Original Article

Differences in pulmonary nodular consolidation and pulmonary cavity among drug-sensitive, rifampicin-resistant and multi-drug resistant tuberculosis patients: the Guangzhou computerized tomography study

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Background: Pulmonary nodular consolidation (PN) and pulmonary cavity (PC) may represent the two most promising imaging signs in differentiating multidrug-resistant (MDR)-pulmonary tuberculosis (PTB) from drug-sensitive (DS)-PTB. However, there have been concerns that literature described radiological feature differences between DS-PTB and MDR-PTB were confounded by that MDR-PTB cases tend to have a longer history. This study seeks to further clarify this point.

Methods: All cases were from the Guangzhou Chest Hospital, Guangzhou, China. We retrieved data of consecutive new MDR cases [n=46, inclusive of rifampicin-resistant (RR) cases] treated during the period of July 2020 and December 2021, and according to the electronic case archiving system records, the main PTB-related symptoms/signs history was ≤3 months till the first computed tomography (CT) scan in Guangzhou Chest Hospital was taken. To pair the MDR-PTB cases with assumed equal disease history length, we additionally retrieved data of 46 cases of DS-PTB patients. Twenty-two of the DS patients and 30 of the MDR patients were from rural communities. The first CT in Guangzhou Chest Hospital was analysed in this study. When the CT was taken, most cases had anti-TB drug treatment for less than 2 weeks, and none had been treated for more than 3 weeks.

Results: Apparent CT signs associated with chronicity were noted in 10 cases in the DS group (10/46) and 9 cases in the MDR group (10/46). Thus, the overall disease history would have been longer than the assumed <3 months. Still, the history length difference between DS patients and MDR patients in the current study might not be substantial. The lung volume involvement was 11.3%±8.3% for DS cases and 8.4%±6.6% for MDR cases (P=0.022). There was no statistical difference between DS cases and MDR cases

both in PN prevalence and in PC prevalence. For positive cases, MDR cases had more PN number (mean of positive cases: 2.63 *vs.* 2.28, P=0.38) and PC number (mean of positive cases: 2.14 *vs.* 1.38, P=0.001) than DS cases. Receiver operating characteristic curve analysis shows, PN ≥4 and PC ≥3 had a specificity of 86% (sensitivity 25%) and 93% (sensitivity 36%), respectively, in suggesting the patient being a MDR cases.

Conclusions: A combination of PN and PC features allows statistical separation of DS and MDR cases.

Keywords: Differential diagnosis; pulmonary; tuberculosis (TB); multidrug-resistant (MDR); computed tomography (CT)

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Introduction

The emergence of drug-resistant (DR) tuberculosis (TB) increases the burden of TB control. Multidrug-resistant tuberculosis (MDR-TB) refers to TB infection resistant to at least two first-line anti-TB drugs, isoniazid and rifampicin. About 0.5 million people developed DR-TB in 2018, of these 78% were MDR-TB, while only 1/3 of the confirmed MDR-TB cases were adequately treated (1). Extensively drug-resistant TB (XDR-TB) is defined as TB that has evolved resistance to rifampin and isoniazid, as well as to any member of the quinolone family and at least one of the second-line injectable drugs: kanamycin, amikacin, and capreomycin. Of MDR-TBs, XDR-TB accounts for 4–20% of these infections (2,3). Recently, a new category of DR *Mycobacterium tuberculosis* (*M.tb*) strain named totally drug-resistant TB (TDR-TB) has been identified, which is resistant to all first- and second-line drugs used to treat TB (4). Moreover, it is estimated that there are 1.9 million latent MDR-TB infected individuals around the world (5). When resistant mutants arise during treatment with anti-TB drugs, it is considered as acquired resistance (previously treated MDR-TB). Patients infected with an already drug-resistant strain develop primary resistance (new MDR-TB), which is observed in newly diagnosed TB patients. It has been estimated that globally 3.5% (which can be much higher in some regions) of newly diagnosed TB patients, and 20.5% of previously treated patients, are MDR-TB (1,6).

Despite that a wide range of geno- and phenotypic tests are available to detect DR *M.tb* strains and their susceptibility to drugs used, delay of appropriate MDR-TB treatment is common. Specimens used to detect MDR-pulmonary tuberculosis (PTB) are mostly sputum and bronchoalveolar lavage fluid, but when effective samples are not available, the utility of existing detection methods is limited. There have been interests to use chest imaging as a supporting tool to suggest the diagnosis of MDR-PTB (7). The suspicion of MDR/XDR-PTB by chest imaging can further guide and even intensify the diagnostic process for MDR-TB. A number of published articles described the potential imaging features difference between drug-sensitive (DS) and MDR-PTB (7-24). It had been suggested that MDR-TB cases tended to have more extensive disease, more likely to be bilateral, to have pleural involvement, to have bronchiectasis, and to have lung volume loss (7). XDR-TB overall appears even more aggressive than MDR-TB, with a greater number of cavities, larger cavities, and cavities of thicker wall (7,17). However, these signs alone are considered not sufficient for the differential diagnosis of MDR/XDR-PTB from DS-PTB (7). On the other hand, there may be no biological rationale that MDR-PTB shall demonstrates higher lung lesion extent or more lung destructions than DS-PTB. Some studies did not show imaging feature differences between DS-PTB *vs.* MDR-PTB or did not show imaging feature differences between MDR-PTB *vs.* XDR-PTB (25-27). In fact, that there is no imaging feature difference between DS-PTB and MDR-PTB is also the perception of many practicing radiologists (personal communications). There have been concerns that reported radiological feature differences between DS-PTB and MDR-PTB were confounded by that MDR cases tend to have a longer history prior to being diagnosed as MDR, thus the radiological features shown in MDR-PTB may not be intrinsic to MDR-PTB pathology. The variation in imaging manifestations across the studies could be a consequence of differential time intervals between disease onset and chest imaging (7).

