2022.2.21 제 285회 대한결핵 및 호흡기학회 심포지엄

Bronchiectasis-COPD Overlap (BCO) Patients with Low Lung function and Frequent Exacerbations: What is the best Treatment Strategy?

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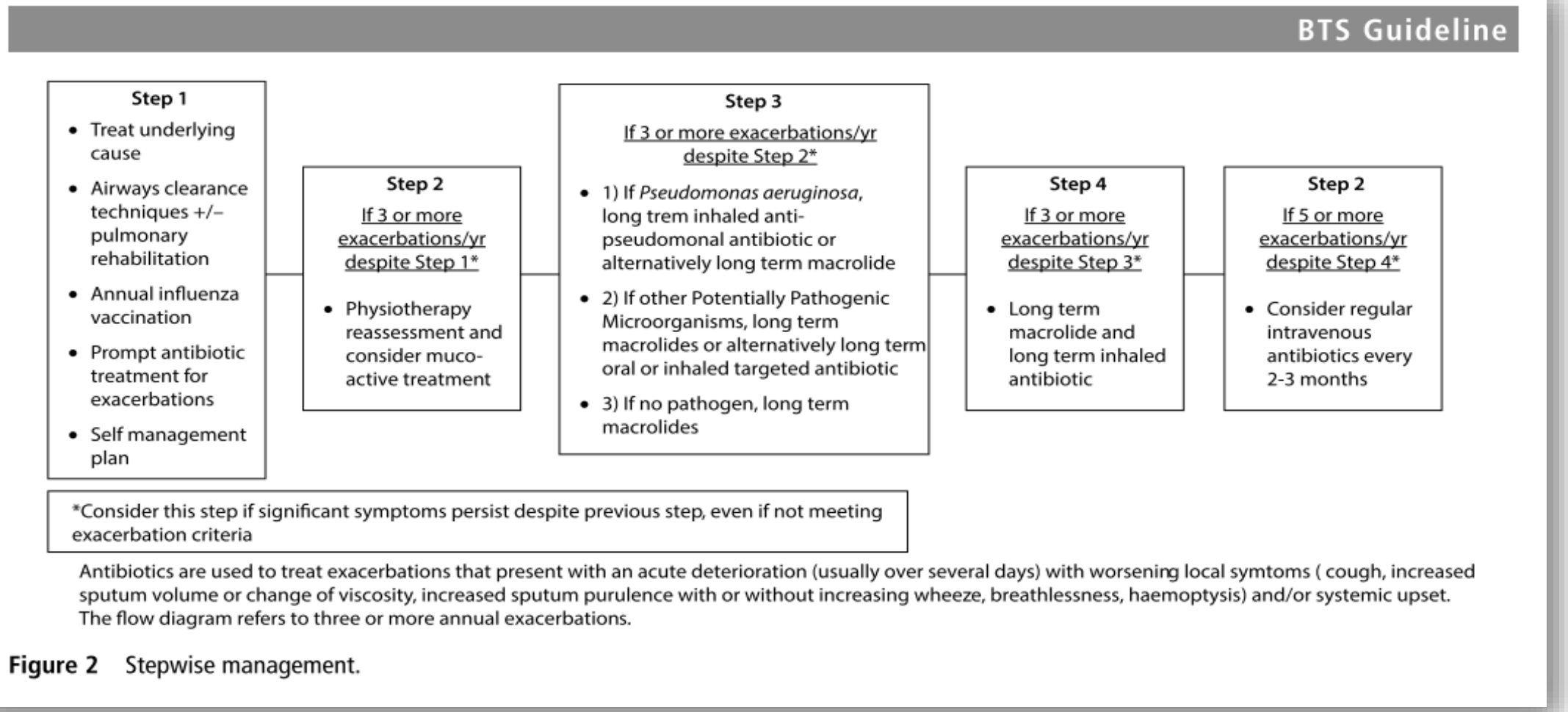
Management of Bronchiectasis



Antibiotics are used to treat exacerbations that present with an acute deterioration (usually over several days) with worsening local symtoms (cough, increased sputum volume or change of viscosity, increased sputum purulence with or without increasing wheeze, breathlessness, haemoptysis) and/or systemic upset. The flow diagram refers to three or more annual exacerbations.

Figure 2 Stepwise management.

British Thoracic Society Guideline for bronchiectasis in adults. Thorax. 2019

Treatment of bronchiectasis

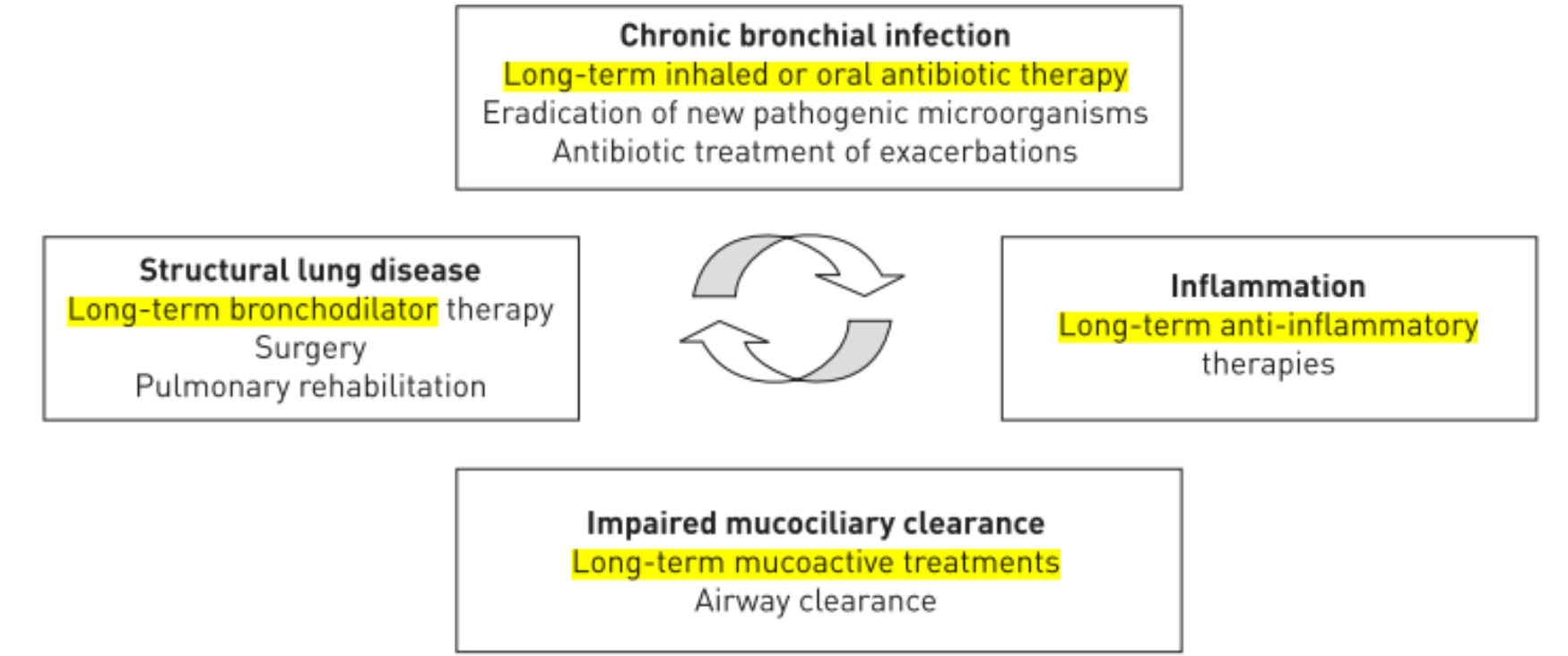


FIGURE 1 Treatments for bronchiectasis considered in this guideline according to the vicious cycle concept of bronchiectasis.

European Respiratory Society guidelines for the management of adult bronchiectasis. ERJ. 2017;50(3).

Treatment of bronchiectasis

Treatable (therapeutic) traits

Chronic airway infection
- Antibiotic therapy
  - Inhaled
  - Targeted
  - Macrolides

Pathogen acquisition
- *Pseudomonas aeruginosa* eradication therapy

Immunodeficiency
- Immunoglobin replacement
- Prophylactic antibiotics

NTM
- Antibiotic therapy

ABPA
- Corticosteroids
- +/– antifungals

Airflow obstruction and functional impairment
- Pulmonary rehabilitation
- Bronchodilators

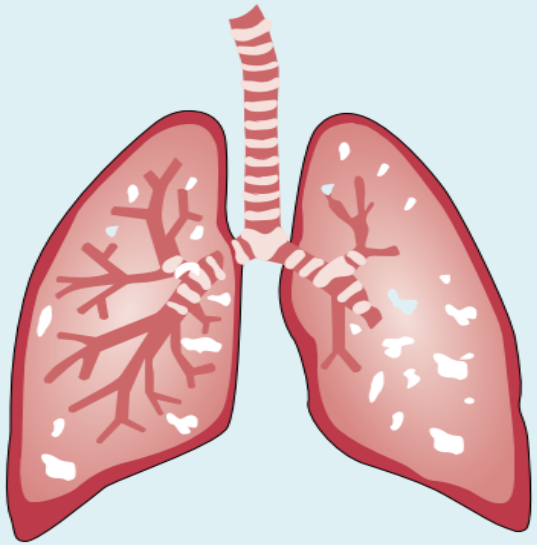
Sputum production
- Airway clearance
- Mucoactive drugs

