

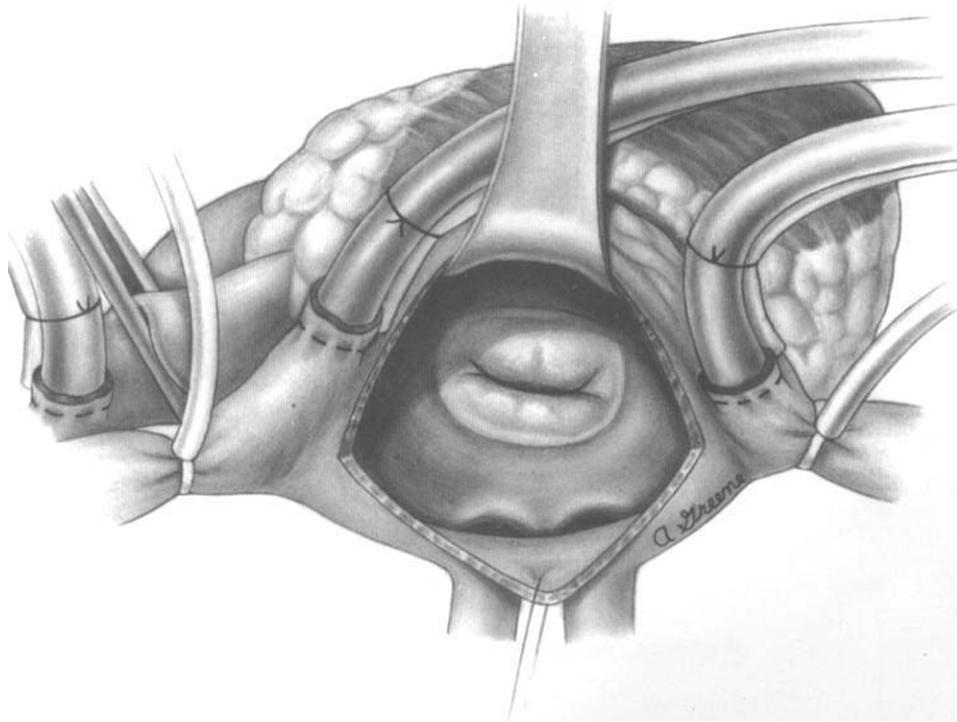
Operative Approaches to the Left Atrium and Mitral Valve: An Update

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Approximately 30,000 to 40,000 operations per year in the United States involve exposure of the left atrium and the mitral valve. In the future we will see an increase in mitral valve procedures because of the growth of programs in the emerging countries where the incidence of rheumatic mitral valve disease remains high, especially in children and young adults. Mitral valve operations, and especially repairs of the valve, demand excellent exposure for precise, anatomical definition and for decisions regarding mitral valve repair, reconstruction, or replacement with preservation of the subvalvular apparatus. Complex operations within the left atrium for tumor resection or for endocarditis involving the fibrous trigone similarly demand excellent exposure and innovative approaches. In addition, the teaching of surgical techniques requires the ability of all to visualize the operation as it evolves.

This review updates a previous experience in 1983,¹ with particular emphasis on newer approaches and techniques for the necessary exposure within the left atrium. Also included are the newer techniques to complement the evolving minimally invasive procedures. This review is limited to the exposure techniques. Specific procedures are discussed in the subsequent articles. No attempt is made to describe the specific operative procedures on the mitral valve or within either the left or right atrium. The major anatomical point to keep in mind with all of the techniques described is that the mitral valve is vertically oriented from the sternum to the thoracic spine. It is also in fibrous continuity with the aortic valve. Exposure involves bringing the vertical position to the view of the surgeon by adjusting the surgical incision, rotation on the horizontal axis, and retraction.

SURGICAL TECHNIQUE

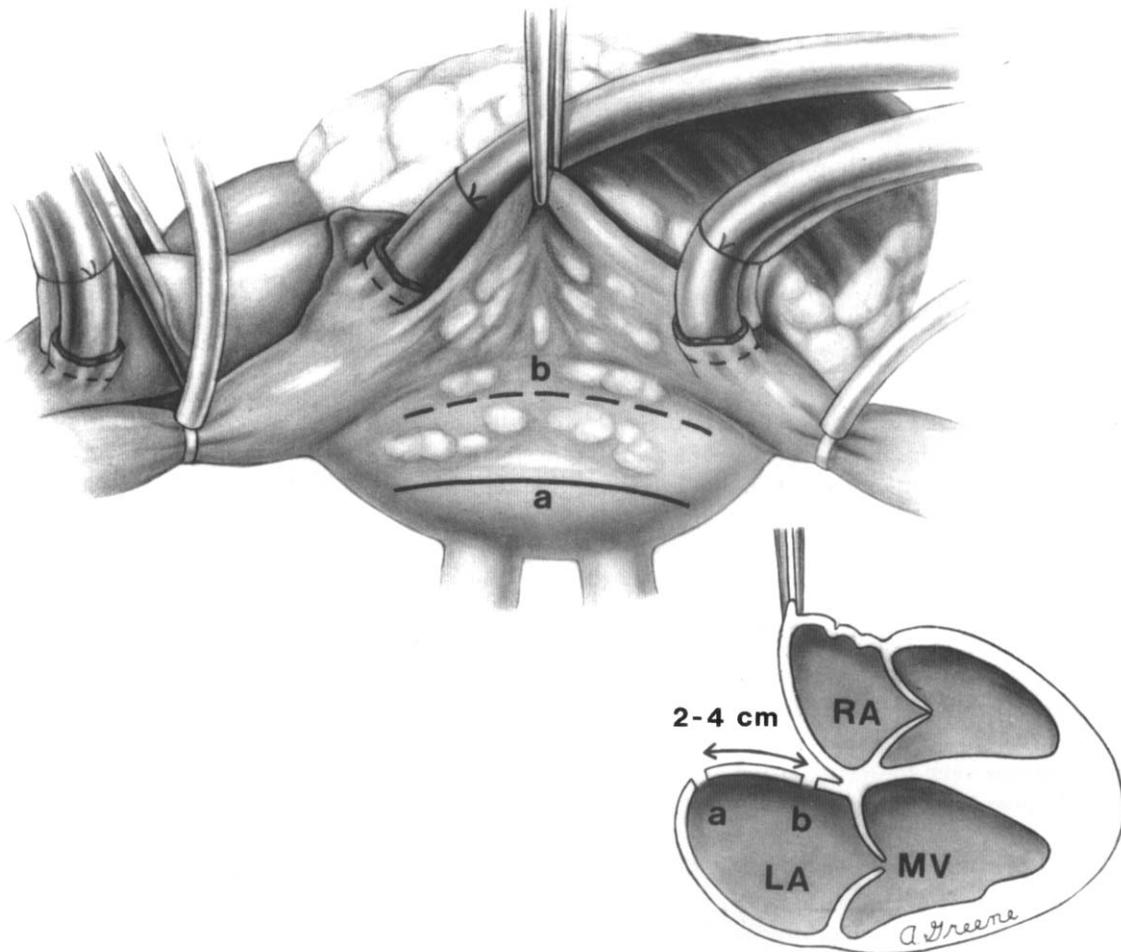


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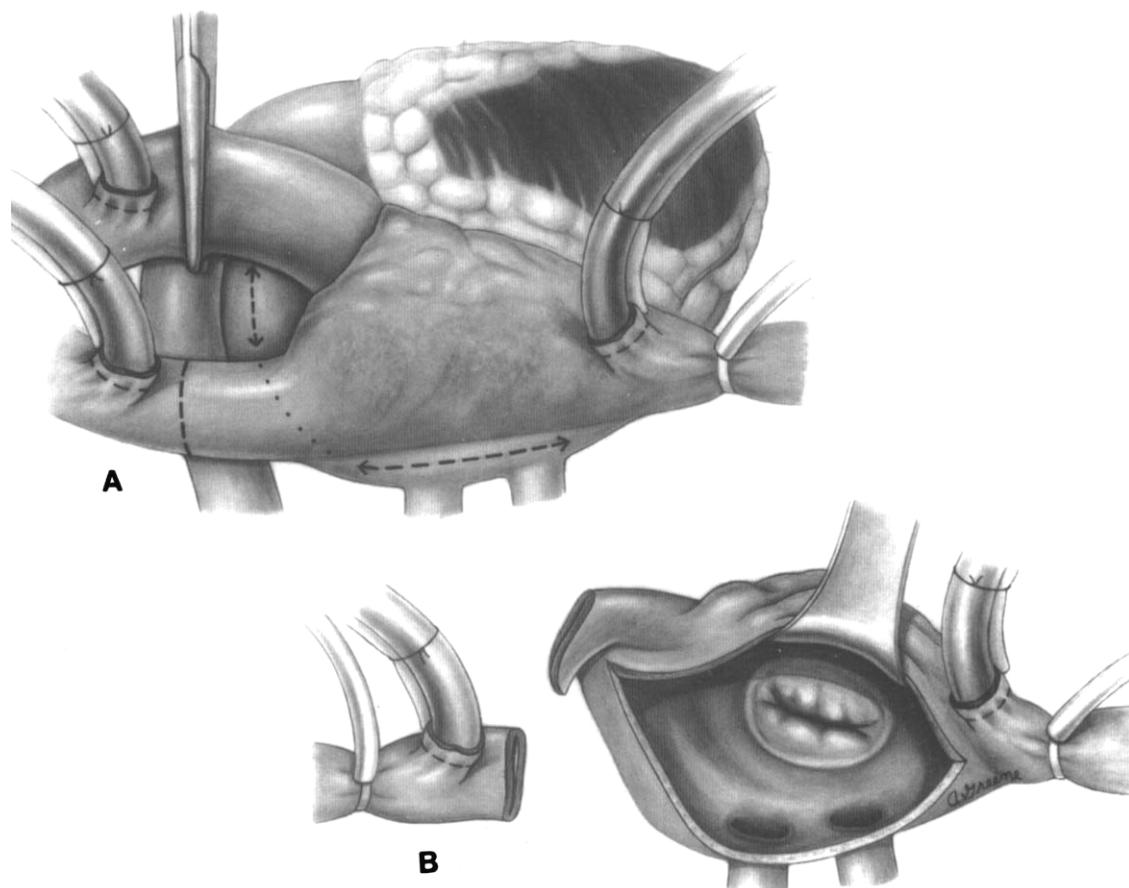
I Traditional approach: Vertical left atriotomy. After a median sternotomy, incise the pericardium longitudinally and firmly suspend the right side to the pectoralis fascia, the drapes, or the retractor, while leaving the left side unsuspended. This allows elevation of the heart, and the rotation of the apex of the heart posteriorly improves the ease of mitral valve visualization. In redo situations, free the pericardial adhesions to allow the heart to fall posteriorly. If the adhesions are dense or dissection is not desired, opening the left chest allows the apex with the attached pericardium to fall posteriorly. Institute total cardiopulmonary bypass through aortic and bicaval venous cannulation. The recent development of vacuum-assisted venous drainage permits the use of smaller venous cannulas. Insert antegrade and retrograde cardioplegia cannulas, and dissect the intrapericardial caval attachments a short distance (2 to 3 cm), using care to avoid injury to the posteriorly located azygos or hepatic veins.² After cardioplegic arrest, apply caval tourniquets or Cooley caval clamps (Pilling Week, Research Triangle Park, NC). Anterior and leftward traction on the inferior vena caval tourniquet further improves exposure. Initiate the vertical left atriotomy anterior to the right superior pulmonary vein and posterior to the interatrial sulcus (Sondergaard's groove). Extend it in a "C" fashion superiorly behind the superior vena cava (SVC), avoiding injury to the right pulmonary artery, and inferiorly into the oblique fissure behind the inferior vena cava (IVC).

