Chapter 16
Intensive Care Treatment of Critical Tuberculosis

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16.1 Introduction

Despite recent advancements in tuberculosis (TB) treatment, 1–3 % of patients progress to critical TB, which has a high rate of mortality (Agarwal et al. 1977; Frame et al. 1987; Levy et al. 1987). In critical TB, the biological functions of heart, lungs, brain, liver, kidneys, gastrointestinal tract, and other major organs are damaged and cannot maintain proper electrolyte balance. Because critical TB patients are usually highly infectious, the intensive care and support they need must be provided in isolation, away from the general hospital population and from the other critically ill patients. Therefore, specialized TB intensive care units (TBICUs) should be set up in high incidence areas. Sufficient medical personnel and equipment should be provided to ensure treatment.

16.2 Candidates for TB Intensive Care Unit Treatment

Critical TB includes severe pulmonary TB, tuberculous meningitis, severe abdominal TB, tuberculous pericarditis, and severe osteoarthrosis TB. Severe pulmonary TB is defined as more than three lung lesions, the formation of cavities and/or regular emission of tubercle bacillus, as well as serious constitutional symptoms (loss of

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appetite, weight loss, fever, night sweats, and fatigue) with complications such as severe pneumonia and respiratory failure (Zhang 2004). Severe tuberculous meningitis patients have more than two of the following characteristics: disturbance of consciousness (drowsiness, lethargy, and/or coma); serious systemic TB symptoms and/or a temperature above 39 °C for 3 days; protein content progressively increases in the cerebrospinal fluid or is greater than 2100 mg/L; imaging indicates hydrocephalus; presence of cranial nerve palsy, paralysis, or other complications (Wang et al. 2006). Abdominal TB could cause intestinal obstruction, intestinal perforation, and tuberculous pericarditis with pericardial tamponade symptoms. Spinal TB with paraplegia indicates severe osteoarthrosis TB.

16.2.1 TBICU Admission Criteria

As a general rule, the decision to treat TB patients in TBICU should be based on the following criteria: failure of one or more organs; hemodynamic instability; and requirement of endotracheal intubation, mechanical ventilation, or other invasive medical procedures for monitoring (Nava et al. 1998; Task Force of the American College of Critical Care Medicine Society of Critical Care Medicine 1999; Webb 1999; Cai 2006).

Common serious complications in critical TB patients requiring care in the TBICU are as following:

- Acute respiratory failure (requiring mechanical ventilation)
- Possible suffocation in patients with active massive hemoptysis
- Refractory or life-threatening tension pneumothorax
- Severe lung infection
- Multiple organ dysfunction syndrome (MODS)
- Shock due to various causes
- Right-sided heart dysfunction caused by acute pulmonary vascular disease
- Heart, lung, brain, and kidney function need to be closely monitored after surgery
- Severe water, electrolyte, or acid–base imbalance; malnutrition
- Intracranial hypertension and hernia caused by severe tuberculous meningitis

Patients in a terminal state of illness or having irreversible disease are generally not treated in the TBICU.

16.2.2 Critical TB Patients in the TBICU

Respiratory failure is a serious complication which first appeared in critical TB-associated multiple organ dysfunction syndrome (MODS). It is also the main reason to be treated in ICU (Erbes et al. 2006; Silva et al. 2010). Secondary pulmonary infection is the primary cause of increased respiratory failure in cases of

critical TB, followed by hemoptysis and pneumothorax (Rao et al. 1998; Zahar et al. 2001; Lee et al. 2003; Ryu et al. 2007). Respiratory failure can occur for many reasons, including impaired lung function due to lung lesions as well as respiratory muscle fatigue caused by long-term malnutrition and protein degradation, which leads to decreased reactivity to anoxia, carbon dioxide retention, and pump failure (Shneerson 2004; Zhang 2004). The inhospital mortality of respiratory failure caused by pulmonary TB is as high as 69 % (Agarwal et al. 1977; Frame et al. 1987) and is twice that of respiratory failure caused by pneumonia (Levy et al. 1987; Confalonieri et al. 1999; Jolliet et al. 2001).

From a clinical viewpoint, TB is a chronic wasting disease. More than 90 % of critical TB patients suffer anemia, in which more than half have hemoglobin levels <9 g/dL. About 67.2 % of severe TB patients also suffer hypoproteinemia (Erbes et al. 2006). At the same time, an impaired immune system leaves patients vulnerable to secondary pulmonary infection or sepsis. In response to sepsis, the effector cells release inflammatory mediators uncontrollably, which leads to MODS. Multiple studies have shown that 30–90 % of TB patients in the intensive care units suffer sepsis, while the incidence of MODS ranges from 19 % to as high as 80 % (Zahar et al. 2001; Lee et al. 2003; Erbes et al. 2006; Ryu et al. 2007; Chen and Zhu 2010; Silva et al. 2010). Domestic and international research has shown that sepsis and MODS are independent factors which affect the mortality of hospitalized critical TB patients (Lee et al. 2003; Erbes et al. 2006; Ryu et al. 2007; Chen and Zhu 2010).

16.2.3 APACHE II Scoring System for TB Patients with Respiratory Failure

The Acute Physiology and Chronic Health Evaluation II (APACHE II) is the most widely used scoring systems in intensive care units in China and abroad. The APACHE II score is closely associated with disease severity and can predict mortality in patients. A number of studies have shown that the scores in patients with respiratory failure due to pulmonary TB are between 16.8 and 22.8 and this APACHE II score indicates a mortality rate of 20–50 % (Knaus et al. 1985). But the actual mortality was 59–69 %, which indicates the APACHE II scoring system may not be so accurate for patients with pulmonary TB and a prognosis for respiratory failure (Zahar et al. 2001; Silva et al. 2010; Lee et al. 2003; Erbes et al. 2006; Ryu et al. 2007).

16.3 TBICU Requirements

The settings of TBICUs vary among geographic regions and hospital sizes. The following basics are required: a dedicated, separate space with a reasonable layout; sufficiently experienced and specially trained healthcare workers; a comprehensive monitoring technology support system; and air purification devices (Cai 2006).

Most patients in the TBICU have respiratory failure as result of pulmonary TB. TBICUs should pay particular attention to the air handling systems. Negative pressure laminar flow systems should be established in ICUs in first-class hospitals (WHO 1999). The double door entrance to the TBICU should include an airlock and should be designed to restrict access to authorized personnel only. The inner doors of the air-lock chamber should remain locked until the outer doors of the chamber are closed. Air filtration or disinfection equipment is required in the air-lock chamber. The directional flow of air in the TBICU should be controlled by positive pressure and the incoming air should pass through a laminar flow device. The air handling system should be able to maintain the air at appropriate temperature and humidity, with a reasonable distribution of pressure and airflow throughout the interior (WHO 1999). In order to ensure a low level of pathogenic microorganisms within the unit, the total air volume should be replaced 10–15 times per hour, dust particles should be kept below 100,000 parts/m^3, the temperature should be between 22 and 24 °C, and the relative humidity should be maintained between 55 and 75 %. The unit should be disinfected by ozone or UV (>10 uW/m^3, 1–2 h) every 24 h. There should be at least 15–20 m^2 of floor space for every sick bed and there should be at least 1.5–3 m between beds to decrease the chance of cross-infection (Cai 2006). An intensive care unit setup for a single individual would require approximately 20–30 m^2 (Cai 2006), and can be used for isolating and treating drug-resistant TB patients. The exhale end of the respirator requires filtration. Closed suction tubes and a closed suction system should be used. Patient mouth, nose, and respiratory tract secretions must be strictly controlled and sterilized before disposal to prevent releasing TB into the environment. All materials contaminated by respiratory tract secretions must be sterilized.

TBICU staff, including doctors, nurses, care workers, and cleaners, must be trained in TB infection control measures. The changing of clothes and shoes and the wearing of N95 masks and hats before entering the TBICU must be strictly enforced. A hand washing system which requires hand washing before and after checking each patient, before technical procedures, after handling waste, and when entering or leaving the intensive care unit must be instituted.

16.4 Monitoring of Critical TB

16.4.1 Routine Clinical Monitoring

16.4.1.1 Symptoms

Coughing and Expectoration

The character of coughing and expectoration should be observed, including the time occurred, tone, intensity of coughing, expectoration volume, and expectoration character. An increase of expectoration volume indicates severe infection. A sudden decrease in amount of expectoration may be related to inadequate airway

humidification. Yellow purulent expectoration is suggestive of bacterial infection. Foul-smelling expectoration indicates anaerobic infections. Pink foamy expectoration may be pulmonary edema (Cai 2006). The amount and color and impurities of hemoptysis should also be observed.

