical diagnostic work-up of patients with risk for pulmonary hypertension

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Background: Pulmonary hypertension (PH) is diagnosed by right heart catheterization while Doppler Echocardiography is widely accepted as the most specific non-invasive screening tool. The role of other routine measures in the diagnostic work-up of patients has not been clearly defined. We hypothesized that a diagnostic algorithm using a combination of simple non-invasive parameters might help to identify patients with PH.

Methods: We retrospectively analyzed all patients who received a right heart catheterization and a routine non-invasive assessment including ECG, blood gas analysis, pulmonary function tests, laboratory tests and six-minute walk test in our department between 2005 and 2010. The pretest probability for PH was about 50 %. In the first step, the ratio of the S and R waves in lead I of the ECG were determined; a value ≥ 1 (≥ 90°) was considered as right axis deviation (RAD). In a second step, further non-invasive parameters were analyzed by logistic regression for their association with PH. The investigator was blinded to the right heart catheterization results.

Results: We included $n = 395$ patients in this study. RAD was present in $n = 87$ of these patients. Within these, PH was detected in $n = 82$ patients, and was missing in $n = 5$ subjects, revealing a positive predictive value of 94 %. In the remaining $n = 308$ patients, we identified $n = 60$ patients with a combination of NT-proBNP < 393 pg/ml, DlCOcSB > 65 %, arterial $SO_2 \geq 95$ % and Borg dyspnoe score < 3 at the end of the six-minute walk test, of which only $n = 4$ suffered from PH revealing a negative predictive value of 93 %.

Conclusions: Our retrospective analysis on a relatively large, heterogenous cohort of subjects including patients with and without PH suggests that the combination of simple, non-invasive parameters allows a reliable identification of subjects both with a very high and with very low probability of PH, allowing diagnostic decisions on a more solid basis. The suggested method should be further validated in prospective, population based studies.

P26

Is spirometry properly used to diagnose COPD? Results from the population-based BOLD study in Salzburg, Austria

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Background: Current guidelines reccommend post-bronchodilator spirometry to confirm a diagnosis of COPD. We investigated whether a self-reported diagnosis of COPD was associated with prior spirometry and, whether a correct diagnosis of COPD was more likely when spirometry was reported.

Methods: We used data from the population-based Austrian Burden of Obstructive Lung Disease (BOLD) study. Participants were aged >40 years, and completed the BOLD questionnaire and post-bronchodilator spirometry.

Reported COPD diagnosis and reported prior lung function test were based on questionnaire. Non-reversible airways obstruction (AO) was defined as post-bronchodilator FEV1/FVC <0.7, corresponding with COPD GOLD stage I+, and GOLD stage II+ was also investigated.

A correct diagnosis of COPD was defined, when subjects reported a prior COPD diagnosis and demonstrated non-reversible airways obstruction on post-bronchodilator spirometry.

Results: 68 (5.4 %) of 1258 participants reported a prior physician's diagnosis of COPD. Among those only 25.0 % (17/68) reported a lung function test within the past 12 months, and 67.6 % (46/68) at any time in the past. The likelihood for a correct COPD GOLD stage I+ diagnosis was similar among subjects reporting (likelihood ratio 2.07 [95 % CI; 0.89–5.50 C.I.]) and subjects not reporting (likelihood ratio 2.78 [95 % CI; 1.58–4.87]) a lung function during the last 12 months. Similar likelihood ratios were seen when GOLD stage II+ was investigated and, when lung function was reported at any time in the past.

Conclusions: One third of subjects with a reported diagnosis of COPD never had a lung function test. When spirometry was reported, this did not increase the likelihood for a correct COPD diagnosis.

P27

Indirect costs of non-malignant respiratory diseases caused by smoking in Poland

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Background: Smoking is a large socioeconomic problem in Poland causing direct costs due to treatment of tobacco-induced diseases and indirect costs due to loss of productivity. In this study we calculated annual indirect costs caused by smoking-induced non-malignant respiratory diseases in Poland.

Methods: Calculations were made for both genders (M/F) based on population data according the human capital method considering loss of productivity until reaching statutory retirement age and gross income. Costs of premature mortality due to non-malignant respiratory diseases (chronic obstructive pulmonary disease (COPD), influenza, pneumonia) and costs of premature disability and absences were calculated.