Based on earlier literature reviews (20,21,28) and our

own analysis (9), we considered that pulmonary nodular (PN) and pulmonary cavity (PC) represent the two most promising imaging signs in differentiating MDR-PTB from DS-PTB. In a recent study [Dalian study (29)], using history length matched DS-PTB and MDR-PTB cases from a well-defined urban region in Dalian, China, we analysed the CT feature differences of these paired cases with a focus on PN and PC. There were 33 consecutive MDR-PTB cases [inclusive of rifampicin-resistant (RR) cases], with 19 cases had a history of <1 month, and 8 and 6 cases had a history of 1–6 and >6 months respectively. To pair the MDR-PTB cases according to the history length, matched 33 cases of DS-PTB patients were included. The first computed tomography (CT) exams prior to treatment were analysed. It was found that, compared with DS cases, MDR cases had a higher prevalence of PN and a higher number of PN per positive case for PN. For the cases >1 month history, MDR-PTB had a higher number of PC per positive case than that of DS-PTB cases. The lung field distribution of all lesions tended to be wider for MDR-PTB cases. Since the Dalian study only had a limited sample size (29), we conducted another study (the Guangzhou study) using patient data from another hospital in Guangzhou, China, with the goal to confirm these newly noted results.

Methods

Patient data

This study was approved by our institutional ethics committee and conducted in accordance with the Declaration of Helsinki (as revised in 2013). The patient consent was waived due to the retrospective nature of this study. All PTB cases were from the Guangzhou Chest Hospital, Guangzhou, China. Data was retrieved from the electronic case archiving system of the hospital. According to the 2016 World Health Organization (WHO) update, MDR-PTB management strategy is recommended for all patients with RR-PTB, regardless of confirmation of the isoniazid resistance (30); therefore, in this study RR-PTB was included as MDR-PTB cases. We retrieved data of consecutive MDR/RR cases treated during the period of July 2020 and December 2021, and according to the electronic case archiving system records, the main PTB-related symptoms/signs history was ≤3 months till the first CT scan in Guangzhou Chest Hospital was taken. We only included new cases who had never been treated for TB. In total we retrieved 46 MDR-PTB cases (34 males, 12 females, age: 38.5±16.85 years, range: 19–84 years, among them 22 cases were RR resistant cases, 47.8%). For the 24 (non-RR) MDR-PTB cases, 13 cases, 8 cases, 2 cases, and 1 case were resistant to 2, 3, 4, and 5 anti-TB drugs respectively (Table S1). The Drug sensitivity confirmation tests included a combination of sputum culture and Genexpert test results. There was no XDR-PTB among our cases. To pair the MDR-PTB cases with equal disease history length, from our hospital database we retrospectively collected 46 cases of PTB patients (31 males, 15 females, age: 46±18 years, range: 18–83 years) who were confirmed to be DS-TB. These DS cases were diagnosed and treated in our hospital also during July December 2020 and December 2021. All patients were HIV-negative, and none had immunocompromised status.

The first CT in Guangzhou Chest Hospital was analysed in this study. For all cases, lung CT was performed with a TOSHIBA Asteion 16-slice spiral CT scanner. The slice thickness was 5.0 mm. Only plain CT scans without contrast agent administration were analysed in this study. Since in many cases earlier chest X-ray or CT conducted in primary care clinics were available, some patients started anti-TB treatment before the CT examination in Guangzhou Chest Hospital (*Figure 1*).

All PTB lesions were read for their extent. A longitudinal axis was taken from the upper apices of the lungs down to the diagram, and then this axis was divided into three segments of equal length with each segment correlated to a zone. In this way, two lungs were divided into six zones. Modifications were made to the Fleischner Society Glossary definitions for PN and PC (29,31). A PN was a rounded or oval (but not band-like) solid opacity with a relatively clear boundary measuring between >6 mm to 3 cm in diameter (*Figure 2*), and quantified for their number. Smaller nodules and aggregation of smaller nodules were not counted as PN in this study. A PC was a gas-filled space, seen as a lucency area within pulmonary consolidation or a nodule. PC was counted only for those with a lumen diameter >5 mm. Multiple cavities in a single consolidation is counted as one cavity. Worm-eroding like cavity (WELC) is more likely to be numerous, these usually small cavities in one consolidation were together counted as one cavity. A PC within a PN was counted as both one PC and one PN. PC was also differentiated from bulla and cyst with a thin wall. CT images were jointly read by a radiology trainee (SNT) and a specialist radiologist (YXJW), with consensus all achieved.

The percentage lung volume involvements by TB lesions were evaluated quantitatively, using PyCharm (JetBrains

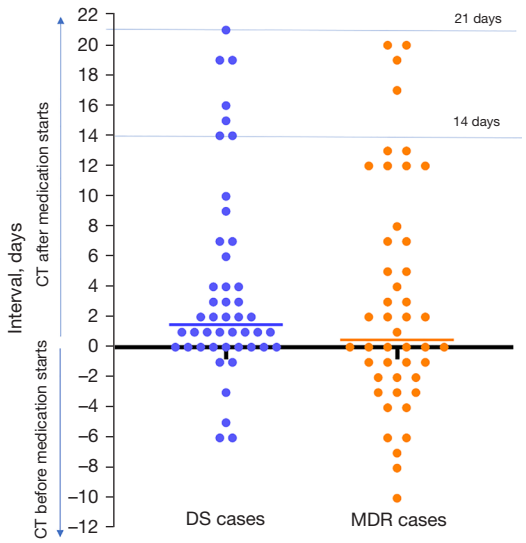

Figure 1 The interval period (days) between when anti-tuberculosis treatment started and when the first CT scan in Guangzhou Chest Hospital was taken. Bars in the graph indicate median time. For cases who had treatment started before the CT in Guangzhou Chest Hospital, they had earlier chest imaging (CT or X-ray) in another primary care clinics. DS, drug-sensitive; MDR, multidrug-resistant.

s.r.o., Prague, Czech Republic). Lung parenchyma regions were initially extracted by a combination of CT density thresholding and morphology. Then CT density thresholding was applied to segment diseased parts of the lung parenchyma (i.e., areas with increased CT density), sparing healthy lung areas. Graphical operation was applied to fill in the blood vessels in the lungs as well as to divide the boundaries of the bronchi. Finally, the volume of the diseased lung was calculated by counting the number of voxels in all slices.

