Abstracts

43. Jahrestagung der Österreichischen Gesellschaft für Pneumologie
3. Jahrestagung der Österreichischen Gesellschaft für Thoraxchirurgie

Wien, 10.–12. Oktober 2019

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Ein 61-jähriger Patient mit rezidivierenden Hämoptysen, progressiver Dyspnoe und bilateralen pulmonalen Infiltraten

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Patientencharakteristik, Anamnese und Symptome: Ein 64-jähriger Patient wird mit Hämoptysen seit 2 Wochen, zunehmender Müdigkeit, Dyspnoe, Gliederschmerzen und Inappetenz zugewiesen. Aufgrund eines stattgehabten STEMI wird ASS 100 mg einmal täglich eingenommen. Der Patient ist seit über 10 Jahren ehemaliger Raucher mit ca. 30 Packyears.

Diagnostik und Diagnose: In der CT-Thorax zeigt sich eine weichteildichte Raumforderung am Abgang des linken Unterlappenbronchus mit subtotaler Obstruktion der Segmentbronchien (Abb. 1a). Zusätzlich zeigt sich eine inhomogene Konsolidierung im posterioren Oberlappensegment rechts (Abb. 1b). Das Blutbild ist unauffällig. Bronchoskopisch zeigt sich alblutiges Sekret im linken Unterlappen; keine aktive Blutung. ASS wird präventiv abgesetzt. Histologisch finden sich chronisch-entzündliche Veränderungen, jedoch kein Tumorgewebe.

Einen Monat später erfolgt bei rezidivierenden Hämoptysen eine weitere Bronchoskopie, dabei zeigen sich erneut chronisch-entzündliche Veränderungen. Histologisch zeigt sich ein unveränderter Befund. Da eine maligne Grunderkrankung nach wie vor plausibel erscheint, erfolgt eine transbronchiale Biopsie der linken Unterlappenbronchus und Prednisonol 1 mg/kg Körpergewicht/d sistieren die Hämoptysen.

Zwei Wochen nach Entlassung wird der Patient aufgrund neuerlicher Hämoptysen und AZ-Verschlechterung aufgenommen. Es zeigt sich ein Hämoglobinwert von 7 mg/dl. Die CT-Thorax zeigt nun eine vollkommene weichteildichte Konsolidierung des linken Unterlappens.

Therapie und endgültige Diagnose: Der Patient wird zur Resektion auf die Thoraxchirurgie des Universitätsklinikums Graz verlegt. Die histologische Diagnose ergab ein primäres Angiosarkom der Lunge.

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54-jähriger adipöser Patient mit Atemnot im Liegen

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Patientencharakteristik, Anamnese und Symptome: Der 54-jährige Patient wird im Dezember 2018 zur Abklärung einer seit 2 Monaten bestehenden Dyspnoe in Rückenlage an unserer Abteilung stationär aufgenommen. Anamnestisch gibt der Patient an etwa zwei Monate zuvor einen viralen Infekt durchgemacht zu haben, danach habe er auch heftige Schulterschmerzen linksseitig verspürt. Etwa zwei Wochen nach Abklingen der Schulterbeschwerden, bemerkt der Patient eine ausgeprägte Kurzatmigkeit.

Vorbekannt sind bei dem Patienten eine koronare Herzkrankheit (Eingefäßerkrankung bei Zustand nach NSTEMI mit...
In der Bodyplethysmographie zeigte sich eine leichtgradige Restriktion. Eine bronchiale Obstruktion konnte ausgeschlossen werden. Die Diffusionskapazität bezogen auf das Alveolervolumen war normal.

Der Ausschluss einer Pulmonalembolie erfolgte mittels einer Computertomographie der Pulmonalgefäße.

Differentialdiagnostisch ergaben sich für uns folgende Überlegungen: OSAS, Shunt, ILD, Herzinsuffizienz und Atemmuskelschwäche.

Anhand der weiteren Abklärung ergab sich eine unerwartete Diagnose.

Überraschende Diagnose eines stenosierenden gastrointestinalen Tumors

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Patientencharakteristik, Anamnese und Symptome: Ein 49-jähriger Patient ohne Vorerkrankungen stellte sich mit diffusen abdominellen Schmerzen beim Hausarzt vor. In der klinischen Untersuchung zeigte sich eine Druckempfindlichkeit bei tiefer Palpation im rechten Mittel-/Unterbauch. Der Patient berichtete über regelmäßigen Stuhlgang ohne Übelkeit oder Erbrechen. Keine weiteren Symptome, insbesondere kein Fieber, Gewichtsverlust oder Nachtschweiß. Es bestand ein aktiver inhalativer Tabakkonsum mit kumulativ ca. 40 pack-years.

PCI der RCA), arterielle Hypertonie, Depression und ein multi-segmentaler Diskus-Prolaps (L3/L4, L4/5, L5/S1).

Diagnostik und Diagnose, Differentialdiagnostik: Es erfolgte neben einer ausführlichen Anamnese und körperlichen Untersuchung zunächst eine pneumologische Basisdiagnostik inklusive Thoraxröntgen, Lungenfunktion und arterieller Blutgasanalyse. Die körperliche Untersuchung fiel bis auf eine Adipositas unauffällig aus, insbesondere die Lungen und das Herz auskultorisch unauffällig und keine Ödeme. Im Thoraxröntgen zeigte sich ein beidseitiger Zwerchfellhochstand. Ein Infiltrat, Erguss oder höhergradige Stauungszeichen konnten ausgeschlossen werden (Abb. 1).

Da beim Patienten die Atemnot besonders im Liegen ausgesprochen war, erfolgte zunächst die Analyse der arteriellen Blutgaswerte im Sitzen: paO2 79 mmHg, paCO2 40 mmHg, pH-Wert 7,43. Im Liegen fiel das paO2 auf 63 mmHg ab (~20 % im Vergleich zur sitzenden Position), paCO2 und pH blieben unverändert. Zusammenfassend lässt sich eine deutliche Oxygenierungsstörung im Liegen erheben.

Endoskopisches Bild einer stenosierenden Tumormasse im Bereich des Zökums
Diagnostik und Diagnose: In einer ersten orientierenden Sonographie des Abdomens zeigte sich eine inhomogene, steiniernde wandende Verdickung im Bereich des rechten Kolon. Die Computertomographie (CT) des Abdomens bestätigte den Befund, so dass eine weiterführende Abklärung mittels Koloskopie erfolgte. Dabei imponierte ein exophytischer, 2/3 der Zirkumferenz umfassender, polyppöder Tumor im Zökum. Die maximale Ausdehnung lag bei ca. 10 Zentimeter (Abb. 1). Labormäßig zeigte sich ein leicht erhöhter CEA Wert mit 6,1 ng/ml bei einem normwertigen CA 19-9. Bei dem hochgradigen Verdacht auf einen malignen Prozess wurde zur Komplettierung des Stagings ein CT des Thorax durchgeführt. Dabei zeigten sich ausgeprägte Lungenveränderungen mit teilweise kleinfleckigen, retikulär imponierenden Infiltraten im linken Oberlappen, sowie ein Rundherd mit zentraler Einschmelzung im rechten Oberlappen. Zwischenzeitlich ergab sich aus der Histologie der Tumorbiopsie des Zökums der Nachweis von epitheloidzelligen Granulomen, aber ohne Hinweis auf Malignität. Die PCR auf Mycobacterium tuberculosis-Komplex war hingegen negativ. Bei dem hochgradigen Verdacht auf eine pulmonale Tuberkulose mit gastrointestinalem Beteiligung wurde der Patient auf eine pneumologische Station verlegt und schutzisoliert. In einer ersten Sputum Untersuchung waren mikroskopisch keine säurefesten Stäbchen in der Ziehl-Neelsen Färbung darstellbar, aber die PCR auf M. tuberculosis-Komplex war positiv. Eine weiterführende Diagnostik mittels PET CT und cMRT ergab keinen Hinweis auf weitere Tuberkulose-Manifestationen.

Therapie: Es wurde eine antimykobakterielle Therapie mit Rifampicin, Isoniazid, Ethambutol und Pyrazinamid eingeleitet. Die Therapie entschied mit hohen nächtlichen Fieberzacken, starke Cephalea und eine Pneumonie sind typisch [1].

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bilisierung. Radiographisch zeigen sich ausgeprägte Milchglasverschattungen beidseits mit Aussparrung der Mantelzone. Lungenfunktionell eine hochgradig eingeschränkte Diffusionskapazität bei nur leichtgradig eingeschränkten mobilisierbaren Atemvolumina und keiner formalen Obstruktion oder Restriktion. Bronchoskopisch kein Hinweis auf Alveardarmproteinose, CD4/CD8 Ratio in der BAL mit verminderten CD4/CD8 Quotienten, in den peripheren Probenexzisionen Hinweise auf organi- nierende Pneumonie, in der Immunfluoreszenz spärlicher Nachweis von Pneumocystis jiroveci, ansonsten kein Erreger- nachweis.  

**Therapie:** Nach Diagnosestellung erfolgt die leitliniengerechte Therapie mit Trimethoprim-Sulfamethoxazole (TMP-SMX) intravenös 15 mg/kg Körpergewicht (1). Hierunter kommt es zu einer deutlich verbesserten der klinischen Symptomatik. In einer radiologischen Verlaufskontrolle zeigen sich die bilateralen Milchglasverschattungen deutlich regredient, jedoch noch neu aufgetretene bis 14 cm messende bilaterale Pneumatozellen im interlobär-Bereich. Ein solche Entwicklung ist nur in Einzelfällen in Kombination mit einer Immundefizi- enz beschrieben (2). Da nur einzelseitig PEs entnommen wurden, kann differentialdiagnostisch ein postinterventioneller Interlo- bärpneumothorax ausgeschlossen werden. Unter fortgeführter Therapie inklusive Atemphysiotherapie zeigen sich die Pneu- matocele in regelmäßigen Kontrolluntersuchungen regre- dient.

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**F06 Ungewöhnliche Nebenwirkung durch Checkpoint-Inhibitor**

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**Anamnese:** Bei einem 57-jährigen wird ein TTF-1 positiv- es Adenokarzinom mit einem PD-L1 Status von 100 % diag- nostiziert. Das initiale Tumorstadium ist IIIA (cT4 cN0 mM0), die Mutationsanalysen sind negativ. Im Tumorboard wird ein individuelles Vorgehen mit 4 Zyklen Immun-Chemotherapie mit Cisplatin/Pemetrexed/Pembrolizumab in „neoadjuvan- ten“ Absicht, mit anschließender Evaluierung für eine operative Sanierung, beschlossen.

**Verlauf:** Kurz nach dem 1. Zyklus Immun-Chemotherapie entwickelt der Patient eine Divertikulitis, welche konserva- tiv erfolgreich behandelt werden kann. 2 Wochen später wird der Patient erneut vorzeitig wegen grijpper Symptomatik. Im Labor zeigen sich zunächst nur gering ausgelente Infektpara- meter. Rasch kommt es zu einer Zunahme der Beschwerden mit Schüttelfrost, Fieber, Kopfschmerzen, Tachykardie, Schwef- ausbrüche, Dyspnoe, Hypertonie und Ödeme. Es zeigt sich das Bild wie bei Sepsis, jedoch ohne Fokus oder Erregnachweis. Der Patient wird auf die Intensivstation transferiert. Nun ist das Interleukin-6 (IL-6) deutlich ausgelöst mit 1129 pg/ml, CRP 20,2 mg/dl, PCT 0,7 ng/ml bei normaler Leukozytenzahl. In der Thorax-Computertomographie imponiert das Bild einer ausge- dehnten Pneumonitis bei gleichzeitiger Verkleinerung des Pri- mártumors.

