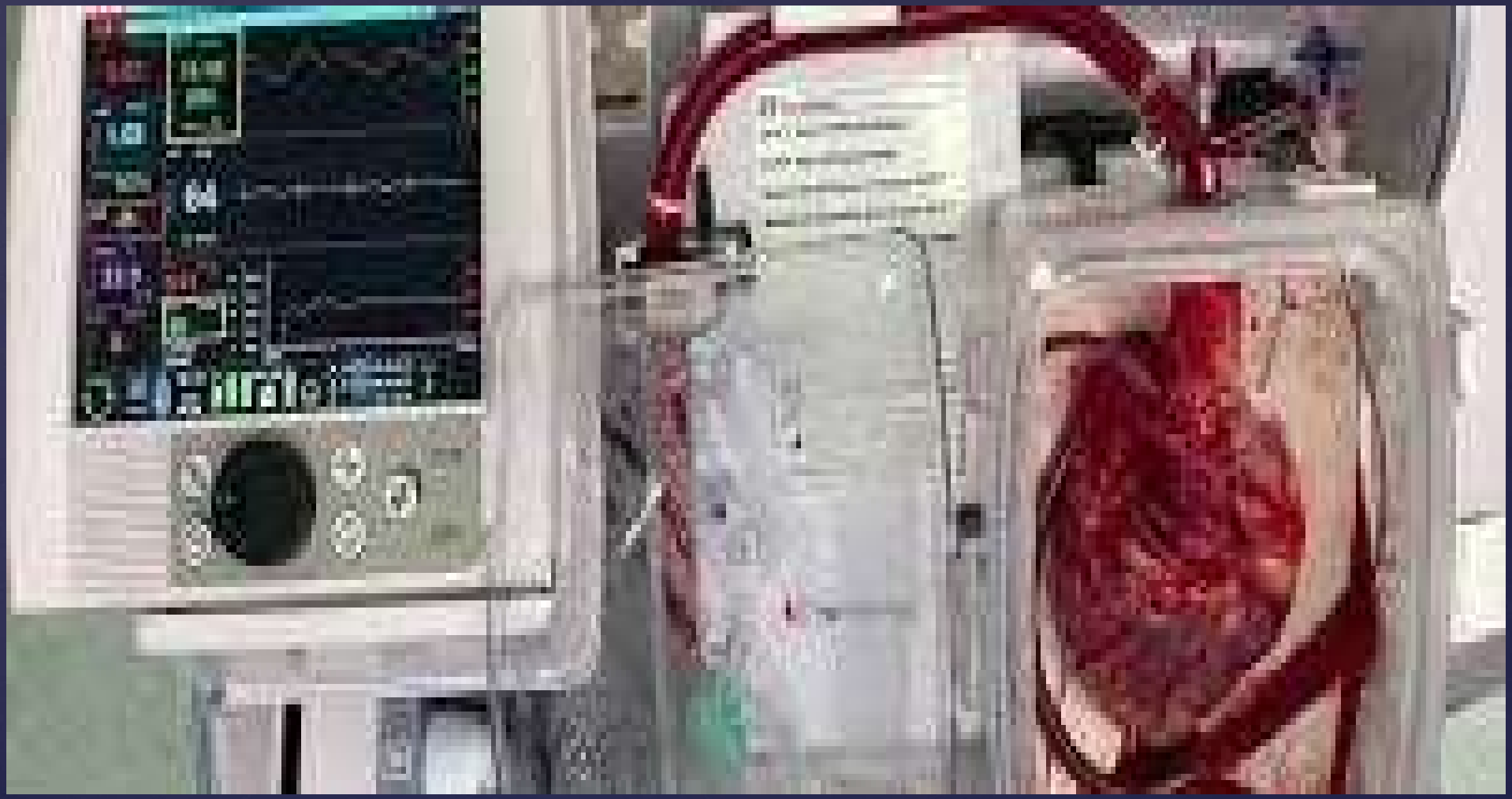
Pediatric Heart Transplantation



Dr. Bahar Dehghan, Ped. Cardiologist, Isfahan UMS

The first pediatric heart transplant was performed on December ۶th, ۱۹۶۷, by Dr. Adrian Kantrowitz in Brooklyn, New York.

- Approximately ۳۵۰ to ۴۰۰ heart transplants are performed in children under the age of ۱۸ annually in US, and over ۷۰۰ are performed worldwide.

- As of ۲۰۱۹, average survival rates after ped. HTX are:

۸۵%, ۷۴%, and ۶۳% at ۱, ۵ and ۱۰ yr respectively.

Indications:

- Children with lethal cardiomyopathy (more in adolescents),
- Some forms of complex CHD (HLHS in infants),
- Some infants and children with failed surgical interventions.
- Rare causes of heart failure: complications of Kawasaki disease, cardiac tumors, uncontrollable arrhythmias, and retransplants for graft failure.

PRETRANSPLANT EVALUATION

- A large amount of historical, anatomic, hemodynamic, metabolic, immunologic, and psychosocial information is required.

- With the exception of some infants with unoperated CHD (e.g. HLHS), most children require *a cardiac catheterization* before HTX.

History and Physical

- Current history, including NYHA / Ross functional class
- Age, height, weight, body surface area, body mass index and BMI%ile
- Complete cardiac anatomy history
- Complete surgical and procedure history, from primary documents
- Past medical history
- Developmental history
- Neuropsychiatric history
- Family history
- Medications
- Medication allergies
- Immunization record
- Vital signs, oxygen saturation
- Complete routine physical exam

Cardiopulmonary Data

- Echocardiogram
- Resting electrocardiogram
- Cardiac catheterization and angiography, as applicable, with pulmonary vascular resistance testing when elevated
- Cardiac MRI, when applicable (cardiac anatomy)
- Chest CT, when applicable (cardiac anatomy, re-entry risk)
- Cardiopulmonary exercise stress testing, with VO_2 measurement (functional capacity)
- Chest x-ray (heart size)
- Endomyocardial biopsy for possible reversible causes (e.g., myocarditis), or multisystem disorders (e.g., storage diseases in suspected cases)
- Abdominal ultrasound (liver, kidney)
- Neck and groin vascular ultrasound (vascular anatomy for vascular access)
- Liver biopsy for older Fontan patients
- Pulmonary function testing, when applicable
- Nuclear GFR (renal function)

Laboratory Data

- Blood type, and second separately drawn sample for confirmation
- Infants: isohemagglutinins: anti-A and anti-B titers
- HLA typing, high resolution
- HLA antibody screening (or Panel Reactive Antibody)
- Infection screening: CRP, blood and urine culture

- Urine for urinalysis and 24-hr urine for computation of glomerular filtration rate
- Coagulation status: prothrombin time, partial thromboplastin time, vitamin K–dependent factors for patients with liver disease
- Platelet function analysis when applicable
- Blood counts and differential
- Chemistries, including electrolytes, renal function and hepatic function tests
- Prealbumin
- Erythrocyte sedimentation rate
- Thyroid function studies
- Hemoglobin A1c
- Lipid panel, fasting
- B-type natriuretic peptide or NT-proBNP
- Serology for human immunodeficiency virus, hepatitis vaccination, toxoplasma gondii, syphilis, cytomegalovirus, Epstein–Barr virus, herpes simplex virus, and vaccination statuses
- PCR for EBV and CMV
- Pharmacogenetic testing, when applicable
- Metabolic screening for systemic illness, when applicable
- Pregnancy test when applicable
- PPD when applicable
- Micronutrients: Vitamin D, Zinc, etc
- Iron level and ferritin
- IgG level in patients with repeated infections or protein loss

Pretransplant Management

- ***Immunology:*** ABO, HLA-Ab
- ***Cardiac:*** PVR (contraindicated if > ۶-۹ W/m^2), Heart-Lung Tx
- ***Nutrition:*** specially for whom have a Fontan operation and either plastic bronchitis or PLE

Considerations for Multiorgan Transplantation

- ***Heart–Kidney Tx:*** There is a comparative benefit of combined heart–kidney Tx over isolated HTx when GFR is under ٣٧ mL/min (Infants are not candidates.)