Rotate the table to the left. Exposure of the left atrium is accomplished with the hand held Cooley mitral valve retractors (Pilling Week) or the self retaining Cosgrove (Cosgrove Mitral Valve Retractor, Kapp Surgical Instrument, Inc, Cleveland, OH) or Carpentier (Bonchek Modified Carpentier or Lemole-Pilling Mitral Valve Retractor Systems, Pilling Week) systems. Particularly when the IVC-pericardial reflection has been transected, use great care to avoid excessive left atrial traction and the possible consequence of IVC avulsion. Dissection under the SVC with ligation and division of the azygos vein allows extension of the cephalad limb of the atriotomy onto the superior aspect of the left atrium.³

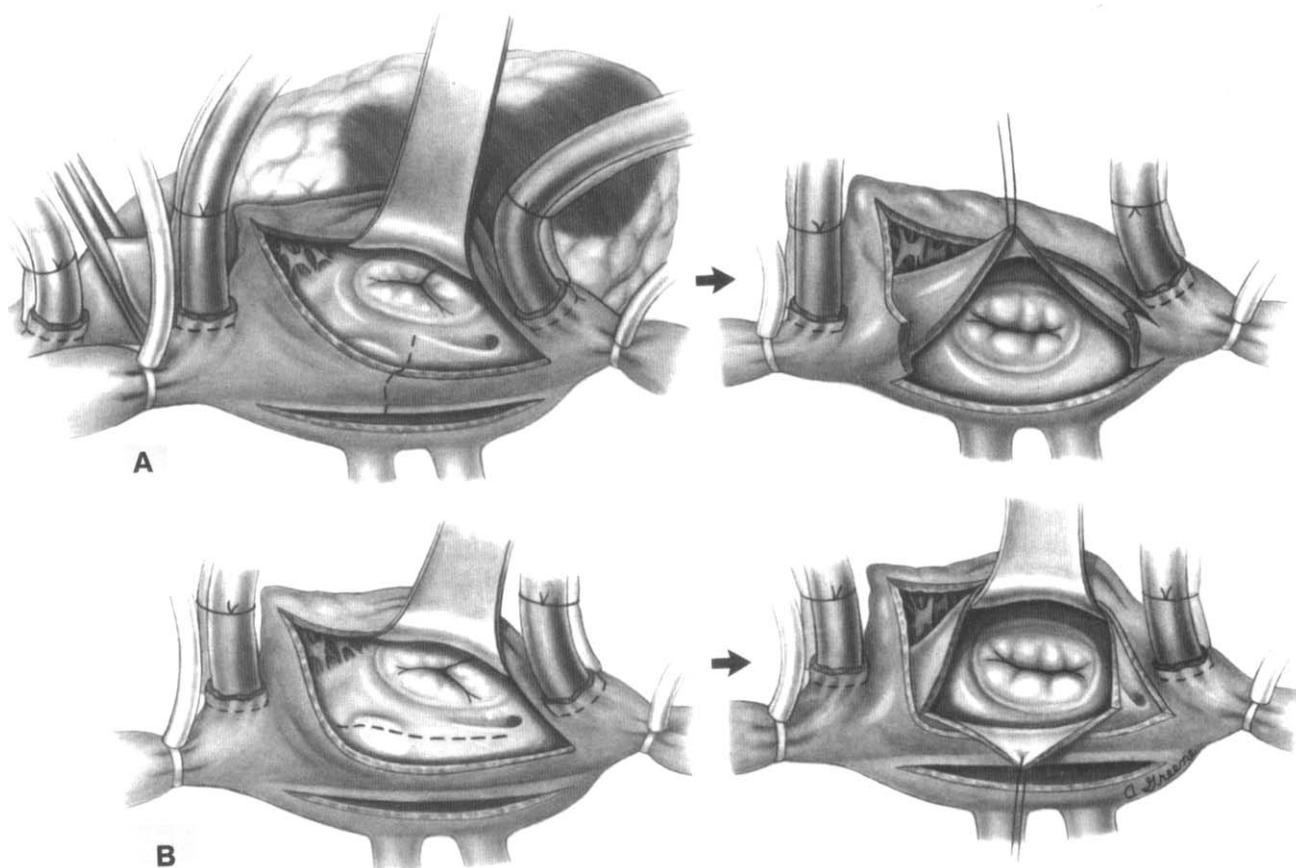
A headlight improves lighting in the tunnel-like exposure of the mitral valve. A pericardial pack behind the apex of the left ventricle increases exposure of the anterolateral papillary muscle, whereas a pack between the inferior diaphragm and the heart increases exposure of the posteromedial papillary muscle. Pushing against difficult-to-see areas of the mitral annulus also aids in visualization. Left heart venting may be achieved through the right superior pulmonary vein, pulmonary artery, left ventricular apex, or the aortic root. Flooding the pericardial cavity with CO₂ reduces the amount of intracardiac air retention. Readminister cardioplegia as appropriate (usually every 10 to 15 minutes). After completion of the intracardiac procedure, close the left atriotomy with a single layer 3-0 polypropylene suture, taking care to approximate the endocardial surfaces in order to achieve maximal closure strength and avoid an intramural atrial dissection.



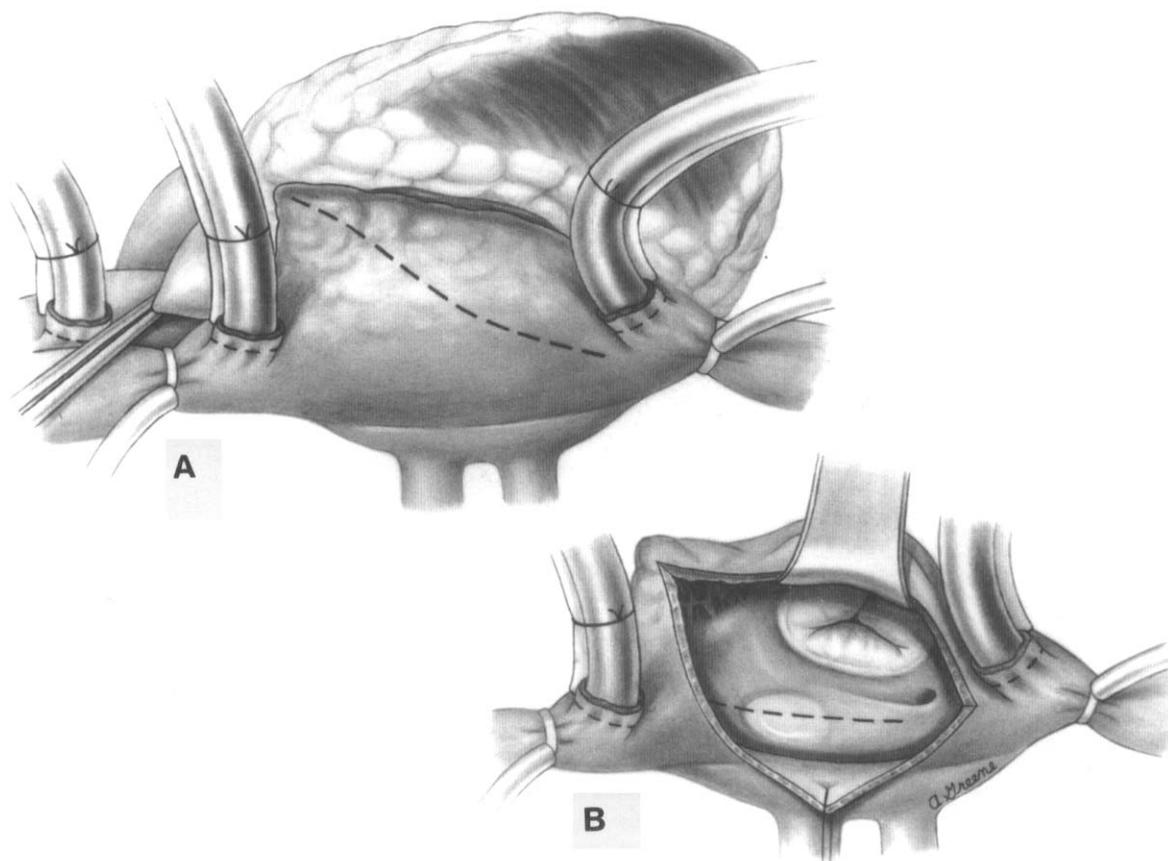
2 The site of the vertical left atriotomy may be at the fatty interatrial junction or may be located closer to the mitral valve by dissecting the Sondergaard's groove, separating the left atrium from the right, and allowing the surgeon to perform left atriotomy 2 to 4 cm medially.^{2,4} This latter incision requires closure where the left atrium is thinner and may carry a greater risk of suture line bleeding.⁵ Accidental entry into the right atrium can allow air lock and obstruction of venous drainage. This is easily controlled by oversewing the entry point.



