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Retrospective study of clinical and lesion characteristics of patients undergoing surgical treatment for Pulmonary Tuberculosis in Georgia

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Abstract

Objectives—Our aim was to retrospectively compare clinical data and characteristics of removed lesions of the cohort of patients undergoing therapeutical surgery for their tuberculosis.

Design and methods—Demographic and epidemiological details, clinical data, data on the surgery performed, macroscopic characteristics of the TB lesions removed, and outcome were recorded retrospectively from the 137 patients who underwent therapeutical surgery for their TB in Tbilisi, Georgia during 2014 and 2015.

Results—Men represented 70% of the included patients, presented more comorbidities and underwent operation earlier in terms of days between diagnostic and surgery. Women underwent operation at younger ages, and in MDR/XDR-TB cases, showed higher percentages of sputum conversion at >2 months and of fresh necrosis in the surgical specimens, suggesting a worse evolution. Half of cases were MDR/XDR-TB cases. In spite of being considered microbiologically cured according to WHO, a non despricable percentage of cases showed viable bacilli in the

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surgical specimen. Even if no causality could be statistically demonstrated, differences could be encountered according to gender and drug susceptibility of the responsible strains.

Conclusions—According to our results, host factors such as gender, type of necrosis found in the lesions, size of lesions and presence of viable bacilli in the surgical specimen, should be included in future studies on therapeutical surgery of TB. As most of studies are done in MDR/XDR-TB, more data on DS-TB operated cases are needed. Our results also highlight that, in spite of achieving the microbiologically cured status, sterilization might not occur, and thus new biomarkers and new methods to evaluate the healing process of TB patients are urgently needed and radiological assays should be taken into account.

Keywords

Tuberculosis; Surgery; Gender; DS-TB; MDR/XDR-TB; Necrosis

1. Introduction

According to the World Health Organization (WHO), Georgia has a high incidence of tuberculosis (TB) cases (116/100.000 habitants), with a high Multi-Drug Resistant TB (MDR-TB) burden (51% of all declared cases in 2015).[1] In countries with high incidences, therapeutical surgery is still a good option to cope with TB complications and sequelae, as well as to reduce the bacilli burden[2]; and might be essential as an adjuvant to the appropriate chemotherapy in the MDR-TB cases.[3] In this manuscript, we present a study that aimed to retrospectively compare clinical data and characteristics of removed TB lesions of a cohort of patients undergoing therapeutical surgery for their TB, in the National Center for Tuberculosis and Lung Diseases (NCTLD, Tblisi, Georgia).

2. Materials and methods

2.1. Design

The project was reviewed and approved by the Ethics Committee IRB00007705 NCTLD Georgia #1, IORG0006411 (Tbilisi, Georgia) and the Ethics Committee of Germans Trias i Pujol Hospital (Badalona, Catalonia, Spain) to ensure compliance with all current national and European laws on clinical studies. The study was registered at the clinicaltrials.gov database with the identifier NCT02715271. The results presented here were extracted from a retrospective cohort including all patients operated per clinical routine at the NCTLD.

2.2. Data

Data were recorded retrospectively and anonymously from the 2014 and 2015 surgical notebooks in a Spreadsheet created ad-hoc, including different categories on both the patients and the lesions' characteristics. WHO definitions were used whenever possible.[4] Table 1 includes all data categories recorded, definitions and possible answers. Graph Pad Prism 6 software (La Jolla, CA, USA) was used to draw the figures. Statistical analysis was done using the independent 2 samples t-test to compare continuous variables. The associations with other categorical variables were tested with the Chi-square test or Fisher

exact test. All tests were two-tailed, and p-values less than 0.05 were considered statistically significant.

3. Results

3.1. Demographic and epidemiological features

A total of 137 patients underwent therapeutical surgery for their TB at the NCTLD during the years 2014 and 2015, 96 males (69.8%) and 41 females (30.8%). Men were older (median age = 43.5 years old) than women (28 years old). 25% of men had comorbidities: Hepatitis C Virus Infection (n = 15), Diabetes mellitus (n = 5), HCV and Diabetes (n = 3), and HCV plus HIV infection (n = 1). A total of 49 patients were smokers, 48 on a daily or mostly daily basis; representing a 48.9% and 2.4% of total male and female populations, respectively. The majority of women (92.6%) declared never drinking alcohol. The alcohol intake in men increased with age. While men declaring themselves abstemious (13.5%) had a median age of 26 years old, those declaring drinking on less than monthly (33.3%), monthy (52%) or weekly basis (8.3%) had a higher median age (45.6 years old). No statistically significant differences were encountered between DS-TB and MDR/XDR-TB groups.