- ***Heart–Liver Tx:*** homozygous FHC with MI, amyloidosis, CHD and Fontan-associated liver disease (cardiac patients diagnosed with biopsy-proven decompensated cirrhosis).

Ped. data suggest some degree of reversibility of liver findings in Fontan patients < ١٨ yr who undergo HTx.

- ***Heart–Lung Tx:*** Patients with cardiac dysfunction due to PPHN or lung disease (cor pulmonale) recover after LTx. Children with such severe CHD that HTx alone is not possible: PA and MAPCAs can't be unifocalized, or patients with such severe PVOD & PVR elevation.

Donor Evaluation

- *Size:*

a larger allograft relative to their native heart (e.g., patients with elevated PVR)**, but oversized grafts (donor: recipient height >١/٢) are a risk factor for early mortality.**

Accepted range of donor: recipient weight is ٠/٨ to ٢/٠, though ratios up to ٣/٠ have been utilized in some cases.

- *Extra Vessels:*

In HLHS for Ao reconstruction, Central PA reconstruction, donor SVC and innominate vein tissue for patients with abnormal venous anatomy, previous Fontan, LSVC,….

- *Graft Function:*

Donor EF < ٥٠% is an independent risk factor for early mortality.

Coronary angiography is commonly requested for donors >٣٥ or ٤٠ years.

Surgical Technique

- ۲ basic transplant surgical techniques are commonly used: *bicaval* and *biatrial*.
- In both types, LA is left intact posteriorly to avoid surgical intervention on PVs.
- LA anastomosis is made first.
- Aorta and PA are anastomosed, often by end-to-end technique, with attention to any congenital or residual narrowing.
- RA can either be anastomosed as a cuff to the recipient atrium (*biatrial anastomosis*), or the recipient SVC and IVC can be separately anastomosed to the donor (*bicaval anastomosis*).

- *Biatrial anastomosis* is thought by some surgeons to be a simpler solution to prevent SVC stenosis, especially in small children, and is occasionally needed to include LSVC to CS drainage to donor heart.

- *Bicaval anastomosis* has a lower incidence of pacemaker requirement and long-term atrial arrhythmias.

- Patients with abnormal situs or other abnormal connections may have modifications of these techniques to allow for proper positioning of allograft.

- In the US, the time/date that LA anastomosis is started is recorded as the transplant time.
- This is important only for documentation when the surgical time is near midnight.
- The donor ischemic time is recorded as the time from cross-clamp and cardioplegia of the donor heart, until the aortic cross-clamp is released after implantation.

- Primary graft dysfunction and failure are a function of cold ischemic time, and are more common when ischemic time surpasses ۴ hours, although the contribution of long warm ischemic time (time from removal of donor organ from ice storage to removal of aortic cross-clamp) to graft dysfunction is being increasingly recognized and strategies to minimize both cold and warm ischemic times are important.

- Cold ischemic time of up to ۶ hours is usually well tolerated for younger-age donors and standard risk recipients.

Assessment of the Postoperative Heart by TEE

- TE is usually performed postop. to check for patency of the anastomoses (especially SVC and PAs), to assure that redundant LA tissue is not obstructing MV, and evaluate RV and LV function.

- Hyperacute rejection can be diagnosed immediately on these TE images, but is often apparent by visual inspection of beating heart, which turns dark colored or even black due to complement activation and intravascular thrombosis.

Rate/Pacing

- Postop. transplanted heart will respond to circulating catecholamines and to inotropic agents infused, but it is not connected to the recipient's parasympathetic or sympathetic nervous system directly.

- Thus, the allograft has limited ability to raise its own HR appropriately during recovery.

- C.O is typically rate dependent due to diastolic dysfunction of transplanted heart.

- Some centers use IV catecholamine infusions only (epinephrine, isoproterenol), while others will use temporary atrial pacing to overcome inappropriately low HR.

- For babies and toddlers, a lower rate may initially be set near ١٣٠ to ١٥٠ bpm, while for older children a rate of ١١٠ to ١٣٠ may be chosen early after transplant.

Right Ventricular Function

- RV is subjected to considerable stress in the transplant process.
- In the donor after death, it may be subjected to stress from resuscitative efforts, or strained by aggressive pulmonary recruitment for lung transplant.

- After cold ischemia for transplant, the muscle may be required to pump against secondary PH due to a history of recipient left heart diastolic dysfunction and chronic pulmonary vascular disease.

- In such cases, RV may struggle or even fail, and RV support often mandates at least several days of inotropic support after transplant.

- Uncommonly, RV failure is immediate and requires temporary mechanical support in the form of temporary RVAD or ECMO.

Cardiac Support

- By the time a transplant is completed, a donor heart has had several insults including the original cause of donor death, potential CPR or trauma and resuscitation, and cold ischemia.
- It is common for a recipient to require several days of inotropic support after transplant to allow the allograft to recover.
- In addition, the metabolic stress of the transplant should not be ignored.

- The cold heart is still somewhat metabolically active and has not been receiving oxygen or glucose.

- After reperfusion, and in the setting of steroid therapy, ATP depletion impairs glucose transport into cardiac myocytes.

- **Dextrose and insulin infusions** are often critically important to the early recovery of heart in the first hours after operation.

POSTTRANSPLANT IMMUNOSUPPRESSION

- *Oversuppression:*

  Minimizing immune suppression is important so that patients do not develop infections or malignancy (PTLD). Other major concerns include renal dysfunction, DM, HTN, osteopenia and HLP, which are dose-related toxic effects.

- *Immunosuppressive Medications:*

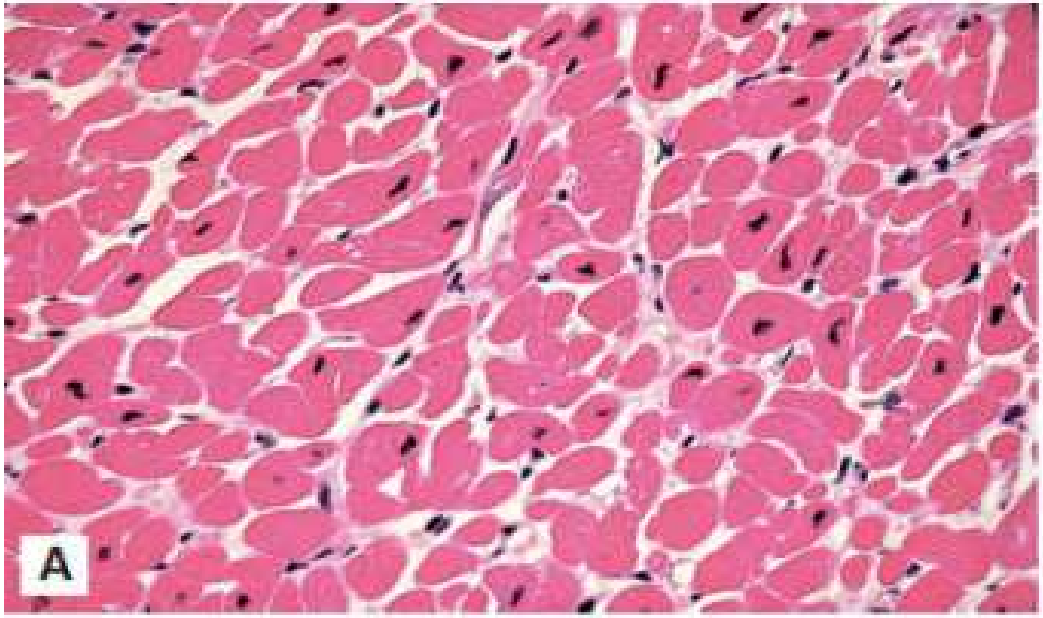
  CNIs. **Mainstay of immune suppressive therapy for ped. HTx prevent IL-۲ production and T-cell activation: Cyclosporine-A, Tacrolimus,….**