**Diagnose:** Es handelt sich um ein Zytokin-Release-Syn- drom (Zytokinsturmsyndrom) unter „Triple Therapie“. Dies- ses wird verursacht durch eine high-level Immunereaktion. Es wird häufig beobachtet bei CAR T-Zell Therapie, GvHD, Rituximab, sowie rezent auch bei Checkpoint-Inhibitoren (1). Typischerweise sind hohe Werte von Interleukin-6 und Interleukin-Gamma messbar. Symptome sind Fieber, Übelkeit, Schüttelfrost, Tachykardie, Asthenie, Kopfschmerz, Hyperto- nie, Exanthem, Ödeme und Dyspnoe. Es handelt sich um einen onkologischen Notfall (1).

**Weiterer Verlauf:** Der Patient erhält eine hochdosierte Glukokortikoidtherapie (1 g Prednisolon) in ausschleichender Dosierung, darunter kommt es zu einem Rückgang von IL-6 und der Infektparameter und deutlicher Symptombesserung. Initial benötigt der Patient hohe Mengen an O2, bei Entlassung ist kein Sauerstoff mehr notwendig. Die weitere Therapie wird mit Pembrolizumab als Monotherapie fortgeführt. Nach 6 Zy- len zeigt sich ein guter Response und eine Lobektomie inklusive Thoraxwand-Resektion kann durchgeführt werden.

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Nach einem Monat kommt der Patient jedoch abermals mit einer akuten Verschlechterung der respiratorischen Situation zur Aufnahme. Im CT-Thorax kann diesmal als Ursache eine zentrale Pulmonalembolie beidseits festgestellt werden. Initial benötigt der Patient zur ausreichenden Oxygenierung eine Highflow-Sauerstofftherapie. Unter Therapie mit niedermolekularem Heparin kann auch die bereits dritte pulmonale Problematik innerhalb von 3 Monaten verbessert werden. Im Labor zeigten sich jedoch massiv erhöhte Leber-bzw. Cholestaseparameter, washebald der Patient auf eine gastroenterologische Abteilung zur weiteren Abklärung transferiert werden muss.

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2. Kroegel C, Costabel U (Hrsg) Klinische Pneumologie. Thieme Verlag, Stuttgart; 2013.

Bronchuskarzinom – personalisiert
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Patientencharakteristik, Anamnese und Symptome: 38-jähriger Mann, Niemals-Raucher, leere Anamnese. Seit 14 Tagen Husten, leichte Hämoptoe, „Durchzuatmen nicht möglich“. Leuco: 26,2 G/l; LDH 351 U/l; CRP 21,6 mg/l.

Diagnostik: USGK und TTE: 4,8 x 1 cm echoarme Struktur von der li. Lungenvene ausgehend, im Vorhof flottierend und durch die Mitralklappe in den li. Ventrikel durchschlagend. Verdacht auf Vorhofmyxom. Wegen Gefahr der Mitralklappenobstruktion Akuttransfer in Herzchirurgie.

Thorax-CT: 12 x 8 x 4 cm Raumforderung von parastrachale rechts entlang des li. Hauptbronchus bis unter die Trachealbifurkation nach links; Infiltration V. pulmonalis li, li. Vorhof und Oesophagus. Ösophagektomie.

Bronchoskopie: Tumorgewebe ab dem li. Lob-Bronchus-Ostium, Totalverschluss.

PET-CT: Primium (SUV 40) und VX Konglomerate ipsi- und kontralateral parastrachale/mediastinal.

Biopsie: Solides Adenokarzinom des Bronchus. PD-L1 100 % positiv, ALK-Rearrangement.

Therapie und Verlauf: Geplanter Induktions-Therapiebeginn mit Alectinib 5 Tage post Biopsie. AZ-Verschlechterung, Subileus, abdomineller Vernichtungsschmerz, verstärkte Dyspnoe.

Thorax/Abdomen-CT: Deutliche, locale Progression, Pleuraerguss links, thromboembolischer Subtotalverschluss A. mesenterica superior, Subileus. Thoraxdrainage links. Versuch radiologisch-interventioneller Aspiration der Thromben (negativ). Laparotomie: Ausgedehnte, ischämische Dünnarmnekrose. Thrombektomie aus der A. mesenterica superior. Resektion von 1,5 m Jejunum.

3. postoperativer Tag: Beginn mit Alectinib 600 mg 4x/die. 9 Tage nach Therapiebeginn: deutliche, klinische Besserung. Nach 2 Monaten: Tumorvolumen minus 80 %. Vorhoff-Infiltiration nur noch marginal nachweisbar.

Nach 5 Monaten: Restthorakotomie, komplette mediastinale Lymphknotenausräumung Histologie: Partielle, epitheloidzellige Granulome (PCR auf Mycobakterien neg.) Vierzehn Tage später: Thoracotomie links, Unterlappenlobektomie, komplette mediastinale Lymphknotendissektion. Histologie: Kein Tumorgewebe mehr feststellbar.

Die Erhaltungstherapie mit Alectinib bis dato. Patient weiterhin tumorfrei und in gutem AZ.

F09

Akute Dyspnoe bei einer Patientin mit einem Mammakarzinom
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Patientencharakteristik, Anamnese und Symptome: Eine 55-jährige Patientin präsentierte sich in der Notfallambulanz mit einer progredienten belastungsabhängigen Dyspnoe. Anamnestisch bestand bei der Patientin ein kutan metastasiertes Mammakarzinom rechts und Zustand nach Ablatio, Bestrahlung und Chemotherapie.

Diagnostik, Differentialdiagnostik und Diagnose: Laborchemisch waren folgende Parameter auffällig: D-Dimer (4,87 mcg/mL), CRP (5,97 mg/dL), Laktat (11 mmol/l) und die Thrombozytanzahl (17 G/L). Die Echokardiographie zeigte Zeichen einer deutlichen Rechtsherzbelastung und eines pulmonalen Hochdrucks mit einem geschätzten systolischen pulmonalerteriellem Druck (sysPAP) von 65 mmHg. Die echokardiographisch durchgeführte pulmonale CT Angiographie lieferte keinen Hinweis auf eine zentrale Pulmonalembolie, zeigte allerdings multiple, uncharakteristische Unterlappen, betonte, kleine milchglasartige Rundherde. In Zusammenschau mit dem erhöhten Entzündungsparameter und der ausgeprägten Thrombozytopenie stellte sich der Verdacht auf eine atypische Pneumonie. Aufgrund der Rechtsherzbelastung und des nodulären Musters im CT (Abb. 1) erschien jedoch differenzialdiagnostisch eine tumorthrombotische Mikroangiothse wahrscheinlich.

Therapie: Es wurde umgehend eine antibiotische Therapie mit breitbasigem Spektrum eingeleitet. Trotz adäquater intensivmedizinischer Maßnahmen kam es in weiterer Folge zu einem therapieresistenten Schockzustand und Ableben der Patientin. Als Korrelat zum CT Bild, zeigte die Obduktion als Todesursache eine ausgedehnte intravasale Tumorausbreitung, histologisch dem bekannten Mammakarzinom entsprechend.
sich zur Voruntersuchung progrediente bullöse Veränderungen beidseits mit Beteiligung der UL. Die Bildgebung und Anamnese ergaben bereits bei der initialen Behandlung den Verdacht einer seltenen erblichen Erkrankung mit Formation multipler pulmonaler Zysten, mit anschließender genetischer Diagnostik und Verifizierung des Birt-Hogg-Dubé-Syndroms (BHDS).

**Therapie:** Das BHDS ist außer extrapulmonalen Manifestationen der Mutation des Follikulin-Gens durch unzählige in allen Lungenabschnitten vorhandene Zysten gekennzeichnet, wodurch eine Resektion aller Läsionen unmöglich ist. Das Standardverfahren – Bullektomie mit partieller Pleurektomie – ist beim BHDS oftmals frustran. Erfolge mit einer totalen pleuralen Deckung mittels eines Netzes aus oxidierter regenerierter Zellulose, welche zur Verdickung der viszeralen Pleura ohne Adhäsionen führt, wurden rezent berichtet [1]. Bei der letzten VATS führten wir zusätzlich zu einer Zystenresektion eine Abdeckung der freien Lungenoberflächen inklusive des großen Interlobaria mit 10 × 20 cm Equitamp durch. Derzeit ist die Lunge vollständig entfaltet.

**Literatur**

1. Mizobuchi T, et al. A total pleural covering of absorbable cellulose mesh prevents pneumothorax recurrence in patients with Birt-Hogg-Dubé syndrome. Orphanet J Rare Dis. 2018;13(1):78.

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**F10**

*Alternative zur Pleurodese bei seltener Ursache eines rezidivierenden Pneumothorax*

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*Patientencharakteristik, Anamnese, Symptome:* Wir berichten über einen 28-jährigen männlichen Patienten mit plötzlich beim Tennis aufgetretenem, stechendem Schmerz rechtsthorakal. Anamnestisch sind 3 Episoden mit Spontanpneumothorax vorbekannt, wobei bereits VATS mit Keilresektion der Blebs und partieller oder subtotaler parietaler Pleurektomie vor 15 (rechts) bzw. 3 Monaten (links) durchgeführt wurden. Die Vitalparameter waren unauffällig, ebenso die restliche Eigenanamnese. Erwähnenswert ist eine zystische Lungenerkrankung mit rezidivierenden Pneumothoraces bei der Mutter.

*Diagnostik und Diagnose:* Das Lungenröntgen ergab keinen sicheren Hinweis auf einen neuerlichen Pneumothorax. Aufgrund der Anamnese und persistierender Symptomatik wurde ein Thorax-CT durchgeführt, welches einen geringen Pneumothorax mit Prädominanz basal zeigte. Zudem fanden wir bereits bei der initialen Behandlung den Verdacht einer seltenen erblichen Erkrankung mit Formation multipler pulmonaler Zysten, mit anschließender genetischer Diagnostik und Verifizierung des Birt-Hogg-Dubé-Syndroms (BHDS).

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**Literatur**

1. Mizobuchi T, et al. A total pleural covering of absorbable cellulose mesh prevents pneumothorax recurrence in patients with Birt-Hogg-Dubé syndrome. Orphanet J Rare Dis. 2018;13(1):78.

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**F11**

*Lunge – Niere – Haut: ein interdisziplinärer „case of the year“*

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Herr S. wird im Mai 2019 an der nephrologischen Abteilung zur Transplantationsevaluierung bei chronischer Niereninsuffizienz stationär aufgenommen. Diagnostisch vorbekannt ist eine terminale Niereninsuffizienz auf Basis einer fokalen sklerosierenden Glomerulonephritis. Eine Nierentransplantation von 2005 endete letztlich bei wiederkehrender FSGS im chronischen Transplantversagen. Nebendiagnostisch weist der Patient eine KHK, PAVK, lymphoide Papulose sowie Z.n. Kalziphylaxie der Unterschenkel von 2017 auf. In den nun durchgeführten Check-up-Untersuchungen zeigt sich in der Thorax-CT ein seltener Befund mit multiplen, partiell verkalkten Oberlappenveränderungen. Atemfunktionell ergibt sich kein Hinweis auf eine Ventilations- oder Diffusionsstörung. Laborchemisch kann keine unterstützende Information gewonnen werden. Der Patient wird aufgrund der unklaren Lungenveränderungen uns konsiliarisch vorgestellt. Hier ist auch für uns die Ätiologie der Lungenveränderungen zunächst unklar, zumal nach Durchsicht vorheriger CT-Aufnahmen von 2016 und 2017 sich die Veränderungen deutlich progredient zeigen. Aufgrund der geplanten NTX-Listung entscheiden wir uns zunächst zur Erweiterung der nichtinvasiven Diagnostik mittels PET-CT. Hier weisen die apikalen Lungenverkalkungen keinen erhöhten FDG-Uptake auf. Kein Hinweis für malignomsuspekte Veränderungen. Nun stellt sich die Frage nach der Notwendigkeit einer weiteren invasiven Diagnostik (Bronchoskopie/CT-Stanzbiopsie?). In Zusammenhang mit der vorliegenden Grunderkrankung mit dialysepflichtiger Niereninsuffizienz, daraus sekundärem Hyperparathyreoidismus und vor allem aufgrund der Kalziphylaxie von 2017 können wir die Diagnose letztlich ohne weitere Abklärung stellen.
Glück im Unglück, vom Tumor zur SOP

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Anamnese und Symptome: Der 72jährige Herr K. wird uns wegen zunehmender Belastungsdyspnoe, Husten, reduziertem AZ und vermehrter Schweißneigung bei Bronchusokklusion des rechten OL (im auswärtigen CT V. a. TU re OL) vom niedergelassenen Lungenfacharzt zugewiesen.