Dyspnea

The respiratory rate should be observed, including breath depth and rhythm and whether there is orthopnea or use of accessory muscles of inspiration.

Chest Pain

The location and character of chest pain should be observed. Pneumothorax, acute pleurisy, and pulmonary embolism often result in severe pain in the affected side. The pain of angina and myocardial infarction or esophagus, mediastinal disorders always located in the precordium or breastbone.

16.4.1.2 Physical Signs

In order to adjust treatment as needed, the physical signs of critical TB patients should be monitored in TBICU, including continuous monitoring of vital signs and transcutaneous pulse oxygen saturation. Timely physical examinations of organ systems should also be performed.

Body temperature should be closely monitored. Choose the temperature measuring method/device according to the patient's disease condition: underarm thermometer, oral or rectal thermometer, nasopharyngeal temperature probe, continuous measurement of skin temperature, etc. A rise in body temperature will increase oxygen consumption and carbon dioxide production and can damage the central nervous system to delirium and coma. A drop in temperature can result in circulatory disturbance, hypoxia, or even ventricular fibrillation.

Breath should be monitored for the depth of breathing exercise, respiratory rate, rhythm, symmetry, and whether spontaneous breathing and mechanical ventilation are coordinated.

Pulse rate should be monitored along with pulse rhythm, tension, strength/weakness, and whether waveforms are symmetric.

Blood pressure can be monitored by noninvasive or invasive means (see Sect. 16.4.6). Arterial blood pressure and cardiac output have a direct relationship with total peripheral resistance. These factors reflect the heart afterload, myocardial oxygen consumption, and perfusion pressure. They are useful indicators to determine the circulation, but not the only indicators.

Transcutaneous pulse oxygen saturation (SpO_2) is monitored with a percutaneous pulse oximeter placed at the end of the finger, earlobe, etc. Infrared light sensors measure oxygenation levels of hemoglobin, which continuously and instantaneously

monitor blood oxygen saturation (SpO_2) which has a high correlation (normal greater than 95 %) with the patient's actual arterial oxygen saturation (SaO_2). The main factors affecting the percutaneous SpO_2 measurement are peripheral perfusion status and the color and/or thickness of keratinized layer of skin where the pulse oximeter is placed (Cai 2006).

Skin and mucous membranes should be observed for temperature, elasticity, and presence of any edema or hemorrhage. Note skin color with or without jaundice.

Observe patient's head and neck; pay attention to the eyes and note whether there is jaundiced sclera or edema of the conjunctiva. Observe jugular vein filling, tracheal position, neck lymph nodes, and thyroid.

Heart rate and rhythm should be noted along with whether heart sounds are strong or weak, whether there is heart murmur or other abnormal heart sounds, and the size of any cardiac dullness.

Lungs: note thorax morphology, respiratory rate, rhythm, and breathing movement symmetry. On percussion, note areas of drumlike sound or dullness or percussion drum so. On auscultation, note the nature, location, and phase of rales or pleural friction rub.

Abdomen: watch for abdominal distention, mass, ascites, tenderness, and/or rebound tenderness, and change in bowel sounds. Note liver and spleen size.

16.4.1.3 Fluid Intake and Output

Urine is an important indicator of heart and kidney function. Record daily intake and output fluid volume to monitor fluid balance. Decreased urine output (positive balance) should be considered a sign of inadequate intake, shock, renal insufficiency, or urinary retention (Cai 2006). Electrolyte balance should be maintained if urine output increases.

16.4.2 Nutritional Status Monitoring

In patients with critical TB, correct evaluation of nutritional status and the implementation of sound nutritional support is an important prerequisite. Methods include patient inquiry (perform a detailed investigation of the patient's daily diet, lifestyle, and economic conditions), observation (note the presence or absence of weight loss, muscle weakness, reduced body fat, dehydration or edema, and whether hair is sparse and/or lacks luster), and physiological measurements. There are many physiological indicators of nutritional status. Each has its limitations; combine a number of indicators to better evaluate the nutritional status of the patient.

Body mass index (BMI) is calculated by dividing the patient weight (kg) by height squared (m^2). A normal male BMI is 20–25, and less than 20 may be underweight. A normal female BMI is 19–24 and less than 19 may be underweight (Zhang and Gao 2006; Jiang 2008).

Triceps skinfold thickness (TSF) reflects the storage of body fat. To measure, keep patient's left upper arm down and relaxed. Find the midpoint of the triceps between the top of the shoulder (acromion) and the elbow (olecranon). Pinch the skin with the left thumb and index finger to make a vertical skinfold 1 cm from the measurement point and measure with calipers. Normal adult measurements are 12.5 mm for males and 16.5 mm for females. Measured values of 80–90 % of normal indicates mild malnutrition; 60–80 % indicates moderate malnutrition; below 60 % indicates severe malnutrition (Zhang and Gao 2006; Jiang 2008).

Mid Upper Arm Circumference (MUAC) includes upper arm muscles and any subcutaneous fat, and reflects nutritional status. Keep left upper arm hanging down and relaxed. At the midpoint between the acromion and the olecranon, measure the girth of the arm with a soft tape (Zhang and Gao 2006; Jiang 2008).

Arm muscle circumference (AMC) reflects the somatic protein status. AMC is calculated from the MUAC and TSF measurements above (in centimeters) as follows:

$$\mathrm{AMC} = \mathrm{MUAC} - \left(3.14 * \mathrm{TSF}\right)$$

Normal AMC is 25.3 cm for males and 23.2 cm for females. A measurement equivalent to 80–90 % of normal indicates mild malnutrition, 60–80 % indicates moderate malnutrition, and less than 60 % indicates severe malnutrition. AMC closely relates to serum albumin levels. If the patient's serum protein is less than 28 g/L, AMC is also decreased in about 87 % of patients (Zhang and Gao 2006; Jiang 2008).

Serum protein, transferrin, prealbumin, and other indicators may be useful as part of a comprehensive evaluation, but care should be taken in interpretation, as these are variable indicators of stress, infection, and hypoxia effects.

Creatinine Height Index (CHI) is calculated by dividing the 24-h urine creatinine excretion (mg) by patient height (cm). In the case of constant protein intake, a result of less than 6.0 indicates that there is a protein deficiency (Zhang and Gao 2006; Jiang 2008).

The Absolute Lymphocyte Count normal value is 1.5×10^9 cells/L. A count of less than 1.2×10^9 cells/L may indicate malnutrition or immune dysfunction (Zhang and Gao 2006; Jiang 2008).

16.4.3 Brain Function Monitoring

General brain function monitoring includes checking consciousness, language ability and mental status, pupil size and light reflex, and limb activity and muscle tone. Use the Glasgow Coma Score (GCS) for assessment in adult patients. A GCS of less than or equal to 8 is indicative of severely damaged brain function (see Table 16.1).

Intracranial pressure (ICP) is the pressure of the cranial cavity and thus cerebrospinal fluid and brain tissue. Normal (lateral position) ICP is 5–15 mmHg in adults, 3.5–7.5 mmHg in children. Increased ICP (more than 15 mmHg) is common in severe tuberculous meningitis. Currently, ICP is measured invasively. A hole is

Table 16.1 Glasgow coma score (GCS) (Teasdale and Jennett 1974)

Points	Motor response	Language response	Eye response
6	Moves as requested		
5	Purposeful movements toward pain	Oriented	
4	Withdrawal from pain	Confused	Active eyes
3	Flexion in response to pain	Random or inappropriate words	Eyes open in response to speech
2	Hyperextension in response to pain	Incomprehensible sounds	Eyes open in response to pain
1	No motor response	No verbal response	Cannot open eyes

Interpretation of GCS total to evaluate brain injury: minor at 13 or more, moderate at 9–12, severe if less than 9

drilled into the skull and a catheter with a pressure sensor is placed in the ventricle or in the subdural, epidural, or subarachnoid space. ICP measured by intraventricular catheter is currently considered the most accurate and reliable and allows direct discharge of cerebrospinal fluid to reduce ICP. ICP monitoring may leave the patient vulnerable to intracranial infections. Great care should be taken during prep and catheter insertion to minimize infection, and catheter time should generally be limited to less than 72 h (Liu and Yan 2009).

