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Diagnosis of IPA in HIV: the role of the chest X-ray and radiologist

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Abstract The role of clinical information and chest film for the discrimination between invasive pulmonary aspergillosis (IPA) and its differential diagnoses in human immunodeficiency virus (HIV) infection was studied. The diagnostic performance of clinical information and chest film alone and in combination was studied for eight internists and eight radiologists with regular exposure to IPA patients. The multicenter case sample consisted of 25 patients with proven IPA and 25 with other pulmonary diseases typical for HIV. The cases were presented on a CD-ROM. Receiver operating characteristics (ROC) methodology was employed. With clinical information alone, internists achieved the highest diagnostic performance (area under curve/AUC=0.84). Viewing the chest films did not contribute to their performance (AUC=0.80, P=0.26). The radiologist's performance on the basis of viewing the chest film (AUC=0.75) increased significantly (P=0.012) when clinical information (AUC=0.83) was supplied. IPA cases with characteristic radiological appearance were correctly identified in 90% with chest film. For radiologists with regular exposure to HIV patients, chest films hold relevant information and contribute to the determination in cases with charac-

teristic radiological appearance. Overall and especially in cases with less characteristic radiological appearance, they have significant profit from full access to the clinical data. For internists with regular exposure to HIV patients, chest films do not provide information essential for the verification or differentiation of potential IPA.

Keywords Aspergillosis · Fungal lung disease · HIV infections · Acquired immunodeficiency syndrome · ROC analysis · ROC curve

Introduction

Invasive pulmonary aspergillosis (IPA) is a life-threatening opportunistic infection in the advanced stage of HIV infection. The disease normally takes a lethal course when antifungal therapy is not started in time. Compared to other types of immunosuppression, it is, however, rare in AIDS, with its prevalence having been further reduced by highly active antiretroviral therapy (HAART) [1, 2]. An analysis of the US American HIV archives revealed an average risk of IPA of 0.4% in HIV-infected patients. Risk increases to 1.0% when CD4 counts decline below 50/µl and 3.0% in neutropenic patients [3, 4].

Numerous studies have demonstrated that invasive fungal infections are underdiagnosed in life and their incidence is higher than stated. Despite HAART [5, 6], progression from HIV infection to AIDS continues, particularly in cases of resistance to antiretroviral drugs, of poor compliance and among immigrants. In addition, the epidemic spread of HIV infection in countries without sufficient antiretroviral therapy has resulted in a huge worldwide increase of AIDS [7].

A reliable and fast diagnosis of IPA in HIV patients thus remains essential [8]. A number of factors hinder the effort. First, the clinical symptoms of IPA are nonspecific. However, certain pulmonary infections do occur commonly in association with one type of immunosuppression, but rarely with others. Knowledge of these associations assists in narrowing down the differential diagnosis and in deciding upon the most appropriate next confirmatory diagnostic step. Second, as species of the genus *Aspergillus* (*Aspergillus* spp.) are ubiquitous, respiratory isolation may not represent disease. Third, no pathogen may be isolated from sputum or bronchial lavage in the early stages of IPA, delaying diagnosis [8]. Fourth, while serum detection systems appear promising, they are still under clinical evaluation [9–11].

Conventional chest radiography is the imaging modality for initial evaluation of patients with AIDS and pulmonary complications. Low radiation exposure, low cost and overall availability are major advantages [12, 13]. Generally known problems of conventional chest film are limited sensitivity and specifity since any infection can present with several different patterns in immune compromised patients. Their evaluation has hitherto been felt to have a decisive influence on the diagnostic and therapeutic course in the initial phase of the pulmonary disease. Studies investigating the role of computed tomography showed uniformally higher sensitivity, but different results concerning the differential diagnoses [14–16]. The purpose of the study was to measure the diagnostic performance of the chest film and the corresponding clinical information in the correct discrimination of IPA in HIV patients.

Patients and methods

This study was a randomized and blinded multicenter receiver operating characteristics (ROC) study design. A total of 125 patients infected with HIV were selected from the files of three institutions (North Manchester General Hospital, Manchester, UK, Charité and Auguste-Viktoria-Klinikum, both Berlin, Germany). All patients suffered from AIDS-defining diseases and had been admitted with acute pulmonary complaints compatible with IPA. Twenty-five consecutive proven cases of IPA were included in the ROC analysis (Fig. 1, 2).