During the course of CT assessment, it became clear to the authors that some of the patients had PTB history much longer than 3 months. Apparent radiological signs associated with chronicity, such as extensive fibrosis, apparent lesion calcifications, or contraction of the chest cage due to lung destruction, were noted in 10 cases in the DS group (10/46) and 9 cases in the MDR group (10/46). Further discussions were held with respiratory physicians, and it was informed that such a phenomenon is relatively common among Guangzhou Chest Hospital patients. A substantial portion of patients often ignore mild symptoms initially, and only report the history when the symptoms become more apparent. Additional checking showed that,

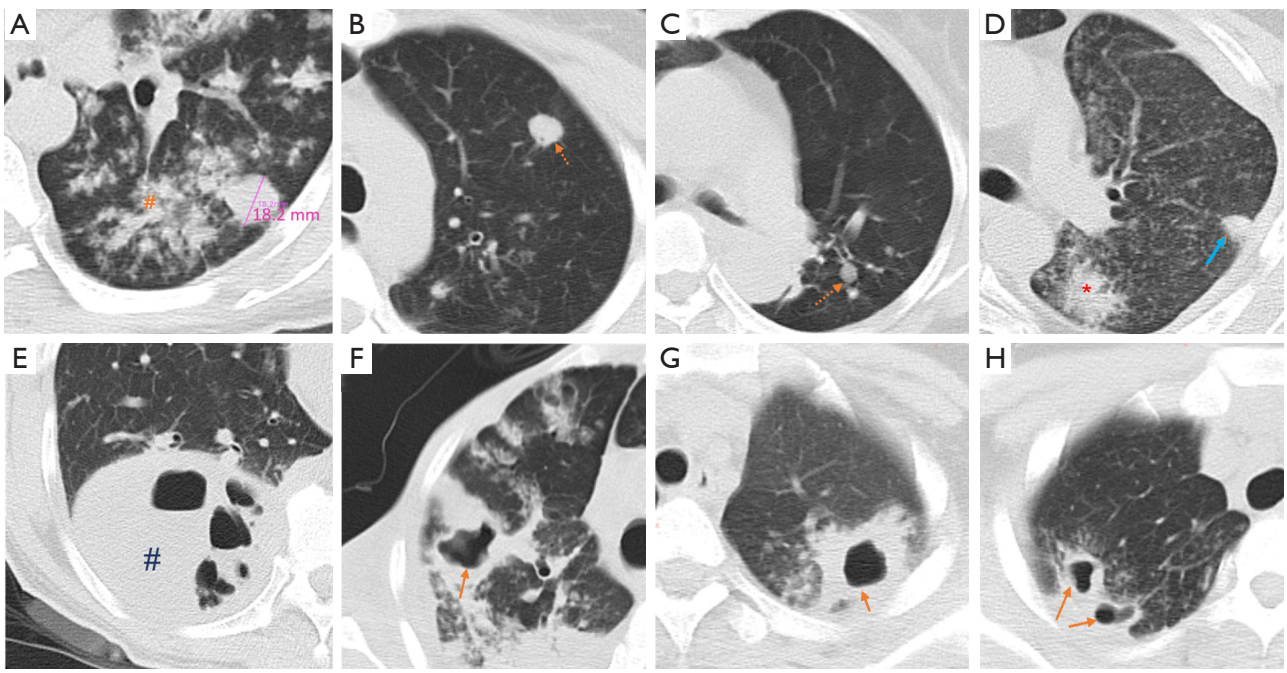

Figure 2 Illustration of PN and PC. (A) A PC of 18.2 mm is noted, and # indicates these small nodules are not counted as PN; (B,C) orange arrow indicates a PN; (D) * indicates ill-defined lesion noted counted as PN, and blue arrow indicates a triangle lesion not counted as PN; (E-H) cavities are counted as once in each figure. #, multiple cavities in a consolidation; orange arrow, cavity. PN, pulmonary nodular consolidation; PC, pulmonary cavity.

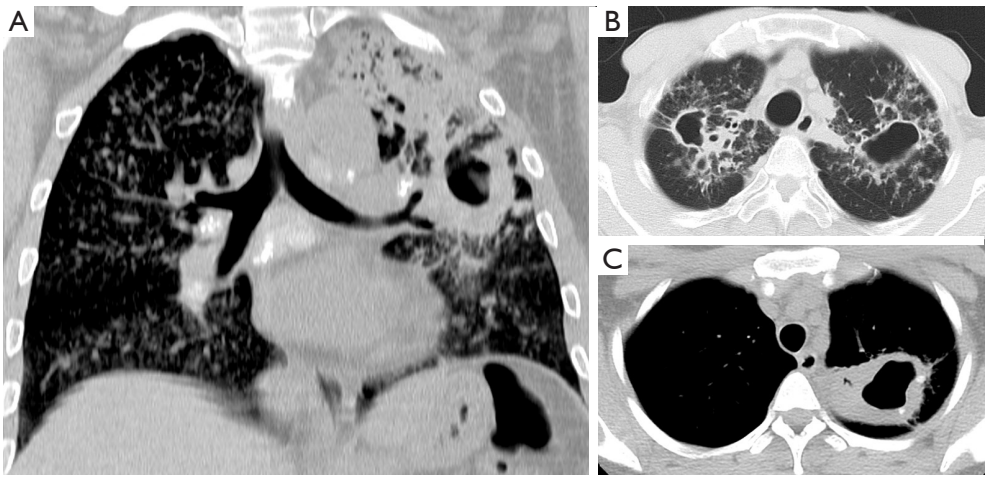

Figure 3 CT of three DS-PTB cases. The case in (A) shows extensive bilateral lung lesion with calcifications suggesting chronicity, and left lung lesion with cavities, and slight shrinkage of left chest cage (note the left diaphragm is higher than the right diaphragm). The case in (B) shows extensive bilateral lesions with bilateral cavities. The case in (C) shows left lung consolidation and thick-walled cavity (note calcifications in the cavity wall). DS-PTB, drug sensitive pulmonary tuberculosis.

22 (47.8%, 22/46) of the DS patients and 30 (65.2%, 30/46, P=0.09) of the MDR patients were from rural communities.

Statistical analysis was processed using GraphPad Prism (San Diego, CA, USA). Comparisons between two groups were conducted with Chi-squared test for categorical variables and Mann-Whitney *U* test for continuous variable. Receiver operating characteristic (ROC) curve analysis was used to determine the diagnostic performance, reporting the area under the ROC (AUROC) and optimal cut-off values with sensitivity and specificity. A P value of less than 0.05 was considered statistically significant.

Results

With both DS and MDR cases, some patients had lesions that only involved a small part of the lungs, whereas some patients had very extensive lesions including thick-walled cavities (*Figures 3*,*4*). The lung volume involvement was 11.3%±8.3% for DS cases and 8.4%±6.6% for MDR cases (P=0.022, *Figure 5*). DS cases showed a slightly higher extent of lung volume involvement than MDR cases.