Diagnostik: Konventionell-radiologisch zeigt sich ein Infiltrat im rechten OL, die Entzündungszeichen sind deutlich erhöht (CRP 11 mg/dl). Es wird eine antibiotische Therapie mit Meropenem eingeleitet. Blutgasanalytisch findet sich bei bekannter COPD III eine milde respiratorische Partialinsuffizienz. Mit dem Bronchoskop ist der rechte OL durch eine Kalzium- und Phosphataushaltstherapie um Metronidazol erweitert.

Eine 27-jährige Patientin präsentiert sich in der Internistischen Notaufnahme, nachdem sie auf der Couch liegend plötzlich starke linkss seitige Schmerzen verspürt hat und danach starke Luftnot. Die Vitalparameter zeigen keine Auffälligkeiten und die physikalische Untersuchung ergibt einen unauffälligen Befund. Bei leicht erhöhtem D-Dimer wird nach schriftlicher Aufklärung ein PTE-CT durchgeführt und eine pulmonal arterielle Embolie ausgeschlossen. Allerdings zeigt sich eine ca. 10 cm (transversal) × 7 cm (kraniokaudal) Durchmesser haltende, relativ glatt begrenzte, flau Kontrastmittel aufnehmende, rundliche, vornehmlich subpleurale Expansion im linken Unterlappen mit scholligen Verkalkungen im kaudalen Aspekt. Aufgrund der Herkunft der Patientin (Rumänien) wurde in erster Linie eine Echinokokkus Zyste vermutet und eine Therapie mit Albendazol begonnen. Außerdem wurde die Patientin zu einer operativen Sanierung vorgemerkt. Zur weiteren Abklärung wurde eine PET-CT Untersuchung durchgeführt. Dabei präsentierte sich die Expansion als pericardial, nahe zum Mediastinum hin gelegen mit inhomogen, aber signifikant gesteiger tem Tracer Uptake. Aufgrund dieses Befunds erschien eine Echinokokkuszyste als sehr unwahrscheinlich, sodass eine CT gezielte Punktion durchgeführt wurde. Die Histologie ergab ein atypisches hyperzelluläres spindelzelliges Proliferat mit hylä nisiertem Stroma, fokalen Nekrosen und SMA-Expression.

Es wurde nun rasch eine Unterlappenresektion mit medias tinaler Lymphadenektomie über eine linksseitige posterolaterale Thorakotomie vorgenommen. In der entsprechenden Histologie zeigten die spindeligen Zellen immunhistochemisch wieder eine positive Reaktion auf SMA, während ALK1, CD34, Desmin, EMA, Pankeratin, Keratin, E1/3, Keratin, CAM5.2, S100, SOX10, STAT6 und TLL1 negativ waren. Die zusammenfassende histologische Beurteilung ergab ein Myofibroblastom ohne Hinweis für Malignität.

Der postinterventionelle Verlauf gestaltete sich komplikationslos und die Patientin war bereits nach wenigen Tagen beschwerdefrei.

Das Myofibroblastom ist ein mesenchymaler Tumor, der in verschiedenen Organen vorkommt, meist jedoch in der Haut. In der Lunge ist er sehr selten und keinesfalls immer benign. Inflammatorische Formen wurden in der Literatur beschrieben. Die Therapie der Wahl ist die vollständige Resektion.

Weiterer Verlauf: Im weiteren Verlauf kommt es zu einem deutlichen Rückgang der Entzündungszeichen und zu einer Besserung der Symptome. Allerdings finden sich, trotz weiterhin ofenem OL Eingang, zunehmende Schmerzen mit infiltrativen Veränderungen des rechten OL, passend zu einer sekundären organisierenden Pneumonie. Es wird eine Cortisontherapie eingeleitet.
Impairment of NKT cells is involved in excessive vascular collagen deposition in PH due to lung fibrosis

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Background: Lung fibrosis is a devastating disease that is further complicated by the presence of pulmonary hypertension (PH). Vascular remodeling is an underlying cause of PH, and associated with increases in cellularity as well as extracellular matrix. Currently, it is not known whether changes in the immune cell profile can affect the deposition of collagen into the vascular bed in lung fibrosis. In our preliminary results, we identified a marked decrease in the numbers of natural killer T-cells (NKT) in the pulmonary arteries (PA) of PH patients due to lung fibrosis. We therefore aim to investigate the role of NKT-cells on vascular remodelling in this disease.

Methods: We analysed vascular collagen deposition and the inflammatory signature of PAs and blood of PH patients due to lung diseases, as well as in an animal model of pulmonary fibrosis. The effect of immunomodulation of NKT by a specific agonist (α-Galactosylceramide) on collagen deposition and vascular remodeling was assessed in vivo, ex-vivo and in vitro.

Results: This study identified that vascular remodeling in lung fibrosis with PH is accompanied by increased collagen deposition in the vessel wall and a simultaneous absence of NKT cells. Decreased numbers of NKT-cells were also observed in peripheral blood. In experimental pulmonary fibrosis, treatment with the NKT-cell agonist decreased parenchymal and vascular remodelling, while partially restoring the inflammatory profile. In human peripheral blood mononuclear cells (PBMC), pharmacological NKT-cell activation induced anti-fibrotic secretome. Consequently, extrinsic application and activation of PBMC reduced the collagen content of 1) TGF-beta activated PASM and 2) on human precision-cut lung slices of fibrosis patients.

Conclusion: NKT cells present a potential target for immunomodulatory therapy with the capacity to act in an anti-fibrotic fashion both on vascular and parenchymal remodelling.

Fragment of Collagen IV is a mediator of endothelial dysfunction in pulmonary hypertension

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Background: Pulmonary hypertension (PH) is a common complication of lung diseases. Vascular remodelling due to excessive extracellular matrix (ECM) deposition and endothelial dysfunction are key features of PH. High ECM turnover may lead generation of matrikines, which are biologically active peptides released upon proteolytic cleavage of ECM proteins. The basement membrane (BM), specialised ECM proteins underlying endothelial cells, is not only important for sustaining tissue integrity but also important for vascular endothelial cell function. Type IV collagen (ColIV) is the predominant collagen in the BM, in situ analysis suggests the potential of proteolytic fragmentation. Whether biologically active fragments of ColIV are released in PH, and whether those matrikines are involved in the pathophysiology of vascular remodelling and associated endothelial dysfunction is yet to be known.

Methods: Localization of ColIV in vessels was identified by immunohistochemistry staining. Presence of ColIV fragments in pulmonary arteries (PAs) was assessed with western blotting. Barrier integrity function and apoptosis on human pulmonary artery endothelial cells were elucidated by using ECIS and by flow cytometry, respectively.

Results: We identified increased gene expression of ColIV in small PAs in PH patients due to lung diseases compared to controls. Stainings localized ColIV to the intima and media layer of PAs. Protein analysis from isolated PAs identified the presence of ColIV fragments. Shorter fragments, which potentially contain an active sequence, were increased in PH patients. By using a synthesized peptide of that sequence, we observed a potent disruption of endothelial barrier function and induction of cell death, which is even more prominent when the endothelial barrier integrity is not yet fully established.

Conclusion: The increased presence of matrikine of ColIV in PH patients can contribute the associated endothelial dysfunction. Thus, matrikines of BM proteins may present new future therapeutic targets in the treatment of PH in lung diseases.
abstracts

P03

MiRNA34a levels in exosomes from human lung fibroblasts. A senescence model

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Background: Idiopathic pulmonary fibrosis (IPF) is a progressive pulmonary disease of unknown origin with a high mortality rate and limited treatment options. Fibroblasts are central to matrix homeostasis and thus critical for the development and progression of IPF. Cellular senescence plays an important, however, controversially discussed role in IPF for having both pro- and anti-fibrotic effects. Senescent lung fibroblasts have been reported to express increased amounts of miRNA34a, which has anti-fibrotic effects and promotes apoptosis in the cells that express it. However, nothing is known about the levels of miRNA34a in exosomes as providers of intercellular communication.

Methods: Proliferating (early passage) and senescent (late passage) human lung fibroblasts (LL47 (MADO) ATCC CCL-135) were cultured and the degree of senescence was quantified by β-galactosidase-expression. MiRNA34a was quantified in exosomes purified from the cell-culture media, and subjected to quality control using 2100-Bioanalyzer and Nanodrop analysis. MiRNA concentration was determined by qPCR. Fold changes in the expression level of miRNA34a and pre-RNA34a in exosomes from proliferating and senescent fibroblasts were compared using a two-sided student t-test.

Results: We validated our senescence model by showing strong β-galactosidase in senescent fibroblasts whilst proliferating fibroblasts were negative. Up-regulation of miRNA34a by senescent lung fibroblasts has previously been reported by others and we confirmed this in our system in which there was significantly more pre-miRNA34a in senescent fibroblasts than in proliferating fibroblasts (fold change = 1.95; p = 0.023). More importantly, miRNA34a was also significantly increased in exosomes purified from senescent fibroblast culture-fluid than from exosomes originating from proliferating fibroblast (fold change = 2.58; p = 0.002).

Conclusion: MiRNA34a concentrations are not only increased in senescent lung fibroblasts, but also in exosomes derived from them. This provides a potential mechanism for bystander apoptosis induced by human lung fibroblasts which, if confirmed, would have obvious implications for the pathogenesis of IPF.

P04

Targeting innate immunity exacerbates inflammation and pulmonary fibrosis in a systemic sclerosis-associated lung disease model

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Background: Systemic sclerosis (SSc) is a progressive fibrotic autoimmune disorder with frequent lung involvement that relates to poor outcome and increased mortality. The exact pathomechanisms are unknown, but a strong inflammatory component, including cytokines of the innate immune response, such as interleukin-1 (IL-1) or transforming growth factor β (TGFβ), have been associated with disease pathogenesis. We investigated the feasibility of anti-inflammatory/-fibrotic drugs targeting the innate immunity to treat the development of pulmonary vascular and interstitial remodelling in the Fra-2 transgenic (TG) mouse model of SSc.

Methods: Fra-2 TG and wild-type (WT) control mice were treated with the IL-1 receptor antagonist anakinra or the anti-fibrotic drug pirfenidone. Pulmonary fibrosis was assessed by determining lung function and collagen deposition. Inflammatory cell populations were measured in bronchoalveolar lavages and lung homogenates of treated and untreated WT and TG mice using flow cytometry and real-time PCR analysis of inflammatory mediators.

Results: Fra-2 TG mice treated with either anakinra or pirfenidone exhibited augmented collagen deposition, restrictive lung function and increased amounts of inflammatory cells in the lung. Both treatments shifted inflammation towards a Th2 predominant response: For example, anakinra significantly increased the expression of IL-4 and markers of pro-fibrotic, alternatively activated macrophages, e.g. Arg1, in Fra-2 TG mice, without affecting WT mice. Similarly, pirfenidone increased the amount of eosinophils and expression of Th2 cytokines and eosinophil chemoattractants in the lungs of TG mice.

Conclusion: Blockade of innate immunity cytokines, such as IL-1 or TGFβ, led to a shift towards Th2 inflammation and augmented collagen deposition in the lungs of Fra-2 TG mice, thereby worsening lung function. These findings have important clinical implications as they indicate that inappropriate anti-inflammatory/-fibrotic treatments may aggravate pulmonary fibrosis associated with systemic sclerosis.

