JOURNAL OF PHARMACEUTICAL ANALYSIS

A COMPARATIVE STUDY OF TOTAL THORACOSCOPIC AORTIC VALVE SURGERY AND TRADITIONAL OPEN-CHEST AORTIC VALVE SURGERY: A PROPENSITY SCORE-MATCHED STUDY

Running Title: Total thoracoscopic aortic valve surgery

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Research aim:
By collecting and analyzing the clinical data of total thoracoscopic aortic valve replacement, and comparing it with the relevant data of traditional midline thoracotomy aortic valve replacement, in order to ensure the accuracy of the comparison, the study adopted sophisticated propensity score matching technology. To identify the significant advantages and unique features of total thoracoscopic surgery. In addition, this study also included a detailed compilation and analysis of domestic and foreign literature on minimally invasive aortic valve replacement surgery, compared the application effects of different minimally invasive surgical methods in clinical practice, and in-depth analysis of the advantages and disadvantages. These research results provide important reference for the promotion and application of total thoracoscopic surgery in clinical practice. To scientifically evaluate the feasibility, safety, minimally invasive and cosmetic effects of total thoracoscopic technology in aortic valve replacement. Verify the reliability of the total thoracoscopic heart valve surgery model and the surgical operation specifications and clinical treatment standards, and lay a theoretical and clinical foundation for the application and promotion of total thoracoscopic technology in cardiac surgery.

Research methods:
Selected patients: We screened a total of 24 eligible patients in the thoracoscopic group who underwent thoracoscopic surgery in our hospital from January 2020 to December 2023, and 366 patients who underwent traditional median sternotomy aortic valve replacement. By propensity score matching, 24 patients in the total thoracoscopic aortic valve replacement group were compared with 24 patients in the traditional midline thoracotomy group (control group). Surgical technique: 1.1 Anesthesia management: same as mitral valve. 1.2 Establishment of peripheral extracorporeal circulation: same as mitral valve. 1.3 Surgical method: 1.3.1 Setting of three holes on the chest wall: The first hole is the entry hole for the left hand instrument, 1 to 2 cm long, located between the anterior axillary line and the mid-axillary line on the right side of the third intercostal space. The second hole is the right-hand instrument entrance hole, 2.5-3 cm long, located between the midclavicular line and the

anterior axillary line. The third hole is the thoracoscopic entrance, located at the junction of the anterior axillary line and the mid-axillary line in the fourth intercostal space on the right side, and is about 1.5-2cm long. 1.3.2 The sequence of three-port incision is as follows: Same as the mitral valve. 1.3.3 Pericardial incision and suspension: same as mitral valve. 1.3.4 Place left ventricular drainage: same as mitral valve. 1.3.5 Insert the perfusion tube into the aortic root: same as the mitral valve. 1.3.6 Block the ascending aorta: Insert the aorta blocking forceps into the operating hole of the left hand. Myocardial protective solution can be injected through the aortic root, and this method is suitable for perfusion in patients with aortic valve stenosis. 1.3.7 Perfuse the left and right coronary arteries separately under direct vision: For patients with aortic regurgitation, use an oblique incision near the aortic root, about 1.5-2 cm from the front wall of the aorta, and observe the openings of the left and right coronary arteries. , and then use a three-way perfusion tube to perfuse the left and right coronary arteries simultaneously. 1.3.8 Aortic incision and traction: Gradually extend the aortic incision from the left side to above the junction of the left and right coronary arteries, and then further expand to the right. Near the border of the left coronary sinus, the surgical team will A 5-0 Prolene suture is applied to the center of the upper end and combined with a spacer for lifting. This step is to properly draw the incision edge superiorly and to the right and ensure that it is stably attached to the inferior right edge of the pericardiotomy area. At the same time, 5-0 Prolene sutures and spacers were also used for suspension on both sides of the lower end of the aortic incision, and were respectively pulled and safely fixed on the left edge of the pericardiotomy and the surface of the diaphragm to ensure the stability of the incision. 1.3.9 Treatment of the aortic valve: Use a 2/0 double-ended needle with a gasket, place the gasket on the left ventricular side or aortic side of the aortic valve annulus, and perform mattress-style interrupted sutures along the aortic valve annulus. The order of suturing is first the right coronary annulus, then the left coronary annulus, and finally the non-coronary annulus. All sutures are pulled out through the right-hand operating hole and evenly stuck on the wire clamping ring. After the external thoracic valve is sutured, they are inserted into the aortic valve annulus through the right-hand operating hole and tied and fixed with a special knotter. The aortic incision is sutured with 4-0 Prolene sutures with pads using a combination of mattress and continuous methods to reduce incisional bleeding.

Research result:

After propensity score matching, there was no significant statistical difference in the basic data between the total thoracoscopy group and the control group. The results of the study showed that compared with traditional open surgery, the average operation time of the total thoracoscopic AVR group increased (188.39±41.78 vs. 169.93±43.56, p=0.0027). Similarly, the average cardiopulmonary bypass time and aortic cross-clamping time in the thoracoscopic group were significantly longer than those in the control group (179.87±47.65min vs. 109.47±19.46min, p<0.0001; 119.53±30.89min vs.68.12±18.08min, p <0.0001. Moreover, the proportion of patients in the thoracoscopic AVR group with extracorporeal circulation time greater than 120 minutes and aortic cross-section time greater than 90 minutes was significantly higher than that in the control group (25.0% vs. 4.1%, p < 0.0001; 16.7% vs. 4.1 %, p=0.0105). In addition, the average tracheal intubation time of patients in the thoracoscopic AVR group was significantly lower than that of the control group (16.13±6.88h vs. 25.01±17.41h, p=0.0029). The average intraoperative blood loss in the thoracoscopic AVR group was significantly lower than that in the control group. The difference was significant (P=0.0017). (142.59 ± 108.56ml vs. 261.08 ± 79.78, P < 0.0001) Similarly, the average postoperative drainage volume of patients in the thoracoscopic AVR group was also significantly lower than that in the control group (288.45 ± 201.17ml vs. 399.75 ± 298.08ml, p = 0.0298.). None of the 48 AVR patients died during hospitalization or within one month after surgery, and there was no significant difference in the incidence of major complications after surgery (8.3% vs. 12.5%, p=0.8987).

Conclusion and significance:

This study shows that compared with conventional open surgery, total thoracoscopic aortic replacement is feasible, safe, reduces hospitalization time, and achieves better minimally invasive and cosmetic effects, providing support for the promotion of thoracoscopic technology. This initiative has established a solid theoretical foundation and clinical experience and is of great and lasting significance to the scientific community.

Key words: Total thoracoscopic valve surgery, minimally invasive aortic valve replacement, propensity score matching

Background

In the 1990s, video-assisted thoracoscopy had been used in cardiac surgery abroad for more than 30 years and had made great progress, especially the application of robot-assisted systems, which enabled it to complete various cardiac surgeries. The popularization of thoracoscopic cardiac surgery in China was relatively slow. It was not until the early 2000s that it began to be used in the field of cardiac surgery, with robot-assisted surgery as the mainstream method. It can not only effectively perform minimally invasive operations, minimize surgical injuries, reduce postoperative pain, shorten recovery periods, but also reduce surgical expenses and meet modern people's pursuit of beauty. In addition, on the basis of ensuring the quality of surgery, this technology also indicates a broader development space. At present, in the field of cardiac surgery technology, thoracoscopic surgery represents an important technological revolution and can be used to complete most cardiac surgeries. It is a typical representative of modern minimally invasive cardiac surgery.

Heart valve disease can cause complete loss of heart function and eventually lead to heart failure[1]. In Western industrialized countries such as the United States, the age-adjusted incidence of moderate to severe valvular heart disease is estimated to be about 2.5%, and its confidence interval falls between 2.2% and 2.7%[2]. In these developed countries, valvular heart problems are mainly caused by degenerative changes, and the prevalence of such diseases is increasing as the population ages[3]. In contrast, the latest epidemiological data in China reveal that the weighted incidence of valvular disease is about 3.8%, which is estimated to affect about 25 million patients nationwide[4]. As a representative of developing countries, the main cause of valvular heart disease in China is rheumatic fever[5]. Rheumatic fever affects the heart valves and may promote the development of rheumatic heart disease (RHD). Although RHD is essentially an autoimmune disease, its exact cause is not yet fully understood. It is generally believed that the disease is secondary to the immune response after hemolytic streptococcal infection[5]. Rheumatic heart disease usually affects the mitral valve and aortic valve most often. In severe cases, it may cause valvular stenosis and/or regurgitation, causing serious health problems.