The following gold standard was used for verification [17]:

- Autopsies (n=2)
- Positive microscopy and culture of transbronchially or transthoracically acquired biopsies positive for *Aspergillus* spp. (n=9)

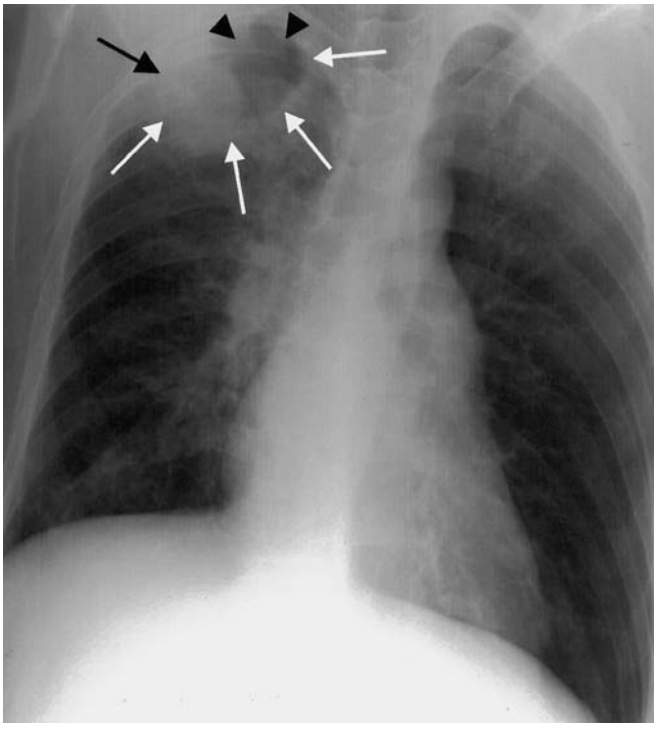

Fig. 1 Chest film of a typical IPA with cavity (*white arrows*), fungus (*black arrow*) and air crescent sign (*arrow heads*) in the right upper lobe

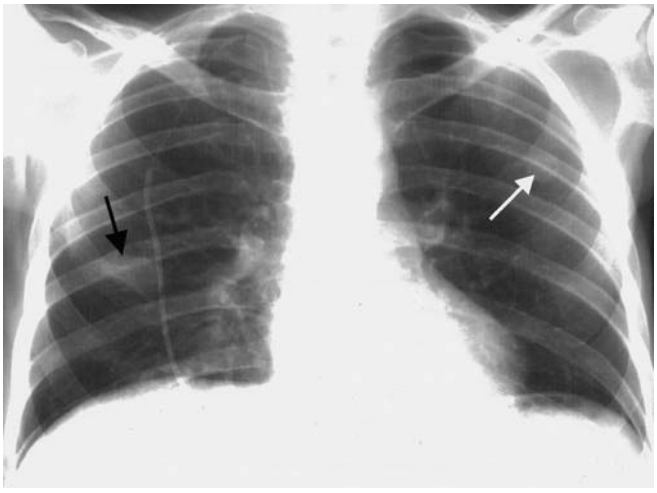

Fig. 2 Chest film of a typical IPA with nodules in the middle fields (*black and white arrow*) of both lungs

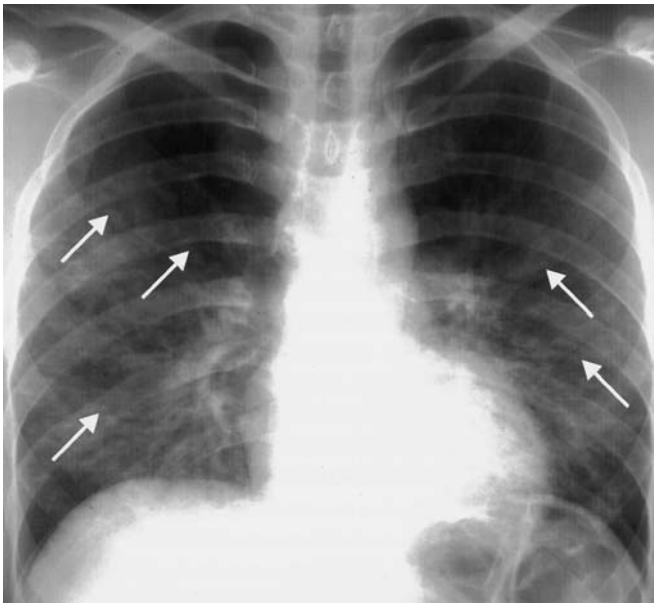

Fig. 3 Chest film showing typical infiltrations in *Pneumocystis* pneumonia (*white arrows*)