P05

Adult pulmonary vascular remodeling is independent of ephrin-b2/EphB4 guidance system

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Background: Pathological vascular remodeling in pulmonary arterial hypertension patients is characterized by excessive coverage of pulmonary arteries by smooth muscle cells, termed muscularization. Deletion of vascular guidance molecule, ephrin-b2 in smooth muscle cells and pericytes leads...
were recorded in the national Alpha1 Lung Registry and monitored for their augmentation therapy. AAT level, genotype, disease progression and health-related quality of life were analysed.

Results: Among the 353 patients (57% male, 66% smokers any time) recorded in the Registry, 78% had a PiZZ genotype, 12% a PiSZ genotype and 10% patients had other genotypes. The average follow-up period of patients recorded was 5.1 years with a maximum time of 21 years. Patients treated with augmentation therapy showed a median AAT level of 83.5 mg/dL vs 59 mg/dL at baseline. In comparison, patients without augmentation treatment showed median AAT level of 27 mg/dL at baseline and 27.5 mg/dL at the end of follow-up period.

Post-bronchodilator FEV1 at baseline was 54.6% and 52.8% at the end of follow-up. Amount of patients on treatment experiencing exacerbations and a FEV1 35–50% (n=78) was 46%, and for patients with a FEV1 50–60% (n=47) it was 11% at end of follow-up.

Conclusion: AAT augmentation therapy ensures that the protective threshold of AAT serum levels are reached, slows the decline in FEV1, which is generally associated with a decreased number of exacerbations. Early diagnosis and treatment is important in preventing ongoing damage to lung and liver.

P07 | Fig. 1 Prevalences of chronic cough in male and female

P07 | Prevalence and characteristics of chronic cough in a general population study

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Background: Chronic cough impairs life quality and drives health care utilisation significantly. However, general population prevalence has been rarely reported. Aim of our study was to investigate the prevalence of chronic cough in a general population and to describe characteristics of these individuals.
Methods: The LEAD study is a longitudinal, observational, population-based cohort study of a random sample of >11,000 individuals aged 6 to 80 years stratified by age and sex. Chronic cough (coughing nearly every day and/or in the morning during the last 12 month independent of common cold for at least 3 month), smoking habit and sputum production was evaluated by questionnaire.

Results: Out of 11,387, chronic cough prevalence was 7.9% (n=900). Mean duration of chronic cough was 6.6±9.4 years. There was no gender predominance (mean prevalence in male 8.1%, in female 7.7%; p=0.57; Fig. 1). However, chronic cough increased with age in both sexes (p<0.001). From all participants with chronic cough 356 (39.6%) were current and 251 (27.9%) former smokers. 59.8% (n=538) reported increased sputum production.

Conclusion: In a well characterized general population sample, chronic cough is substantially prevalent both in men and female and lasts for many years. Thus, it seems that appropriate therapy is lacking and urgently needed.

Effect of intravenous iron (Ferinject®) on exercise capacity and quality of life of stable COPD patients

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Background: The repletion of iron improves exercise capacity and symptoms in patients with chronic heart failure. In COPD iron deficiency is found in up to 50% of patients, potentially contributes to reduced exercise capacity and is therefore a potential therapeutic target. The aim of this study was to estimate the positive effect of intravenous ferric carboxymaltose on exercise capacity and quality of life in patients with COPD.

Methods: We included stable COPD outpatients in this non-randomized, interrupted time series pilot trial with one pre-intervention measurement and one post intervention measurement. Inclusion criteria were FEV1%predicted between 30% and 80% as well as iron deficiency (ferritin level <100 μg/l or ferritin level between 100 and 299 μg/l with transferrin saturation <20%). Hemoglobin was required to be <15 g/dl. Patients with cardiac disease as well as inflammatory disease including acute exacerbation were excluded. Exercise capacity was assessed by the six-minute walking distance (6 MWD) as well as maximum oxygen uptake (VO2max) during symptom-limited cardiopulmonary exercise testing. Quality of life was measured using the Saint-George Respiratory Questionnaire (SGQR). Patients received a single intravenous administration of one gram of ferric carboxymaltose (Ferinject®). Pre versus post intervention data were compared using the paired T-test.

Results: 12 patients (67% male, 63±8 years, FEV1%predicted 44±14) were included and ten patients could be followed up. Mean ferritin and hemoglobin were 70±41 μg/l; 13.8±1.7 g/dl, respectively. One month after iron infusion 6 MWD increased by 54 (14 to 94) meters, p=0.014. VO2max increased by 1.9 (0.8 to 3) ml/kg/min, p=0.006. SGQR increased by 0.2 (0.09 to 0.3) points, p=0.002. FEV1 and hemoglobin were unchanged.

Conclusion: Intravenous iron was associated with improved exercise capacity and quality of life in stable COPD patients independent from hemoglobin. Our data provide an estimate for the sample size calculation of a larger randomized trial.

CLARA – COPD in Österreich (Austria) – Lebensqualität und Einschränkungen im Alltag – Quality of Life and Limitations in Daily Life

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Background: COPD patients suffer from respiratory symptoms and limitations in daily life. We aimed to characterize COPD outpatients regarding the impact of their disease on overall health, daily life, and perceived well-being.

Methods: A national, multicentre, cross-sectional study was conducted in offices of pulmonologists and general practitioners. The St. George’s Respiratory Questionnaire for COPD patients (SGRQ-C) was used. Inclusion criteria were spirometrically defined COPD and age ≥40 years. Subjects with a history of lung surgery, lung cancer or a last four weeks COPD exacerbation were excluded.

Results: 67 pulmonologists and 6 general practitioners participated and collected data from 1,175 COPD patients; of those 77 were excluded due to missing data, and 248 patients were found unobstructed (FEV1/FVC ≥0.7). Finally, 850 patients (62.8% men; mean age 66.2±8.3 (SE) years; mean FEV1%pred. 51.5±6.6 (SE) were analysed. 55.4% had at least one exacerbation in the last year, and 12.5% were therefore hospitalised. 50.3% reported not being able to do any sports and only 21.3% stated that their chest symptoms allow them doing anything they would like to do.

Conclusion: In Austria, COPD patients are strongly symptomatic and experience grave limitations in daily life due to their disease.
Microvascular coronary perfusion and hyperinflation in COPD – data from the LEAD (Lung, hEart, sociAl, boDy) study

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Background: The subendocardial viability ratio (SEVR), a novel surrogate for microvascular coronary perfusion, is strongly determined by left ventricular diastolic function. Diastolic dysfunction is a common finding in COPD and might be explained by lung hyperinflation. So far, no study investigated the role of SEVR in COPD and assessed a potential association to hyperinflation. We aimed to conduct the non-invasive assessment of microvascular coronary perfusion in patients with COPD and to investigate a potential association to hyperinflation.

Methods: We analysed participants from the population-based Austrian LEAD study aged 40–80 years. Patients were identified via the previous diagnosis of COPD. Controls were characterized by the absence of COPD and/or asthma. SEVR was assessed via applanation tonometry at the radial artery. We quantified airflow limitation by FEV1 on spirometry. Hyperinflation was measured via the ratio of residual volume to total lung capacity (RV\%TLC) on bodyplethysmography.

Results: From the entire LEAD cohort (n = 11,423) we analysed 421 patients with COPD (age 62 ± 10 years, male 48.2%) and 5,192 controls without obstructive airway disease (age 58 ± 10 years, male 46.8%). SEVR was significantly lower in COPD patients than controls (149.2 ± 29.6 versus 156.4 ± 29.4, p = 0.000) even when considering effects of age and gender. In our study sample we did not find an association between SEVR and FEV1. However, in the multivariate analysis we found a significant inverse correlation between SEVR and RV\%TLC (r = –0.266, p = 0.000).

Conclusion: Microvascular coronary perfusion is significantly reduced in COPD and is associated with the amount of hyperinflation.
Results: 265 patients (male 66%, mean age 67 years) with moderate and very severe COPD (GOLD 2–4: 96.2%) and persistent symptoms (GOLD B: 62.3%, GOLD D: 34%) according to GOLD report 2018 were included. Lung function parameters (FEV1, FVC and MEF50; \( p < 0.001 \)) and symptoms (cough, sputum and shortness of breath; \( p < 0.001 \)) improved significantly in comparison to baseline.

A clinically relevant improvement of the CAT score was observed after 12 weeks in COPD patients with symptom severity GOLD B (from 22.1 to 16 points; \( p < 0.001 \)) and GOLD D (from 25.5 to 19.3 points; \( p < 0.001 \)). 96.2% of the patients were satisfied with BDP/FF/G and 95% of the patients wished to continue treatment. 18 adverse reactions were reported, of which three were serious, but not drug-related.

Conclusion: The results demonstrate the safety and efficacy of BDP/FF/G in COPD patients in a real-world setting with an improvement in lung function and symptom control, a reduction of COPD symptoms and a high treatment satisfaction perceived by the patients.

Benralizumab is effective in Austrian severe eosinophilic asthma patients: preliminary real-life data

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Background: Benralizumab is a monoclonal interleukin-5-receptor antibody that has shown efficacy and safety in patients with severe eosinophilic asthma (SEA) in randomized controlled trials (RCTs). Patients included in RCTs are not representative of real-life patients. There is little real-life data of asthmatics receiving Benralizumab. The objective of this study is to investigate the effectiveness of Benralizumab in Austrian real-life SEA patients.

Methods: So far 45 adult SEA patients eligible for anti-eosinophilic monoclonal antibody therapy based on current global initiative for asthma (GINA) guidelines from our severe asthma clinic received Benralizumab 30 mg s.c. every 4 weeks for the first 3 doses and afterwards every 8 weeks. Data are collected at baseline, 24 hours and 7 days after the first treatment and at every subsequent treatment.

Results: There was a highly significant \( (p < 0.001) \) reduction in peripheral blood eosinophils already 24 hours after the first treatment. Asthma control as measured by the asthma control test (ACT) and the asthma control questionnaire (ACQ6) improved significantly and rapidly (both \( p < 0.001 \) 4 weeks after the first treatment). This improvement in asthma control was sustained through all visits. Forced expiratory volume in 1 second (FEV1) significantly improved already after 7 days (\( p < 0.05 \)) although some patients already showed an impressive FEV1 increase after 24 hours. The FEV1 improvement remained significant through most visits. No severe adverse events occurred.

Conclusion: Benralizumab is effective in Austrian SEA patients. These preliminary results support the use of Benralizumab in SEA patients eligible for anti-eosinophilic monoclonal antibody therapy.

The German Severe Asthma Registry: FeNO values correlate with medical therapy, quality of life and smoking

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FeNO as a marker of airway inflammation lacks large-scale validation for severe asthma. This study aims to elucidate correlations of FeNO with medical therapy, quality of life and smoking in the population of the German Severe Asthma Registry including ≤ 8 year follow-ups of 1340 patients (49 ± 17 yrs., 58 % female, FEV1 2.07 ± 0.82 L).

Medical therapy included ICS+LABA+LAMA in 1283 and oral steroids (OCS) in 905 of 2582 appointments.

Patients depending on OCS had significantly higher baseline FeNO (52 ± 49 ppb; \( n = 448 \)) than without OCS (40 ± 37 ppb; \( n = 694; \) \( p < 0.0001 \)). Therapy with low-moderate ICS-dose was associated with significantly higher FeNO compared to high-dose ICS (47 ± 44 ppb; \( n = 713 \) vs. 41 ± 39 ppb; \( n = 287; \) \( p = 0.03 \)).

Omalizumab treatment leads to reduction in FeNO (therapy start: 43 ± 40 ppb; \( n = 181 \)) in ≥ 3 yearly follow-up (29 ± 23 ppb; \( n = 47; \) \( p = 0.001 \)).

