The Official journal of Indian College of Cardiology, Kerala Chapter

Vol. 2, Issue - 2 September 2018

KJC 3

Kerala Journal of Cardiology

Focussed topic: **Interventions of inter atrial septum**

KJC

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"I can't go out on the track and do the same old things, it won't work...!"
– Lightning McQueen (Cars -3)

Dear Teachers and Friends,

Thank you very much for the overwhelming reception given to first two editions of Kerala Journal of Cardiology (KJC), the official publication of Indian College of Cardiology, Kerala Chapter. In fact, within one year of its humble beginning as a regional journal, KJC was able to grab national attention among post graduate students in cardiology. We received mails and messages not just from Kerala and Tamil Nadu, but also from Managalore, Pune, Chandigarh, New Delhi…..truly we were overwhelmed and honoured. This should make us more grounded and responsible. The bar has been raised several notches above…. and we need to deliver every time!

The initial two editions of KJC focused on clinical aspects of congenital heart diseases and valvular heart diseases. And with the KJC 3, we are shifting gears to the exciting world of interventional cardiology. This does not mean, KJC will not cover clinical topics in future; KJC will include anything that is important in learning and clinical practice. We are trying to have totally different content with each edition and we hope this unpredictability will help to sustain reader's interest in KJC. Just like 'Lightning McQueen' in 'Cars -3', we know, "we can't go out on the track and do the same old things, it won't work…!"

KJC 3 is a mix of senior master teachers and young academic teachers as in previous editions. With every passing month KJC is getting bigger – this time we have a record number of six master teachers (5 in Diamonds section and 1 in Pearls section) with their teaching articles; Making KJC 3, the biggest KJC ever in terms of content and pages. As you go through the pages of KJC 3, you will realise the ''Pan India' focus of journal with more teachers contributing from various parts of India. The **'Diamonds'** section of KJC 3 deals with interventions of inter atrial septum and focuses on interatrial septal anatomy, atrial septal defect and trans-septal puncture.

For a resident/fellow in cardiology, one of the challenging things to learn in interventional cardiology is to master the technique of inter atrial septal puncture. At least at some point of our career, we all felt that learning trans-septal puncture was 'the thing' and it distinguished true interventionists from kids! I can remember the days, myself spending hours on articles and videos of tran-septal puncture; only to get frightened with the innumerable techniques and complications starting from cardiac perforation to aortic valve injury. The seniors/teachers who were experts in trans-septal procedures were bigger heroes than many Hollywood celebrities..!

In this edition of KJC, we have three master teachers trying to simplify the transeptal puncture techniques. The aim of this section is not to enumerate all the techniques of trans-septal puncture and confuse the juniors further. For a systematic and in depth learning, any number of classic text books are available. Aim is to simplify it and describe only the commonly used methods by the masters in the field. In order to have a balanced learning, three different perspectives of trans-septal punctures are included.

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Dr Rajiv C is the Clinical Professor at Amrita Institute of Medical Sciences (AIMS), Kochi, Kerala and is a renowned senior adult interventional cardiologist dealing with structural interventions. As mentioned already, the intention is not to have a comprehensive review of all the techniques but to elaborate on the methods usually done in his lab. We can feel his clear approach to the techniques and his lucid way of teaching in this article. Approach to septal puncture can vary in an electrophysiology lab when only venous access is taken for radio frequency ablations. **Dr Ajit Thachi**l, an acclaimed academic speaker and senior electrophysiologist at Lisie Hospital, Kochi describes how trans-septal puncture is performed in an electrophysiology lab. In addition, he describes the newer methods of trans-septal punctures using intra cardiac echo-cardiography and trans-oesophageal echocardiography. In difficult situations like very large left atrium or structural abnormalities, an understanding of the trans-jugular approach to puncture inter atrial septum is very useful. KJC is proud to have **Dr George Joseph**, Professor of cardiology, Christian Medical College (CMC), Vellore, Tamil Nadu, dealing with this topic; Dr George Joseph being one of the pioneers of this technique in India. This article is co-authored by **Dr Dibya Ranjan Behera**, Assistant Professor in cardiology CMC, Vellore.

After discussions on tran-septal puncture, KJC-3 will move to another important topic, 'anatomy and embryology of inter atrial septum' by **Dr Deepa S Kumar,** Assistant Professor in cardiology at Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Thiruvananthapuram, Kerala. For every student in cardiology, hemodynamic assessment of cardiac shunt lesions is generally considered a difficult nut to crack! **Dr Kannan B R J**, senior interventional cardiologist and paediatric cardiologist at Vadamalayan Hospitals, Madurai, Tamil Nadu, deals with this tough topic. Dr Kannan B R J is well known for his teaching classes and this master teacher has managed to assemble approach to all the cardiac shunt lesions in an amazing small article….read it to believe it!