Results: Relative risks (RR) of death were highest for COPD in actual (S; M: 9.65, F: 10.47) and ex-smokers (ex-S; M: 8.75, W: 7.04) and lower for influenza and pneumonia (S: ≤2.18, ex-S: ≤1.56). Premature death of S/ex-S resulted in costs of 525.3 Mio. PLN (M: 460.3 Mio. PLN, F: 65.0 Mio. PLN; 1 EURO ≈ 4 PLN) predominantly by COPD (259.9 Mio. PLN) reflecting 8.6 % of all costs caused by premature death including cancer and cardiovascular disease. Annually 319 persons (M: 220, F: 99) lost their ability to work generating costs of 92.7 Mio. PLN (M: 70.8 Mio. PLN, F: 21.9 Mio. PLN) which is 10.2 % of all costs caused by smoking-induced premature disability. Additionally, there were costs of 2.1 Mrd. PLN (M: 1.4 Mrd. PLN, F: 0.7 Mrd. PLN) caused by 14.0 Mio. (M: 8.7 Mio., F: 5.3 Mio.) days of absence reflecting 75.5 % of all costs caused by absences due to illness in S/ex-S.

Conclusions: Data demonstrate the amount of smoking-induced indirect costs in Poland and show large differences between distinct cost fractions. Consideration of the partial amounts is crucial for further optimisation of measures for cost reduction (e. g. specific prevention).

P28

CPAP-adherence in a clinical sleep apnea population

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Background: The aim of this study was to assess adherence with mask continuous positive airway pressure (CPAP) in patients with polysomnographically diagnosed obstructive sleep apnea syndrome (OSAS).

Methods: We studied 88 patients (mean Age 55 ± 11 yrs, mean BMI 36 ± 7 kg/sqm, mean AHI 48 ± 30/h, ESS 10 ± 5) who received fixed or auto-adjusted mask CPAP treatment for OSAS at our institution. All patients underwent a standardized educational session and mask fitting by experienced staff. Data on treatment adherence, residual sleep disordered breathing, and mask leakage were collected at mean ± standard deviation 318 ± 143 days after CPAP initiation. Patients with good adherence (>4 h/night on at least 70 % of days) were compared with those who used their device less frequently.

Results: In the overall population, CPAP therapy was used 84 ± 18 % of the days since treatment initiation with 6.0 ± 1.4 h CPAP use/night. Percentage of days with at least 4 h CPAP use/night was 70 ± 23 %. There was no significant relationship between baseline AHI, arousal index, ESS score, or therapeutic CPAP pressure with CPAP adherence. Patients with good adherence ($n = 60$) were slightly older (57 ± 17 yrs vs. 51 ± 12 yrs, $p < 0.05$) and had higher minimum oxygen saturation (74 ± 5 SaO_2 min vs. 68 ± 8 SaO_2 min, $p < 0.05$) at baseline compared to patients with poor adherence ($n = 28$). In contrast, mask air leakage flow (34 ± 7 L/min vs. 39 ± 9 L/min, $p < 0.05$), residual sleep disordered breathing (5.1 ± 3.5 AHI vs. 3.5 ± 0.9 AHI, $p < 0.05$), and the Epworth Sleepiness Score (9.6 ± 4.7 vs. 5.8 ± 4.0, $p < 0.05$) were significantly higher in patients with poor adherence.

Conclusions: Adherence with CPAP therapy in our cohort was satisfactory, however, factors such as mask air leakage may contribute to poor adherence and thus residual sleep disordered breathing in a subset of patients.

P29

ADAM 33 protein in bronchial brushings and biopsies is increased in bronchial carcinomas*

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Background: The asthma and COPD susceptibility gene, *ADAM33,* is selectively expressed in mesenchymal cells and the activity of soluble ADAM33 has been linked to angiogenesis and airway remodeling.

Aims: We hypothesized that *ADAM33* mRNA & protein are differentially expressed in bronchial biopsies from healthy airways and bronchial carcinomas.

Methods: Paired primary bronchial fibroblasts ($n=4$) from healthy and tumor tissue were grown +/−TGFβ2 to induce myofibroblast differentiation. Fibroblasts, bronchial biopsies ($n=12$) and brushings ($n=12$) were analyzed for ADAM33 expression using quantitative RT-PCR and western blotting. Immunohistochemistry for ADAM33 was performed on bronchial biopsies.

Results: TGFβ2 caused induction of β-*SMA* and suppression of *ADAM33* mRNA expression in normal and tumor fibroblasts. *ADAM33* mRNA expression tended to be decreased in tumor biopsies whereas ADAM33 protein expression was significantly increased (bands of 45 and 75 kDa). In bronchial brushings *ADAM33* mRNA was not detectable. However, there was single band at ~75 kDa for ADAM33 and also specific staining for ADAM33 in the epithelium of bronchial biopsies.

