

Original Article

Predictors of post operative outcomes and time to full recovery among first time thoracotomy cases at Tikur Anbessa Specialized Hospital in Ethiopia.

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Abstract

Background: Thoracotomy is a major surgical procedure requiring a thorough understanding of cardiorespiratory mechanics. Postoperative care requires a high-dependency environment and trained and well-experienced staff. The aim of this study was to determine the post-op outcomes, estimate the time to full post-op recovery, and identify predictors associated with these outcomes among patients who underwent first time thoracotomy at Tikur Anbessa Specialized Hospital (TASH) from April 1, 2011 to March 31, 2012 in Ethiopia.

Methodology: A retrospective chart review was conducted among 148 patients. Descriptive analysis using frequencies with percentages and mean survival times were used to characterize the study population. To compare the mean time to post-thoracotomy recovery between groups, Kaplan-Meier survival plot together with Log-rank test was used. To identify significant predictors of post-thoracotomy outcomes and time to post-thoracotomy recovery, a robust Poisson regression model and Cox proportional hazard survival model were run at 5% level of statistical significance.

Results: From the 148 patients, 115 (77.7%, 95% CI=71.5%-85.6%) fully recovered, 27 (18.2%, 95% CI=12.0%-23.6%) have recovered with complications and 6 (4.1%, 95% CI=1.4%-6.9%) died. The overall mean time to post-thoracotomy recovery was 13.2 days (95% CI=10.1-16.4). Significant predictors of major complications and death were being male (ARR=1.99, 95% CI=1.02, 3.94, p=0.049), pre-op WHO Performance status score of 3 and 4 (ARR=2.56, 95% CI=1.19, 5.48, p=0.015), developing intraoperative complication (ARR=2.29, 95%CI=1.14, 4.59, p=0.020) and taking systemic analgesia (ARR=4.13, 95% CI=1.05, 16.23, p=0.042). Significant predictors of time to post-op recovery were being male (AHR=0.62, 95% CI=0.42,0.92, p=0.017) and developing intraoperative complication (AHR=0.38, 95% CI=0.18, 0.80, p=0.011).

Conclusion: The post-thoracotomy morbidity and mortality in the study population is similar to previous reports, and the mean recovery time is within the expected range for a good outcome. For further improvement in these outcomes, it is crucial to mitigate risks during the preoperative period and closely monitor and manage high-risk patients during the postoperative period.

Keywords: Post-thoracotomy outcomes, time to post-thoracotomy recovery, robust Poisson regression, Cox proportional Hazard survival model, Ethiopia

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Thoracotomy is a major surgical procedure that is used to diagnose and treat many benign and malignant lesions of the lungs, pleura, esophagus, and other mediastinal structures (1). It is one of the most difficult surgical incisions to deal with in the postoperative period. Postoperative complications result in significant morbidities and mortalities in patients subjected to thoracic surgeries (2). The procedure might cause reduction of lung capacity (forced vital capacity [FVC] and forced expiratory volume in one second [FEV1]). It might also impair gas exchange, cough and mucociliary clearance, eventually developing micro-atelectasis and postoperative hypoxemia (2, 3).

The overall incidence of complications following thoracotomy is variable and ranges between 15% to 37.5% and cardiopulmonary complications may occur in 30-60% of cases in the postoperative period (4-6). Different authors reported life threatening complications in as low as 2% to as high as 27% of their patients (7-9). This is primarily due to the differences in the type of pulmonary complications studied, the clinical criteria used in the definition of the complications and the type of surgery included (10). Various risk factors for complications following thoracic surgery have been identified. The most frequent risk factors include age of the patient, preoperative pulmonary function tests, presence of cardiovascular comorbidity, poor performance status (ASA III and IV) smoking status, and COPD (7,11-23). Furthermore, the incidence of perioperative mortality associated with thoracic surgery ranges from 1 to 12% (24,25). In the presence of these major complications, delayed recovery is expected to occur followed by all potential hospital acquired infections and complications (23,26).