As expected patients reaching asthma control (ACQ < 1.5: 35 ± 30 ppb; \( n = 429 \)) showed significantly lower FeNO than uncontrolled patients (49 ± 50 ppb; \( n = 470; \) \( p < 0.0001 \)). High FeNO levels were also associated with lower FEV1 (FEV1 > 80%: 39 ± 37 ppb; \( n = 349 \) vs. FEV1 < 40%: 56 ± 60 ppb; \( n = 118; \) \( p = 0.004 \)) and with blood eosinophilia (≥ 300 cells/µL: 57 ± 46 ppb; \( n = 272 \) vs. < 300 cells/µL: 37 ± 36 ppb; \( n = 580; \) \( p = 0.0008 \)).

Current smokers had significantly lower FeNO (24 ± 22 ppb; \( n = 30 \)) than exsmokers (41 ± 40 ppb; \( n = 442; \) \( p = 0.0004 \)), and non-smokers had the highest FeNO (50 ± 46 ppb; \( n = 470; \) \( p < 0.0001 \)).

Conclusion: In this carefully selected severe asthma cohort, increased FeNO levels are associated with OCS-dependency, eligibility for biologics-therapy, lower FEV1, higher blood eosinophils, lower ICS-doses and lower asthma control, as well as never smoking status.
Discordance of asthma therapy with the new GINA Guideline 2019: real world data from the LEAD Study

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Background: The new GINA guidelines 2019 provide a drastic change in treatment of mild asthma. Therapy with short acting beta agonists (SABA) are no longer recommended. “SABA-only-users” should be changed to as-needed inhalative corticosteroid (ICS) and long acting beta agonist (LABA). We were wondering how many current asthmatics may need a treatment change with this novel recommendation.

Methods: The LEAD study is a longitudinal, population-based Austrian cohort study, consisting of 11423 randomly recruited male and female, aged 6-80 years. We derived data from participants with current doctor’s diagnosed asthma for the analysis of their recorded therapy.

Results: 1028 participants (45.7% male, mean age 44.6) had an ever diagnosis of asthma. Current asthma (CA) was reported in 572 patients (45.8% male, mean age 46.9). Of these, asthma control by the asthma control test (ACT, n=433) was good (>20 points) in 72.7% and rather good (>15 <20 points) in 18.7% and 8.5% were uncontrolled (<15 points). In CA, 26.1% (n=149) of the patients were using short acting bronchodilators (SABA 14.2% or SABA/SAMA 12.2%) as reliefer therapy. Short acting bronchodilators only were used by 10%, ICS only by 9.3% of the CA population (former GINA step 1 therapy). 31% used ICS/LABA, and 7.2% LAMA (GINA step 2 or higher). Nearly half of the patients (47.6%) used no therapy at all.

Conclusion: According to our real life data, we found an urgent therapy change from SABA only to ICS combination (as needed) in 10% of current asthma patients; in total, in 26% of current asthma the SABA reliever therapy has to be abandoned.

Use of nebulized saline solutions in theory and practice

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Background: The nebulization of isotonic and hypertonic saline solutions (IS/HS) is recommended in guidelines as a supportive therapy for various respiratory diseases. Whereas HS (3-7%) is used more frequently to mobilize mucus in serious diseases like cystic fibrosis or bronchiectasis, IS is mainly mentioned in respiratory physiotherapy. The aim of the survey was to query the actual use of IS/HS and to compare it with the current German and European therapy guidelines.

Methods: In 2000 PARI saline solution packs, a flyer with QR code was enclosed, leading to an online questionnaire with 25 questions. In total, 807 users/parents (age: 0.1-85y) finalized the questionnaire across Germany.

Results: Respondents (RP) inhaled most frequently IS (70%), followed by 3% HS (20%) and 6% HS (10%). Cough/bronchitis were the main reasons for the inhalation therapy (81% for IS, 75% for 3% HS and 59% for 6% HS). This common therapeutic approach is not yet sufficiently reflected in guidelines. IS was used by 52% of RP for humidification and/or for prevention (25%) and less often for the treatment of serious diseases (20%). By contrast, 33%/50% of RP used 3%/6% HS in serious diseases in accordance with the therapy guidelines. Nearly 50% of RP used IS/HS for more than half a year. The self-assessment of tolerability showed that 99% of RP rated IS as “good”, “very good” or “excellent”, as did 98% the 3% HS and 91% the 6% HS. A reduction in symptoms was noted by 96% of IS, 95% of 3% HS and 94% of 6% HS users. A high portion of users (IS: 97%; 3% HS: 89%; 6% HS: 91%) wanted to continue the nebulization with the chosen inhalation solution “probably” or “definitely”.

Conclusion: According to this user survey, the nebulization of IS/HS in certain indications and in this frequency is not yet represented appropriately in all respiratory therapy guidelines reviewed here.

Prevalence and risk factors of abnormal lung function at different age bins through life in the general population

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Background: Abnormal lung function predicts cardio-respiratory mortality but how different associated factors vary and interact through life is unclear.

Methods: We investigated the prevalence of abnormal lung function and its interaction with a large number of potentially associated factors (n=55) in 11,423 individuals (aged 6-82 years) recruited into the LEAD Study, an observational, population-based cohort in Austria.

Results: We found that: (1) the prevalence of abnormal lung function, identified either by pre-bronchodilator FEV1/FVC < the lower limit of normal (LLN) or FEV1 < LLN, ranged from 4.5% to 8.8%, increased with age and is reduced after bronchodilation;
and, (2) there are many factors associated with abnormal lung function, which change, interact and accumulate through life.

**Conclusion:** Abnormal lung function in the general population is not rare, even in the youngest age bins. Factors associated with abnormal lung function are dynamic (i.e. they change with time), are inter-related, accumulate over a life-time. Importantly, some of them may be amenable to preventive interventions.

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**P18**

Outpatient pulmonary rehabilitation in Austria

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**Background:** Outpatient pulmonary rehabilitation (OPR) is a novel nonpharmacological therapeutic option for pulmonary patients in Austria. We wanted to elucidate the effects of WHO Phase II and III OPR in a real-world setting.

**Methods:** 294 consecutive patients, 121 WHO Phase II and 173 WHO Phase III (56% COPD, 13% Asthma, 31% other) were included in this prospective multicenter (Graz, Innsbruck, Vienna, Wels) interventional trial. They underwent a multidisciplinary OPR. Primary endpoint was the improvement in 6-minute walking test (6MWT).

**Results:** 6MWT improved from 461±11.9 to 494±12.4 m (+33 m, P<0.001), in asthmatics +26 m, in COPD +36 m, MCID +14–30 m) in Phase II. Additional Phase III OPR led to a further increase of 20.4 m, P<0.05. Watt max increased from 81.5±3.9 to 86.9±4.6 W (+5.4 W, P<0.001, MCID +4 W) and additionally +5.7 W in Phase III, Sit to stand test from 21.8±0.8 to 26.3±0.9

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**Retrospective evaluation of pulmonary rehabilitation outcome parameters in 2595 consecutive patients – a single center experience**

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**Background:** Pulmonary rehabilitation (PR) has become an essential part in the management of COPD and other chronic respiratory diseases, supported by growing evidence about its efficacy. In an extension of a former study evaluating first year results, we now report on the assessment of pulmonary rehabilitation outcome parameters collected within 44 months at the "Rehaklinik Enns", a PR center in close cooperation with a tertiary care university hospital.

**Methods:** Patients attended an individually tailored three-week in-patient PR program according to the 2013 ATS/ERS guidelines between June 2015 and January 2019. Spirometry, a 6-minute walk test (6MWT) and a COPD assessment test (CAT) were performed at the beginning and the end of the program. Changes were compared to the validated minimal clinically important difference (MCID). Additionally the smoking cessation rate and its association with outcome parameters were analyzed.

**Results:** Among 2595 patients (mean age 61.9 y, 42.9% female) the most frequent diagnosis was COPD (64.1%), followed by asthma (13.5%), lung cancer (5.9%) and pulmonary embolism (2.7%). An increase in 6MWT above the MCID of 30 meters was observed in 51.8% of all patients. Greater benefits were seen in younger patients. A reduction in CAT score of at least the MCID of 2 points was evident in 74.4% of all patients. There were no differences for sex or baseline smoking status concerning 6MWT or CAT changes. Of a total of 639 current smokers 166 (26.0%) stopped smoking at the end of PR, independent of age or sex. Successful cessation resulted in a greater increase in 6MWT (41.4 m vs. 30.1 m).

**Conclusion:** PR showed beneficial effects irrespective of the entity and severity of pulmonary disease, sex and age. Patients who accomplished smoking cessation during PR had a greater 6MWT improvement than those who did not.
Development and implementation of a management tool for a pulmonary rehabilitation concept based on the International Classification of Functioning, Disability and Health

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Increasing prevalence, morbidity and mortality in COPD have so far become a heavy socio-economic burden as well as a demanding challenge for health systems and medical professionals working in multi-professional teams. Smoking is the primary reason for the development and progression of this irreversible chronic disease. The diversity of COPD symptoms and frequent multi-morbidity require an integrative approach focusing on the individual patient in order to optimize treatment and self-management of the disease. This aims at improving the individual’s quality of life, at avoiding hospitalization as well as the need for care, and at maintaining the ability to work, which eventually leads to a reduction of primary and secondary costs for the health systems. The present master thesis intends to answer the research question if – by using an ICF-based assessment tool that integrates a bio-psycho-social approach – the pulmonary rehabilitation of severe COPD patients leads to a higher-quality outcome than it has been possible so far with the use of non-ICF assessment tools. In order to carry out an empirically led pilot study based on the ICF-Core-Sets for obstructive lung diseases the author has developed a questionnaire in the design of a Pre-Post-test method following the principals of haphazard sampling. Fifty patients in the severe and very severe stage of COPD have been included in the process of a participation-oriented qualitative analysis. In the Pre-Post-test comparison the items in the components „activity/participation” and „body function” have improved significantly, which verifies the hypothesis. Consequently an ICF-based tool can represent personal situations more precisely than the established assessment methods. This enables patients and medical professionals to more specifically define the therapy aims and to individually adapt therapy programs in pulmonary rehabilitation.

Das Rauchfrei Ticket – the direct link to professional tobacco cessation and relapse prevention on the Rauchfrei Telefon

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Background: Tobacco cessation is an important intervention for prevention and therapy of various diseases, especially concerning lung health. There are effective and evidence based offers throughout Austria, which are available and often cost free. Still—many smokers do not seek professional support for cessation or know about those offers. Addressing smokers to stopp and directly connect them to a support offer when seeing them in a mural or extramural setting can improve the abstinence rates.

Methods: To ask the smoking behaviour, to advice the stopp and to instantly connect to an evidence based offer is a very good strategy to support smokers on their way to exit the nicotine addiction. The strategy is efficient and only little time consuming.

The “Rauchfrei Ticket” offers this possibility. Smokers and ex-smokers can be registered directly at the quitline (Rauchfrei Telefon)—via fax,san, mail or online.

The Rauchfrei Team, all health psychologists with education in tobacco cessation call back, once the patient is registered at the quitline for a counselling either for cessation or for relapse prevention. If the telephone is not the suiting medium for the Rauchfrei Telefon informs about cessation services all over Austria.

Results: This cooperation is helpful for all involved parties. Health professionals appreciate the possibility to assign their patients to a tobacco cessation program. For smokers and ex-smokers it is easier to make use of support, when proposed and connected by their trusted health professional. The Rauchfrei Telefon reaches about 80% of those patients, registered via “Rauchfrei Ticket”. In 2018 about 700 patients were registered by health professionals at the Rauchfrei Telefon.

Conclusions: Tobacco cessation is easier with professional help. In order to get smokers and ex-smokers, who would not seek support, into treatment, the Rauchfrei Ticket has proven efficient and available.

The prevalence of restrictive lung function in a general population obtained by spirometry and bodyplethysmography – Data from the LEAD study

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Background: Published prevalence data on restrictive lung function (RLF) in the general population vary widely from 5–20% and are obtained by spirometry only. Therefore, the aim of our study was to determine the prevalence and severity of RLF in a general population according to both spirometric and bodyplethysmographic excepted equations.