Conclusions: Similar to cells from healthy and asthmatic volunteers TGFβ suppressed expression of *ADAM33* mRNA in normal or tumour fibroblasts. ADAM33 protein was increased in bronchial tumour biopsies suggesting potential roles in tumourigenesis and –growth. The presence of ADAM33 protein in bronchial brushings and biopsies in the absence of ADAM33 mRNA expression in brushings suggests that the mesenchyme is the source for ADAM33 protein in the epithelium.

P30

The study of thermal kinetic fingerprints and rapid detection of bacterial growth by microcalorimetry

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Background: Bacterial growth produces heat secondary to increasing substrate metabolism. We have used Differential Scanning MicroCalorimetry (μDSC) to study the metabolic growth curves of bacteria and evaluate detection criteria. Although not new to microbiology, μDSC has not been used to extensively characterize bacterial growth patterns and distinguish between bacterial species.

Methods: Plated colonies of either of the bacteria were suspended overnight in sterile Trypton Soy Broth (TSB). A new inoculum was prepared using fresh medium and incubated until mid-exponential growth was reached. The suspension was then introduced in the microcalorimetry cells and refrigerated until the experiment was registered. The reference cell required for microcalorimetry was filled with equal amount of sterile TSB.

Results: The growth patterns of *Staphylococcus aureus* and *Escherichia coli* differ highly in their morphology. We chose a set of parameters including time to bacterial growth detection (defined as a 15 μW shift from baseline), height and time to peak heatflow as well as the return to baseline and compared the results between different replicates of the same bacteria and between species. *Escherichia coli* had the fastest detection time and highest peak, but also exhausted its nutritive substrate quickest. In contrast, *Staphylococcus* samples had a longer growth time, with samples returning to baseline close to 24 h later.

Discussion: The different curves obtained from the studied bacteria allows for their differentiation – they represent a kinetic fingerprint for the specific bacteria. Our investigations can aid in rapid detection and differentiation, allowing for rational use of antibiotics in a clinical setting.

Conclusions: Microcalorimetry is a powerful tool for the study of bacterial metabolism and as such has potential role in the evaluation of bacterial response to antibiotics. This method provides rapid information without employing difficult and costly genetic tests.

P31

Bronchoscopic findings and interventions in patients with long-term tracheostomy

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Aims: To describe airway abnormalities as identified by flexible bronchoscopy (FB) in a cohort of patients with long-term tracheostomy (LTT), and to report on interventions as a consequence of FB findings.

Methods: Records of patients with LTT followed from January 2009 to December 2011 were reviewed. FBs were performed as routine surveillance endoscopies, as additional scheduled endoscopies, or because of disease and/or tracheostomy related complications. Interventions and extra caregiver trainings that were implemented as a result of detected airway pathologies were identified.

Results: In 52 patients (20 f, 32 m) 163 diagnostic FBs were performed. Thirty patients had a tracheostomy for long-term ventilation, and 22 as a bypass for upper airway obstruction. Median age was 4.2 years (0.1–32.7). In 79 instances FBs were performed transnasally, in 66 via the cannula, and in 18 via both routes. In 10 instances (6 %) complications led to FBs; in 16 (10 %) additional scheduled FBs, and in 137 (84 %) surveillance FBs were performed. The mean frequency of FBs was 1.1/patient and year (0.3–2.3). The most common findings were airway malacia in 37 %, clinically relevant granulation tissue in the suprastomal region in 7 %, at the end of the cannula in 6 %, and in other regions in 12 %. Cannula changes were performed in 22 %, ventilator changes in 2 %, and surgical interventions in 3 %. 14 % of the caregivers received extra training on correct suction techniques.

Conclusions: In this series of patients on LTT we found a high incidence of airway abnormalities. As FB findings resulted in interventions in a quarter of our patients we recommend that FB should be performed at least once a year. Patients with significant airway pathology, however, may benefit from more frequent endoscopic evaluations.

P32

Thrombotic microangiopathy after lung transplantation

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Background: Thrombotic microangiopathy (TMA) has an incidience of 0,8–14 % after solid organ transplantation with thrombotic-thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS) as the two major clinical syndromes. Adverse reactions to drugs, especially calcineurin inhibitors (CNI) are reported as a potential cause of TTP/HUS. The purpose of this study was to describe the incidence and course of TMA in a large collective of patients after lung transplantation (LUTX).