Electroencephalography (EEG) uses scalp electrodes to monitor brain activity. Though not required, EEG can be used to monitor critical TB symptoms of the central nervous system, including coma. Increased intracranial pressure shows mainly on the EEG as abnormalities of diffuse slow activity in the context of simultaneous attacks on both sides with high volatility of θ or δ rhythm. EEG manifestations of pulmonary encephalopathy are characterized by diffuse abnormalities, mainly α irregular, slow, diffuse δ or θ wave to the forehead. A resting EEG with no electrical activity is one of the diagnostic criteria of brain death (Liu and Yan 2009).

16.4.4 Monitoring of Respiratory Function

Basic monitoring of respiratory function includes checking vital signs, respiratory rate, respiratory motion, breath sounds, and peripheral circulation and other limbs.

16.4.4.1 Lung Capacity Monitoring

Static lung capacity and tidal volume should be monitored to detect changes. Common indicators include inspiratory reserve volume (IRV), expiratory reserve volume (ERV), functional residual capacity (FRC), vital capacity (VC), total lung capacity (TLC), and the residual volume/total lung capacity ratio (Cai 2006).

16.4.4.2 Lung Function Monitoring

The determination of pulmonary ventilation can be more meaningful than lung volume measurements because it can reflect dynamic changes in pulmonary ventilation. Common monitoring indicators include minute ventilation (V_E), maximal voluntary ventilation (MVV), forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), etc.

The dead space volume/tidal volume ratio (V_D/V_T) reflects alveolar ventilation. Normal values range from 20 to 40 %. The ratio can be calculated using the Bohr equation

$$\frac{V_D}{V_T} = \frac{\left(PaCO_2 - P_ECO_2\right)}{PaCO_2}$$

where P_ECO_2 is the partial pressure of expired CO_2 (Zhang and Gao 2006).

16.4.4.3 Pulmonary Ventilation Function Monitoring

Measures of pulmonary ventilation include the ventilation/perfusion (V/Q) ratio, alveolar-arterial oxygen gradient ($A\text{-}aO_2$) which may show hypoxia, Oxygen delivery (DO_2) which shows oxygen delivered over time, and the oxygenation index. The ratio PaO_2/FiO_2 is one of the main monitoring indicators of pulmonary ventilation; the calculation is simple, and the normal range 430–560 mmHg. Combined with medical history and other indicators, $PaO_2/FiO_2 < 300$ mmHg suggests acute lung injury (ALI) and $PaO_2/FiO_2 < 200$ mmHg is a sign of acute respiratory distress syndrome (ARDS) (Cai 2006; Zhang and Gao 2006; Yu 2008).

16.4.4.4 Respiratory Muscle Function Test

Maximum inspiratory pressure (MIP) reflects the overall strength of inspiratory muscles. Maximum expiratory pressure (MEP) reflects the expiratory muscle strength and overall ability to cough and expectorate. Maximum transdiaphragmatic pressure (Pdimax) evaluates diaphragm function (Zhang and Gao 2006; Yu 2008).

16.4.4.5 Blood Gas Monitoring

Noninvasive monitoring of pulse oxygen saturation (SPO_2) is important. Normal SPO_2 is 95–100 % while breathing normal air, and has good correlation with SaO_2 ($\gamma = 0.9$). Simple, noninvasive, continuous display of arterial oxygen saturation and pulse waveform monitoring is extremely important in critically ill patients (Cai 2006).

End-tidal carbon dioxide partial pressure (PetCO2) has a good correlation with $PaCO_2$ and can be measured by an artificial airway gas sampling device which continuously monitors exhaled CO_2. Normal $PetCO_2$ is 35–40 mmHg. This data can be affected by the CO_2 volume produced by the tissue, pulmonary blood flow (cardiac output), alveolar ventilation, and other factors. It may indirectly reflect changes in these indicators (Cai 2006).

16.4.5 Ventilator Monitoring

Respiratory failure is a serious complication of TB. Ventilator technology and mechanical lung ventilation has become an important therapeutic treatment for respiratory failure. Ventilator monitoring is very complex and important; any changes of parameter could not only infect the pulmonary ventilation function, but also influence hemodynamics and organ function.

16.4.5.1 Artificial Airway Monitoring

Endotracheal intubation should be checked for proper depth and stability, and balloon pressure should be monitored. Maximum balloon pressure is maintained at 20–25 mmHg. Too high a pressure can lead to tracheal mucosal ischemia or necrosis; too low a pressure can lead to leakage and aspiration of oropharyngeal secretions (Yu 2008).

16.4.5.2 Ventilation Monitoring

Include tidal volume and minute ventilation. Tidal volume is usually set to 5–12 mL/kg; adult minute ventilation can be set to 6–10 L/min. The ventilator, which has the function of monitoring exhaled carbon dioxide, can monitor the amount of dead space/tidal ratio (V_D/V_T) as discussed in Sect. 16.4.4.2.

16.4.5.3 Monitoring of Respiratory Mechanics

Peak inspiratory pressure (PIP) is the maximum pressure in the respiratory cycle of mechanical ventilation. Mechanical ventilation with a high PIP is related to barotrauma; PIP should generally be limited to below 40 cmH_2O (Zhang and Gao 2006; Yu 2008).

Plateau pressure (Pplateau), also called end-inspiratory pressure, depends on the factors of tidal volume and respiratory system compliance. If tidal volume is stable, the worse the respiratory system compliance, the higher the plateau pressure. Set some pause time on the ventilator to display the end-inspiratory plateau pressure, to reflect the respiratory system compliance indicators.

End-expiratory pressure (EEP) is the sum of setting positive end-expiratory pressure (PEEP) and endogenous PEEP ($PEEP_i$). If the patient's end-expiratory airway pressure cannot return to zero or the setting PEEP level, the excess pressure from the lungs' failure to empty is called the endogenous PEEP value. $PEEP_i$ is caused by increased airway resistance due to trapped gasses or too short an expiratory time which is then inadequate to complete breath-related activity and is not conducive to patient ventilation.

Airway resistance pressure (Praw) is the resistance to airflow in the patient's respiratory tract that must be overcome by mechanical positive pressure ventilation. P_{raw} and plateau pressure combined constitute peak inspiratory pressure. Increased P_{raw} may be a sign of retention of airway secretions.

Airway resistance (Raw) equals P_{raw} divided by the flow rate. Normal airway resistance is in the range of 0.6–2.4 $cmH_2O/(L\ S)$. The airway resistance of an endotracheal intubation patient is up to 6 $cmH_2O/(L\ S)$; the airway resistance of a bronchial asthma patient is up to 3–18 $cmH_2O/(L\ S)$ (Zhang and Gao 2006; Yu 2008).

Compliance refers to the changes in capacity produced by pressure changes and reflects the elasticity of the lungs. Compliance can be static or dynamic according to different methods of detection.

Static compliance (C_{st}) or respiratory system compliance (C_{rs}), including lung and thoracic compliance, is measured when there is no airflow (during inspiratory pause).

$$C_{st} = \frac{V_T}{\left(P_{plateau} - \text{PEEP}\right)}$$

Dynamic compliance (C_{dyn}) is measured when there is airflow and includes lung compliance and airway resistance factors.

$$C_{dyn} = \frac{V_T}{\left(\text{PIP} - \text{PEEP}\right)}$$

16.4.5.4 Mechanical Ventilation Waveform Monitoring

Waveform displays allow real-time observation of respiratory mechanics. This gives the medical staff a better understanding of patient pathophysiology characteristics. Ventilation settings can be reasonably adjusted in order to achieve better therapeutic effect. Mechanical ventilation waveform displays include the pressure–time curve, volume–time curve, flow rate–time curve, the pressure–volume loop, and flow rate–volume loop.

The pressure–time curve reflects airway pressure changes over time period in real time. This curve reflects PIP, $P_{plateau}$, P_{raw}, and PEEP changes (Yu 2008; see Fig. 16.1).