The aortic valve is composed of three leaflets, which are evenly arranged on the curved edge of the valve and together form a semilunar structure. It is worth noting that the aortic valve also has special forms, such as a single leaflet or a double leaflet structure. Aortic valve disease is a wide range of diseases, including both primary diseases originating from the valve itself and secondary lesions caused by damage to the supporting structure. Based on the hemodynamic characteristics, aortic valve disease can be divided into two categories: stenosis and regurgitation. In the case of mild aortic valve abnormalities induced by infective endocarditis or rheumatic fever, drug intervention is a feasible strategy to curb infection and prevent the disease from worsening during the subtle period of initial pathological signs. However, patients at this stage often show insignificant symptoms and signs, and the early lesions of the aortic valve are difficult to detect immediately. Until signs such as dizziness or even fainting appear, the condition has mostly progressed to moderate to severe, accompanied by problems such as contraction, calcification and perforation of the valve. At this stage, drug therapy has limited effect, and surgical repair or replacement of the aortic valve can achieve the purpose of radical cure. Aortic regurgitation is a common heart valve disease, which is mainly manifested by the inability of the aortic valve to close normally during diastole, resulting in blood flowing back from the aorta to the left ventricle. Among the many treatment methods, surgical repair or plasty of the aortic valve has been proven to be a treatment method that is particularly suitable for patients with aortic regurgitation, and has good results. Surgical repair or plasty of the aortic valve is a delicate surgical operation that aims to restore the normal function of the valve by repairing or adjusting the valve structure. Compared with traditional valve replacement, this surgical method has a lower complication rate and better long-term effect. During the operation, a variety of technical means are used to repair the valve according to the specific situation of the patient, such as annuloplasty ring implantation and valve edge repair. These technologies can effectively improve patients' aortic valve regurgitation and improve their quality of life. In 1958, WARREN J. TAYLOR first publicly reported the implementation of aortic valvuloplasty[6][7]. Other literature indicates that the method of reducing the size of the aortic valve annulus by implanting an external annular plasty ring has shown certain results, but the long-term therapeutic effect of this method still needs further scientific research to confirm [8].

With the continuous advancement of artificial valve technology and the improvement of surgical implant technology, aortic valve replacement surgery has become the first choice for treating patients with aortic valve disease. In 1960, Harken and his team first attempted to perform aortic valve stenosis and regurgitation replacement surgery through median sternotomy [9]. Since then, aortic valve replacement surgery has been recognized as a safe and feasible treatment method, characterized by low surgical mortality and low complication rate. Traditional median thoracotomy involves an incision of approximately 10 to 15 cm in length. This method greatly optimizes the surgical field of view and provides surgeons with sufficient working space. It not only meets the needs of aortic valve replacement, but is also widely used in various cardiovascular surgeries, such as coronary artery bypass grafting and aortic arch replacement. Despite this, median sternotomy surgery also has its inherent limitations and challenges. The sternum, as an important part of the human thorax, plays a key role in protecting important organs such as the heart and lungs. However, in certain specific medical situations, doctors may choose to perform a "median sternotomy" operation, which will inevitably damage the integrity of the sternum. Median sternotomy is a surgical procedure whose main purpose is to gain direct access to the heart and other important thoracic organs. This procedure is often used in cardiac surgery, mediastinal tumor resection, or other surgeries that require exposure of the heart and great blood vessels. During the operation, the doctor needs to cut the sternum to gain access to the chest cavity for operation. Although this operation is necessary for the treatment of certain diseases, it also carries certain risks. Therefore, when performing a median sternotomy, the doctor needs to weigh the necessity of the operation against the possible risks and take appropriate measures to reduce the occurrence of complications. Because median sternotomy requires sawing the sternum, the wound surface is very large, and the postoperative pain is severe and the patient cannot tolerate it. The recovery period of the operation is long [10], especially for the elderly and patients with hypertension, the recovery time may be longer, which increases the risk of infection.

With the continuous development of cardiac surgery technology, surgeons have developed many different minimally invasive aortic valve replacements to meet the needs of patients to reduce bed rest time and recover quickly. RaoPn et al. [11] first reported minimally invasive aortic valve replacement through right parasternal thoracotomy in 1993. Although this method maintains the integrity of the sternum and allows for a relatively fast postoperative recovery, it is still difficult to avoid a certain degree of damage to the costal cartilage. In addition, there are some shortcomings in the visual exposure of aortic valve surgery. In 1996, aortic valve replacement via a small upper sternal incision was successfully reported by German doctor Konertz et al. [12]. The upper sternal small incision surgical method is a delicate and efficient surgical technique that is widely used in the field of cardiothoracic surgery. This method can accurately and quickly reach the surgical area through a carefully designed incision path, reduce damage to surrounding tissues, and improve surgical results. First, the incision is located in the center of the sternum near the upper part [12]. This incision is usually small, and the length depends on the needs of the operation, generally ranging from a few centimeters to more than ten centimeters. The purpose of this incision is to expose the structure of the sternum and ribs, which facilitates subsequent surgical operations. Next, the sternum is cut to the third or fourth intercostal space on the right side, and then the sternum is sawed open with an arc incision [12]. The shape and length of this arc-shaped incision are also determined according to the needs of the operation. Through this arc-shaped incision, the mediastinum is opened and the heart is operated on. Due to the small incision, the patient's pain and complication rate after the operation will be reduced, and the damage to the surrounding tissues will be reduced accordingly [13]. In actual application, the small incision surgery method in the upper sternum is usually suitable for some specific cardiothoracic surgeries, such as heart valve replacement and coronary artery bypass grafting. These surgeries require precise and meticulous operations, and the small incision surgery method in the upper sternum can just meet these requirements. Usually, due to the similar shape of the skin incision, this incision is vividly called a "T-shaped" or "J-shaped" incision because of its shape [13]. Compared with the traditional right parasternal incision, the small incision in the upper sternum can better display the aortic valve area and facilitate surgical operations. This method has been accepted by most surgeons [14]. Although this method reduces damage to the sternum, it still cannot completely avoid the impact on the overall structural integrity of the sternum. In order to reduce the impact of cardiac surgery on the sternal structure, thoracoscopic technology has gradually matured and applied in practice

[15]. Thoracoscopic surgery is based on different access designs, including the popular "three-port technique" and the more streamlined "single-port method". The latter may use the Choker device to deploy the thoracoscopic device or as an auxiliary channel during the operation. Currently, many medical institutions have routinely performed mitral and tricuspid valve repair surgery under full thoracoscopic surgery. Studies have shown that this type of minimally invasive thoracoscopic surgery can significantly reduce the scope of injury, reduce postoperative pain, shorten the necessary time for mechanical ventilation, and show a lower risk of bleeding compared with traditional median thoracotomy [16].

With the continuous development of thoracoscopic technology in the field of cardiac surgery, more and more medical experts tend to adopt this modern method in aortic valve surgery. As early as 2005, Folliguet et al. first published an article introducing five cases (four of which were aortic valve stenosis and one was aortic valve regurgitation). They successfully completed aortic valve replacement surgery using thoracoscopic combined with robot-assisted surgery[17]. The core advantages of this thoracoscopic robot-assisted surgery are the three-dimensional visual effects, remote control capabilities, precise scaling of movements, and delicate operating skills it provides, all of which surpass traditional non-robot-assisted surgical methods[18]. However, the robotic technology equipment currently available on the market cannot fully meet the needs of removing extensive calcified tissue. Therefore, for patients with extensive and severe calcification in and around the valve, robotic surgery is not the best treatment option for the time being[19].

With the continuous advancement of thoracoscopic technology in the field of aortic valve surgery, clinicians have begun to explore the practice of fully thoracoscopic aortic valve surgery without robot assistance. For example, in 2014, Vola et al. recorded the first case of fully thoracoscopic aortic valve replacement surgery in the United States using a full bioprosthesis (manufactured by Medtronic) with needleless fixation technology [20]. In 2016, Vola et al. conducted a follow-up study on 14 patients who underwent fully thoracoscopic aortic valve replacement surgery, and the results showed that the technology was still effective [21]. However, the learning curve of thoracoscopic technology is long, and the duration of extracorporeal circulation and aortic block is more likely to be prolonged, especially in the early stages of development. This may increase the risk of myocardial ischemia, death, and postoperative complications [22][23]. Therefore, before deciding to undergo thoracoscopic aortic valve replacement surgery, a comprehensive preoperative evaluation of the patient is a necessary step, and such surgery should be performed under the guidance of a professional cardiac surgery team with extensive thoracoscopic surgery skills. Once complications such as valve edge leakage or significant obstruction of thoracoscopic operation are encountered, conversion to traditional median sternotomy should be considered in a timely manner to ensure that patient safety is always the primary consideration in all decisions. Since the mortality rate of many elderly patients is very high, many elderly patients are unable to undergo surgery for a long time[24]. Therefore, the use of minimally invasive surgical methods can improve surgical efficiency, reduce surgical time, and play a key role in accelerating the patient's postoperative recovery process.

With the development of interventional treatment technology, transcatheter aortic valve replacement (TAVR) provides a new treatment option for these patients. However, when the aortic valve is dysfunctional, blood flow may be obstructed, resulting in increased heart burden and even symptoms such as heart failure. To solve this problem, the medical community has developed a treatment method called transcatheter aortic valve replacement. There are two common transcatheter aortic valve replacements, namely transapical aortic valve replacement and transfemoral aortic valve replacement[25]. These two methods have their own characteristics and are suitable for patients with different conditions. First, transapical aortic valve replacement: a small incision is made through the apex of the heart, and a catheter is inserted into the left ventricle through this incision. Subsequently, the new artificial aortic valve is delivered to the position of the aortic valve through the catheter[26]. This method is suitable for some special cases, such as when the patient's femoral artery is not suitable for surgery or the patient's heart structure is more complex. The second is the transfemoral aortic valve replacement method: a small incision is made in the patient's groin area, and then a catheter is inserted into the femoral artery and guided to the aortic valve position. Next, the new artificial aortic valve is delivered to the aortic valve position through the catheter [26]. This method is relatively simple, with less surgical trauma and faster recovery, so it is widely used in clinical practice. Peter Stachon et al. conducted a subgroup comparative analysis of the high-risk groups for transcatheter interventional treatment and surgery at the apex of the heart and found that it is safer to perform surgery in patients under 75 years old with a lower surgical risk. The study by Lucia Junquera and her team pointed out that the aortic valve replacement surgery performed through the femoral artery and carotid artery showed similar trends in the two groups in terms of postoperative mortality and complication rates [26].