Device closure of atrial septal defects (ASDs), is an important intervention in children as well as in adults. A great teacher with the experience of thousands of ASD device closures, **Dr Krishnamoorthy K M**, Professor of cardiology at SCTIMST, Thiruvananthapuram, Kerala is presenting a step wise approach to ASD device closure in his inimitable way. This chapter has 61 figures from his personal collection to make it as simple as possible to the students in cardiology. **Dr Sarin Mathew**, Senior Fellow, Aortic and Adult Cardiac Surgery, Manchester University Hospital, United Kingdom (UK), gives the surgeon's approach to ASD closure, adding variety to this section. Truly we are becoming international with this article from UK!!

Unlike previous editions, KJC 3 in its **'Pearls'** section carries a master teacher as well. **Dr Ramakrishna Pillai V**, currently senior interventional cardiologist at Kerala Institute Medical Sciences (KIMS), Thiruvananthapuram has decades of teaching experience including at SCTIMST, Thiruvananthapuram. He has prepared "STEMI management – an update" a comprehensive article incorporating all the recent guidelines. We are sure that the residents in cardiology will find this article as a very useful quick reference to STEMI management. **Dr Praveen Jayan**, consultant cardiologist at Bharat Hospital, Kottayam, discusses medical management of valvular heart diseases subsequently. Finally, **Dr Arun Gopi** and **Dr Sajan Ahmad Z**, editorial board members of KJC, complete the 'Pearls' section of KJC 3.

Editorial board would like to thank **Dr Ramakrishna Pillai V**, President of Indian College of Cardiology, Kerala chapter; **Dr Mangalanandan P**, Vice President of Indian College of Cardiology, Kerala chapter; and **Dr Binu S S**, Secretary of Indian College of Cardiology, Kerala chapter. Without the unconditional support offered by them, KJC 3 would not have been possible.

It has been close to two years since I joined the duty of chief editor of KJC and I must say, I have enjoyed the job given to me thoroughly. It feels wonderful to be associated with KJC; but just as all good things out there, an end is inevitable. KJC is going to be handed over to better hands and this will be my last assignment as chief editor of KJC. Expect a totally revamped and a lot better KJC 4 from the new editor. I would like to thank all the teachers and friends for the support and encouragement.

'Smokey' in Cars - 3 said…..

"*You can't turn back the clock, kid. But, you* ***can*** *wind it up again..!*"

I am trying to wind it up again!!
Bye. With regards.

Abhilash S P
Editor in chief
KJC

KJC Diamonds

Trans-septal Puncture: How I do It

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Editor's Note: ***Trans-septal puncture is an important aspect of interventional cardiology. Approach and technique vary cosiderably between operators. This article is the perspective of this distinguished senior adult interventional cardiologist.***

INTRODUCTION

Cardiologists Drs John Ross Jr, Eugene Braunwald and Andrew G Morro chief of cardiac surgery at the National Institutes of Health (now the National Heart, Lung and Blood Institute), Bethesda first developed and published the concept and technique of trans septal left sided heart catheterization[1] in 1959. Subsequently important refinements were made to the needle and catheter. Edwin C. Brockenbrough's description[2,3] of the technique in 1962 differs hardly from that in current use. Charles E. Mullins developed a combined catheter and dilator set designed precisely to fit over the Brockenbrough needle, which gives a smooth taper from the tip of the needle, over the dilator to the shaft of the sheath[4]

Initially septal puncture was used for hemodynamic left atrial pressure measurement[5,6,7] and LV pressure measurement in severe aortic stenosis[1]. This technique found great practical use since balloon mitral valvotomy was popularised by Kanji Inoue et al[8,9] in 1984. Subsequently more and more expanding indications have surfaced especially for Transcatheter mitral valve repair (MitraClip), left atrial appendage closure, mitral valve in valve implantation, mitral paravalvar leak closure, percutaneous left ventricular assist device placement. and electrophysiologic procedures like Pulmonary vein isolation for AF/left side pathway ablation.

Safe and successful septal puncture needs a thorough knowledge of the septal anatomy and the hardware needed with intelligent use of imaging, primarily fluoroscopy.