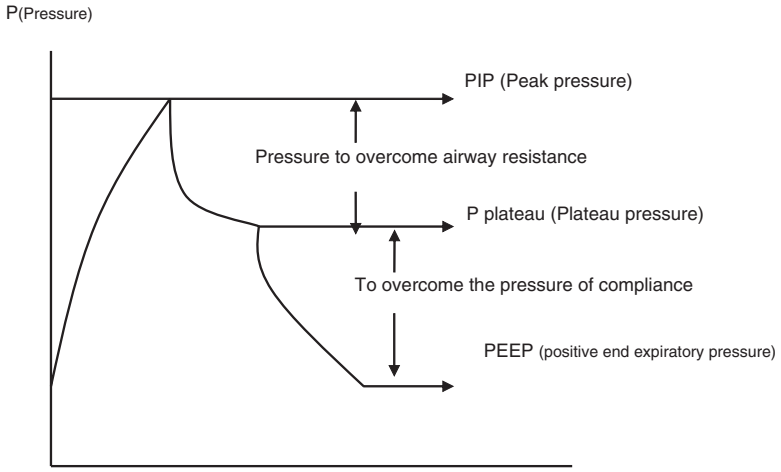

Fig. 16.1 Relationship of pressure–time curves and airway resistance and compliance

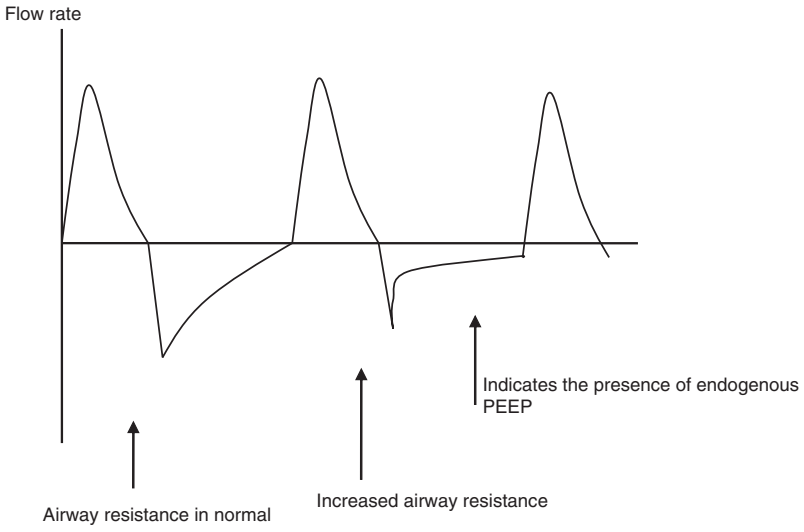

Fig. 16.2 Airway resistance effects on the flow rate–time curve

The volume–time curve reflects the tidal volume changes in the ventilation cycle.

The flow rate–time curve reflects the flow rate of the inspiratory phase and expiratory phase in the ventilation cycle. When patients present with obstructive ventilatory dysfunction, peak expiratory flow rate decreases and the flow rate quickly slows down. The curve shows a shaped bend and extension of the expiration time. The end-expiratory flow rate cannot be reduced to 0, and the tips at the end of exhalation indicate the presence of $PEEP_i$ (Yu 2008). See Fig. 16.2.

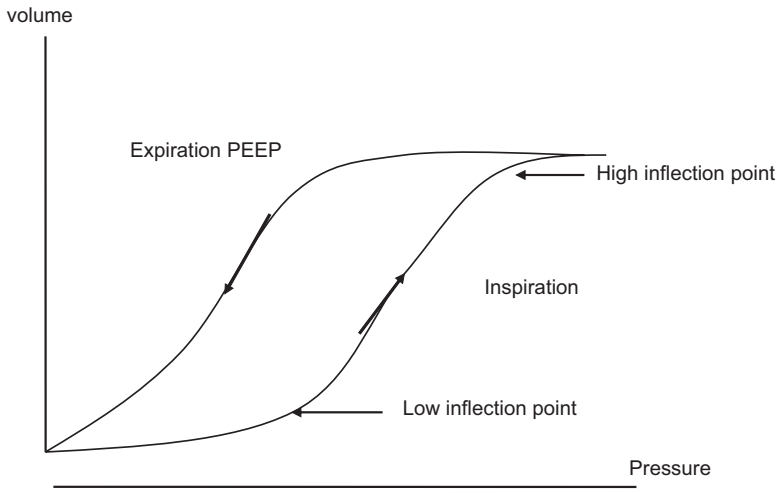

Fig. 16.3 Pressure–volume loop of ARDS patients, low and high inflection point

The pressure–volume loop is formed by the changes of inspiratory phase and expiratory phase in the breathing cycle. Real-time monitoring of the volume related to the mechanical ventilation pressure changes reflects lung compliance. The low inflection point indicates when opening pressure is reached and the alveoli begin to expand. This inflection point is used to select the best PEEP, which is generally more than 2 cmH_2O. The high inflection point reflects the degree of chest flexibility at maximum expansion. High pressure of mechanical ventilation should be lower than the high pressure inflection point in order to avoid barotrauma and circulatory function suppression (Yu 2008; see Fig. 16.3).

The flow rate–volume loop tracks airflow rate and volume changes in a respiratory cycle. This loop reflects the set flow rate type (constant, decreasing type, etc.) in inspiratory phase, and can indicate a probable increased airway resistance in the expiratory phase, gas trapping, or pipeline leak. See Fig. 16.4 (Yu 2008).

16.4.6 Hemodynamic Monitoring

16.4.6.1 Arterial Blood Pressure (ABP) Monitoring

In cases of severe hypotension, invasive blood pressure monitoring is more accurate than noninvasive blood pressure monitoring. It is usually performed via arterial puncture of the radial artery or the dorsal artery in the foot. Some of the indications are severe shock, hypotension, individuals taking vasoactive drugs, and individuals needing frequent arterial blood gas examination. Some common complications of invasive blood pressure monitoring are infection, embolisms, hemorrhaging, and aneurysms.

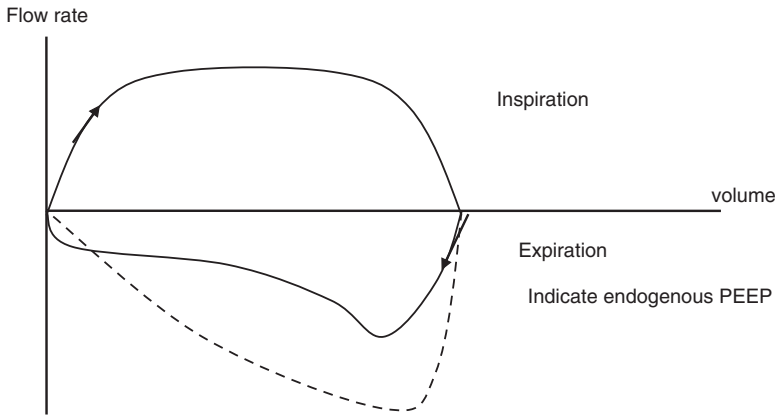

Fig. 16.4 Flow rate–volume loop of increased airway resistance. *Dotted line* is the normal expiratory tracing

16.4.6.2 Central Venous Pressure Monitoring

Central venous pressure (CVP) is the pressure in the chest section when the blood flows through the right atrium and the inferior vena cava. This measurement mainly reflects the right ventricular preload. Normal CVP is 4–12 mmHg. CVP is a function of blood volume, level of cardiac function, venous tone, intrathoracic pressure, venous return flow, and pulmonary vascular resistance, among other factors. Causes and treatment of abnormal central venous pressure are shown in Table 16.2. CVP is an indirect indicator of cardiac function. Therefore, continuous observation of dynamic changes is more meaningful than a single absolute value.

16.4.6.3 Pulmonary Artery Pressure and Pulmonary Capillary Wedge Pressure Monitoring

Insert a floating catheter (Swan-Ganz catheter) through the superior vena cava or inferior vena cava, then through the right atrium and right ventricle and into the pulmonary arteries. This allows measurement of the right atrial pressure (RAP), right ventricular pressure (RVP), pulmonary artery systolic pressure (RADP), mean pulmonary artery pressure (PAP), and pulmonary capillary wedge pressure (PCWP). When the left ventricle and mitral valve function is normal, pulmonary capillary wedge pressure is only 1–2 mmHg higher than left atrial pressure, so pulmonary capillary wedge pressure can be used to estimate the state of pulmonary circulation and left ventricular function. It is also a useful and reliable indicator of left ventricular preload. In pulmonary arteries the normal systolic pressure is 15–30 mmHg, the diastolic pressure is 6–12 mmHg, the mean pressure is 9–17 mmHg, and the PCWP is 6–12 mmHg. A PCWP < 6 mmHg can indicate a serious shortage of vessel capacity; a PCWP of 12–15 mmHg indicates a normal vessel capacity or an insufficient

Table 16.2 Causes and treatment of central venous pressure changes (Liu and Yan 2009)

CVP	Arterial pressure	Cause	Treatment
Low	Low	Hypovolemia	Add blood volume
Low	Normal	Good heart function, low blood volume	Appropriate to add blood volume
High	Low	Poor cardiac function, reduced cardiac output	Administer cardiac stimulant, oxygen, diuretics, and/or vasodilator. Correct acidosis. Carefully control fluid intake
High	Normal	Excessive contraction of vascular capacity, pulmonary vascular resistance increased	Control fluid intake, increase vascular and pulmonary capacity with a vasodilator
Normal	Low	Reduced cardiac ejection function, excessive contraction of capacity vessels	Perform cardiac infusion test. In cases of hypovolemia, infuse fluid

vessel capacity with left ventricular dysfunction; a PCWP > 15 mmHg indicates too much vessel capacity or left ventricular dysfunction with an associated risk of pulmonary edema (Yu 2008; Liu and Yan 2009).

