0.4; 95% CI, 0.2–0.9), an effect that was heterogeneous across studies and may also be confounded by factors that predisposed to poor outcomes in these patients (271). Alternatively, patients who were healthy enough to withstand surgery may have intrinsically lower mortality, so it is difficult to predict the direction of potential bias.

Additional Considerations

In the MDR-TB treatment guidelines updated in 2016, WHO recommended elective partial surgery as an intervention complementary to chemotherapy in specifically selected individuals (23). The committee acknowledged there is significant uncertainty, with a paucity of publications and data regarding patient preferences, acceptability by surgical personnel, cost, and feasibility of performing elective surgery as an intervention for MDR-TB.

Conclusions

On the basis of the limited evidence that is available, there appears to be a net benefit from an elective partial lung resection (e.g., lobectomy or wedge resection) when offered together with a recommended MDR-TB regimen, compared with medical therapy alone. Committee members believed that this therapeutic option would probably be more beneficial when clinical judgement, supported by bacteriological and radiographic data, suggests a strong risk of relapse or treatment failure with medical regimen alone. We found no currently available evidence that pneumonectomy would be beneficial for patients with MDR TB receiving a background drug regimen.

Research Needs

Rigorously designed and conducted studies, ideally well-done randomized trials that measure and report benefits but also adverse effects and quality of life, are needed to clarify the role of surgery in the management of patients with MDR-TB. The following specific issues need to be addressed: the optimal timing for surgery, the optimal drug regimens and their duration before and after surgery, the role of surgery in special populations and patients with comorbid conditions (e.g., those living with HIV), the optimal surgical approaches, the optimal infection control measures to be implemented perioperatively, and the role of pulmonary rehabilitation (263, 267, 270, 273).

Treatment of Isoniazid-Resistant TB

Isoniazid is an important first-line agent for the treatment of TB, possessing potent early bactericidal activity against *M. tuberculosis*. However, monoresistance to isoniazid is frequent worldwide, with an estimated prevalence of 8% (range, 5–11%) of TB cases (12). A recent systematic review and meta-analysis compared the treatment outcomes of isoniazid-resistant TB to outcomes of drug-susceptible TB and found that treatment of isoniazid-resistant TB with first-line drugs resulted in suboptimal outcomes, with higher treatment failure (11% vs. 1%) and relapse (10% vs. 5%) (274). In addition, the study found that standardized empirical treatment of new isoniazid-resistant TB cases may be contributing to higher rates of acquired drug resistance (8% vs. 0.3%). Prior ATS, CDC, and IDSA guidelines recommended treatment with a standard four-drug regimen (isoniazid, rifampin, pyrazinamide, and ethambutol) for 6 months, with discontinuation of isoniazid after the results of DST are known and if isoniazid resistance was found (275).

Summary of the Evidence

Procedures and methodology to assemble and rank the certainty in the evidence are reported in Appendix A, with evidence profiles for PICO questions reported in Appendix B. An IPDMA of 33 datasets with 6,424 patients, of whom 3,923 patients in 23 studies received regimens related to isoniazid-resistant TB, was used as the evidence (276). Regimens of interest for our analyses (all with or without isoniazid) were *1*) rifampin, ethambutol, and pyrazinamide; and *2*) rifampin, ethambutol, and pyrazinamide, plus a fluoroquinolone. For these analyses, isoniazid-resistant TB was defined based on phenotypic resistance to isoniazid and susceptibility to rifampicin, with or without additional resistance to pyrazinamide, ethambutol, or streptomycin. Critical concentrations of 0.1 μg/ml or 0.2 μg/ml were used in 21 out of 23 centers for the definition of resistance to isoniazid (276). For PICO Question 20a, we found few studies that used regimens of 6 months of rifampin, ethambutol, and pyrazinamide, plus a fluoroquinolone, but several that used regimens of 8 to 9 months of this regimen; hence, we combined 6 with >6 months for this PICO. For the comparator of rifampin, ethambutol, pyrazinamide with or without isoniazid, we similarly combined regimens of 6 and >6 months' duration regimens, after comparison between these durations showed outcomes were not significantly different. For PICO Question 20b, few patients received regimens that had a fluoroquinolone, rifampin, ethambutol, and a shorter duration of pyrazinamide. A total of 118 patients received 1 to 3 months of pyrazinamide in conjunction with 6 and >6 months' durations of rifampin, ethambutol, and fluoroquinolone-containing regimen and were available for analyses.

Benefits

Compared with 6 months of daily rifampin, ethambutol, and pyrazinamide (with or without isoniazid), adding a fluoroquinolone to this regimen was associated with significantly greater treatment success (aOR, 2.8; 95% CI, 1.1–7.3) but with no significant effect on mortality (aOR, 0.7; 95% CI, 0.4–1.1) or acquired rifampicin resistance (aOR, 0.1; 95% CI, 0.0–1.2). When evaluating the impact of shortening the duration of pyrazinamide (ranging from 1–3 mo) in a regimen that contains a fluoroquinolone, the treatment success was very high, with 117 of 118 patients achieving treatment success. On the other hand, comparisons of shorter pyrazinamide regimens to regimens including both a fluoroquinolone and pyrazinamide for ⩾6 months did not show significantly different results (aOR, 5.2; 95% CI, 0.6–46.7). Similar results were obtained when the comparisons were restricted to patients receiving later-generation fluoroquinolones, namely moxifloxacin, levofloxacin, and gatifloxacin (data not shown).

Harms

The outcome of adverse events from TB drugs was intended to be assessed in the IPDMA but could not be analyzed because these outcomes were either not reported or reported with very different definitions. The adverse events associated with TB drugs, especially pyrazinamide, are well established (227, 277).

Additional Considerations

We note that the estimates of effect were imprecise from the IPDMA because of the small number of patients who received the