Asthma and eosinophilia
- Inhaled corticosteroids

Low BMI
- Nutrition

GORD
- PPI
- +/– prokinetics

Other comorbidities
- Treat appropriately



Other factors
- Ethnic differences
- Environmental exposures
- Climatic variation
- Lifestyle
- Psychosocial

Targetable (endophenotypic) traits

Microbial (bacterial) dysbiosis
- Probiotics

Mycobiome (fungal) dysbiosis
- Antifungals

Neutrophil dysfunction
- Neutrophli elastase inhibitors

Protease-mediated lung damage
- Protease inhibitors

Ciliary dysfunction (primary or secondary)
- Airway clearance
- CFTR potentiator therapy

Systemic inflammation and vascular dysfunction
- Anti-inflammatory therapy

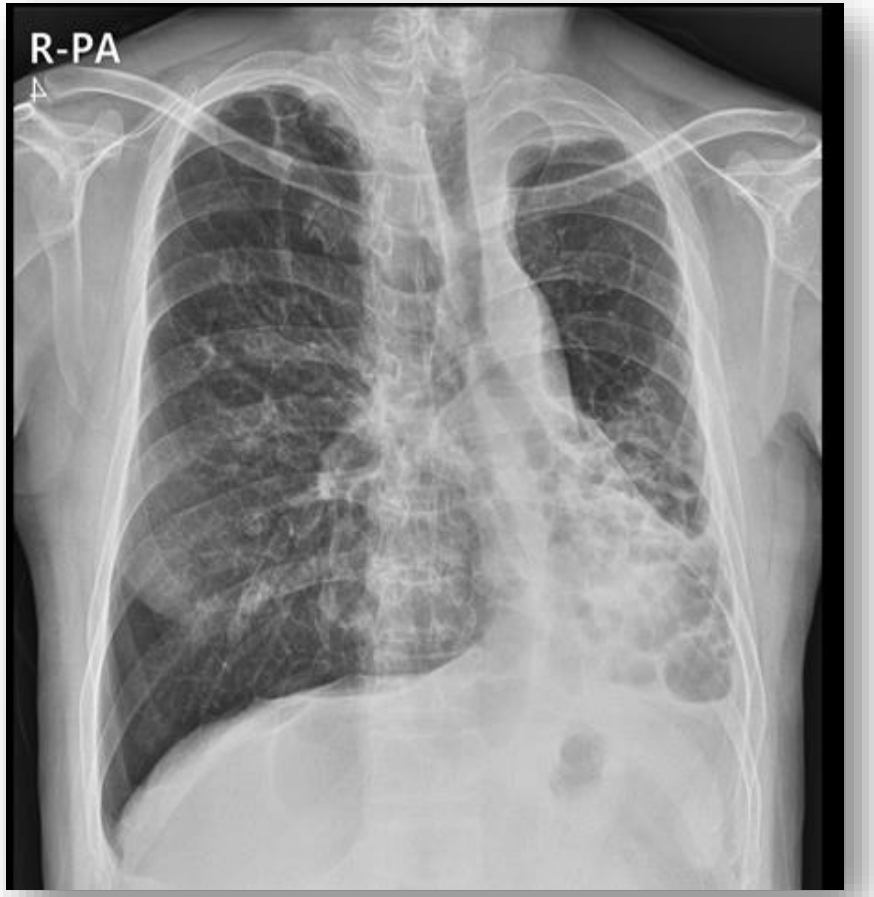
CFTR dysfunction
- CFTR potentiators
- CFTR correctors

Innate immune deficiency
- TLR-based therapeutics
- Antibiotic prophylaxis

Chalmers JD et al. Lancet Respir Med. 2018;6(9):715-26

Case #1st visit : 2021.9.24 opd

- M/57
- CC: Pre-op evaluation (inguinal hernia 로 수술계획)
- PHx:
  - old TB treatment (10대)
  - Bronchiectasis 로 2013년부터 타병원에서 추적 중 (진해거담제 복용)
  - s/p Bronchial artery embolization : 2013
- Smoking: 25pys, 2012 quit



Case #1st visit : 2021.9.24 opd

- Medication
  - Spiriva, foster 2 puff bid
  - axima, meptin, erdos
  - 악화시마다 methylon 2T or 3T daily + Levofloxacin 일주일여 사용
- Exacerbation history
  - 3년 전 1회 입원 치료, 이후 입원력은 없었다.
  - 1년에 1~2회 steroid, 항생제 opd 에서 복용하였다
- Initial saturation : 94% (room air), mMRC : 2, CAT score : 12
- BSI: 4 (mild), FACED: 2 (mild)
- Height: 174cm, wt: 68kg, BMI: 22.4

Table 4 Variables involved in calculating the severity score in the Bronchiectasis severity index

	Factor and points for scoring system			
Age (years)	<50 (0 points)	50–69 (2 points)	70–79 (4 points)	>80 (6 points)
BMI (Kg/m^2)	<18.5 (2 points)	18.5–25 (0 points)	26–30 (0 points)	>30 (0 points)
FEV_1% predicted	>80 (0 points)	50–80 (1 point)	30–49 (2 points)	<30 (3 points)
Hospital admission within last 2 years	No (0 points)		Yes (5 points)	
Number of exacerbations in previous 12 months	0 (0 points)	1–2 (0 points)	≥3 (2 points)	
MRC breathlessness score	1–3 (0 points)	4 (2 points)	5 (3 points)	
P. aeruginosa colonisation	No (0 points)		Yes (3 points)	
Colonisation with other organisms	No (0 points)		Yes (1 point)	
Radiological severity	<3 lobes affected (0 points)	≥3 lobes or cystic bronchiectasis in any lobe (1 point)		

0-4 Points=mild disease; 5–8=moderate disease; 9 and over=severe disease.

Table 5 Variables involved in calculating severity in the FACED score

	Factor and points for scoring system	
FEV_1% predicted	<50 (2 points)	≥50 (0 points)
Age (years)	≤70 (0 points)	>70 (2 points)
Colonisation by *P. aeruginosa*	No (0 points)	Yes (1 point)
Radiological extension of bronchiectasis	1–2 lobes (0 points)	>2 lobes (1 point)
Modified MRC dyspnoea scale	1–2 (0 points)	III-IV (1 point)

0–2 Points=mild disease; 3–4=moderate disease; 5–7=severe disease.

Case #1st visit : 2021.9.24 opd

- 2021.9.24 PFT

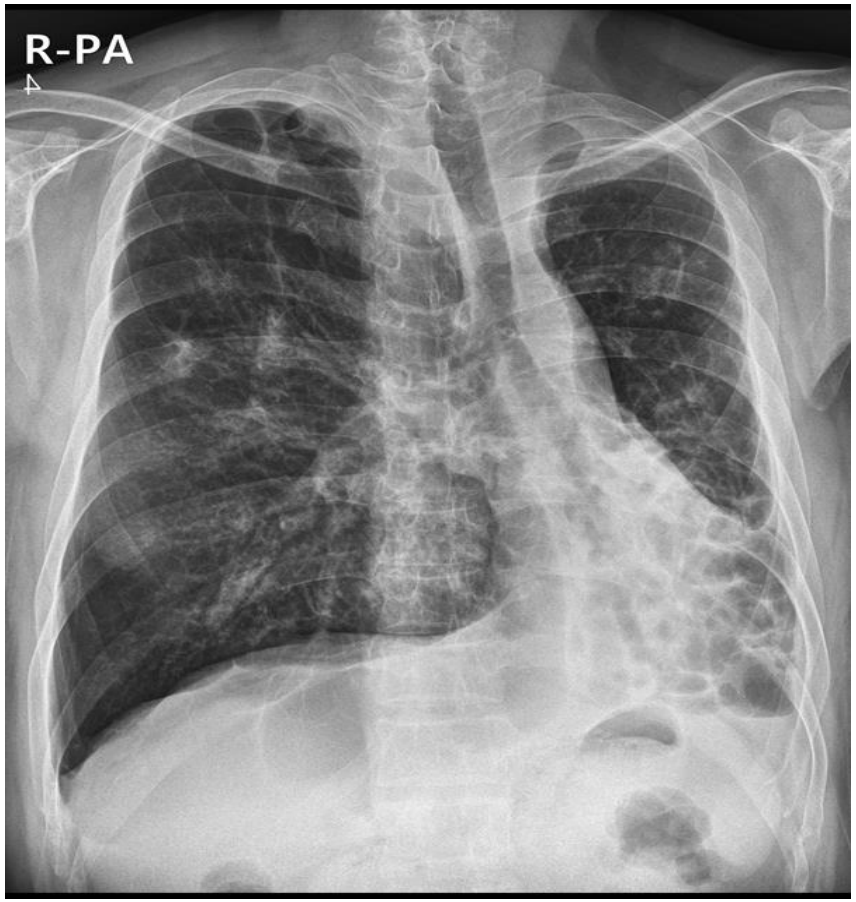
Date: 09/24/21

		Ref	Pre	% Ref	Post	% Ref	%Chg
Spirometry							
FVC	Liters	4.93	2.66	54	2.81	57	6
FEV1	Liters	3.84	1.19	31	1.15	30	-3
FEV1/FVC	%	75	45		41		
FEV3	Liters		1.81		1.82		0
FEV6	Liters		2.29		2.35		3
FEF25-75%	L/sec	3.21	0.36	11	0.32	10	-11
IsoFEF25-75	L/sec	3.21	0.36	11	0.47	15	30
FEF50%	L/sec	4.41	0.50	11	0.34	8	-31
PEF	L/sec	8.55	5.15	60	4.51	53	-12
FET100%	Sec		9.91		12.24		23
FIF50%	L/sec		3.58		3.75		5