16.4.6.4 Cardiac Output (CO) Monitoring

Cardiac output is defined as the total volume of blood pumped by one ventricle per minute (normal left and right ventricular output is basically the same). CO is an important indicator of cardiac function. A Swan-Ganz catheter can be used with the thermal dilution method to measure cardiac output. This is done by injecting cold saline solution into the right atrium and measuring the blood temperature change as it passes the catheter tip in the pulmonary artery. One can then calculate the right ventricular output. There are four factors that affect cardiac output: myocardial contractility, cardiac preload, cardiac after load, and heart rate. Normal CO is 4–8 L/min and is expressed as

$$CO = SV * HR$$

where SV is ventricular stroke volume and HR is heart rate. Other hemodynamic parameters can be derived from CO.

Cardiac index (CI) more accurately reflects heart function by factoring in the effect of body size (represented by body surface area, BSA) when estimating cardiac output.

$$CI = \frac{CO}{BSA}$$

The reference value for CI in a healthy population is 2.5–4 L/(min m^2). A cardiac index of <2.5 L/(min m^2) indicates heart failure, and if the CI falls below 1.8 L/(min m^2) the patient may be in cardiogenic shock.

Stroke volume (SV) and stroke index (SI) reference values in a healthy population are 60–130 mL and 35–55 mL/m^2, respectively.

Pulmonary vascular resistance (PVR) must be overcome for blood to flow through the circulatory system. A normal PVR is 10~25 (kPa s)/L. Elevated PVR is associated with pulmonary vascular disease, lung disease with pulmonary hypertension and hypoxemia. Dynamic monitoring of PVR is beneficial to understanding disease progression. *Pulmonary vascular resistance index (PVRI)* is indexed to body mass. A normal PVRI is 22.5–31.4 (kPa S)/(L m^2) (Liu and Yan 2009).

Systemic vascular resistance (SVR) is used in the diagnosis of vascular disease. The reference value for SVR is 90–150 (kPa s)/L. The reference value for *systemic vascular resistance index (SVRI)*, which is the SVR over body surface area, is 195–240 (kPa S)/(L m^2) (Liu and Yan 2009).

16.4.6.5 Pulse Indicator Continuous Cardiac Output (PiCCO) Monitoring

PiCCO is a simple technology that uses hyperactivity dilution and pulse wave contour analysis to continuously and accurately monitor cardiac output (see a list of parameters in Table 16.3). This technology, which was developed more than 10 years ago, is widely used in critically ill patients requiring hemodynamic monitoring. Because PiCCO does not require the use of a pulmonary artery catheter, the cost and risk to patients are reduced. Instead, PiCCO uses a central venous catheter and a femoral artery catheter to monitor cardiac output in both adults and children. PiCCO can be used in patients requiring cardiovascular and circulatory volume status monitoring such as after transplant surgery and in cases of shock, cardiac dysfunction, sepsis, and/or acute respiratory distress syndrome (ARDS). Single measurement methods for estimating cardiac output have given way to stroke-based continuous cardiac output monitoring methods such as PiCCO (Fig. 16.5). For normal ranges for main PiCCO parameters, see Table 16.4.

PiCCO is contraindicated in patients with complications such as hemorrhagic disease, aortic aneurysm, arteritis, arterial stenosis, limb embolism, lung resection, pulmonary embolism, cardiopulmonary bypass, unstable body temperature or blood pressure, severe arrhythmia, severe pneumothorax, heart and lung compression disorders, heart cavity cancer and/or a heart shunt.

Due to PiCCO's quick response time and convenience, it is possible to make timely comparisons and judgments from multiple hemodynamic data. Intrathoracic blood volume (ITBV) gives a better estimate of heart preload than the right ventricular end-diastolic pressure (RVEDP) and CVP and shows better accuracy. If catecholamines, mechanical ventilation, or other parameters are changed, the intrathoracic blood volume index (ITBVI) can reflect changes in preload. Extravascular lung water (EVLW) is a measure of pulmonary interstitial fluid volume, and is a more accurate indicator in the diagnosis and treatment of pulmonary edema than PCWP.

Table 16.3 Main parameters of PiCCO (Yu 2008; Liu and Yan 2009)

Thermodilution parameters (single measurement)	Parameters of pulse contour (continuous measurements)
Cardiac output (CO)	Pulse continuous cardiac output (PCCO)
Global end-diastolic volume (GEDV)	Stroke volume (SV)
Intrathoracic blood volume (ITBV)	Heart rate (HR)
Extravascular lung water (EVLW)	Stroke volume variation (SVV)
Pulmonary vascular permeability index (PVPI)	Arterial pressure (AP)
Cardiac index (CFI)	Systemic vascular resistance (SVR)
Global ejection fraction (GEF)	Maximum slope of arterial pressure (dPmx)

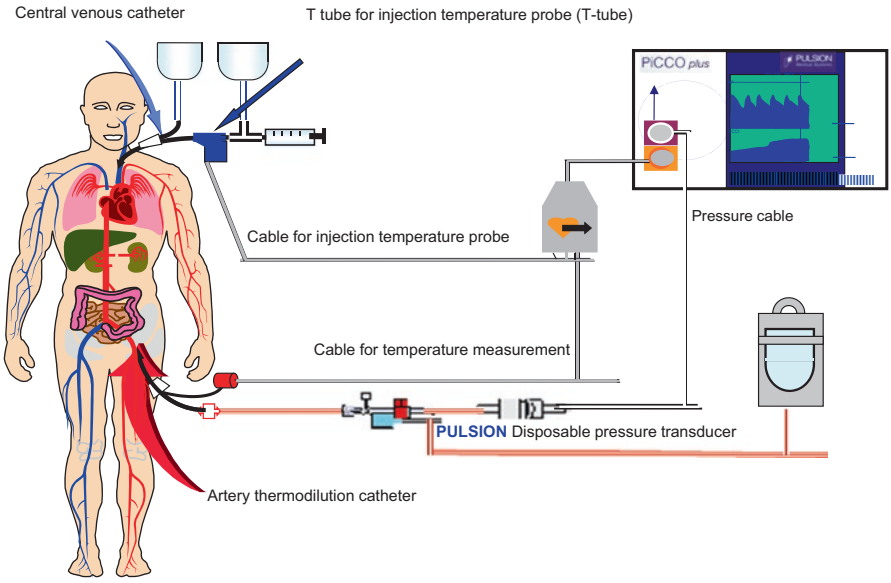

Fig. 16.5 PiCCO tubing connection diagram (Yu 2008)

Table 16.4 Normal values of PiCCO parameters (Yu 2008; Liu and Yan 2009)

Parameters	Normal range	Unit
Cardiac index (CI)	3.0–5.0	L/min/m^2
Stroke volume index (SVI)	40–60	mL/m^2
Global end-diastolic volume index (GEDI)	680–800	mL/m^2 mL/m^2
Thoracic blood volume index (ITBI)	850–1000	mL/kg
Extravascular lung water index (ELWI)	3.0–7.0	mL/kg
Pulmonary permeability index (PVPI)	1.0–3.0	
Stroke volume variation (SVV)	≤10	%
Global ejection fraction (GEF)	25–35	%
Cardiac function index (CFI)	4.5–6.5	1 min^{-1}
Mean arterial pressure (MAP)	70–90	mmHg
Systemic vascular resistance index (SVRI)	1700–2400	(kPa S)/(L m^2)

16.4.7 Gastrointestinal Mucosal pH (pHi) Monitoring

Given the importance of the gastrointestinal mucosal barrier and its vulnerability due to the effects of ischemia and hypoxia, steps should be taken to protect the gastrointestinal mucosa of critical TB patients. Because ischemia and hypoxia can lead to local tissue lactic acid accumulation and acidosis, the measurement of acidity in the gastrointestinal mucosa may be an alternative indicator of tissue perfusion and oxygen metabolism. The pHi is assessed by gastric tonometry, which measures the gastric partial pressure of carbon dioxide in the stomach, and then converts it to pHi. A normal pHi ranges from 7.35 to 7.45. The risk of MODS and mortality significantly increases when the pHi < 7.32 (Liu and Yan 2009).

