VIH e doença de orgão –O desafio a longo prazo

CICLO DE REUNIÕES TEMÁTICAS

1ª Reunião
Patologia Pulmonar

Organização: NEDVIH e Consulta de Medicina Interna/ Infeciologia do C. H. Barreiro Montijo

Patologia Pulmonar
C.H. Barreiro-Montijo

COPD AND LUNG CANCER – EARLY DIAGNOSIS AND FOLLOW-UP

Raquel Paulinetti Camara
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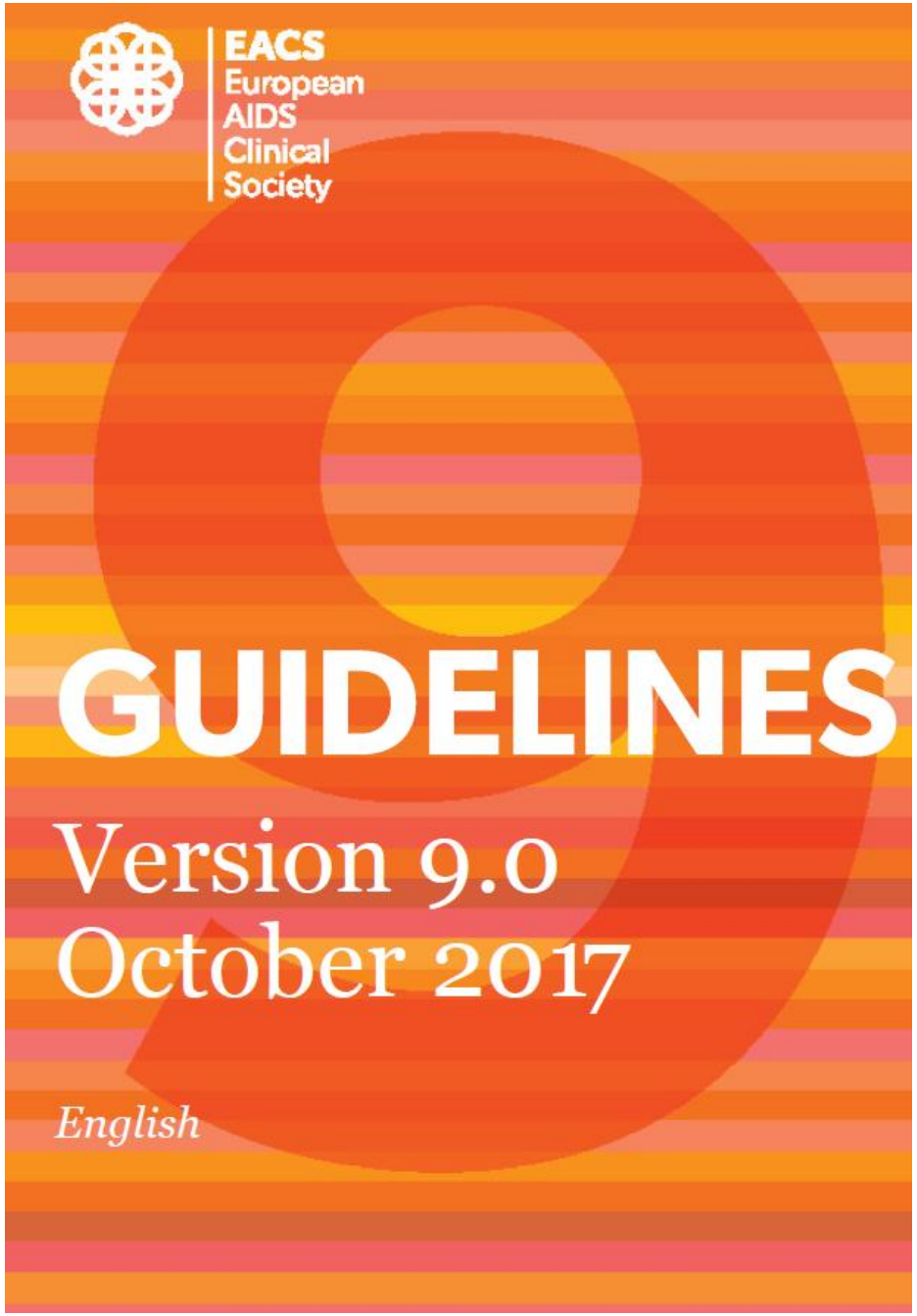

NCCN National Comprehensive Cancer Network®

NCCN

Cancer in People Living With HIV, Version 1.2018

Clinical Practice Guidelines in Oncology

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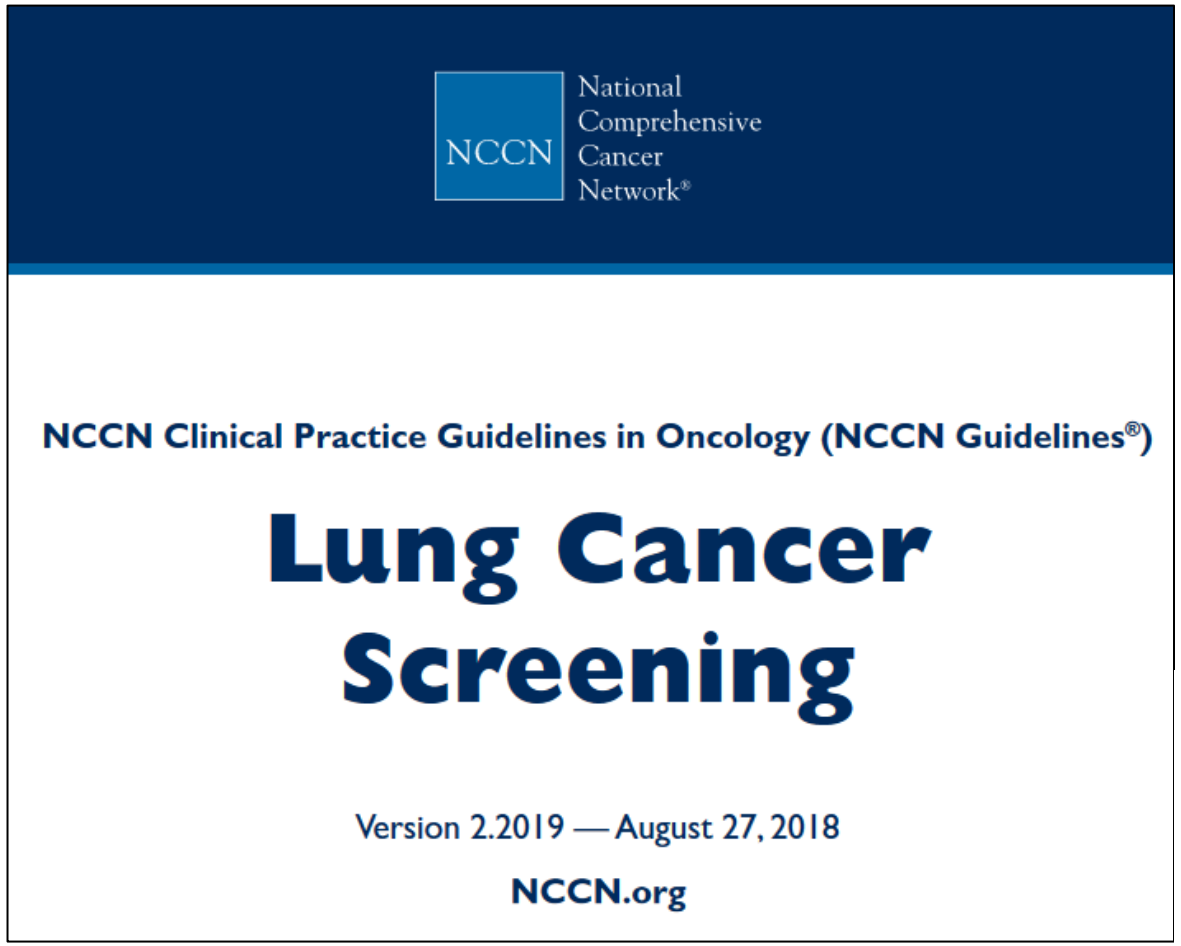


Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017[1]

Radiology

INTRODUCTION: HIV & PULMONARY FUNCTION

AIDS. 2018 Jan 14;32(2):227-232. doi: 10.1097/QAD.0000000000001691.

HIV is associated with airway obstruction: a matched controlled study.

Makinson A[1,2], Hayot M[3], Eymard-Duvernay S[1], Ribet C[4], Raffi F[5], Pialoux G[6], Zucman D[7], Poizot-Martin I[8], Bonnet F[9], Abgrall S[10], Tattevin P[11], Cheret A[12], Ferry T[13], Mauboussin JM[14], Marchand L[15], Rouzaud C[16], Reynes J[1,2], Zins M[4], Le Moing V[1,2]; ANRS EP48 HIV CHEST study Team.

Author information

Abstract

OBJECTIVE: To explore whether airway obstruction is associated with HIV in a cohort of HIV-infected and uninfected smokers.

METHODS: People living with HIV (PLWHIV) participated in the ANRS EP48 HIV CHEST study, an early lung cancer diagnosis study with low-dose chest tomography. HIV-uninfected study participants were from the CONSTANCES cohort. Inclusion criteria were an age greater than 40 years, a smoking history of at least 20 pack-years, and for PLWHIV, a CD4 T-lymphocyte nadir less than 350/µl and last CD4 cell count more than 100 cells/µl. Two randomly selected HIV-uninfected study participants were matched by age and sex with one PLWHIV. Prebronchodilatator forced expiratory volume in 1s (FEV1) to forced vital capacity (FVC) ratio was the primary outcome, and association of FEV1/FVC ratio less than 0.70 and FEV1 less than 80% of the theoretical value, as a proxy of chronic obstructive pulmonary disease, the secondary outcome.

RESULTS: In total, 351 PLWHIV and 702 HIV-uninfected study participants were included. Median age was 50 years, and 17% of study participants were women. Plasma HIV RNA was less than 50 copies/ml in 89% of PLWHIV, with a median CD4 cell count of 573 cells/µl. HIV (β -2.19), age (per 10 years increase; β -2.81), tobacco use (per 5 pack-years increase; β -0.34), and hepatitis C virus serology (β-2.50) were negatively associated with FEV1/FVC. HIV [odds ratio (OR: 1.72)], age (per 10 years increase; OR 1.77), and tobacco use (per 5 pack-years increase; OR 1.11) were significantly associated with the secondary outcome.

CONCLUSION: Our study found a significant association of airway obstruction with HIV status in smokers aged more than 40 years with previous immunodeficiency.

PMID: 29135582 DOI: 10.1097/QAD.0000000000001691

Thorax. 2018 May;73(5):431-438. doi: 10.1136/thoraxjnl-2017-211079. Epub 2018 Jan 13.

Airflow limitation in people living with HIV and matched uninfected controls.

Ronit A[1], Lundgren J[2], Afzal S[3], Benfield T[4], Roen A[5], Mocroft A[5], Gerstoft J[1], Nordestgaard BG[3,6], Vestbo J[7], Nielsen SD[1]; Copenhagen Co-morbidity in HIV infection (COCOMO) study group.

Author information

Abstract

INTRODUCTION: Whether HIV influences pulmonary function remains controversial. We assessed dynamic pulmonary function in people living with HIV (PLWHIV) and uninfected controls.

METHODS: A total of 1098 PLWHIV from the Copenhagen Co-morbidity in HIV infection study and 12 161 age-matched and sex-matched controls from the Copenhagen General Population Study were included. Lung function was assessed using FEV_1 and FVC, while airflow limitation was defined by the lower limit of normal (LLN) of FEV_1/FVC and by FEV_1/FVC<0.7 with FEV_1predicted <80% (fixed). Logistic and linear regression models were used to determine the association between HIV and pulmonary function adjusting for potential confounders (including smoking and socioeconomic status).

