

Chest computed tomography scores in patients with cystic fibrosis and MRSA lower airways colonization

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Introduction

- MRSA – an emerging pathogen in CF
- A dramatic increase over the last decade, from 2.1% in 1996 to 25.7% in 2010
- As opposed to *Pseudomonas aeruginosa* (PA), which has clearly been associated with clinical deterioration in CF, there is more debate about the role of MRSA
- Is it just a marker of severe lung disease¹, or an independent risk factor²?

¹Sawicki et al., Ped Pulm 2008

²Dasenbrook et al., AJRCCM 2008

Introduction - 2

- A greater proportion of CF patients with normal/slightly decreasing FEV1 → PFTs do not monitor progression of disease
- HRCT - the gold standard to detect bronchiectasis, an early sign of irreversible lung disease in CF
- Some centers perform routine chest CT every 2 or 3 years
- CT scoring systems enable a standardized interpretation and quantification of pulmonary changes

Aim

Our aim was to examine the association between bacterial colonization in the sputum (MRSA with or without PA) and CT scores in CF patients

Methods

- A cross-sectional, single center retrospective study
- **Inclusion criteria:**
 - A confirmed diagnosis of CF (sweat chloride ≥ 60 mmol/l and/or two CF-causing mutations)
 - Follow up at CFC Verona
 - MRSA in sputum (≥ 3 positive cultures in a year, taken every three months)
 - chest CT performed after acquisition of MRSA
- **Exclusion criteria:**
 - Lung transplantation

Methods - 2

- CT scans were performed as a routine practice in the center - every 2-3 years, in stable clinical conditions
- The study patients were divided according to sputum culture results: MRSA positive, PA negative (MRSA+); MRSA positive, PA positive (MRSA+/PA+)
- Controls - patients with CF, matched for gender and age at CT, with only PA (PA+) or no MRSA, no PA in their sputum (PA-)

Methods - 3

- CT scans - blinded to patient identification, scored independently by two radiologists previously trained to use the scoring system
- "Brody score" - bronchiectasis, mucus plugging, peribronchial thickening, parenchymal opacity, and hyperinflation in the periphery and the center of each lobe. The sum of the sub scores provides a total score¹
- CF-CT scoring system - an upgraded version of the Brody II system; clear definitions of the structural abnormalities, reference images and training sets²

1Brody et al., J Thorac Imaging 2006

2Tiddens et al., Pediatr Radiol 2014

Objectives

- **Primary** - to compare the CT scores of study and control patients in each group
- **Secondary** - to compare the clinical status of study and control patients in each group: FEV1, BMI, pancreatic and diabetic status