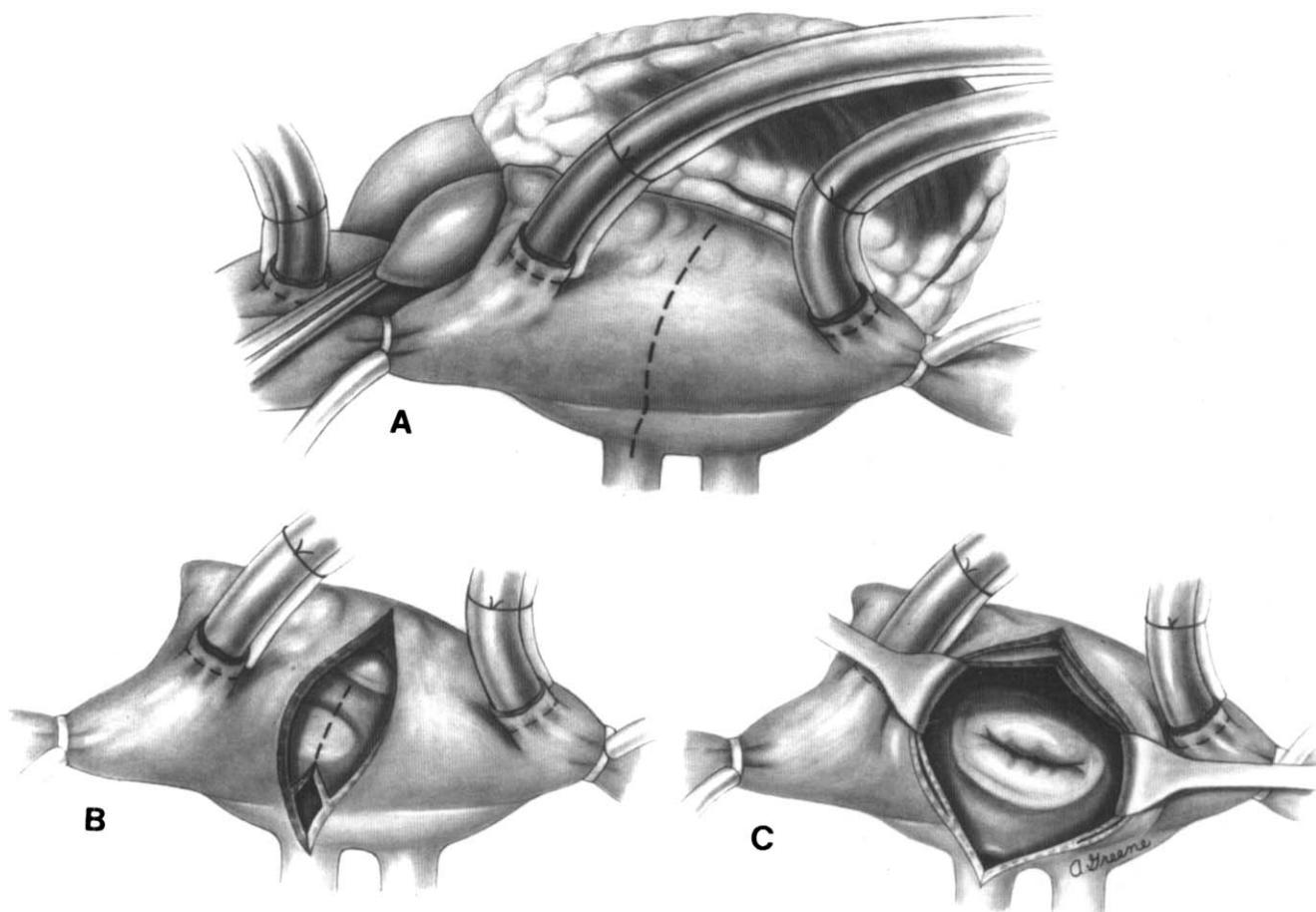
3 Transection of the SVC also allows extension of the cephalad limb of the atriotomy onto the superior roof and permits further rotation of the right atrium and atrial septum to the left and away from the surgeon.^{6,7} The transection should leave at least a 1- to 2-cm cuff on the right atrium and may require moving the SVC cannulation site from the right atrium to the SVC or innominate vein.⁸ Air lock or compromised venous drainage may occur during this transfer. SVC stenosis or thrombosis and sinoatrial node injury have been described with this technique.



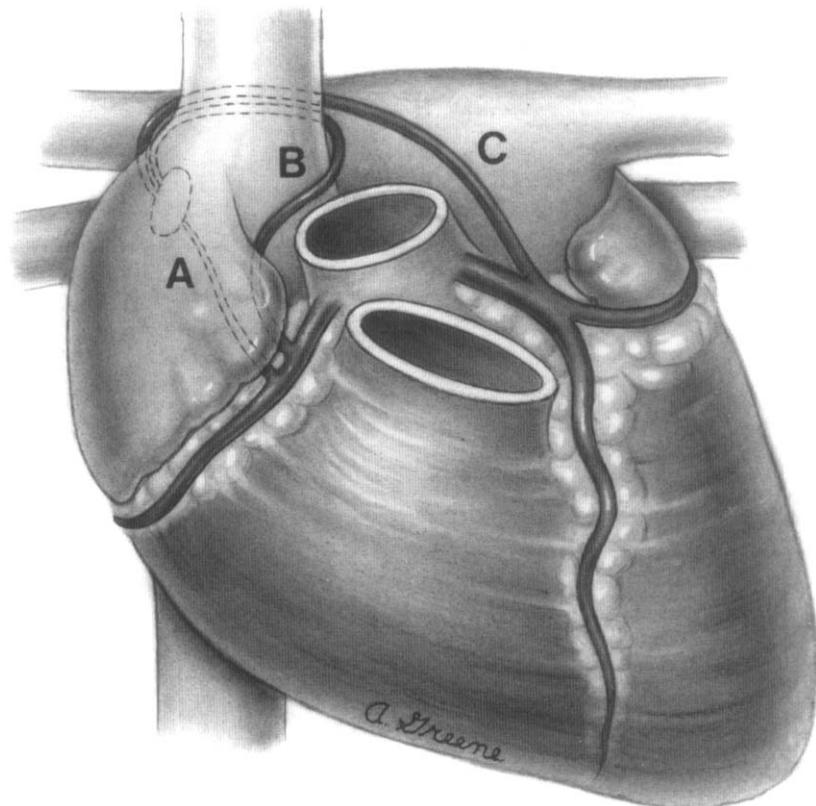
4 Transseptal approach. (A) The vertical left atriotomy may also be converted to a transseptal approach if exposure is inadequate. Begin by performing a vertical right atriotomy parallel to the left atriotomy.^{9,10} Then, open into the left atrium through the septum, with a transverse incision through the fossa ovalis, perpendicular to the two atriotomies, and transecting the bridge of tissue between them. (B) Alternatively, open into the left atrium through a vertical septal incision through the fossa ovalis, parallel to the two atriotomies. With this incision, avoid encroaching on the coronary sinus inferiorly or the dome of the left atrium superiorly. With either of these transseptal incisions, avoid excessive medial displacement that may impinge on the mitral annulus. A lower transverse septal incision has been described but is not illustrated here.¹¹



5 If exposure can be predicted to be difficult, as in the case of a small left atrium or deep chest, a planned transseptal approach may be used.¹²⁻¹⁸ With a vertical right atriotomy, parallel to the atrioventricular sulcus, make a secondary, vertical septal incision through the fossa ovalis, avoiding the coronary sinus.



6 The classic Dubost approach. Make a transverse right atriotomy and extend it laterally into the superior pulmonary vein or between the pulmonary veins into the left atrium. Then, beginning at the edge of the septal incision, carry the incision medially through the fossa ovalis to expose the mitral valve.¹⁹



7 Superior septal approach—Anatomical aspect. The superior septal approach²⁰⁻³⁰ gives superb exposure. Its liability is the possibility of atrial dysrhythmia. Because this may be caused by disruption of the sinoatrial node artery, thorough understanding of its anatomy is important. Three variations of this arterial supply probably explain the inconsistent reports of the incidence of postoperative dysrhythmias.^{31,32} Pathway A, the most common (48% to 80%) courses along the inner anterior border of the right atrium. Pathway B courses anteriorly then behind the SVC to the sino atrial (SA) node. Pathway C arises from the circumflex and also courses posteriorly over the left atrium, behind the SVC to the SA node. A summary of the recent literature fails to solve this dilemma. (Table 1) Utley et al²⁶ have reviewed the incidence of atrial dysrhythmias with the superior septal, the standard vertical left atrial, and the transseptal approaches and concluded that the superior septal approach might better be confined to patients in atrial fibrillation preoperatively, whereas with normal sinus rhythm, the traditional or transseptal approach is preferred. This is borne out with the transseptal approach causing virtually no arrhythmias or heart block (Table 2).