RESULTS: In predominantly white men with mean (SD) age of 50.6 (11.1) the prevalence of airflow limitation (LLN) was 10.6% (95% CI 8.9% to 12.6%) in PLWHIV and 10.6% (95% CI 10.0 to 11.1) in uninfected controls. The multivariable adjusted OR for airflow limitation defined by LLN for HIV was 0.97 (0.77-1.21, P<0.78) and 1.71 (1.34-2.16, P<0.0001) when defined by the fixed criteria. We found no evidence of interaction between HIV and cumulative smoking in these models (P interaction: 0.25 and 0.17 for LLN and fixed criteria, respectively). HIV was independently associated with 197 mL (152-242, P<0.0001) lower FEV_1 and 395 mL (344-447, P<0.0001) lower FVC, and 100 cells/mm^3 lower CD4 nadir was associated with 30 mL (7-52, P<0.01) lower FEV_1 and 51 mL (24-78, P<0.001) lower FVC.

CONCLUSION: HIV is a risk factor for concurrently decreased FEV_1 and FVC. This excess risk is not explained by smoking or socioeconomic status and may be mediated by prior immunodeficiency.

TRIAL REGISTRATION NUMBER: NCT02382822.

Ann Am Thorac Soc. 2018 Feb;15(2):192-199. doi: 10.1513/AnnalsATS.201606-492OC.

Decreased Lung Function and All-Cause Mortality in HIV-infected Individuals.

Gingo MR[1], Nouraie M[1], Kessinger CJ[1], Greenblatt RM[2,3], Huang L[3], Kleerup EC[4], Kingsley L[5], McMahon DK[1], Morris A[1,6].

Author information

Abstract

RATIONALE: Human immunodeficiency virus (HIV) infection is associated with pulmonary disease and worse lung function, but the relationship of lung function with survival in HIV is unknown.

OBJECTIVES: To determine whether lung function is associated with all-cause mortality in HIV-infected individuals.

METHODS: HIV-infected participants from cohorts in three locations underwent pre- and post-bronchodilator spirometry and determination of single-breath diffusing capacity of the lung for carbon monoxide (DI_{CO}) in 2008-2009, computed tomographic (CT) scanning of the chest for quantitative emphysema and airway measures, and echocardiography for estimated left ventricular systolic and diastolic function and tricuspid regurgitant velocity. Bivariate analysis and multivariable Cox proportional hazards models were used to determine whether decreased lung function was independently associated with increased all-cause mortality. Models were adjusted for covariates including age, sex, body mass index, smoking status, self-reported hepatitis C status, HIV viral levels, $CD4^+$ T-cell counts, hemoglobin, antiretroviral therapy, and illicit drug use.

RESULTS: Overall, 396 HIV-infected participants underwent pulmonary function testing. Thirty-two participants (8%) died during a median follow-up period of 69 months. A post-bronchodilator FEV_1-to-FVC ratio less than 0.7 (hazard ratio [HR], 2.47; 95% confidence interval [CI], 1.10-5.58) and a DI_{CO} less than 60% (HR, 2.28; 95% CI, 1.08-4.82) were independently associated with worse mortality. Also, hepatitis C (HR, 2.68; 95% CI, 1.22-5.89) and baseline plasma HIV RNA level (HR per ln RNA copies/ml, 1.50; 95% CI, 1.22-1.86) were associated with mortality in HIV-infected participants. The only CT or echocardiographic measure associated with greater mortality in univariate analysis was greater wall thickness of medium-sized airways (HR for wall area percent, 1.08; 95% CI, 1.00-1.18; P = 0.051), but none of the CT or echocardiogram measures were associated with mortality in multivariable analysis.

CONCLUSIONS: Airflow obstruction and impaired diffusing capacity appear to be associated with all-cause mortality in HIV-infected persons over an average of 6 years of follow-up. These data highlight the importance of lung dysfunction in HIV-infected persons and should be confirmed in larger cohorts and with extended follow-up periods. Clinical trial registered with www.clinicaltrials.gov (NCT00869544, NCT01326572).

J Acquir Immune Defic Syndr. 2018 Jul 6. doi: 10.1097/QAI.0000000000001797. [Epub ahead of print]

Smoking and Accelerated Lung Function Decline in HIV-Positive Individuals: A Secondary Analysis of the Start Pulmonary Substudy.

MacDonald DM[1], Melzer AC[1,2], Collins G[2], Avihingsanon A[3], Crothers K[4], Ingraham NE[1], Mugerwa H[5], Ristola M[6], Shuter J[7], Kunisaki KM[1,2]; INSIGHT START Pulmonary Substudy Group.

Author information

Abstract

BACKGROUND: Chronic obstructive pulmonary disease (COPD) is a leading cause of death and disability globally. Both cigarette smoking and HIV have been identified as independent risk factors for COPD. We used data from the Strategic Timing of Antiretroviral Treatment (START) Pulmonary Substudy to quantify the impact of smoking on rate of lung function decline in HIV.

METHODS: We included START Pulmonary Substudy participants who contributed at least two good quality spirometry measures during the study. Slope of forced expiratory volume in 1 second (FEV1) was estimated using a repeated measures model adjusted for treatment group (immediate vs. deferred treatment arm of START), age, sex, race, baseline COPD, and region.

RESULTS: Of 1,026 START Pulmonary Substudy participants, 915 (89%) were included in this analysis. Median follow up time was 3.9 years. Smokers and non-smokers were similar in baseline age (median 36 y), but smokers were more likely to be white, male, and from Europe/Israel/Australia. Smokers had faster average FEV1 decline compared to non-smokers (-38.3 mL/y vs -25.1 mL/y; difference of -13.2 mL/y [95% CI: -23.6 to -2.7]; p=0.013), were more likely to meet criteria for rapid FEV1 decline (7.2% to 11.7% more likely [p=0.09 to p=0.002], depending on the definition of rapid decline), and had borderline, but not statistically significant, higher incident COPD during follow-up (9.7% vs 5.8%, p=0.06).

CONCLUSION: Compared to non-smokers, HIV-positive smokers experience faster decline in lung function. These results underscore the need for a better understanding of how to best support smoking cessation among HIV-positive populations.

PMID: 29985804 DOI: 10.1097/QAI.0000000000001797

Respir Res. 2018 Jul 27;19(1):140. doi: 10.1186/s12931-018-0835-7.

Decreased microbiome diversity in the HIV small airway epithelium.

Xu S[1], Tsai A[2], Sze MA[3], Vucic EA[4], Shaipanich T[5], Harris M[6], Guillemi S[6], Yang J[1], Sinha S[7], Nislow C[7], Montaner J[6], Lam W[4], Lam S[4], Sin DD[1,5], Paul Man SF[1,5], Leung JM[8,9,10].

Author information

Abstract

BACKGROUND: Persons living with human immunodeficiency virus (PLWH) face an increased burden of chronic obstructive pulmonary disease (COPD). Repeated pulmonary infections, antibiotic exposures, and immunosuppression may contribute to an altered small airway epithelium (SAE) microbiome.

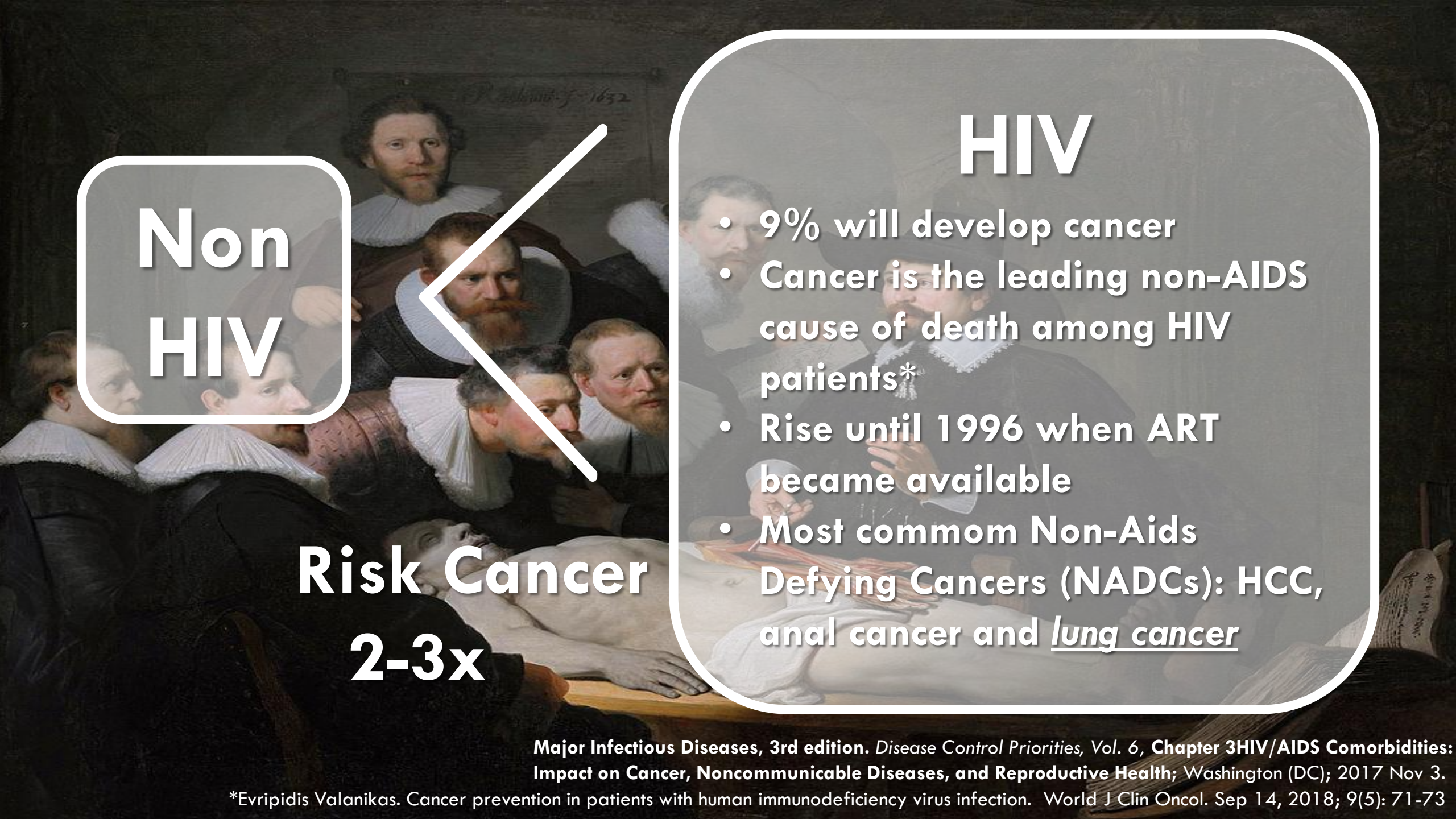
METHODS: SAE cells were collected from 28 PLWH and 48 HIV- controls through bronchoscopic cytologic brushings. DNA extracted from SAE cells was subjected to 16S rRNA amplification and sequencing. Comparisons of alpha and beta diversity between HIV+ and HIV- groups were performed and key operational taxonomic units (OTUs) distinguishing the two groups were identified using the Boruta feature selection after Random Forest Analysis.

RESULTS: PLWH demonstrated significantly reduced Shannon diversity compared with HIV- volunteers (1.82 ± 0.10 vs. 2.20 ± 0.073, $p = 0.0024$). This was primarily driven by a reduction in bacterial richness (23.29 ± 2.75 for PLWH and 46.04 ± 3.716 for HIV-, $p < 0.0001$). Phyla distribution was significantly altered among PLWH, with an increase in relative abundance of Proteobacteria ($p = 0.0003$) and a decrease in Bacteroidetes ($p = 0.0068$) and Firmicutes ($p = 0.0002$). Six discriminative OTUs were found to distinguish PLWH from HIV- volunteers, aligning to Veillonellaceae, Fusobacterium, Verrucomicrobiaceae, Prevotella, Veillonella, and Campylobacter.

CONCLUSIONS: Compared to HIV- controls, PLWH's SAE microbiome is marked by reduced bacterial diversity and richness with significant differences in community composition.