3.2. TB data

The 92.7% of total cases recorded were pulmonary TB exclusively (127 patients), while in 7.3% (10 patients) pleura involvement (as empyema) was found (being more frequent in males, not statistically significant). Pleura involvement was present in the 80% of MDR/XDR-TB cases.

Approximately the half of the patients included were DS-TB (56.9%), and the other half, MDR or XDR (40.1%). Mono resistance was rare. Table 2 shows the number of cases for each category, as well as the number and percentage according to gender. The percentage of men and women were very similar regardless of the drug-sensitivity of the strains involved.

The chest X-ray assay (previous to surgery) showed the presence of a single lesion (only cavities and tuberculomas considered) for most of the patients (76%), while 19.2% showed 2 lesions, and 4.8% up to three.

Most patients undergoing surgery had been considered bacteriology cured according to WHO's definitions (96.3%). No statistically significant differences according to gender or drug susceptibility were found in the non microbiologically cured group of patients.

Figure 1 shows the results of time to culture's negativization, in totals and stratified by gender and by the drug-sensitivity of the strains. As women included in this cohort were younger (28 vs 43.5 years old), we stratified the results by dividing the male cases in ≤43 and >43 years old, to see if the gender itself could be an influence free from the age input. Differences were encountered between females and males of ≤43 years old, being statistically significant for DS-TB cases ($p \leq 0.0001$). A high percentage of patients negativized the culture in ≤2 months (51.8%), especially if they were women or younger (median age of 33). The culture was always negative in a non despicable 31.3% of the

cases; and up to 40.6% of male cases when stratified by gender. Patients with culture negative at ≤2 months were younger than those in whom it had always been negative (median age of 33 vs 43 years old, respectively; $p < 0.0001$). When stratified by gender, this difference was only seen in males (median age: 37 vs 47 years old; $p = 0.022$); but the overall percentage of negative cultures in females was significantly lower. Statistically significant differences in terms of negativization of culture were encountered between DS-TB and MDR/XDR-TB, both in total ($p \leq 0.0001$) and when stratifying the results by age and gender (males ≤43, $p = 0.0009$; males >43, $p = 0.0007$; and females, $p = 0.0169$).

Nearly half of DS-TB cases negativized the culture at ≤2 M (47.4%), while in MDR/XDR-TB cases, the proportion of patients with negative results at >2 M (29.0%) were increased but due to a decrease of always negative results (a 44.8% in DS-TB vs a 12.7% in MDR/XDR-TB). Males and females were different, both in DS and MDR/XDR-TB cases, even if these differences were statistically significant only in DS-TB ($p \leq 0.0001$). Negative cultures were more frequent in MDR/XDR-TB cases, especially if women or males >43 years old.

3.3. Surgery

The main indication for surgery was the presence of lesions (cavities and tuberculomas or empyemas) in the chest X-ray assays (73.7%), both in DS (65.3%) and MDR/XDR-TB (85.4%), in spite of a good treatment adherence. In case of MDR/XDR TB, patients had had a sputum conversion but high risk of failure or relapse according to WHO's recommendations.[5] The other indications were those cases not microbiologically cured (2.9%) and a miscellania that we called the "others" group (23.3%) and which included severe complications of the TB. This group was significantly larger for males (31.2%) than for females (4.8%), something expected as men undergoing surgery wexre older and had comorbidities. Surgery for complications of TB was more frequent in DS-TB cases (32.0% vs a 12.7% in MDR/XDR-TB; ($p = 0.03$)).

Men underwent surgery earlier compared to women, according to days between diagnosis and surgery date (208.5 and 263 days, respectively; $p = 0.0037$). In DS-TB cases, there was a remarkable increase in days between diagnosis and surgery date in womens' cases vs mens' (225.5 vs 81.5; $p = 0.0002$). Statistically significant differences were found between DS-TB and MDR/XDR-TB, both in total and when stratifying by gender. Table 3 shows all these results.

No statistically significant differences were encountered between DS and MDR/XDR-TB according to age, neither in total nor stratified by gender; even if MDR/XDR-TB operated patients tended to be younger than DS-TB: 34 (28–48) vs 43 years old (26.75–50.25).

Differences between DS and MDR/XDR-TB were found in terms of history of previous treatment ($p = 0.0053$). While relapse patients were more frequent among DS-TB cases (26.47% vs 3.77% for MDR/XDR-TB), more operated MDR/XDR-TB cases were new (64.15% vs 55.88% for DS-TB), had a history of previous treatment (26.41% vs 16.18% for DS-TB), or were under treatment after lost follow-up (5.66% vs 1.47% for DS-TB).