Even though there are recent advances in anesthesia and perioperative care, complications such as myocardial ischemia, thromboembolism, infection, hemorrhage, and death still occur (27). Various authors analyzed outcomes in a specific group of patients with specific diagnoses like lung carcinoma, pulmonary hydatid cyst, pneumonectomy or lobectomy to determine possible risk factors for poor outcome (7-9,28-30). However, our study included all types of thoracic surgeries undertaken for variable diagnoses. Accordingly, the purpose of this study was to determine the post-op outcomes, estimate the time to full post-op recovery, and identify factors associated with these outcomes among patients who underwent first time thoracotomy at Tikur Anbessa Specialized Hospital (TASH) from April 1, 2011 to March 31, 2012 in Ethiopia.

Methods

Study Design and Population

A retrospective chart review study was conducted among patients aged 13 years and older and who had first time thoracotomy for various indications at

TASH, the largest referral hospital in Ethiopia, over a period of one year from April 1, 2011 to March 31, 2012. During the one-year observation period, a total of 167 thoracotomies were performed, out of which five were re-thoracotomies for postoperative complications and 14 cases did not have complete information on their chart. Finally, after excluding the 19 ineligible cases, 148 patients were included in the study.

Operational Definition

Full Post-thoracotomy Recovery: Is the absence of major non-fatal life-threatening events occurring in the first 30 postoperative days or the absence of death within the first 30 post-thoracotomy days.

Major complication: Non-fatal life-threatening events occurring in the first 30 postoperative days, if pharmacological or technical support was required, if permanent disability ensued or life expectancy was threatened and is classified as respiratory complications or non-respiratory complications.

Operative mortality: Death occurring within 30 days of operation in patients who remained hospitalized since the time of the operation and death occurring later during the same hospitalization.

Event: Full post-thoracotomy recovery

Censoring: Includes patients who were lost to follow-up, transferred out, died or completed the follow-up period before achieving full recovery.

Time to event or censoring: time between thoracotomy to recovery or censoring (in days).

Data Collection and Quality Assurance

A pre-tested data abstraction tool was used to extract data from the charts of the patients. Data on pre-operative, operative, and post-operative characteristics of the patients and their post-op outcomes and time to full post-op recovery were collected. To assure data quality, data was collected by two senior surgery residents. Double data entry and data cleaning through checking for inconsistencies, numerical errors, and missing parameters was also performed. After the data cleaning was complete, the data was exported to SPSS version 25.0 software for analysis.

Statistical analysis

To characterize the study population, descriptive statistics using frequencies with percentages and mean survival times were run. To compare the mean time to post-thoracotomy recovery between groups, Kaplan-Meier (KM) survival plot together with Log-rank test was used, where p-value ≤ 0.05 indicated a statistically significant difference.

To identify significant predictors of post-thoracotomy outcomes, a robust Poisson regression model was run. Univariate analysis was run at 25% level of significance to identify significant exposures that are going to be modeled into the final analysis. Then, a multivariable analysis was run at 5% level of significance where adjusted relative risk (ARR), P-value and 95% CI for ARR were used to test significance and interpretation of results. The final multivariable robust Poisson regression model was tested for model adequacy and it showed a good fit to the data based on Omnibus test result of p-value=0.009.

To identify predictors of time to post-thoracotomy recovery, Cox proportional hazard (PH) survival model was used. At 25% level of significance, a univariate analysis was run to screen out significant exposures to be included in the final model. Accordingly, the selected variables were included into the final multivariable Cox PH survival model at 5% level of significance where adjusted hazard ratio (AHR), 95% CI for AHR and p-value were used to interpret the results. The proportional hazards assumption, the basic assumption of the model, was tested using log minus log function and all plots

revealed parallel lines between groups showing that the model is a good fit for the data.