KEYWORDS: COPD; Epithelium; HIV; Microbiome

INTRODUCTION:
HIV
LUNG CANCER



Non HIV

Risk Cancer 2-3x

HIV

- 9% will develop cancer
- Cancer is the leading non-AIDS cause of death among HIV patients*
- Rise until 1996 when ART became available
- Most commom Non-Aids Defying Cancers (NADCs): HCC, anal cancer and *lung cancer*

Major Infectious Diseases, 3rd edition. *Disease Control Priorities, Vol. 6,* **Chapter 3HIV/AIDS Comorbidities: Impact on Cancer, Noncommunicable Diseases, and Reproductive Health;** Washington (DC); 2017 Nov 3.

*Evripidis Valanikas. Cancer prevention in patients with human immunodeficiency virus infection. World J Clin Oncol. Sep 14, 2018; 9(5): 71-73

HIV – LUNG CANCER

Cancer development:

- ADC: usually soon after HIV diagnosis
- NADCs: >= 5 years after HIV diagnosis

Worst Cancer Survival:

- HIV patients versus non infected patients - average survival 10% at 24 months*
- NADCs versus ADCs

Particularities:

- CD4 T-cell > 200 cells mm3 were found protective against ADCs
- Older patients and doing weaker ART were more likely to be diagnosed with an NADC

Major Infectious Diseases, 3rd edition. *Disease Control Priorities, Vol. 6,* Chapter 3HIV/AIDS Comorbidities: Impact on Cancer, Noncommunicable Diseases, and Reproductive Health; Washington (DC); 2017 Nov 3.

*Alison Morris. An Official ATS Workshop Report: Emerging Issues and Current Controversies in HIV-Associated Pulmonary Diseases. Am Thor Soc. September 2010.

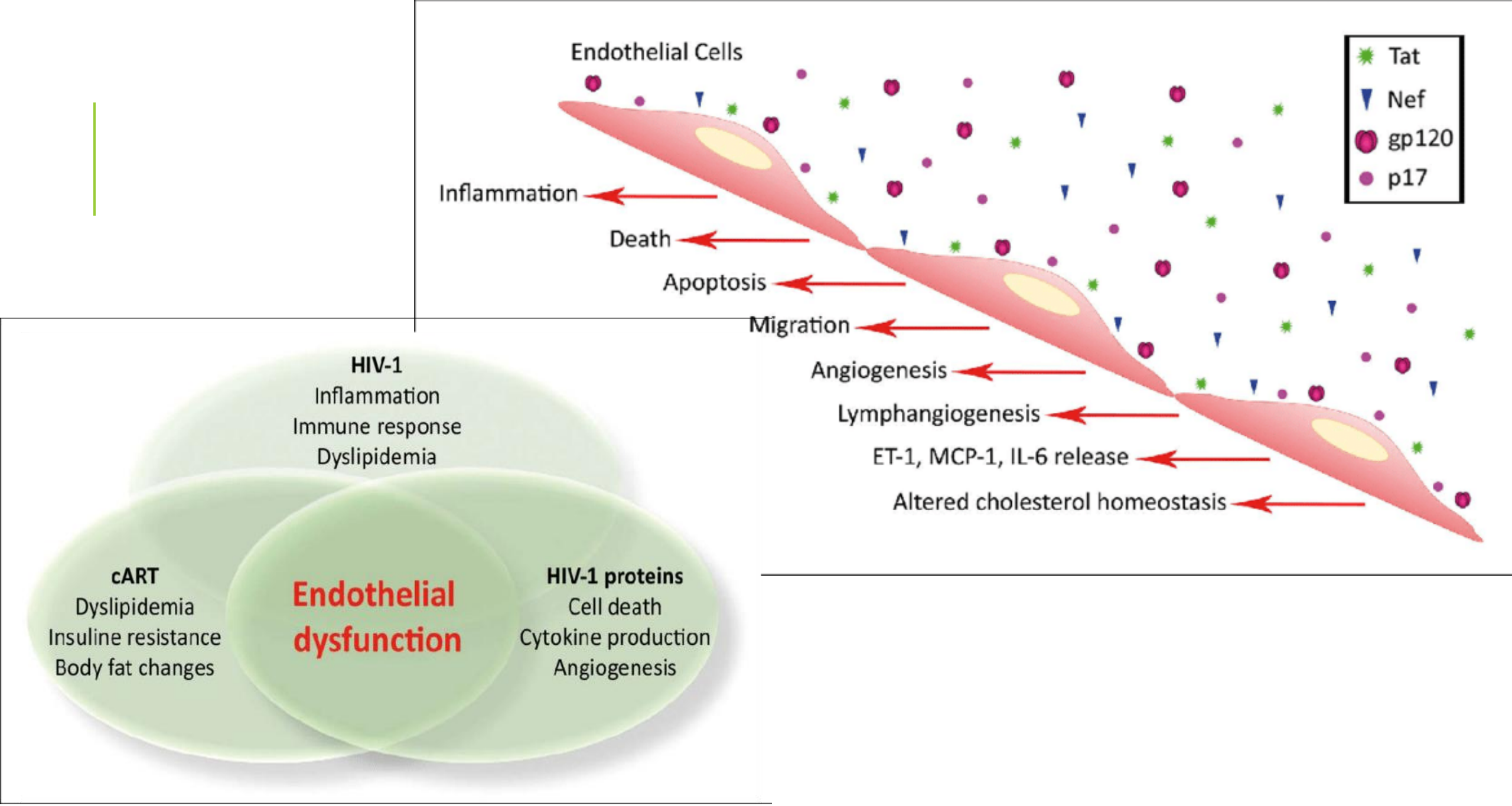
HIV – LUNG CANCER

How HIV plays an oncogenic role in the development of lung cancer is not clear:

- Microsatellite alterations: > in cancer + HIV-infected patients than in uninfected patients.

- An enhanced susceptibility to carcinogens or the occurrence of lung injury as a result of prior infections may also be involved in the increased risk for lung cancer in HIV.

Alison Morris. An Official ATS Workshop Report: Emerging Issues and Current Controversies in HIV-Associated Pulmonary Diseases. American Thoracic Society. September 2010.



The New Microbiologica: official journal of the Italian Society for Medical Virology (SIVIM) 39(3):163-173 · April 2016

Cancer Sci. 2018 Oct;109(10):3105-3114. doi: 10.1111/cas.13768. Epub 2018 Sep 3.

Human immunodeficiency virus Tat-TIP30 interaction promotes metastasis by enhancing the nuclear translocation of Snail in lung cancer cell lines.

Liu YP[1,2,3,4,5], Chen CH[4], Yen CH[3,5,6,7], Tung CW[8], Chen CJ[4,9], Chen YA[3,4], Huang MS[10,11].

Author information

Abstract

Lung cancer patients with human immunodeficiency virus (HIV) have a poorer prognosis than do patients without HIV infection. HIV1 Tat is a secreted viral protein that penetrates the plasma membrane and interacts with a number of proteins in non-HIV-infected cells. The loss of function of Tat-interacting protein 30 (TIP30) has been linked to metastasis in non-small cell lung cancer (NSCLC). However, it is unknown how the interaction of HIV1 Tat with TIP30 regulates the metastasis of NSCLC cells. In this study, the overexpression of TIP30 decreased tumor growth factor-β-induced epithelial-to-mesenchymal transition (EMT) and invasion of NSCLC cells, whereas the knockdown of TIP30 promoted EMT, invasion and stemness. Exposure to recombinant HIV1 Tat proteins promoted EMT and invasion. A mechanistic study showed that the interaction of HIV1 Tat with TIP30 blocked the binding of TIP30 to importin-β, which is required for the nuclear translocation of Snail. Indeed, the loss of TIP30 promoted the nuclear translocation of Snail. In vivo studies demonstrated that the overexpression of TIP30 inhibited the metastasis of NSCLC cells. In contrast, the coexpression of HIV1 Tat and TIP30 diminished the inhibitory effect of TIP30 on metastasis. Immunohistochemistry confirmed that TIP30 overexpression reduced the nuclear localization of Snail, whereas the coexpression of HIV1 Tat and TIP30 increased nuclear Snail in metastatic tumors. In conclusion, the binding of HIV1 Tat to TIP30 enhanced EMT and metastasis by regulating the nuclear translocation of Snail. Targeting Tat-interacting proteins may be a potential therapeutic strategy to prevent metastasis in NSCLC patients with HIV infection.

KEYWORDS: Snail; Tat-interacting protein; epithelial-to-mesenchymal transition; non-small cell lung cancer; nuclear translocation

PMID: 30099830 DOI: 10.1111/cas.13768

DISPARITIES IN CANCER CARE FOR PLWH

PLWH who develop cancer have higher mortality compared with the general cancer population. Reasons for this include:

- Delayed diagnoses
- Advanced cancer stage
- Other co-morbidities
- Immunosuppression

There is also significant disparity in cancer treatment between PLWH and the general cancer population:

- Many PLWH don't receive any cancer treatment at all.

Results of a survey of 500 oncologists in the United States suggest that lack of consensus guidelines contributes to ***the substandard cancer care often offered to patients with HIV*** and cancer.

Clinical Practice Guidelines in Oncology, NCCN - Cancer in People Living With HIV, Version 1.2018

RECOMMENDATIONS FOR CANCER MANAGEMENT IN PLWH

The NCCN panel recommends that ***most PLWH who develop cancer should be offered the same cancer therapies as HIV-negative individuals***, and modifications to cancer treatment should not be made solely on the basis of HIV status.

Inclusion of PLWH in cancer clinical trials should be encouraged whenever feasible.

Clinical Practice Guidelines in Oncology, NCCN - Cancer in People Living With HIV, Version 1.2018

INTRODUCTION:
HIV
COPD

Lancet Glob Health. 2018 Feb;6(2):e193-e202. doi: 10.1016/S2214-109X(17)30451-5. Epub 2017 Dec 16.

Prevalence of chronic obstructive pulmonary disease in the global population with HIV: a systematic review and meta-analysis.

Bigna JJ[1], Kenne AM[2], Asangbeh SL[3], Sibetcheu AT[4].

Author information

Abstract

BACKGROUND: In recent years, the concept has been raised that people with HIV are at risk of developing chronic obstructive pulmonary disease (COPD) because of HIV infection. However, much remains to be understood about the relationship between COPD and HIV infection. We aimed to investigate this association by assessing studies that reported the prevalence of COPD in the global population with HIV.

METHODS: In this systematic review and meta-analysis, we assessed observational studies of COPD in people with HIV. We searched PubMed, Embase, Web of Science, and Global Index Medicus, with no language restriction, to identify articles published until June 21, 2017, and we searched the reference lists of the retrieved articles. Eligible studies reported the prevalence of COPD or had enough data to compute these estimates. We excluded studies in subgroups of participants selected on the basis of the presence of COPD; studies that were limited to other specific groups or populations, such as people with other chronic respiratory diseases; and case series, letters, reviews, commentaries, editorials, and studies without primary data or an explicit description of methods. The main outcome assessed was prevalence of COPD. Each study was independently reviewed for methodological quality. We used a random-effects model to pool individual studies and assessed heterogeneity (I^2) using the χ^2 test on Cochrane's Q statistic. This study is registered with PROSPERO, number CRD42016052639.

FINDINGS: Of 4036 studies identified, we included 30 studies (151 686 participants) from all WHO regions in the meta-analysis of COPD prevalence. 23 studies (77%) had low risk of bias, six (20%) had moderate risk of bias, and one (3%) had high risk of bias in their methodological quality. The overall prevalence of COPD was 10·5% (95% CI 6·2-15·7; I^2=97·2%; six studies) according to the lower limit of normal definition of COPD, and 10·6% (6·9-15·0; 94·7%; 16 studies) according to the fixed-ratio definition. COPD prevalence was higher in Europe and among current and ever smokers, and increased with level of income and proportion of participants with detectable HIV viral load. Prevalence of COPD was significantly higher in patients with HIV than in HIV-negative controls (pooled odds ratio 1·14, 95% CI 1·05-1·25, I^2=63·5%; 11 studies), even after adjustment for tobacco consumption (2·58, 1·05-6·35, 74·9%; four studies).