Methods: We retrospectively analyzed all primary LUTX in our centre performed between 2001 and 2011. Combined heart-lung transplantations, re-transplantations and patients who died within the first month postoperatively were excluded. 619 bi-lateral and 99 uni-lateral transplantations entered the analysis. All cases of TMA were identified according to laboratory findings and outcomes were analyzed.

Results: TMA occurred in 14 patients (1.9 %) after 405.0 ± 450.9 (mean ± SD) days post LUTX. All patients received tacrolimus or cyclosporine (combined with MMF and steroids) as primary immunosuppression (IS) and 8 patients received induction therapy with ATG or Alemztuzumab. Therapy consisted of a modification in IS in all patients and additionally plasmapheresis was performed in 6 patients. Overall survival after LUTX was significantly lower in patients with TMA (1046.9 ± 849.2) compared to patients without TMA (1422.2 ± 1104.1). No other significant differences or risk factors for TMA could be found. However all patients with TMA had a clinical relevant infection shortly prior to the diagnosis of TMA and 3 patients died within 3 months after the diagnosis of TMA due to multi-organ failure. Overall survival after TMA diagnosis was 635.6 ± 840.9 days (mean ± SD).

Conclusions: TMA after LUTX is a rare complication but has an significant impact on patient survival. TMA may be triggered by the use of calcineurin inhibitors and infections. Therapy is carried out stepwise starting with a switch of IS up to plasmapheresis in severe cases.

P33

Product failures in in-vitro diagnostics for rapid testing of blood gases and electrolytes – Results of the market surveillance by the BfArM until end 2010

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Background: The European Directive 98/79/EC on In-vitro Diagnostics (IVD) regulates marketing and post market surveillance of IVD in the European Economic Area. In cases of incidents and field corrective actions/preventive actions (CAPA) manufacturers have to inform the responsible Competent Authority (CA; D: BfArM for most IVD, AU: BASG).

Methods: In this study we analysed all notifications regarding IVD for rapid testing (point of care testing, POCT) of blood gases and electrolytes received until end 2010 by the BfArM in respect to source of notification, underlying product defects and performed CAPA.

Results: From 2851 notifications regarding IVD 49 were related to IVD for rapid testing of blood gases and electrolytes (analysers: 33, tests/consumables: 16). Notifications were received from manufacturers (24/14), other CAs (2/2), users (6/0) and other sources (1/0). Causes of product failure were identified in 29/16 cases. In the other cases the causes remained unclear (1/0) or a user error was the cause (3/0). Most frequent causes were software errors (11/0), errors in manufacturing/quality control (4/7), constructional faults (5/2), interferences (3/2) and labelling errors (0/3). CAPA were performed in 29/16 cases. Based on the risk caused by the product failure and the underlying causes these were (multiple entries possible) customer information (26/14, mandatory in case of a recall), recalls (17 (including software-update)/12), modifications in production/quality management (5/11), software-update (12/2), modifications of the instructions for use (8/3), the design (6/2), raw materials (4/1) or labelling (0/2).

Conclusions: Our data suggest that IVD for rapid testing of blood gases and electrolytes are an important product group. Analysers are typically at risk for software failure, whereas tests are prone to production errors. Accordingly, CAPA were different in both groups. In summary, the European system for post marketing surveillance of IVD is a valuable tool to enhance product safety.

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The clinical utility of plasma DNA concentration and integrity measurement for NSCLC diagnostics and radical therapy effectiveness monitoring*

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Our aim was to evaluate the clinical value of quantitative plasma DNA analysis, including DNA concentration and integrity (fragmentation) measurement, for early NSCLC diagnostics and assessment of radical therapy effectiveness.

Plasma DNA concentration and integrity index (DII) was measured in 60 resectable NSCLC patients (stage I-IIIA) prior and following the radical treatment using real-time PCR. Patients with chronic respiratory inflammation (34 COPD, 35 sarcoidosis and 32 asthma) were included into the study to assess the diagnostic accuracy of plasma DNA quantification in NSCLC detection. 10 orthopedic patient undergoing hip joint surgery and 40 healthy volunteers comprised control groups.