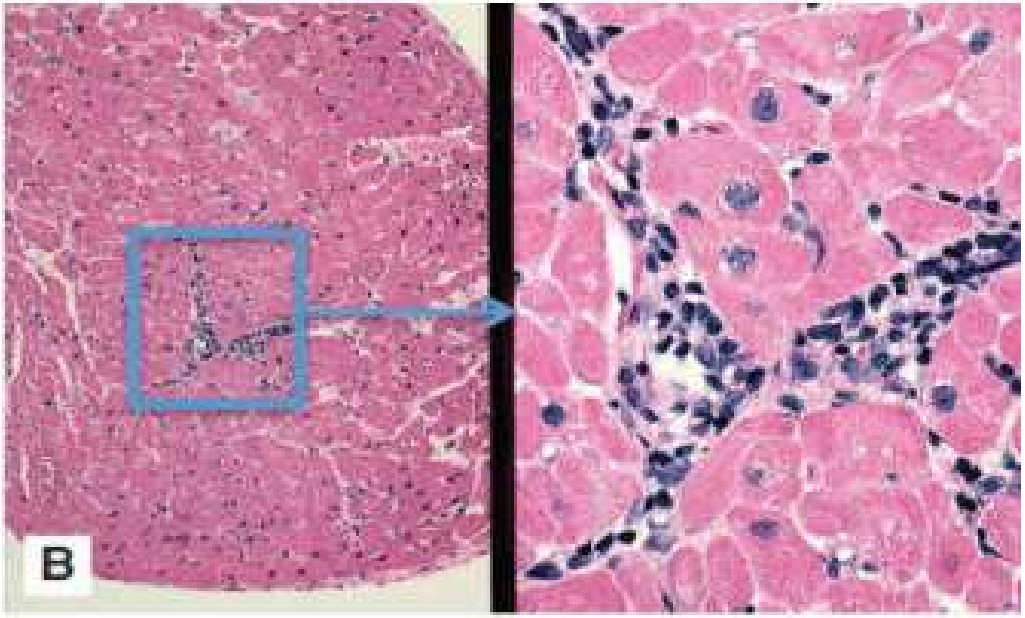
  Glucocorticoids.

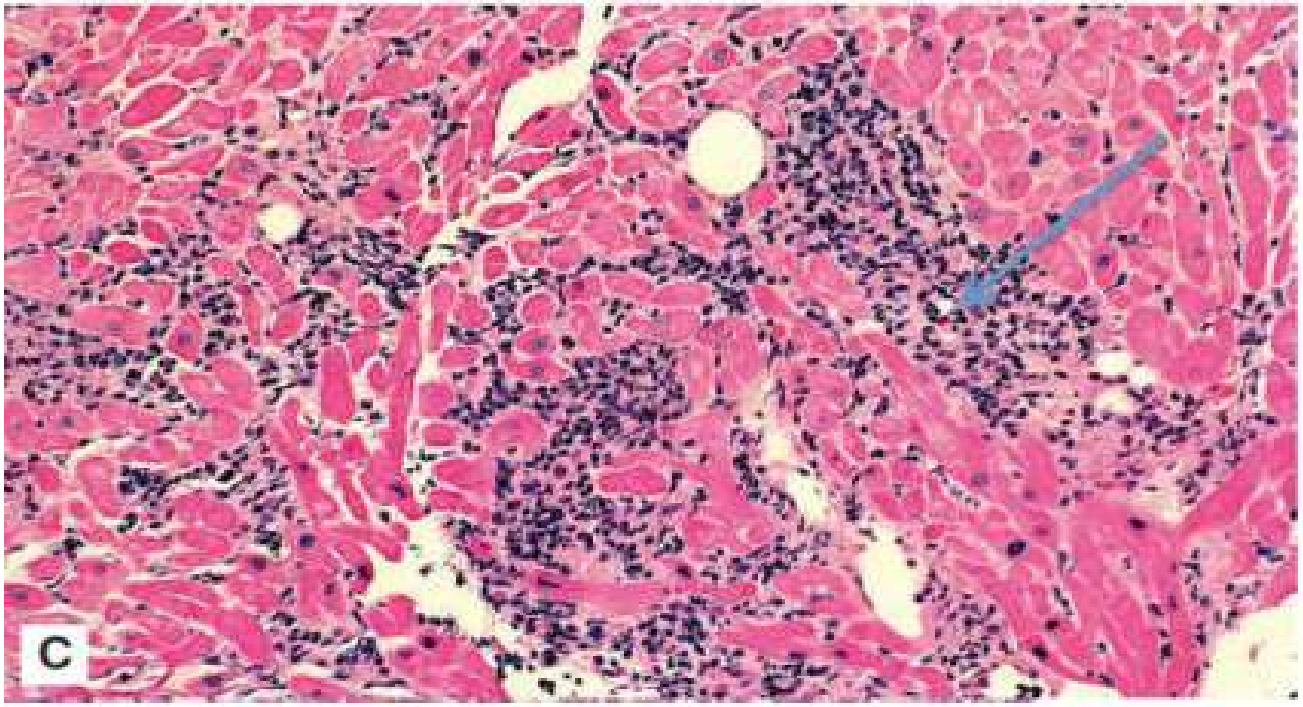
COMPLICATIONS

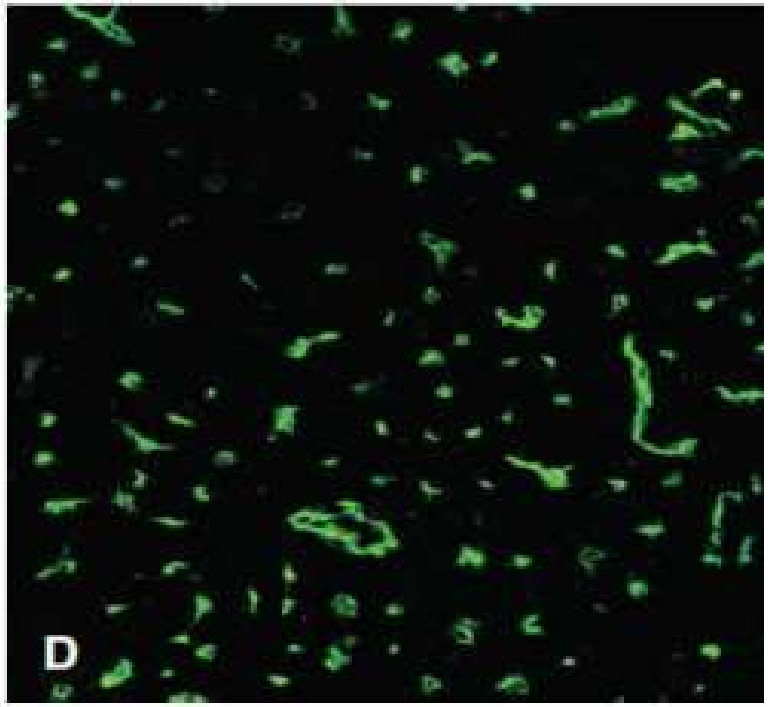
- Rejection
- Transplant CAD, Coronary Angiography
- Infections
- PTLD
- Chronic Kidney Disease
- Diabetes
- Hypertension
- Hyperlipidemia
- Other Immunologic Complications:

Immune dysregulation is common after ped HTx, when chronic immune suppression is administered. Chronic steroid therapy and CNI administration can be associated with chronic allergies, eczema, asthma, celiac disease.