Results

Baseline (Pre-operative) characteristics

From the 148 first time post-thoracotomy patients, the majority of the study participants were younger than 40 years old (64.2%). The minimum and maximum ages were 13 and 80 years old, respectively. Seventy-nine patients (53.4%) were male and 15 (10.1%) patients were smokers. Over a quarter of them (27.7%) had one or more comorbid illness at the time of their presentation. Pulmonary tuberculosis and its chronic sequelae were seen in 17/41 patients followed by hypertension in 9/41 patients, bronchial asthma in 5/41 patients, diabetes mellitus in 4/41 patients and toxic goiter in 3/41, HIV in 2/41 and COPD in 1/41. From the 69 females, one was in her second trimester pregnancy. Seventy-two (48.6%) patients had a World Health Organization performance status (WHO-PS) score of 1 while 9 (6.1%) were asymptomatic with a score of 0 and only 2 (1.4%) patients were bed-bound with a score of 4. (**Table1**)

Table 1: Baseline characteristics of the participants who underwent first time thoracotomy (n=148)

Variables	Frequency (%)	Variables	Frequency (%)
Age		Comorbidities	
< 40	95 (64.2)	No	107 (72.3)
≥ 40	53 (35.8)	Yes	41 (27.7)
Sex		Pulmonary tuberculosis	7/41
Male	79 (53.4)	Hypertension	8/41
Female	69 (46.6)	Bronchial asthma	5/41
Smoking		Diabetes mellitus	4/41
No	15 (10.1)	Toxic goiter	3/41
Yes	133 (89.9)	HIV	2/41
WHO-PS		COPD	1/41
0 (Asymptomatic)	9 (6.1)	Others	10/41
1 (Symptomatic but ambulatory)	72 (48.6)		
2 (<50% in bed during the day)	42 (28.4)		
3 (>50% in bed during the day)	23 (15.5)		
4 (bed bound)	2 (1.4)		

Operative and Post-operative characteristics

The commonest indication for thoracotomy was empyema thoracis seen in 38 (25.7%) of the patients followed by esophageal cancer in 20 (13.5%) patients, hydatid cyst of the lung in 19 (12.8%), and mediastinal tumor in 13 (8.8%). The commonest surgical approach was posterolateral thoracotomy performed in 117 (79.1%) patients. Among the posterolateral thoracotomies and the axillary thoracotomies, 73 (49.3%) were performed in the right chest. Decortication was the commonest operative procedure performed on 35 (23.6%) patients followed by hydatid cystectomy in 19 (12.8%) patients. In 118 (79.7%) patients, the operation lasted less than 3 hours; it lasted less than 1 hour in 7, 1 to 2 hours in 66, and 2 to 3 hours in 45 patients. Intraoperative complications occurred in 15 (10.1%) patients. The commonest intraoperative complication was significant bleeding (>1500ml) which occurred in 9 (6.1%) patients. One hundred five (70.9%) patients were transferred to surgical Intensive care unit (ICU) immediately following surgery and 50 (33.8%) of them stayed for 24 hours or less, 34 (23%) of them stayed for 48 hours and 21 (14.2%) of them stayed for more than 48 hours. The most common type of analgesia utilized in the postoperative period was a combination of intravenous (IV) narcotics, parenteral non-steroidal anti-inflammatory drugs (NSAIDS) and Tramadol used in 95 (64.2%) patients.

Postoperative complications occurred in 31 (20.9%) patients. Respiratory complications occurred in 21/33 of them and non-respiratory complications in 6/33 patients. Both respiratory and non-respiratory complications occurred in 6/33 patients. The commonest respiratory complication was pneumonia which occurred in 12/21 patients followed by broncho pleural fistula which occurred in 6/21 patients. Anastomotic leak and anemia were the most common non-respiratory complications which occurred in 3/6 patients each. Reoperation was required in 5 (3.4%) patients. Post-op control Chest X-ray (CXR) revealed that 112 (75.7%) had a normal finding. (Table 2).