This article retrospectively analyzes and summarizes the clinical data of aortic valve replacement surgery performed through a fully thoracoscopic approach, and compares it with the data of traditional median thoracotomy aortic valve replacement surgery. To further define the unique nature and benefits of fully thoracoscopic surgery, an in-depth analysis was performed through propensity score matching. At the same time, by reviewing international and domestic literature on minimally invasive aortic valve replacement technology, this study analyzed the different results of various minimally invasive surgical techniques in practical applications, aiming to reveal the pros and cons of each minimally invasive method and provide a scientific basis for the clinical promotion of minimally invasive surgical practice.

Materials and Methods

1. Selected patients

Compared with traditional open heart surgery, thoracoscopic surgery has the advantages of less trauma, faster recovery, and fewer complications. Therefore, it has become the preferred treatment option for many heart patients if they meet the conditions. However, not all heart patients are suitable for thoracoscopic surgery, and the grasp of surgical indications is crucial to ensure the success of the operation and patient safety.

The surgical indications for thoracoscopic cardiac surgery are basically the same as those for conventional open heart surgery. At the same time, the preoperative evaluation criteria for thoracoscopic surgery are also roughly the same as those for traditional surgery, including comprehensive consideration of factors such as the patient's age, physical condition, and cardiac function.

However, despite the many advantages of thoracoscopic surgery, there are still some cases where this type of surgery is not suitable. First, if the patient has a history of cardiac surgery, especially if he has undergone open-chest surgery before, there may be complex conditions such as adhesions in the chest cavity, which increases the difficulty and risk of surgery. Secondly, for patients with acute or subacute infections such as infective endocarditis and connective tissue disease, the damage to the aortic valve and the perivalvular area cannot be assessed due to the presence of inflammation and infection, which increases the difficulty of surgery. In addition, patients with severely calcified aortic valve rings are also not suitable for thoracoscopic surgery, because calcification may cause valve stiffness and increase the difficulty of surgical operation. Finally, patients who need to undergo coronary artery bypass grafting at the same time are more suitable for traditional open-chest surgery because they need to deal with more complex vascular problems. In addition to the above-mentioned contraindications, thoracoscopic surgery also has relative contraindications such as severe damage to the patient's cardiopulmonary function and severe chest deformity. In these cases, although they are not absolute contraindications, the surgical risk will increase significantly, and doctors need to weigh and decide based on the specific conditions of the patient. It is worth mentioning that with the continuous advancement and innovation of medical technology, thoracoscopic surgery is also expanding and improving in terms of surgical indications and contraindications. In the future, we have reason to believe that thoracoscopic surgery will play an important role in more areas and bring better treatment effects and quality of life to patients with heart disease.

None of the following indicators are suitable for thoracoscopic surgery: aortic CT features aortic dissection; severe chest deformation; patients with severe chest adhesions who have undergone right-sided thoracic surgery; single-lung ventilation, extremely limited lung activity, and intolerance; severe femoral artery distortion and deformation, and severe femoral artery calcification [26]. In addition to determining surgical suitability based on the patient's condition, it is also necessary to carefully consider the patient's age, the specific type of aortic valve injury, the degree of calcification of the valve and aortic valve ring, and their overall health status.

In order to ensure the safety and effectiveness of the operation, a series of strict inclusion criteria are usually used when selecting surgical subjects.

① Patients with simple aortic valve disease without other heart diseases are selected to ensure that the operation is only for the problem of the aortic valve itself without interference from other heart diseases. In complex heart diseases, the treatment of a single lesion is often more clear and effective.

② The diameter of the aortic root is greater than 25mm, the diameter of the aortic valve ring is greater than 20mm, and the diameter of the ascending aorta is greater than 45mm. This series of size requirements is to ensure that there is enough space for the operation of the blood vessels during the operation, and to avoid the surgical risks caused by too small blood vessels. These specific values are based on a large number of clinical practices and medical research, and are intended to ensure the safety and success rate of the operation.

③ No chest deformity or chest surgery history on the right side, which is to ensure that no additional damage is caused to the existing deformity or surgical scar during the operation. Chest deformity or surgical scars may increase the difficulty and risk of surgery, so this standard is crucial to ensure the smooth progress of the operation.

④ The aorta and femoral artery have no obvious malformations and no severe atherosclerosis, which is to ensure the patency and elasticity of the blood vessels during the operation. Vascular diseases such as atherosclerosis may increase the risk of surgery, and the patency and elasticity of blood vessels are the key to the success of the operation.

This is a retrospective study. We screened 24 eligible patients in the thoracoscopic group who underwent thoracoscopic surgery in our hospital from January 2020 to December 2023, and 366 patients who underwent traditional median sternotomy aortic valve replacement. Among patients with aortic valve disease, 24 patients who underwent total thoracoscopic aortic valve replacement surgery were paired and compared with 24 patients who underwent traditional median thoracotomy (control group) by propensity score matching.

2. Propensity score matching

The thoracoscopic group and the control group were accurately matched using the propensity score matching (PSM) method [43]. The clinical baseline indicators that are matched are: age, gender, weight, smoking history, preoperative left ventricular ejection fraction (LVEF), hypertension, diabetes, and chronic obstructive pulmonary disease (COPD). The propensity score matching method (PSM) is a commonly used statistical technique that can help researchers effectively process and analyze binary treatment indicator data to draw more accurate experimental conclusions. First, it is necessary to select an appropriate caliper value (such as 0.2 in this case), and then match the thoracoscopic group and the control group based on this value. The matching ratio is set to 1:1, which means that each subject in the thoracoscopic group will be matched with a subject in the control group. In this way, the potential confounding factors between the two groups will be balanced as much as possible, thereby improving the reliability of the research results. Next, it is necessary to calculate the propensity score (PS value), which is a value that reflects the probability of a subject receiving a certain treatment (such as thoracoscopic surgery). By calculating the PS value, various characteristics of the subject before receiving the treatment can be evaluated to determine which factors may affect the effect of the treatment. In this case, the calculation of the PS value will be based on various potential confounding factors between the thoracoscopic group and the control group, such as age, gender, and severity of the disease. After the PS value is calculated, the PSweight after matching needs to be further calculated [43]. This is a weight value used to adjust the statistical weight of the matched sample to ensure the representativeness of the research results. By calculating the PSweight, the treatment effect can be evaluated more accurately and the interference of potential confounding factors on the results can be eliminated. Finally, after obtaining the data after propensity score matching, various statistical methods can be used to conduct in-depth statistical analysis of the thoracoscopic group and the control group. These analyses may include comparing the average effect between the two groups, assessing the confidence interval and significance level of the treatment effect, etc. Through these analyses, comprehensive and accurate conclusions about the effect of thoracoscopic surgery can be drawn, providing strong support for clinical practice. This means that every patient in the thoracoscopic group will be paired with a patient in the control group to match the characteristics of the two groups as much as possible. 24 patients were enrolled in the thoracoscopic group. Among the 366 patients who underwent AVR through a midline incision, 24 were matched 1:1 and served as the control group of the thoracoscopic group. See Table 2.

3. Surgical techniques

1 Complete thoracoscopic group

1.1 Anesthesia management

Arrange the patient to lie in a supine position and raise the right chest to an angle of 20 to 30 degrees. Then, attach external defibrillation electrodes to the patient's left anterior chest wall and left dorsal chest wall. Single-lumen endotracheal intubation for general anesthesia. When performing internal chest surgery, a bronchial occluder is required to achieve left-sided single-lung ventilation. Use 100% high-purity oxygen for ventilation, and set the tidal volume (VT) at 6 to 8 ml/kg. The respiratory rate is 12 to 16 times/min, and the Sa02 is maintained above 97% by adjusting the respiratory rate. After anesthesia takes effect, an esophageal ultrasound probe is inserted, and the aortic valve replacement operation and the gas discharge status in the left heart system are regularly checked during the operation.

1.2 Establishment of peripheral extracorporeal circulation

One of the common and effective means of establishing extracorporeal circulation is through peripheral cannulation. This method mainly uses the femoral artery and femoral vein as the inlet and outlet of the cannula to achieve extracorporeal circulation of blood. The positions of these two blood vessels are relatively fixed and their diameters are moderate, which provides convenient conditions for peripheral cannulation. Advantages of peripheral cannulation: Compared with traditional median thoracotomy cannulation, peripheral cannulation has many advantages. First, peripheral cannulation is less traumatic and can avoid complications caused by central venous cannulation, such as pneumothorax and hemothorax. Second, the operation of peripheral cannulation is relatively simple and can be performed at the bedside without entering the operating room. Make a longitudinal incision 1.5 cm long at the most prominent position of the femoral artery in the right inguinal area. Take 5-0 slip sutures and perform purse-string sutures on the femoral artery and femoral vein respectively. After heparinization, insert a rigid guide wire, and cannulate the artery to the appropriate position along the guide wire. Remove the guide wire and the cannula core, completely expel the bubbles, connect it to the extracorporeal circulation tube, and then fix it. Puncture the femoral vein in the same way, and then insert the guide wire. Under the guidance of esophageal ultrasound, the bipolar femoral vein cannula is slowly moved up along the direction of the guide wire [10]. The tip of the femoral vein catheter is placed in the superior vena cava, guided by esophageal ultrasound, while its lower end is retained in the inferior vena cava. Conventional venous drainage uses natural gravity and negative pressure assistance, and its negative pressure range is maintained at 20 to 40 mmHg. During the operation, it is necessary to ensure that the central venous pressure is maintained at no more than 15 cmH2O. In the operation management of cardiopulmonary bypass, the key is to balance blood flow, achieve full circulation flux, and support arterial oxygen partial pressure to maintain at least 120 mmHg. If this standard cannot be achieved, consider adding a jugular vein catheter to the superior vena cava to enhance drainage, or abandon peripheral extracorporeal circulation to correct extracorporeal circulation.