Methods: Data was obtained from the Austrian LEAD Study, a longitudinal, observational, population-based cohort study. In total, 9998 participants (46.6% male) were included in
this analysis. rLF was defined spirometrically by FEV1/FVC > Lower Limit of normal (LLN) and FVC<LLN and bodyplethysmographically by TLC<LLN. Severity of rLF was defined as mild (>80%pred), moderate (40–60%pred) and severe (<40%pred).

Results: Overall, the prevalence of rLF by spirometric criteria is 3.4% (N=337) and by bodyplethysmographic criteria 0.9% (N=85; p<0.001). rLF is more prevalent in male vs. female (1.6 vs 0.2; p<0.001; Table 1) and independent of age, although no rLF was found in age <18 years. Nearly all rLF were mild, independently from the parameter used (FVC% or TLC%), which both are highly correlated (R=0.6, p<0.001).

Conclusion: The prevalence of rLF in our general population is significantly less than previously reported; especially when bodyplethysmographic criteria are applied. Therefore, existing prevalence data on rLF may be interpreted with caution and should be validated by bodyplethysmography in the future.
Therapy line and associated predictors of response to PD-1/PD-L1 inhibitor monotherapy in advanced NSCLC – a retrospective bi-centric cohort study

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Background: Evidence on the efficacy of PD-1/PD-L1-directed immune checkpoint inhibitor (ICI) therapies for advanced non-small cell lung cancer (NSCLC) is mainly based on clinical trials in first- or second line settings. We aimed to investigate response and prognostic factors with special regard to third or later line therapy.

Methods: We retrospectively analyzed all patients having received ICI monotherapy with nivolumab, pembrolizumab or atezolizumab for advanced NSCLC at the two study sites in Linz and Salzburg. Computed tomography evaluations were analyzed using response evaluation criteria in solid tumors (RECIST, version 1.1). Kaplan-Meier analyses were conducted to calculate progression-free (PFS) and overall survival (OS), the impact of influencing variables was evaluated using uni- and multivariate Cox-regression analyses.

Results: Among 153 patients (59% men, mean age 66 years), median PFS was 4 months (M; 95% confidence interval (95%CI) 3,5), OS was 13M (10,17) and objective response rate (ORR) was 22%. In multivariate analyses among all patients, PFS was significantly influenced by PD-L1 expression (p=0.002) and
ECOG performance status \( (p = 0.029) \), for OS only therapy line \( (p = 0.025) \) had significant impact. Therapy line \( \geq 3 \) was associated with significantly inferior PFS \( (p = 0.003) \) and OS \( (p = 0.001) \).

In first line therapy PFS, OS and ORR were 7M (3,11), 17M (9, not evaluable—n. e.) and 36%, in second line 4M (3,7), 18M (13, n. e.) and 19% and in \( \geq 3 \) third line 2M (1,3), 9M (4,12) and 13%. PFS was significantly influenced by PD-L1 expression in first line therapy \( (p = 0.006) \), while there were no significant findings for second line. In 23rd line three line PFS performance status significantly affected PFS and OS (both \( p < 0.001 \)).

Conclusions: Third or later line single-agent anti-PD-1/ PD-L1 therapy is less efficacious as compared to first- and second-line treatment. In that setting, ECOG performance status predominates known predictors like PD-L1 expression or presence of an alteration in EGFR or ALK.

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EGFR, EML4-ALK, ROS 1 and BRAF testing in Austrian patients with NSCLC

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Background: Targeted therapy is becoming increasingly important in lung cancer and has improved the overall survival for patients with NSCLC. EGFR and BRAF mutations, EML4-ALK and ROS1 fusions are currently available targets. The aim of the study was to evaluate these molecular alterations in a large sample of Austrian patients with NSCLC.

Methods: Tumor tissue of patients with histologically confirmed adenocarcinoma or NSCLC NOS excluding squamous cell carcinoma and neuroendocrine carcinoma from 4 hospitals in Austria were routinely analyzed independent of the tumor stage and clinical characteristics for molecular alterations (reflex testing). EGFR- and BRAF-Mutations were detected using quantitative Real Time PCR assays (cobas\(^\text{®}\), Roche). Targeted ALK Fusions were detected by Immunohistochemistry (IHC) (Ventana anti ALK (D5F3), positive or not clearly interpretable cases were further tested by RT-qPCR (AmoyDx\(^\text{®}\)). For ROS1 fusion IHC-screening with ROS1 D4-D6-antibody was followed in stained cases by RT-qPCR (AmoyDx\(^\text{®}\)) or FISH ROS1 break-apart probe (Zyto Vision\(^\text{®}\)) for confirmation.

Results: Since January 2011 3922 patients were analyzed for EGFR mutation which was found positive in 488 patients (12.4% of total samples). 428 patients (10.9%) carried an activated mutation (Exon Del 19 and Exon 21 L858R). Since August 2011 2970 patients were tested for EML4-ALK and positive IHC staining was found in 180 patients (6.1%). Out of 332 not clearly interpretable IHC tests only 7 were positive in PCR testing. 1816 patients were screened for ROS1 fusion with IHC beginning in January 2014. In only 6 (0.3%) patients ROS-1 fusion could be confirmed. Out of 300 tested cases for BRAF mutation 8 were positive (2.6%).

Conclusion: Frequency of EGFR (12.4%), EML4-ALK (6.1%), ROS1 (0.3%) and BRAF (2.6%) in a large sample of Austrian patients with NSCLC was quite similar to other Caucasian subgroups. Consequently, we recommend reflex testing independent of any clinical characterization.

P25

Sensitive diagnostic of a pleural carcinosis based on ctDNA in pleura effusion of melanoma patients – A system for companion diagnostic for BRAF

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Background: The sensitivity of conventional immunocyto-chemical analysis of pleural effusions for the diagnosis of pleural carcinosis is only 10-65%. The diagnostic based on circulating tumor DNA (ctDNA), which can be detected in pleura effusion, similar to the blood-based liquid biopsy test could show an increased sensitivity and the detection of actionable gene alterations, making targeted therapy possible. The test could be used as companion diagnostic (CDx).

BRAF-V600 mutation occurs in about 50% of malignant melanoma and serves as actionable mutation for BRAF/MEK-inhibitor-therapy.

Therefore BRAF-V600 appears to be an ideal indicator gene-alteration.

Methods: For the test a fully automated PCR system which detects semiquantitative V600E/E2/F600K/R/M-mutations in codon 600 of BRAF-gene, was used.

From a mixture of 200 µl pleural effusion and 800 µl PAX—puffer, 1ul was used for PCR analysis.

Results: Two patients with melanoma and known BRAF V600 mutation of primary tumor, were extracted ct-DNA from pleura effusion. In both cases a BRAF V600 mutation could be detected despite a negative immunocytology. Pleuracarcinosis was approved by VATS. After BRAF/MEK inhibitor-therapy both patients are in complete remission (15 and 11 months).

Conclusion: Detection of indicator gene-lesion based on ctDNA of pleural effusion could increase the sensitivity for the diagnosis of pleural carcinosis. Moreover it could be used for CDx prior to targeted therapy.

A clinical study addressing this question is initiated.
P26

Delay to surgical treatment in lung cancer patients and its impact on survival

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Background: Outcome in early stage lung cancer might be influenced by the preoperative delay between first radiologic examination and surgical resection. Herein we aim to analyse the impact of the preoperative delay on survival in lung cancer patients.

Methods: The institutional database was queried to identify patients with primary lung cancer who were treated with primary surgery. Time intervals were defined as date of first suspicious medical imaging until date of surgical treatment. All patients received PET-CT staging and tissue confirmation prior to treatment planning in a multidisciplinary tumour board. Patients with unknown date of first contact, follow-up CT scans of pulmonary nodules, or neoadjuvant therapy were excluded. In total, 287 patients treated between 2009 and 2017 were included for further analysis.

Results: Median time between first suspicious medical imaging and surgical therapy was 62 days (range 23–120) and did not differ between male and female patients. Patients were then classified into two groups according to the duration of the medical work-up: group A up to 60 days and group B from 61 to 120 days. Clinical T- and N- stages were comparable between the groups. Overall survival did show trends for improved survival in group A, however failed to reach statistical significance. In the subgroup of cT2 tumours (87 patients, no difference in comorbidities and nodal status between group A and B), there was a significant survival benefit for patients in group A (p = 0.043).

Conclusion: Delay between diagnosis and treatment of lung cancer may result in dismal outcome. Efforts need to focus on improving and streamlining patient pathways to shorten the delay until surgical treatment to a minimum. Process improvement might be achieved by stringent interdisciplinary work-up and a patient-centred approach.

P27

Favorable long-term survival after palliative resection for a giant primary rib osteosarcoma with severe mediastinal shifting

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Background: Osteosarcoma is the most common malignancy of the bone with high morbidity and mortality. Treatment of choice is chemotherapy (CHT) followed by surgery and adjuvant CHT. Primary rib osteosarcoma is a rare disease. We present a case of a young patient with a giant primary rib osteosarcoma undergoing palliative resection.

Methods: A 29-year-old woman presented with dyspnea and pain in the left chest wall in August 2012. Computed tomography (CT) showed a large lesion destructing the 3rd left rib with extension to the left upper lobe. Biopsy revealed an osteoplastic OS and staging examinations showed no distant metastases (DM).

Results: CHT by the EURAMOS-1-protocol was started but the patient refused any further treatment after 1 cycle due to side effects. 1.5 years later, CT scan showed a major tumor progression with severe mediastinal shifting and total atelectasis of the left lung. Due to the extreme large tumor size and lack of treatment alternatives, surgery in palliative intent was the only option. A complete resection of the tumor including chest-wall reconstruction was performed. The postoperative course was challenging, but she recovered well and was discharged after several months with no evidence of disease. Thereafter, the patient again refused any further treatment and checkups. 4.5 years later she presented again with local recurrence in the left chest wall and in excellent overall condition without evidence for DM. Accordingly, a re-thoracotomy, partial resection of ribs 6–9, left diaphragm and pericardium and reconstruction were performed. The postoperative course was without complications and the surgery was well-tolerated.

Conclusion: This case report shows an unexpected favorable outcome after palliative resection for a giant primary rib OS with severe mediastinal shifting. Currently, 7 years after diagnosis, the patient is free from disease.

P28

Respiratory symptoms prevalence and spirometric changes among non-smoker male wood workers

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Background: Occupational lung disease comprises a broad spectrum of disorders as a result of inhalation or ingestion of noxious chemicals or dust particles. Prolong unprotected inhalation of wood smoke leads to series of respiratory symptoms including nasal congestion, cough, chest tightness and wheezing, on the other hand wide-ranging chemicals, including cellulose, hemicelluloses, lignin as well as extraneous materials may result in respiratory health challenges.

Methods: Two hundred seventy-six, non-smoker male wood workers and equal number of non-smoker male office worker, referred to pulmonology clinic included in this study. Evaluation of study participants included completion of a questionnaire regarding respiratory symptoms and baseline spirometry was measured according to the actual recommendations.

Results: Respiratory symptoms including cough, phlegm, chest tightness, and wheezing were significantly higher in wood workers than office workers (40.2% versus 29.3%) for...
Methods: HRCT scans of 128 subsequent patients (mean age 65 years, 65% male) discussed by the local ILD board were reviewed and scored by an expert ILD radiologist, creating a semi-quantitative mapping of HRCT findings: Each lung was divided into three equally large portions defined by the maximum cranio-caudal diameter, each part was subdivided into a subpleural (<10 mm within the pleura), central and peripheral area (separated by half distance hilus-supleural space). Standardized patterns included noduli, reticulation, honeycombing, ground glass, consolidations, emphysema, bronchiectasis, visual signs of volume reduction and pulmonary hypertension (pulmonary artery/aorta ≥1). Using the Akaike information criterion, cut-off values for each semi-quantified HRCT finding were created regarding FVC and DLCO. Multivariate stepwise regression-analyses were used to evaluate the predictive value of HRCT findings on FVC and DLCO.