INTERPRETATION: Our findings suggest a high prevalence of COPD in the global population with HIV, and an association with HIV. As such, COPD deserves more attention from HIV health-care providers, researchers, policy makers, and stakeholders for improved detection, overall proper management, and efficient control of COPD in people with HIV. Efforts to address this burden should focus on promoting the decrease of tobacco consumption and adherence to highly active antiretroviral therapy to reduce viral load.

HIV - CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Reasons for increased COPD in HIV-infected patients are not completely understood:

- HIV infection may result in increased **pulmonary inflammation**, including increased numbers of CD8 1 T cells and IFN-G production in the alveolar space. Altered antioxidant balance occurs in HIV infection, and BAL glutathione levels decrease over time.
- **HIV itself and its peptides** may also induce apoptosis of endothelial cells, an important factor in the pathogenesis of COPD.
- **Microbial colonization** of the respiratory tract may play a key role in the pathogenesis of COPD in the HIV-uninfected population
- **Lung infections** could perpetuate lung injury and inflammation, thus contributing to COPD progression.
- The role of **Pneumocystis** in the pathogenesis of COPD is of particular interest in HIV, as HIV-infected patients are commonly colonized with Pneumocystis. Lung colonization has been associated with COPD severity in HIV-uninfected patients.

Alison Morris. An Official ATS Workshop Report: Emerging Issues and Current Controversies in HIV-Associated Pulmonary Diseases. Am Thor Soc. Sep 2010.

J Acquir Immune Defic Syndr. 2018 Aug 16. doi: 10.1097/QAI.0000000000001840. [Epub ahead of print]

Factors Associated with Progression of Lung Function Abnormalities in HIV-Infected Individuals.

Li Y[1], Nouraie SM[1], Kessinger C[1], Weinman R[1], Huang L[2], Greenblatt RM[3], Kleerup E[4], Kingsley L[1], McMahon D[1], Fitzpatrick M[1], Morris A[1].

Author information

Abstract

BACKGROUND: HIV is an independent risk factor for chronic obstructive pulmonary disease (COPD); however, baseline risk factors for lung function decline remain largely unknown in this population.

METHODS: HIV-infected participants in the Pittsburgh Lung HIV Cohort with at least three pulmonary function measurements between 2007-2016 were included. Pulmonary function testing (PFT) including post-bronchodilator (BD) spirometry and diffusion capacity for carbon monoxide (DLco) was performed every 18 months. We used a mixed effect linear model to evaluate factors associated with PFT and DLco decline and logistic regression models to evaluate factors associated with rapid FEV1 decline (defined as >80ml per year) and any DLco decline.

RESULTS: 285 HIV-infected participants were included. Median baseline CD4 cell count was 521 cells/μl, 61.9% had an undetectable HIV viral load at baseline, and 78.5% were receiving ART. Approximately 20% of participants met Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria for a diagnosis of COPD at baseline. Older age and baseline GOLD stage 1 compared with stage 0 were associated with faster decline in post-BD FEV1%, while female sex was associated with slower decline. Similarly, female sex was associated with slower decline in DLco%. HIV-related factors including CD4 cell count, viral load and ART use were not significantly associated with pulmonary function decline.

CONCLUSION: Older age, male sex and higher baseline GOLD stage were associated with more rapid Post-BD FEV1% decline in HIV-infected individuals.

PMID: 30142142 DOI: 10.1097/QAI.0000000000001840

HIV - CHRONIC OBSTRUCTIVE PULMONARY DISEASE

The role of ART in the development or progression of COPD in HIV-infected patients is under investigation.

One intriguing study reported that ART use was an independent predictor of airflow obstruction.

ART might be associated with COPD through:

- Direct effects of antiretroviral medications
- Development of a "modified immune reconstitution inflammatory syndrome" to low levels of pathogens or self-antigens
- Some modifying factor associated with ART use (82).

Alison Morris. An Official ATS Workshop Report: Emerging Issues and Current Controversies in HIV-Associated Pulmonary Diseases. Am Thor Soc. Sep 2010.

RISK FACTORS, PREVENTION AND SCREENING FOR LUNG CANCER

RISCK FACTORS – SMOKING

Principal direct cause of lung cancer

- Responsible for 90% of all lung cancer cases

The risk of lunf cancer for a smoker is 10 to 20 times higher then a non-smoker individual

- Age of beginning
- Type of tobacco
- Packs/year
- Number of cigarrets/day
- (…)

RISK FACTORS – SMOKING

Cigarette smoking has been associated with decreased markers of lung immune function in HIV-infected patients.

Prevalence of tobacco use is several-fold higher among patients with HIV.

Smoking is associated with lung-cancer-specific mortality, and increased after ART era.

The incidence of lung cancer appears to be in part independent of tobacco use

Mortality from LC was not associated with immunosuppression or HIV viral load

Major Infectious Diseases, 3rd edition. *Disease Control Priorities, Vol. 6,* **Chapter 3HIV/AIDS Comorbidities: Impact on Cancer, Noncommunicable Diseases, and Reproductive Health;** Washington (DC); 2017 Nov 3.

HIV – SMOKING – LUNG CANCER

These patients should be made aware of smoking cessation benefits and behavioral interventions to reduce smoking.

Pharmacotherapy (including nicotine replacement therapy, varenicline and bupropion), cognitive behavioral counseling and/or motivational strategies can be employed.

Major Infectious Diseases, 3rd edition. *Disease Control Priorities, Vol. 6,* **Chapter 3HIV/AIDS Comorbidities: Impact on Cancer, Noncommunicable Diseases, and Reproductive Health;** Washington (DC); 2017 Nov 3.

RISK FACTORS – ENVIROMENTAL FACTORS

Abestos

- Risk 10 times higher (50 if smoker)
- Cumulative effect and interval (>10 years)

Radon

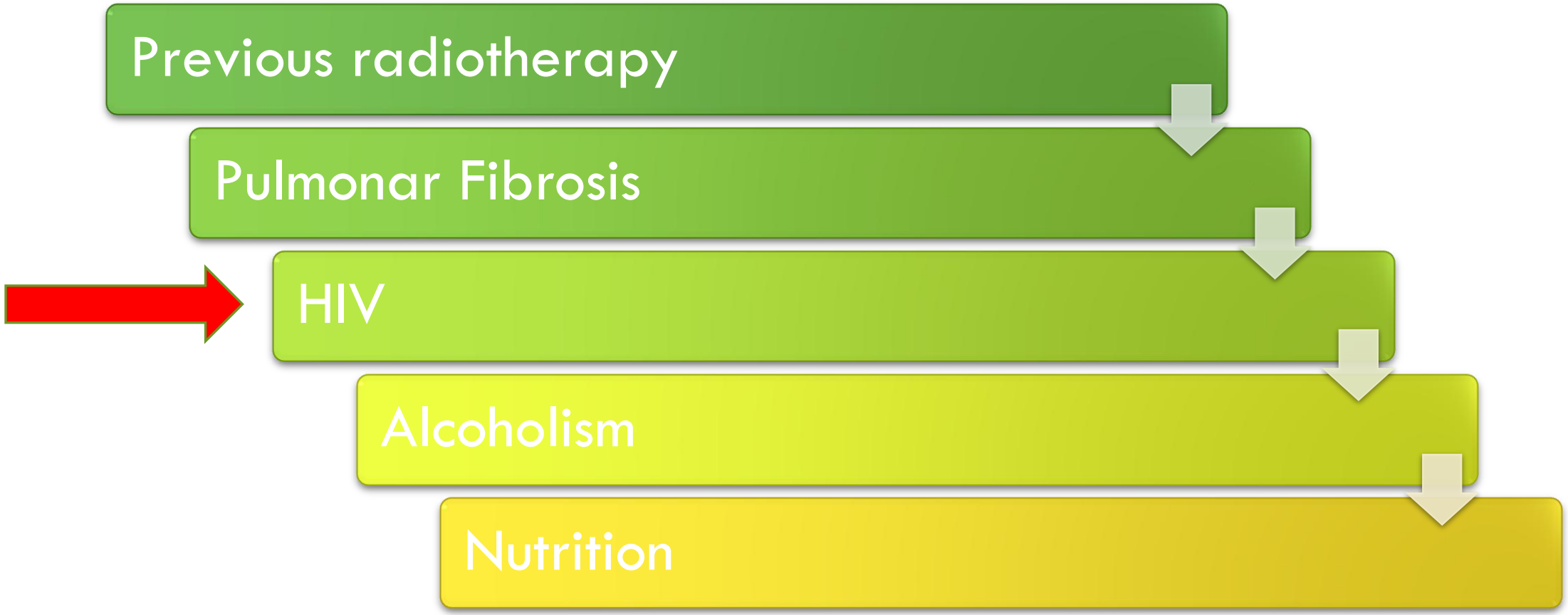
- In granitic áreas, houses are made with this material reaching danger concentrations

Enviromental pollutants

- Cars, industry

Sílica; Arsenic; Berillyum; Cadmium; Níckel; Tar; Soot

OTHER RISK FACTORS



CONSUMO DE TABACO

Valores em milhões de unidade, referentes ao período de janeiro a junho

NOTA: As representações gráficas entre os diferentes produtos não estão em proporção

PREVENTION – ENVIRONMENTAL FACTORS

- Respect security mesures (masks)
- Healthy eating with vegetables and fruit
- Obesity control
- Physical exercise

Ann Am Thorac Soc. 2018 Apr;15(Supplement_2):S132-S133. doi: 10.1513/AnnalsATS.201707-614MG.

Effects of Household Air Pollution in Malawi and Human Immunodeficiency Virus Status on Respiratory Symptoms and Inflammation, Injury, and Repair Markers.

Kim C[1], Jary H[2,3], Mortimer K[3], Schweitzer KS[4], Curran-Everett D[1,4], Gordon S[5], Petrache I[1,4].

Author information

Abstract

RATIONALE: Household air pollution (HAP) and human immunodeficiency virus (HIV) are associated with increased risk for chronic obstructive pulmonary disease. Both HAP and HIV are widespread in Sub-Saharan Africa, including Malawi, where HIV has 10.6% prevalence in patients 15-49 years old.

OBJECTIVES: We hypothesized that HIV infection (HIV^+) and habitual exposure to HAP (HAP^+) synergize to cause systemic inflammation and vascular injury, which may herald early onset of chronic respiratory diseases.

METHODS: In this pilot study, 50 subjects from Malawi with known HIV status were administered surveys recording demographics, HAP exposure, and respiratory symptoms/diagnoses. Peripheral blood was collected, and Meso Scale Discovery V-Plex assay was used to measure the levels of 41 serum markers.

RESULTS: Almost all subjects (96%) reported HAP^+, 30 were HIV^+, 20 were HIV^-, with a mean age of 22 years in both groups. More females (73%) were HIV^+, whereas 65% of those who were HIV^- were males. The vast majority were never-smokers (70% of HIV^- and 83% of HIV^+ subjects, respectively). Forty-six percent of all subjects (57% of HIV^+HAP^+ and 33% of HIV^-HAP^+) reported respiratory diagnoses and/or respiratory symptoms, with breathlessness and cough being most common. Although HIV^+HAP^+ individuals had a trend to increased proinflammatory cytokines and vascular injury markers, and decreases in proangiogenic factors compared with HIV^-HAP^+, only the decrease in serum interleukin-16 (by 44%) was statistically significant ($P = 0.03$). Also, compared with other subjects, serum interleukin-2 levels were significantly decreased (by 31%; $P = 0.02$) in HIV^+ subjects with persistent respiratory symptoms.

CONCLUSIONS: This study suggests a high prevalence of respiratory symptoms in HIV^+ individuals exposed to HAP. The significant decrease in interleukin-2 and interleukin-16, cytokines associated with HIV clearance, may contribute to viral persistence, and because their low levels were found to correlate with chronic obstructive pulmonary disease severity, they may serve as biomarkers for risk of chronic obstructive pulmonary disease in this vulnerable population.