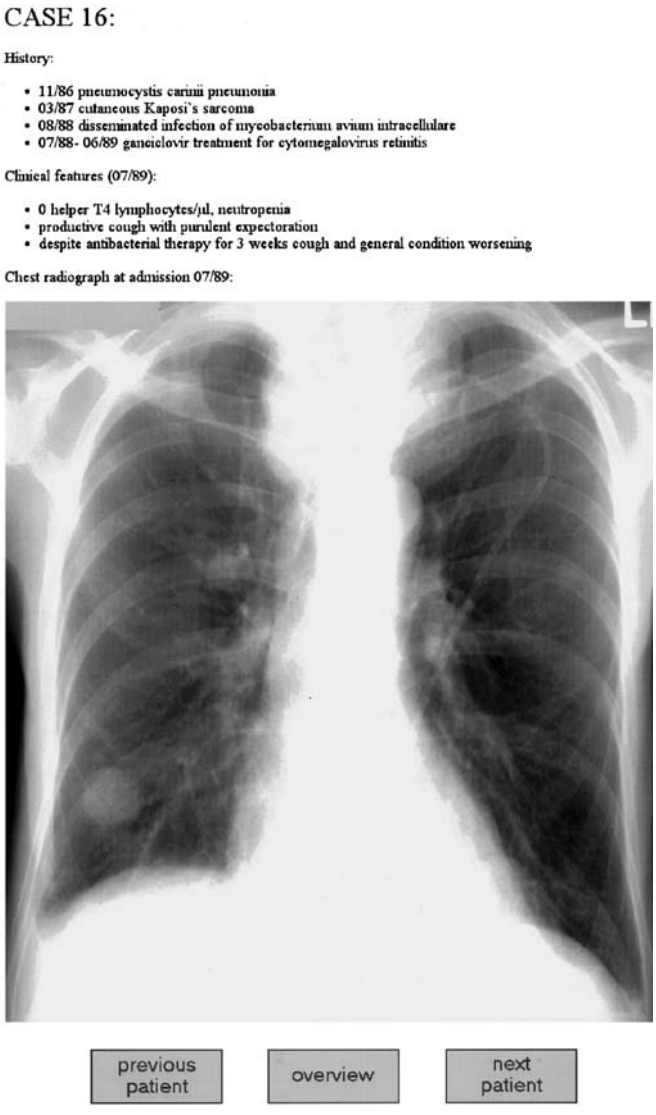

Fig. 4 Example of a case presented on the CD-ROM with clinics, chest film and buttons for navigation

– Positive microscopy and culture of bronchial lavages for *Aspergillus* spp. (*n*=10)
– Repeated positive culture of bronchial lavages without concomitant pathogens (*n*=1)
– Repeated microscopy of induced sputum and of sputum showing hyphae consistent with *Aspergillus* spp. without evidence of concomitant pathogens together with a therapeutic response over 3 months (*n*=3)

Patients not included in the IPA group had other pulmonary diseases. They were used for the recruitment of the differential diagnoses (25 proven consecutive cases) with the frequency distribution corresponding to the relative frequency in German AIDS patients (*Pneumocystis* pneumonia (*n*=12) [(Fig. 3)], bacterial pneumonia (*n*=10), pulmonary tuberculosis (*n*=1), pneumonia from *Mycobacterium avium intracellulare* (*n*=1) and pulmonary Kaposi's sarcoma (*n*=1)). The diagnoses were verified by the demonstration of the pathogen in bronchial lavages (*n*=21), transbronchial biopsy (*n*=1), by autopsy (*n*=1) and by successful therapy (*n*=1). Patients not included in the database had either no proven diagnosis or more than one pulmonary disease.

Radiological pathologies with variously intense morphologies were selected. Cases were blinded and randomized to compile the case CD-ROM based on HTML (Fig. 4). The films were digitized with 180 dpi (matrix: 2,000×2,000, system resolution 0.14 mm, gray scale range 8 bits). Images were primarily displayed with an 800×600 matrix. They were enlarged to their maximal size on demand. As lateral films and CT images were not available in every case, only p.a. films were employed. The location of the relevant pathology was stated in each evaluation form in order to make sure that the correct lesion was analyzed. Previous unrelated lesions were indicated to the readers.