Rejection histology

Cardiac Status

- The "normal" posttransplant course involves an evolution of heart function over hours, and then a gradual improvement over days and weeks.
- Not all cardiac dysfunction after transplant is caused by rejection, and so assessment of the posttransplant patient needs to include an understanding of their expected cardiac performance.

- Normal postop. recovery—including hypoxic injury, metabolic depletion (intracellular glucose) and excessive demands of the postop. state: first ۵ days.

- Mild dysfunction, moderate inotrope dependence, or overt failure requiring mechanical support can occur, and need to be differentiated from rejection.

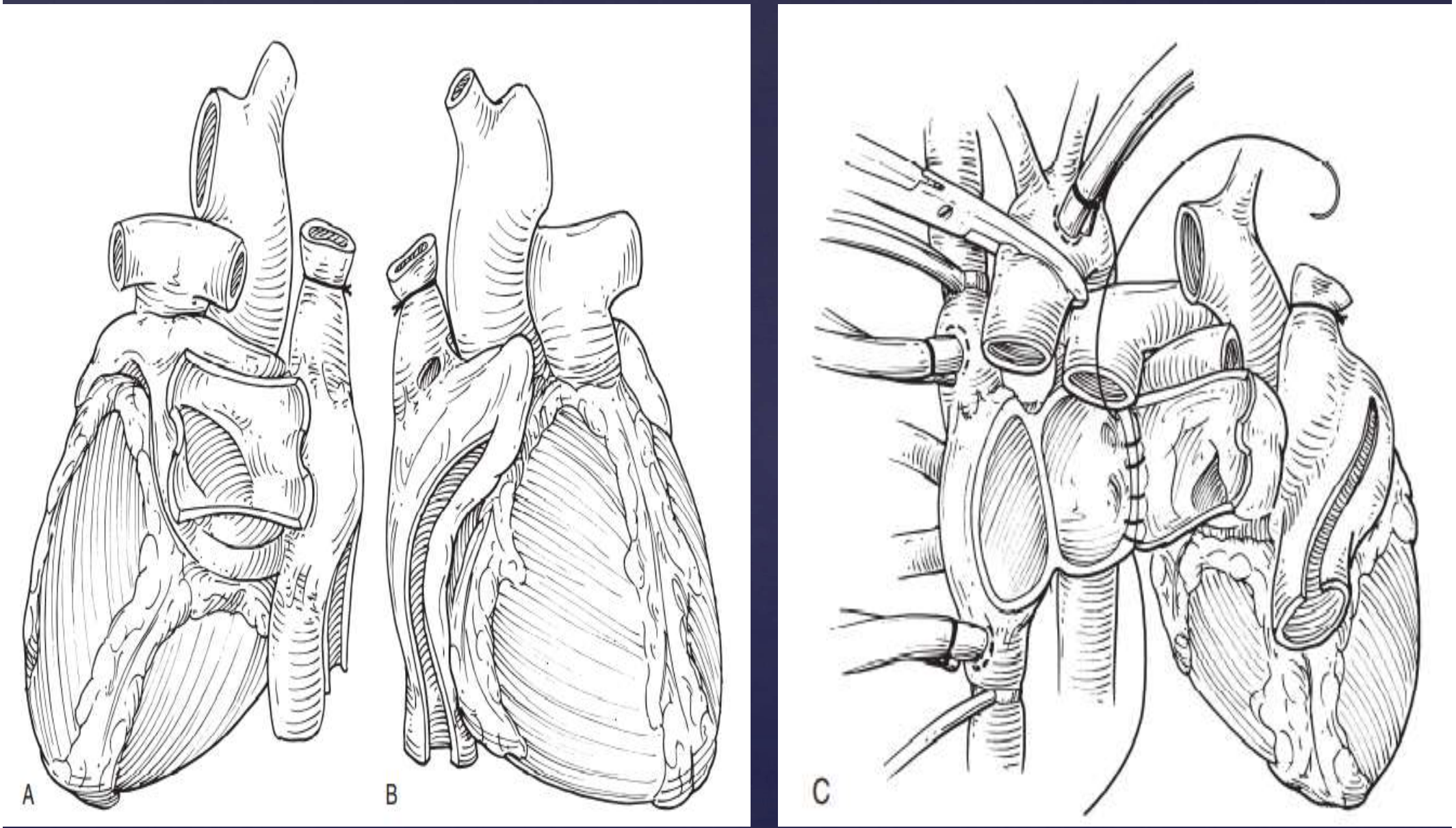
- Myocardial edema—in first ۲ to ۵ days postop. often related to reperfusion injury
- Hypertrophy—over first ۲ months, generally steroid-related.
- After recovery, and as steroid-related hypertrophy resolves, there is generally an expectation of normalization of cardiac diastolic function, an improvement in overall cardiac performance, improvements in minor valve regurgitation.