The DS-PTB *vs.* MDR-PTB differences of prevalence (positive rate) and lesion number for PN and PC are shown in *Tables 1*,*2*, and *Figures 6*,*7*. PC and any lesion distributions tended to be slightly wider for MDR-PTB cases. There was no statistical difference between DS cases and MDR cases both in PN prevalence and in PC prevalence. For positive cases, MDR-PTB had more PN number and PC number, and this was statistically significant for PC.

AUROC analysis results are selectively shown in *Table 3*. Together with Dalian results, data suggests PC/PN number ≥3 or 4 were associated with a high probability of the PTB patient to be MDR. Graphic analysis shows a combination of PC number and maximum diameter of PC allowed a separation of DS cases and MDR cases on probability term (*Figure 8*); and a combination of PC number, maximum diameter of PC, and PN number might even allow an even better statistical separation of DS cases and MDR cases (*Figure 9*).

Discussion

Despite our initial intention to recruit patients with clearly defined short disease history length of <3 months, the results of recruitment were not as anticipated but these still reflect clinical practice in many scenarios. This experience was different from that of the Dalian study (29), and mostly likely related to the hospital setting and patient sources. Moreover, this Guangzhou study is a radiologist-initiated study, being less sensitive to the issues of history taking during the initial patient inclusion. It may be possible that DS cases could have had an overall slightly longer disease history, due to that 10 cases (21.7%) of DS cases had apparent chronicity CT sign while 9 cases (19.6%) of MDR cases had apparent chronicity CT sign. This may also help explain that lung involvement volume percentage was higher for DS patients than for MDR patients, being

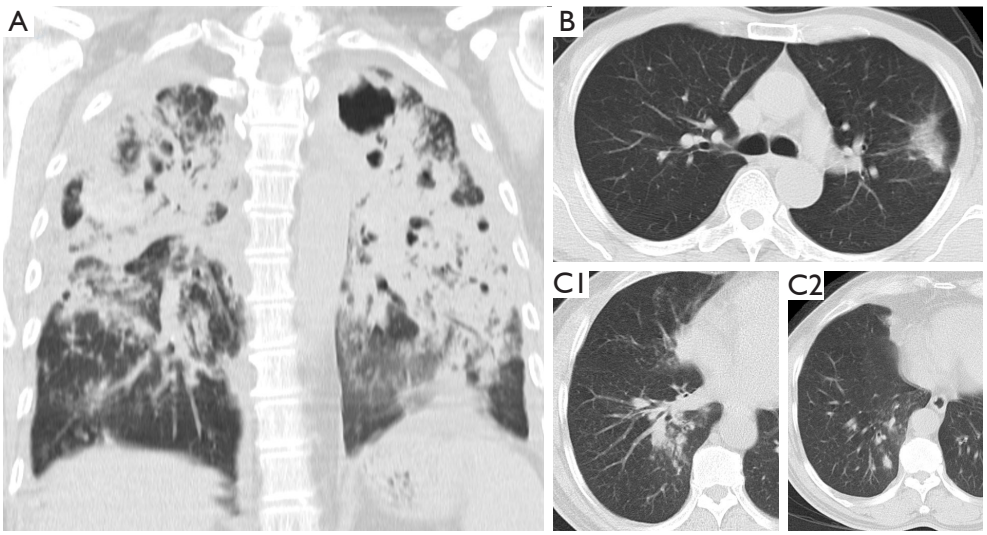

Figure 4 CT of three MDR-PTB cases. The case in (A) shows extensive bilateral lung lesion with bilateral cavities (note thickening of the pleura, and the left diaphragm is higher than the right diaphragm). The case in (B) shows a patch of infiltration in the left lung, and this is the only lesion in this patient. (C1,C2) The same case and show small areas of infiltration and consolidation in the right lung. MDR-PTB, multi-drug resistant pulmonary tuberculosis.

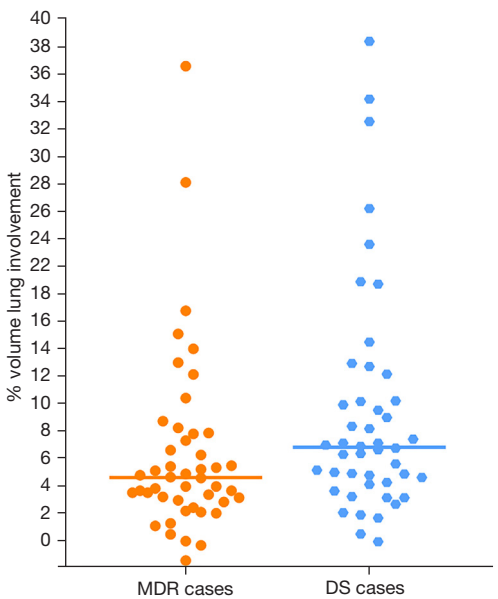

Figure 5 Percentage lesion lung involvement volume on CT of DS and MDR cases. A higher percentage lesion lung involvement is noted for DS cases. The bars in the graph indicate median value. DS, drug sensitive; MDR, multi-drug resistant.

Table 1 Prevalence, mean number and mean size (in mm) for PN and PC

Lesions	Prevalence (%)	Mean No. #	Mean size #
PN			
DS-PTB	63.04 (29/46)	2.28	12.75
MDR-PTB	69.57 (32/46)	2.63	11.90
P value	0.508	0.381	0.681
PC			
DS-PTB	63.04 (29/46)	1.38	18.40
MDR-PTB	60.87 (28/46)	2.14	18.36
P value	0.830	0.001	0.967

#, counting per positive case. DS, drug-sensitive; PTB, pulmonary tuberculosis; MDR, multidrug-resistant resistant (including rifampicin); PN, pulmonary nodular; PC, pulmonary cavity.