Segmentectomy was the most frequent surgical procedure (56.9%), regardless of the gender of the patients, followed by lobectomy (30.%), pleural surgery (9.49%) and pulmonectomy (2.9%, which was performed in more MDR/XDR-patients than DS-TB: n = 3 vs n = 1).

In the majority of cases, only one lesion was removed (69.3%; vs n = 2 (17.5%), n = 3 (3.6%) and pleura (9.4%)). In the resected lung tissue, in addition to the cavity or tuberculoma, there could be conglomerates foci, a single foci, areas of fibrosis, bulls, or bronchiectasis. No statistically significant differences were encountered on number of operated lesions when stratifying the results by gender, age, or drug sensitivity.

Only 6 patients suffered post-surgery complications, 5 of them being males of a median age of 41 years old. Haemorragia was the most frequent complication (n = 3). Other complications were pneumonia plus acute respiratory failure (n = 1), bronchopleural fístula (n = 1) and delayed unfolding of the operated lung (n = 1). Half of these patients (n = 3) were new patients and half (n = 3) were relapsed patients, having undergone treatment after failure. Half of the cases were DS-TB, and the other half, MDR (n = 2) or XDR-TB (n = 1, the female case).

3.4. TB lesions

Median size for all lesions was 2.4 cm (25%–75%: 2–2.8). No statistically significant differences in terms of lesions' size were encountered, neither according to gender, patients' age, type of necrosis (fresh, dry, both) or drug-sensitivity.

Despite the fact that out of the 137 patients 132 (96.3%) were WHO cured patients, in 123 (93.1%) there was presence of necrosis in the lesion. Necrosis was macroscopically considered fresh in 71.5% of cases, dry in 6.5%, and both fresh and dry in 21.9%. Figure 2 shows these results according to gender and sensitivity to TB drugs. Results showed statistically significant differences due to drug sensitivity in all cases but men of ≤43 years old (total, $p = 0.0136$; >43 males, $p = 0.0418$); females, $p = 0.0412$). Men of ≤43 years had lesions with a higher percentage of fresh necrosis when compared to women in DS-TB cases (81.8% vs 58.3%, $p = 0.05$) and less in MDR/XDR-cases (65% vs 86.6%, $p = 0.023$). Men of ≤43 years old had a higher percentage of fresh necrosis in lesions when compared to those of >43 in DS-TB cases (81.8% vs 72.7%, $p = 0.014$); and slightly less in MDR/XDR-TB ($p = 0.0106$) Figure 3.

Patients being considered bacteriology non cured according to WHO, presented a higher percentage of fresh necrosis (60%), even if the n of this group (n = 5) was too small to extract conclusions.

Fibrosis/cirrhosis was found in the 89% of lesions, with a majority of cases being fibrotic (98.3%).

Table 4 reports the positive results obtained for AFB stain and culture on samples from surgical specimens, among those patients operated for presence of lesions in X-Ray, with cavities or tuberculomas, and considered bacteriologically cured according to WHO's definitions. In 19 patients the microbiological study of surgical samples could not be done, either because sampling is not done during surgery due to surgical procedures (10 patients

with empyema, 3 with spontaneous pneumothorax, 1 with thoracoplasty), or for technical reasons (n = 5). Even if any statistical analysis is difficult to be performed and interpreted because of the small numbers obtained, a tendency toward higher percentage of positive culture in fresh necrosis vs both fresh and dry necrosis and in those patients always having negative sputum cultures can be seen.

3.5. Outcomes

Statistically significant differences were encountered between outcomes of DS-TB when compared to those obtained for MDR/XDR-TB ($p < 0.0001$). While the percentage of cured patients was similar (30.8% for the DS-TB and 24.5% for MDR/XDR-TB) as well as those not evaluated (1.4% vs 1.8%); the categories lost to follow-up (7.3% vs 16.9%), treatment completed (47.0% vs 1.8%) and outcome still not known (8.8 vs 35.8) showed very different values. For the patients with outcome still not known, they are still on treatment. Moreover, 1.8% and 0% of failed treatment were recorded for MDR/XDR-TB and DS-TB, respectively. No statistically significant differences were encountered when stratifying the results by age or gender.