Results

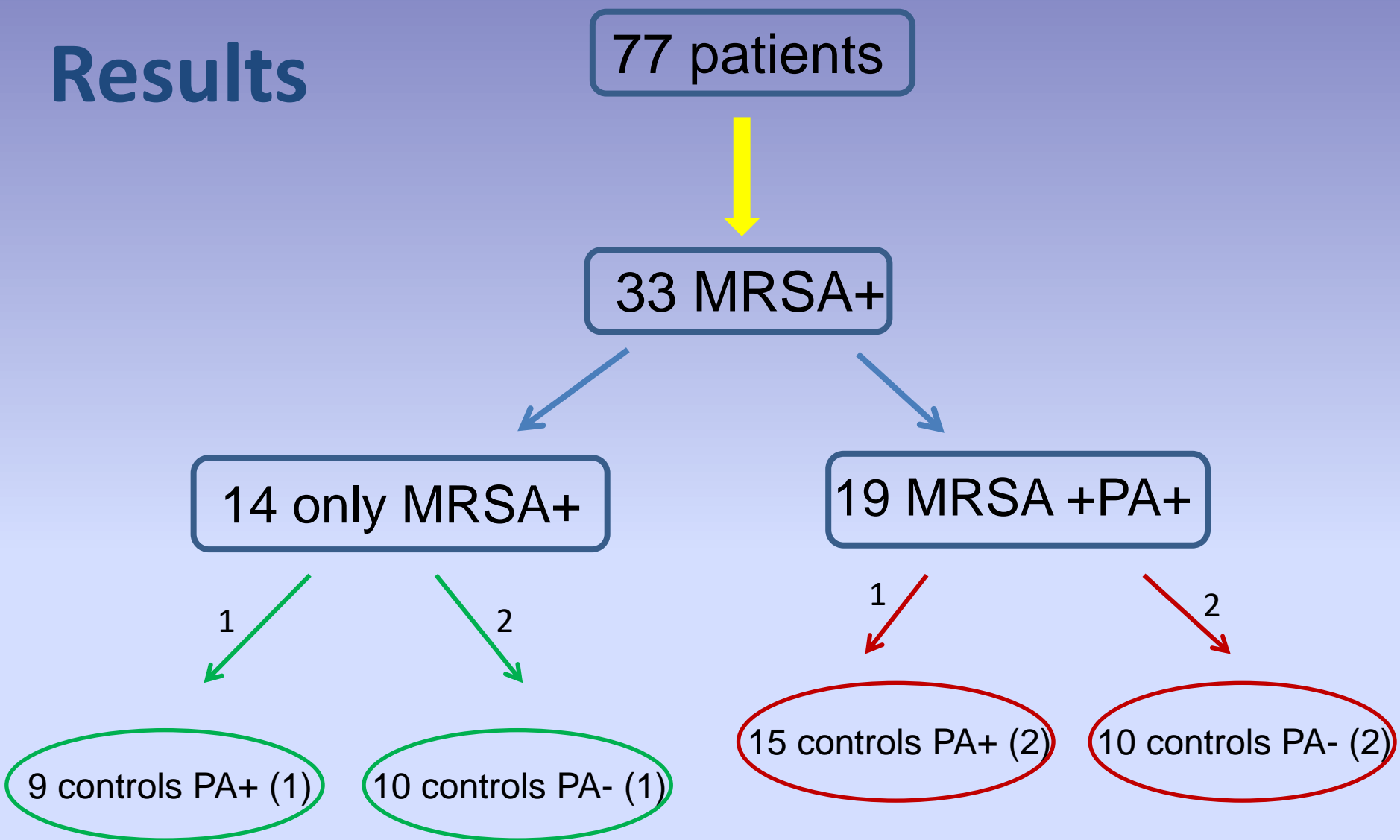


Table 1

	N (%)
Gender	
Male	34 (44.2)
Female	43 (55.8)
Age at CT	
Mean (SD)	22.9 (12.3)
Median, range	21.2 (5.9 - 48.0)
Age at colonization	
Mean (SD)	17.4 (11.5)
Median, range	14.4 (0.5 - 43.7)
Group of colonization	
MRSA+	14 (18.2)
MRSA+ PA+	19 (24.7)
PA+	24 (31.2)
PA-	20 (26.0)

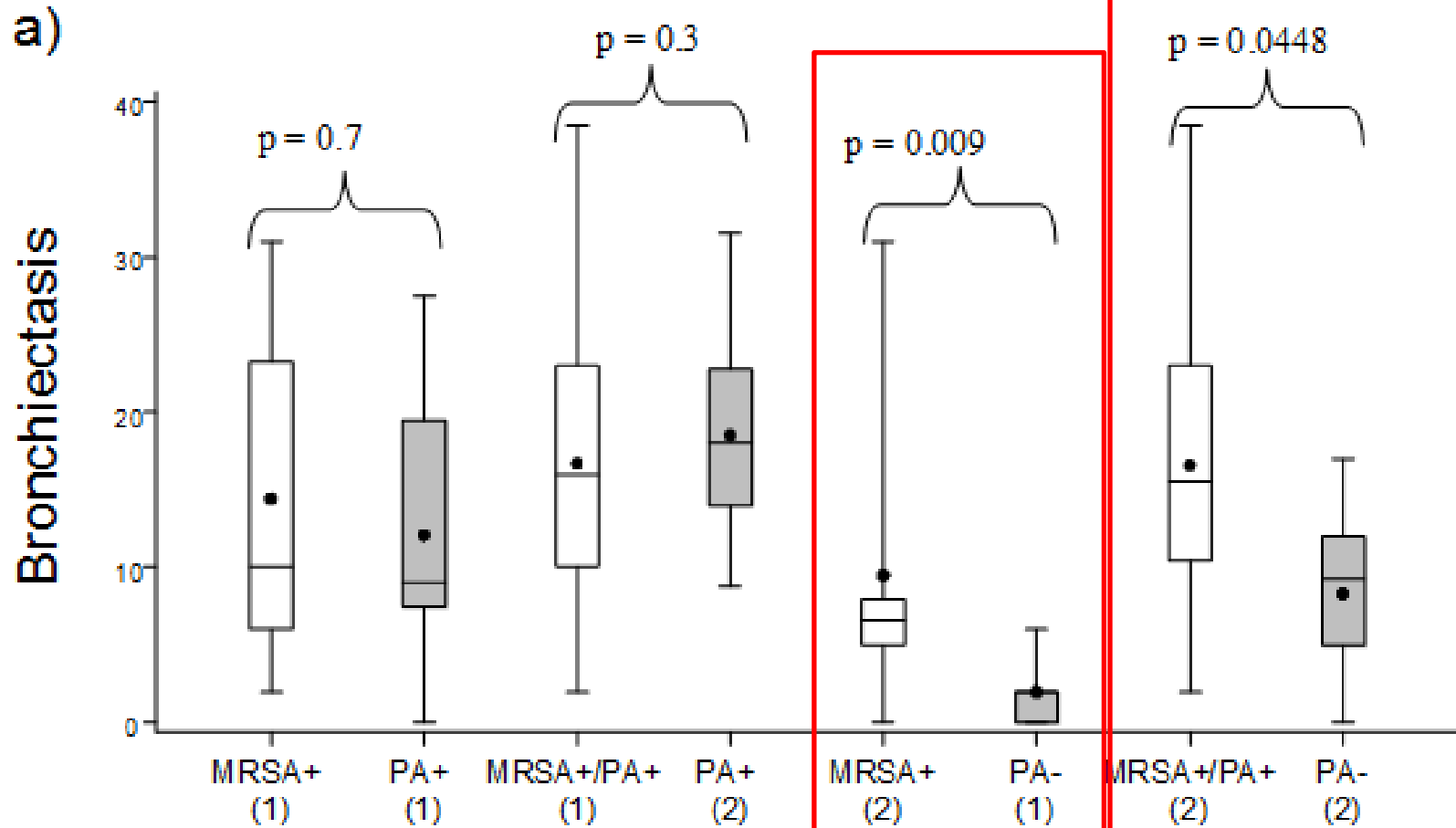
Results – cont.