NSCLC patients (8.0 ng/ml) demonstrated significantly higher mean plasma DNA concentration than patients with chronic respiratory inflammation (3.4 ng/ml), orthopedic patients (3.0 ng/ml) and healthy controls (2.3 ng/ml; $p < 0.0000$). The cut-off point of > 2.8 ng/ml provided 90 % sensitivity and 80.5 % specificity in discriminating NSCLC from healthy individuals (AUC = 0.89, $p < 0.0001$), while 56 % specificity and 90 % sensitivity in distinguishing NSCLC patients from non-NSCLC subjects (AUC = 0.80, $p < 0.0001$). The mean plasma DII was significantly higher in resectable NSCLC (3.1) and chronic respiratory inflammation (3.7) than healthy individuals (1.0; $p = 0.0000$). Comparable dynamics in plasma DNA levels was observed a week

after the surgery in both resected NSCLC (68.7 ng/ml, $p<0.0000$) and orthopedic patients (28.4 ng/ml, $p<0.0015$). During 3–6 month follow-up relapse-free NSCLC patients demonstrated significant reduction in plasma DNA levels (2.8 ng/ml), whereas in relapsed subjects plasma DNA concentration was significantly higher than at baseline.

Although overall diagnostic power of the plasma DNA quantification was insufficient for routine early-stage NSCLC detection, it was still superior to diagnostic parameters presented by conventional serological markers used in lung cancer diagnostics. Significant differences in DII values among the study groups suggested the involvement of certain pathological processes, apoptosis and necrosis in particular, in plasma DNA fragmentation. Drastic increase of plasma DNA concentration after resection in NSCLC group was due to surgical trauma but not to malignancy. In the post-operative long-term follow up plasma DNA quantification proved its potential usefulness for radical NSCLC therapy effectiveness monitoring.

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Exercise induced increase of proANP in connective tissue disease patients may indicate PAP increase.*

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Background: Natriuretic peptides (brain natriuretic peptide (BNP) and atrial natriuretic peptide (ANP)) are produced in cardiomyocytes of different myocardial regions. In case of dilation of the heart, BNP and ANP are excessivly released into the circulation. BNP is used as a biomarker in patients with chronic heart failure and pulmonary hypertension (PH). ANP is a marker of acute cardiac stress and may reflect actual hemodynamic changes during exercise. In connective tissue disease an excessive increase of pulmonary pressure may represent an early stage of pulmonary vascular disease and may be clinically relevant.

Methods: We investigated plasma levels of proANP and NT-proBNP during right heart catheterization at rest and exercise in patients with connective tissue disease without PH. The levels at rest and during exercise were compared by Wilcoxon signed rank test. The correlations between the changes of mean PAP and NT-proBNP as well as mean PAP and proANP were calculated by Spearman's Rho test.

Results: $N=47$ patients (resting mean PAP: 16±3 mmHg, mean PAP at maximal exercise: 37±8 mmHg) were included. NT-proBNP and proANP significantly increased from rest to exercise (NT-proBNP rest: 91±102 pg/mL, maximal exercise: 96±96 pg/mL, $p<0.001$; proANP rest: 2.43±1.22 pg/mL, maximal exercise: 2.92±1.33 pg/mL, $p<0.001$). The increase in proANP levels between rest and maximal exercise significantly correlated with the increase in meanPAP ($p=0.007$, $r=0.404$), but there was no significant correlation for NT-proBNP ($p=0.606$).

Conclusions: Our results suggest that the exercise induced increase of proANP in patients with connective tissue disease may indicate the exercise-induced increase in PAP.

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The measurement of end-tidal CO2 may help to differentiate between PH due to chronic lung or heart disease and CTEPH

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Background: End-tidal CO_2 pressure ($PETCO_2$) is a simple parameter, which may be assessed at rest or during exercise during cardiopulmonary exercise testing (CPET). $PETCO_2$ changes have been described in patients with cardiac failure and acute pulmonary embolism, as well as in pulmonary hypertension (PH), but it is not known if $PETCO_2$ may be helpful in differentiating between PH subgroups.

Methods: We retrospectively investigated $PETCO_2$ data of patients with a meanPAP >25 mmHg at rest, due to chronic left heart (LH-PH), and pulmonary disease (Lu-PH) or CTEPH. $PETCO_2$ was measured at rest and during maximal exercise. Mean values were compared by ANOVA and multiple comparisons were performed with Scheffé equation as post hoc test.