Table 1. Superior Septal Technique: Incidence of Dysrhythmias

Investigators	Year	No. of Patients	Rhythm	
			Preoperative	Postoperative
Guiraudon et al ²⁰	1991	12	NSR 12	NSR 12
Alfieri et al ²¹	1991	111	NSR 52 AF 59	NSR 49/AF 3 AF 57/NSR 2
Berreklouw et al ²²	1991	22	NSR 17 AF 5	NSR 17 AF 5
Kon et al ²⁴	1993	71	NSR 32 AF 37 HB 2	NSR 26/AF 4/Death 2 AF 27/NSR 8/Death 2 HB 2
Smith ²⁵	1993	17	NSR 17	NSR 17 (with ectopic atrial rhythm in 12)
Utley et al ²⁶	1995	46	NSR 28 AF 17 Paced 1	NSR 13/AF 6/Nodal 2/Paced 6 NSR 1/AF 14/Paced 2
Kumar et al ²⁷	1995	65	NSR 36 AF 28 NB 1 Junc 0	NSR 32 AF 26 HB 1 Junc 3
Masuda et al ²⁸	1996	83	NSR 19 AF 62 Junc 1 SSS 1	NSR 15/AF 2/Paced 1/Death 1 AF 54/NSR 7/Paced 2
*Gaudino et al ²⁹	1997	73	NSR 36.9 AF 58.9 Junc 2.7 Block 1.3	NSR 21.8 AF 54.6
Takeshita et al ³⁰	1997	54	NSR 19 AF 35	NSR 17/AF 2 AF 27/NSR 8

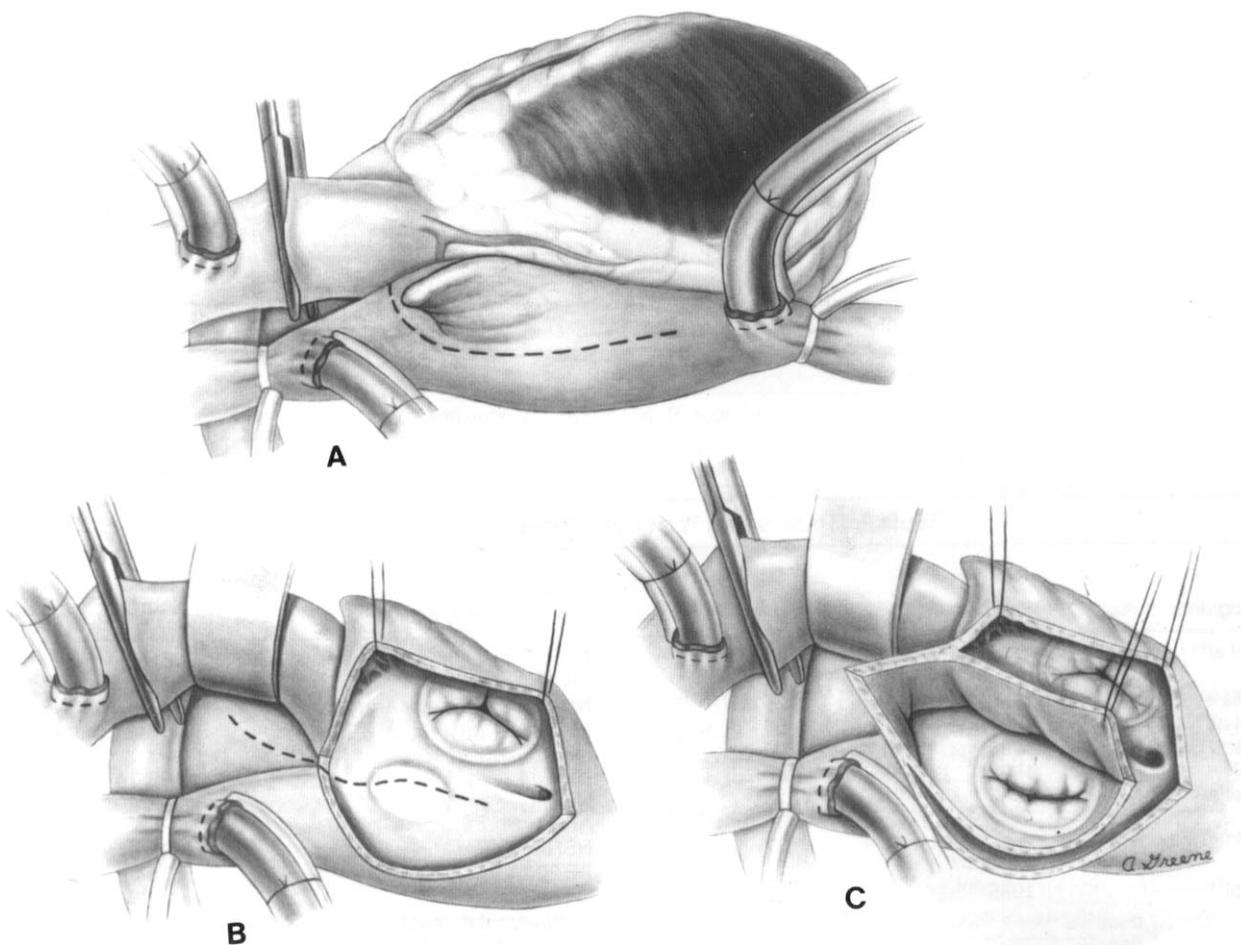
Abbreviations: AF, atrial fibrillation; HB, heart block; Junc, junctional; NSR, normal sinus rhythm; SSS, sick sinus syndrome.

*Numbers represent percentages.

Table 2. Trans-septal Technique: Incidence of Dysrhythmias

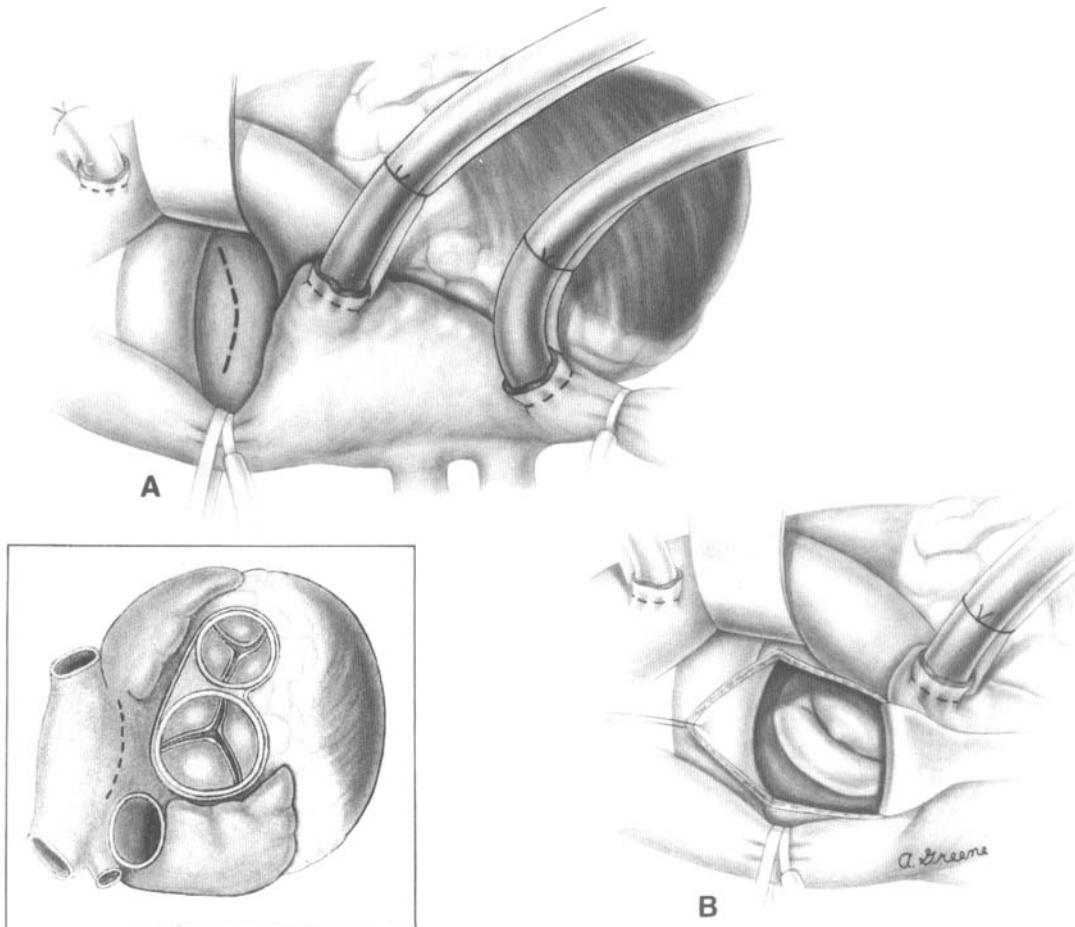
Investigators	Year	No. of Patients	Rhythm Disturbances	
			Preoperative	Postoperative
McGrath et al ¹³	1988	17	NSR 5 AF 12	NSR 5 AF 12
Campanella et al ¹⁰	1990	29	No details; no major arrhythmias	Same
Deloche et al ¹⁵	1990	66	IA	No heart block
Khonsari and Sintek ¹⁶	1990	1,000	NA	—
Hartz et al ¹⁷	1992	20	NSR 14	NSR 14
El-Saegh et al ¹⁴	1993	18	NSR 4 AF 14	NSR 4 AF 14
Utley et al ²⁶	1995	37	NSR 13 AF 20	NSR 9/Nodal 2/Paced 2 AF 14/Paced 4/NSR 1/Nodal 1
Couetil et al ¹¹	1995	25	No details; no apparent damage to conduction system	
Escobar et al ¹⁸	1997	39; (4 superior septal)	NSR 10 AF 29	NSR 10 AF 27/NSR 1

Abbreviations: IA, incomplete analysis; NA, not analyzed.