ANATOMY OF THE INTER-ATRIAL SEPTUM

The inter-atrial septum is bounded posteriorly by a fold of pericardium between the left and right atria, superiorly by the superior vena cava (SVC), antero-superiorly by the aortic non-coronary sinus, anteriorly by the septal tricuspid annulus, antero-inferiorly by the coronary sinus os (Fig 1), and inferiorly by the inferior vena cava. In an autopsy study of 50 patients[5], fossa Ovalis was oval (82%); average transverse diameter was 14.53 mm and vertical 12.60 mm. In 90%, the rim of the annulus was raised; in 20%, a recess was found deep to the margin of the annulus

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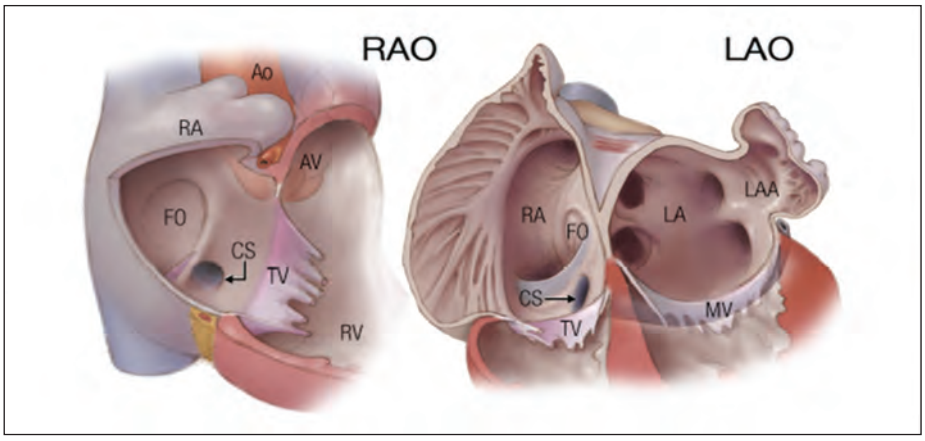

Fig.1 Atrial septum as viewed in RAO & LAO
(AV - Ao valve, FO - Foramen Ovale, CS - Coronary Sinus)

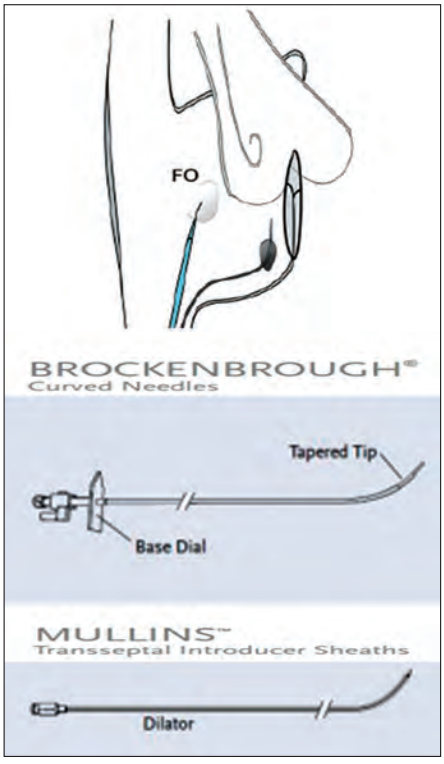

Fig.2 Site of septal puncture and Brockenbrough needle & Mullins Sheath assembly)

THE CLASSIC TECHNIQUE

A femoral venous access is obtained (more commonly the right). When femoral venous access is not available right jugular venous access can be made use of[19]. A terumo guidewire (0 .032-inch) is passed via 6F sheath in the right femoral vein to the superior vena cava and the left innominate vein in the anteroposterior fluoroscopy view. Arterial access is preferably obtained to keep a pig tail catheter in the aortic non coronary sinus as a land mark of the aortic root to avoid aortic puncture which can have disastrous consequences. His bundle catheter is an alternate option (Fig.2). Puncture has to be posterior to the His bundle & coronary sinus os.

A 5F/6F pigtail catheter is positioned in the aortic non coronary sinus. The venous sheath is removed and a Mullins dilator is advanced over the wire into the left innominate vein keeping enough wire beyond and the wire is then withdrawn (Fig.3). The Mullins dilator is pulled back one cm ensuring good blood back flow to prevent its tip poking against the vein. The Brockenbrough needle with a curved tip is then passed up the Mullins dilator gently until its tip is just within the end of the catheter (Fig.4). The direction arrow on the needle is rotated to face posteriorly to 4 o'clock, as viewed from below, if the LA is of normal size, or to 5 or 6 o'clock for a moderately enlarged or very large LA.