Post-thoracotomy outcome, Censoring status and mean recovery time

From the 148 patients, 115 (77.7%, 95% CI=71.5%-85.6%) fully recovered, and the remaining 33 (22.3%, 95% CI=14.7%-28.5%) were censored. Among the censored observations, 27 (18.2%, 95% CI=12.0%-23.6%) have recovered with complications and 6 (4.1%, 95% CI=1.4%-6.9%) died. The overall mean time to post-thoracotomy recovery was 13.2 days (95% CI=10.1-16.4). A comparison of the mean recovery time was made between groups. Accordingly, a significantly delayed post-op recovery was observed for patients who were 40 years and

older (10.1 Vs 18.1 days), male (10.8 Vs 14.9 days), WHO-PS score of 2 and above (10.1 Vs 14.4 Vs 13.2 days), developed intraoperative complication (11.5 Vs 18.6 days), and were on IV Narcotics, NSAIDS, and tramadol ± Epidural analgesia in the post-op period (7.2 Vs 14.9 days). (Table 3)

Table 2: Operative and post-operative characteristics of the participants who underwent first time thoracotomy (n=148)

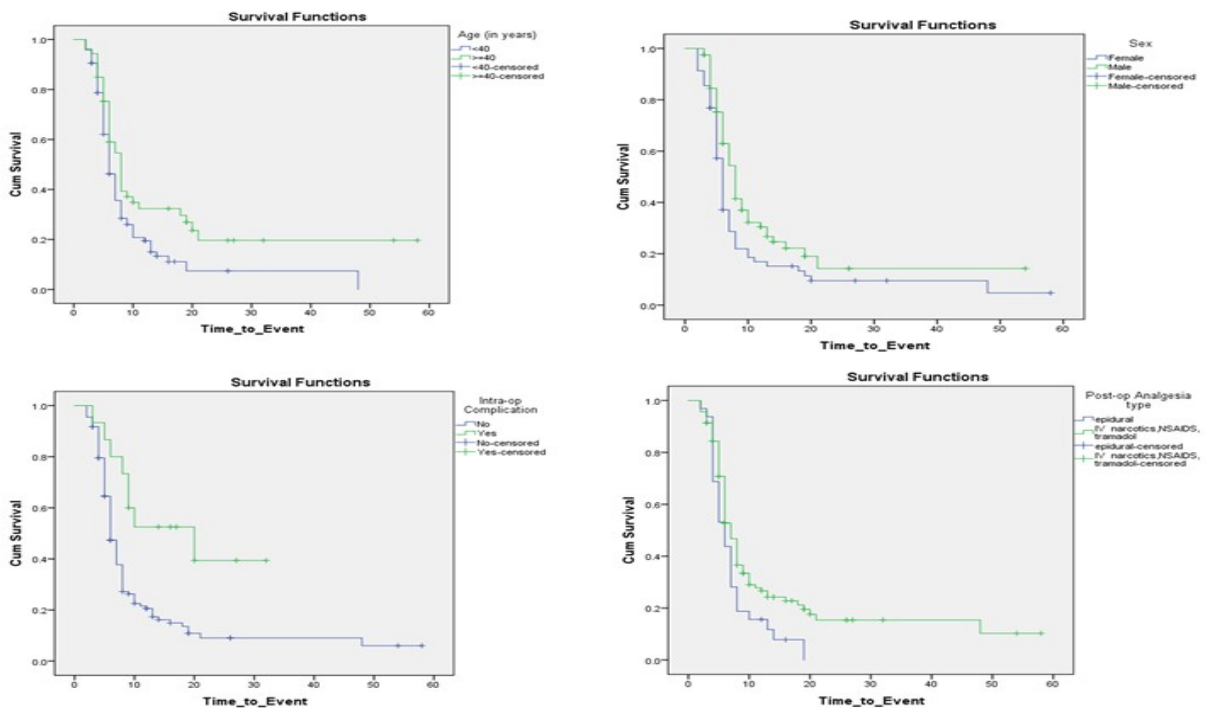
Variables	Frequency (%)	Variables	Frequency (%)
Indications		Intraoperative complication	
Empyema Thoracis	38 (25.7)	No	133 (89.9)
Esophageal Ca	20 (13.5)	Yes	15 (10.1)
Hydatid Cyst	19 (12.8)	Patient transferred to SICU post op	
Mediastinal Tumor	13 (8.8)	No	43 (29.1)
Constrictive Pericarditis	12 (8.1)	Yes	105 (70.9)
PDA	12 (8.1)	Post op analgesia used	
Lung Mass	9 (6.1)	Epidural	32 (21.6)
Giant Bullae with Pneumothorax	9 (6.1)	IV Narcotics, NSAIDS, and tramadol	95 (64.2)
Bronchiectasis	5 (3.4)	Epidural + IV medications	21 (14.2)
Aspergilloma	5 (3.4)	Post-op complications	
Others	6 (4.1)	No	115 (77.7)
Type of surgical approach		Yes	33 (22.3)
Posterolateral thoracotomy	117 (79.1)	Respiratory	21/33
Sternotomy	16 (10.8)	Non-respiratory	6/33
Axillary thoracotomy	14 (9.5)	Both	6/33
Hemi Clamshell	1 (0.7)	Re-operation required	
Operative procedure done		No	143 (96.6)
Decortication	35 (23.6)	Yes	5 (3.4)
Cystectomy	19 (12.8)	Finding on control CXR	
Trans Thoracic Esophageal resection	16 (10.8)	Normal	112 (75.7)
Pneumonectomy	14 (9.5)	Pleural fluid collection	12 (8.1)
Pericardiectomy	12 (8.1)	Fluid + Air with air fluid level	9 (6.1)
PDA Ligation	12 (8.1)	Consolidation	6 (4.1)
Mediastinal Tumor Excision	11 (7.4)	Collapse	3 (2.0)
Bullectomy	7 (4.7)	Atelectasis	2 (1.4)
Explorative Thoracotomy	5 (3.4)	pneumothorax	2 (1.4)
Others	4 (2.7)	subcutaneous air	2 (1.4)
Total time of surgery			
< 3 hours	118 (79.7)		
≥ 3 hours	30 (20.3)		