4. Discussion

Since the first recorded operation for TB, in 1726, therapeutical surgery was frequent and often essential for TB treatment, until the appearance of the chemotherapy in mid 20th century, and then was progressively abandoned. Nowadays, therapeutical surgery for TB is restricted to high TB burden countries, mostly to treat severe complications (as haemoptysis)[6] or sequelae (as important fibrosis),[7] especially if available chemotherapy options are limited (as in MDR/XDR cases),[2,5,8] and with a good overall cure rate.[2,9,10]

As in other published studies,[8,10–12] men was more frequent in our cohort. Men undergoing surgery were older than women, something understandable if we take into account that older men in our series had more comorbidities and toxic habits, more pleural involvement (secondary to the pulmonary disease), and more complications. The highest percentage of complications could also explain why men received surgery earlier compared to women (especially in the DS-TB cases), according to days between diagnosis and surgery date.

In our study, gender also seems to play a role in active TB and its course, as differences were still encountered when stratifying male cases by age and comparing female results with those for males under <43. Women underwent surgery at younger ages, and in MDR/XDR-TB cases, showed higher percentages of sputum conversion at >2 months and of fresh necrosis in the surgical specimens. This could mean that even if overall men suffer more TB, the TB course tends to be worse in women, especially if MDR/XDR. Previous literature has described higher rates of progression to disease for females during reproductive years.[13] Even if this were exclusively described for progression to disease and did not explore a worse evolution or progression within the disease state, we hypothesize that reproductive age might play a role, as women included in our study had a median age of 28 years old. The sex bias has been long debated in tuberculosis field, and even if sociocultural (access to healthcare) and behaviour (as smoking) factors have been demonstrated to have a role in it, there is increasing proof that biological factors (such as sex steroid hormones or variations at

the TLR8 gene) might also have an important influence.[14,15] Our results show no statistical cause-effect relationship between gender and all the other features we recorded, but as differences are still encountered, we do think this might be due to the n included in our cohort (n = 137) is considerably high, but still low to verify the causality between factors. As cohorts of surgically treated TB patients are relatively small, we would like to encourage other scientists to use the same categories we used here, in order to be able to reproduce and even sum up the results obtained.

Our results come to be added to those of previous studies showing the need of therapeutical surgery for MDR/XDR-TB cases, which in our cohort represented nearly half of the patients included.[5,7,8,16] As expected, these cases negativized the sputum culture later than 2 months, and these results were statistically significant when compared to DS-TB cases. Patients with MDR/XDR-TB usually have either thick-walled cavitary lesions or with a destroyed lobe or lung that contains a substantial amount of bacilli, making it difficult for penetration of antibiotics.[17,18] So, pulmonary cavities harbor millions of resistant organisms and the infection in these locations cannot be controlled by the host-specific immunity and, consequently, the surgical removal of these cavities may permit cure.[19] Our data supports what led to Kurbatova et al. to propose culture conversion status at 6 months as a better correlator of treatment success.[20] In 22.2% of these cases, surgical specimens were cultured and a positive result was obtained; a lower percentage than in a previous study conducted in the same center,[21] but still high (22.2%).

More than half of the operated cases were DS-TB cases, in spite of that therapeutical surgery has been lately considered or recommended only for MDR/XDR-TB[5]; the main indication for surgery (65.38%) being the persistence of lesions in X-ray in spite of good adherence to treatment. There are many reasons confirming the legitimacy of surgical treatment of patients with pulmonary DS-TB, including a high risk of relapse, the presence of a localized lesion, the absence of any radiological and/or bacteriological improvements during the initial three to four months of chemotherapy, the irreversible morphological changes of the lungs and other respiratory organs due to the development of the fibrotic tissues during the progress of TB over the long term, or tuberculoma’s size of more than three centimetres.[5] In countries of the former Soviet Union with a high prevalence of TB, there is a characteristically late referral of patients with tuberculosis (all forms) for medical attention. This results in a large number of patients with very advanced, extensive cavernous forms of a DS-TB, with strongly expressed irreversible morphological changes in the lungs, which poorly answer to medical anti-tuberculosis treatment, and therefore relatively more prone to surgical treatment than in the developed countries of Western Europe and America. Moreover, National TB guidelines of many countries of the former USSR include the persistence of cavitary lesions in X-Ray as one of the main indications for surgical treatment of DS-TB.[22,23] Our results on the presence of necrosis (87.1%) and microbiologically persistence of alive bacilli (14%) in surgical specimens of DS-TB, as well as the proportion of relapse patients (26.47% for DS-TB vs 3.77% for MDR-TB) point to the feasibility and need surgery for indicated cases among patients with DS-TB.