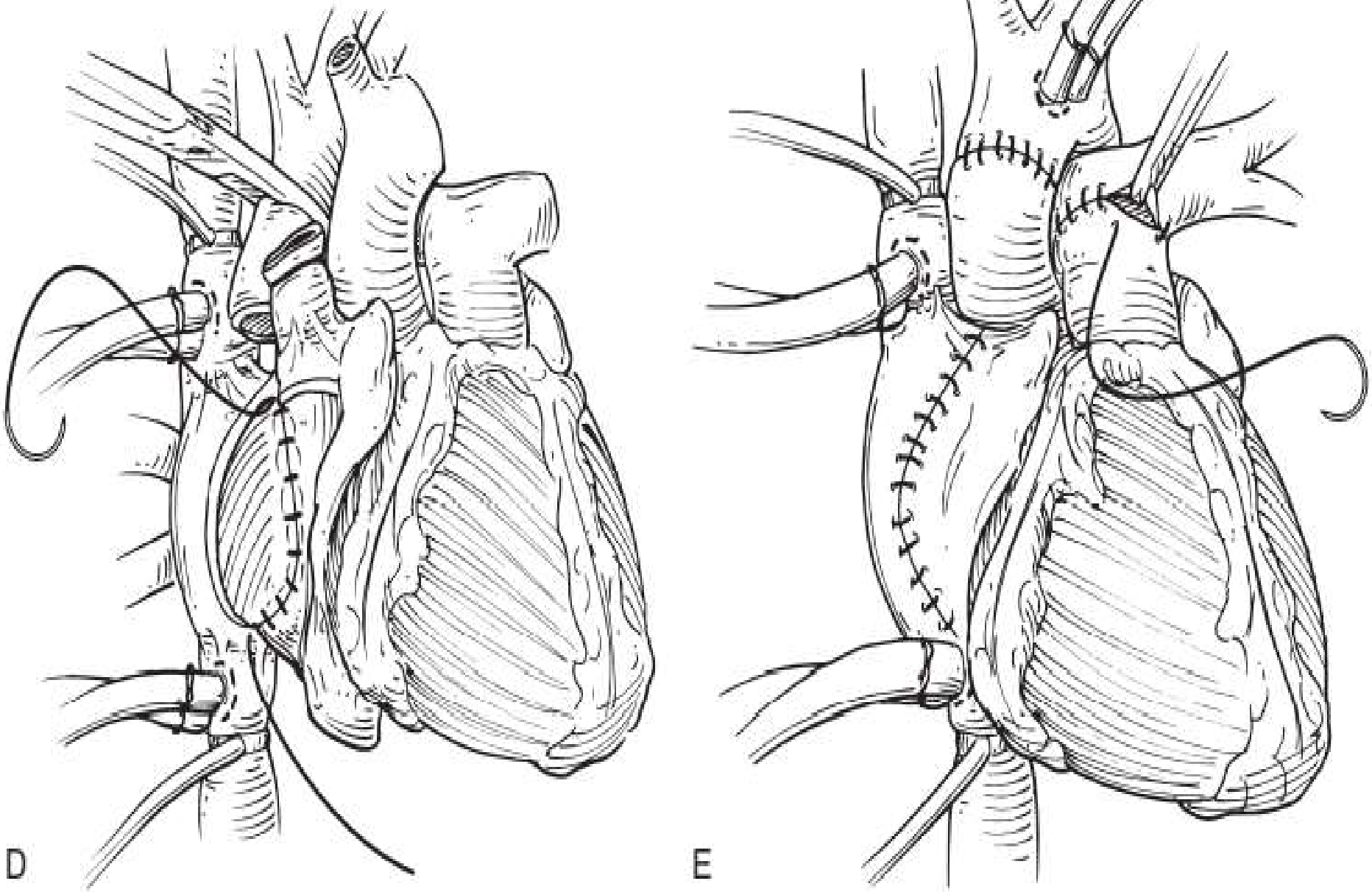
- Cardiac rejection is a consideration whenever there is a failure of the heart to improve, or when there is unexpected worsening of cardiac function especially in patients at high risk for rejection and out of target immunosuppression drug levels.

Pediatric Challenges

- Appropriate hand sanitation can be a challenge, especially in epidemics of viral illness.
- Children can also have a difficult time coping with new medications, certain medication tastes or textures, and it is difficult to reason with a child who may not want to participate in medical testing or procedures, or even medication administration.
- Pediatric hospitals are well equipped with distraction techniques and well-trained child life specialists who can help a child understand medical events and help them cope with these challenges.

Orthotopic cardiac transplantation, biatrial technique




D
E

A, Creating donor heart LA cuff by incising through PV orifices.

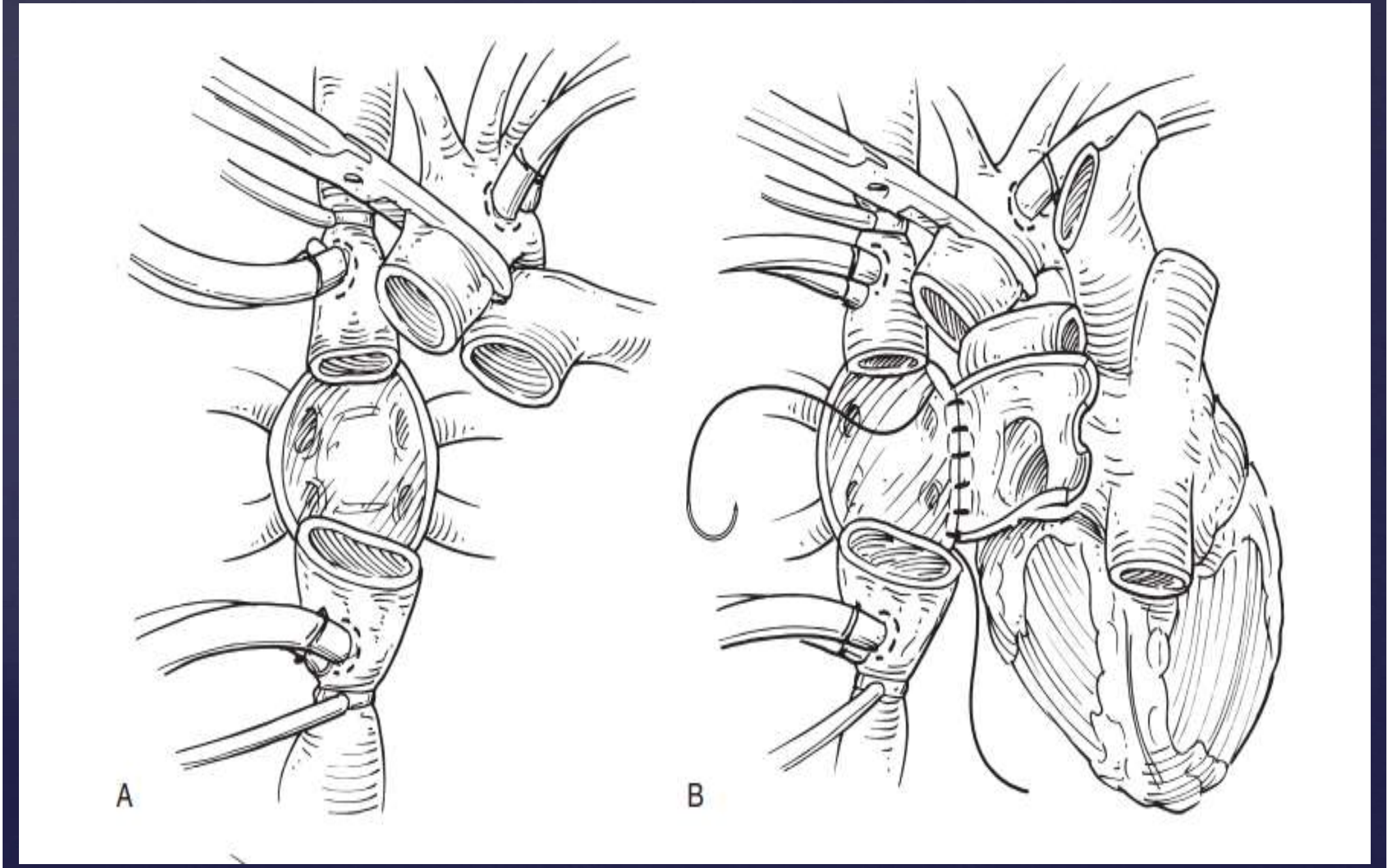
B, Creating donor heart RA cuff. Incision begins at orifice of IVC and extends toward RA appendage approximately halfway between sulcus terminalis and AV groove.