- WBC: 8800/mm^3 (neutrophil 48%, eosinophil: 1%), CRP : 15 mg/L (N: 0~8 mg/L)
- 척수마취로 수술진행, Inguinal hernioplasty with mesh, bilateral [2021-10-04]

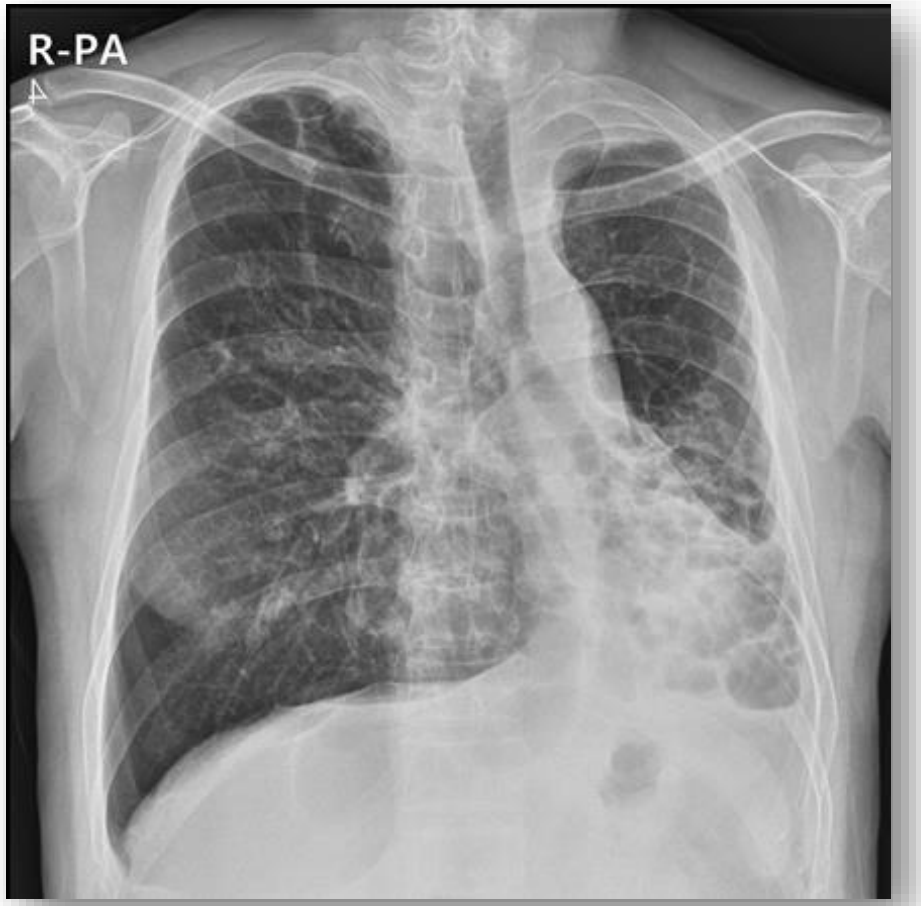
Case #1st admission : 2021.11.4~ 11.10

- 2021.11.4 ER 내원
  - 일주일여 전부터 호흡곤란, 기침, 가래 악화되어 ER 경유 입원.
  - Vital : 120/80, RR: 20 BT: 38 °, PR: 120, Saturation : 88% (room air)
  - EKG : sinus tachycardia
  - PEx: LLL wheezing + crackle
  - WBC : 13000/mm^3 (neutrophil 70%, eosinophil: 0.2%), CRP : 192 mg/L

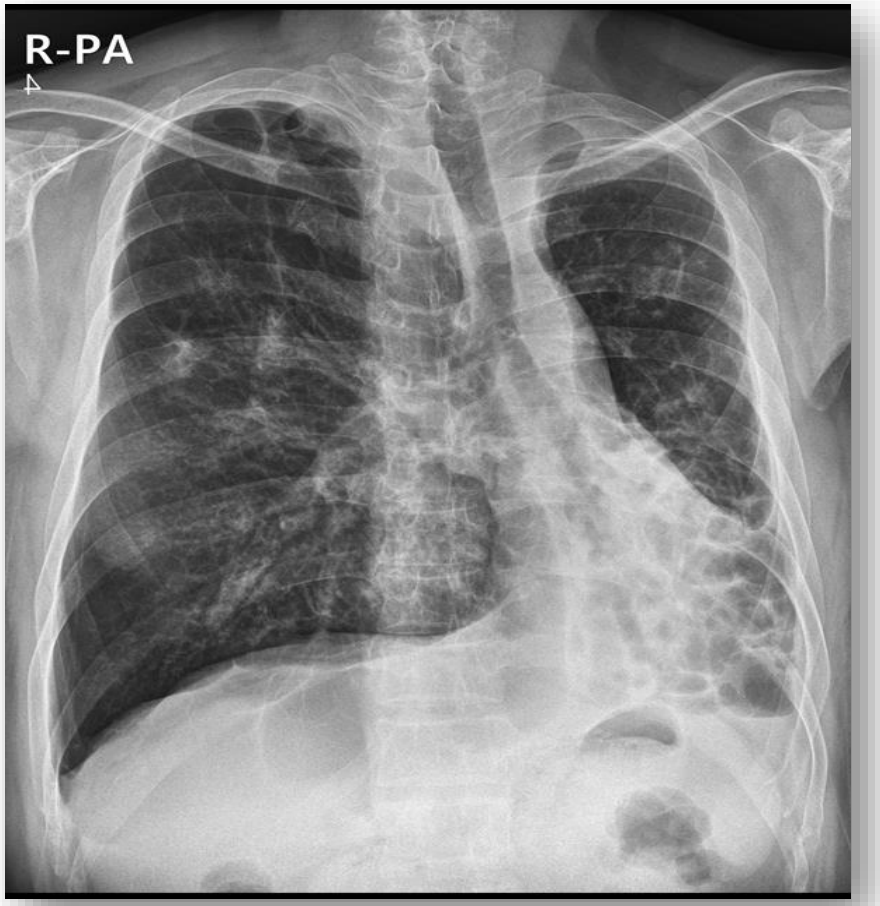


2021.11.4 CXR

Case #1st admission : 2021.11.4~ 11.10



2021.9.24 CXR



2021.11.4 CXR

Chest CT (2021.11.4)

TTE (2021.11.6)

검사결과

Impression

1. Borderline RVE (34/41/70) with normal LV wall thickness
2. No RWMA and normal LV systolic function (EF=61%)
 - Normal RV contractility
3. Grade I LV diastolic dysfunction (E/e`=7.3)
4. Valves: normal morphology and trivial TR
5. Moderate resting pulmonary hypertension (RVSP=62.8mmHg, no IVC plethora)
6. Minimal pericardial effusion.

Conclusion)
Borderline RV enlargement and normal LV systolic function (EF=61%) without RWMA
Moderate pulmonary hypertension (RVSP=62.8mmHg)

Name

Case #1st admission : 2021.11.4 ~ 11.10

- 입원경과
  - Sputum bacterial, mycobacterium culture : No growth
  - Anti: iv piperacillin/tazobactam (일주일)
  - Steroid: methyprednisolon 40mg for 5 days
  - Mucomyst, Ventolin, Atrovent, Pulmicort nebulizer → 증상 호전 후 자가 inhaler
  - 에어로 제시카 교육 (oscillating Positive Expiratory Pressures) 하여 사용시작
  - 발열 호전, leukocytosis 호전, CRP 정상화로 입원 일주일후 퇴원 진행
  - 가정산소 처방 (운동시 2L prn)