Results: $N=46$ patients were included (LH-PH: $n=14$, mean PAP 40±11 mmHg, PVR 327±188 dyn s cm^{-5}, PAWP 21±5 mmHg; Lu-PH: $n=15$, meanPAP 34±8 mmHg, PVR 441±266 dyn s cm^{-5}, FEV1 %pred. 63±27; CTEPH: $n=17$, meanPAP 46±11 mmHg, PVR 732±308 dyn s cm^{-5}). $PETCO_2$ at rest was 4.97±1.04 mmHg, 4.70±1.19 mmHg, and 3.55±0.71 mmHg in LH-PH, Lu-PH and CTEPH patients. The $PETCO_2$ difference between LH-PH and CTEPH was 1.38 (CI 95 % 0.48–2.29, $p=0.001$), and between Lu-PH and CTEPH 1.14 (CI 95 % 0.24–2.04, $p=0.007$). Comperable similar results were obtained with $PETCO_2$ during maximal exercise.

Conclusions: PH caused by CTEPH is characterized by lowered $PETCO_2$ as compared to PH due to chronic heart or lung disease.

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Soluble receptor of advanced glycation endproducts (sRAGE) and endothelial dysfunction during and after acute exacerbations of COPD

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Background: COPD is accompanied by an increased cardiovascular risk which is furthermore aggravated by the incidence of acute exacerbations. Recently, the soluble receptor for advanced glycation endproducts (sRAGE) emerged as a promising biomarker in chronic

inflammatory disorders. The aim of this study was to investigate a possible influence of an acute exacerbation (AE) on sRAGE and endothelial dysfunction in patients with COPD. We hypothesize that both circulating levels of sRAGE and endothelial dysfunction are impaired during AE and improve after clinical recovery.

Methods: We enrolled patients admitted to hospital due to an acute exacerbation of COPD. Study related procedures comprised lung function testing, measurement of plasma sRAGE levels and the quantification of endothelial dysfunction by means of the flow-mediated dilation technique (FMD). The entire spectrum of measurements was scheduled within two days of hospital admission and thereafter when having confirmed clinical stability.

Results: We recruited 29 patients (27 % female) during AE of COPD. Baseline characteristics were as follows: age: 64 ± 8 years, BMI: 25 ± 5.8, FEV1: 37 ± 12 %pred. During AE patients showed a median sRAGE of 525 pg/mL (371–770, 1st to 3rd quartile) and a mean FMD of 6.7 ± 3.6 % indicating severe endothelial dysfunction. After confirmed clinical stability we observed a significant increase of sRAGE [876 pg/mL (633–1371, 1st to 3rd quartile)] ($p < 0.001$) and a simultaneous improvement in FMD (10.0 ± 3.4 %) ($p < 0.001$). In addition, we observed a significant positive correlation between sRAGE and FMD (coeffient = 2.43; $p = 0.01$) in our study sample.

Conclusions: Our results indicate a substantial impairment of sRAGE and endothelial function in exacerbated patients with COPD. AEs transiently deteriorated endothelial function probably via impairment of circulating sRAGE levels.

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Proliferation of alveolar type II pneumocytes is stimulated by Jagged-1 in vitro*

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Notch is an ancient cell-signaling system that regulates the specification of cell fate. Recently, Notch was found to confer antigen presenting cell function on mast cells, induce histamine release in human basophils and regulate migration and survival of eosinophils.

In acute lung injury, alveolar type II cells activate macrophages, secrete soluble mediators, migrate and spread in response to the injury. Additionally, Notch stimulated myofibroblast differentiation and migration of cultured RLE-6TN cells. However, until now, nothing is known on the role of Notch activation regarding proliferation of rat alveolar type II cells.

Rat alveolar type II cells (RLE 6TN) were obtained from the American Type Culture Collection (ATCC no. CRL-2300; Manassas, VA, USA) and were cultured in DMEM/Ham's F12 containing 10 % fetal calf serum and L-glutamine. Cell proliferation was measured by direct cell count and the fluorometric proliferation assay EZ4U basing on tetrazolium salt reduction. Cells were incubated with the test substances in medium containing 0.5 % fetal calf serum for 24 h at 37 °C and 5 % CO_2.

Jagged-1 significantly stimulated proliferation of alveolar epithelial cells within a wide concentration range [5 µg/ml to 100 pg/ml]. The maximum effect was observed at 100 ng/ml. To show specificity of the observed effect, rat alveolar type II cells were preincubated (45 min) and co-incubated with the specific gamma secretase inhibitor DAPT [10^{-4} M] which completely abolished the effect of Jagged-1 [ng/ml].

Herewith, we report for the first time that the Jagged-1/Notch signaling pathway is affecting rat alveolar type II cell proliferation in vitro.

Autorenverzeichnis