Table 3: Censoring status, and comparison of mean time to recovery between groups among patients who underwent first time thoracotomy (n=148)

Variables	Time to recovery		Mean time to recovery (in days)	p-value
	Event	Censored		
Age				
< 40	78	17	10.1	0.013*
≥ 40	37	16	18.1	
Sex				
Female	59	10	10.8	0.011*
Male	56	23	14.9	
Smoking				
No	107	26	12.3	0.056
Yes	8	7	12.6	
Comorbidity				
No	88	19	12.1	0.117
Yes	27	14	11.6	
WHO-PS				
0 and 1	69	12	10.1	0.007*
2	32	10	14.4	
3 and 4	14	11	13.2	
Intraoperative complication				
No	107	26	11.5	0.003*
Yes	8	7	18.6	
Post-op analgesia type				
Epidural	30	2	7.2	0.019*
IV Narcotics, NSAIDS, and tramadol ± Epidural	85	31	14.9	

*Statistically significant

This difference is also demonstrated on the KM survival plot of these groups where a shorter recovery time for the above groups is observed. (**Figure 1**)

**Fig 1:** Kaplan-Meier survival graph of time to post-thoracotomy recovery stratified by age, sex, intraoperative complication, and post-op analgesic type.

Predictors of Post-thoracotomy Outcome

To identify the predictors of post-thoracotomy outcomes, a multivariable robust Poisson regression model was run after adjusting for age, sex, smoking, comorbidity, WHO-PS, intraoperative complications, and post-op analgesia type which were found to be significantly associated on the univariate analysis. From these, sex, WHO-PS, intraoperative complications, and post-op analgesia types were found to be significantly associated with the outcome.

Accordingly, after adjusting for other variables, the risk of developing major complications and/or death among males was almost twice that of females (**ARR=1.99, 95% CI=1.02, 3.94, p=0.049**). Patients with pre-op

WHO-PS score of 3 and 4 were found to have a 2.56 times increased risk of developing major complication and/or death as compared with those with a score of 0 or 1 (**ARR=2.56, 95% CI=1.19, 5.48, p=0.015**). Furthermore, developing intraoperative complication and taking systemic analgesia during the post-op period were associated with an increased risk of developing major complication and/or death by 2.29 times (**ARR=2.29, 95%CI=1.14, 4.59, p=0.020**) and 4.13 times (**ARR=4.13, 95% CI=1.05, 16.23, p=0.042**) as compared with those with no complication and were taking epidural analgesic, respectively. (**Table 4**)