It is difficult to compare these results to other studies, as most literature refers only to therapeutical efficacy of surgery in MDR/XDR-TB cases, and published data on DS-TB are

scarce.[2,9,11] Our results could be partly explained by the high percentage of cases in which fresh necrosis was found in DS-TB, indicating a poor resolving evolution. To our knowledge, this is the first attempt to classify operated lesions during the last years. The classification between proliferative and exudative lesions (with dry and fresh necrosis, respectively), was done years ago describing the coexistence of several type of lesions in time, some tending to fibrosis and calcification (thus with more positive outcomes) and others with a higher exudative component, tending to liquefaction and usually related to a higher bacillary load.[24] In our study, we divided the removed lesions into the presence of dry (considered as positive) or fresh necrosis (considered as negative), or the presence of both (as an intermediate phase). Even if most operated lesions showed fresh necrosis and this made it difficult to establish any statistically significant analysis, results showed differences according to gender, with a remarkable high proportion of presence of fresh necrosis in MDR/XDR-TB female cases, supporting the idea that women's lesions might evolve worse under certain conditions. Despite the fact that almost all patients with MDR-TB and XDR-TB have been treated for a long time (≥1 year) with second-line antitubercular drugs, MDR/XDR patients still have cavities; and in the absolute majority of them (94.44%), necrosis was detected in operating specimens (most of them of the fresh type). AFB stain and culture were found positive (in a 65.96% and 23.4%, respectively) in surgical specimens of those MDR/XDR-TB patients considered microbiologically cured, had cavities or tuberculomas and still had lesions in their X-ray assays. These results are similar to those previously published in the literature,[8] but still frightening.

Presence of bacilli was found in surgical specimens in an important percentage of total cases, which was higher in MDR/XDR-TB cases, older patients and female patients, and in the presence of fresh necrosis. Moreover, from the 98% of DS-TB cases presenting cavities or tuberculomas and considered bacteriology cured according to WHO definitions, a non despricable 56% presented AFB positive at samples from the surgical specimens. Even if a positive AFB stain in a biological sample does not imply the presence of viable bacilli, up to 14% of those cases considered bacteriologically cured were culture positive, including 2 cases in which the AFB stain was negative. For us, this is the most important finding in our study, and poses doubts regarding the clearance effect of anti-TB drugs. During prolonged chemotherapy and decrease of bacterial load, a part of the microbial population remains in the host's organism in the state of persistence, and as proposed by some authors, transformated to L-forms or small-grained forms, characterized with low virulence but proven capacity for reversion and previous virulence.[25–27] The only validated biomarker now available to evaluate the curation of a patient, is to achieve a negative culture along a positive clinical evolution in a patient with a bacteriologically confirmed TB at the beginning of the treatment.[4] And yet, our results in DS-TB which followed treatment correctly, proved that no sterilization was achieved. In our opinion, our results support the idea that the correlators used are not reflecting what is happening in situ, and therefore new biomarkers are urgently needed. During the last years, different genetic profiles and other biomarkers of TB disease have been described in peripheral blood, suggesting that they could be used to establish the key of future therapeutic approaches.[28–32] As results might be different if measured in situ, surgical specimens might be a valuable tool to validate them.

In conclusion, we would like to encourage other scientists to use our categories in their studies conducted with therapeutical surgery, and to publish their results on DS-TB operated cases. Moreover, our results highlight that, in spite of achieving the microbiologically cured status, sterilization might not occur. This suggests that new studies to search biomarkers able to correlate with the in situ disease are urgently needed, and that evolution of radiological assays should be taken into account, as they are essential. Altogether, this information will help us better understand the reality of TB and will foster the development of new appropriate and tailored therapeutic options.

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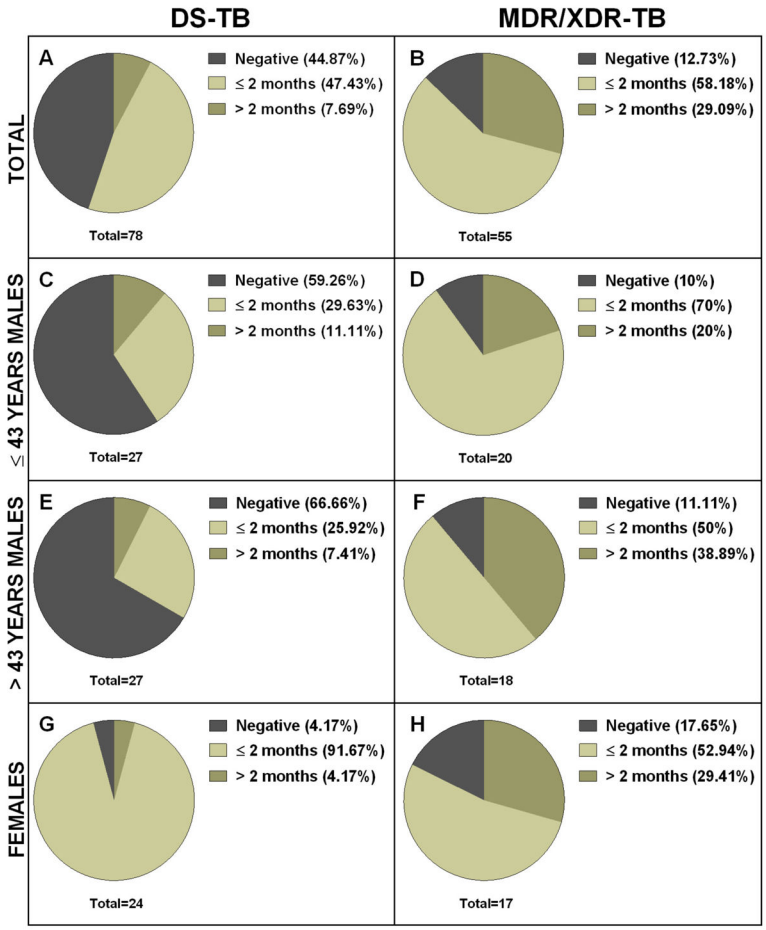