- Since case and control groups were matched for age at CT, ages are similar
- Mean age at CT:
 - MRSA+ (1) and their PA+ controls - significantly higher than MRSA+ (2) and their PA- controls (22.07 vs 11.37 years, $p=0.04$)
 - MRSA+/PA+ (1) and their PA+ controls - slightly higher than MRSA+/PA+ (2) and their PA- controls (29.95 vs 22.99, $p=0.09$)
- Good correlation in scoring between the two radiologists – ICC 0.82 (bronchiectasis score), 0.8 (total score)

Table 2 – CT scores

	Bronchiectasis	Total score
	Mean (SD)	Mean (SD)
MRSA+ (1) (N=9)	14.44 (10.82)	38.25 (20.18)
PA+ (1) (N=9)	12.11 (9.47)	32.22 (18.74)
p	0.7	0.4
MRSA+/PA+ (1) (N=15)	16.72 (9.36)	41.88 (18.18)
PA+ (2) (N=15)	18.53 (5.76)	45.33 (11.50)
p	0.3	0.4
MRSA+ (2) (N=10)	9.53 (9.78)	28.78 (19.73)
PA- (1) (N=10)	2.00 (2.31)	8.70 (8.45)
P	0.009	0.0027
MRSA+/PA+ (2) (N=10)	16.60 (9.91)	40.93 (17.21)
PA- (2) (N=10)	8.33 (5.74)	23.75 (14.82)
P	0.0448	0.0155