11.3%±8.3% for DS cases and 8.4%±6.6% for MDR cases (P=0.022). However, a higher number of MDR cases (MDR: 65.2%; DS: 47.8%) were from rural communities, and rural community patients may seek medical care at a later stage

Table 2 Distribution of PN, PC, and any tuberculous lesions

Distribution	PN		PC		Any lesions	
	DS (n=29)	MDR (n=32)	DS (n=29)	MDR (n=28)	DS (n=46)	MDR (n=46)
Lung fields	1.58±0.76†	1.50±0.61†	1.24±0.43‡	1.64±0.85‡	1.77±0.83§	2.07±1.06§
Bilateral lungs	10 (34.48)	5 (15.63)	4 (13.79)	7 (25.00)	14 (18.75)	14 (20.83)
R upper field	5 (17.24)	9 (28.13)	10 (34.48)	14 (50.00)		
L upper field	12 (41.38)	14 (43.75)	13 (44.83)	13 (46.43)		
Upper fields (R + L)	17 (58.62)	23 (71.88)	23 (79.31)	27 (96.43)		
R middle field	8 (27.59)	5 (15.63)	1 (3.45)	5 (17.86)		
L middle field	9 (31.03)	7 (21.88)	4 (13.79)	10 (35.71)		
Middle fields (R + L)	17 (58.62)	12 (37.50)	5 (19.23)	15 (31.25)		
R lower field	5 (17.24)	6 (18.75)	3 (17.24)	5 (17.86)		
L lower field	7 (24.14)	5 (15.63)	2 (6.90)	2 (7.14)		
Lower fields (R + L)	12 (41.38)	11 (34.38)	5 (17.24)	7 (25.00)		

Data are presented as mean ± standard deviation or number (percentage). †, P=0.819; ‡, P=0.034; §, P=0.106. DS, drug-sensitive; MDR, multidrug-resistant; PN, pulmonary nodular; PC, pulmonary cavity; R, right; L, left.

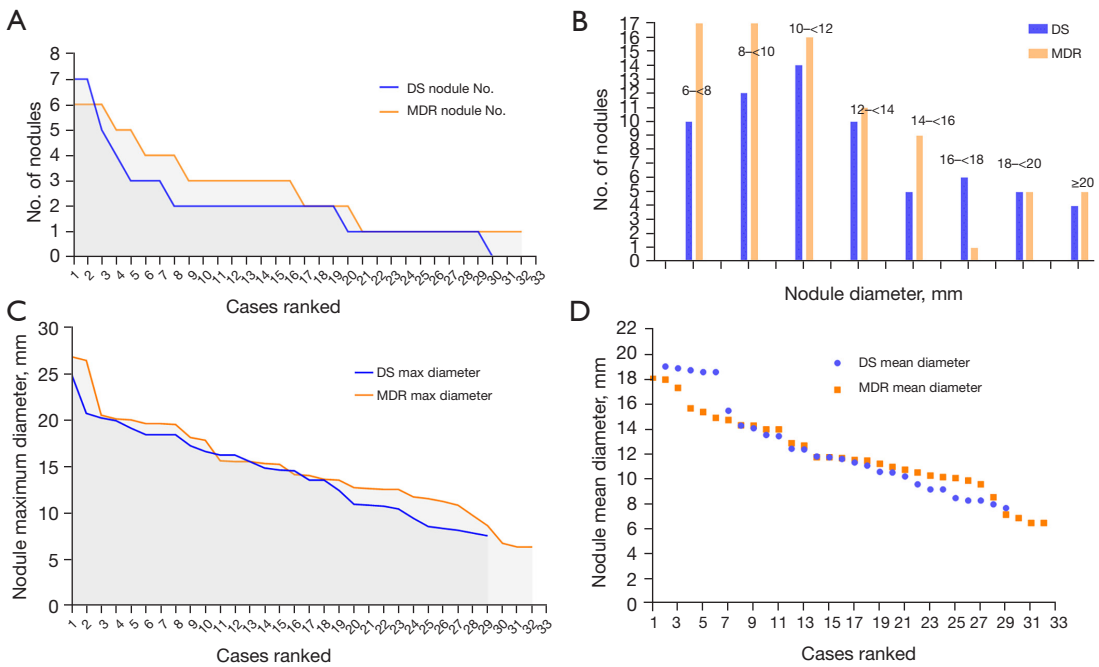

Figure 6 PN distribution characteristics between DS-PTB and MDR-PTB (only PN positive cases are presented). (A) Cases ranked from the case of highest PN number to the case of lowest PN number (n=1); (B) number of PN according to the diameter; (C) cases ranked based on with PN of largest diameter to with PN of smallest diameter; (D) cases ranked according to the mean diameter of the PN. PN, pulmonary nodular; DS-PTB, drug sensitive pulmonary tuberculosis; MDR-PTB, multi-drug resistant pulmonary tuberculosis.

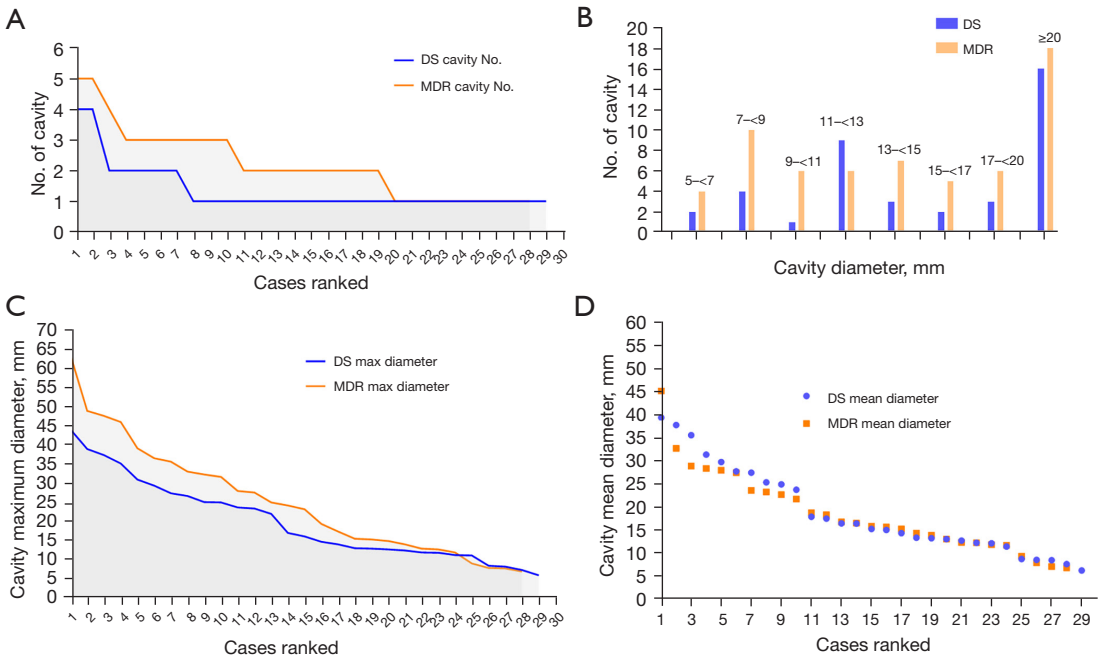

Figure 7 PC distribution characteristics between DS- and MDR-PTB (only cavity positive cases are presented). (A) Cases ranked from those with highest PC number to those with lowest PC number (n=1); (B) number of cavities according to the diameter; (C) cases ranked based on with cavities of largest diameter to with cavities of smallest diameter; (D) cases ranked according to the mean diameter of the cavities. DS-PTB, drug sensitive pulmonary tuberculosis; MDR-PTB, multi-drug resistant pulmonary tuberculosis; PC, pulmonary cavity.