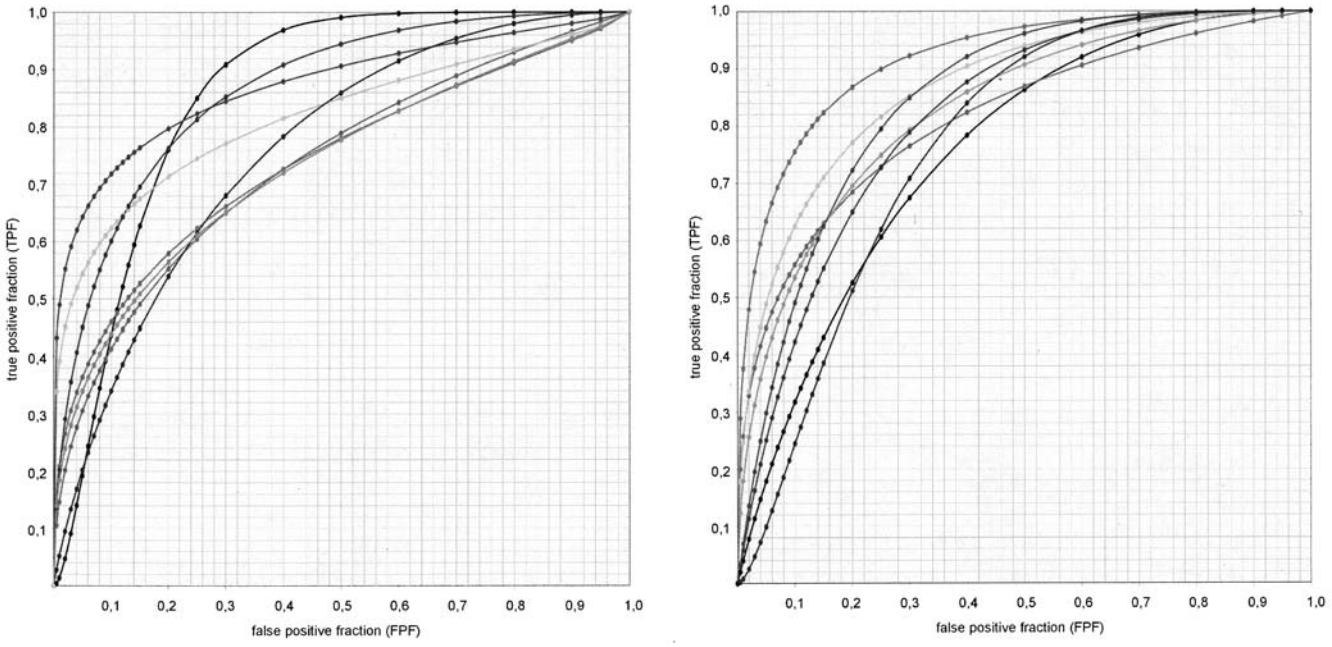

Fig. 5 ROC curves of internists (*right graphic*) and radiologists (*left graphic*) in part 2 of the study having chest film and detailed clinical information

The participants were told that within the study every patient suffered from HIV infection with AIDS and acute pulmonary diseases, half with IPA, half with differential diagnoses including bacterial pneumonia, *Pneumocystis* pneumonia, pulmonary tuberculosis, *Mycobacterium avium intracellulare* and Karposi's sarcoma in characteristic frequency distribution (baseline clinical information).

The specific clinical information provided in short texts for the individual patients in one part of the study comprised relevant history, findings of physical examination, relevant laboratory parameters, former therapies and their clinical impact (e.g., ganciclovir causing neutropenia).

Eight internists and eight radiologists took part in the ROC analysis. They came from referral centers of infectious and oncological diseases. Half of the internists were specialized in oncology and half in infectious diseases. Radiologists were board certified with experience in infectious and oncological diseases. The case presentation on CD-ROM allowed the participation of specialists from France, Germany, Great Britain, The Netherlands and the United States. The participants were able to navigate through the case presentation. An introductory page was placed at the beginning, including the baseline information and working instructions.

First, the internists evaluated the specific clinical information only. Three weeks later, they reviewed the same information in a different case order in combination with the corresponding chest film. The radiologists started with the evaluation of the chest film. After 3 weeks, they analyzed the same images in a different case order together with the specific clinical information. The design of the second study part was identical for radiologists and internists.

The participants determined their degree of certainty of the presence of IPA on a five-point scale for each case. In non-IPA cases, they provided differential diagnoses that were documented, but not analyzed for the ROC analysis. The precise radiological appearances and their impact on the assumed diagnosis as felt by the reader were also documented. Predefined radiological descriptors were used. The confidence scale, which is characteristic of ROC analyses, ranged from "(almost) sure IPA" to "probably IPA" to "undecided" to "probably not IPA" and finally "(almost) sure not IPA." The participants were requested to use the whole scale. ROC curves were calculated for each participant [18, 19]. The area under curve (AUC) was regarded to represent diagnostic performance.

Results

First, the internists achieved an average diagnostic performance (AUC) of 0.84 (SD 0.055) when their decision was based on the specific clinical information alone (Fig. 6). Secondly, with the specific clinical information combined with the chest film they achieved an average AUC of 0.80 (SD 0.043) (Fig. 5, 6) (not significant: P=0.23 Wilcoxon's test for combined samples). Oncologists (AUC first part 0.83, second part 0.79) and infectious disease physicians (AUC first part 0.85, second part 0.79) performed alike (not significant: Wilcoxon's test P=0.73).

The radiologists achieved an average AUC of 0.75 (SD 0.046) with the chest film only (Fig. 6). Their performance increased to an AUC of 0.83 (SD 0.036) when their decision was based on the combination of chest film and specific clinical information (Fig. 5, 6) (significant: P=0.006 Wilcoxon's test). No significant distinction was found between the diagnostic performance of internists and radiologists.

Subgroup analysis of radiologist's results with chest film only showed that the distinction between IPA and *Pneumocystis* pneumonia was achieved with a high degree of accuracy (88%) in contrast to the accuracy of bacterial pneumonia (62%). IPA cases with characteristic