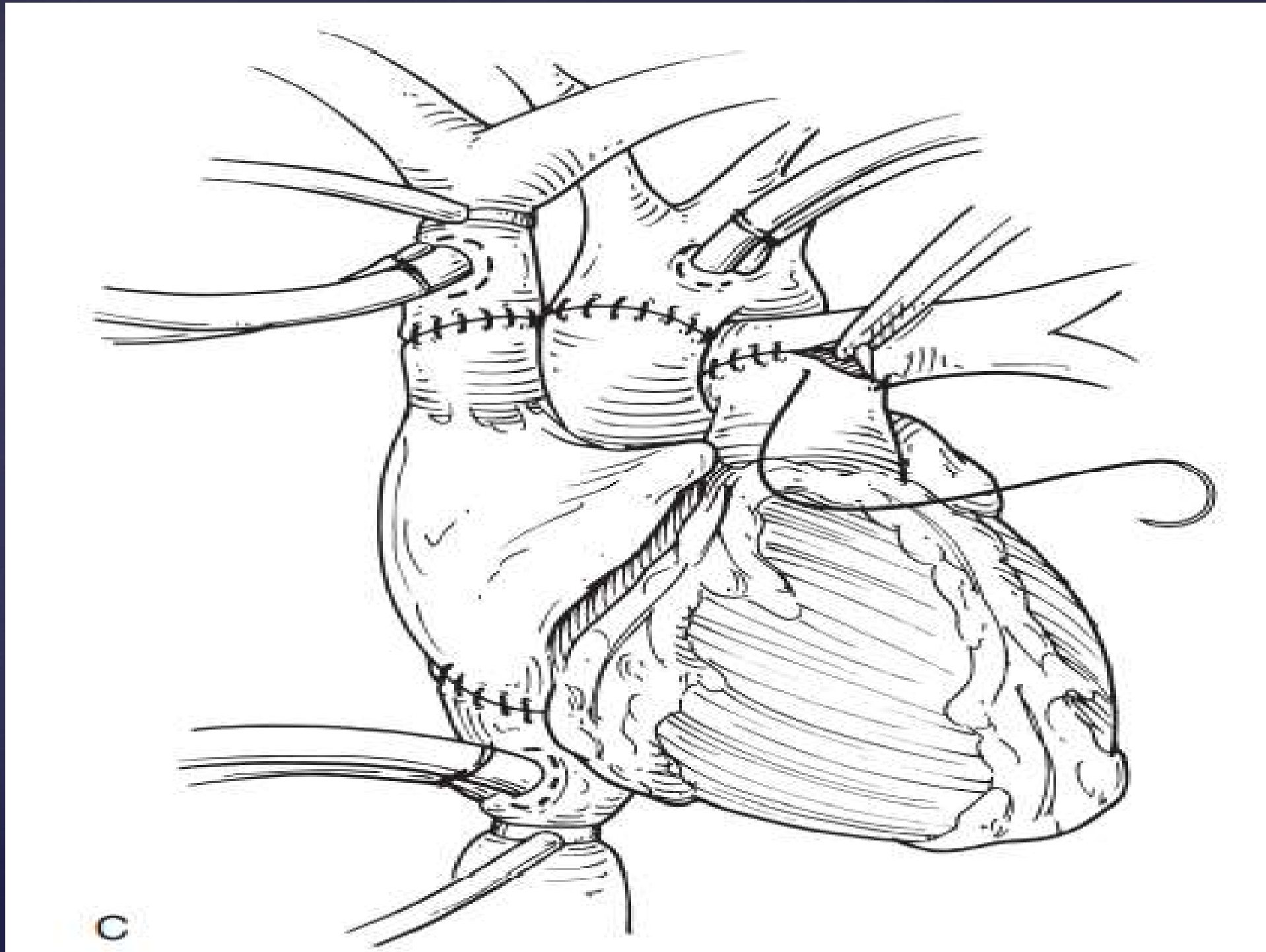
C, LA anastomosis is commenced.

D, RA anastomosis is commenced on IAS. This suture line overlaps atrial septal portion of LA anastomosis.

E, Aortic and pulmonary trunk anastomoses are completed.

Orthotopic cardiac transplantation, bicaval technique.