Table 3 Receiver operating characteristic curve analysis results

Data source	No. of lesions	Specificity, %	Sensitivity, %
PN			
Current study	≥4	86	25
Song *et al.* (29)	≥3	93.9	48.5
PC			
Current study	≥3	93	36
Song *et al.* (29)	≥4	84.9	39.4

Both this Guangzhou study and the Dalian study show PN/PC number of ≥3 or ≥4 suggests relatively high specificity for suggesting MDR, however the sensitivities are relatively low. PN, pulmonary nodular; PC, pulmonary cavity; MDR, multidrug-resistant.

of the disease. Overall, considering our sample strategy, we believe that the history length difference between DS patients and MDR patients in the current study might not be substantial.

The general perception of many practicing radiologists is that there is no imaging feature difference between DS-PTB and MDR-PTB, and it is impossible to differentiate MDR-PTB from DS-PTB subjectively on chest imaging. Indeed, our current quantitative analysis showed lesion volume extent was even higher among DS patients than among MDR patients. The distributions of PC and all lesions were only slightly wider for MDR-PTB cases than for DS-PTB cases (*Table 1*). This is consistent with our Dalian study, where the mean lung field involvement was 3.52 for DS cases and 3.88 for MDR cases, and bilateral lung involvement was 51.5% for DS cases and 66.7% for MDR cases (29).

Our recent Dalian study showed that MDR cases had a higher prevalence of PN and a higher number of PN per positive case for PN (29). The difference was apparent even for the cases with <1 month history. On the other hand, it takes time for PC lesions to develop in the infected lungs (29). In contrast to our Dalian study where for early-stage cases a bigger difference was noted for PN (rather than for PC) between DS-PTB and MDR-PTB, our current study showed for cases with a possibly longer disease history a bigger difference was noted for PC rather than for PN, which is on the other hand consistent with a number of earlier reports (7,10,17,21,22). Thus, this study further supports the notion that we should consider patient history length when

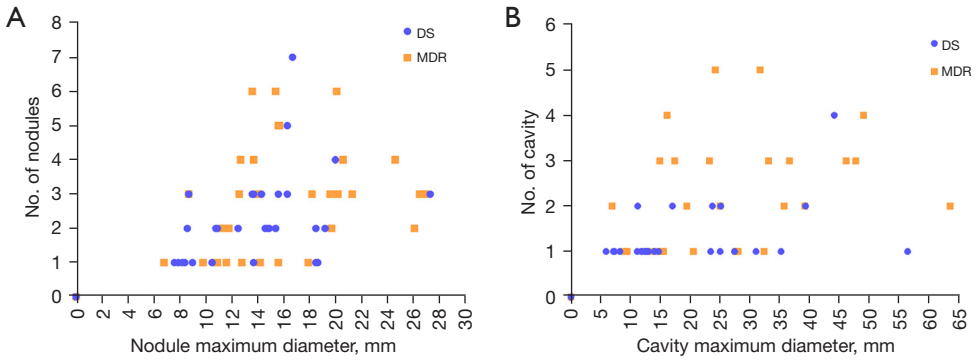

Figure 8 PN and PC distribution characteristics between DS-PTB and MDR-PTB (only PN or PN positive cases are presented, as negative cases concentrate at the zero values). A better separation is noted for PC features than for PN features. (A) On a patient-by-patient basis, relationship between the largest PN a patient had and the number of PN of this patient. (B) On a patient-by-patient basis, relationship between the largest PC a patient had and the number of PC of this patient. PN, pulmonary nodular; PC, pulmonary cavity; DS-PTB, drug sensitive pulmonary tuberculosis; MDR-PTB, multi-drug resistant pulmonary tuberculosis.

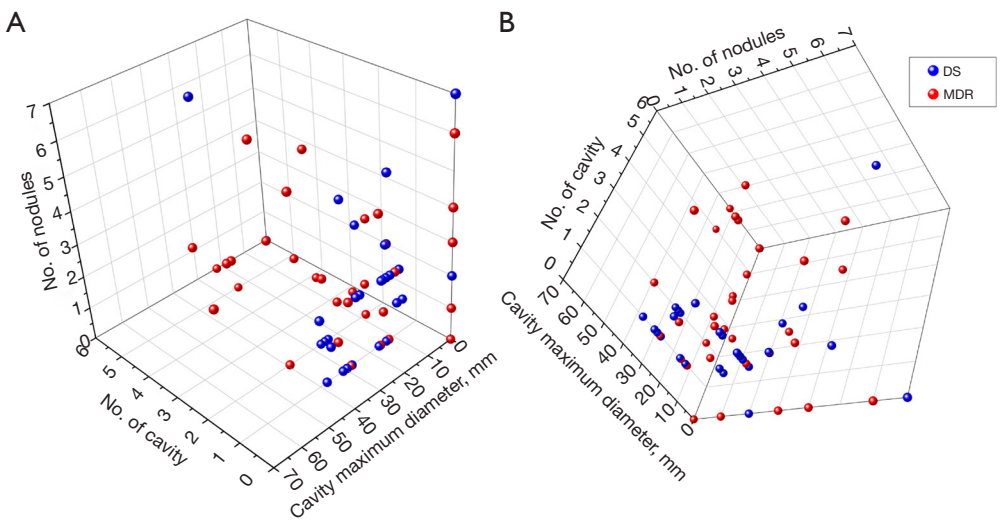

Figure 9 Visual demonstration of a combination of pulmonary cavity number, maximum diameter of pulmonary cavity of the patient, and pulmonary nodule number. One ball represents one patient. This figure shows some MDR patients can be separated from DS patients in statistical terms. DS, drug sensitive; MDR, multi-drug resistant.