16.4.8 Chest X-ray Monitoring

Chest X-ray monitoring is used to monitor the progress of lung disease, the placement of artificial airways, the positioning of central venous catheters, and as a reference value to determine removal from the ventilator.

16.4.9 Liver and Kidney Function Monitoring

Severe chronic consumption, infection, shock, and anti-TB drug treatment can have significant impacts on renal and hepatic function in critical TB patients, so close monitoring is critical.

16.4.9.1 Monitoring of Renal Function

The simplest method to evaluate renal function and the dilution and concentration function of renal tubules is by measuring the specific gravity of the urine.

Glomerular filtration rate assessment includes monitoring values for endogenous creatinine clearance (CCR), creatinine (Cr), and blood urea nitrogen (BUN). However, serum β2-microglobulin (β2-M) levels give a better estimate of the glomerular filtration rate. The glomerular filtration rate and β2-M are negatively correlated; when the glomerular filtration rate decreases, β2-M begins to rise earlier and more significantly than the serum creatinine concentration (Cai 2006; Yu 2008).

16.4.9.2 Monitoring of Hepatic Function

Protein metabolism is one of the liver's major functions. The liver produces albumins, glycoproteins, lipoproteins, and a variety of transporter proteins. When mononuclear cells in the liver are stimulated, γ-globulin is overproduced. This condition

can progress to autoimmune hepatitis, which can lead to hyperthyroidism and other endocrine system dysfunction. Therefore, it is important to monitor levels of serum albumin, immune globulin, and lipoprotein. Most critical TB patients have severe hypoproteinemia.

Glucose metabolism plays an important role in maintaining stable blood sugar levels. Abnormal blood sugar levels can be indicative of dysfunctional glucose metabolism caused by substantial liver damage.

Lipid monitoring is another way to track hepatic function. The liver synthesizes endogenous cholesterol, fatty acids, triglycerides, and other lipids. It also clears exogenous lipids and adipose tissue fatty acid, and decomposes free fatty acid. The liver also synthesizes high-density lipoprotein (HDL), very low density lipoprotein (VLDL), and lecithin—cholesterol acyl transfer enzymes (LCAT).

Bilirubin metabolism is another indicator of liver function and can be monitored by checking serum total bilirubin, 1 min bilirubin test, urine bilirubin, urobilinogen, etc.

Serum enzymes that can also be indicators of liver function include alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), γ-glutamyl transferase (GGT) and its isoenzymes, and cholinesterase.

16.4.10 Coagulation Monitoring

Ninety percent of critical TB patients exhibit the formation of microvascular thrombosis due to endothelial cell dysfunction, insufficient endogenous anticoagulant and thrombosis formation materials, changes in platelet quality and quantity, suppressed bone marrow function, leukocyte adhesion, decreased red blood cell deformability in individuals prone to disseminated intravascular coagulation (DIC), small artery thrombosis associated with ischemia and hypoxia, or hyperfibrinolysis caused extensive bleeding in late stage so that tissue perfusion is in serious deficiency. This accelerates organ dysfunction (Cai 2006; Yu 2008).

It is important to monitor bleeding and clotting time, prothrombin time (PT), and activated partial thromboplastin time (APTT). In patients prone to DIC, it is necessary to perform the 3P test, and to monitor quantitative plasma fibrinogen, fibrin degradation products (FDP), and, when necessary, the patient's clotting factor levels.

16.4.11 Arterial Blood Gas and pH Monitoring

Arterial blood gas analysis and monitoring includes assessment of the patient's oxygenation, gas exchange, and acid–base status. It is performed by collecting arterial blood from the radial artery, dorsal artery, or the femoral artery via direct puncture or through an arterial catheter. The blood analysis data is combined with patient history and clinical examination results.

16.5 Treatment of Critical TB

16.5.1 Anti-TB Treatment

Many studies indicate that delayed treatment of TB patients with active TB reduces the survival rate (Pablos-Méndez et al. 1996; Rao et al. 1998; Sacks and Pendle 1998). For patients with critical TB, delayed anti-TB treatment is also independently associated with factors increasing hospital mortality (Zahar et al. 2001; Ryu et al. 2007). Therefore, patients with critical TB should be started on effective anti-TB treatment as soon as possible if organ function allows. Because of the stress put on the major organs of patients with critical TB, the incidence of MODS can reach 19–80 % (Zahar et al. 2001; Lee et al. 2003; Erbes et al. 2006; Ryu et al. 2007; Chen and Zhu 2010; Silva et al. 2010). Therefore, an anti-TB treatment regimen should be based on the extent of TB disease and the state of liver and kidney function. Likewise, it is important to frequently monitor liver and kidney function during treatment.

Newly diagnosed individuals (and some patients receiving re-treatment) with mild hepatic dysfunction may choose a treatment protocol which includes one drug with potential liver toxicity. For instance, rifampicin can be substituted with rifapentine in the following regimens: isoniazid, rifapentine, ethambutol, and ofloxacin; or rifapentine, ethambutol, and ofloxacin solution. Alternatively, based on the type of TB, one can select multiple drugs with liver toxicity but at the same time administer liver protecting treatment. If there are a number of abnormalities in liver function during treatment, especially levels of transaminase 2 × the upper normal limit, alkaline phosphatase 1.5 × normal, and an increase in bilirubin, TB treatment should be withdrawn immediately and steps taken to protect the liver (American Thoracic Society 2003; Ma and Zhu 2006).

For patients with renal dysfunction, the therapeutic course of treatment should be consistent with initial and recurrent TB. However, this requires careful design of a drug treatment program with the inclusion of toxic and nontoxic drugs and constant adjustment of drug dosages to maintain renal function. Rifampicin and isoniazid are metabolized by the liver so do not require dose adjustments. Although pyrazinamide is metabolized by the liver, its metabolites (pyrazine acid and 5-hydroxy-pyrazine acid) accumulate in patients with renal insufficiency, so kidney function must be monitored closely. Ethambutol, streptomycin, kanamycin, amikacin, and capreomycin are mainly excreted by the kidneys, so their dosages must be adjusted based on renal function (American Thoracic Society 2003; Launay-Vacher et al. 2005). The pharmacokinetic characteristics of anti-TB drugs are concentration dependent, so dose adjustments are made primarily by extending the treatment interval (Launay-Vacher et al. 2005). The reduced dosages for patients with creatinine clearance of less than 30 mL/min and patients receiving hemodialysis treatment are similar. Details are shown in Table 16.5.

Almost 70 % of TB patients suffer severe hypoproteinemia (Silva et al. 2010), which may affect the absorption of anti-TB drugs and result in low plasma concentrations of rifampin and ethambutol in patients with severe TB. Factors such as liver

Table 16.5 Dosages of anti-TB drugs in adult patient with renal dysfunction and dialysis treatment (American Thoracic Society 2003)

Drug	Need to adjust the dosage?	Creatinine clearance values < 30 mL/min or dialysis treatment recommended dosage of drugs
Isoniazid	No	300 mg, 1 time/day or 900 mg/time, 3 times/week
Rifampicin	No	600 mg, 1 time/day or 600 mg/time, 3 times/week
Pyrazinamide	Yes	25–35 mg/kg/time, 3 times/week
Ethambutol	Yes	15–25 mg/kg/time, 3 times/week
Levofloxacin	Yes	750–1000 mg/time, 3 times/week
Cycloserine	Yes	250 mg, 1 time/day or 500 mg, 3 times/week
Ethionamide	No	250–500 mg, 1 time/day
Aminosalicylic	No	4 g, 2 times/day
Streptomycin	Yes	12–15 mg/kg, 2–3 times/week
Capreomycin	Yes	12–15 mg/kg, 2–3 times/week
Kanamycin	Yes	12–15 mg/kg, 2–3 times/week
Amikacin	Yes	12–15 mg/kg, 2–3 times/week

and kidney dysfunction and the metabolism of anti-TB drugs make it difficult to control the effective blood concentration and therapeutic effect of anti-TB drugs. Therefore, drug plasma concentration in patients with liver and kidney dysfunction should be monitored closely (Zahar et al. 2001; American Thoracic Society 2003).