KEYWORDS: HIV; Malawi; chronic obstructive pulmonary disease; household air pollution; indoor air pollution

PREVENTION – ENVIRONMENTAL FACTORS

SCREENING

RISKS

- Futile detection of small aggressive tumors or indolent disease
- Quality of life
  - Anxiety of test findings
- Physical complications from diagnostic workup
- False-positive results
- False-negative results
- Unnecessary testing and procedures
- Radiation exposure
- Cost
- Incidental lesions

NCCN Clinical Practice Guidelines in Oncology, Lung Cancer Screening, Version 2.2019 — August 27, 2018

SCREENING

BENEFITS

- **Decreased lung cancer mortality[1]**
- **Quality of life**
  - **Reduction in disease-related morbidity**
  - **Reduction in treatment-related morbidity**
  - **Improvement in healthy lifestyles**
  - **Reduction in anxiety/psychosocial burden**
- **Discovery of other significant occult health risks (eg, thyroid nodule, severe but silent coronary artery disease, early renal cancer in upper pole of kidney, aortic aneurysm, breast cancer)**

NCCN Clinical Practice Guidelines in Oncology, Lung Cancer Screening, Version 2.2019 — August 27, 2018

SCREENING – TO WHOM?

Recomended by american societies (NCCN):

- Professional exposure (Mines; Buildings)
- ≥ 50 years
- Smokers
- Ex-smokers ≤ 15anos
- ≥ 30 Packs/year

In Europe, only for researching purpose

Specific pathologies

Alison Morris. An Official ATS Workshop Report: Emerging Issues and Current Controversies in HIV-Associated Pulmonary Diseases. Am Thor Soc. Sep 2010.

SCREENING FOR LUNG CANCER IN PLWH

Nowadays there is an increased risk for the development of lung cancer in PLWH.

- In the National Lung Screening Trial, *annual low-dose helical chest CT screening in high-risk smokers* was associated with a reduction in lung cancer–specific mortality.
- One study *assessed annual CT-based lung cancer screening* (up to 4 scans) in 224 PLWH who were *current and former smokers with a ≥20 pack-year* history, between 2006 and 2013, and identified 1 case of lung cancer in 678 patient-years (young age)
- Another study assessed a *single CT scan* to screen for lung cancer in 442 HIV-infected smokers with a *≥20 pack-year* history and a *CD4+ T-cell nadir count of <350 cells/mcL*. Lung cancer was diagnosed via a CT scan in 9 patients (2.0%; 95% CI, 0.9–3.8).

The panel recommends that screening for lung cancer should be performed in PLWH based on the same criteria used in the general population.

Clinical Practice Guidelines in Oncology, NCCN - Cancer in People Living With HIV, Version 1.2018

SCREENING FOR LUNG CANCER IN PLWH

Lung cancer screening is not recommended in the general population; whether HIV-infected smokers represent a group that might benefit from screening and early detection is not known.

Diagnosis and treatment of lung cancer in HIV-infected patients is similar to that in non–HIV-infected individuals.

Alison Morris. An Official ATS Workshop Report: Emerging Issues and Current Controversies in HIV-Associated Pulmonary Diseases. Am Thor Soc. Sep 2010.

SCREENING

Chest xRay + Spumctum Citologic Exam

- *There is no decrease in mortality rate*

Toracic CT Scan (low dose)

- ***20% reduction in mortality***
- National Lung Screening Trial (NLST):
  - 53.456 individuals (USA)
  - **55 - 74 years, smokers or ex-smokers (≤ 15 years) with ≥ 30 Packs/year**
  - Aim: anual CTscan vs Chest xR

More likely to have benign lung nodules.
Infectious granuloma and tuberculosis are possible differential diagnoses. An infectious disease workup should be performed when indicated.
Treatment for possible non-malignant diagnoses can be considered before biopsy.

SCREENING ASSESSMENT

- If concurrent pulmonary Kaposi sarcoma - increased bleeding may occur during biopsies
- Lung biopsies should be cultured for bacteria, fungi, and mycobacteria acid-fast bacilli.
- Brain lesions + NSCLC + HIV: rule out infectious processes (eg, toxoplasmosis) or other malignancies such as non-Hodgkin's lymphoma.

*Screening for lung cancer with CT may be effective, however, the low yield is probably due to the young age of most of these patients, so new strategies for targeting screening efforts are needed**

*Major Infectious Diseases, 3rd edition. *Disease Control Priorities, Vol. 6,* Chapter 3HIV/AIDS Comorbidities: Impact on Cancer, Noncommunicable Diseases, and Reproductive Health; Washington (DC); 2017 Nov 3.

Clinical Practice Guidelines in Oncology, NCCN - Cancer in People Living With HIV, Version 1.2018

Chronic Lung Disease in HIV

Screen for chronic lung disease:
- Are you 40 years or older?
- Have you smoked more than 10 pack years in your entire lifetime?

Then check for respiratory symptoms:
- Do you have ANY of the following on a regular basis: 1) shortness of breath when walking up a slight hill or hurrying on flat ground; 2) cough and/or sputum; 3) wheezing

"Yes" to all three questions

"Yes" to "shortness of breath on light exercise or at rest"

"No"
Repeat questions anually

Assess for airflow limitation with spirometry

Post-bronchodilator $FEV_1/FVC < 0.70$

Diagnose COPD

Post-bronchodilator $FEV_1/FVC > 0.70$, *but reduced lung volumes and/ or altered CO diffusion capacity test*

Consider chest CT for structural changes and/ or referral to respiratory specialist(iii)

Assessment of symptoms/risk of exacerbations(i)

Assessment of concomitant chronic diseases(ii)

Make comprehensive assessment particularly for the risk of concomitant CVD including pulmonary hypertension

European AIDS Clinical Society (EACS) Guidelines 9.0, 2017

SYMPTOMS AND SIGNS THAT ALERT FOR RESPIRATORY DISEASE

SIGNS AND SYMPTOMS OF ALERT

The clinical presentation of lung cancer in HIV-infected patients is similar to that in HIV-uninfected patients.

The majority of symptomatic patients have extended disease at time of diagnose

- Local effect (primary lesion)
- Regional effect/ distancy (methastasis)
- Effects not directly related with the tumor (Paraneoplasic Syndrome)

Alison Morris. An Official ATS Workshop Report: Emerging Issues and Current Controversies in HIV-Associated Pulmonary Diseases. Am Thor Soc. Sep 2010.

SIGNS AND SYMPTOMS OF ALERT

COUGH (50 – 75%)	New beggining, alteration of the usual pattern Scquamous and small cells – central involvement Obstructive pneumonia (tumor growth) Bronquiectasis (slow growth tumors, carcinoides)
HEMOPTISIS (20 – 50%)	Cancer is not the most frequente cause Consider first infection and bronquiectasis. Demands directed study to clear the diagnose (CTscan and broncofibroscopy)
THORACALGIA (20 – 40%)	More frequently in younger patients Pleura or chest wall involvement Obstructive pneumonia Pulmonary tromboembolism

SIGNS AND SYMPTOMS OF ALERT

DYSPNEA (25 – 40%)	Airway obstruction – extrinsic compression; endoluminal involvement Obstructive pneumonia / athelectasy Pneumothorax, pleural effusion PTE Pericardic effusion
DYSPHONIA (10 – 20%)	Recurrent laryngeal nerve involvement

- WEIGHT LOSS
- ANOREXIA
- REPETEAD RESPIRATORY INFETIONS

SIGNS AND SYMPTOMS OF ALERT

SECONDARY INVOLVMENT - METASTASES	
PLEURA:	Pain, cough, dyspnea (¼ are assymptomatics)
BONE:	Pain, cognitive impairment (oncologic emergency)
CNS:	Headache, vomiting, cranial nerves defects, hemiparesis

SIGNS AND SYMPTOMS OF ALERT

PARANEOPLASIC SYNDROMES	
HYPERCALCEMIA	Bone mehastase
HYPONATREMIA	
MIASTENIC SYNDROME OF LAMBERT EATON	Previous to the neoplasy in 80% of cases. Insidious proximal muscle weakness, atrophy, hiporreflexia, transitory involvement of cranial nerves (diplopia, ptosis, disphagia)
HEMATOLOGIC	Anemia, leucocitosis, trombocitosis, eosinophilia, hipercoagulability
HYPERTROPHIC OSTEOARTROPATHY	Chronic proliferative periostite of long bones, digital hipocratism (hands and feet), oligo or poliarthrit (12% of patients with ADC)

WHEN AND WHOM EVALUATE?