1.3 Surgical method

1.3.1 Three-hole setting of the chest wall:

The first hole is the left-hand instrument entry hole, 1~2 cm long, and this hole is designed to be located between the right anterior axillary line and the mid-axillary line of the third intercostal space. First, cut the skin, separate the intercostal muscles, implement left lung ventilation alone, and then enter the chest cavity. The aortic clamp and the pericardial traction wire for occlusion are inserted into this hole [10];

The second hole is the right-hand instrument entry hole [10], which is 2.5-3 cm long and is designed to be located between the midclavicular line and the anterior axillary line. The skin and subcutaneous tissue are cut, the intercostal muscles are separated, the endotracheal tube connector is disconnected, and the main surgical instruments such as the needle holder, scissors, and perfusion needle are placed into the right chest cavity.

The third hole is the entry point for the thoracoscope, which is set at the fourth intercostal space of the right chest, approximately at the intersection of the anterior axillary line and the mid-axillary line. The incision length is about 1.5 to 2 cm. This process involves sequentially cutting the epidermis and subcutaneous tissue, carefully separating the intercostal muscles, and safely disconnecting the endotracheal tube connection, so as to smoothly access the right chest cavity. After each incision is completed, a soft tissue incision protective cover should be installed immediately to protect the subcutaneous fat and muscle. The positions of each hole should be reasonably adjusted based on details such as the patient's body shape, the location of the heart, and the position of the top of the diaphragm when lying flat.

1.3.2 The order of three-hole incision is as follows:

The first step is to make the thoracoscopic hole (third hole) [11]. After putting on the incision protection cover and inserting the thoracoscopic lens, adjust its viewing angle, positioning accuracy, and image brightness, contrast, white balance and focus. Then, use the fingers of the left hand to gently press around the surgical opening, use the field of view of the thoracoscopic lens to confirm the correct position inside the chest cavity, and carefully examine whether the layout is appropriate. Then cut the surgical hole on the left hand and put the incision protection cover into the incision; the incision of the operation hole on the right hand should be completed in the same way.

1.3.3 Pericardial incision and suspension:

After the thoracoscope is placed, adjust its angle and position to perform a comprehensive scan of the right thoracic mediastinum area. The pericardium is incised approximately 2 cm above the right phrenic nerve and parallel to the phrenic nerve. Through the left and right surgical holes, the traction lines of the pericardial incision are pulled out and fixed.

1.3.4 Placement of left heart drainage:

The left hand holds the forceps to enter the hole, and the right hand holds the needle to enter the hole. Use a 4-0 double-headed needle without a gasket to slide the line and perform a "U"-shaped purse-string suture on the right upper pulmonary vein. The left heart drainage tube is inserted and fixed through the left hand operation hole (the first hole) [11].

1.3.5 Insertion of the perfusion tube at the aortic root:

Adjust the position of the thoracoscope to expose the aortic root. Insert forceps into the left surgical hole and needle holder into the right surgical hole. Use a double-ended needle with a gasket to suture the anterior wall of the ascending aorta in a "U" shape to form a purse-like shape. Insert the perfusion needle into the aortic root through the right operating hole and connect it to the infusion tube.

1.3.6 Block the ascending aorta:

After checking that the pipeline connection is normal, start extracorporeal circulation, perform left atrial drainage, and lower the temperature. Insert the aortic clamp into the left operating hole. Appropriately reduce the flow rate of extracorporeal circulation and block the distal end of the ascending aorta at the same time [12]. After blocking, the flow rate is restored.

Myocardial protective fluid can be injected through the aortic root. This method is suitable for perfusion of patients with aortic valve stenosis [11].

1.3.7 Perfuse the left and right coronary arteries separately under direct vision:

Re-adjust the angle and position of the thoracoscope to better observe the condition of the aortic root. For patients with aortic regurgitation, an oblique incision is made near the aortic root, approximately 1.5-2 cm from the anterior wall of the aorta, to observe the openings of the left and right coronary arteries, and then a three-way perfusion tube is used to simultaneously perfuse the left and right coronary arteries. Using Del Nido or HTK cardioplegia solution for myocardial protection can greatly reduce the number of perfusions.

1.3.8 Aortic incision and traction:

After completing the cardioplegia and perfusion process, we need to widen the aortic incision from the left side until it exceeds the intersection of the left and right coronary arteries, and continue to extend to the right until it approaches the edge area of the left non-coronary sinus. Then, the upper center of the aortic incision was suspended using 5-0 Prolene sutures and gaskets, and pulled in the upper right direction, while firmly fixing it to the lower right edge of the pericardial incision. For both sides of the lower end of the aortic incision, we also used 5-0 Prolene sutures and gaskets, each with one stitch for suspension, and pulled and firmly fixed to the left edge and diaphragm of the pericardial incision. By adopting this appropriate aortic incision suspension technique, we can ensure that the structure of the aortic valve and its valve ring is fully exposed.

1.3.9 Treatment of the aortic valve:

After removing the diseased aortic valve leaflets through the left and right operation holes, insert a valve measuring instrument through the right operation hole to measure the aortic valve ring to confirm the size of the artificial valve. Use a 2/0 double-headed needle with a gasket, place the gasket on the left ventricular side or aortic side of the aortic valve ring, and perform mattress-style interrupted sutures along the aortic valve ring [19]. The order of suturing is first the right coronary annulus, then the left coronary annulus, and finally the non-coronary annulus[21]. All sutures are pulled out from the right hand operation hole and evenly clamped on the clamping steel ring. After the suture of the extrathoracic valve is completed, they are inserted into the aortic annulus through the right hand operation hole and fixed with a special knotter. Check the opening and closing of the valve and whether the subvalvular and supravalvular gaskets are flipped[21]. The aortic incision is finely sutured using a combination of mattress suture and continuous suture, and 4-0 Prolene sutures with gaskets can effectively reduce incision bleeding.

1.3.10 Rewarming; opening of the ascending aorta:

The gas in the left heart system is drained by negative pressure through the perfusion needle in the ascending part of the aorta, and rewarming is continued. Change the position and angle of the thoracoscope to fully expose the aortic root, and lower the head of the bed downward to help the gas in the heart to be discharged. After temporarily reducing the flow rate of extracorporeal circulation, the ascending aorta clamp is opened, and the heart begins to beat again. If ventricular rhythm is not effective after drug treatment, external defibrillation can be considered. After removing the perfusion needle, check for bleeding. If bleeding occurs, it can be re-sutured to achieve the effect of hemostasis. Postoperatively, transesophageal ultrasound examination can be routinely used to check the opening and closing of the aortic valve, the left heart exhaust, and the occurrence of paravalvular fistula.

1.3.11 Stop extracorporeal circulation; remove the cannula; stop bleeding

Change the position and angle of the thoracoscope to ensure that the overall image of the mediastinum is fully displayed, and at the same time expose the inner part of the chest wall puncture to observe whether there is bleeding. After re-examination, perform venous blood gas testing when the extracorporeal circulation rewarming reaches a satisfactory state. After the end of extracorporeal circulation, remove the femoral vein cannula and use protamine to neutralize the previously used heparin [15]. Adjust the endoscopic equipment and re-check the bleeding of the heart, pericardium, and chest wall puncture site. After confirming that everything is normal, the thoracoscope is removed and the hole in the chest wall is carefully sutured, and the drainage tube is placed in the chest cavity. When the blood pressure and heartbeat are stable, the femoral artery catheter can be removed and tied. At the same time, the openings of the femoral artery and femoral vein should be checked for bleeding, and the skin should be sutured.

2 Traditional median thoracotomy group

The patient was intubated with a single-lumen endotracheal tube and placed in a supine position[9]. The surgery used a median sternotomy to cut the skin and subcutaneous tissue, and the sternum was further sawed with a saw and the sternum was spread open[10]. The extracorporeal circulation system was cannulated through the aorta and right atrium, and the heart was exposed under direct vision. A left heart drainage tube was placed in the left ventricle, cannulated through the right upper pulmonary vein, and the aortic valve replacement surgery was exposed through an oblique incision in the aorta[10]. After completing the aortic valve replacement and venting the left ventricle, the ascending aorta clamp is released, the heart resumes beating autonomously, and the extracorporeal circulation support is gradually terminated after the blood pressure and heart rate stabilize. Protamine is used to neutralize heparin, and then the heart-lung machine tube is removed, hemostasis measures are thoroughly implemented, a drainage tube is placed, the sternum is closed with steel wire, and the incision is sutured layer by layer.