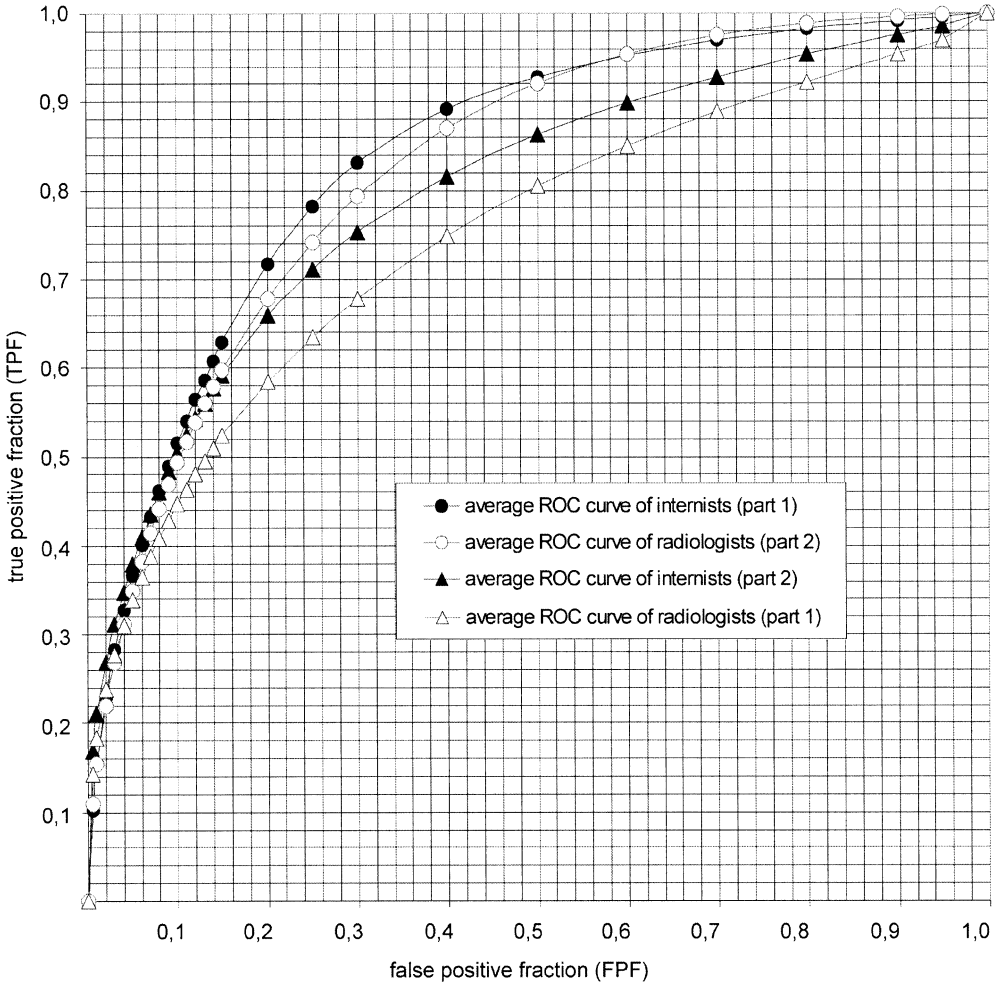

Fig. 6 Average ROC curves of internists and radiologists in part 1 and part 2—part 1 with either chest film (radiologists) or clinical information (internists) and part 2 with both chest film and clinical information

radiological appearance (48%) were correctly identified in 90%. They had evident nodules (92%), cavitations (75%), air crescent sign (33%) or subpleural infarctions (17%). IPA cases with less characteristic or evident findings (52%) were correctly discriminated in 23%. Of these IPA cases, 30% showed various pathologies consisting of interstitial, peribronchial opacities, consolidations and nodules. They were correctly diagnosed in 50%. The other 70% of the less characteristic or evident cases presented with interstitial (100%) and peribronchial (85%) opacities and were diagnosed in only 11%. Tuberculosis was mentioned as differential diagnosis in 42% of the characteristic and 38% of the less characteristic cases of IPA.

Discussion

Neutropenic hematologic patients are at high risk of getting IPA over a limited period of time. The establishment of early thoracic computed tomographic scans has reduced the mean time to diagnosis dramatically, which is decisive for the therapeutic course [20–22]. The role of imaging in AIDS patients suspected to have IPA is less clear, partly because IPA has become an unusual complication in AIDS patients nowadays [3, 5] and a variety of differential diagnoses that afford a different therapy have to be distinguished. Conventional chest radiography is the first line imaging modality when pulmonary complications are apparent. It localizes the disease process, establishes additional diseases and has the major advantages of low radiation exposure, low cost and overall availability [12, 13]. In the present ROC study, the contribution of chest films to the differential diagnoses and the corresponding clinical information to the correct discrimination of IPA in HIV patients was evaluated.

Radiologists had an acceptable mean performance of 0.75 when analyzing the chest film alone, but the lowest perfomance of all four groups. The subgroup analysis showed that the radiological appearance of IPA-characteristic findings (air crescent sign, cavitary, nodule, subpleural infarction) usually led to the correct diagnosis with the help of chest film. Less characteristic or complex radiographs were often misinterpreted, being de-

scribed as consolidations, interstitial or peribronchial opacities. Furthermore, cases of IPA with subtle findings illustrated the limits of detection with conventional images since diagnostic performance depends on size and attenuation of the radiological lesion [23]. Differential diagnoses that were most often misinterpreted showed nodules, cavities and consolidations frequently seen in IPA. Tuberculosis was frequently perceived as the main differential of IPA. On the contrary, the typical radiological appearance of *Pneumocystis* pneumonia usually led to the correct diagnosis.