The catheter and needle are withdrawn together until they are seen to slip medially on entering the RA. They are slowly withdrawn further till a small jump of the catheter is seen and/or felt as the tip drops over the limbic edge into the foramen ovale. The assembly is gently advanced slightly upward to confirm that it is catching on the atrial septal wall. Most of the time, especially in patients with mitral stenosis tactile feel of left atrial pulsations will be discernible. Now the position of the catheter with the needle can be confirmed in multiple views.

RAO view (Fig.5) ensures that the catheter tip is away from the right atrial wall, inferior and posterior to the aortic non coronary sinus and superior and posterior to the coronary sinus ostium. LAO view ensures that the catheter is pointed towards the left atrium and the catheter tip is posterior and inferior to the aorta. Electrophysiologists, who usually deal with normally sized LAs, use the left anterior oblique position because it better profiles the drop of the catheter over the limbic edge. Some operators prefer the right anterior oblique (which has the atrial septum enface). I prefer to puncture in the lateral view (Fig.6). A gentle counter clockwise motion may be done to confirm that the needle curve is pointing posteriorly to prevent a very anterior puncture. However any change in position of the catheter tip should be followed by review of the position in the RAO view before attempting puncture. Once satisfied with good position in RAO & lateral views and LA pulsation, puncture can be done under fluoroscopy.

With the catheter held immobile and steady, the needle is advanced forward beyond the dilator tip. A "give way" feel can be felt by the operator as the needle crosses the septum. LA entry can be confirmed by a gentle contrast puff in the left atrium. Backflow of bright red blood is another method to ensure successful left atrial entry. Occasionally, when a patent foramen ovale is present, both the catheter and needle may jump forward together into the LA when the initial upward pressure is applied. However such an entry may not be the preferred one in many indications.

Once the needle tip position in the left atrium is confirmed, the Mullins dilator is gently advanced over the needle into the left atrium(Fig.7). Heparin is given either in the left atrium or in the pigtail catheter in the aorta. An ACT of ≥300 sec. is ideal. A 0.025 inch stainless steel guidewire terminating in spring coils is advanced through the Mullins dilator into the left atrium. This ensures subsequent safe procedures in the left heart. The Mullins dilator is removed and larger dilators depending on the procedure needed are used to dilate the femoral venous entry and the atrial septal entry sites.

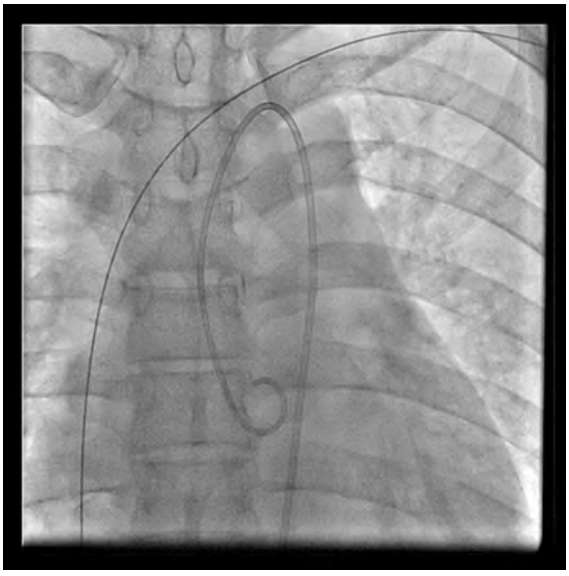

Fig.3 AP view: Terumo wire through the left innominate vein. Pig tail catheter in the aortic sinus.

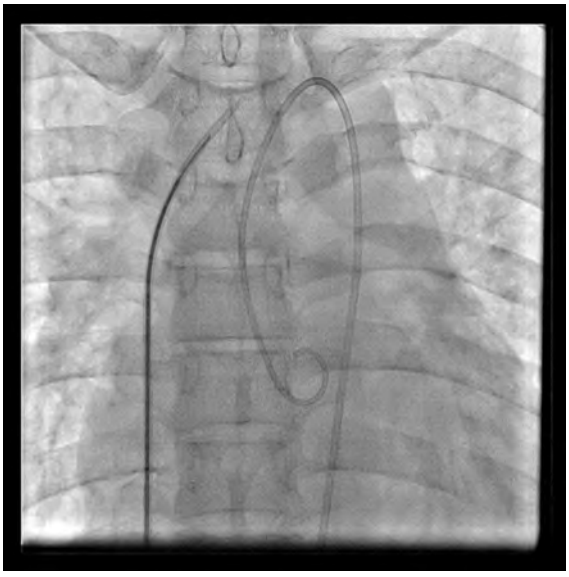

Fig.4 AP view: Brockenbrough needle within the Mullin's dilator.