Figure 1.

Time in sputum culture conversion.

Time to sputum culture conversion (always negative, less than 2 months (≤2 months) and more than 2 months (>2 months)) is represented in percentages, for DS-TB and MDR/XDR-TB cases. Total values and results stratified by gender (males (of more or less than 43 years old) and females) are graphically represented.

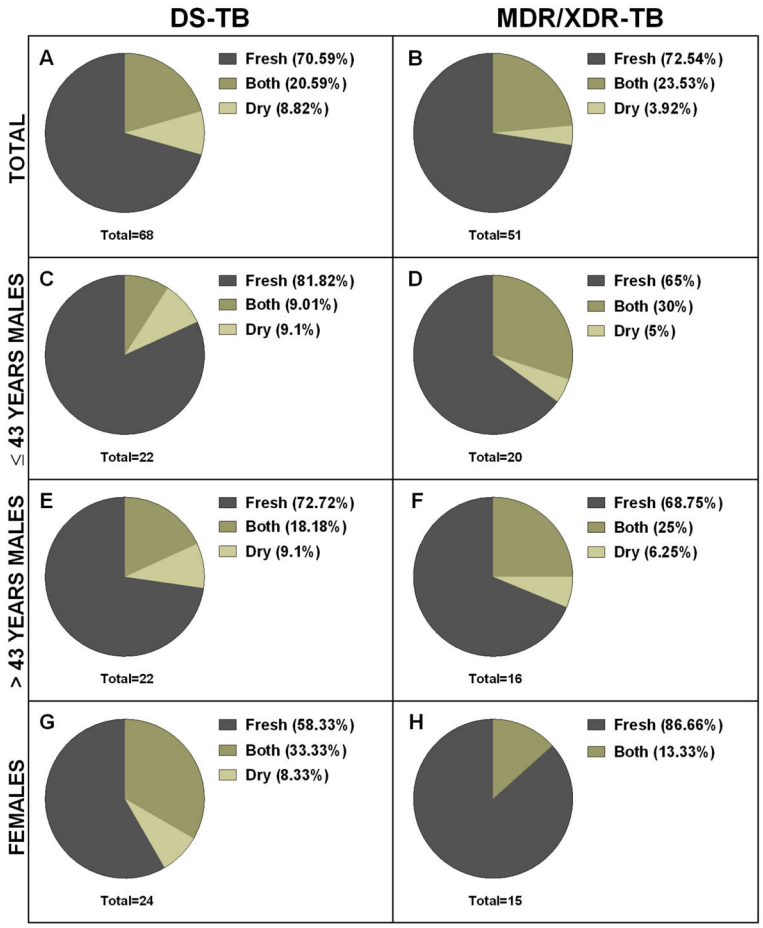

Figure 2.

Necrosis type found in lesions.

Percentages of presence of the different type of necrosis (fresh, dry and both) are represented for DS-TB and MDR/XDR-TB cases. Total values and results stratified by gender (males (of more or less than 43 years old) and females) are graphically represented.