≥ 50 years

Smokers

Ex smokers ≤ 15 years

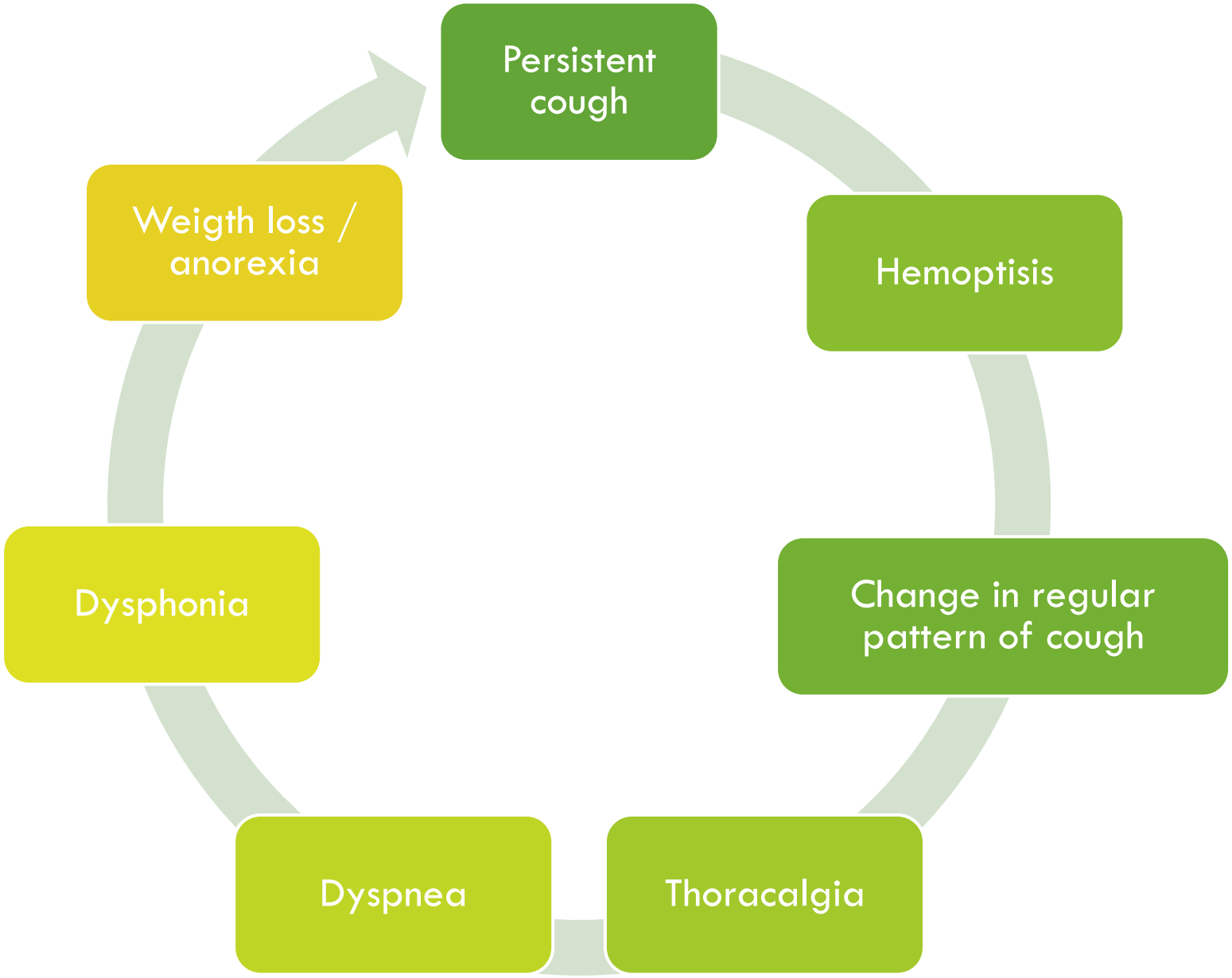
≥ 30 PY

Chronic respiratory pathology

Oncologic history

Patients submitted to radiotherapy

Family history of malignancies



WHEN AND WHAT COMPLEMENTARY DIAGNOSTIC METHODS SHOULD BE DEMAND

	Assessment	At HIV diagnosis	Prior to starting ART	Follow-up frequency	Comment
CO-MORBIDITIES					
Haematology	FBC	+	+	3-12 months	
	Haemoglobinopathies	+			Screen at risk persons
	G6PD	+			Screen at risk persons
Body Composition	Body-mass index	+	+	Annual	
Cardiovascular Disease	Risk assessment (Framingham score[iii])	+	+	2 years	Should be performed in all men > 40 years and women > 50 years without CVD
	ECG	+	+/-	As indicated	Consider baseline ECG prior to starting ARVs associated with potential conduction problems
Hypertension	Blood pressure	+	+	Annual	
Lipids	TC, HDL-c, LDL-c, TG[iv]	+	+	Annual	Repeat in fasting state if used for medical intervention (i.e. ≥ 8h without caloric intake)
Glucose	Serum glucose	+	+	Annual	Consider oral glucose tolerance test / HbA1c if fasting glucose levels of 5.7-6.9 mmol/L (100-125 mg/dL)
Pulmonary Disease	Respiratory symptoms and risk factors[xii]	+	+	Annual	If severe shortness of breath is reported with preserved spirometry, echocardiography may be performed to rule out heart failure and/or pulmonary hypertension
	Spirometry			As indicated	Spirometry should be performed in all symptomatic persons[xii]
Liver Disease	Risk assessment[v]	+	+	Annual	
	ALT/AST, ALP, Bilirubin	+	+	3-12 months	More frequent monitoring prior to starting and on treatment with

European AIDS Clinical Society (EACS) Guidelines 9.0, 2017

Analysis

Spumctum exam

- Direct and cultural exam plus molecular tests
- Microbiologic
- Micologic
- Citologic

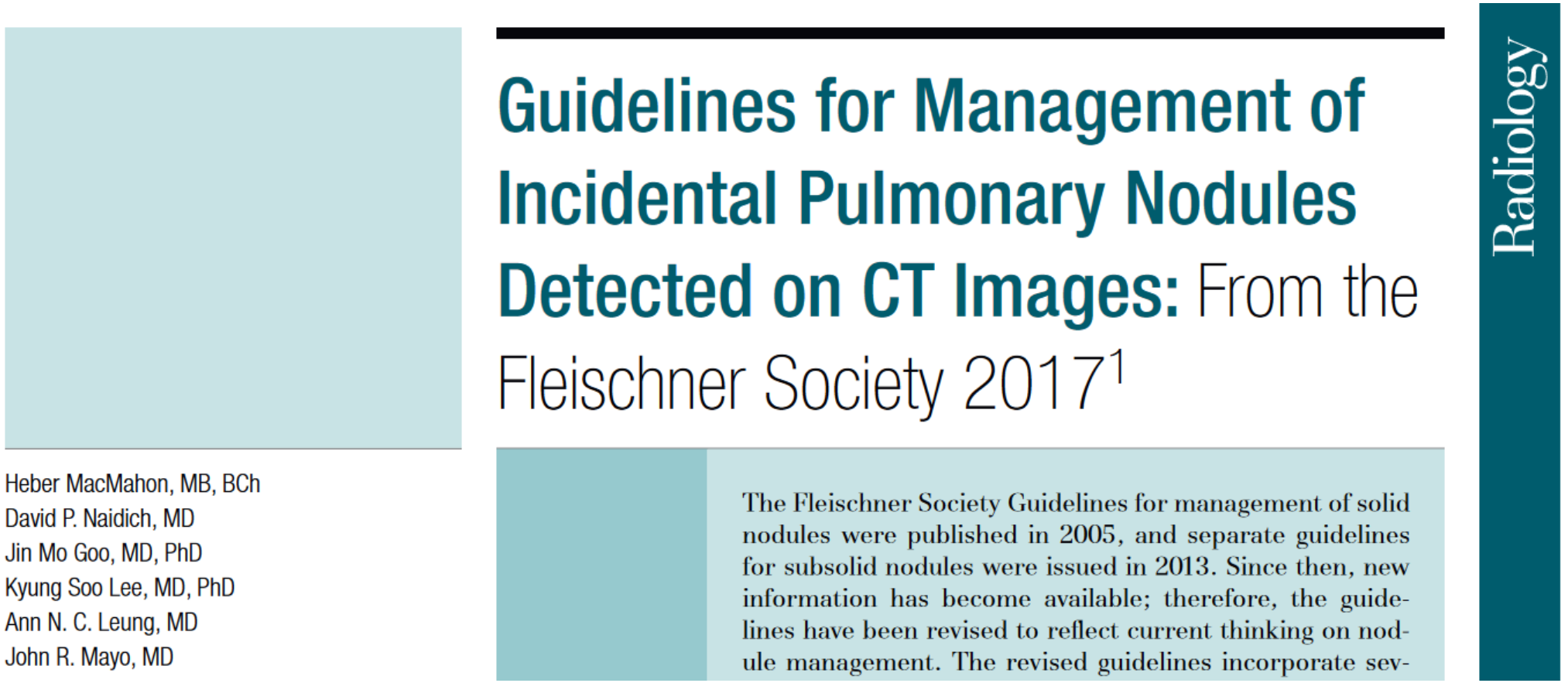
Funtional Respiratory Tests

- Spirometry
- Pletismografy
- Broncodilatation
- CO difusion

Chest xRay

CT Scan

WHEN AND WHAT COMPLEMENTARY DIAGNOSIS METHODS SHOULD BE DEMAND



Radiology

Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017[1]

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The Fleischner Society Guidelines for management of solid nodules were published in 2005, and separate guidelines for subsolid nodules were issued in 2013. Since then, new information has become available; therefore, the guidelines have been revised to reflect current thinking on nodule management. The revised guidelines incorporate sev-

Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017

Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017[1]

The revised guidelines incorporate several substantive changes that reflect current thinking on the management of small nodules:

- The minimum threshold size for routine follow-up has been increased
- Recommended follow-up intervals are now given as a range rather than as a precise time period

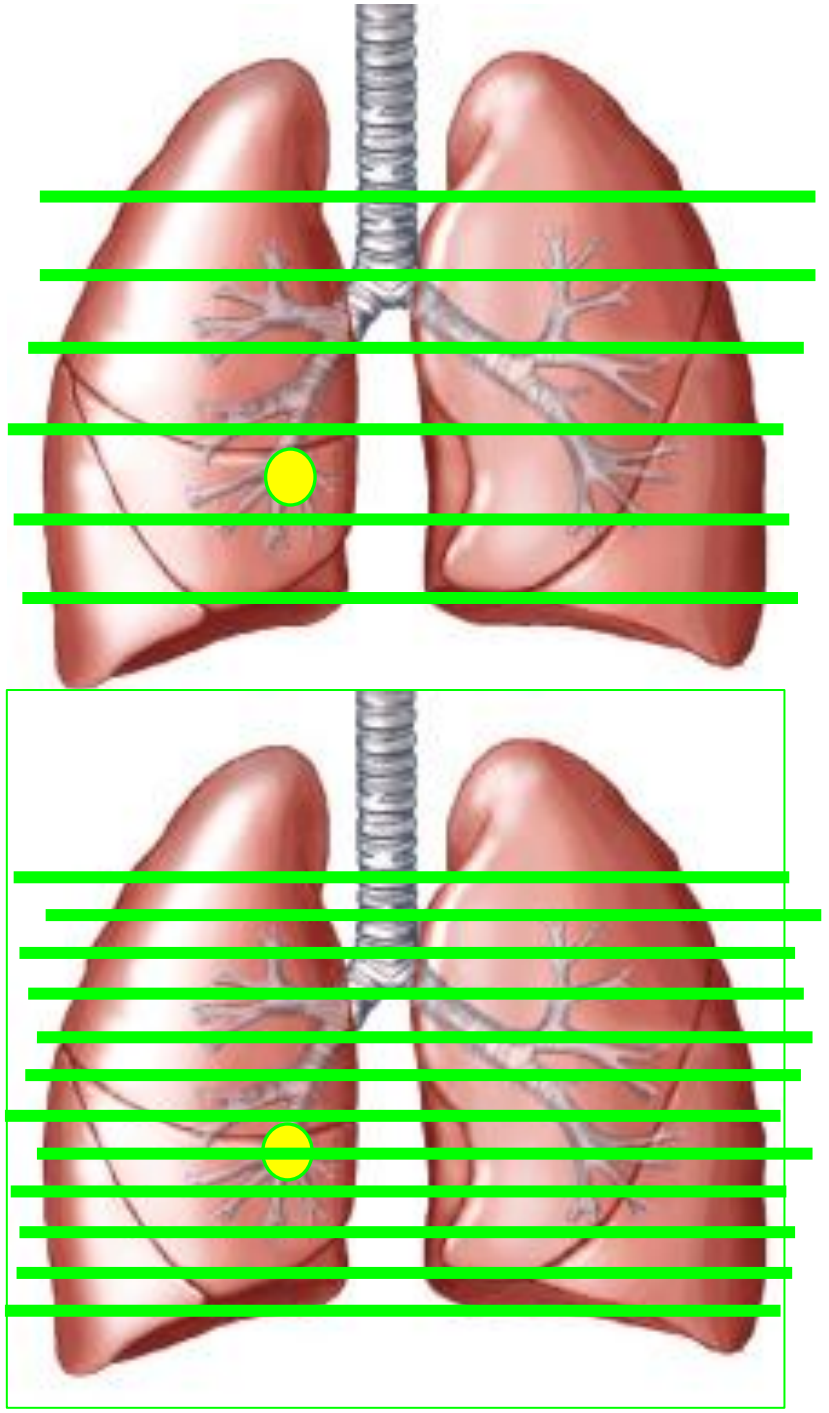
The purpose of these recommendations is to reduce the number of unnecessary follow-up examinations, accounting for multiple factors and patient preference.

Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017[1]

For diagnose and follow up: *Normal CT scan* instead of High Resolution CT Scan (HRCTS)

For follow up, most nodules smaller than 1 cm will not be visible on chest radiographs

Larger solid nodules of low risk: follow-up with radiography rather than CT (lower radiation)



Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017[1]

Risk Factors for Malignancy - General Considerations:

- Size and Morphology (larger, spiculation)
- Location (upper lobes, right lobe)
- Multiplicity
- Growth Rate
- Emphysema and Fibrosis
- Age, Sex, Race, and Family History (older, female, black)
- Tobacco and Other Inhaled Carcinogens

A: Solid Nodules*

Nodule Type	Size: <6 mm (<100 mm^3)	Size: 6–8 mm (100–250 mm^3)	Size: >8 mm (>250 mm^3)	Comments
Single				
Low risk†	No routine follow-up	CT at 6–12 months, then consider CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Nodules <6 mm do not require routine follow-up in low-risk patients (recommendation 1A).
High risk†	Optional CT at 12 months	CT at 6–12 months, then CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A).
Multiple				
Low risk†	No routine follow-up	CT at 3–6 months, then consider CT at 18–24 months	CT at 3–6 months, then consider CT at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).
High risk†	Optional CT at 12 months	CT at 3–6 months, then at 18–24 months	CT at 3–6 months, then at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).

Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017

B: Subsolid Nodules*

Nodule Type	Size: <6 mm (<100 mm³)	Size: ≥6 mm (>100 mm³)	Comments
Single			
Ground glass	No routine follow-up	CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years	In certain suspicious nodules < 6 mm, consider follow-up at 2 and 4 years. If solid component(s) or growth develops, consider resection. (Recommendations 3A and 4A).
Part solid	No routine follow-up	CT at 3–6 months to confirm persistence. If unchanged and solid component remains <6 mm, annual CT should be performed for 5 years.	In practice, part-solid nodules cannot be defined as such until ≥6 mm, and nodules <6 mm do not usually require follow-up. Persistent part-solid nodules with solid components ≥6 mm should be considered highly suspicious (recommendations 4A-4C)
Multiple	CT at 3–6 months. If stable, consider CT at 2 and 4 years.	CT at 3–6 months. Subsequent management based on the most suspicious nodule(s).	Multiple <6 mm pure ground-glass nodules are usually benign, but consider follow-up in selected patients at high risk at 2 and 4 years (recommendation 5A).

Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017

WHAT CAN BE DONE BEFORE THE PULMONOLOGY APPOINTMENT

SMOKING CESSATION IN PLWH WHO HAVE CANCER

Should be offered to all PLWH who smoke and have cancer.

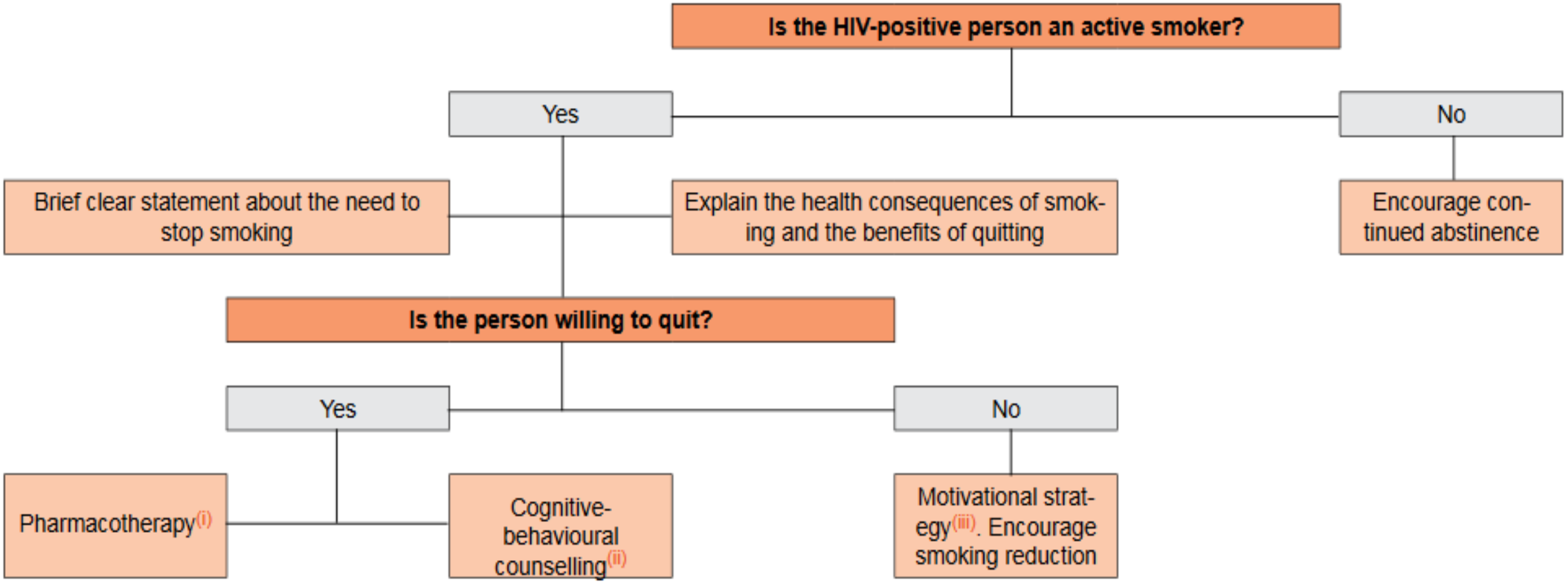
In the general population improved general health and well-being, reduced treatment-related complications, decreased cancer recurrence, fewer second primary tumors, and improved survival

There is lack of data specific to PLWH after a cancer diagnosis.

Clinical Practice Guidelines in Oncology, NCCN - Cancer in People Living With HIV, Version 1.2018

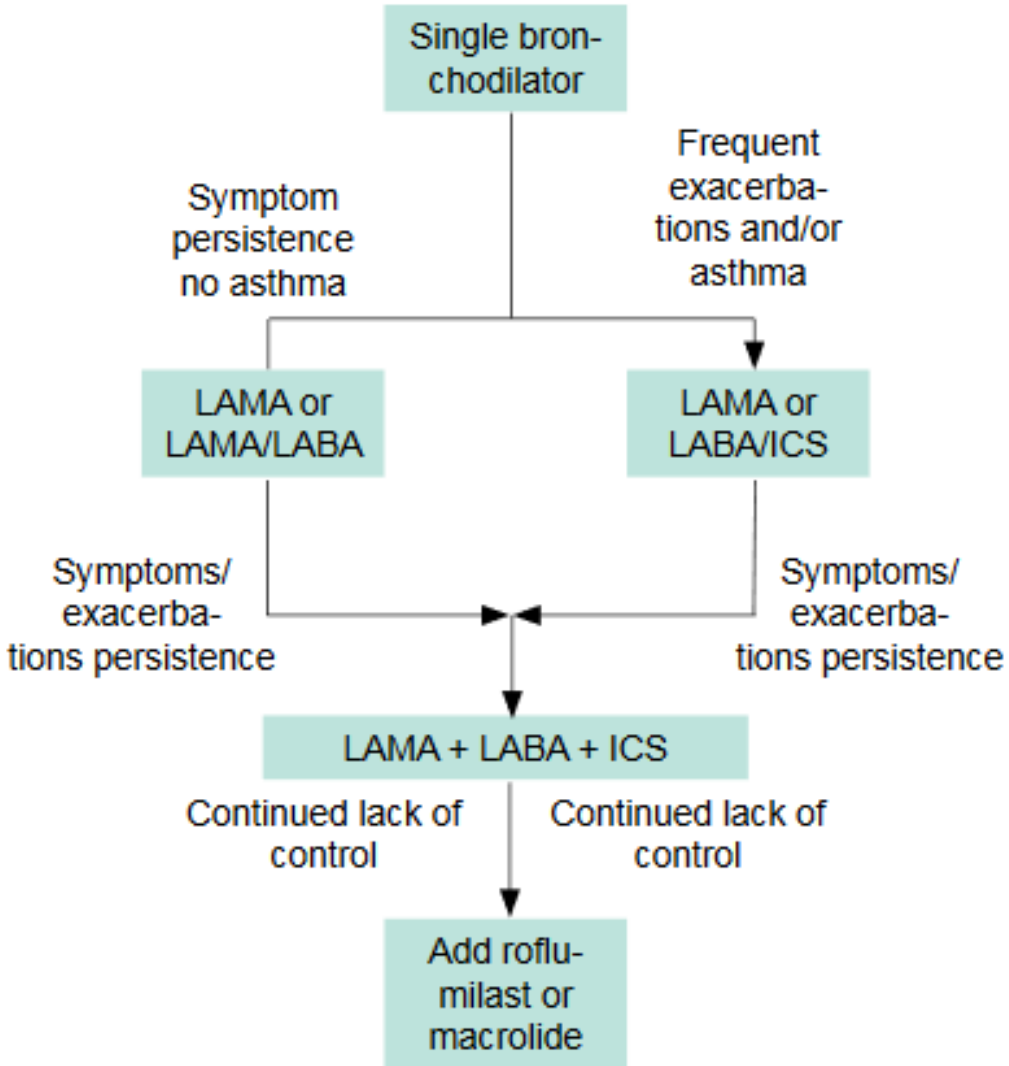
Smoking cessation

HIV-positive tobacco users should be made aware of the substantial health benefits of smoking cessation which include reducing the risk of tobacco-related diseases, slowing the progression of existing tobacco related disease, and improving life expectancy by an average of 10 years.
Regularly consider the following algorithm with two major questions:



European AIDS Clinical Society (EACS) Guidelines 9.0, 2017

Treatment of COPD[iv]



LABA: long-acting β2-agonist
LAMA: long-acting muscarinic antagonist
ICS: inhaled corticosteroid

i Assessment of either dyspnoea using mMRC, see https://www.verywell.com/guidelines-for-the-mmrc-dyspnea-scale-914740 or symptoms using CAT™, see http://www.catestonline.org/ and history of exacerbations (including prior hospitalisations)

ii COPD itself has significant extra-pulmonary (systemic) effects including weight loss, nutritional abnormalities and skeletal muscle dysfunction

iii Based on expert opinion

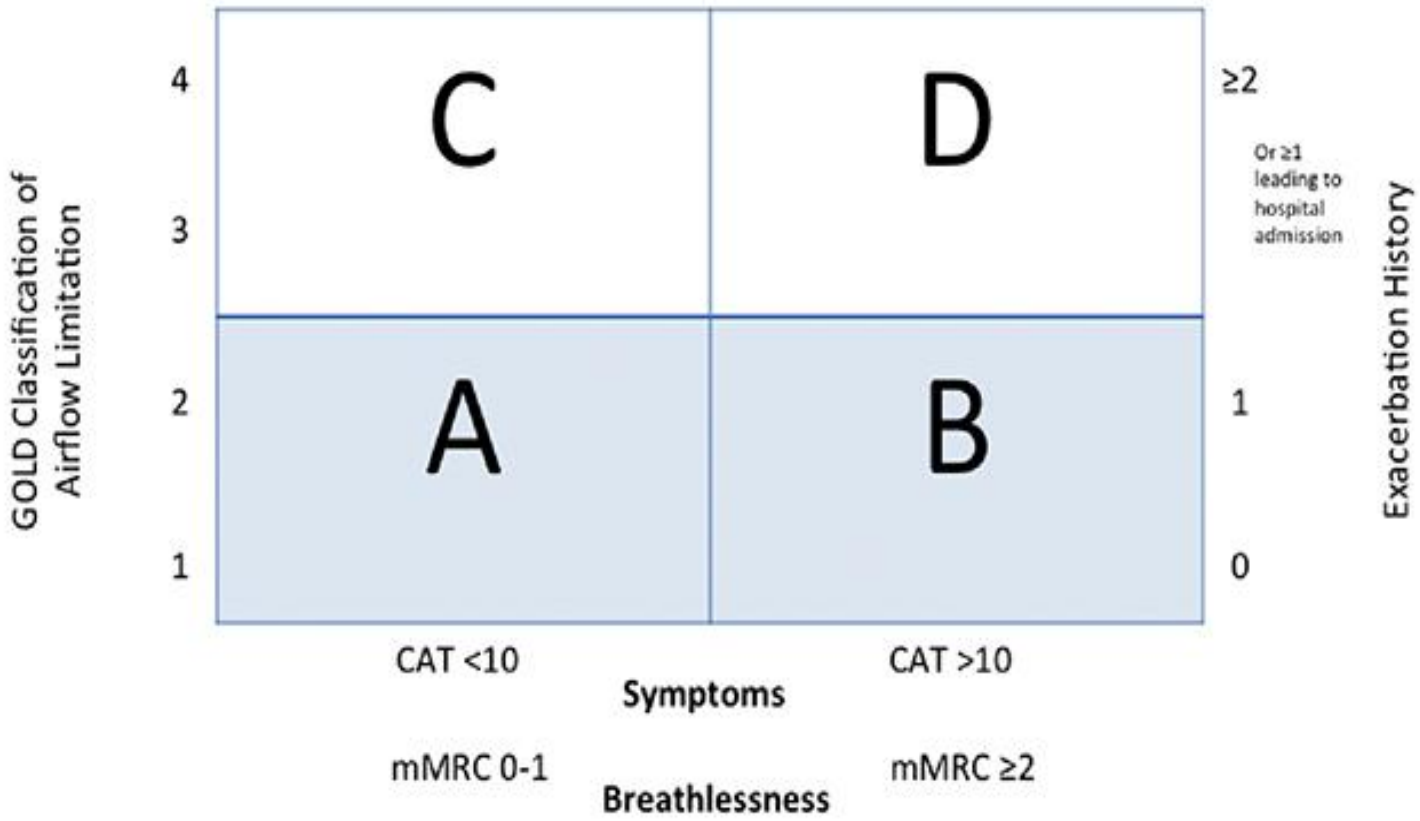
iv Each pharmacological treatment should be individualised and guided by the severity of symptoms, risk of exacerbations, adverse effects, co-morbidities, drug availability and cost, and the individual's response, preference and ability to use various drug delivery devices.
Inhaler technique needs to be assessed regularly.
Long-term use of oral glucocorticoids has no evidence of benefits in COPD. Because of the risk of pneumonia and because of proven superiority of LABA/LAMA over LABA/ICS, the addition of ICS to LABA is recommended only in individuals with history of frequent exacerbations and/or asthma or in individuals not adequately controlled by LAMA/LABA combination. Do not use inhaled glucocorticoids with boosted ART regimens, see Drug-drug Interactions between Corticosteroids and ARVs.
Influenza and pneumococcal vaccination decreases rates of lower respiratory tract infections, see Vaccination