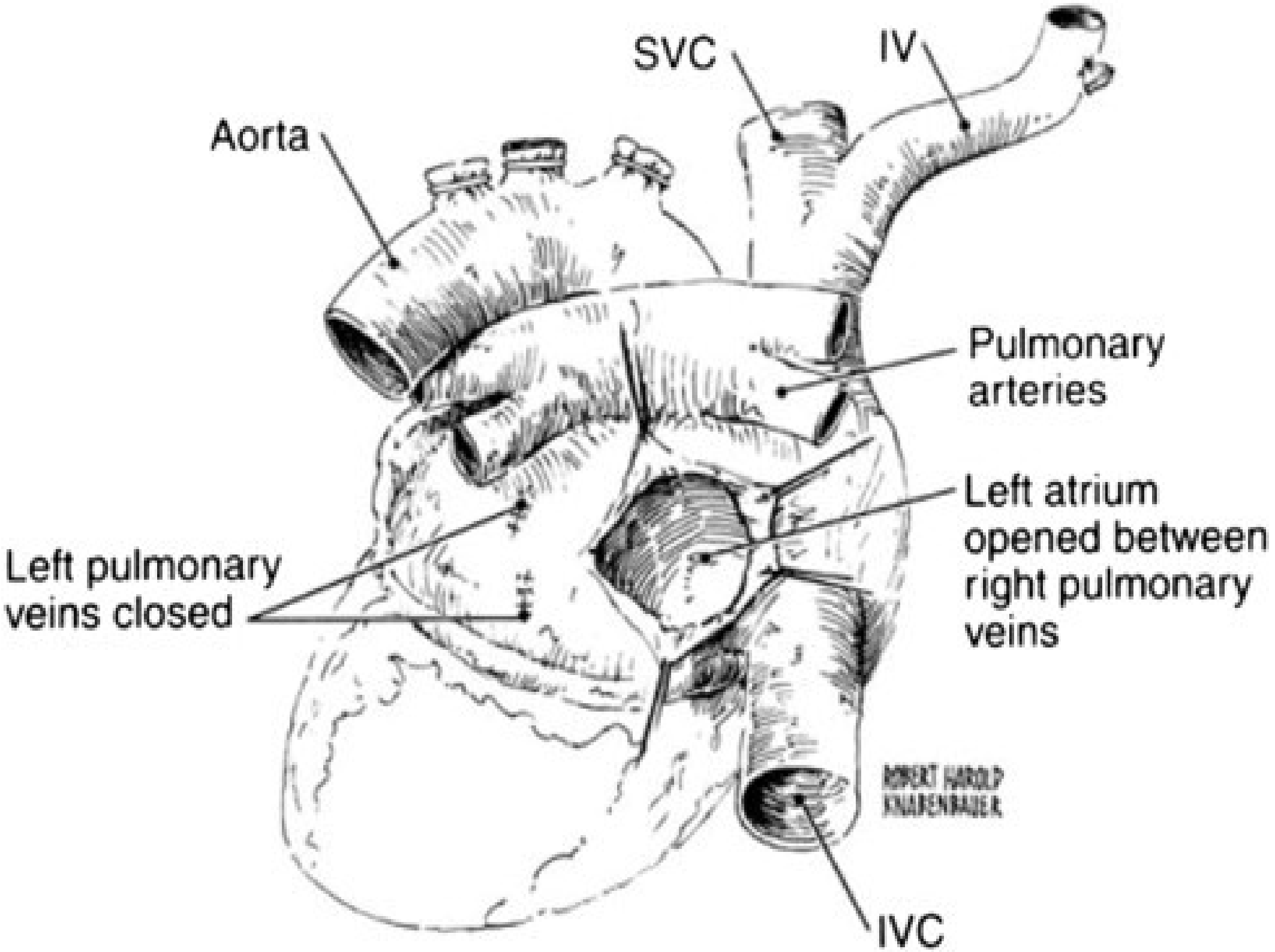


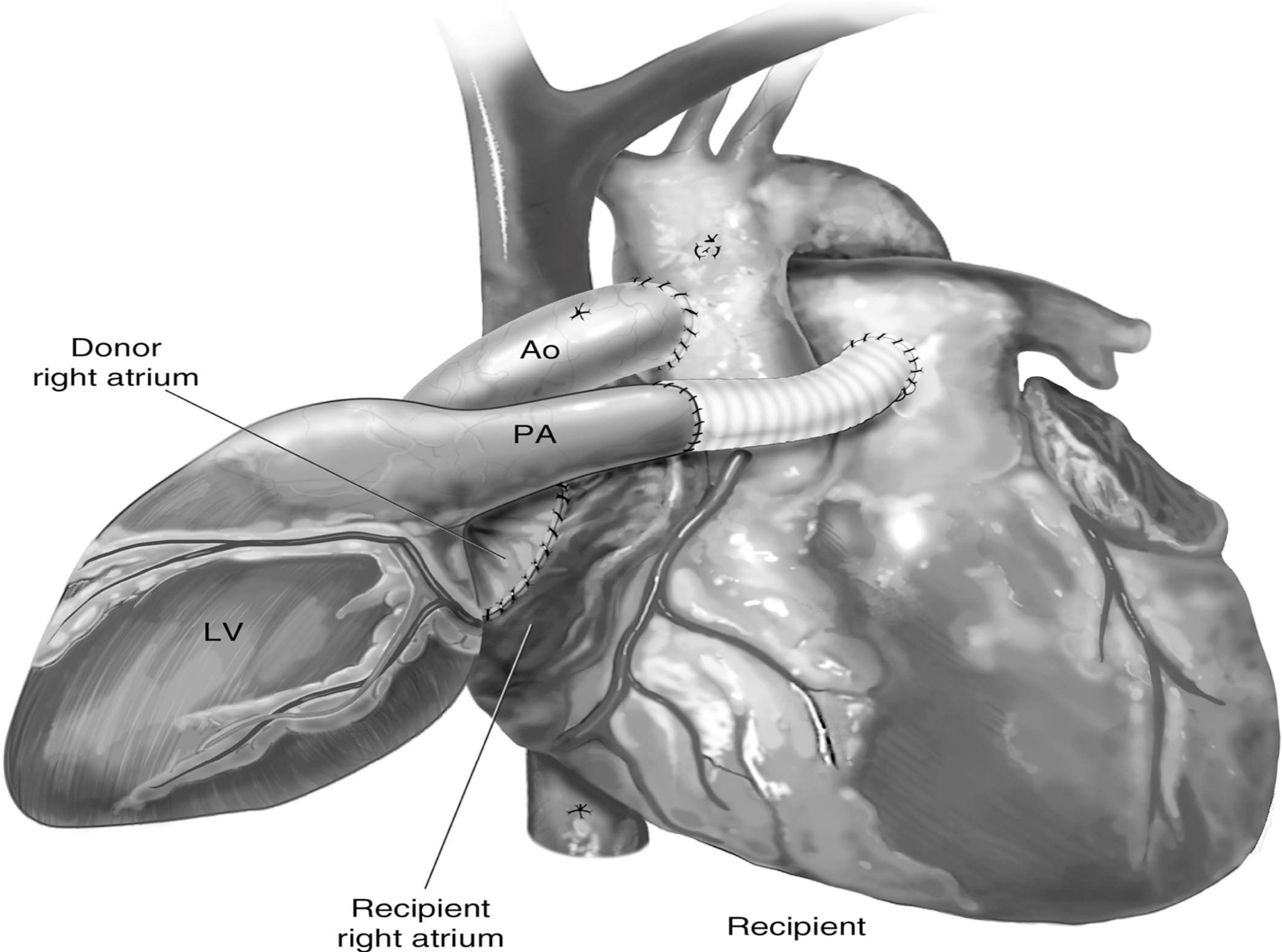

C

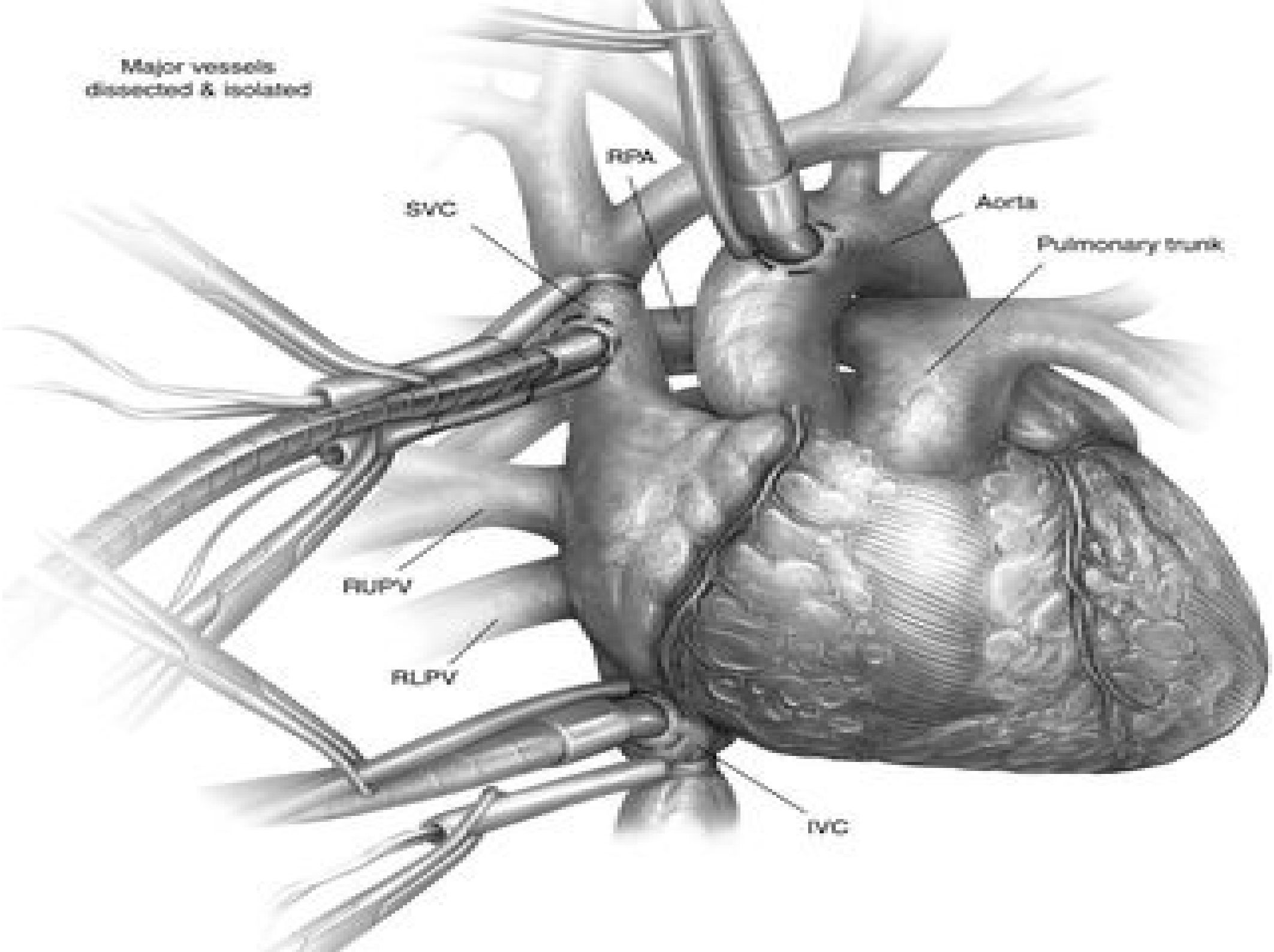
A, RA is divided to create SVC and IVC cuffs. Great vessels are divided as in biatrial method.