Results: FVC was significantly determined by the extent of bronchiectasis ($F = 8.25; p < 0.001$) and consolidations ($F = 6.53; p = 0.012$). Including age and sex into the model, bronchiectasis remained the only significant HRCT variable ($F = 11.49; p < 0.001$), next to age ($F = 10.43; p = 0.001$). DLCO was significantly influenced by the extent of emphysema ($F = 16.27; p < 0.001$), reticulation ($F = 4.99; p = 0.008$), bronchiectasis ($F = 3.61; p = 0.016$) and signs of pulmonary hypertension ($F = 5.34; p = 0.023$). Age and sex did not have significant implications on the DLCO model.

Conclusion: FVC was found to be mainly determined by the extent of bronchiectasis and age, while emphysema, reticulation, bronchiectasis and signs of pulmonary hypertension predicted DLCO.

Standardized semi-quantitative computed tomography findings and associated changes in FVC and DLCO in a real-life cohort of interstitial lung disease patients

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Background: Forced Vital Capacity (FVC) and Diffusion Capacity for Carbon Monoxide (DLCO) are standard parameters used to measure functional impairment in interstitial lung diseases (ILD). Both correlate with disease severity and mortality and can be used to assess disease progression. Still, it is largely unknown which exact features routinely described in high-resolution computed tomography (HRCT) chest scans determine those functional alterations.

Methods: HRCT scans of 128 subsequent patients (mean age 65 years, 65% male) discussed by the local ILD board were reviewed and scored by an expert ILD radiologist, creating a semi-quantitative mapping of HRCT findings: Each lung was divided into three equally large portions defined by the maximum cranio-caudal diameter, each part was subdivided into a subpleural (<10 mm within the pleura), central and peripheral area (separated by half distance hilus-supleural space). Standardized patterns included noduli, reticulation, honeycombing, ground glass, consolidations, emphysema, bronchiectasis, visual signs of volume reduction and pulmonary hypertension (pulmonary artery/aorta ≥1). Using the Akaike information criterion, cut-off values for each semi-quantified HRCT finding were created regarding FVC and DLCO. Multivariate stepwise regression-analyses were used to evaluate the predictive value of HRCT findings on FVC and DLCO.

Results: FVC was significantly determined by the extent of bronchiectasis ($F = 8.25; p < 0.001$) and consolidations ($F = 6.53; p = 0.012$). Including age and sex into the model, bronchiectasis remained the only significant HRCT variable ($F = 11.49; p < 0.001$), next to age ($F = 10.43; p = 0.001$). DLCO was significantly influenced by the extent of emphysema ($F = 16.27; p < 0.001$), reticulation ($F = 4.99; p = 0.008$), bronchiectasis ($F = 3.61; p = 0.016$) and signs of pulmonary hypertension ($F = 5.34; p = 0.023$). Age and sex did not have significant implications on the DLCO model.

Conclusion: FVC was found to be mainly determined by the extent of bronchiectasis and age, while emphysema, reticulation, bronchiectasis and signs of pulmonary hypertension predicted DLCO.

Prognostic significance of the Shock Index in patients with hemodynamically unstable pulmonary embolism

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Background: The shock index (SI), defined as the ratio between heart rate and blood pressure, has a prognostic sig-
nificance in relation to inhospital mortality in patients with pulmonary embolism.

Methods: Our retrospective study included 63 patients with previously diagnosed hemodynamically unstable PE who were treated at the Institute of Pulmonary Diseases of Vojo-
dina, Sremska Kamenica. Sex, age, SI (heart rate/systolic blood
pressure), the Early Warning Score (EWS) and the Modified
Early Warning Score (MEWS), risk factors for fatal outcome
(obesity via BMI (Body Mass Index), hypotension, tachycardia,
and long-term smoking), the outcome of treatment, the indi-
vidual variables of the EWS and MEWS score systems, and
the prognostic significance of the SI and EWS and MEWS scoring
systems were analyzed. A comparison of values of numeri-
cal features between the two groups was carried out using the
Student’s t-test. Testing the difference in the frequency of the
attributes was done using the χ2 test. In order to investigate the
connection between two or more features, or to generate ade-
quate statistical models, univariate and multivariate regression
analysis were used. Values of significance level p < 0.05 are con-
sidered statistically significant.

Results: The positive prognostic value of the Shock Index
against the outcome of treatment has not been established.

Conclusion: The Shock Index according to the results of
our study, has no prognostic significance in relation to the
death outcome. However, there are significantly more deceased
patients at high risk according to the MEWS score system.

Real-world clinical management of CTEPH
patients – a single center experience

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Background: The gold-standard therapy for patients with
chronic thromboembolic pulmonary hypertension (CTEPH)
is pulmonary endarterectomy (PEA). For inoperable patients
medical treatment and balloon pulmonary angioplasty (BPA)
should be considered. According to international registry stud-
ies around 60% of CTEPH patients undergo PEA, however, the
number of subjects not enrolled in registry studies is unknown.

Methods: In this retrospective single-center study we
assessed all patients diagnosed with CTEPH at the Medical Uni-
versity of Graz between 2002 and 2018. We stratified patients
according to their clinical management based on the anatomical
distribution of obstructive lesions, pulmonary hemodynamics,
comorbidities and patients’ preferences. Four major clinical
groups were defined: patients undergoing PEA after complete
evaluation (E-PEA), patients not eligible for PEA after complete
evaluation (E-noPEA), patients refusing PEA (NE-REF) and
patients with unfavorable risk-benefit ratio for PEA based on
non-surgical evaluation (NE-RB).

Results: We included n = 75 patients (age: 63 ± 15 yr, males:
55%). Out of these, n = 45 (60%) were evaluated for PEA (E-PEA:
n = 24 (32%), E-noPEA: n = 21 (28%)). Thirty (40%) patients did
not undergo surgical evaluation for PEA (NE-REF: n = 11 (15%),
NE-RB: n = 17 (23%), no information: n = 2 (3%)). The patients
not considered for referral to the surgical center were signifi-
cantly older (E-PEA: 55 ± 16 yr, E-noPEA: 59 ± 16 yr, NE-REF:
66 ± 9 yr, NE-REF: 74 ± 9 yr), had the highest number of cardiopul-
monary comorbidities (E-PEA: 0.9, E-noPEA: 1.5, NE-REF: 1.1,
NE-RB: 1.8), the lowest 6-minute walk test (E-PEA: 373 ± 113,
E-noPEA: 345 ± 98, NE-REF: 327 ± 136, NE-REF: 260 ± 117) and the
poorest 3-year survival (E-PEA: 88%, E-noPEA: 81%, NE-REF:
91%, NE-RB: 53%).

Conclusion: In a real-world setting, the number of CTEPH
patients who are not referred to a surgical center for PEA is sub-
stantial and may have been underestimated in previous PEA
registries. The main reasons for no referral are patients’ refusal
and poor risk/benefit ratio after non-surgical evaluation due to
old age, comorbidities, and poor physical capacity.

Sjögren syndrome and pulmonary vascular
disease (PVD) – Results from a prospective cross-sectional study

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Background: Pulmonary hypertension (PH: mPAP ≥
25 mmHg) has been reported as severe complication in patients
suffering from primary- and secondary Sjögren syndrome.
However, there are no epidemiological data available from
prospective studies regarding its true prevalence. Moreover, no
data exist regarding the frequency of borderline mPAP (mPAP
21–24 mmHg) or exercise PH (EPH: mPAPexercise > 30 mmHg+
total pulmonary resistance [TPR] exercise > 3WU) in this collect-
ive of patients. Therefore, we aimed to prospectively assess the
prevalence of PVD including PH, borderline mPAP and EPH in
patients with primary and secondary Sjögren syndrome.

Methods: Consecutive patients with Sjögren syndrome from
our ophthalmological- and rheumatological outpatient clinics
were prospectively recruited. All patients underwent echocar-
diography at rest and during exercise. They were assigned to a
low-, intermediate- or high-risk group according to their rest-
ing SPAP and their mPAP/C0 slope during exercise. In high-risk
patients (SPAP ≥30 mmHg, suspected PH) right heart cath-
terization (RHC) was suggested. Intermediate-risk patients
(SPAP 30–37 mmHg [suspected borderline mPAP] or exercis-
eSPAP ≥ 46 mmHg + TPR > 3WU [suspected EPH]) RHC was
recommended in case of symptoms or significantly decreased
peakVO₂.

Results: 86 patients were screened (female N = 81, age 58 ±10
years, primary Sjögren N = 46). N = 6 patients had a resting SPAP
≥38 mmHg, all of them also meeting criteria for suspected EPH.
N = 19 and N = 18 fulfilled criteria for suspected borderline mPAP
and/or EPH, respectively. Patients with suspected EPH were
older (64 ±10 vs 55 ±10, p < 0.001), had higher SPAP (32 ±7 vs
24 ±4, p < 0.001) and E/e’ (9.3 ±2.5 vs 7.3 ±2.4, p < 0.001) at rest.
No significant differences were observed regarding peakVO₂ and
6MWD. RHC was performed in 10 patients. EPH was confirmed
in N = 8, borderline mPAP in N = 1. No patient had PH.
Conclusion: In this first prospective study evaluating the prevalence of PVD in Sjögren syndrome no patient had PH whereas EPH was more prevalent. EPH seems to be associated with higher age, higher resting SPAP and mild diastolic left-ventricular-dysfunction.

Red blood cell distribution width in pulmonary hypertension – a useful biomarker?

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Background: According to the current guidelines, treatment decisions in patients with pulmonary hypertension (PH) should be based on the disease severity and the expected 1-year-mortality risk of each patient. Most available risk assessments include multiple parameters. Consequently, risk assessment is an extensive and time-demanding process. Finding a biomarker which is associated with poor outcome and is easily detectable in the blood would simplify prognostic evaluation and treatment decisions, ideally without compromising performance. One of these potential biomarkers is the red blood cell distribution width (RDW). The aim of this study was to identify whether the RDW is a useful biomarker in patients diagnosed with PH.

Methods: This is a retrospective study of 120 patients diagnosed with PH, including 59% with PH type 1. Clinical assessment, laboratory tests, blood gas analyses and results from right heart catheterisation and echocardiography from the patients’ first presentation and the years 2015 to 2018 were analysed in order to investigate associations between RDW and known determinants of prognosis in PH. Mortality risk was assessed using the modified Risk Assessment Score (mRASP).

Results: Mortality-risk groups significantly differed in RDW, which was also significantly higher in patients who deceased during follow-up. Cumulative survival was significantly worse in patients with RDW >14.5%, whereas NT-proBNP was significantly higher in this group. There was a significant difference in RDW between the WHO functional classes as well as in different categories of 6-minute walk distance.

Conclusion: RDW was associated with worse prognosis in accordance with recent publications. Thus, RDW may perform as a convenient, non-invasive prognostic biomarker in PH whose significance should be further validated.

Is idiopathic pulmonary arterial hypertension caused by insulin resistance?

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Background: The growing interest in metabolic profiling of pulmonary hypertension (PH) is fueled by current findings suggesting that there are significant metabolic changes causing the disease and linking pulmonary arterial hypertension (PAH) to insulin resistance. Glucose intolerance has been reported as a common feature of idiopathic PAH (IPAH) and insulin resistance is considered as a risk factor, which might impact survival. Unfortunately, the available studies did not investigate whether insulin resistance is related to the development of PH or rather to loss of physical activity; furthermore, they rely only on surrogate markers of insulin resistance rather than direct assessment of insulin sensitivity. The technical gold standard for assessment of insulin sensitivity is the hyperinsulinemic-euglycemic (Botnia) clamp, which has never been implemented on IPAH patients.