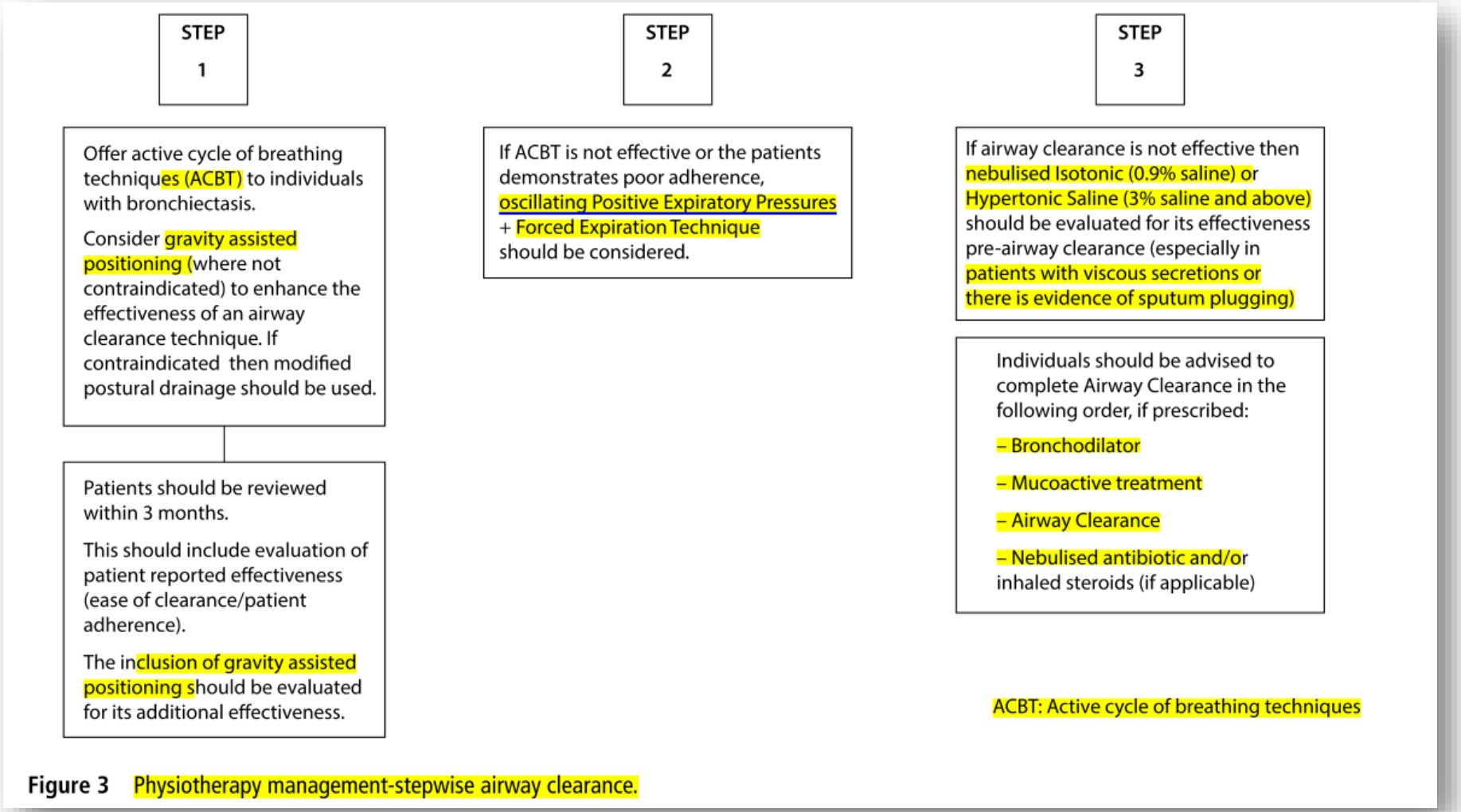
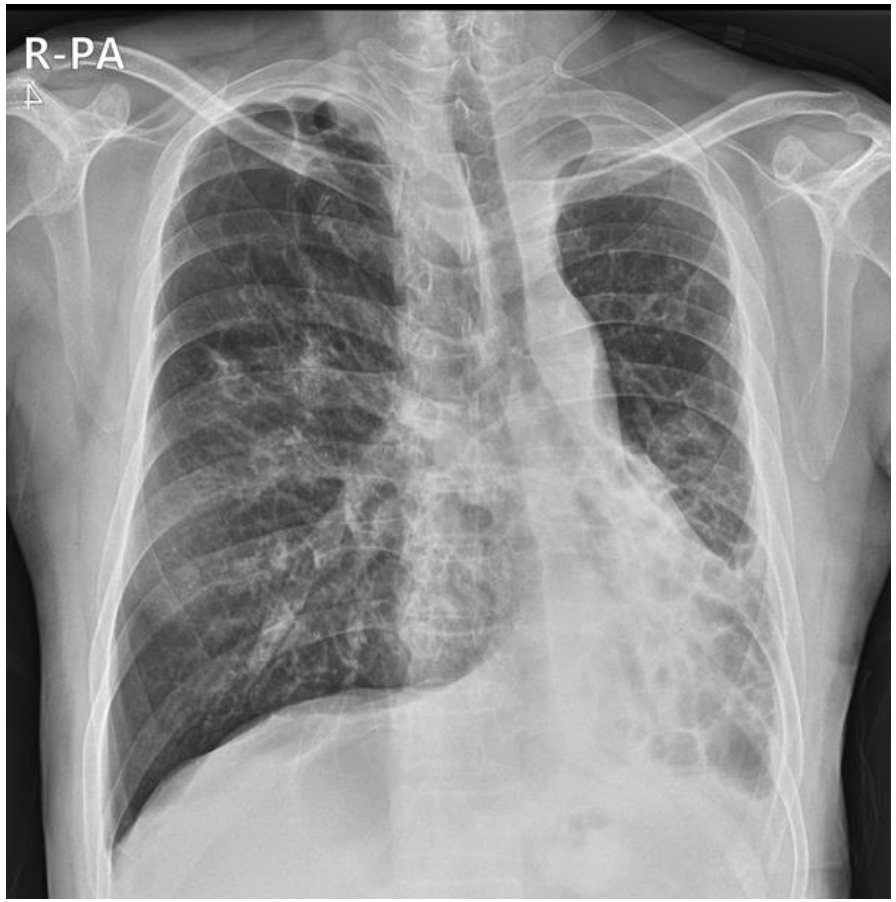


Figure 3 Physiotherapy management-stepwise airway clearance.

British Thoracic Society Guideline for bronchiectasis in adults. Thorax. 2019

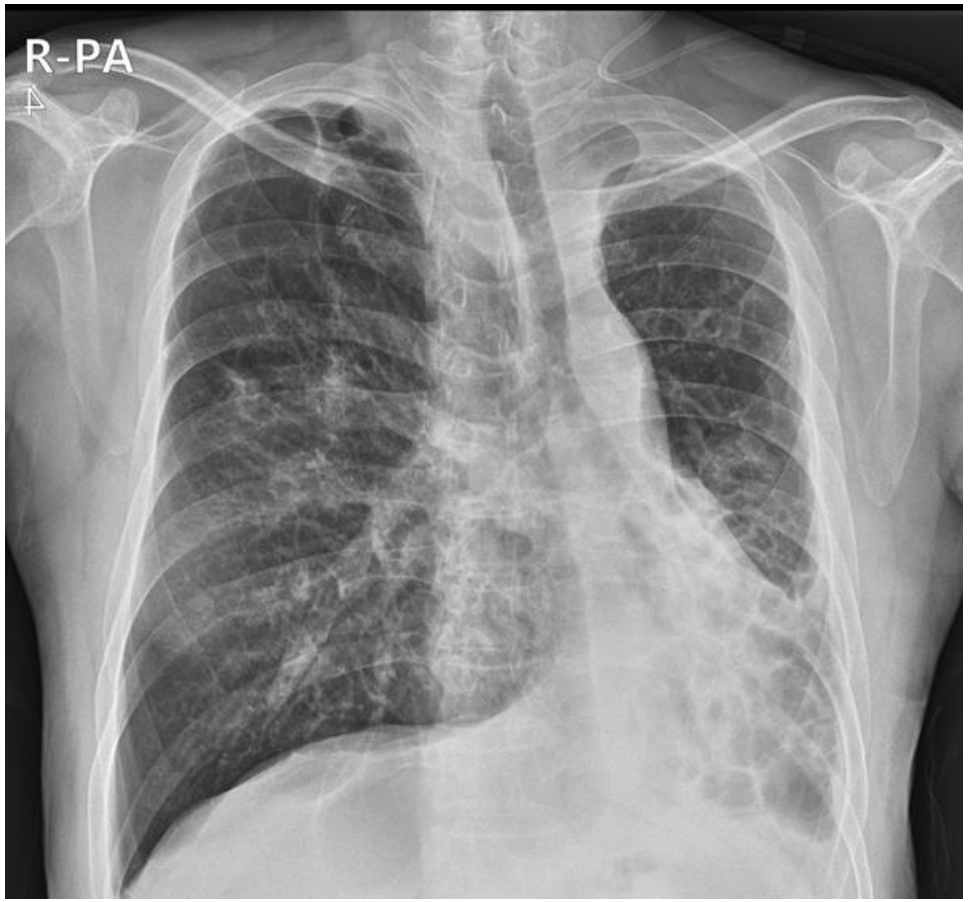
#2nd admission : 2021.12.17~ 2021.12.31

- 2021.12.17 ER 내원
  - 2021.11.4~11.10 BE 악화로 입원치료한 환자로, 내원 전일부터 호흡곤란, 가래 악화되어 ER 경유 입원.
  - Vital : 115/70, RR: 23 BT: 37.6 °, PR: 130, Saturation : 90% (room air)
  - EKG : sinus tachycardia
  - PEx: LLL wheezing + crackle
  - WBC : 10500/mm^3 (neutrophil 65%, eosinophil: 0.1%), CRP : 195 mg/L