8 The superior septal approach is also variously known as extended vertical transatrial, extended vertical transseptal, combined superior-transseptal, septal-superior, extended superior septal, extended transseptal, and the transplant approach.²⁵ Begin by placing the SVC cannula lateral to the right atrial appendage or in the SVC directly. Make a longitudinal (vertical) right atriotomy anterior to the sulcus terminalis. Carry the incision cephalad around the superior base of the atrial appendage, or directly through the appendage, to reach the atrial septum. Avoid the sino-atrial node, but keep the incision 1 to 2 cm from the right ventricle to allow safe closure. Incise the septum vertically through the fossa ovalis, directly under and parallel to the right atriotomy, extending the incision superiorly to the superior apex of the right atriotomy. Continue the confluence of these two incisions superiorly into the dome of the left atrium. Keep this incision away from the thin tissue at the base of the left atrium near the aorta and left ventricle, away from the right pulmonary artery, and away from the posterior side of the ascending aorta near the left coronary artery. Tagging or marking the junction of these three incisions facilitates subsequent reapproximation and closure. Retract the atrial septum gently to avoid atrioventricular nodal injury.

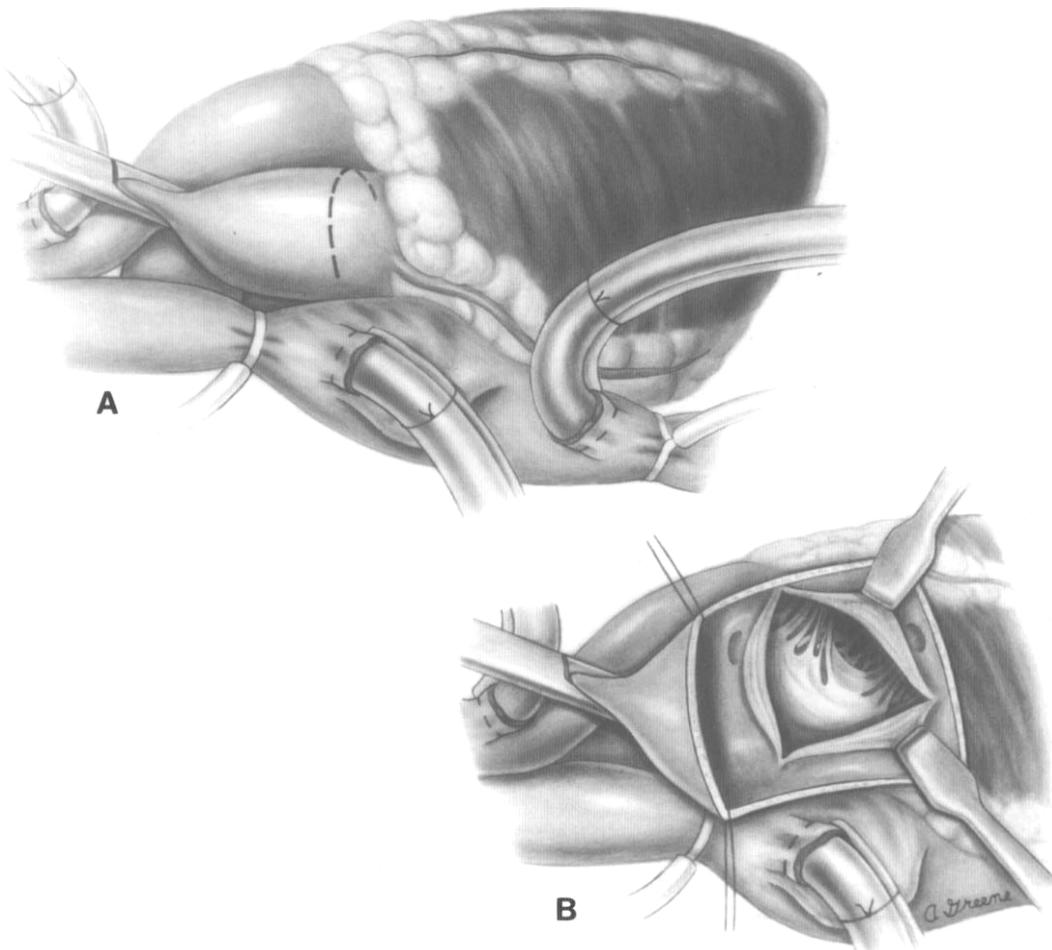
Reconstruct the atria with 3-0 or 4-0 polypropylene sutures, beginning one suture line at the superior pole of the left atriotomy and another at the inferior pole of the septal incision. Join these suture lines at the junction of the three incisions in the left atrium, septum, and right atrium. Then complete the closure of the right atriotomy.



9 The superior approach to the mitral valve was described by Meyer et al,³³ and advocated by Saksena et al,³⁴ Molina,³⁵ and Hirt et al.³⁶ This approach allows adequate exposure of the mitral valve, with minimal to moderate retraction of the aorta and SVC. It also allows a view of the mitral annulus more perpendicular to its plane than do other approaches.

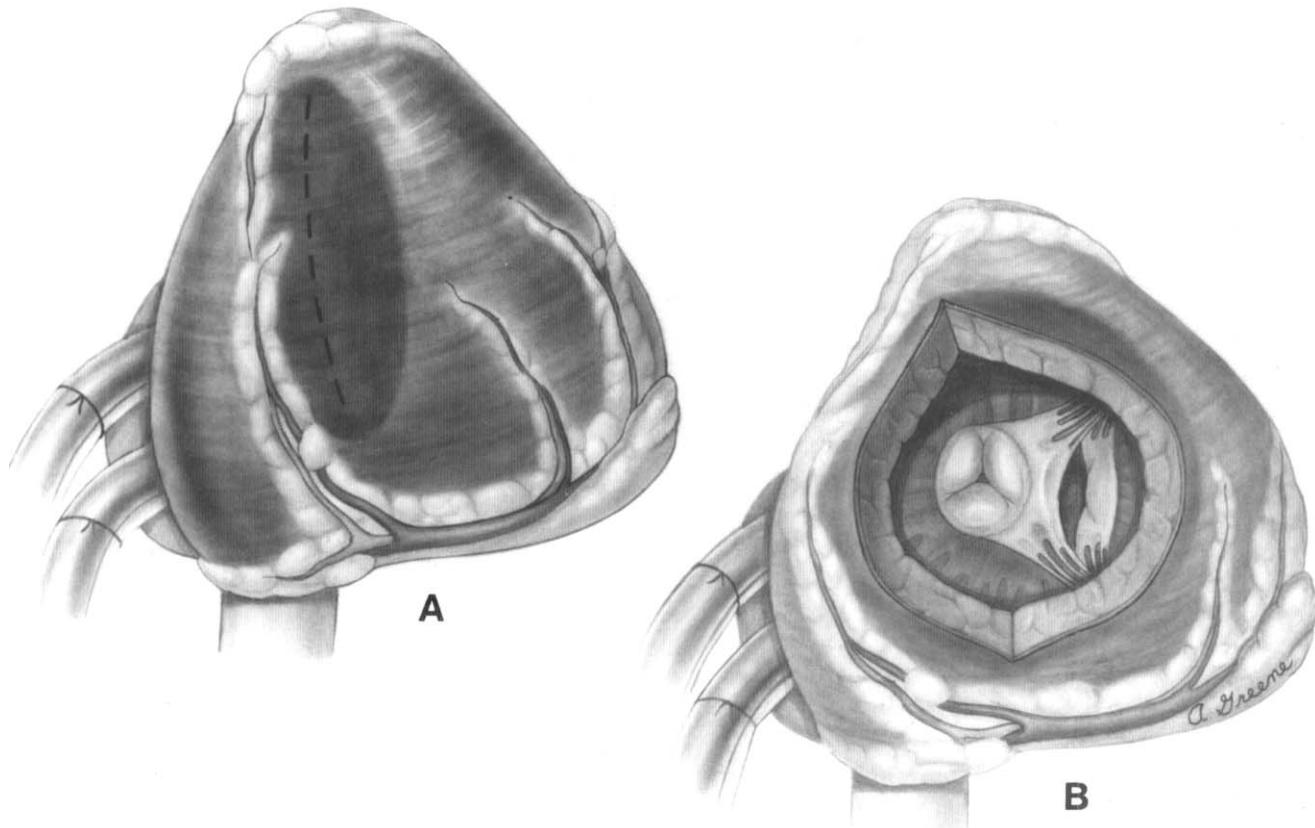
Dissect the aorta and the SVC from the right pulmonary artery behind them. Avoid injuring the left coronary artery behind the aorta. Mobilize the SVC from cephalad to the right pulmonary artery inferiorly to the groove between the SVC and the right atrium (sulcus terminalis). In the presence of pulmonary hypertension, care must be taken not to injure an enlarged pulmonary artery. Retract the aorta anteriorly and to the left, and the SVC anteriorly and to the right, to expose the left atrial dome. Excessive aortic retraction causes aortic insufficiency. With the aorta occluded, excessive retraction renders ineffective the administration of antegrade cardioplegia. A calcified or debris-laden aorta increases the hazard of emboli and constitutes a relative contraindication to the use of this approach. Be careful not to injure the sinoatrial node artery during this dissection.³⁷

Incise the superior dome of the left atrium transversely as shown. Avoid extending the incision too far to the left under the aortic root and into the thin-walled left atrial appendage. Instead, provide greater exposure if necessary by extending the incision to the right and into the right superior pulmonary vein. If exposure is still inadequate, the incision may be converted into a modified superior septal approach.