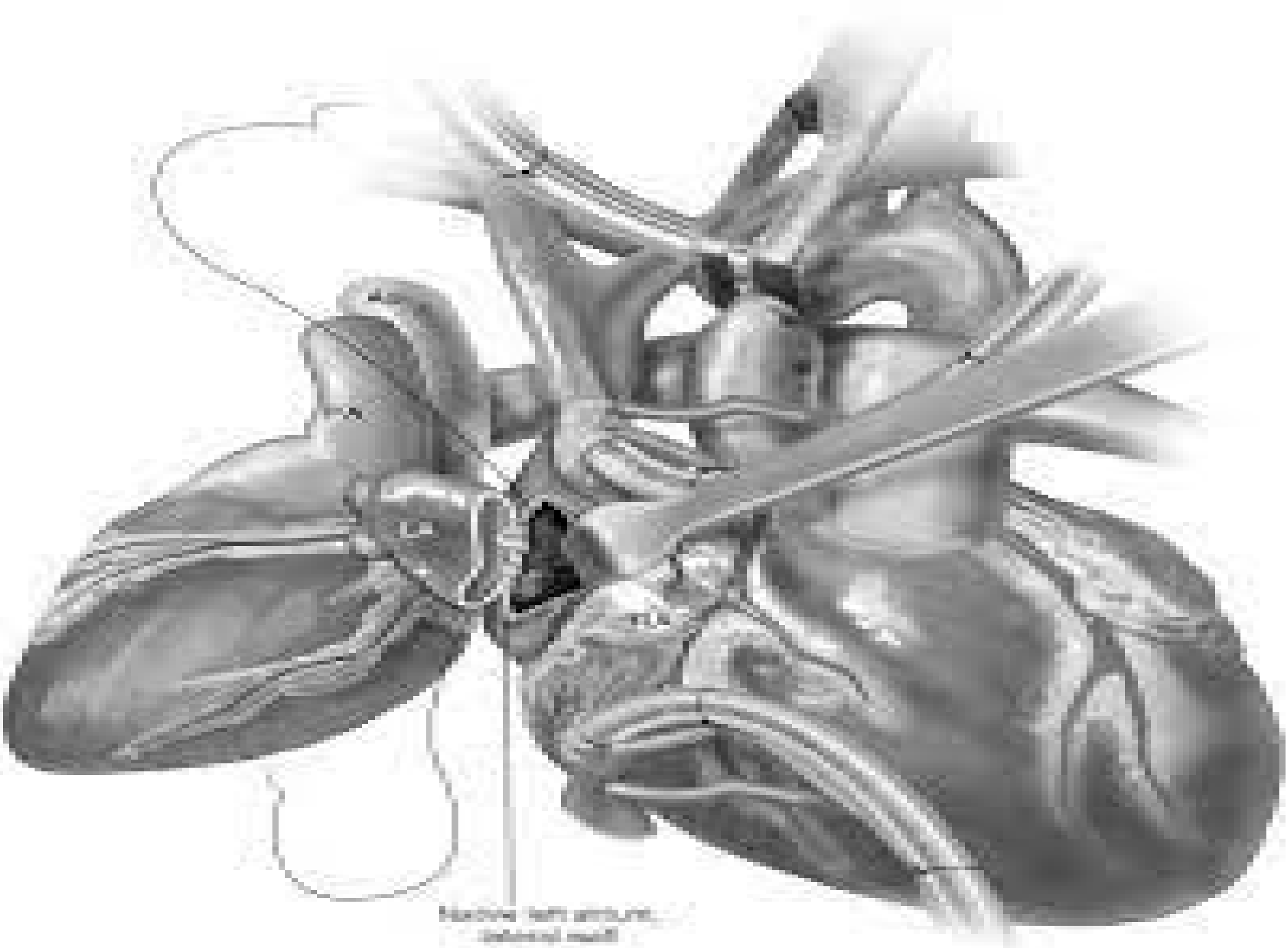
B, Commencement of LA anastomosis.

C, Completion of bicaval transplant technique, showing IVC, SVC, aortic, and pulmonary trunk anastomoses.


SVC
IV
Aorta
Pulmonary arteries
Left atrium opened between right pulmonary veins
Left pulmonary veins closed
IVC


Donor
right atrium
Ao
PA
LV
Recipient
right atrium
Recipient


Major vessels
dissected & isolated
RPA
SVC
Aorta
Pulmonary trunk
RUPV
RLPV
IVC



پیوند قلب کودکان در ایران

به گزارش خبرگزاری مهر:

- تاکنون بیش از ۱۵۰ مورد پیوند قلب در کودکان در مرکز قلب شهید رجایی طی ۶ سال گذشته انجام شده (از۸ تا ۴۸ کیلوگرم) شامل DCM, RCM, ARVC, hepatobastoma, ...
- در سال ۹۹: ۲۲ مورد و در ۶ ماه نخست ۱۴۰۰: ۲۵ مورد (یک مورد فوت)
- در کل دنیا سالانه ۴۰۰ تا ۴۵۰ مورد
- مهم‌ترین دلیل این موفقیت کار تیمی منسجمی شامل تمام همکاران از واحد نقلیه تا ریاست بیمارستان و اتاق عمل، تیم جراحی قلب، بیهوشی قلب، perfusionist وECMO و تیم داخلی است.
- مهمترین مشکلات در کشور ما: فرهنگ اهدا عضو، داروها

03 August 2020

Sajjad Darwishali, a 9-year-old boy from Yazd, was brain dead after a car accident in his hometown while cycling in a street on August 31, 2019. Upon his family's consent, his organs including his heart, liver, cornea and kidneys were donated to patients in need.

On September 1, 2019, Iran's emergency flight team headed to Yazd to quickly transfer Sajjad's heart to Tehran in order to be transplanted to another 10-year-old boy, Mahyar Issaei. The transplant operation was successful. Mahyar had been suffering from cardiomyopathy, a disease of the heart muscle, for four years as a result of Kawasaki disease. He had been waiting for heart transplant for four months. Mahyar was discharged from the hospital after 19 days and is recovering. Doctors recommended him to rest at home for three months due to low immunity of his body and then gradually return to normal life. From now on, the hearts of the two families are beating for Mahyar's health, wishing him a bright future.

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Doctors at Shahid Rahnemoon Hospital in Yazd prepare Sajjad's heart for transfering to Tehran and transplanting to 10-year-old Mahyar.

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Emergency technician takes Sajjad's heart to helicopter for transfering to Shahid Rajaee Hospital in Tehran. For a heart transplant, the patient needs to be transplanted within four hours after the aorta is removed, otherwise the heart will die.

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Mahyar, in the intensive care unit (ICU) of Shahid Rajaee Hospital in Tehran, is ready to be transferred to the hospital ward a few days after the heart transplant operation.

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Mahyar's mother is happy to see his son being transferred from intensive care unit (ICU) to the hospital ward.

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More than a month after the heart transplant operation, Mahyar has partially recovered and is getting a haircut at their home in Karaj.