There are 3 life saving interventions:
1. Smoking cessation
2. Chronic oxygen when stable (non-exacerbated) resting $SpO_2 \leq 88\%$ (or $PaO_2 \leq 55$ mmHg)
3. Non-invasive ventilation (NIV) in individuals with acute hypercapnic respiratory failure

The MRC Breathlessness Scale

Grade	Degree of breathlessness related to activities
1	Not troubled by breathlessness except on strenuous exercise
2	Short of breath when hurrying on the level or walking up a slight hill
3	Walks slower than most people on the level, stops after a mile or so, or stops after 15 minutes walking at own pace
4	Stops for breath after walking about 100 yds or after a few minutes on level ground
5	Too breathless to leave the house, or breathless when undressing

Figure 1. GOLD Strategy for COPD Categorization




Duaklir Genuair

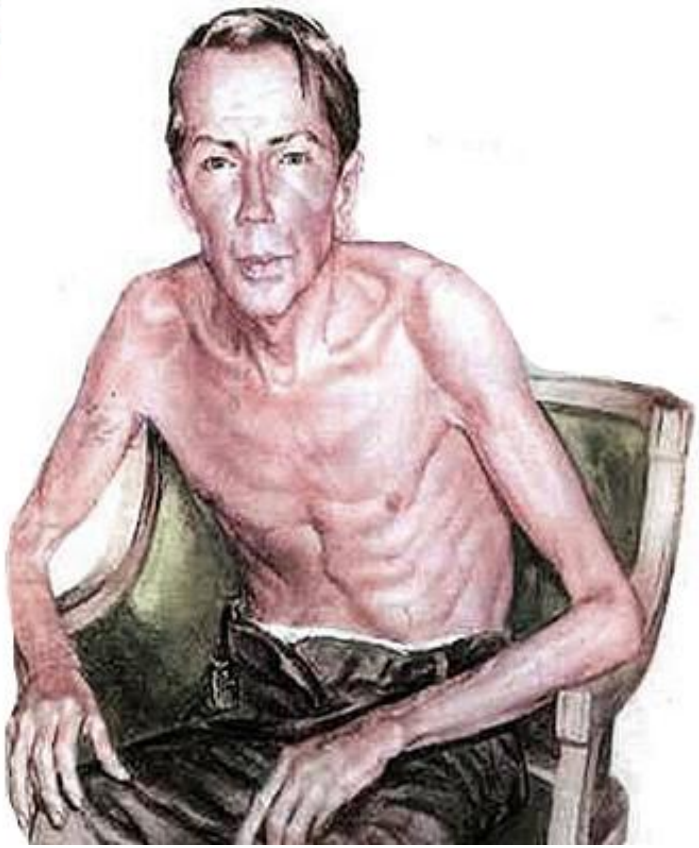

100/50
ADVAIR


RELVAR
92/22 µg
30


ultibro
breezhaler
NOVARTIS


HandiHaler


120
flutiform



DRUG-DRUG INTERACTIONS

	Non-ARV drugs	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c	RAL	ABC	FTC	3TC	TAF	TDF	ZDV
	bupropion	↔	↓	↔	↓	↓57%	↓55%	↔	↓	↔	↔	↔	↑?	↔	↔	↔	↔	↔	↔	↔
Miscellaneous	antacids	D	D	↔	↔	↔	↔	↔	↔	D	↔	D	D	D	↔	↔	↔	↔	↔	↔
	PPIs	D	D	↔	↔	↔	↔	↔	↔	D	↔	↔	↔	E	↔	↔	↔	↔	↔	↔
	H2 blockers	D	D	↔	↔	↔	↔	↔	↔	D	↔	↔	↔	E	↔	↔	↔	↔	↔	↔
	alfuzosin	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
	beclometasone inhal.	↑[v]	↑[v]	↑?[v]	↓11%	↑[v]	↔	↔	↔	↔	↔	↔	↑[v]	↔	↔	↔	↔	↔	↔	↔
	buprenorphine	↑	↑67%	↑	↑[vi]	↔	↓50%	↓25%	↔	↔	↔	↔	↑35%	↔	↔	↔	↔	↔	↔	↔
	budesonide inhal.	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
	ergot derivatives	↑	↑	↑	↑	↑	↑	↑	↓	E	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
	ethinylestradiol	↔	↓19%[vii]	↑30%	↓44%	↓ 2%	↔[viii]	↑22%	↓20%	↑14%	↔	↑3%	↓25%	↔	↔	↔	↔	↔	↔	↔
	fluticasone inhal.	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
	methadone	↑?[iii]	↓[ii, iii]	↑?	↓16%	↓53%[iii]	↓52%	↑6%	↓≈50%	↓16%	↔	↔	↑7%	↔	↓	↔	↔	↔	↔	E29-43%
	salmeterol inhal.	↑[iii]	↑[iii]	↑	↑	↑[iii]	↓	↓	↓	↔[iv]	↔	↔	↑[iii]	↔	↔	↔	↔	↔	↔	↔
	sildenafil (erec. dys.)	↑	↑	↑	↑	↑	↓	↓37%	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
	St John's wort	D	D	D	D	D	D	D	D	D	D	D	D	D?	↔	↔	↔	D	↔	↔
	varenicline	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔

European AIDS Clinical Society (EACS) Guidelines 9.0, 2017

Drug-drug Interactions between Bronchodilators (for COPD) and ARVs

	Bronchodilators	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c	RAL	ABC	FTC	3TC	TAF	TDF	ZDV
LAMA	aclidinium bromide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
LAMA	glycopyrronium bromide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
LAMA	tiotropium bromide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
LAMA	umeclidinium bromide	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
SAMA	ipratropium	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
LABA	formoterol	↔[a]	↔[a]	↔	↔	↔[a]	↔	↔	↔	↔[a]	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
LABA	indacaterol	↑[d]	↑[d]	↑[d]	↑[d]	↑[d]	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
LABA	olodaterol	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
LABA	salmeterol	↑[b]	↑[b]	↑[b]	↑[b]	↑[b]	↓	↓	↓	↔[a]	↔	↔	↑[b]	↔	↔	↔	↔	↔	↔	↔
LABA	vilanterol	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
SABA	salbutamol (alb-uterol)	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
MX	aminophylline	↔	↓	↔	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
MX	theophylline	↔	↓	↔	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
PDE4	roflumilast	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
ICS	beclometasone	↑[c]	↑[c]	↑?[c]	↓11%	↑[c]	↔	↔	↔	↔	↔	↔	↑[c]	↔	↔	↔	↔	↔	↔	↔
ICS	budesonide	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
ICS	fluticasone	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔

European AIDS Clinical Society (EACS) Guidelines 9.0, 2017

Drug-drug Interactions between Corticosteroids and ARVs

Corticosteroids	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c	RAL	ABC	FTC	3TC	TAF	TDF	ZDV
Inhaled, oral, topic and/or injected corticosteroids: beclometasone (inhalation)	↑[a]	↑[a]	↑?[a]	↓[b]	↑[a]	↔	↔	↔	↔	↔	↔	↑[a]	↔	↔	↔	↔	↔	↔	↔
betamethasone	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	D	D	↔	↑[c]	↔	↔	↔	↔	↔	↔	↔
budenoside (inhalation)	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	↔	↔	↔	↑[c]	↔	↔	↔	↔	↔	↔	↔
clobetasol (topical)	↑[c,d]	↑[c,d]	↑[c,d]	↑[c,d]	↑[c,d]	↔	↔	↔	↔	↔	↔	↑[c,d]	↔	↔	↔	↔	↔	↔	↔
dexamethasone	↑[c] D	↑[c] D	↑[c] D	↑[c] D	↑[c] D	↓ D	↓ D	↓ D	D	D	↔	↑[c] D	↔	↔	↔	↔	↔	↔	↔
fluocinolone (topical)	↑[c,d]	↑[c,d]	↑[c,d]	↑[c,d]	↑[c,d]	↔	↔	↔	↔	↔	↔	↑[c,d]	↔	↔	↔	↔	↔	↔	↔
fluticasone (inhalation)	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	↔	↔	↔	↑[c]	↔	↔	↔	↔	↔	↔	↔
hydrocortisone (oral)	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	↔	↔	↔	↑[c]	↔	↔	↔	↔	↔	↔	↔
hydrocortisone (topical)	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
methylpredni-solone	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	↔	↔	↔	↑[c]	↔	↔	↔	↔	↔	↔	↔
mometasone (inhalation)	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	↔	↔	↔	↑[c]	↔	↔	↔	↔	↔	↔	↔
prednisolone (oral)	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓ 40%	↓	↓	↔	↔	↔	↑[c]	↔	↔	↔	↔	↔	↔	↔
prednisone	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓ 40%	↓	↓	↔	↔	↔	↑[c]	↔	↔	↔	↔	↔	↔	↔
triamcinolone	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	↔	↔	↔	↑[c]	↔	↔	↔	↔	↔	↔	↔

European AIDS Clinical Society (EACS) Guidelines 9.0, 2017

HIV THERAPY DURING CANCER TREATMENT

HIV specialist + oncology team.

Already on ART: continue during cancer treatment (+-modifications).

Not yet on ART: initiate ART either ≥7 days before starting the cancer treatment or long enough after cancer therapy has been initiated (distinguish adverse effects of each therapy).

ART interruptions during cancer treatment should be avoided, increases the risk of:

- Immunologic compromise
- Opportunistic infection
- Death.

Clinical Practice Guidelines in Oncology, NCCN - Cancer in People Living With HIV, Version 1.2018

HIV THERAPY DURING CANCER TREATMENT

- Poor performance status of PLWH is multifactorial.
- Treatment with ART may improve PS.
- Continuation of ART may also result in better tolerance of cancer treatment, higher response rates, and improved survival.

- Drug interactions can occur in patients with NSCLC and HIV.
- Both an HIV pharmacist and an oncology pharmacist should be consulted.

Clinical Practice Guidelines in Oncology, NCCN - Cancer in People Living With HIV, Version 1.2018

TAKE-HOME MESSAGES

- At present time, PLWH should be screened, treated and followed for COPD and lung cancer by the same criteria of non-infected patients
- Screening for lung cancer could be done in ≥ 50 years, smokers, ex-smokers ≤ 15years, ≥ 30 PY, family history and comorbidities (…)
- Low-dose CT scan is more appropriate then Chest x-Ray for screening
- Being aware of alert signs and symptoms is crucial to make the diagnose
- PLWH should have the same diagnostic and therapeutic opportunities

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VIH e doença de orgão –O desafio a longo prazo

CICLO DE REUNIÕES TEMÁTICAS

1ª Reunião
Patologia Pulmonar

Organização: NEDVIH e Consulta de Medicina Interna/ Infeciologia do C. H. Barreiro Montijo

Patologia Pulmonar
C.H. Barreiro-Montijo

COPD AND LUNG CANCER – EARLY DIAGNOSIS AND FOLLOW-UP

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