Bronchiectasis scores



Total scores

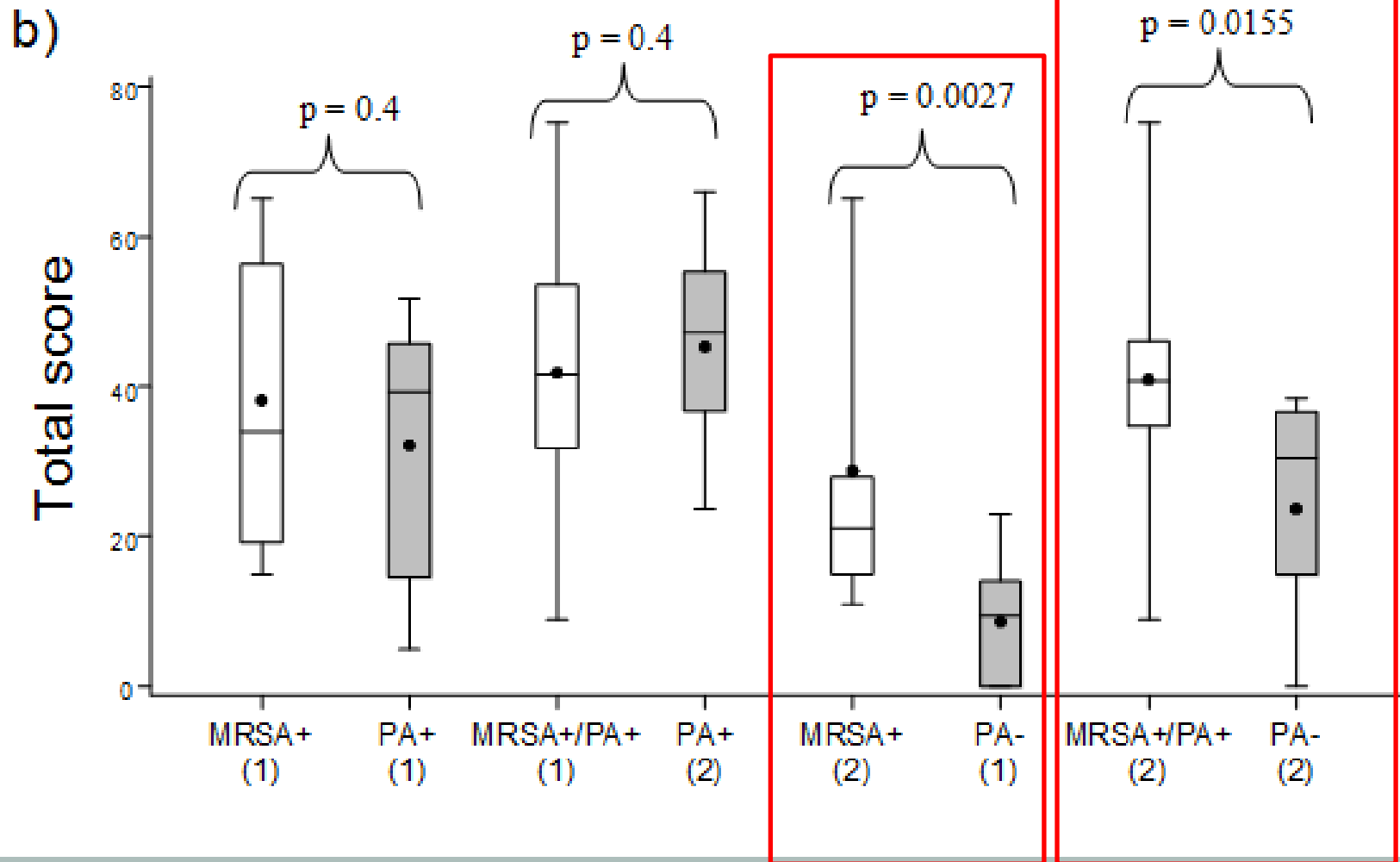


Table 3 – clinical status

	Age at CT Mean (SD)	FEV1 CT Mean (SD)	BMI		Pancreatic status		Diabetes	
			Normal or over weight	Under weight	PS	PI	No	Yes
MRSA+ (1) (N=9)	21.98 (12.83)	78.00 (22.24)	8 (88.9)	1 (11.1)	2 (22.2)	7 (77.8)	8 (88.9)	1 (11.1)
PA+ (1) (N=9)	22.07 (12.89)	62.00 (30.43)	5 (55.6)	4 (44.4)	2 (22.2)	7 (77.8)	6 (66.7)	3 (33.3)
p	0.9	0.3	0.3		1		0.6	
MRSA+/PA+ (1) (N=15)	29.91 (10.59)	55.40 (23.41)	13 (86.7)	2 (13.3)	5 (33.3)	10 (66.7)	13 (86.7)	2 (13.3)
PA+ (2) (N=15)	29.95 (10.58)	53.27 (21.40)	9 (60.0)	6 (40.0)	3 (20.0)	12 (80.0)	12 (80.0)	3 (20.0)
p	1	1	0.2		0.7		1	
MRSA+ (2) (N=10)	11.37 (5.35)	86.00 (20.43)	9 (90.0)	1 (10.0)	1 (10.0)	9 (90.0)	10 (100.0)	0 (0.0)
PA- (1) (N=10)	11.37 (5.34)	98.40 (10.32)	9 (90.0)	1 (10.0)	4 (40.0)	6 (60.0)	10 (100.0)	0 (0.0)
p	0.9	0.1	1		0.3		-	
MRSA+/PA+ (2) (N=10)	22.80 (9.76)	60.90 (24.88)	7 (70.0)	3 (30.0)	2 (20.0)	8 (80.0)	10 (100.0)	0 (0.0)
PA- (2) (N=10)	22.99 (9.89)	86.89 (18.57)	9 (90.0)	1 (10.0)	5 (50.0)	5 (50.0)	9 (90.0)	1 (10.0)
p	0.9	0.0373	0.6		0.3		1	