IV. Statistical analysis

We used SPSS 22.0 software to process and analyze the data of the thoracoscopic group and the control group in detail to reveal the possible differences between the two groups. In order to more clearly present the distribution of continuous measurement data, we used mean ± standard deviation or median and quartiles to express it. This expression not only provides the central trend of the data, but also reflects the degree of dispersion of the data, so that readers can have a more comprehensive understanding of the distribution of the data. For the categorical variables in the data, we used the chi-square test to test [43]. The chi-square test is a statistical method used to compare the difference between the actual observed frequency and the expected frequency. The chi-square test is used to determine whether there is a significant difference between the two groups of categorical variables. If the data follow a normal distribution, the T test is used for analysis of continuous variables; if the data do not conform to a normal distribution, a non-parametric test is used [43]. The P value indicates the probability that the observed effect is caused by random error. If the P value is less than 0.05, it is generally believed that the observed effect is not caused by random error but is statistically significant.

V. Ethical Review

This study was approved by the Ethics Committee of Shanghai Yuanda Cardiothoracic Hospital, with approval number: yd2021-025-01.

Research Results

I. Comparison of basic data of the two groups of patients

From the data, it can be seen that there are some significant differences in the basic data of the two groups of patients before surgery (see Table 1 for details). In terms of average age, the average age of patients in the thoracoscopic group was 49.47±11.24 years old, which was significantly lower than that of the control group (55.86±13.92 years old) (P=0.0000); in addition, the proportion of patients over 60 years old was also lower in the thoracoscopic group than in the control group (20.8% vs. 38.4%, p=0.0175). The proportion of patients with aortic regurgitation was significantly higher in the thoracoscopic group than in the control group (22 (91.7%) vs. 70.2%, p=0.0132). The diameter of the aortic annulus was significantly higher in the thoracoscopic group than in the control group (29.96±3.17 vs. 26.17±6.59, p=0.0128). The history of smoking, hypertension, and hyperlipidemia was significantly different between the thoracoscopic group and the control group. The other preoperative clinical information, such as past medical history (stroke, coronary heart disease, diabetes, chronic renal failure, peripheral vascular disease, etc.), NYHA grade, and left ventricular ejection fraction before surgery, did not differ significantly between the two groups. (Table 1)

Table 1: Comparison of basic data between the thoracoscopic group and the control group (before propensity score matching)

parameter	Thora. group（n=24)）	Control group（n=366	P
Sex（male/female）	17/7	269/97	0.0172
age	49.47±11.24	55.86±13.92	0.0000
≥60	5（20.8%）	141（38.4%）	0.0175
BMI（Kg/m2）	23.52±8.18	23.66±9.12	0.8791
Smoking history	4（16.7%）	178（48.7%）	0.0000
History of diabetes	1（4.2%）	17（4.7%）	0.5769
History of high blood pressure	3（12.5%）	91（24.8%）	0.0000
History of hyperlipidemia	1（4.2%）	81（22.1%）	0.0000
History of chronic renal failure	1（4.2%）	4（1.2%）	0.2123
History of stroke	1（4.2%）	4（1.2%）	0.2123
Peripheral vascular disease	1（4.2%）	7（1.8%）	0.4327
NYHA（III or IV）	5（20.8%）	74（20.1%）	0.8897
History of coronary heart disease	1（4.2%）	14（3.8%）	0.8755
Left ventricular ejection fraction	60.58%±6.98	59.45%±7.36	0.4653
Aortic annulus diameter（mm）	29.96±3.17	26.17±6.59	0.0128
Aortic regurgitation	22（91.7%）	257（70.2%）	0.0132
Aortic stenosis	2（8.3%）	109（29.8%）	0.0465

After Propensity score matching, 24 patients were selected as the control group of the thoracoscopic surgery group through 1:1 matching among patients who underwent median incision aortic valve replacement (AVR). The matching model was: gender + age + BMI + NYHA + LVEF, etc. After analysis, there was no significant statistical difference in the basic data between the thoracoscopic group and the control group (after propensity score matching) (see Table 2).

Table 2: Comparison of basic data between the thoracoscopic group and the control group (after propensity score matching)

parameter	Thora. group（n=24）	Control group（n=24）	P
Sex（male/female）	17/7	19/5	0.3348
age	49.47±11.24	50.17±10.43	0.8634
≥60	5（20.8%）	6（25.0%）	0.3063
BMI（Kg/m2）	23.52±8.18	23.19±8.47	0.907
Smoking history	4（16.7%）	5（20.8%）	0.6351
diabetes	1（4.2%）	2（8.3%）	0.4308
hypertension	3（12.5%）	3（12.5%）	1.0000
High cholesterol	1（4.2%）	2（8.3%）	0.4308
Chronic renal failure	1（4.2%）	2（8.3%）	0.4308
History of stroke	1（4.2%）	1（4.2%）	1.0000
Peripheral vascular disease	1（4.2%）	3（12.5%）	0.3086
NYHA（III or IV）	5（20.8%）	5（20.8%）	1.0000
History of coronary heart disease	1（4.2%）	1（4.2%）	1.0000
Left ventricular ejection fraction	60.58%±6.98	60.77%±7.03	0.8179
Aortic annulus diameter（mm）	29.96±3.17	29.34±4.15	0.8963
Aortic regurgitation	22（91.7%）	21（87.5%）	0.6386
Aortic stenosis	2（8.3%）	3（12.5%）	0.6967

2: Surgery-related clinical results of the two groups of patients

The results of the study showed that compared with the control group of traditional open surgery, the average operation time of the thoracoscopic AVR group was improved (188.39±41.78 vs. 169.93±43.56, p=0.0027). The average cardiopulmonary bypass duration and aortic cross-clamping duration in the thoracoscopic group were significantly increased compared with the control group (179.87±47.65min vs. 109.47±19.46min, p<0.0001; 119.53±30.89min vs.68.12±18.08 min, p<0.0001. Moreover, the proportion of patients in the thoracoscopic AVR group who received cardiopulmonary bypass for more than 120 minutes and the aortic cross-section duration for more than 90 minutes was significantly higher than that of the control group (25.0% vs. 4.1% , p<0.0001; 16.7% vs. 4.1%, p=0.0105) In addition, the average ICU observation time of the two groups of patients did not show a significant difference (50.48±37.13 hours vs. 53.05±28.47 hours, p=0.8297.). However, it is worth noting that the average tracheal intubation time of patients in the thoracoscopic AVR group was significantly lower than that of the control group (16.13±6.88h vs. 25.01±17.41h, p=0.0029). In terms of time, the time for patients in the thoracoscopic group was 8.24±4.77 days, compared with 12.03±6.13 days for patients in the control group. After statistical processing, the difference between the two groups was significant (P=0.0017) (Table 3).

There were no significant differences in hemoglobin levels and platelet counts between the two groups of aortic valve replacement (AVR) patients after surgery. In terms of average intraoperative blood loss, the thoracoscopic AVR group had a significantly lower volume than the control group (142.59±108.56ml vs. 261.08±79.78, P<0.0001). Similarly, the average postoperative drainage volume of patients in the thoracoscopic AVR group showed a significantly reduced trend compared with the control group (288.45±201.17ml vs. 399.75±298.08ml, p=0.0298). As for the number of patients who needed to receive blood product treatment after surgery, there were 10 patients in the thoracoscopic group, accounting for 41.7%, and 11 patients in the control group, accounting for 45.8%. There was no significant statistical difference between the two groups. . There was no significant difference between the two groups in terms of average total hospitalization costs. (table 3)

None of the 48 AVR patients died during hospitalization or within one month after surgery, and there was no significant difference in the incidence of major postoperative complications between the two groups (8.3% vs. 12.5%, p=0.8987). Infection-related complications such as lung infection or wound infection were not seen in the thoracoscopic group. One person in the control group was observed to have a pulmonary infection and was successfully discharged after receiving continuous anti-infective treatment. A total of 3 patients in the two groups developed bradyarrhythmias, and sinus rhythm was restored within 14 days of temporary pacemaker treatment. One patient in the control group developed delayed hemopneumothorax after surgery, manifesting as shortness of breath and decreased oxygen saturation, which improved after symptomatic treatment.

Table 3: Comparison of perioperative clinical outcomes and complications between patients in the thoracoscopic group and the control group (after propensity score matching)

parameter	Thora. group（n=24）	Control group（n=24）	P
Total operation time（min）	188.39±41.78	169.93±43.56	0.0027
>200min	5（20.8%）	3（12.5%）	0.0591
Extracorporeal circulation time（min）	179.87±47.65	109.47±19.46	<0.0001
>120min	6（25.0%）	1（4.1%）	<0.0001
Aortic clamping time（min）	119.53±30.89	68.12±18.08	<0.0001
>90min	4（16.7%）	1（4.1%）	0.0105

parameter	Thora. group（n=24）	Control group（n=24）	P
Intraoperative blood loss（ml）	142.59±108.56	261.08±79.78	<0.0001
Postoperative ICU observation time（h）	50.48±37.13	53.05±28.47	0.8297
Postoperative endotracheal intubation time（h）	16.13±6.88	25.01±17.41	0.0029
Postoperative hemoglobin（g/L）	105.89±24.06	106.02±26.38	0.9157
Postoperative platelet（10'9/L）	158.06±65.77	151.66±44.12	0.7638
Postoperative drainage volume（ml）	288.45±201.17	399.75±298.08	0.0298
Blood product use	10（41.7%）	11（45.8%）	0.8563
RBC（U）	0.75±1.28	0.48±1.56	0.4197
plasma（ml）	75.34±104.66	112.77+298.14	0.4963
Postoperative complications	2（8.3%）	3（12.5%）	0.8987
Infection (incision and lung)	0（0%）	1（4.17%）	0.7968
Reoperation due to bleeding	0（0%）	0（0%）	1
Arrhythmias	2（8.3%）	1（4.17%）	0.7253
New postoperative cerebrovascular accident	0（0.8%）	0（0%）	1
Hemothorax	0（0%）	1（4.17%）	0.7968
New onset renal failure after surgery	0（0%）	0（0.8%）	1
die	0（0）	0（0）	-
Postoperative hospital stay（d）	8.24±4.77	12.03±6.13	0.0017
Total hospitalization cost (yuan) (median)	127617	110765	0.5083