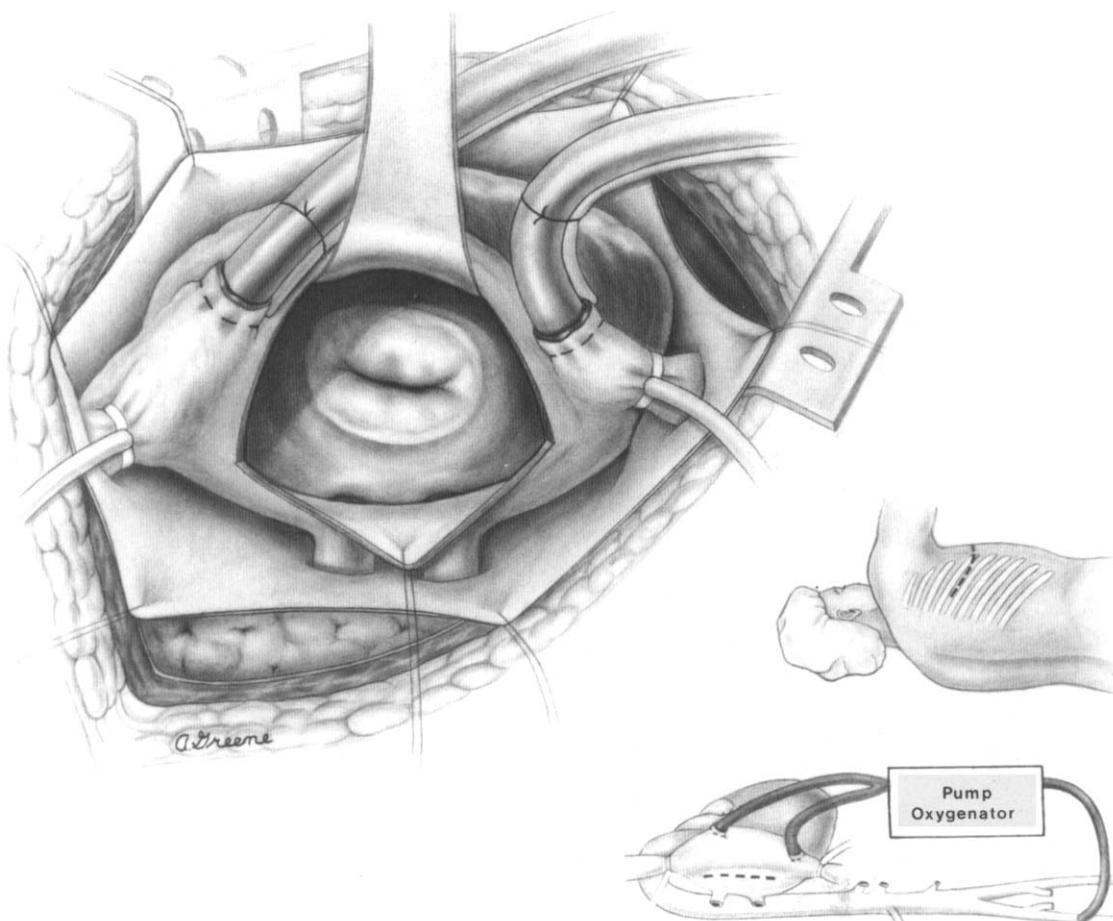
10 **Transaortic approach—Perform a standard aortotomy.** After excising the aortic leaflets, retract the aortic root and annulus to expose the anterior leaflet of the mitral valve. Excise the anterior leaflet and chordae. The posterior leaflet may be retained or excised. Place the valve sutures from the left atrium into the left ventricle and then through the mitral prosthetic annulus from the superior to the inferior (ventricular) side, where the sutures are tied. The prosthetic annulus thus lies below the native mitral annulus. Then proceed with the aortic valve replacement.

During replacement of both mitral and aortic valves, it may be possible to attain adequate exposure to replace the mitral valve through the aortotomy incision.³⁸⁻⁴⁰ This is feasible in the presence of a dilated aortic root and aortic annulus, such as that found in Marfan's syndrome; the dilated aorta is necessary not only for exposure, but the annulus must be sufficiently large to allow passage of the mitral valve prosthesis. David et al⁴¹ have used this approach for endocarditis involving the fibrous trigone, and Cowgill and Adamick⁴² have used it to excise an anterior mitral leaflet causing left ventricular outflow tract obstruction after a mitral valve replacement.



II Left ventricular approach. Concomitant mitral valve and left ventricular operations for ventricular septal defect or aneurysm may both be performed through the ventriculotomy. This approach has also been used with partial left ventricular reduction (Batista operation).^{43,44}

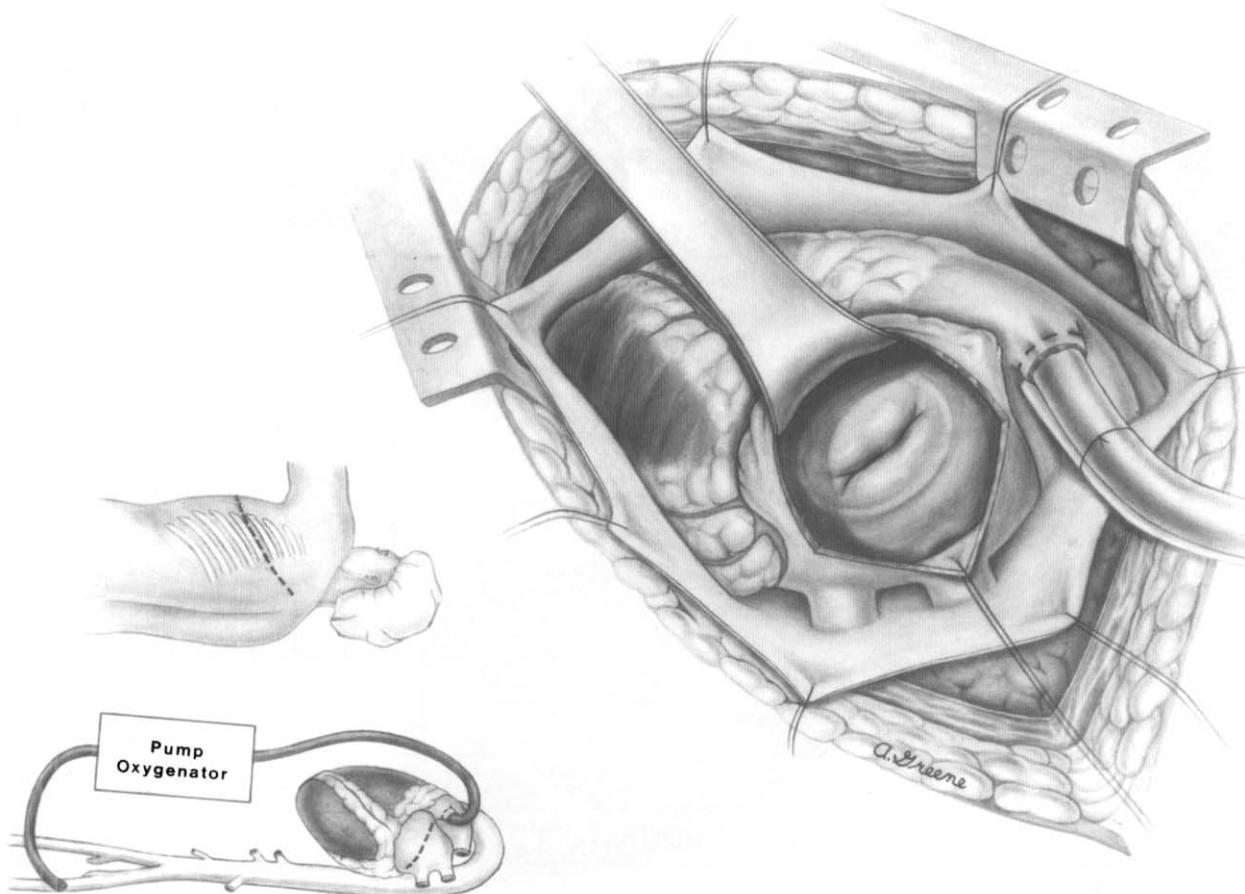
Open the left ventricle parallel to the septum, through the scarred or infarcted tissue. Extend the incision towards the apex to improve exposure without endangering the mitral subvalvular apparatus. Either mitral valve repair or replacement may be performed through this approach.^{45,46} With mitral replacement, remove the prosthesis from the valve holder, which, if used with this approach, may result in the valve being inserted upside down. Place the valve sutures from the atrial side to the ventricular side and then through the prosthetic annulus from its superior to inferior (ventricular) side. Competency of valvular repair is more difficult from the ventricular than from the atrial approach and must be ascertained with transesophageal echocardiography after weaning from cardiopulmonary bypass.