Methods: We assessed insulin sensitivity by applying Botnia clamp on 5 pairs of non-diabetic IPAH patients and their age-, sex-, and body composition-matched non-diabetic healthy controls. All participants underwent DEXA-scan and received standardized nutrition in accordance to their calorie demand, and then fasted for 20 hours. Then dynamic insulin regulation and -sensitivity was assessed by Botnia clamp. Differences between patients and their matched controls were tested with 2-sided exact test. P<0.05 was considered statistically significant.

Results: The two groups were comparable in terms of fasting blood glucose and -lipid levels, as well they both displayed normal efficacy of glycemic control. The Botnia clamp measurements showed no differences in insulin response or insulin sensitivity in any of the IPAH patients when compared to their healthy controls. In IPAH, the whole-body glucose disposal capacity in response to insulin infusion showed the same characteristics as in healthy controls.

Conclusion: This study provides no evidence for insulin resistance as an underlying mechanism for idiopathic PAH.

Inhalation of anti-infectives in cystic fibrosis and bronchiectasis – current status of treatment

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In the last decades inhalation of antibiotics (liquid and powder) became an established treatment in cystic fibrosis (CF) patients but also in patients with non-cystic fibrosis bronchiectasis. It was followed by a strong increase in life expectancy and quality of life mainly in CF patients. A number of drugs (amikacin, aztreonam, tobramycin, colistin, ciprofloxacin, combination fosfomycin/tobramycin) has been approved for CF by U.S. or European regulatory authorities (FDA, EMA) for...
Assessment of body composition parameters in elderly lung transplantation recipients using chest computed tomography scans

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Background: Pre-transplant body composition is increasingly recognized as prognostic factor for the outcome after lung transplantation (LuTx). In this study, we aimed to establish an objective, computed tomography (CT)-based quantification of the body composition in elderly recipients and its association with the clinical outcome after LuTx.

Methods: In this retrospective study, patients 60 years and older who received LuTx at the Medical University of Vienna from December 1998 to December 2018 with appropriate pre-transplant (≤ 1 year prior to transplant) CT scans were included.

Results: A total of 114 patients were included in the analysis (86 (75.4%) male and 28 (24.6%) female). The mean age at transplantation was 63 ± 2.7 years. COPD (50.9%) and fibrosis (40.4%) were the two most common diagnoses. Three groups, according to body composition, were formed: “high risk” group: low muscle mass and high mediastinal fat; “low risk” group: high muscle mass and low mediastinal fat and “intermediate” group: any other combination. In the “high risk” group, there were significantly more post-transplant complications including VAC-implantation (p = 0.001), the need for tracheostomy (p = 0.017) and delirium (p = 0.042). Similarly, “high risk” patients had a prolonged respiratory weaning (p = 0.022), intensive care unit stay (p = 0.001) and hospitalization (p = 0.001).

Conclusion: The evaluation of body composition parameters based on chest CT scans in LuTx candidates seems to be a promising, objective tool in the evaluation of elderly LuTx recipients in order to predict post-transplant complications.

Pleural empyema: intracavitary fibrinolysis compared with video-assisted toracoscopy

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Background: The less invasive VATs has replaced the treatment of pleural empyema with open thoracotomy. Although the MIST2 trial confirmed a role for intrapleural fibrinolysis, debate still exists regarding its efficacy, also after a recent revision in a Cochrane Review.

Methods: We compared 35 patients (group A) treated with intracavitary fibrinolysis (100,000 UI Urokinase +/– 5 mg DNAse) for thoracic empyema with 54 patients (group B) treated with VATs. For the group B we made a literature research and choose 3 studies [1–3], which favored VATs.

Results: Group A: n patients: 35, average age 65, n comorbidity 3.7, drainage duration 11 d, length of stay 17 d, failure of treatment (secondary VATs) 6. Group B: n patients 54, average age 41.7, n comorbidity not noted, drainage duration 5 d, length of stay 7 d, failure of treatment 4.

The group A differs considerably from the group B for a higher age of the patients with a high number of comorbidities. The patients treated with intracavitary fibrinolysis have been treated more often with bronchiectasis (34% vs. 10%) and with intracavitary fibrinolysis (34% vs. 10%) and with intracavitary fibrinolysis (34% vs. 10%).
drained longer, have been hospitalized longer, but the failure of fibrinolytic therapy with the consecutively secondary VATs was low (17%).

**Conclusion:** The advantages of intracavitary fibrinolysis are the good efficacy (therapeutic success of 83%), lower invasiveness and the safety of the method. The disadvantages, the longer drainage duration and the longer hospitalization, depend on the higher age and the many comorbidities and not on the method. So we think that the intracavitary fibrinolysis can be recommended the first line therapy of empyema especially in old patients with many comorbidities.

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**Postoperative Air Leak – an interdisciplinary report**

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**Background:** SUV positive round foci right upper lobe cT3 cN0 M0, FEV1 67%, COPD GII-III, m, 61 a (09/15) Lobectomy with LK Diss. N2 Position incl. parietal pleurectomy near the apex using open anterolat. Thoracotomy (10/15).

**Methods:** Postoperative persistent pneumothorax in the right middle and upper field

Little diff. Plates CA pt3 pN0 (0/12) Rx (pleura parietalis) L0 V0 Pn0 GIII UICC IIB

Adj. polychemotherapy with 4 cycles of cisplatin and navelbine

Radiation of the tumor bed parietal with 60Gray in 30 fractions

Intermediate pneumatic supply 11/15–12/15

Recurrent infection exacerbations, unchanged pneumothorax up to 11/17

02/18 discrete enlargement of the pneumothorax cavity

03/18 True Close valve for about 5 weeks

05/18 inflammatory pleural effusion, E. coli evidence

09/18 pos. mould myphae culture, Empyem

VATS—VAC system with Vera Forte flushing

10–12/18 VAC and then open dressing change due to air leak

Results: 19.12.2018 bronchoscopic valve system Otto Wagner Hospital (Doz. Dr. Arschang Valipour). On 31.01.2019 defect toma was possible.

Conclusion: In cooperation with interventional pneumology and plastic surgery, the closure of the airleak and thoracostoma was possible.

**Surviving a rare case of rapidly progressive cryptogenic organizing pneumonia in a 75-year old male patient**

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**Background:** Rapidly progressive cryptogenic organizing pneumonia (rpCOP) is a rare disease with a high mortality after the first 2–3 weeks of disease-onset. It can occur in healthy, vigorous individuals or can be associated with other systemic disorders. The course can be rapid, with 1–3 days of symptoms followed by respiratory hypoxemic failure afterwards. These rapidly progressing patients might present with symptoms similar to ARDS or acute interstitial pneumonia.

**Methods/Case-presentation:** We present a rare case of a 75-year-old male who survived a rpCOP with diffuse opacities in both lungs and severe hypoxemic failure. An infectious etiology and lymphoproliferative causes (LIP) of the underlying respiratory disease were ruled out with bacterial and fungal cultures and serologic testing of blood and BAL fluid (common bacteria, Legionella pneumophila, Chlamydia pneumoniae, mycobacteria, fungi, cytomegalovirus, adenovirus, herpes simplex, influenza and parainfluenza, syncytial respiratory virus, cytomegalovirus, adenovirus, herpes simplex, Pneumocystis jiroveci). There was no evidence of iatrogenic causes of immunosuppression, toxic exposure, cancer, undergoing cytotoxic chemotherapy, pre-existing interstitial lung disease or pre-existing collagen-vascular disease (e.g. EAA). Collected data included medical history with tobacco history, type and duration of symptoms, initial physical examination, laboratory findings, results of microbial cultures. BAL was carried out within 2 days of hospitalization. BAL results showed a massive lymphoctic alveolitis with more than 90% lymphocytes.

**Course:** After exclusion of the above mentioned causes, the patient was treated immediately with high dose i.v. corticosteroids and then switched to an, initially overlapping, pulse therapy with i.v. cyclophosphamide. He recovered fully after a 4 week-stay at our intensive care unit followed by a 4 week-program at our remob-ward.

**Conclusion:** One has to consider rpCOP as a cause of respiratory failure with bilateral opacities in the CT-Scan which requires a prompt high dose immunosuppressive therapy regime in order to improve survival in these patients.

**Changes in blood derived biomarkers reflect PAH progression and response to targeted therapy**

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Treatment of pulmonary fibrosis by the use of AAV2-L1 encoding an IL-17A decoy receptor

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Background: Idiopathic pulmonary fibrosis (IPF) is believed to be a result of a dysregulated healing process involving multiple signaling pathways, including Interleukin-17 (IL-17). Therefore, we propose to elucidate the impact of lung-directed gene therapy targeting IL-17a in pulmonary fibrosis.

Methods: In order to modulate pulmonary IL-17a signaling, we designed an adeno-associated virus (AAV) with selective lung tropism (AAV2-L1), targeting fibrosis-associated inflammation through pulmonary expression of a newly designed soluble IL-17a decoy receptor (decoyR).

C57BL/6 mice will be transfected either with AAV2-L1-Luc (Luciferase) or AAV2-L1-IL-17a decoyR. After 14 days, efficient transfection of the lungs will be verified by in vivo imaging. Subsequently, irradiation of the lungs will be performed, after which leukocyte kinetics in BALF and lung tissue will be monitored at early and late time-points i.e. up to 6 months. Severity of fibrosis will be assessed using trichrome stainings. IL-17a signaling analysis and in-depth immune-phenotyping including bioactive mediator lipidomics will be performed. In a second approach, gene therapy will be conducted in mice with already established pulmonary fibrosis, i.e. at time-points 1 as well as 3 months after lung irradiation or endotracheal bleomycin instillation, and monitored for additional 3 and 6 months, in order to understand whether our AAV2-L1-IL-17a decoyR will have the potential to prevent progression, or even to reverse pulmonary fibrosis.

Conclusion: Our approach constitutes an innovative attempt to introduce gene therapy in IPF and progressive ILDs of known cause.

Pathophysiological involvement of exosomes in idiopathic pulmonary fibrosis

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Background: Idiopathic pulmonary fibrosis (IPF) is the most common and most severe form of fibrosing interstitial lung disease. Cells of special interest in the development and progression of IPF are fibroblasts as they are central to the matrix homeostasis. Cellular senescence is recognized, although controversially discussed, for having an essential role in IPF by having both pro- and anti-fibrotic effects. Recent studies link the aging process to miRNAs circulating amongst others through exosomes. Senescence-associated exosomes may be meaningful players in the pathogenesis of IPF, however, their pathophysiological involvement in IPF remains largely unexplored.

Methods: In this study, tissue samples from patients diagnosed according to the ATS/ERS guidelines with IPF, non-specific interstitial pneumonia, hypersensitivity pneumonitis and healthy controls are obtained via biopsy, from explants or donor lungs. Cells are cultivated and purified for fibroblasts. Cellular senescence is quantified by specific cellular markers. Exosomes are isolated by polyethylene-glycol-enrichment and ultracentrifugation and are characterized by analysis with density gradients, immunoblot, transmission-electron-microscopy and nanoparticle-tracking. MiRNA and pre-miRNA (miRNA-34a and miRNA-21) are isolated from purified exosomes and quantified by qPCR. For assessing the influence of miRNAs on cellular senescence, we established a senescence model using commercially available human lung fibroblasts (MADO). This model is used to investigate changes towards senescence by transfection of purified exosomes. In senescent cells we aim to block miRNAs with locked nucleic acids to inhibit miRNAs and measure downstream RNAs and proteins. All obtained data of this study are analysed with STATA version 14. A two-sided p-value <0.05 is considered statistically significant.

Outlook: The purpose of this study is to discover the distribution of exosomes and investigate senescence-associated miRNA profiles, with a special focus on miR-21 and miR-34a. The results will provide new insights into the pathogenesis of IPF and the involvement of exosomes in the senescence of fibroblasts.
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