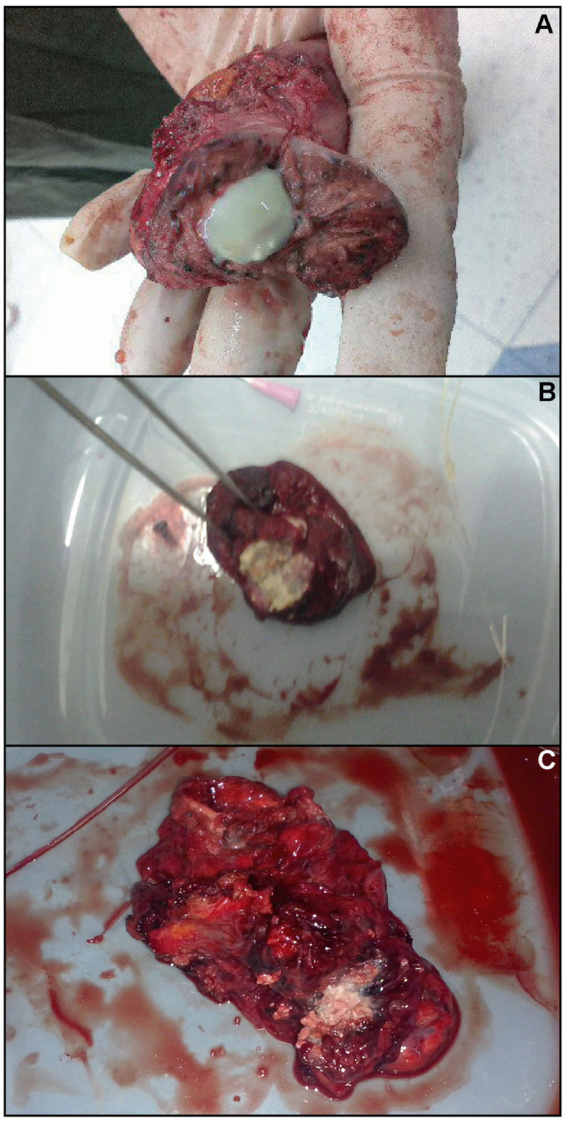

Figure 3.

Types of necrosis in surgical specimens.

Macroscopic photographs of removed surgical specimens showing fresh necrosis (A), both fresh and dry necrosis (B) and dry necrosis (C).

Table 1

Data recorded

Group	Category	Variables
Demographic and epidemiological data	Age (years old)	In years old
	Gender	Male/Female
	Smoking habit	on daily or almost daily basis, weekly, monthly, less than monthly, never
	Alcohol intake	on daily or almost daily basis, weekly, monthly, less than monthly, never
General clinical data	Presence of comorbidities	Diabetes mellitus, HIV infection, immunosupression other than HIV-infection, renal failure, chronic obstructive pulmonary disease (COPD) previous to TB, Hepatitis C Virus infection, hepatic cirrosis, others
Clinical data regarding the TB	history of previous treatment	new patient, relapse patient: treatment after failure, treatment after loss to follow-up patient, other previously treated patient, unknown previous TB treatment
	anatomical site of TB	Pulmonary, extrapulmonary
	drug-sensitivity	Drug Sensitive (DS-TB), Rifampicin Resistant only, Monoresistance to any other drug other than rifampicin, polydrug resistance, MultiDrug Resistant (MDR), extradrug resistance (XDR)
	date of diagnosis of the present TB episode	dd/mm/yy
	date of treatment initiation	dd/mm/yy
	number of lesions found in the chest X-ray assay	n
	bacteriology cured or not at the time of surgery according to WHO's guidelines	Yes/No
	time in negativization of culture	Recorded in months, and analyzed as always negative, negative at ≤2 months (M) or negative at >2 M
	time from TB diagnosis and surgery	In days
Data regarding the surgery performed	main indication for surgery	Still lesions in X-ray assays, Clinically not cured, Microbiologically not cured, Others (spontaneous pneumothorax, pulmonary haemorrhage, pleural empiema)
	number of operated lesions	n
	type of surgery performed	segmentectomy (for lesion resection or removing lung segment), lobectomy (for lung resection or removing lung lobe), Pulmonectomy (for removal of the whole lung)
	date of surgery	dd/mm/yy
	post-surgery complications	Open answer
Data on macroscopical characteristics of the TB lesions removed (surgical specimens)	lesion size	in cm, considering the maximum lenght
	type of lesion operated	tuberculoma, cavitation
	presence of necrosis	no necrosis, necrosis: moderate growth of connective tissue, alternating with unmodified lung tissue, cirrosis: complete substitution of lung tissue by the connective tissue with damage of vessels and bronchies
	type of necrosis	fresh: necrosis macroscopically looking like of a liquid consistency, dry: necrosis macroscopically looking like of a dry consistency, both: coexistence of fresh and dry necrosis
	Presence of Acid Fast Bacilli (AFB)	Yes/No

Group	Category	Variables
	Positivity of culture of samples in solid medium (Lowenstein-Jensen) for *M.tuberculosis*	Yes/No
Outcome	Official final outcome according to WHO definitions	Treatment completed, Treatment success, Cured, Lost of follow-up, Treatment failed, Still not known, Not evaluated, Death (if death, date of death in dd/mm/yy recorded)

Table 2

Distribution of tuberculosis patients by drug-resistance according to WHO classification.