12 Right thoracotomy approach. Perform a right anterolateral thoracotomy through the fourth intercostal space, with fifth rib resection if necessary to improve exposure. This may be extended across the sternum to improve access. Alternatively, perform a posterolateral thoracotomy through the fourth intercostal space. Retract the lung posteriorly, and open the pericardium with a vertical incision, anterior and parallel to the phrenic nerve. Cannulate the ascending aorta or, if this is too difficult, the right femoral artery. Obtain venous drainage either through bicaval right atrial cannulation, or SVC/right femoral vein cannulation. Femoral-femoral cardiopulmonary bypass with deep hypothermia has been reported in complex redo operations.^{47,48} Insert antegrade and retrograde cardioplegia cannulas as indicated. Thorough intracardiac air removal at operative completion is difficult; we recommend flooding the operative field with CO₂.

After institution of cardiopulmonary bypass and cardioplegic arrest, open the left atrium through the interatrial groove. Because this approach is from the lateral side of the heart, the visualization of the mitral valve is excellent, with the plane of the mitral valve oriented nearly perpendicular to the surgeon's line of sight.

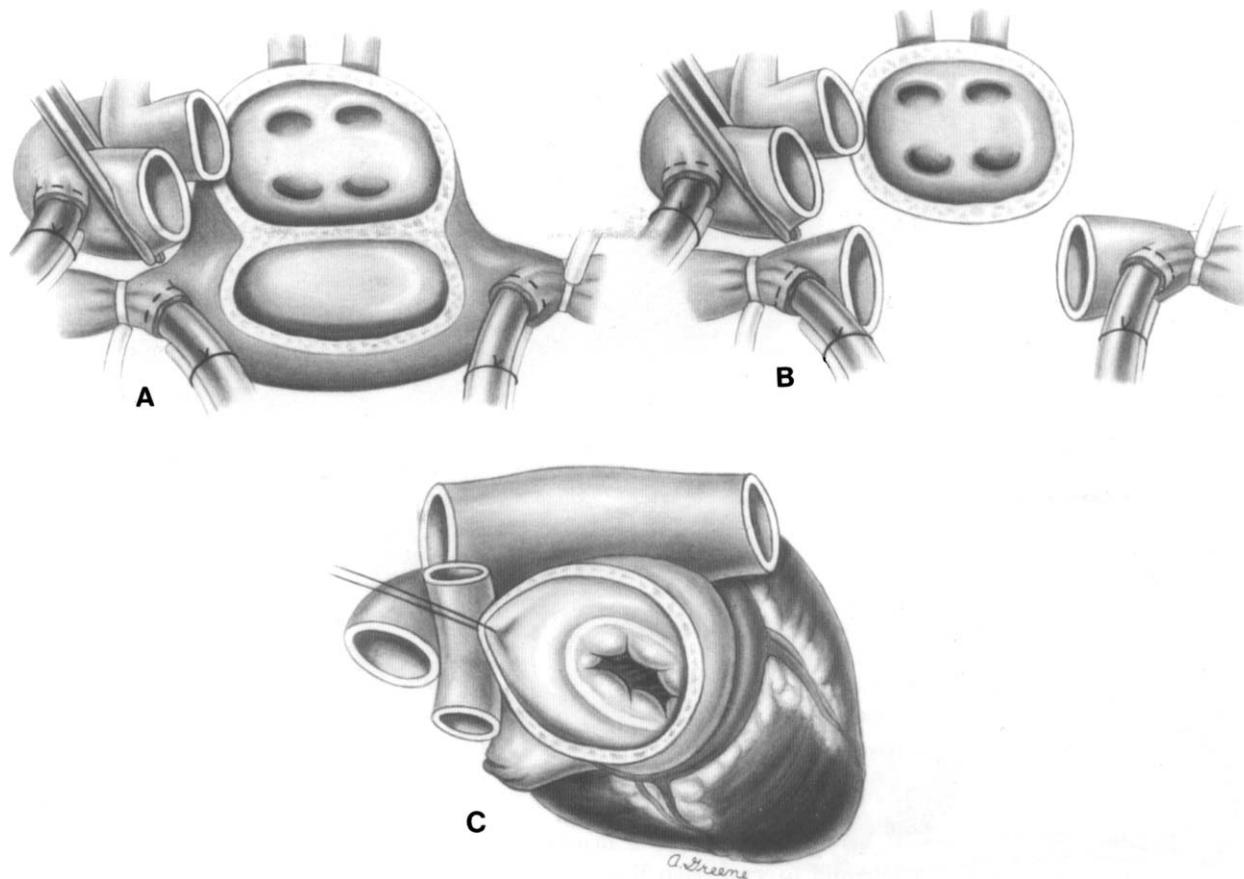
During the early years of open mitral valve operations, a right thoracotomy was frequently used to gain valvular exposure.⁴⁹⁻⁵² It remains an excellent approach in patients with a deep chest or when exposure is otherwise expected to be difficult from a median sternotomy. It may also be the preferred incision for mitral valve surgery as a redo or in patients with patent coronary grafts previously constructed by a median sternotomy.⁵³⁻⁶⁰ Disadvantages include difficulty in gaining access to other areas of the heart, difficulty in air aspiration from the left ventricle, and difficulty in cannulating and cross-clamping the aorta. However, access to the tricuspid valve is excellent. The use of retrograde cardioplegia facilitates myocardial protection. Double lung ventilation expedites exposure.



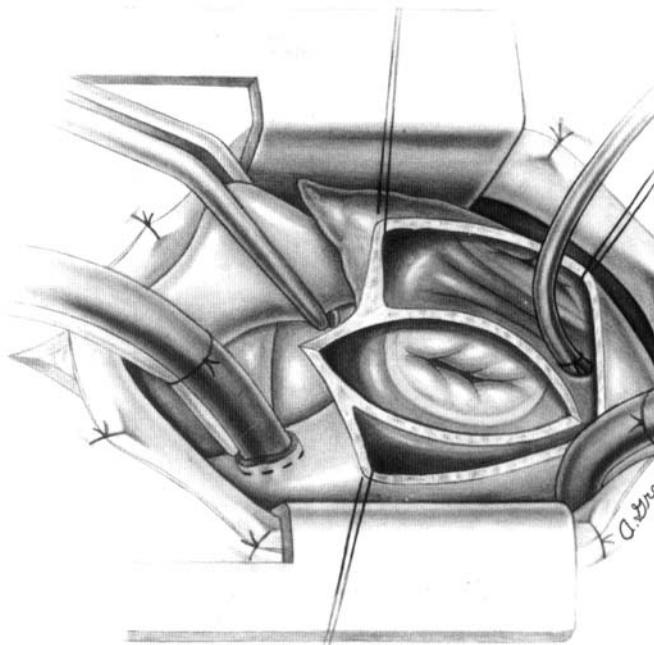
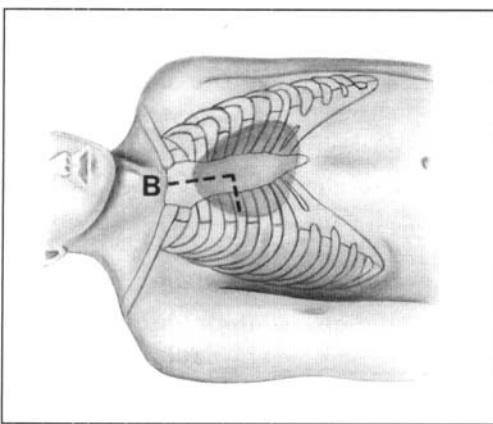
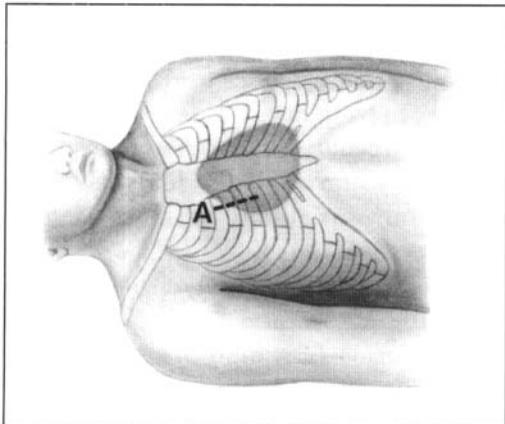
13 Left thoracotomy approach. Perform a left posterolateral thoracotomy through the fourth or fifth intercostal space, with the addition of fifth rib resection if necessary to improve exposure, and open the pericardium anterior and parallel to the phrenic nerve. Place one long venous drainage cannula through the left femoral vein, into the IVC-right atrial junction. A second drainage catheter may be placed in the right atrial appendage,⁶¹ in pulmonary artery at its infundibulum, or at the origin of the left pulmonary artery.⁶² Cannulate the left femoral artery or descending aorta for arterial return. Rarely, the left iliac artery has been used for arterial cannulation.

Vent the left ventricle by the ventricular apex or through the ascending aorta, if it is accessible. Open the left atrium with an incision parallel to the atrioventricular groove. Because this incision is carried through the thin-walled atrial appendage, the closure requires some delicacy.

Nichols et al⁶³ and Clowes et al⁶⁴ described using a left thoracotomy to approach the mitral valve. It is not applicable when either aortic or tricuspid valve procedures are also necessary. As with the right thoracotomy approach, double lung ventilation facilitates exposure. Familiarity with this technique is necessary when a closed mitral commissurotomy through a left thoracotomy requires conversion to an open mitral valve replacement or repair.