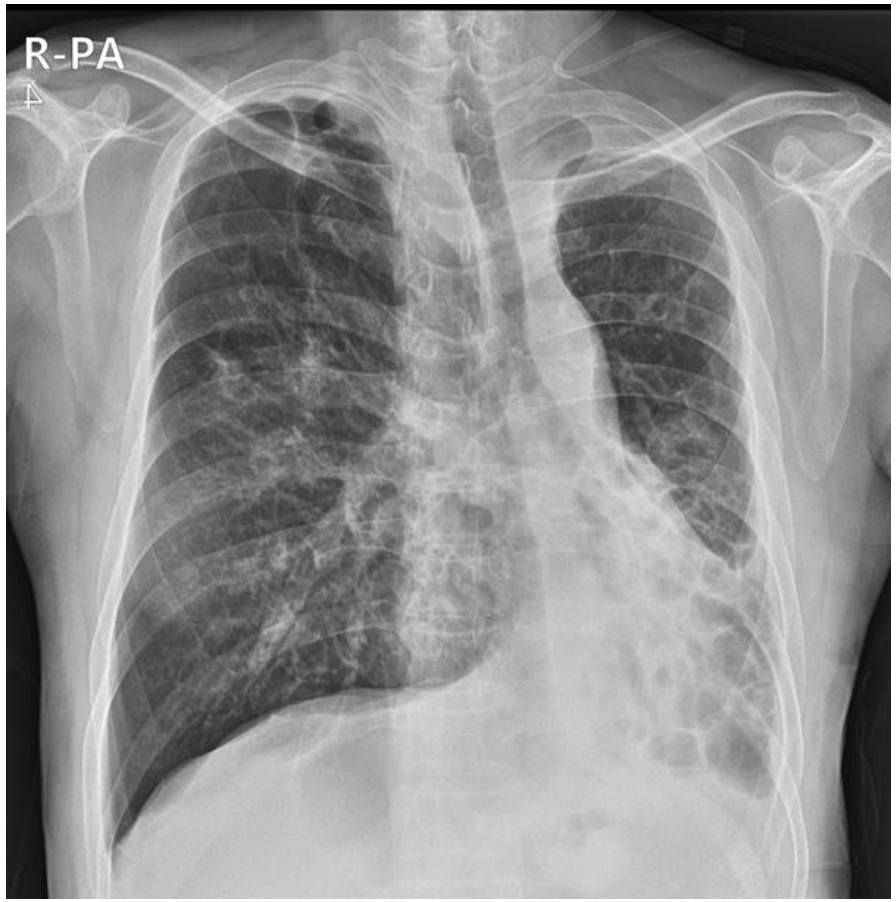


2021.12.17 CXR

#2nd addmission : 2021.12.17~ 2021.12.31



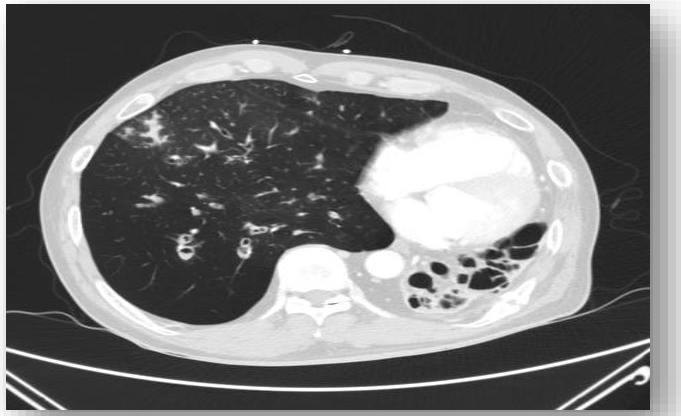
2021.11.17 CXR

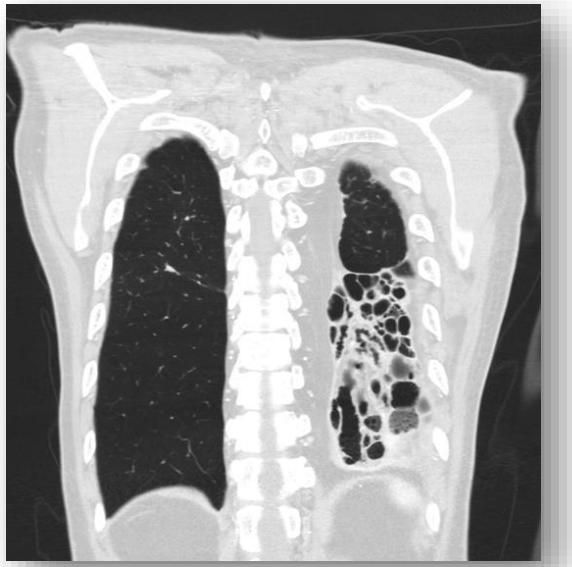


2021.12.17 CXR

Chest CT (2021.12.17)

Lt. 8th rib fracture





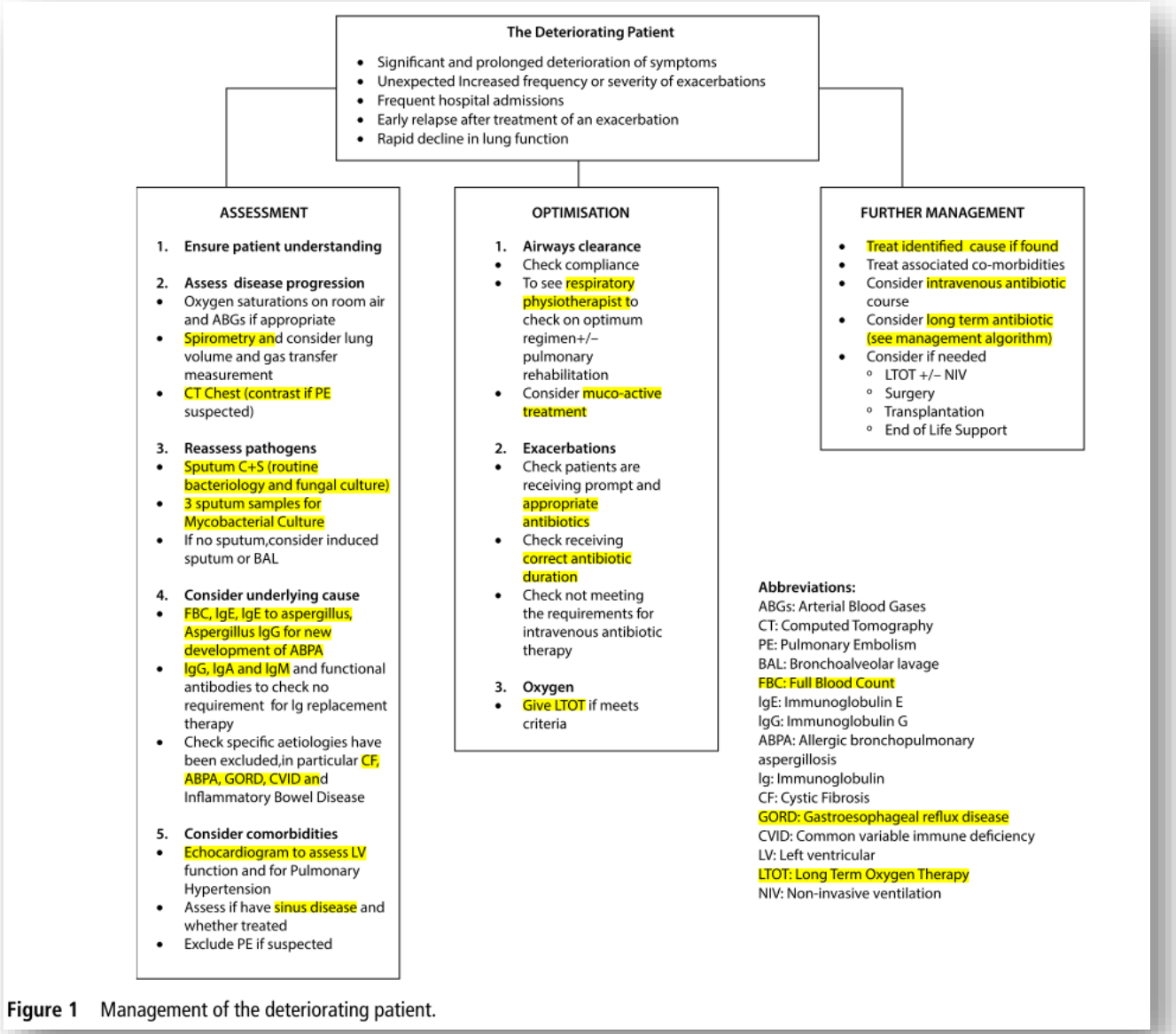


Figure 1 Management of the deteriorating patient.

British Thoracic Society Guideline for bronchiectasis in adults. Thorax. 2019

#2nd admission : 2021.12.17~12.31

- 기타검사
  - FENO : 14 ppb
  - Induced sputum : neutrophil predominant
  - Total IgE: 102
  - MAST: Mite-farinae(진드기) 2+, Mite-pterony(진드기) 3+
  - Gm3 IgG Aspergillus fumigatus : 68.9
  - ANA, MPO Ab, PR3 Ab: negative
  - Immunoglobulin

검체명	검사명	의뢰	결과	서식	참고치	R	단위
Serum	IgG Quantitation		1274		841~1743		mg/dL
Serum	IgG1 Subclass		7720.0		다중참고치		mg/L
	IgG2 Subclass		3830.0		다중참고치		mg/L
	IgG3 Subclass		146.0		다중참고치		mg/L
	IgG4 Subclass		521.0		30~2010		mg/L
검체명	검사명	의뢰	결과	서식	참고치	R	단위
Serum	IgA Quantitation		237		70~400		mg/dL
	IgM Quantitation		68		40~230		mg/dL

2022.12.18 PNS: bilateral maxillary sinusitis

#2nd admission : 2021.12.17~12.31

- **골다공증 내분비 협진**
  - 환자 T score -2.3으로 osteopenia range 이나 TBS 1.265 로 poor bone quality소견을 보이며 steroid의 장기적 투여가 예상되는 분으로 추가골절 예방위해 bisphosphonate의 재사용이 beneficial할 것으로 판단됩니다. Fosamax plus D 주1회 사용 시작해주시기 바랍니다.