The interindividual variability was lowest in the group of radiologists. The diagnostic decision seemed to depend more on the characteristics of the chest films than on the experiences of the radiologists. Another reason could be that board-certified radiologists with experience in opportunistic infections have similar levels of knowledge.

The radiologists' performance improved significantly when chest film and clinical information was pooled. Radiologists were able to employ clinical information with significant benefit for diagnostic performance. The results of previous observer performance studies looking into the reading performance of radiologists with and without clinical information are heterogeneous. The majority of studies found a positive impact of clinical information on performance [24–29]. A few studies detected an increased number of false positive diagnoses especially provoked by false and/or suggestive history of equivocal and normal chest radiographs [26, 29] or no effect by clinical history [30, 31]. The results of this study warrant the conclusion that radiologists should be given maximum information for image interpretation.

The results showed the internists having the highest diagnostic performance when their diagnostic decision was based on the clinical information only, but the spread of diagnostic performance within this group was highest as well. In our opinion, these results have limited significance. The artificial preselection of the detailed clinical information might have missed the real clinical situation and might have been suggestive. Additionally, internists were more specialized than radiologists usually are. Radiologists have to be both: specialist and generalist. In analyzing the chest film together with the clinical information, the diagnostic performance of the internists surprisingly decreased slightly (but statistically not significantly); thus, internists did not profit from interpreting the chest film. This is consistent with a study that showed that board-certified radiologists' performance in interpreting radiographs is significantly superior to that of non-radiologist physicians [32]. For internists, the clinical data were decisive for the distinction of IPA. To the best of our knowledge, no other studies exist that look into the role of clinical information in comparison to imaging information for the decision-making process of internists either in the HIV setting or elsewhere.

Employing both chest film and detailed clinical information, radiologists and internists achieved similar diagnostic performances. Although equal preconditions seemed to exist for both participating groups, we believe that the comparison between radiologists and internists is rather critical because the clinical data presented in the study were selected; thus, the internists' results are artificially improved. Results showed that most of the internists were perfect in interpreting the preselected clinical data, but tended to be confused by interpreting chest films. On the contrary, radiologists' results showed the benefits of chest film in cases with typical radiological pattern, but also the limits in cases with subtle or atypical or equivocal pathology. But it was clearly shown that radiologists were able to increase the diagnostic performance using clinical information in those cases. There may have been a disadvantage in the lack of lateral chest films.

The results of this study were influenced by the applied methodology. The maximal display-format of the digitized chest films was comparable to digital images of 2,048×2,048 pixels (2K). Evaluations have shown equivalent perception of pulmonary lesions with analog films and digital radiographs of this matrix [33, 34]. A few studies imply inferior diagnostic performances with compressed digital images for the detection of interstitial opacities [35–43]. In the case of our study, a systematic bias would have affected all study parts alike. The reading conditions, such as the reading time, differed individually. The image quality on the computer screen also may have varied; adjustments for the screen display were recommended on the introductory page of the CD-ROM. Naturally, the experimental reading situation did not reflect the true clinical decision process. To ensure that the right lesion would be analyzed, its location was indicated. This so-called direct search has been said to result in higher diagnostic performances [44], but a substantial increase of false-positive decisions has also been observed [45]. The participants knew that half of the patients were positive for IPA, in contrast to clinical practice where the prevalence of IPA in patients with HIV is less than its differential diagnoses. Thus, they tended to overdiagnose IPA. Again, this was true for all parts of the study and should not alter the comparative evaluation.

In conclusion, the study's results demonstrated that radiologists should be given full access to clinical data (patient's clinical symptoms, laboratory data, immune status level, demographic information, drug therapy) and that the internists need the radiologists' competence in interpreting chest films. Both points could be realized with close cooperation between internists and radiologists. Furthermore, the study showed that the chest radiograph provided adequate information in typical cases; on the other hand, it confirmed the diagnostic limitations of chest films in subtle and equivocal cases. Radiologists and internists have to be aware of these limitations and

to decide upon the next diagnostic step in those cases. Studies proved the CT to be the best second imaging modality in selected cases with higher sensitivity for pathologies, but also superior performance in differential diagnoses [12, 46]. Finally, the results illustrated the importance of knowledge about opportunistic diseases that are associated with the different types and levels of immunosuppression.