analyzing the CT features of PTB patients. The current study and the Dalian study both suggest that PN/PC number ≥3 or 4 may be associated with a high probability of a PTB patient being MDR (*Table 3*). This is particularly interesting considering that in this study the lesion lung involvement percentage is higher in DS patients than in MDR patients. Our current study further supports that a combination of PC number, PC maximum diameter, and PN number might allow a separation of DS-PTB cases and MDR-PTB cases on statistical terms. Current difficulties include that qualification of PC/PN numbers and sizes are not only time consuming but also are associated with some subjectivities for smaller lesions or clustered lesions quantifications. It is noted that, for PC and PN positive cases, the Dalian results had a higher PC/PN number per case for the high-count cases than the current study. We will further investigate to understand if this was due to genuine patient differences, or it was due to PC/PN identification subjectivity. Further development of artificial intelligence technology may allow better consistency in lesion characterization with high time-

efficiency (32-35). We also plan to publish a teaching atlas to standardize human reading.

According to the 2016 WHO update, MDR-PTB management strategy is recommended for all patients with RR-PTB, regardless of confirmation of the isoniazid resistance (30). Therefore, in clinical practice, the differentiation between RR cases and true MDR cases may be less important. However, we tentatively checked the PN/PC differences between RR cases and true MDR cases in this study, and the results are shown in Figure S1 and Table S2. The lung volume involvement was 9.37%±8.57% for RR cases, and 7.43%±4.04% for true MDR cases (P>0.05). Table S2 shows a slight trend of more PN and PC changes among true MDR cases than among RR cases, though there was no statistical significance. We additionally reviewed our Dalian results (29) (Figure S2). The data also tentatively suggest that MDR cases might have demonstrated higher PN/PC counts for true MDR cases than for RR cases. More studies are required to confirm this point.

There are many limitations to this study. The first limitation is that we failed to quantify disease history length which is a subjective measure by patients themselves. Due to the nature of the setup of Guangzhou Chest Hospital, a large proportion of the patients (56.5% in total) in this study were from rural areas, it is understandable that some of the patients only presented to the hospital till their discomforts reached a certain degree, or their discomforts had protracted for a long period of time. However, such a phenomenon may represent a real-world possibility. It should be noted that the patients were not all treatment naive when the first CT scan was taken in Guangzhou Chest Hospital. While how this would have affected the results of this study is unknown, however, we expect the impact on the analysed results would be small. In the study of Lee *et al.* (36), 1 month after anti-TB treatment, 59.2% (45/76) cases had chest X-ray improvement whereas 34.2% (26/76) did not show chest X-ray changes. Two months after anti-TB treatment, 71.9% (100/139) cases had chest X-ray improvement whereas 34.2% (35/139) did not show chest X-ray changes. In the study of How *et al.* (37), 8 weeks after anti-TB treatment, 61.7% (71/115) cases had chest X-ray improvement while 30.4% (35/115) did not show chest X-ray changes. In a more recent quantitative ^{18}F-FDG PET-CT study, Malherbe *et al.* (38) described that 1 month into anti-TB treatment, most cases had slight improvement in metabolic lesion volume and mean lesion intensity. For the cases in the current study, when the CT was taken, most cases had drug treatment for less than 2 weeks, and none had been treated for more than 3 weeks (*Figure 1*). We can anticipate this duration of treatment may have only slightly improved some exudative lesions or some infiltrative lesions but change for the PN (which is more solid) and PC (which is known to be slower in drug treatment response) may be group-wise minimal statistically. Another limitation is our relatively small sample size, which also limits the further analysis for the differences between RR patients and true MDR-patients. Since all our cases were new MDR-PTB, whether these features can be generalized to previously treated PTB or child patients should be further investigated (7,39,40).

Conclusions

In conclusion, following the Dalian study (29), this study continues to suggest a combination of PC number, maximum PC diameter, and PN number may statistically suggest the probability of MDR-PTB. This study further supports the notion that we should consider patient disease history length when analyzing the CT features of MDR-PTB patients.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-694/coif). Y.X.J.W. serves as the Editor-in-Chief of *Quantitative Imaging in Medicine and Surgery*. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by our institutional ethics committee and conducted in accordance with the Declaration of Helsinki (as revised in 2013). The patient consent was waived due to the retrospective nature of this study.