	선택	검체명	검사명	의뢰	결과	시식	참고치	R	단위	판정
1	☐	Serum	25-hydroxy Vitamin D (total)		23,2		30~60		ng/mL	L
2	☐		PTH (Parathyroid hormone)		42,0		15~65		pg/mL	
3	☐		CTX (C-telopeptide of Collagen Crosslinks)		0,36		다중참고치		ng/mL	
4	☐		PTNP (Procollagen I N-terminal Propeptide)		14,5		24,3~84,1		ng/mL	L

성별 ◉ 남 ○ 여

검사일 2022-01-10

신장 174.0 cm 체중 68.0 Kg

Findings ◉ T ○ Z score

L1 - L4	-2.3	Comment
Femur Neck	-1.8	Comment
Total Hip	-1.5	Comment

Conclusion ○ normal ◉ osteopenia ○ osteoporosis

**상기 결과는 2015 Adult ISCD 및 2013 Pediatric ISCD Official Positions 에 따른 판독입니다.

Radius (distal 1/3) -3.5 Comment

10년 내 골절위험도 (FRAX model)

Major osteoporotic fracture % Hip fracture (%)

BMD flowsheet

Date	LS BMD	LS T	FN BMD	FN T	TH BMD	TH T	Rd BMD	Rd T	LS Z	FN Z	TH Z	Rd Z
2022-01-10	0.754	-2.3	0.626	-1.8	0.73	-1.5	0.623	-3.5	-1.2	-0.9	-1.1	-2.8

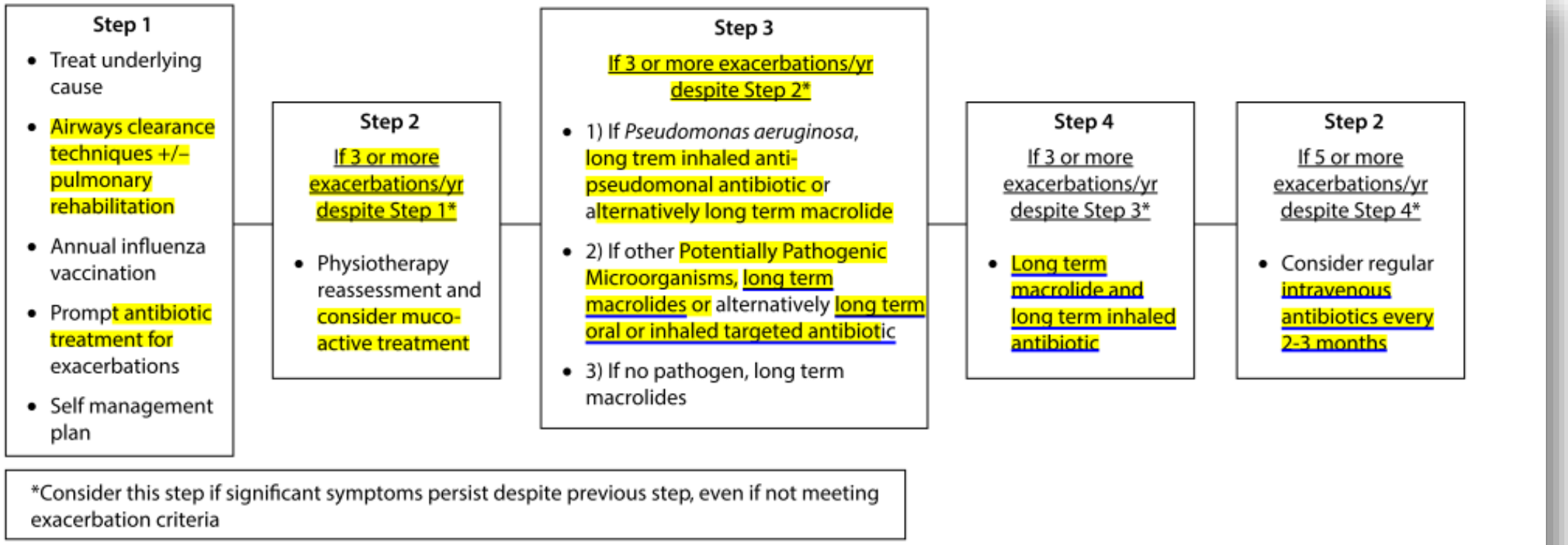


Figure 2 Stepwise management.

British Thoracic Society Guideline for bronchiectasis in adults. Thorax. 2019

TABLE 2 Summary of PICO questions and recommendations

Question	Title	Recommendations
Question 1	Is standardised testing for the cause of bronchiectasis beneficial when compared with no standardised testing?	We suggest the minimum bundle of aetiological tests in adults with a new diagnosis of bronchiectasis *(conditional recommendation, very low quality of evidence)* is: 1) Differential blood count 2) Serum immunoglobulins (total IgG, IgA, IgM) 3) Testing for allergic bronchopulmonary aspergillosis It is expected that sputum culture is undertaken for monitoring purposes of bacterial infection. Mycobacterial culture may be helpful in selected cases where non-tuberculous mycobacteria are suspected as an aetiological cause of bronchiectasis. Additional tests may be appropriate in response to specific clinical features, or in patients with severe or rapidly progressive disease.
Question 2	Are courses of 14–21 days of systemic antibiotic therapy compared to shorter courses (<14 days) beneficial for treating adult bronchiectasis patients with an acute exacerbation?	We suggest acute exacerbations of bronchiectasis should be treated with 14 days of antibiotics (*conditional recommendation, very low quality of evidence*). It is possible that shorter or longer courses of antibiotics may be appropriate in some cases, depending on specific clinical conditions (such as exacerbation severity, patient response to treatment, or microbiology).
Question 3	Is an eradication treatment beneficial for treating bronchiectasis patients with a new isolate of a potentially pathogenic microorganism in comparison to no eradication treatment?	We suggest that adults with bronchiectasis with a new isolation of *P. aeruginosa* should be offered eradication antibiotic treatment (*conditional recommendation, very low quality of evidence*). We suggest not offering eradication antibiotic treatment to adults with bronchiectasis following new isolation of pathogens other than *P. aeruginosa* (*conditional recommendation, very low quality of evidence*).
Question 4	Is long-term (⩾3 months) anti-inflammatory treatment compared to no treatment beneficial for treating adult bronchiectasis patients?	We suggest not offering treatment with inhaled corticosteroids to adults with bronchiectasis (*conditional recommendation, low quality of evidence*). We recommend not offering statins for the treatment of bronchiectasis (*strong recommendation, low quality of evidence*). We suggest that the diagnosis of bronchiectasis should not affect the use of inhaled corticosteroids in patients with comorbid asthma or chronic obstructive pulmonary disease (*best practice advice, indirect evidence*).

European Respiratory Society guidelines for the management of adult bronchiectasis. ERJ. 2017;50(3).

Case #2nd addmission : 2021.12.17~12.31

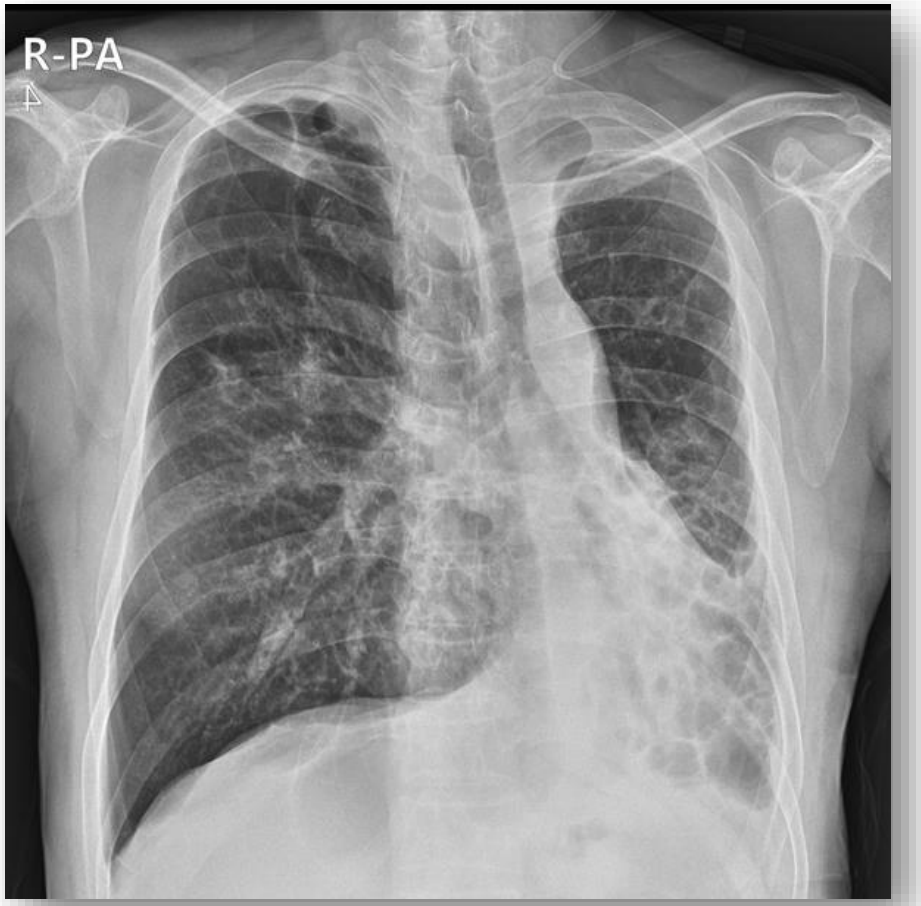
- 입원경과
  - Sputum bacterial, mycobacterium culture : No growth
  - Anti: iv piperacillin/tazobactam (2주일)
  - Steroid: methyprednisolon 40mg for 5 days then 20mg 5days
  - Mucomyst, Ventolin, Atrovent, Pulmicort nebulizer → 증상 호전후 자가 inhaler
  - 에어로 제^이카 + 가정에^서 mucomyst nebulizer ^사용
  - 발열 호전, leukocytosis 호전, CRP 감소 (12mg/dL) 로 입원 2주일후 퇴원 진행
  - 경구 항생제 퇴원약 유지. Levofloxacin
  - 가정산소 처방 (운동^시 2L prn)