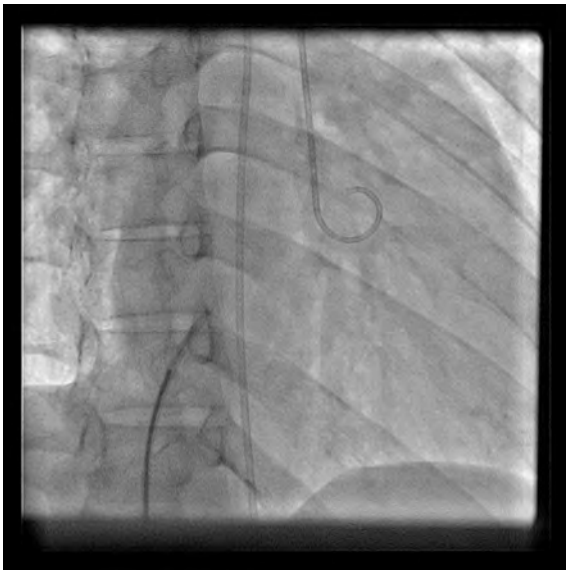

Fig.5 RAO view: Site of puncture below and posterior to aortic sinus, above and posterior to coronary sinus OS and away from RA wall.

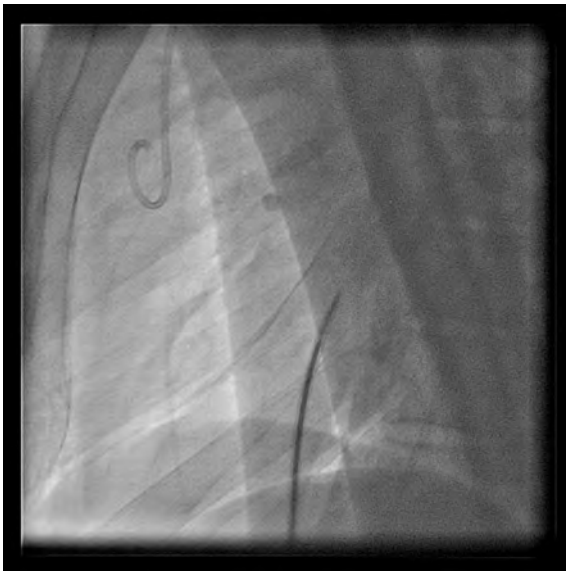

Fig.6 Lateral view: Puncture site below and posterior to aortic sinus.

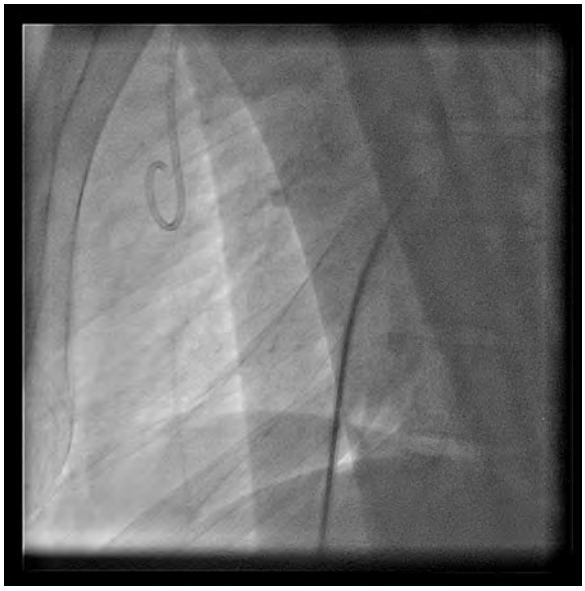

Fig.7 LA entry in the lateral view

The Visual Target

If no drop across the limbic edge is observed,which is common with dilated atria, a visual target must be used. In the AP view the lower border of the LA is visible when the LA is enlarged, and the upper border can be estimated from the bifurcation of the trachea. The crossing point will usually be approximately two thirds of the way down the vertical height of the LA. Hung proposed aiming for a position at the height of one vertebral body from the lower edge of the LA [9]. This takes into account the need to seek a lower position when the LA is very enlarged.