Conclusion

Total thoracoscopic cardiac surgery relies entirely on thoracoscopic images under TV monitoring, which is significantly different from thoracoscopic-assisted cardiac surgery. The surgical procedure is performed using surgical instruments through three tiny incisions set in the chest. Compared with traditional open surgery, thoracoscopic surgery has obvious advantages, that is, it has a significantly enlarged surgical field of view, allowing the surgeon to accurately observe the tiny details in the field of view, thus greatly improving the accuracy and meticulousness of the operation. . Thoracoscopic surgery uses a high-definition camera to transmit images of the inside of the chest to a display screen, allowing operations to be performed within a wider field of view. This expansion of the field of view can more accurately determine the location and scope of lesions, reducing the possibility of misjudgment and omission. The camera used in thoracoscopic surgery has high resolution and high definition, and can capture more subtle diseased tissues. This clear image display enables more accurate identification of diseased tissue during surgery, improving the accuracy and safety of surgery. This advantage enables a more comprehensive understanding of the distribution and adjacency of diseased tissues, providing more precise guidance for surgery. The only drawback is that the minimally invasive holes in the chest wall limit the range of movement of thoracoscopic surgical instruments, making the operation more difficult and the curve long. The operation of thoracoscopy is quite challenging in some aspects, and it requires surgeons to have superb operating skills and rich practical experience. Minimally invasive valve replacement technology reduces surgical injuries by minimizing surgical openings, and its core purpose is to successfully complete surgical tasks in a safe and efficient manner. In 2003, the American Thoracic Society (STS) defined minimally invasive cardiac surgery as a type of cardiac surgery that does not require a complete incision of the sternum or the use of extracorporeal circulation equipment. Similarly, Chitwood and Gulielmos et al also expressed the same view [27]. With the rapid development of medical technology, the concept of minimally invasive surgery has gradually become popular and has become an important development direction of modern medicine. In the field of cardiovascular surgery, the widespread application of thoracoscopic technology has promoted the innovation and upgrading of surgical methods. Some heart surgeries, such as mitral valve repair, aortic valve replacement, etc., have been successfully completed through thoracoscopic technology. The widespread application of thoracoscopy technology benefits from doctors' in-depth understanding of the concept of minimally invasive surgery and the continuous improvement of their skills. Thoracoscopic cardiac surgery is a type of cardiac surgery that combines traditional cardiovascular surgery and endoscopic surgery [28]. Currently, with improved techniques and instruments, the operation time has been shortened compared to the past. The indications for thoracoscopic cardiac surgery are also gradually expanding [29], and its advantages are significant: the surgical approach does not use the traditional median sternal incision, but a true minimally invasive incision, entering the chest cavity from the right intercostal space, and the incision is It is small, about 1-5cm, which reduces trauma and relieves postoperative pain for patients [30]. It also has less blood loss, fast recovery, good cosmetic effect, clear vision, and is easier for patients to accept psychologically [31].

Over the past decade, with the rapid development of surgical techniques and instruments, the use of thoracoscopy in cardiac surgery has become increasingly common. At present, total thoracoscopic technology has been widely used in repair surgeries of atrial septal defect (ASD) and ventricular septal defect (VSD), as well as mitral valve and tricuspid valve plasticity or replacement surgeries. In addition, it also plays an important role in surgical procedures such as atrial fibrillation radiofrequency ablation and cardiac tumor resection. Coronary artery bypass grafting has also been reported sparingly. Thoracoscopic surgery refers to the magnification effect of the thoracoscope, the use of tiny incisions to expand the field of view, and observe the fine details of the surgery [32][33]. It combines traditional surgical techniques with the use of modern photography technology and high-tech surgical instruments [31]. Compared with traditional midline sternal incision surgery, video-assisted thoracoscopic surgery can not only reduce patient trauma and intraoperative blood loss, but also promote rapid recovery of patients. It is especially suitable for treatment of patients with poor physical condition [34][35] . However, reports on the use of total thoracoscopy in the treatment of aortic valve disease are relatively sparse.

Aortic valve disease involves valve opening and closing dysfunction, which may be caused by rheumatism, degeneration, congenital defects, infection or immune-related diseases, affecting the structure and function of the aortic valve and the surrounding aortic valve annulus. The aortic valve, the vital connection between the heart and the aorta, is also affected. Degenerative changes, rheumatic diseases, and congenital abnormalities are intertwined factors that together lead to the occurrence of aortic stenosis (AS). One of the main causes of aortic stenosis in the elderly is degenerative changes. As we age, the aortic valve gradually becomes calcified, causing the valve to become stiff and unable to fully open. This change restricts the flow of blood from the heart to the aorta, causing aortic stenosis. This narrowing not only increases the burden on the heart, but may also lead to a gradual decline in heart function. On the other hand, rheumatic diseases cause valve adhesion, and the adhered valve cannot open and close normally, causing aortic valve stenosis [36]. In this case, patients may experience symptoms such as palpitations, difficulty breathing, and fatigue, which may even be life-threatening in severe cases. In addition to the elderly and patients with rheumatic diseases, congenital aortic valve abnormalities such as bicuspid or unileaf malformation are also an important factor leading to aortic stenosis. [36]. This abnormal valve may cause blood to form a vortex between the heart and the aorta. The vortexed blood continuously impacts the valve, which may cause fibrosis and calcification of the valve, thereby causing aortic valve stenosis. Aortic valve reflux (AR) is mainly caused by rheumatic and infectious diseases. These diseases lead to lesions of the aortic valve and aortic root, resulting in shortening of the distance between the valve and the annulus, resulting in aortic regurgitation. Insufficient valve function. Aortic root dilation, such as Marfan syndrome, can lead to aortic annulus dilatation and aortic valve regurgitation even if the valve structure is normal [36].

The aortic valve is located in an important part of the heart, playing a key role in the blood supply of the coronary arteries and ensuring blood circulation throughout the body. Aortic stenosis causes greater pressure on the left ventricle, causing ventricular hypertrophy to compensate to keep the heart's output constant. The systole of the ventricle becomes longer, and the oxygen consumption of the myocardium also increases. At the same time, the end-diastolic pressure of the left ventricle increases and the blood flow of the coronary arteries decreases, resulting in reduced subendocardial perfusion, which may cause insufficient blood supply to the myocardium; if the area of the valve orifice is less than 1 square centimeter, the transvalvular pressure difference will Increased cardiac output becomes difficult to maintain, resulting in corresponding clinical manifestations. When aortic valve regurgitation occurs, blood will flow back into the ventricles during diastole, resulting in increased blood reception in the ventricles during diastole. Secondly, aortic valve regurgitation will cause the heart to increase myocardial contractility in order to maintain normal pumping function, which will increase myocardial oxygen consumption. At the same time, reflux will also affect the blood flow of the coronary arteries, preventing the myocardium from receiving adequate blood supply, leading to myocardial ischemia and compensatory left ventricular hypertrophy.

In view of the unique anatomical characteristics of the aortic root, its surrounding space is relatively narrow, making minimally invasive surgical procedures extremely complex, further promoting the application and development of total thoracoscopic surgery in the field of aortic valve replacement. Vola M et al. [37] first reported the world's first total thoracoscopic aortic valve replacement surgery in 2014, and conducted a detailed study on 14 low-risk patients who underwent total thoracoscopic aortic valve replacement surgery in 2016. Subsequent studies ultimately achieved significant and encouraging therapeutic effects [38].

For half a century, traditional midline incision and total sternotomy have been widely used in the surgical treatment of cardiac and macrovascular diseases. This method was first reported for in situ aortic valve replacement in 1964 [39]. This method has the characteristics of good visual field display, accurate surgical results, convenient handling of intraoperative bleeding and emergency situations, and high safety, and is suitable for treating various aortic valve problems. However, the incision of this operation is deep and wide, resulting in large wounds and excessive bleeding. Various sternal complications are prone to occur after the operation, such as sternal infection and sternal incision and other serious conditions, which may lead to the death of the patient. With the widespread application of minimally invasive concepts in surgery, thoracoscopic AVR technology has gradually matured [40][41]. This study aims to select the most appropriate treatment plan for patients with aortic valve disease in our hospital. Therefore, a comparative analysis was conducted on these patients who underwent conventional thoracotomy and total endoscopic aortic valve replacement surgery.

This study used propensity score matching technology to accurately match the basic clinical data of patients with traditional thoracotomy and patients with total thoracoscopic aortic valve replacement, and compared the short-term prognosis of patients with traditional midline thoracotomy. The study showed that there was no significant difference in surgical mortality or reoperation rates between the thoracoscopic group and the control group during hospitalization. This result is consistent with the results of foreign studies, indicating that minimally invasive thoracoscopic technology is also a safe and reproducible operation for the treatment of aortic valve disease in China.