Table 4: Predictors of post-thoracotomy outcomes among patients who underwent first time thoracotomy (n=148)

Variables	Post-thoracotomy outcome		CRR (95% CI)	ARR (95% CI)	p-value
	Full recovery	Complication/death			
Age					
< 40	78	17	1	1	
> = 40	37	16	1.69 (0.93, 3.06)	1.27 (0.64, 2.51)	0.497
Sex					
Female	59	10	1	1	
Male	56	23	2.01 (1.03, 3.92)	1.99 (1.02, 3.94)	0.049*
Smoking					
No	107	26	1	1	
Yes	8	7	2.39 (1.26, 4.53)	0.85 (0.35, 2.08)	0.725
Comorbidity					
No	88	19	1	1	
Yes	27	14	1.92 (1.07, 3.47)	1.57 (0.82, 2.99)	0.171
WHO PS					
0 and 1	69	12	1	1	
2	32	10	1.61 (0.76, 3.41)	1.28 (0.64, 2.55)	0.487
3 and 4	14	11	2.97 (1.49, 5.89)	2.56 (1.19, 5.48)	0.015*
intraoperative complication					
No	107	26	1	1	
Yes	8	7	2.39 (1.26 (4.53)	2.29 (1.14, 4.59)	0.020*
Post-op analgesia type					
Epidural	30	2	1	1	
IV Narcotics, NSAIDS, and tramadol ± Epidural	85	31	4.23 (1.08, 16.92)	4.13 (1.05, 16.23)	0.042*

CRR, Crude relative risk; AHR, Adjusted relative risk; CI, Confidence interval; *Statistically significant

Predictors of Time to Post-thoracotomy Recovery

To identify predictors of time to full post-thoracotomy recovery, Cox proportional hazard (PH) survival model was run. From univariate analysis, age, sex, smoking, comorbidity, WHO-PS, intraoperative complications, and post-op analgesia type were found to be significant and were fed into the final multivariable regression model.

In the final model, at a 5% level of significance, sex and intraoperative complication were found to be significantly associated with time to post-thoracotomy recovery.

Accordingly, after adjusting for other covariates, the rate of achieving full post-thoracotomy recovery among males was 38.0% lower than females (AHR=0.62, 95% CI=0.42,0.92, p=0.017). In addition, intraoperative complication was associated

with a 62.0% lower rate of achieving full post-thoracotomy recovery as compared to those with no complication (AHR=0.38, 95% CI=0.18, 0.80, p=0.011). (Table 5)

Table 5: Predictors of time to full post-thoracotomy recovery among patients who underwent first time thoracotomy (n=148)

Variables	CHR (95% CI)	AHR (95% CI)	p-value
Age			
< 40	1	1	
> = 40	0.63 (0.42, 0.94)	0.73 (0.48, 1.13)	0.156
Sex			
Female	1	1	
Male	0.65 (0.45, 0.93)	0.62 (0.42, 0.92)	0.017*
Smoking			
No	1	1	
Yes	0.53 (0.26, 1.09)	1.05 (0.44, 2.46)	0.920
Comorbidity			
No	1	1	
Yes	0.73 (0.47, 1.12)	0.86 (0.52, 1.41)	0.544
WHO PS			
0 and 1	1	1	0.129
2	0.65 (0.42, 0.99)	0.77 (0.49, 1.20)	0.253
3 and 4	0.49 (0.27, 0.87)	0.56 (0.31, 1.01)	0.055
intraoperative complication			
No	1	1	
Yes	0.38 (0.18, 0.78)	0.38 (0.18, 0.80)	0.011*
Post-op analgesia type			
Epidural	1	1	
IV Narcotics, NSAIDS, and tramadol ± Epidural	0.63 (0.42, 0.96)	0.78 (0.50, 1.21)	0.266

CRR, Crude relative risk; AHR, Adjusted relative risk; CI, Confidence interval; *Statistically significant

Discussion

In this study, we assessed the potential post-thoracotomy outcomes, estimated the mean time to full post-op recovery, and identified predictors associated with these outcomes among 148 eligible patients who underwent first-time thoracotomy at Tikur Anbessa Specialized Hospital in Ethiopia from April 1, 2011 to March 31, 2012. Of the 148 patients, 115 (77.7%) fully recovered, 27 (18.2%) recovered with complications, and 6 (4.1%) died. The rate of major complications was in the lower range of expected rates, based on reports from other studies. Life-threatening complication rates of up to 27%-60% have been reported in many studies, while rates as low as 2-10% have been reported in a few studies (4,7-9). Similarly, the perioperative mortality rate was also in the lower range of reported rates from other studies (24,25).