Drug-Resistance (WHO)	TOTAL	Males		Females	
		N	%	N	%
DS-TB	78	54	69.23	24	30.76
monoR	2	2	100	0	0
Rifampicin only	2	2	100	0	0
MDR/XDR-TB	55	38	69.09	17	30.09
MDR-TB	42	33	78.57	9	21.42
XDR-TB	13	5	38.46	8	61.53

Abbreviations: WHO: World Health Organization; DS-TB: Drug-Sensitive Tuberculosis; monoR: mono Resistant; MDR/XDR-TB: Multi Drug-Resistant/Extensively Drug-Resistant Tuberculosis.

Table 3

Days between diagnosis and surgery date.

Drug-Resistance (WHO)	Median (25% – 75%)		
	TOTAL	Males	Females
All patients[a]	233 (100 – 252.5)	208.5 (50.5 – 344)[b]	263 (210 – 373.5)[b]
DS-TB	178.5 (38.25 – 258.75)[d]	81.5 (17.5 – 225.25)[c,e]	225.5 (192.5 – 275)[c,f]
MDR/XDR-TB	351 (233 – 455)[d]	308.5 (215.75 – 405.5)[e]	373 (266.5 – 654)[f]
MDR-TB	305.5 (232 – 399.75)	307 (225 – 400.5)	304 (237 – 511)
XDR-TB	532 (276 – 666)	454 (166 – 610)	533 (372.25 – 891.5)

Abbreviations: WHO: World Health Organization; DS-TB: Drug-Sensitive Tuberculosis; monoR: mono Resistant; MDR/XDR-TB: Multi Drug-Resistant/Extensively Drug-Resistant Tuberculosis.

[a] All patients include: mono resistant, rifampicin only resistant, DS-TB and MDR/XDR-TB patients.

[b] Statistically significant differences between males and females, p = 0.0037.

[c] Statistically significant differences between DS-TB Males and DS-TB females, p = 0.0002.

[d] Statistically significant differences between TOTAL DS-TB and TOTAL MDR/XDR-TB, p <0.0001.

[e] Statistically significant differences between DS-TB males and MDR/XDR-TB males, p <0.0001.

[f] Statistically significant differences between DS-TB females and MDR/XDR-TB females, p = 0.0005.

Table 4

Percentage of AFB and culture positive in samples from surgical specimens.

	TOTAL	Lesions in X-Ray	Cavities and tuberculomas	WHO Bacteriologically Cured	Samples from surgical specimens	
					AFB +	Culture +
Characteristics according to Drug-resistance						
DS-TB	78	51 (65.38%)	51 (100%)	50 (98.04%)	28 (56%)	7 (14%)
MDR/XDR-TB	55	47 (85.45%)	47 (100%)	47 (100%)	31 (65.96%)	11 (23.40%)
Characteristics according to gender						
Males >43 years old	48	29 (60.42%)	29 (100%)	28 (96.55%)	19 (67.86%)	3 (10.71%)
Males ≤43 years old	48	34 (70.83%)	34 (100%)	34 (100%)	19 (55.88%)	6 (17.65%)
Females	41	38 (92.68%)	38 (100%)	38 (100%)	23 (60.53%)	9 (23.68%)
Characteristics according to type of necrosis						
Fresh necrosis	88	70 (79.55%)	70 (100%)	70 (100%)	41 (58.57%)	15 (21.43%)
Dry necrosis	8	6 (75%)	6 (100%)	6 (100%)	5 (83.33%)	0
Both	27	23 (85.18%)	23 (100%)	22 (95.65%)	15 (68.18%)	3 (13.64%)
Characteristics according to negativization time						
Always negative	43	15 (34.88%)	15 (100%)	14 (93.33%)	9 (64.28%)	5 (35.71%)
≤2 months	71	68 (95.77%)	68 (100%)	68 (100%)	42 (61.76%)	9 (13.23%)
>2 months	23	18 (78.26%)	18 (100%)	18 (100%)	10 (55.55%)	4 (22.22%)

Abbreviations: WHO: World Health Organization; AFB: Acid Fast Bacilli; DS-TB: Drug-Sensitive Tuberculosis; MDR/XDR-TB: Multi Drug-Resistant/Extensively Drug-Resistant Tuberculosis.