The three-incision technique under total thoracoscopic surgery is also the core method of minimally invasive mitral valve surgery in our center. Combining domestic and foreign technical experience, we have more than ten years of experience in thoracoscopic surgery. The technical key points of faster and more effective total thoracoscopic aortic valve replacement are summarized as follows:

① The main incision is made between the third or fourth ribs on the right front side of the chest. This method can clearly display the aortic valve and facilitate surgical operation. It also has the advantages of small trauma and exquisite and beautiful incision.

②For patients with good peripheral vascular conditions (including iliac vessels and femoral arteries and veins), the use of direct inguinal cannulation technology can help reduce surgical time.

③ During the process of freeing the intercostal muscles, its length can be appropriately extended, and its size can be slightly larger than the skin incision to minimize damage when opening the intercostal muscles.

④ The use of soft tissue protective devices can not only protect the incision during surgery, but also effectively prevent tissue fragments from entering the heart and causing adverse consequences.

⑤ On the one hand, surgeons must cultivate three-dimensional awareness and practice hard to solve the spatial dislocation problem caused by two-dimensional vision during surgery. On the other hand, to meet the needs of minimally invasive cardiac surgery, specific surgical instruments are required, such as carefully designed long pen-shaped needles and special endoscopic knotting devices.

⑥ When performing purse-string suturing on the ascending aorta, it is crucial to accurately control the depth and shallowness of the needle insertion. Especially when performing purse-string suturing on the aortic root, a cold perfusion needle must be used and ensure proper operation. Once bleeding occurs or the hematoma expands and cannot be remedied, it is necessary to quickly change to a normal position and open the chest.

⑦ During the process of blocking the ascending aorta, the upper clamp should be used gently to avoid damaging the posterior wall of the aorta, right pulmonary artery and main pulmonary artery.

⑧ In the entire process of thoracoscopic aortic valve replacement, all visual information is captured by the thoracoscope. In particular, every detail of the aortic valve needs to be maintained within the core visual range. Therefore, the surgeon's assistant responsible for thoracoscopic surgery must have a deep understanding of various parameters and characteristics, and have a deep and solid understanding of the entire surgical process and the anatomy of the aortic valve. In order to assist the surgeon in exposing the surgical field well, quickly and accurately during the entire operation process, it is convenient for the surgeon to perform the operation.

⑨ Once during the thoracoscopic surgery, intracardiac malformation or hemostasis difficulty that was not recognized before the operation are discovered, the original median thoracotomy incision method should be flexibly adjusted according to the patient's specific situation to prevent unforeseen adverse effects. as a result of.

⑩ During the operation, the surgeon also needs to work closely with the anesthesiologist or cardiopulmonary bypass doctor to complete the operation.

Regarding patient screening: In the initial stage, it is recommended to give priority to those cases with mild stenosis that mainly manifests aortic regurgitation or aortic regurgitation. The size of the aortic root and ascending aorta is also one of the key factors that determine the outcome of surgery. Considering that the operating space in the aortic valve area is relatively limited, even in the case of midline thoracotomy, the lower flap processing and knotting operations of the valve will be quite difficult, and the difficulty will be further increased when operating under endoscopic surgery. big. Therefore, neither the ascending aorta nor the aortic root size should be undersized when screening patients. For patients whose aortic root diameter is less than 25 mm, we need to select carefully, because a sufficiently large aortic root is one of the important factors to ensure the success of the operation. Of course, the diameter of the aorta should not be too large, so that the aortic clamp cannot completely clamp the aorta. At the same time, if there is severe calcification of valve leaflets and annulus, the difficulty and complexity of surgery will increase significantly [38]. This is because the hardened valve and annulus are difficult to operate during surgery and can easily cause complications such as valve tear or annulus rupture. Therefore, selection of the appropriate case and timing of surgery are crucial for this situation. With the accumulation of experience, this technology can be applied to patients with more difficult surgical procedures who require biological valve replacement.

Regarding hospital stay: Almost all current research reports on minimally invasive valve surgery point out that this surgical method can significantly shorten the patient’s hospital stay [42]. In order to avoid the potential impact of selection bias, Sharony et al. used PSM to conduct a comparative study on the clinical outcomes of 233 cases of minimally invasive AVR with the same number as midline incision AVR [43]. It was found that the average hospital stay of patients in the minimally invasive aortic valve replacement (AVR) group was significantly shorter than that of patients in the traditional median sternotomy group (6 days vs. 8 days, $p < 0.001$). This article uses PSM technology to conduct a comparative analysis of the postoperative hospital stay of patients in the thoracoscopic minimally invasive group and the median incision control group. The results showed that the duration of postoperative hospitalization in the minimally invasive thoracoscopic group was significantly reduced compared with the traditional midline incision group (8.24±4.77d vs. 12.03±6.13d, p=0.0017). This result is consistent with earlier studies. The advantages of minimally invasive thoracoscopic cardiac surgery include reduced intraoperative and postoperative blood loss, shortened endotracheal intubation and ICU monitoring time, faster postoperative recovery, and shorter hospital stay. In addition, the study also showed that the total thoracoscopic minimally invasive aortic valve surgery group did not show a significant difference in total hospitalization costs compared with the midline incision surgery group. However, there is currently a lack of accurate and in-depth research on the cost of minimally invasive thoracoscopic surgery. Therefore, it is necessary to further explore the economic benefits of minimally invasive thoracoscopic surgery in the future to better evaluate its application value in clinical practice. But this is evident from the low number of days patients stay in the hospital. In terms of limited medical resources and costs, minimally invasive thoracoscopic valve surgery can save more [44].

Regarding surgical complications: With the advancement of technology, there is no difference between the number of deaths after thoracoscopic surgery and the number of deaths after surgery reported abroad in recent years [45]. This study strictly matched the clinical indicators of the two groups of patients, and the postoperative results showed that there was no difference in the incidence of new stroke between the two groups. In addition, the statistical results showed no significant difference between the two groups of patients in terms of early severe complications, including arrhythmia and new postoperative renal failure, which further supports the need for total thoracoscopic minimally invasive aortic valve surgery. security.

Regarding perioperative bleeding and blood transfusions: Numerous studies have conducted detailed comparisons between thoracoscopic and midline incision valve surgery, and generally found that the amount of blood loss after thoracoscopic surgery was significantly reduced. Dogan and his team conducted a prospective randomized controlled study to compare the differences between the two surgical methods. Their research data show that patients using thoracoscopic technology have significantly less postoperative thoracic drainage volume than patients with traditional midline incision (240±69ml vs. 495±165ml, P=0.008) [46]. In this study, we made detailed statistics and analysis of bleeding during AVR surgery and postoperative drainage data. The results clearly showed that the average blood loss during surgery and postoperative drainage volume of patients in the total thoracoscopy group were significantly lower than those in the control group. This finding further supports the advantages of thoracoscopic surgery in reducing postoperative bleeding. The patient's postoperative bleeding is reflected in the amount of postoperative drainage [35]. Therefore, it is easy to understand that it is easy to understand that the total thoracoscopic cardiac surgery, which abandons the median sternotomy incision and uses three tiny incisions on the right side, results in relatively less blood loss during the operation and thus the postoperative drainage volume.

Other perioperative issues: Total thoracoscopic aortic valve surgery from the right side of the chest requires independent ventilation of the left lung. At this time, the right lung will be in a state of atelectasis. Postoperatively, the risk of recruitment pulmonary edema (RPE) may be increased. The causes of RPE are mostly closely related to the mechanical or biological damage to pulmonary microvessels after VATS, and its formation mechanism is quite complex. At the same time, free radicals and polymorphonuclear leukocytes play a crucial role in the occurrence of retinal pigment epithelium (RPE). Ischemia-reperfusion injury of the lungs and the inflammatory response induced by cardiopulmonary bypass (CPB) may accelerate the development of these pathological processes. Extracorporeal membrane oxygenation (ECMO) has shown high efficacy in treating patients with extremely severe RPE. Current research shows that a single dose of dexamethasone after induction of anesthesia can effectively prevent the occurrence of postoperative RPE [47]. In this study, no obvious symptoms directly related to RPE were observed. Long-term lung ischemia during surgery can be avoided, and RPE can be prevented by intermittent ventilation of the right lung during surgery.

Currently, there are still few studies in China on the comparison of intraoperative and postoperative treatment and clinical data between total thoracoscopic aortic valve replacement surgery and conventional thoracotomy surgery. This study provides an in-depth analysis of the advantages and disadvantages of these two surgical methods, aiming to provide valuable statistical data and practical clinical experience for clinical research and treatment. Although this article is a single-center, retrospective analysis, there are some limitations, and the level of evidence is not as high as that of randomized controlled trials (RCTs). However, the preoperative clinical characteristics of the study and control groups were effectively balanced through the propensity score matching method (PSM). In addition, this study only deeply explored the perioperative clinical data of patients. In the future, long-term follow-up of all patients is needed, and the long-term prognosis of patients with the two surgical methods will be comparatively analyzed in subsequent studies.