#3rd admission : 2022.2.4~ 2022.2.14

- 2022.2.4 ER 내원
  - 2021.11.4~11.10/ 2022.12.17~12.31 BE 악화로 입원치료한 환자로, 내원 전일부터 호흡곤란, 가래 악화되어 ER 경유 입원함.
  - Vital : 130/80, RR: 22 BT: 37.5 °, PR: 125, Saturation : 89% (room air)
  - EKG : sinus tachycardia
  - PEx: LLL wheezing + crackle
  - WBC : 10180/mm^3 (neutrophil 67%, eosinophil: 0.1%), CRP : 159 mg/L

2022.2.4 CXR

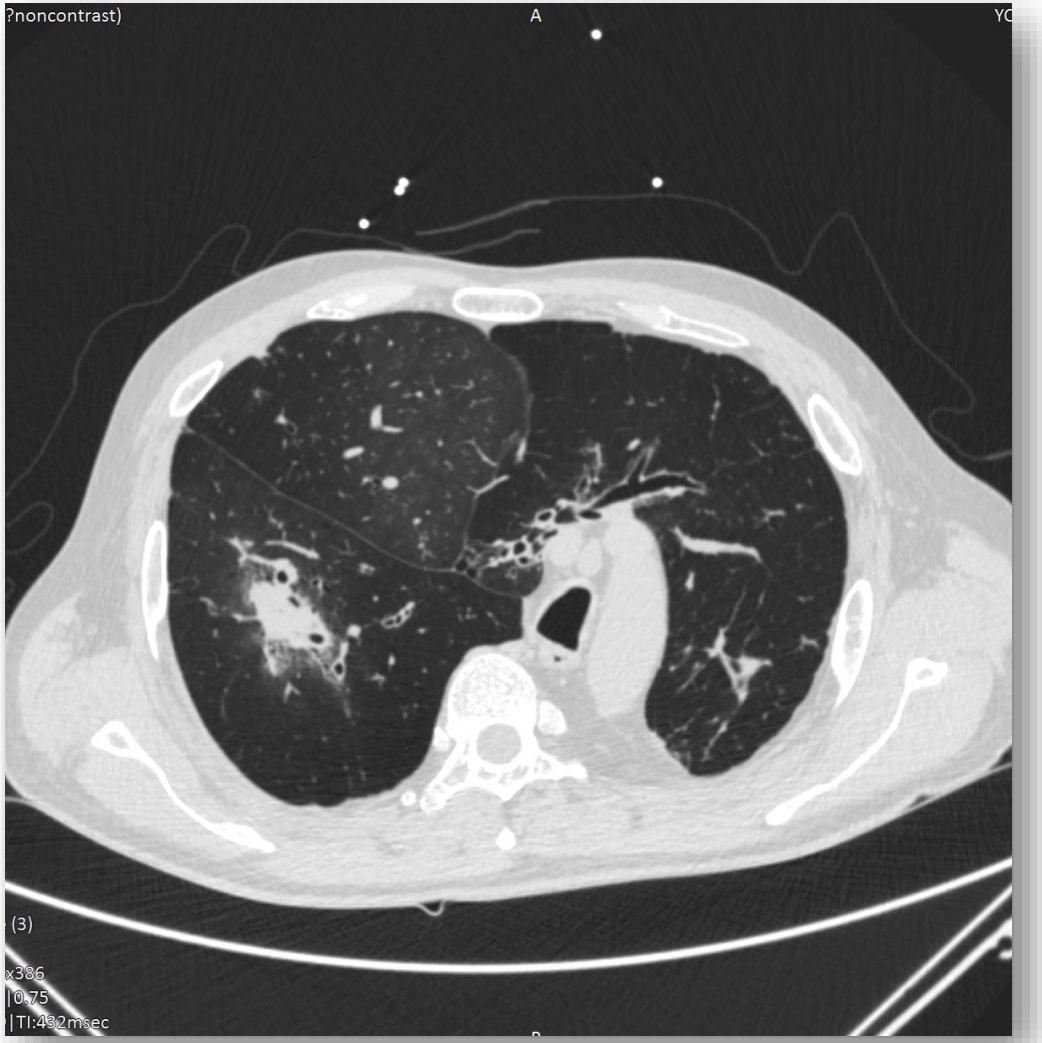
#3rd admission : 2022.2.1~ 2.14



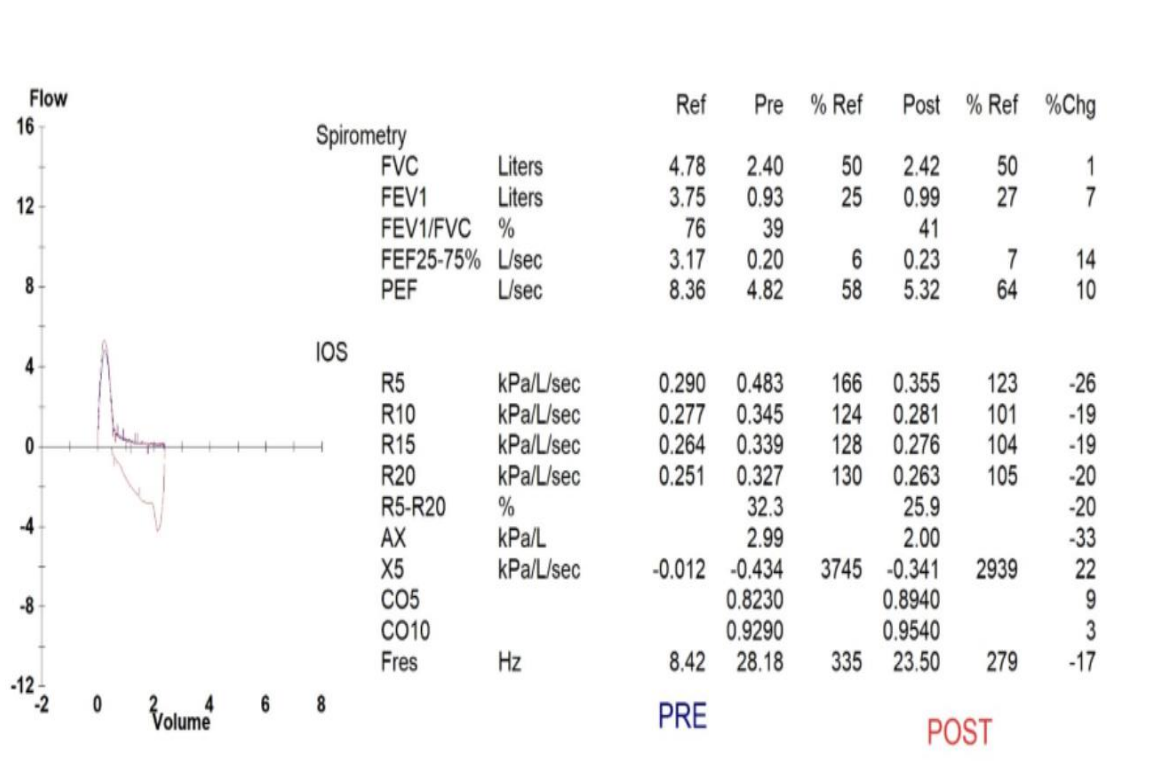
2021.12.31 CXR

2022.2.1 CXR

Chest CT (2022.2.1)

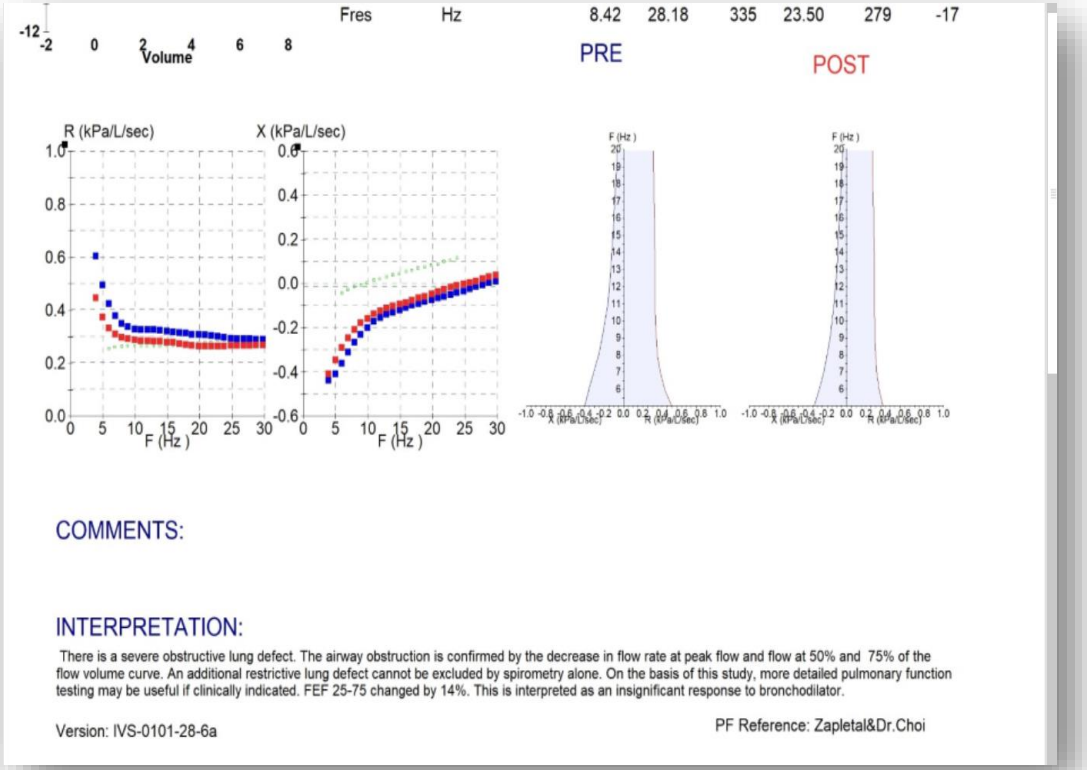


PFT (2022.2.10)