RA angiography can be used to delineate the anatomy of the septum (Fig.8). To achieve satisfactory images a volume of 30 ml of contrast is injected into the RA at 12–15 ml/s using a power injector via a pigtail catheter in both the RAO and LAO projections. This will delineate the vena cavae, tricuspid valve, posterior wall of the RA and the intra-atrial septum. The stored images can then be used to guide the transseptal puncture.

Inoue introduced injecting contrast into the RA and maintaining acquire-mode fluoroscopy until the LA cavity is outlined[17]. The area of RA/LA overlap can then be memorized in relation to the vertebral bodies and used as a visual target. This is particularly helpful if there is distorted anatomy.

IVC angiogram[18] could directly or indirectly show all the anatomical references mentioned earlier. The optimal puncture site was easily identified as the point inferior-posterior to the Non coronary aortic sinus (NCAS) and superiorposterior to the CS os in RAO 45 projection. This was subsequently validated on 3D CTimages. In 78 (96%) patients, the appropriate puncture site was to the left of the midline between NCAS and CS os.

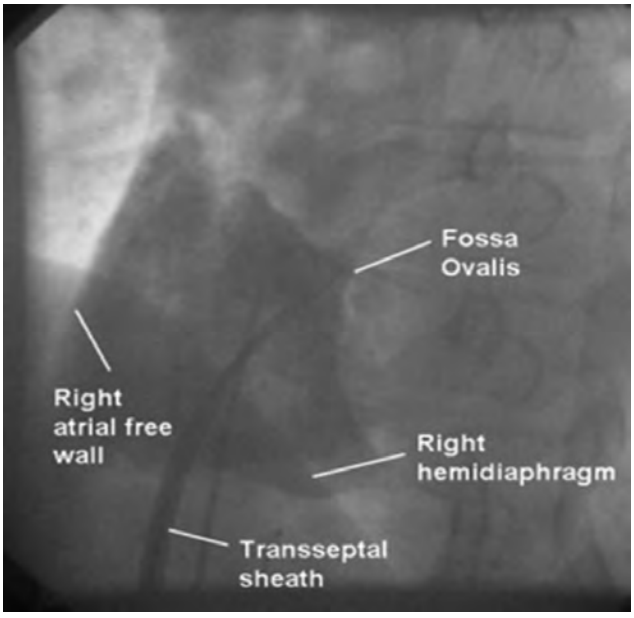

Fig.8 Right atriogram at LAO 40°. From Rogers DP, Lambiase PD, Dhinoja M, et al. Right atrial angiography facilitates transseptal puncture for complex ablation in patients with unusual anatomy17. J Interv Card Electrophysiol 2006;17:29–34

Additional Visualization with Ultrasound

Trans esophageal echocardiography 2D/3D and Intracardiac echocardiography can be complimentary modalities to aid successful and safe septal puncture. They may be useful in selecting sites for puncture ideal for the indication (Fig.9).

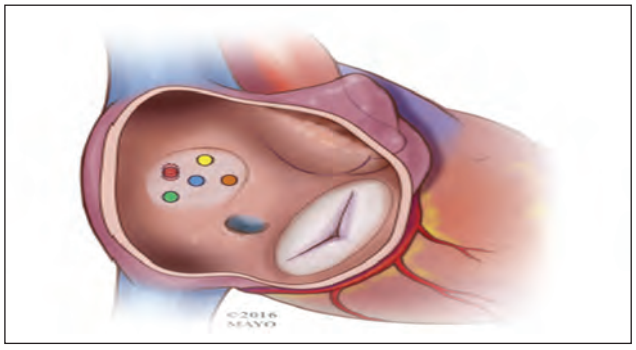

Fig.9 Site specific trans septal puncture for various cardiac interventions[23]

Red: MitraClip, paravalvular leak closure (a higher crossing site is recommended for medial leaks, and a lower crossing site is recommended for lateral leaks; dashed red circles). Yellow: transseptal patent foramen ovale closure. Blue: percutaneous left ventricular assist device placement, hemodynamic studies. Green: left atrial appendage closure. Orange: pulmonary vein interventions. From Alkhouli et al. Transseptal Puncture Techniques. JACC : Cardiovascular Interventions:2465 – 8

TEE provides high quality images from mid esophagus directly behind the left atrium. This will require anaesthesia and also in addition an echocardiographer. ICE provides direct visualization of the inter atrial septum[10,12,13]. It neither needs anaesthesia nor additional personnel for image acquisition or interpretation. However it is costly.