This study focused on monitoring indicators in the early perioperative period and conducted a propensity score matching analysis between patients undergoing total thoracoscopic aortic valve replacement and patients undergoing traditional open surgery. Research shows that the use of thoracoscopic surgery can improve the aesthetics of the incision, relieve the patient's pain during the operation, and promote the patient's rapid recovery. Compared with traditional surgery, this method does not lead to early postoperative mortality and serious complications. It will not increase the treatment costs and risks for patients, so it can be considered as a surgical option for patients with aortic valve disease. The study also showed that compared with conventional open surgery, total thoracoscopic aortic valve replacement for aortic valve disease is feasible, safe, reduces hospital stay and hospitalization time, and achieves better minimally invasive and aesthetic results. The facial effect has laid a theoretical and clinical foundation for the application and promotion of thoracoscopy technology, which has important scientific significance.

In the past two decades, total thoracoscopic cardiac surgery has rapidly developed and become widely accepted due to its advantages such as minimal trauma, accelerated recovery process, and good cosmetic results. Although total thoracoscopic aortic valve replacement surgery has longer external circulation time and aortic cross-clamp time compared with traditional midline thoracotomy surgery, scientific research has shown that there is a lower risk in postoperative mortality, stroke incidence, and arrhythmia. In terms of incidence, etc., it is not significantly different from traditional surgical methods, and the long-term results are comparable. Therefore, more and more patients with aortic disease prefer total thoracoscopic surgery due to its advantages of mild pain, rapid recovery, lower hospitalization costs, and excellent cosmetic results.

References

1.Yan Haiqiang, He Changjin. Current status and development of valvular heart disease treatment[J]. Fujian Medical Journal, 2014, 36 (02): 140-141+143.

2. Gao Runlin. Current status of valvular heart disease in China[J]. West China Medical Journal, 2018, 33 (02): 127- 131.

3.BAUMGARTNER H, FALK V, BAX J J, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease[J]. Eur Heart J, 2017, 38 (36): 2739-91.

4.YANG Y, WANG Z, CHEN Z, et al. Current status and etiology of valvular heart disease in China: a population-based survey[J]. BMC Cardiovasc Disord, 2021, 21 (1): 339.

5. Cui Ming, Chen Fengrong. Overview of the causes of valvular heart disease in the 21st century [J]. Lingnan Cardiovascular Diseases, 2012, 18 (02): 202-204.

6. Lu Zirun, Wang Dongjin. Advances in the treatment of aortic valvuloplasty for aortic regurgitation [J]. Chinese Journal of Clinical Thoracic and Cardiovascular Surgery, 2018, 25 (02): 177-180.

7. TAYLOR W J, THROWER W B, BLACK H, et al. The surgical correction of aortic insufficiency by circumclusion [J]. The Journal of thoracic surgery, 1958, 35 (2): 192-205 passim.

8.BASMADJIAN L, BASMADJIAN A J, STEVENS L M, et al. Early results of extra-aortic annuloplasty ring implantation on aortic annular dimensions[J].The Journal of thoracic and cardiovascular surgery,2016,151(5):1280-5 e1.

9. HARKEN D E,TAYLOR W J,LEFEMINE AA,et al.Aortic valve replacement with a caged ball valve[J].The American journal of cardiology,1962,9(292-9.

10. BORGER MA,MO USTAFINE V,CONRADI L,et al.A randomized multicenter trial of minimally invasive rapid deployment versus conventional full sternotomy aortic valve replacement[J].Ann Thorac Surg,2015,99(1):17-25.

11. RAO P N,KUMAR A S.Aortic valve replacement through right thoracotomy[J].Texas Heart Institute journal, 1993, 20 (4): 307-8.

12. KONERTZ W, WALDENBERGER F, SCHMUTZLER M, et al. Minimal access valve surgery through superior partial sternotomy: a preliminary study [J]. J Heart Valve Dis, 1996, 5 (6): 638-40.

13. UENO G, OHNO N. Aortic valve approaches in the era of minimally invasive cardiac surgery [J] . Surg Today, 2020, 50 (8): 815-20.

14. MALAISRIE S C, BARNHART G R, FARIVAR R S, et al. Current era minimally invasive aortic valve replacement: techniques and practice [J]. The Journal of thoracic and cardiovascular surgery, 2014, 147 (1): 6-14.

15.HOSOBA S,ITO T,ORII M.3D-endoscopic assisted concomitant mitral and aortic valve

surgery[J].The Annals of thoracic surgery,2021,
16.SCHMITTO J D,MOKASHI S A,COHN L H.Minimally-invasive valve surgery[J].Journal of the American College of Cardiology,2010,56（6）:455-62.
17.FOLLIGUET T A,VANHUYSE F,KONSTANTINOS Z,et al.Early experience with robotic aortic valve replacement[J].European journal of cardio-thoracic surgery:official journal of the European Association for Cardio-thoracic Surgery,2005,28（1）:172-3.
18.TAMADON I,MAMONE V,HUAN Y,et al.ValveTech:A Novel Robotic Approach for Minimally Invasive Aortic Valve Replacement[J].IEEE Trans Biomed Eng,2021,68（4）:1238-49.
19.BALKHY H H,LEWIS C T P,KITAHARA H.Robot-assisted aortic valve surgery:State of the art and challenges for the future[J].Int J Med Robot,2018,14（4）:e1913.
20.VOLA M, FUZELLIER J F, CHAVENT B, et al. First human totally endoscopic aortic valve replacement: an early report [J]. J Thorac Cardiovasc Surg, 2014, 147（3）: 1091-3.
21.VOLA M,FUZELLIER J F,CAMPISI S,et al.Closed chest human aortic valve removal and replacement:Technical feasibility and one year follow-up[J].Int J Cardiol,2016,211（71-8.
22.BORGER M A.Introduction:minimally invasive aortic valve surgery supplement[J].European journal of cardio-thoracic surgery:official journal of the European Association forCardio-thoracic Surgery,2018,53（suppl_2）:ii1-ii2.
23.SCHLOMICHER M,HALDENWANG P L,MOUSTAFINE V,et al.Minimal access rapid deployment aortic valve replacement:initial single-center experience and 12-month outcomes[J].The Journal of thoracic and cardiovascular surgery,2015,149（2）:434-40.
24. Gao Runlin. Current status of valvular heart disease in China [J]. West China Medicine, 2018, 33 (02): 127-131.
25. STACHON P, KAIER K,OETTINGER V,et al.Transapical aortic valve replacement versus surgical aortic valve replacement:A subgroup analyzes for at-risk populations[J].The Journal of thoracic and cardiovascular surgery,2021,162(6):1701-9 e1.
26. JUNQUERA L,KALAVROUZIOTIS D,COTE M,et al.Results of transcarotid compared with transfemoral transcatheter aortic valve replacement[J].The Journal of thoracic and cardiovascular surgery,2022,163(1):69-77.
27. Felger JE,Nifong LW,Chitwood WR,Jr.The evolution of and early experience with robot-assisted mitral valve surgery[J].Surg Laparosc Endosc Percutan lech,2002,12(1):58-63.
28. Wang Gaifei, Wang Wujun, Cheng Yunge, et al. Chinese expert consensus on thoracoscopic cardiac surgery. Chinese Journal of Thoracic and Cardiovascular Surgery, 2012, 28: 193-194.
29.Wang Qiang, Xiao Mingdi, Yuan Zhongxiang, et al. Animal experimental study and clinical application of thoracoscopic aortic valve and mitral valve double valve replacement. Chinese Journal of Minimally Invasive Surgery, 2006, 6: 845-846.
30. Zhang Min, Wu Qingchen. Research progress of minimally invasive cardiac surgery. Chongqing Medicine, 2014, 19: 2517-2520.
31. Dogan S, Aybek T, Risteski PS, et al. Minimally invasive port access versus conventional mitral valve surgery: a prospective randomized study. Ann Thorac Surg, 2005, 79: 492-498.

32. Wang Lei, Zhang Zhenzhong. Comparison of clinical efficacy of coronary artery bypass grafting under extracorporeal circulation and without extracorporeal circulation [J]. Contemporary Medicine, 2016, 22 (30): 89-90.
33. Guo Nengrui, Sun Pengfei, Zhang Sen, et al. Clinical summary of minimally invasive cardiac surgery through a small incision on the right anterolateral chest under closed extracorporeal circulation [J]. Chinese Journal of Circulation, 2016, 31 (9): 888-891.
34.Long Yanli, Zhou Rong, Qi Ming, et al. Clinical analysis of 14 cases of thoracoscopically assisted minimally invasive mitral valve and aortic valve bivalve replacement [J]. Journal of Cardiopulmonary and Vascular Diseases, 2016, 35 (1): 38-40+67.
35. Chen Chong, He Yong. Case-control study of aortic valve replacement with small incision and traditional incision [J]. Chinese Journal of Clinical Thoracic and Cardiovascular Surgery, 2018, 25 (4): 1-4.
36. Lu Feng. Clinical study of minimally invasive aortic valve replacement via right parasternal second intercostal transverse incision[D]. Nanchang University (Medical College), 2020.
37.VOLA M, FUZELLIER J F, CHAVENT B, et al. First human tota.

Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials.

Statements and Declarations

Funding

The authors declare that no fund, grant, or other support were received during the preparation of this manuscript.

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Authors' Contributions

All the authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [Xiaofei Zhang] and [Bin Ni]. The first draft of the manuscript was written by [Xiaofei Zhang], and all the authors commented on previous versions of the manuscript. All the authors read and approved the final manuscript.

Ethical Standards

We declare that all human and animal studies have been approved by the ethics committee and have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All patients provided informed consent prior to their inclusion in the study.

Consent to participate

Informed consent was obtained from all participants who were included in the study.

Consent to publish

The authors affirm that human research participants provided informed consent for publication of the findings.