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References

1. Guermazi A, Benchaib N, Zagdanski AM, Hocqueloux L, Rili M, Molina JM, de Kerviler E (2002) Cerebral and spinal cord involvement resulting from invasive aspergillosis. Eur Radiol 12:147–150
2. Guermazi A, Gluckman E, Tabti B, Miaux Y (2003) Invasive central nervous system aspergillosis in bone marrow transplantation recipients: an overview. Eur Radiol 13:377–388
3. Holding KJ, Dworkin MS, Wan PC, Hanson DL, Klevens RM, Jones JL, Sullivan PS (2000) Aspergillosis among people infected with human immunodeficiency virus: incidence and survival. Adult and Adolescent Spectrum of HIV Disease Project. Clin Infect Dis 31:1253–1257
4. Woitas RP, Rockstroh JK, Theisen A, Leutner C, Sauerbruch T, Spengler U (1998) Changing role of invasive aspergillosis in AIDS—a case control study. J Infect 37:116–122
5. Moreno A, Perez-Elias M, Casado J, Navas E, Pintado V, Fortun J, Quereda C, Guerrero A (2000) Role of antiretroviral therapy in long-term survival of patients with AIDS-related pulmonary aspergillosis. Eur J Clin Microbiol Infect Dis 19:688–693
6. Tumbarello M, Ventura G, Caldarola G, Morace G, Cauda R, Ortona L (1993) An emerging opportunistic infection in HIV patients: a retrospective analysis of 11 cases of pulmonary aspergillosis. Eur J Epidemiol 9:638–644
7. Dehne KL, Khodakevich L, Hamers FF, Schwartlander B (1999) The HIV/AIDS epidemic in eastern Europe: recent patterns and trends and their implications for policy-making. AIDS 13:741–749
8. Buckingham SJ, Hansell DM (2003) Aspergillus in the lung: diverse and coincident forms. Eur Radiol 13:1786–1800
9. Ulusakarya A, Chachaty E, Vantelon JM, Youssef A, Tancrede C, Pico JL, Bourhis JH, Fenaux P, Munck JN (2000) Surveillance of Aspergillus galactomannan antigenemia for invasive aspergillosis by enzyme-linked immunosorbent assay in neutropenic patients treated for hematological malignancies. Hematol J 1:111–116
10. Verweij PE, Erjavec Z, Sluiters W, Goessens W, Rozenberg-Arska M, Debets-Ossenkopp YJ, Guiot HF, Meis JF (1998) Detection of antigen in sera of patients with invasive aspergillosis: intra- and interlaboratory reproducibility. The Dutch Interuniversity Working Party for invasive mycoses. J Clin Microbiol 36:1612–1616
11. Costa C, Costa JM, Desterke C, Botterel F, Cordonnier C, Bretagne S (2002) Real-time PCR coupled with automated DNA extraction and detection of galactomannan antigen in serum by enzyme-linked immunosorbent assay for diagnosis of invasive aspergillosis. J Clin Microbiol 40:2224–2227
12. Boiselle PM, Aviram G, Fishman JE (2002) Update on lung disease in AIDS. Semin Roentgenol 37:54–71
13. Haramati LB, Jenny Avital ER (1998) Approach to the diagnosis of pulmonary disease in patients infected with the human immunodeficiency virus. J Thorac Imaging 13:247–260
14. Diehl SJ, Lehmann KJ, Thienel F, Georgi M (1997) Value of high-resolution CT of the lungs in acute pulmonary symptoms of patients with HIV infections. Rofo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr 167:227–233
15. McGuinness G, Gruden JF, Bhalla M, Harkin TJ, Jagirdar JS, Naidich DP (1997) AIDS-related airway disease. Am J Roentgenol 168:67–77
16. Sider L, Gabriel H, Curry DR, Pham MS (1993) Pattern recognition of the pulmonary manifestations of AIDS on CT scans. Radiographics 13:771–784; discussion 785–776
17. Yu VL, Muder RR, Poorsattar A (1986) Significance of isolation of Aspergillus from the respiratory tract in diagnosis of invasive pulmonary aspergillosis. Results from a three-year prospective study. Am J Med 81:249–254
18. Metz CE (1989) Some practical issues of experimental design and data analysis in radiological ROC studies. Invest Radiol 24:234–245
19. Metz CE (1978) Basic principles of ROC analysis. Semin Nucl Med 8:283–298
20. Won HJ, Lee KS, Cheon JE, Hwang JH, Kim TS, Lee HG, Han J (1998) Invasive pulmonary aspergillosis: prediction at thin-section CT in patients with neutropenia—a prospective study. Radiology 208:777–782
21. Maschmeyer G (2001) Pneumonia in febrile neutropenic patients: radiologic diagnosis. Curr Opin Oncol 13:229–235
22. Staples CA, Kang EY, Wright JL, Phillips P, Muller NL (1995) Invasive pulmonary aspergillosis in AIDS: radiographic, CT, and pathologic findings. Radiology 196:409–414
23. Kelsey CA, Moseley RD, Brogdon BG, Bhave DG, Hallberg J (1977) Effect of size and position on chest lesion detection. Am J Roentgenol 129:205–208
24. Tudor GR, Finlay D, Taub N (1997) An assessment of inter-observer agreement and accuracy when reporting plain radiographs. Clin Radiol 52:235–238
25. White K, Berbaum K, Smith WL (1994) The role of previous radiographs and reports in the interpretation of current radiographs. Invest Radiol 29:263–265
26. Babcook CJ, Norman GR, Coblentz CL (1993) Effect of clinical history on the interpretation of chest radiographs in childhood bronchiolitis. Invest Radiol 28:214–217
27. Berbaum KS, Franken EA Jr, Dorfman DD, Barloon T, Ell SR, Lu CH, Smith W, Abu-Yousef MM (1986) Tentative diagnoses facilitate the detection of diverse lesions in chest radiographs. Invest Radiol 21:532–539