Additional imaging can be useful in patients with lipomatous hypertrophy of the atrial septum, atrial septal aneurysm, previous ASD/ PFO device closure[14], prior surgical repair of an atrial septal defect (ASD). Pericardial or Dacron patches can easily be punctured to obtain transseptal access, whereas Gore-Tex patches are harder and difficult to penetrate. In patients with atrial septal aneurysm, during the transseptal puncture, ICE imaging from the RA can clearly show the dilator tip and needle tenting against the interatrial septum[16] The best plane for the transseptal puncture depends on the type of procedure . The level of the left pulmonary veins or slightly anterior to that is ideal for pulmonary vein isolation, allowing the maximal distance possible from the right inferior pulmonary vein and correct alignment with the long axis of the LAA/left pulmonary veins ridge, whereas a more anterior plane toward the MV is preferred for ventricular tachycardia ablations. The optimal view should encompass a safe space between the septum and LA lateral wall.

ICE can help localize the thinner portion of the foramen ovale to be crossed and avoid the hypertrophied atrial septum. In patients with atrial septal aneurysm[21], the septum may tent deep into the LA and get dangerously close to the heart border during transseptal catheterization. ICE is particularly useful to control the needle direction and monitor the space between the bulging septum and LA wall. In the presence of a percutaneous closure device, ICE can identify portions of the native septum not covered by the device that can be targeted for the transseptal puncture usually at the posterior and inferior portions of the septum. Clot formation can also be easily detected[15]. For ablation procedures, ICE can give additional information on ablation position and complications.

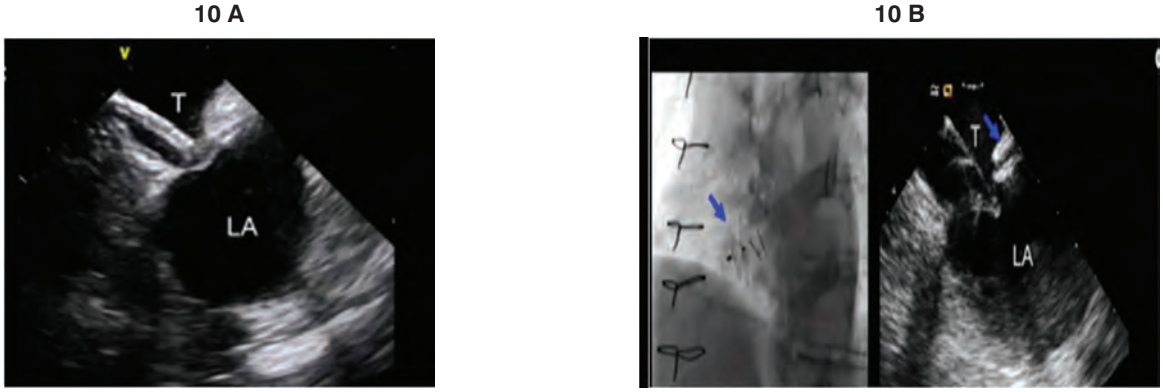

Fig.10 A - Use of ICE to identify thinner portion of the fossa in a patient with lipomatous hypertrophy of the interatrial septum. Fig.10 B - Trans septal puncture in a patient who had ASD device closure earlier. ICE can identify part of septum not covered by the device. From “Use of Intracardiac Echocardiography in Interventional Cardiology”. Enriquez A et al, Circulation 2018;137(21): 2282[13]

Alternative options in challenging cases

Septal puncture has been done using Radiofrequency enabled transseptal needles[20] (Baylis Medical Company) or the SafeSept Transseptal Guide wire (Pressure Products), a 150-cm-long, 0.0315-inch-diameter nitinol guide wire tipped with a flexible J-curve needle. Once the needle is across the septum and out of the dilator, it assumes a J shape, rendering it incapable of further tissue penetration.

TECHNICAL DIFFICULTIES

- Some patients have a very tough septum that resists needle puncture. Usually, this can be overcome by applying even greater pressure to the septum, but in some cases, an alternative crossing point has to be sought.
- Very high LA pressure can cause the atrial septum to bulge markedly into the RA cavity, displacing the catheter/needle as it descends the septum. Marked torque on the needle may be required to find a suitable crossing point.
- Giant LA: Very markedly enlarged LAs can be difficult targets. A very low position may be needed.
- Aneurysms of the atrial septum appear formidable on echocardiography but are surprisingly easy to cross, in part because of a high incidence of associated patent foramen ovale.[16]