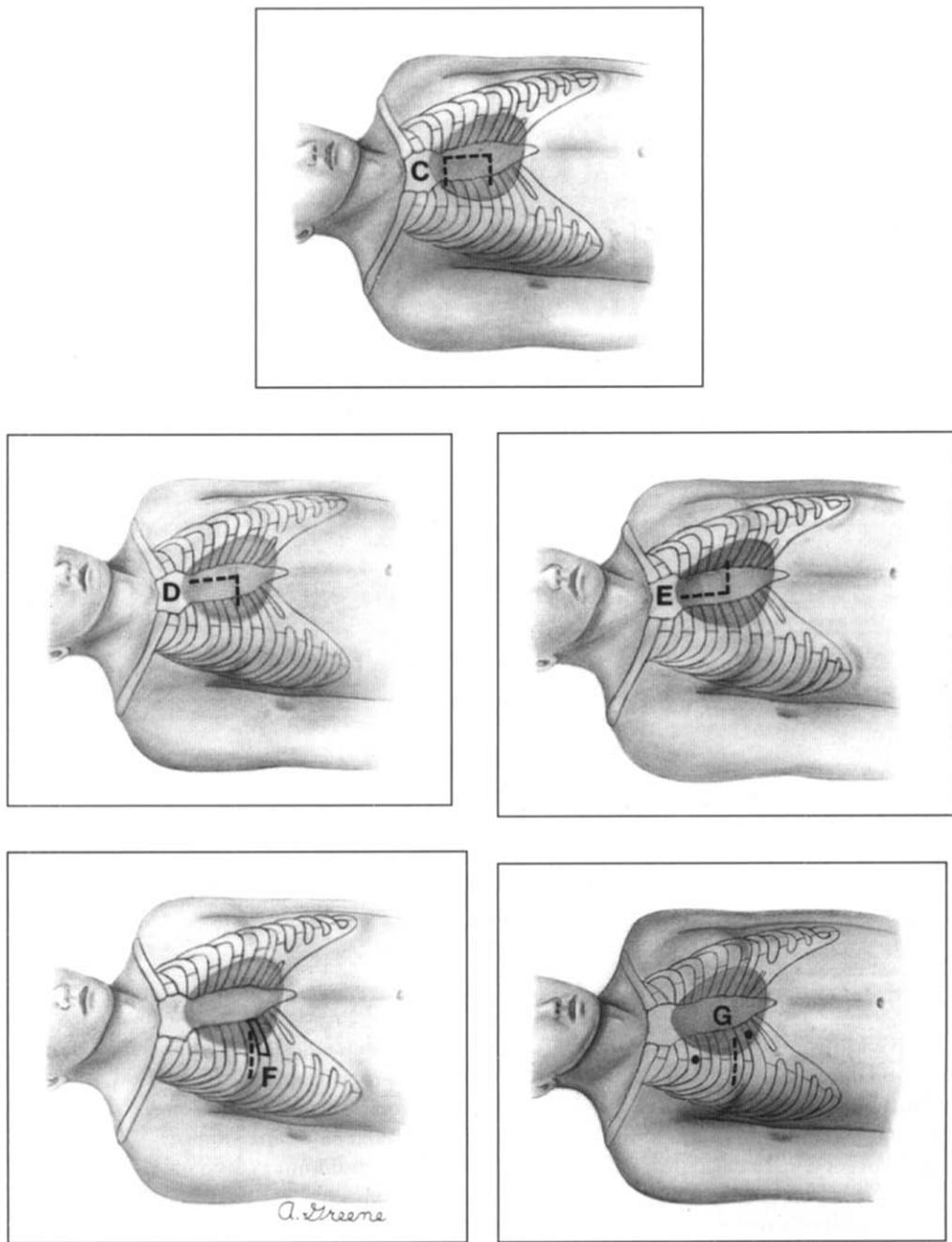


14 Autotransplantation. Two major techniques for cardiac transplantation have been described. The traditional technique as described originally by Lower and Shumway⁶⁵ involves preserving the major posterior portions of the right and left atria.^{65,66} The newer, total heart Wythenshawe technique described by El Gamel et al⁶⁷ leaves only the posterior left atrial cuff. In either method the explanted heart is delivered into an ice or slush containing basin. This allows a bench surgery approach to the mitral valve apparatus. Explantation of the heart with subsequent reimplantation as in a cardiac transplant allows a period of time during which bench surgery may be performed on the heart. Cooley et al⁶⁸ has described this for resection of extensive intracardiac pheochromocytoma, and Batista⁶⁹ has reported 45 cases of left atrial and mitral valve operations performed as bench procedures before reimplanting the heart. In a subsequent report, Batista et al⁷⁰ updated the series to 154 patients, with the predominant indication being to reduce the size of an excessively dilated left atrium (ie, > 6 cm). Although a procedure of considerable magnitude, autotransplantation might be considered for patients requiring complex intra-atrial operations in whom other techniques provide inadequate exposure. Repair of the mitral valve in an ex-vivo donor heart before its transplantation has also been reported.⁷¹



15 Minimally invasive approaches. Mitral valve operations may be performed through incisions smaller than standard median sternotomy.⁷²⁻⁷⁴ Although a number of different incisions have been used, only two basic and distinctly different techniques have been described. The first uses traditional cannulation techniques and traditional instruments to work on the mitral valve through small incisions.^{72,73} The second, port-access mitral valve surgery, uses catheter techniques for both cardiopulmonary bypass and cardioplegia and specially designed instruments to enable working through a small port.^{74,75} With either approach, video-assisted observation of the mitral valve may be useful.^{76,77}

Traditional cannulation. Several incisions can be used. For the right paramedian approach, make an incision over the third and fourth costal cartilages and either resect or transect and fold these two cartilages laterally. The internal mammary vessels can usually be preserved. If exposure of the aorta is limited, use the right femoral artery and vein cannulation, plus a second transatrial SVC venous cannula. Use a right atrial-transseptal, superior septal, or standard left atriotomy approach to access the mitral valve. For the upper sternotomy approach, begin the sternotomy with an oscillating saw at the sternal notch and extend it caudally to the fourth or fifth intercostal space. Saw through the right hemisternum into the fourth or fifth intercostal space, creating an “L”-shaped sternotomy, with preservation of the right internal mammary vessels. Cannulate the ascending aorta and right atrium directly. Because of the smaller operating space afforded by this incision, smaller than usual cannulas may be used. Vacuum assistance will allow adequate venous drainage with cannulas as small as 20 to 22F. Both antegrade and retrograde cardioplegia may be used with this and with the following technique. Use either a right atrial-transseptal approach or a superior septal approach. Access through a left atriotomy is difficult. Both of these approaches require preoperative placement of cutaneous defibrillation pads; space is limited such that internal defibrillator paddles can usually not be used.



15 (continued) (C, D, E) Using variations of these incisions, other similar approaches have been described. Notice the manubrium is left intact.

Port-access technique. Developed by Heartport, Inc (Redwood City, CA), and usually referred to by that name, the port-access technique obtains mitral valve access through a limited lateral right fourth intercostal space thoracotomy (F), and achieves cardiopulmonary bypass, venting of the heart, aortic occlusion, and cardioplegia through peripherally placed catheters. From the internal jugular vein, the anesthesiologist passes a retrograde coronary sinus catheter for retrograde cardioplegia administration, and a pulmonary artery vent for left ventricular decompression.

From the femoral vein, pass a long venous drainage catheter into the inferior vena cava or right atrium, to which vacuum drainage will be applied. Place a femoral arterial perfusion cannula, and through one of its side arms, pass a balloon occlusion catheter into the ascending aorta. This provides aortic occlusion with a balloon, and allows suction decompression of the aortic root and antegrade cardioplegia administration. Place these catheters under fluoroscopic and transesophageal echocardiographic control. With difficulty gaining aortic occlusion, the aortic cross-clamp can be placed transthoracically through the right third interspace (upper dot, G). The clamp passes in front of the superior vena cava and through the transverse sinus.

Through the thoracotomy incision, cannulate the superior vena cava, and then proceed with the mitral valve operation, usually through a standard vertical left atriotomy in the interatrial groove. Video-assistance is usually achieved through an upper port in the second or third interspace (upper dot, G) no further lateral than the anterior axillary line. The endoscope can also be comfortably placed in the surgical incision itself or a lower stab incision (lower dot, G).

The motivation for all these minimally invasive techniques is the hope that the cosmetic appearance is improved, and that painful disability will be decreased when compared with the standard approach performed by a full median sternotomy.

DISCUSSION

In summary, the relative indications for a planned alternative technique include a small left atrium, a deep chest, previous lung resection or pneumonectomy with pronounced mediastinal deviation, previous coronary bypass grafting (especially patent saphenous vein and mammary arteries), large or posterior sessile left atrial tumors, combined mitral/tricuspid access, left atrial clot, left ventricular hypertrophy secondary to calcific aortic stenosis, Kent bundle resection in Wolff-Parkinson-White (WPW) syndrome, idiopathic hypertrophic subaortic stenosis (IHSS) with mitral valve replacement (MVR) and septal resection, redo mitral valve surgery, and more recently pain and cosmesis considerations. Preoperative planning allows the median sternotomy, right or left chest approach, and minimally invasive strategies. Intraoperatively, the median sternotomy offers the most alternatives. Once committed to the vertical left atriotomy approach, conversion to allow better and safer exposure is available. A planned interseptal or extended approach allows obvious better exposure of the right atrium, left atrium, and mitral valve apparatus. The left ventricular approach affords access for the rare situation requiring mitral valve replacement and ventricular wall procedures. The minimally invasive techniques are continuing to evolve. Peripheral cannulation is common to most of them. Partial sternotomy, parasternal, or various thoracotomy approaches are used. Video-assisted thoracic surgery (VATS) offers increased visualization and complements the exposure. Long-term results are anticipated. The recent short-term results with port-access minimally invasive mitral valve repair or replacement showed a series of 309 patients from April 1, 1998 through January 1, 1998. The mortality was 1.5% in the repair group and 3.3% in the replacement group.⁷⁸ The present review has collated the various approaches and placed them in an organized perspective to permit the surgeon to choose the best approach for any given patient.

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