28. Berbaum KS, Franken EA Jr, Dorfman DD, Lueben KR (1994) Influence of clinical history on perception of abnormalities in pediatric radiographs. Acad Radiol 1:217–223
29. Doubilet P, Herman PG (1981) Interpretation of radiographs: effect of clinical history. Am J Roentgenol 137:1055–1058
30. Good BC, Cooperstein LA, DeMarino GB, Miketic LM, Gennari RC, Rockette HE, Gur D (1990) Does knowledge of the clinical history affect the accuracy of chest radiograph interpretation? Am J Roentgenol 154:709–712
31. Cooperstein LA, Good BC, Eelkema EA, Sumkin JH, Tabor EK, Sidorovich K, Curtin HD, Yousem SA (1990) The effect of clinical history on chest radiograph interpretations in a PACS environment. Invest Radiol 25:670–674
32. Potchen EJ, Cooper TG, Sierra AE, Aben GR, Potchen MJ, Potter MG, Siebert JE (2000) Measuring performance in chest radiography. Radiology 217:456–459
33. Schaefer CM, Greene R, Oestmann JW, Hall DA, Llewellyn HJ, McCarthy KA, Pile-Spellman ER, Rubens JR (1990) Digital storage phosphor imaging versus conventional film radiography in CT-documented chest disease. Radiology 174:207–210
34. Hayrapetian A, Aberle DR, Huang HK, Fiske R, Morioka C, Valentino D, Boechat MI (1989) Comparison of 2048-line digital display formats and conventional radiographs: an ROC study. Am J Roentgenol 152:1113–1118
35. Beall DP, Shelton PD, Kinsey TV, Horton MC, Fortman BJ, Achenbach S, Smirnoff V, Courneya DL, Carpenter B, Gironda JT (2000) Image compression and chest radiograph interpretation: image perception comparison between uncompressed chest radiographs and chest radiographs stored using 10:1 JPEG compression. J Digit Imaging 13:33–38
36. Kido S, Ikezoe J, Kondoh H, Takeuchi N, Johkoh T, Kohno N, Tomiyama N, Naito H, Arisawa J, Nakamura H (1996) Detection of subtle interstitial abnormalities of the lungs on digitized chest radiographs: acceptable data compression ratios. Am J Roentgenol 167:111–115
37. Kihara Y (2001) Evaluation of diagnostic accuracy of CRT monitor display for personal computer in the detection of small lung nodules: with particular emphasis on comparison between JPEG and wavelet compression. Nippon Igaku Hoshasen Gakkai Zasshi 61:231–237
38. Kido S, Ikezoe J, Takeuchi N, Kondoh H, Johkoh T, Kohno N, Tomiyama N, Yamagami H, Naito H, Arisawa J et al (1994) Interpretation of subtle interstitial lung abnormalities: conventional versus film-digitized radiography. Radiology 192:171–176
39. Cox GG, Cook LT, McMillan JH, Rosenthal SJ, Dwyer SJ III (1990) Chest radiography: comparison of high-resolution digital displays with conventional and digital film. Radiology 176:771–776
40. Otto D, Bernhardt TM, Rapp-Bernhardt U, Ludwig K, Kastner A, Liehr UB, Dohring W (1998) Subtle pulmonary abnormalities: detection on monitors with varying spatial resolutions and maximum luminance levels compared with detection on storage phosphor radiographic hard copies. Radiology 207:237–242
41. Buckley KM, Schaefer CM, Greene R, Agatston S, Fay J, Llewellyn HJ, Mrose HE, Rubens JR (1991) Detection of bullous lung disease: conventional radiography vs digital storage phosphor radiography. Am J Roentgenol 156:467–470
42. MacMahon H, Vyborny CJ, Metz CE, Doi K, Sabeti V, Solomon SL (1986) Digital radiography of subtle pulmonary abnormalities: an ROC study of the effect of pixel size on observer performance. Radiology 158:21–26
43. Lams PM, Cocklin ML (1986) Spatial resolution requirements for digital chest radiographs: an ROC study of observer performance in selected cases. Radiology 158:11–19
44. Parker TW, Kelsey CA, Moseley RD Jr, Mettler FA Jr, Garcia JF, Briscoe DE (1982) Directed versus free search for nodules in chest radiographs. Invest Radiol 17:152–155
45. Swensson RG, Hessel SJ, Herman PG (1985) The value of searching films without specific preconceptions. Invest Radiol 20:100–114
46. Kang EY, Staples CA, McGuinness G, Primack SL, Muller NL (1996) Detection and differential diagnosis of pulmonary infections and tumors in patients with AIDS: value of chest radiography versus CT. Am J Roentgenol 166:15–19