16.5.2 Anti-infection Treatment

Nosocomial respiratory infections occurred in 20–69 % of patients with critical TB in hospital intensive care units (Zahar et al. 2001; Lee et al. 2003; Erbes et al. 2006; Ryu et al. 2007; Silva et al. 2010). In recent years, multidrug-resistant pathogens causing hospital-acquired pneumonia have also increased sharply, especially in intensive care units. The most common pathogens causing hospital-acquired pneumonia are aerobic, gram-negative bacteria, including *Pseudomonas aeruginosa, Klebsiella pneumoniae,* and *Acinetobacter* spp. Less common are gram-positive bacteria, such as *Staphylococcus aureus*, the majority of which are methicillin-resistant. Lower respiratory tract secretions must be collected for inspection before anti-infection treatment; however, treatment should not be delayed to collect samples in critically ill patients. In these cases, early broad-spectrum treatment should be based on trends of area pathogens with the goal of having the best anti-inflammatory effect. Once the culture results and clinical evaluation are clear, treatment should be promptly adjusted (American Thoracic Society and Infectious Disease Society of America 2005).

In addition to the use of antimicrobial drugs to control infection, attention should be paid to airway humidification, postural drainage of sputum, and the use of bronchial expectorants and diastolic drugs. Mechanical ventilation and intubation equipment should be replaced when wet, and suction should be used to ensure that

air bag pressure is greater than 20 cmH_2O and to prevent subglottic secretions from accumulating around the balloon into the lower airway. Also, patients should be kept in a semi-recumbent position to prevent aspiration of gastric reflux (American Thoracic Society and Infectious Disease Society of America 2005).

16.5.3 Mechanical Ventilation (MV) Treatment

Respiratory failure is a serious complication of TB, and the main reason for admittance into the ICU for the treatment of TB (Erbes et al. 2006; Silva et al. 2010). After years of development, ventilator technology and mechanical lung ventilation for the purpose of gas exchange has become an important therapeutic treatment for respiratory failure.

Mechanical ventilation can serve multiple purposes. It can correct respiratory acidosis by improving alveolar ventilation, $PaCO_2$, and pH. Usually the blood $PaCO_2$ and pH should be maintained at the level of remission. Mechanical ventilation can also be used to correct hypoxemia and alleviate tissue hypoxia by improving alveolar ventilation, increasing inspired oxygen concentrations, increasing lung volume, and reducing breathing power. The basic goal of mechanical ventilation is to improve oxygenation such that $PaO_2 > 60$ mmHg or $SaO_2 > 90$ %. Mechanical ventilation also reduces respiratory power and relieves respiratory muscle fatigue. In patients with respiratory failure due to TB, airway resistance is increased, pulmonary compliance is decreased, and endogenous end-expiratory pressure ($PEEP_i$) leads to a significant increase in respiratory work consumption. In addition, TB patients often have poor nutritional status, and patients with severe TB are prone to respiratory muscle fatigue. Mechanical ventilation can relieve respiratory muscle fatigue in these patients. Additionally, mechanical ventilation can help expectoration and control infection, allow the safe use of sedatives and muscle relaxants, and reduce intracranial pressure in patients with tuberculous meningitis by controlling hyperventilation (Yu 2008; Liu and Yan 2009).

Indications

- When conditions continue to deteriorate despite active treatment; symptoms of pulmonary encephalopathy appear; there is a disturbance of consciousness.
- There is a serious abnormity in breathing; a respiratory rate >35 or <6–8 breaths/min, respiratory rhythm abnormalities, spontaneous breathing becomes weak or disappears.
- Blood gas analysis shows severe ventilation and/or oxygenation disorder: after full oxygen therapy, $PaO_2 < 50$ mmHg and $PaCO_2 > 80$ mmHg and continuously increased, or arterial $pH \leq 7.20$ which indicates serious decompensated respiratory acidosis.

Contraindications for mechanical ventilation include previous occurrence of bullae, lung cysts, hemoptysis, acute myocardial infarction, or shock. Some believe that

treatment of active TB with invasive mechanical ventilation is contraindicative due to the risk of spreading TB by mechanical ventilation. However, there is no research to support the idea that positive pressure ventilation can lead to the spread of TB. Currently, there are no absolute contraindications for mechanical ventilation as long as the correct strategy is implemented and targeted to take appropriate measures.

16.5.3.1 Mechanical Ventilation Methods

Mechanical ventilation can be implemented invasively or noninvasively. Noninvasive positive pressure ventilation (NIPPV) is provided via a nasal mask or face mask. Invasive positive pressure ventilation is performed via endotracheal intubation or tracheostomy.

16.5.3.2 Noninvasive Positive Pressure Ventilation

NIPPV should be used in patients when conventional methods of oxygen therapy (nasal cannula and mask) cannot maintain satisfactory oxygenation, when the patient exhibits use of auxiliary respiratory muscles or has severe respiratory difficulties, or when the patient has deteriorated oxygenation disorder. However, patients must have a good state of consciousness, the ability to expectorate sputum, adequate breathing ability, good hemodynamic conditions, and be amenable to NIPPV (Zhang and Gao 2006; Critical Care Medicine Branch of the Chinese Medical Association 2007; Yu 2008).

NIPPV is contraindicated when patient exhibits decreased consciousness, weak or intermittent breathing, weak expectoration, severe organ dysfunction (upper gastrointestinal bleeding or hemodynamic instability), pneumothorax or mediastinal emphysema without drainage, severe bloating, or in cases of upper airway or maxillofacial injury, surgery, or deformity. NIPPV is not recommended when the patient is not cooperative or experiences mask discomfort.

Randomized controlled clinical trials have shown that early application of NIPPV in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), acute cardiogenic pulmonary edema (ACPE), or immunosuppression can reduce the need for endotracheal intubation and lower hospital mortality rates (Critical Care Medicine Branch of the Chinese Medical Association 2007). In cases of pulmonary TB with respiratory failure, both Chinese and international studies indicate that early application of NIPPV or mechanical ventilation as a sequential treatment can benefit patients (Agarwal et al. 2005; Deng and Guo 2005; Zhu 2006; Men et al. 2009; Zhou 2010). However, the specific effects need to be confirmed through randomized controlled clinical studies.

The two most common types of NIPPV are continuous positive airway pressure (CPAP) ventilation and bi-level positive airway pressure (BiPAP) ventilation. BiPAP has two modes: S mode and T mode. The S mode is for spontaneous breathing ventilation and is the equivalent of pressure support ventilation (PSV) and PEEP. The T

Table 16.6 BiPAP parameters (Yu 2008)

Parameters	Reference value
IPAP/tidal volume	10–25 cmH_2O/7–15 mL/kg
EPAP	3–5 cmH_2O (Type I respiratory failure with a 4–12 cmH_2O)
Back-up frequency (T mode)	10–20 times/min
Inspiratory time	0.8–1.2 s

mode is for back-up control ventilation and is the equivalent of pressure controlled ventilation (PCV) and PEEP. The BiPAP parameters include inspiratory pressure (IPAP), expiratory pressure (EPAP), and back-up control of ventilation frequency. When the spontaneous breathing interval is below the set value (determined by the back-up frequency), the ventilator is in S mode; when the self-breathing interval exceeds the set value, the ventilator automatically switches to T mode.

CPAP is preferred for use in cases of acute cardiogenic pulmonary edema; however, BiPAP may be considered for use in cases of hypercapnia or in patients who have continued difficulty breathing.

In principle, BiPAP parameter adjustments (IPAP and EPAP) are started from a lower level and then gradually increase until a satisfactory level of ventilation and oxygenation is reached, or until the ventilation has reached the highest level the patient can tolerate. The common reference values for BiPAP ventilation parameters are shown in Table 16.6 (Zhang and Gao 2006; Critical Care Medicine Branch of the Chinese Medical Association 2007; Yu 2008).

If the application of NIPPV does not improve the patient's condition within 1–2 h, invasive ventilation should be used.

16.5.3.3 The Basic Model and Parameters Setting of Mechanical Ventilation

Assist-Control ventilation (ACV) is combination of two kinds of ventilation, assisted ventilation (AV) and controlled ventilation (CV). When the patient's inspiratory force is able to trigger the breathing machine and the ventilation rate is higher than any preset frequency, the machine is operating in AV mode. When the frequency of spontaneous breathing is lower than the preset frequency, or there is an inability to trigger the ventilator through breathing, the ventilator switches to CV mode and gives positive pressure ventilation corresponding to the preset tidal volume and frequency. A-C mechanical ventilation is commonly used in ICU patients. This provides basic synchronized ventilation with spontaneous breathing, and ensures minimum minute ventilation in patients with breathing instability (Zhang and Gao 2006; Critical Care Medicine Branch of the Chinese Medical Association 2007; Yu 2008).

The A-C capacity switch for ACV ventilation has the following parameters: trigger sensitivity, tidal volume, respiratory rate, inspiratory flow/flow waveforms. The A-C pressure switch parameters are trigger sensitivity, pressure level, inspiratory time, and respiratory rate.