			Ref	Pre	% Ref	Post	% Ref	%Chg
Spirometry								
	FVC	Liters	4.78	2.40	50	2.42	50	1
	FEV1	Liters	3.75	0.93	25	0.99	27	7
	FEV1/FVC	%	76	39		41		
	FEF25-75%	L/sec	3.17	0.20	6	0.23	7	14
	PEF	L/sec	8.36	4.82	58	5.32	64	10
IOS								
	R5	kPa/L/sec	0.290	0.483	166	0.355	123	-26
	R10	kPa/L/sec	0.277	0.345	124	0.281	101	-19
	R15	kPa/L/sec	0.264	0.339	128	0.276	104	-19
	R20	kPa/L/sec	0.251	0.327	130	0.263	105	-20
	R5-R20	%		32.3		25.9		-20
	AX	kPa/L		2.99		2.00		-33
	X5	kPa/L/sec	-0.012	-0.434	3745	-0.341	2939	22
	CO5			0.8230		0.8940		9
	CO10			0.9290		0.9540		3
	Fres	Hz	8.42	28.18	335	23.50	279	-17

PRE POST



COMMENTS:

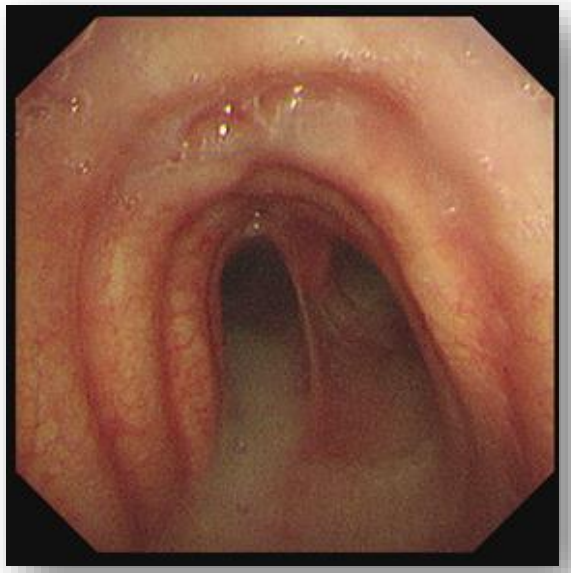
INTERPRETATION:

There is a severe obstructive lung defect. The airway obstruction is confirmed by the decrease in flow rate at peak flow and flow at 50% and 75% of the flow volume curve. An additional restrictive lung defect cannot be excluded by spirometry alone. On the basis of this study, more detailed pulmonary function testing may be useful if clinically indicated. FEF 25-75 changed by 14%. This is interpreted as an insignificant response to bronchodilator.

Version: IVS-0101-28-6a

PF Reference: Zapletal&Dr.Choi

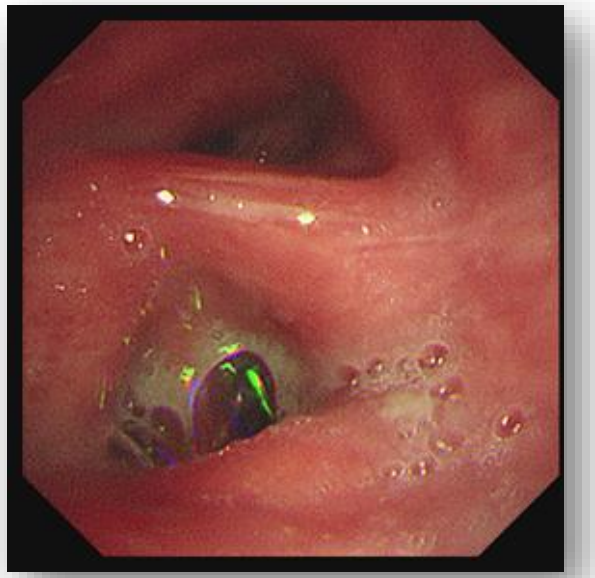
FOB (2022.2.4)



Main carina

Rt bronchus

Lt bronchus



LLL bronchus

- BAL quantitative culture : 60,000 CFU/ml | Actinomyces odontolyticus
- BAL Aspergillus (Galactomannan) Ag : Negative
- Mycobacterial culture : negative

검체명	검사명		의뢰	결과	서식	참고치	R	단위
Bronchoalveolar lavage	Body Fluid Routine Examination	Color		Colorless				
		Turbidity		Cloudy				
		RBC		240				/μL
		TNC(Total nucle		14550				/μL
		WBC		TNC 결과 참조				/μL
		Polymorphonucl		-				%
		Mononuclear ce		-				%
		Neutrophil		97				%
		Lymphocyte		2				%
		Monocyte		1				%
		Eosinophils		0				%
		Basophils		0				%
		Other		0				%
		SG		1.005				
		pH		6.8				

- Actinomyces sp.
  - Actinomyces israelii (m/c)
  - Actinomyces meyeri
  - Actinomyces odontolyticus
  - Actinomyces meyeri
- Primary regimens
  - Penicillin G or Ampicillin or Amoxicillin
  - Beta-lactam : usually effective
  - Quinolone : usually ineffective
  - Macrolide also effective
- Clinical setting
  - Abdominal
  - Cervicofacial
  - Pelvic
  - Pulmonary : mass lesion, dense infiltrate can mimic lung cancer, tuberculosis with or without cavity

#3rd admission : 2022.2.1~ 2.14

- 입원경과
  - FOB c BAL culture: Actinomyces odontolyticus (6x10^4 CFU)
  - Anti: iv piperacillin/tazobactam (2주일)
  - Steroid: methyprednisolon 40mg for 5 days
  - Mucomyst, Ventolin, Atrovent, Pulmicort nebulizer → 증상 호전 후 자가 inhaler
  - 진해거담제 + 에어로 제시카 + 가정에서 mucomyst nebulizer 사용
  - 발열 호전, leukocytosis 호전, CRP 정상화로 입원 2주일 후 퇴원 진행
  - Amoxicillin or Azithromycin 경구 항생제 장기 유지 예정

Question 4	Is long-term (≥3 months) anti-inflammatory treatment compared to no treatment beneficial for treating adult bronchiectasis patients?	We suggest not offering treatment with inhaled corticosteroids to adults with bronchiectasis (*conditional recommendation, low quality of evidence*). We recommend not offering statins for the treatment of bronchiectasis (*strong recommendation, low quality of evidence*). We suggest that the diagnosis of bronchiectasis should not affect the use of inhaled corticosteroids in patients with comorbid asthma or chronic obstructive pulmonary disease (*best practice advice, indirect evidence*).
Question 5	Is long-term antibiotic treatment (≥3 months) compared to no treatment beneficial for treating adult bronchiectasis patients?	We suggest offering long-term antibiotic treatment for adults with bronchiectasis who have three or more exacerbations per year (*conditional recommendation, moderate quality of evidence*). All subsequent recommendations refer to patients with three or more exacerbations per year. We suggest long-term treatment with an inhaled antibiotic for adults with bronchiectasis and chronic *P. aeruginosa* infection (*conditional recommendation, moderate quality of evidence*). We suggest macrolides (azithromycin, erythromycin) for adults with bronchiectasis and chronic *P. aeruginosa* infection in whom an inhaled antibiotic is contraindicated, not tolerated or not feasible (*conditional recommendation, low quality of evidence*). We suggest macrolides (azithromycin, erythromycin) in addition to or in place of an inhaled antibiotic, for adults with bronchiectasis and chronic *P. aeruginosa* infection who have a high exacerbation frequency despite taking an inhaled antibiotic (*conditional recommendation, low quality of evidence*). We suggest long-term macrolides (azithromycin, erythromycin) for adults with bronchiectasis not infected with *P. aeruginosa* (*conditional recommendation, moderate quality of evidence*). We suggest long-term treatment with an oral antibiotic (choice based on antibiotic susceptibility and patient tolerance) for adults with bronchiectasis not infected with *P. aeruginosa* in whom macrolides are contraindicated, not tolerated or ineffective (*conditional recommendation, low quality of evidence*).

European Respiratory Society guidelines for the management of adult bronchiectasis. ERJ. 2017;50(3).

감사합니다

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