Discussion

- At an earlier age, patients with MRSA had worse CT scores than their controls
- With the progression of disease, at an older age MRSA+ patients had similar scores to their PA+ controls
- Similar findings were found in the MRSA+/PA+ groups and bronchiectasis/total score
- **MRSA had a deleterious effect on morphologic changes in the lungs, reflected by CT scores, in our patients**
- Eradication protocols for PA have been thoroughly studied; no definite protocols for MRSA

Discussion - 2

- A few studies investigated the correlation between CT scores and the presence of bacteria in CF airways:
 - CT Bhalla scores of patients with *Staphylococcus aureus* (SA) and PA - higher scores in the PA group¹
 - Risk factors for developing irreversible lesions in CT; only colonization with mucoid PA was significantly correlated with the presence of bronchiectasis²

¹Folescu et al., J Bras Pneumol 2012

²Farrell et al., Radiology 2009

Discussion - 3

- Previous studies examined the clinical effect of MRSA with varying results:
 - Dasenbrook et al. - an increased rate of lung function decline in young patients (8-21 years) with MRSA¹
 - Sawicki et al. - patients with MRSA were treated with more antibiotics and other CF therapies, but did not have a higher rate of FEV1 decline²
- MRSA and PA were found to contribute independently and additively to poorer outcome in CF³

¹Dasenbrook et al., AJRCCM 2008

²Sawicki et al., Ped Pulm 2008

³Hubert et al. J CF 2012

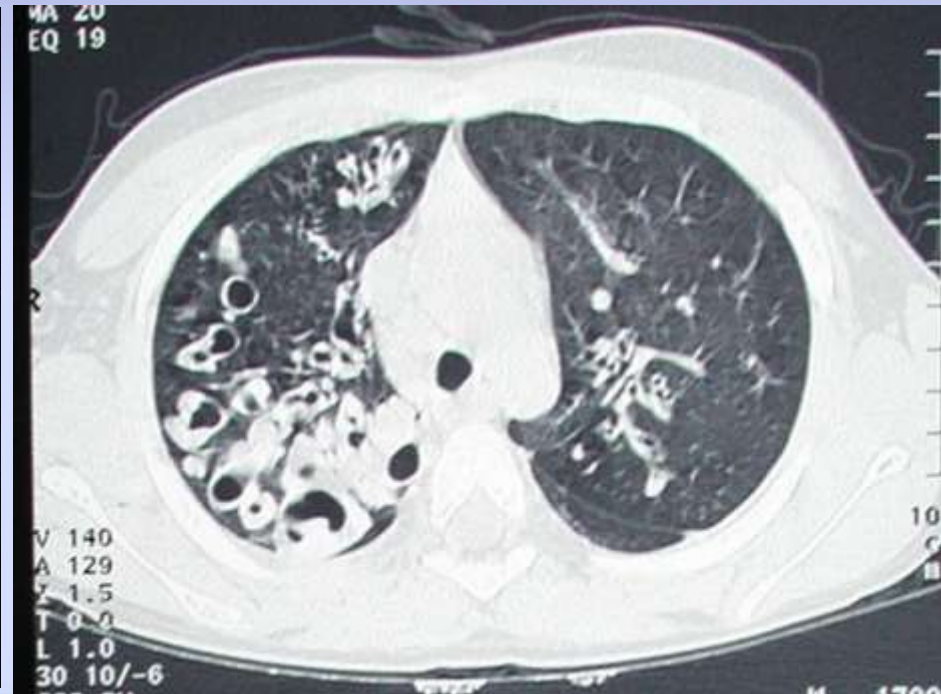
Discussion - 4

- MRSA+ (2) patients had worse CT scores than their matched PA- controls; their FEV1 was similar
- Previous studies - chest CT is more sensitive than FEV1 in detecting early signs of lung disease
 - Farrell et al. - chest CT was fourfold more sensitive than pulmonary function¹
 - Judge et al. - deteriorating CT scores in spite of stable FEV1 in 15% of their cohort²
 - CT score, particularly bronchiectasis score, was found to be associated with future lung disease progression

¹Farrell et al., Radiology 2009

²Judge et al., Chest 2006

11 yrs old patient with MRSA only;
pneumonectomy, died 1 year later
after lung Tx





Limitations

- Small number of patients, retrospective nature
- Assessment of cross-sectional associations, not evolution over time
- No differentiation between Staph. aureus and other pathogens in PA- group
- CT assesses anatomical changes; sensitive functional abnormalities were not studied (LCI)

Conclusions

- MRSA has a substantial effect on CF lung disease, with progression of disease similar to that caused by PA
- CT seemed to be more sensitive than FEV1 at detecting early lung disease
- We support the use of CT in patients infected with MRSA; low-dose protocols
- Studies examining specific eradication protocols for MRSA are warranted

Thank you!!