Synchronized intermittent mandatory ventilation (SIMV) is a combination of spontaneous breathing and controlled ventilation breathing. The synchronous instruction of positive pressure ventilation can be triggered by patient's spontaneous breathing. Between two instructed ventilation cycles, patients could breath spontaneously. Instructed breathing can be proceeded in the form of prebreathing capacity (capacity-controlled SIMV) or pre-pressure (pressure-controlled SIMV). SIMV can cooperate with a patients' spontaneous breathing and reduce the patients' struggle with the ventilator. The level of respiratory support can be changed by changing IMV frequency from full support to partial support. SIMV can be used during the ventilator weaning process for patients who have been on a ventilator for a long time. The parameters for SIMV are tidal volume, flow rate/inspiratory time, controlled frequency, and trigger sensitivity. The pressure level and inspiratory time should be set when SIMV is controlled by pressure.

Pressure support ventilation (PSV) is one of the ventilation support modes in which the patient triggers ventilation and controls the respiratory rate and tidal volume. It switches from inspiratory to expiratory phase when the airway pressure reaches the preset pressure level and inspiratory flow decreases to below the threshold level. If the ventilator is set to the appropriate level, it can effectively reduce the work of breathing and have a positive impact on hemodynamics. Some studies suggest that 5–8 cmH_2O of PSV can overcome the circuit resistance of endotracheal intubation and ventilator, so PSV can be used in the ventilator weaning process. The parameters for PSV are pressure, trigger sensitivity, pressure rise rate, and, in some ventilators, expiratory sensitivity.

Continuous positive airway pressure (CPAP), as previously discussed, assists patients in breathing on their own. The ventilator maintains airway pressure within the entire respiratory cycle (inspiratory and expiratory period). CPAP has all the advantages of PEEP, such as increasing the alveolar pressure and functional residual capacity, increasing oxygenation, preventing airway and alveolar collapse, improving lung compliance, and reducing the work of breathing against $PEEP_i$. However, CPAP pressure that is too high can increase peak pressure and mean pressure of the airway, reduce venous return volume, and reduce blood perfusion of important organs such as the liver and kidneys. In addition, spontaneous breathing produces a slightly lower mean intrathoracic pressure than the same PEEP when CPAP is used. The only CPAP parameter is pressure. *Biphasic positive airway pressure (BIPAP)* gives two different alternating levels of positive airway pressure during spontaneous breathing. It switches between the low pressure and high pressure regularly, and its high-pressure time, low-pressure time, high pressure level, and low pressure level are independent and variable. Functional residual capacity (FRC) reduction, which is produced by switching from high pressure level to low pressure level, can increase expiration volume and improve alveolar ventilation. The BIPAP parameters are high pressure level (*P* high), low pressure level (*P* low), high-pressure time (*T* insp), respiratory frequency, and trigger sensitivity.

The Main Parameters of Mechanical Ventilation

Tidal volume settings in volume-controlled ventilation mode are usually determined based on body weight (5–12 mL/kg) combined with the respiratory system compliance and resistance adjustment. Avoid platform airway pressure exceeding 30–35 cmH_2O. In pressure-controlled ventilation mode, the tidal volume is depended on preset pressure, respiratory system resistance, and compliance, and should eventually be adjusted according to blood gas analysis.

Respiratory rate settings are usually 12–20 breaths/min in adults. In individuals with acute/chronic restrictive lung disease, the setting may be more than 20 breaths/min based on minute ventilation and the PCO_2 level of the target. However, an excessive respiratory rate can lead to increased air trapping and an elevated $PEEP_i$ and should be avoided.

Flow rate for an adult is commonly set between 40 and 60 L/min and adjusted according to minute ventilation, respiratory system resistance, and lung compliance. The ideal peak flow should meet the patient's peak inspiratory flow rate. The velocity waveform commonly used in the clinic is slow wave or square wave. In the pressure-controlled ventilation mode, flow rate is determined by the selected pressure level, airway resistance, and the patient's inspiratory effort.

The *inspiratory time* in spontaneously breathing patients is usually set at 0.8–1.2 s, or a *respiratory ratio* of 1:1.5–1:2. Controlled ventilation patients may have extended inspiratory times and respiratory ratios so as to elevate mean airway pressure and improve oxygenation, but close attention should be paid to $PEEP_i$, patient comfort, and the effects on the cardiovascular system.

Trigger sensitivity under normal circumstances is set with the pressure trigger at −0.5 to 1.5 cmH_2O and the flow trigger at 2–5 L/min. The proper trigger sensitivity settings will make the patient more comfortable and promote human–machine coordination.

Inspired oxygen concentration (FiO2) can be set high (100 %) in the initial phase of mechanical ventilation to quickly correct severe hypoxia, and later adjusted based on target PaO_2, PEEP levels, MAP levels, and hemodynamic status as appropriate. FiO_2 should then be reduced to 50 % or less. If SaO_2 cannot be maintained >90 %, then PEEP should be added to increase mean airway pressure and sedatives or muscle relaxants should be administered. If appropriate, PEEP and MAP may be adjusted as needed to increase $SaO_2 > 90$ % and maintain a minimum FiO_2.

Proper *PEEP settings* will recruit collapsed alveoli, increase mean airway pressure, improve oxygenation and reduce venous return, decrease left ventricular afterload, and reduce the work of breathing caused by $PEEP_i$. PEEP is often used in ARDS as the representative of the type I respiratory failure. When setting PEEP, refer to target PaO_2 and oxygen delivery and consider FiO_2 and tidal volume.

Lung Protective Ventilation Strategy

In order to avoid ventilator-associated lung injury in cases of pulmonary TB with bullae or lung damage, a lung protective ventilation strategy should be designed to avoid excessive inspiratory plateau pressure and tidal volume. The lung protective

ventilation strategy should have a low tidal volume (6 mL/kg), an appropriate level of PEEP, end-inspiratory platform maintained at 30 cmH_2O, and a $PaO_2 > 58–60$ mmHg or oxygen saturation > 90 %. Limiting oxygen concentrations to less than 60 % avoids oxygen toxicity (Zhang et al. 2002; Du et al. 2003).

16.5.4 Supportive Treatment

Supportive treatment includes nutritional support, antishock therapy, and maintenance of the balance of pH, water, and electrolytes. All of these supportive treatments are needed for protein synthesis, for organ function, and to sustain life, especially in patients with critical TB.

16.5.4.1 Nutritional Support

TB is a chronic wasting disease. Critical TB is associated with secondary infections, fever, hypoxemia, and increased work required for breathing. These factors increase the risk of malnutrition. More than half of TB patients have hemoglobin < 9 g/dL, 92.5 % have severe anemia, and 67.2 % have hypoproteinemia (Silva et al. 2010). Malnutrition lowers patient serum total protein and albumin, reduces lesion repair function, damages immune function, and decreases the number and function of lymphocytes in the cellular immune system. Malnutrition delays healing, and this delay increases the chances of transmission. Moreover, malnutrition hypoalbuminemia interferes with anti-TB drug delivery and changes the effective concentration of anti-TB drugs, altering their efficacy (Paton et al. 2004). Nutritional support should be given to severe TB patients as soon as possible. The first choice is enteral nutrition therapy; however, adequate measures must be taken to avoid the occurrence of regurgitation and aspiration. It may be necessary to add a gastrointestinal prokinetic drug. Overfeeding should be avoided in patients with respiratory failure. This is especially true with carbohydrate supplements, which increase carbon dioxide production, increase the respiratory quotient, and increase respiratory load. Patients with intestinal TB complicated by obstruction, fistula, and severe abdominal infection cannot tolerate enteral nutrition, so adequate parenteral nutrition will be necessary (Heyland et al. 2003; Jiang 2008).

16.5.4.2 Antishock Therapy

Hemoptysis, septic shock, and low blood pressure after mechanical ventilation require rapid fluid resuscitation to ensure the effective perfusion of oxygen and blood into the tissues and organs. Vasoactive drugs can be administered in combination with hemodynamic monitoring. Obstructive shock caused by tuberculous pericarditis, pericardial tamponade, or tension pneumothorax requires pericardiocentesis or thoracic drainage to relieve obstructive lesions as soon as possible.

Critical TB, despite being an infrequent cause of multiple organ failure, still has a relatively high mortality rate. There should be a prompt and aggressive diagnostic strategy to identify patients with more than one organ failure and instable hemodynamics who require mechanical ventilation and ICU care. Therefore, specialized TB intensive care units should be set up in high incidence areas. Sufficient medical personnel and equipment should be provided to ensure treatment to reduce TB transmission and patient mortality.

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