The overall mean time to post-thoracotomy recovery was 13.2 days. The average mean time to post-thoracotomy recovery is 7-10 days, but this can vary depending on the type of surgery, the patient's overall health, and other factors (32-34). In this study, the mean time to recovery was a bit longer than the average, but this is likely due to the fact that a considerable proportion of the participants had high-risk factors, such as old age, smoking, and comorbidity. Considering these factors, 13.2 days is a reasonable duration of stay.

The study showed that the risk of major complications and death after thoracotomy was significantly higher in men, in those with a preoperative WHO-PS score of 3 or 4, in those who developed intraoperative complications, and amongst those who received systemic analgesia. In addition, a significantly delayed post-thoracotomy recovery was observed amongst males and those with intraoperative complications. The increased risk with male sex could be because men are more likely to have chronic health conditions that increase the risk of intraoperative complications and poor postoperative outcomes. In addition, in this study, a large proportion of men were smokers and had other comorbidities, which are known to be associated with poor outcomes. Male sex has also been reported as a risk factor for adverse outcomes after surgery in another study (8). Poor preoperative WHO-PS measures a patient's overall health and ability to function. Patients with poor PS are more likely to have chronic health conditions, be older, have a lower BMI, be malnourished, and have other risks. These factors can increase the risk of complications during and after surgery. Other studies have also shown this increased risk (7,21-23, 26).

In addition, intraoperative complications can lead to several negative consequences, including increased length of stay in the hospital and increased risk of

infection, leading to further complications and death. Such increased risk is also demonstrated in other studies (21-23, 26). Furthermore, systemic analgesics are commonly used to manage pain after surgery. However, they can also increase the risk of complications, such as respiratory depression, nausea, and vomiting. These complications can lead to a more extended hospital stay and even death, especially among those with additional underlying medical conditions. Regional analgesics, on the other hand, are less likely to cause these complications. Studies have shown that patients who receive epidural analgesia have a lower risk of death, complications, and a shorter hospital stay (35,36).

The retrospective nature of the study made it impossible to collect data on some important variables, such as preoperative pulmonary function tests, information on the status of diagnosis of COPD, whether chest physiotherapy has been performed, and details of smoking status. These limitations should be considered when interpreting the results of the study.

Conclusions

The post-thoracotomy morbidity and mortality in the study population are similar to previous reports, and the mean recovery time is within the expected range for a good outcome. Male sex and intraoperative complications were significant predictors of increased risk of major postoperative complications, death, and delayed recovery. Preoperative WHO-PS score of 3 or 4 and systemic analgesia were significant predictors of increased risk of major postoperative complications and death. Therefore, mitigating risks during the preoperative period and closely monitoring and managing high-risk patients during the postoperative period is essential. We recommend conducting a prospective cohort study to investigate additional risk factors in a larger patient population.

Declaration

Ethical Considerations

The study was conducted after obtaining ethical clearance from the Department of Surgery Research Committee. The patients' privacy was protected by only using their medical record numbers to identify them, and their identifiers were not used in the research report. Only the research team could access the collected information, and confidentiality was maintained throughout the project.

Availability of data and materials: All relevant data are available upon reasonable request.

Competing interests: The authors declare that they have no known competing interests

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Author's Contribution: FSH conceived and designed the study, performed the statistical analysis and drafted the initial manuscript. AA, DG, SK, and AB contributed to the conception of the study and reviewed the manuscript. TK, SH, and TWL contributed to the conception and design of the study, statistical analysis, and manuscript drafting. All authors revised the manuscript and approved the final version.

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