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Supplementary

Table S1 Paired-patients information for DS and MDR patients

Pair No.	DS-PTB					MDR-PTB					
	Sex	Age, years	History #, months	PN	PC	Sex	Age, years	History #, months	Drugs	PN	PC
Pair 1	F	24	1	2	1	M	43	1	R	2	1
Pair 2	M	30	3	4	2	M	48	3	R	1	5
Pair 3	M	30	1–2	2	1	M	31	1–2	H, R	5	2
Pair 4	M	42	2	2	0	M	50	2	H, R, FLQ	3	4
Pair 5	M	50	2	2	1	M	46	2	H, R, Z, E, S	1	2
Pair 6	M	50	1–2	0	0	M	38	1–2	R	0	0
Pair 7	F	51	<1	1	0	M	56	<1	H, R	1	1
Pair 8	M	56	<1	2	1	M	67	<1	H, R	3	3
Pair 9	F	82	1	0	0	M	73	1	H, R, FLQ	0	0
Pair 10	F	26	<1	3	2	M	39	<1	R	6	0
Pair 11	M	26	<1	2	0	M	26	<1	R	2	1
Pair 12	F	32	1–2	1	1	F	32	1–2	R	0	0
Pair 13	M	57	<1	2	1	F	29	<1	H, R	6	0
Pair 14	M	59	<1	3	1	M	62	<1	R	3	0
Pair 15	M	61	2–3	1	0	M	59	2–3	H, R, S, E	1	0
Pair 16	M	69	2–3	0	1	F	24	2–3	R	5	3
Pair 17	F	18	<1	0	1	M	39	<1	R	1	0
Pair 18	M	20	<1	1	1	M	19	<1	R	0	1
Pair 19	F	26	1–2	0	0	F	26	1–2	R	1	0
Pair 20	F	28	3	3	1	M	30	3	H, R, FLQ	4	0
Pair 21	F	29	<1	1	1	M	24	<1	R	0	0
Pair 22	M	33	<1	0	0	M	20	<1	R	0	0
Pair 23	M	37	1	0	1	M	34	<1	H, R	2	3
Pair 24	F	38	1–2	0	0	F	26	1–2	R	1	3
Pair 25	M	39	2–3	2	1	F	33	2–3	H, R	0	0
Pair 26	M	42	1–2	0	2	F	28	1–2	R	4	0
Pair 27	M	57	2–3	7	4	F	30	2–3	R	1	0
Pair 28	M	63	2–3	2	1	M	69	2–3	R	1	1
Pair 29	M	63	<1	1	0	M	20	<1	R	0	5
Pair 30	M	64	1	0	2	M	34	1–2	R	4	1
Pair 31	F	66	2–3	1	0	M	50	2–3	H, R, FLQ	3	3
Pair 32	M	83	<1	0	1	F	32	<1	H, R, Z, E	0	1
Pair 33	F	29	<1	1	0	M	60	<1	H, R	0	2
Pair 34	M	57	1	1	0	M	22	<1	R	1	2
Pair 35	M	50	3	0	2	M	73	3	H, R	1	2
Pair 36	F	37	<1	0	1	F	33	<1	R	0	2
Pair 37	F	30	2	2	4	M	23	2	R, Ofx	3	2
Pair 38	M	20	1–2	0	0	M	54	< 2	H, R	0	0
Pair 39	M	23	<1	0	1	M	61	2–3	H, R, FLQ	2	2
Pair 40	M	52	<1	2	0	M	51	2	H, R	0	0
Pair 41	M	60	<1	1	1	M	84	2–3	R	0	1
Pair 42	M	27	1	7	0	M	49	3	H, R	3	3
Pair 43	M	80	<1	0	0	M	57	3	H, R	6	3
Pair 44	F	69	<1	2	1	F	58	3	H, R, S	3	2
Pair 45	M	62	<1	0	1	M	59	3	H, R, Z	3	1
Pair 46	M	71	<1	0	0	F	26	3	H, R, E	1	0

History #, the disease history lengths were recorded in the electronic case archiving system. However, later it was noted that these disease history lengths are unreliable, and the real average history length would be much longer. DS, drug sensitive; MDR, multi-drug resistant; PTB, pulmonary tuberculosis; H, isoniazid; R, rifampicin; S, streptomycin; E, ethambutol; Ofx, ofloxacin; Z, pyrazinamide; FLQ, fluoroquinolone; PN, pulmonary nodular consolidation; PC, pulmonary cavity.

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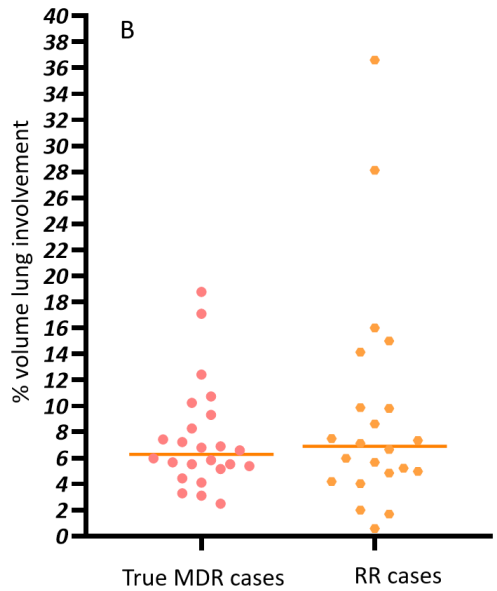

Figure S1 Percentage lesion lung involvement volume on CT of DS and true MDR cases and RR cases. The bars in the graph indicate median value. DS, drug sensitive; RR, rifampicin-resistant pulmonary tuberculosis; MDR, multi-drug resistant pulmonary tuberculosis.

Table S2 Prevalence, mean number and mean size for PN and PC between RR cases (n=22) and true MDR cases (n=24)

	Prevalence	No. of PN or PC (mean) #	Size (mean) #, mm
PN			
RR-PTB	63.3% (14/22)	2.36 (33/14)	11.02
True MDR-PTB	75% (18/24)	2.83 (51/18)	12.59
P	0.403	0.334	0.190
PC			
RR-PTB	54.5% (12/22)	2.17 (26/12)	15.41
True MDR-PTB	66.7% (16/24)	2.25 (36/16)	20.3
P	0.400	0.410	0.104

#, for positive cases. PN, pulmonary nodular consolidation; PC, pulmonary cavity; RR, rifampicin-resistant; MDR, multidrug-resistant; PTB, pulmonary tuberculosis.

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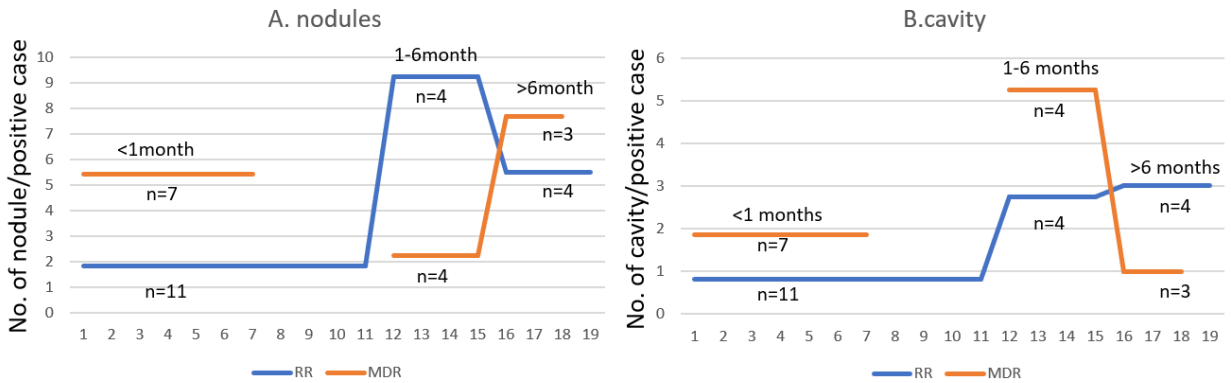

Figure S2 Number of pulmonary nodular consolidation and pulmonary cavity for RR cases and MDR cases. RR, rifampicin-resistant pulmonary tuberculosis; MDR, true multi-drug resistant pulmonary tuberculosis. This Figure is re-used with permission from Song *et al.* (29).

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