COMPLICATIONS OF TRANS-SEPTAL PUNCTURE

Complications include

- Pericardial effusion or tamponade
- Aortic root, right or left atrial wall needle puncture
- Stroke/transient ischemic attack
- Persistence of atrial septal defect
- Death

In a larger multicentre review[11] of 5520 patients, 0.9% of procedures were abandoned because of inability to locate the fossa ovalis, tough atrial septum, perforation of the aortic root or most commonly perforation of the RA into the pericardial space. If this occurs a significant effusion or tamponade is unlikely, provided the sheath is not advanced creating a much larger hole in the atrial wall. If a sheath is passed it should be retained there to prevent exsanguination before either a device closure of the defect or surgical repair can be done. For elective procedures such as AF ablation it is prudent to abandon the procedure, as anticoagulation is required which could exacerbate the problem.

Transient ST elevation in the inferior ECG leads with or without chest pain has been reported in 0.6% of cases. It has been proposed this as a vagal response[22] to the direct mechanical disruption of the autonomic network of the heart by the catheter during the puncture. An alternative explanation, however, is coronary air embolism which may occur due to inadequate de airing of the assembly.

Contraindications to Transseptal Puncture

The only absolute contraindication to atrial transseptal puncture is thrombus at the atrial septum. Relative contraindications are thrombus elsewhere within the LA cavity, ongoing treatment with warfarin, or marked cardiac or thoracic deformity.

Key Points

1. The transseptal puncture is a routine procedure for PTMC and cardiac electrophysiology procedures predominantly for ablation of atrial fibrillation, to access the left atrium.
2. An intracardiac catheter/ pig tail in the posterior aortic sinus should be used as an anatomical marker to avoid puncturing the aortic root.
3. After the initial puncture make sure that the tip of the transseptal needle is in the left atrium before advancing the dilator or sheath further.
4. In view of the risk of stroke, meticulous attention to de-airing/flushing of sheaths and heparinisation(keeping ACT>300s) is necessary.
5. Approximately 1% of procedures are abandoned due to failing to cross the intra-atrial septum.
6. Complications occur in 1% of patients, most commonly inadvertent puncture into the pericardial space. Tamponade is unlikely, providing the sheath/ dilator are not advanced over the needle in this position.
7. Real time visualisation of the intra-atrial septum by TEE/ICE may reduce this small incidence of complications even further.
8. Iatrogenic atrial septal defects usually disappear by 3 months.

CONCLUSION

Atrial transseptal puncture when done by experienced operators is a safe procedure. One must be aware of and be geared to tackle the challenges in the case in question.

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Trans-septal Access in the Electrophysiology Laboratory

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Editor's Note: ***Approach to trans-septal puncture can differ significantly in electrophysiology lab. Author, a well known electrophysiologist describes his techniques of trans-septal puncture.***

Trans-septal access is frequently obtained in the electrophysiology laboratory. This access is required for pulmonary vein isolation and ablation of left atrial arrhythmia, and is often used for mapping and ablation within the left ventricle and on the mitral annulus. The steps involved and hardware used are broadly similar to those employed in trans-septal access in other situations. The conventional fluoroscopic technique used for trans-septal access is sometimes modified in the electrophysiology laboratory; such modifications will be described here.

1) Use of electrophysiology catheters as landmarks

Two electrophysiology catheters that are used as landmarks for septal puncture in the electrophysiology laboratory are the catheters in the coronary sinus and at the His bundle. The point at which the coronary sinus catheter changes in curvature marks the ostium of the coronary sinus (the coronary sinus catheter may lie along the floor or the roof of the coronary sinus in an individual case; this variability is to be accounted for). The compact His bundle potential, recorded just below the non coronary cusp of the aorta, can be used to gauge the location of the non coronary cusp. The fossa ovalis, representing the true interatrial septum, is the target site for septal puncture. Superoinferiorly, the fossa ovalis lies between the level of the non coronary cusp and the ostium of the coronary sinus. The site of puncture should be posterior to the coronary sinus ostium and the non coronary cusp (Figure 1). Thus, fluoroscopically guided septal puncture can be performed without the requirement of a femoral arterial access for pigtail catheter placement in the non coronary cusp. Such avoidance of a femoral arterial access may be desirable for prolonged ablations in the left atrium which require large doses of intravenous heparin. In 40-65 degree left anterior oblique views, the coronary sinus catheter also provides a readily visible reference for the boundary of the left atrium (Figure 1). This provides the operator a clear idea regarding how far into the left atrium the trans septal hardware can be safely introduced.

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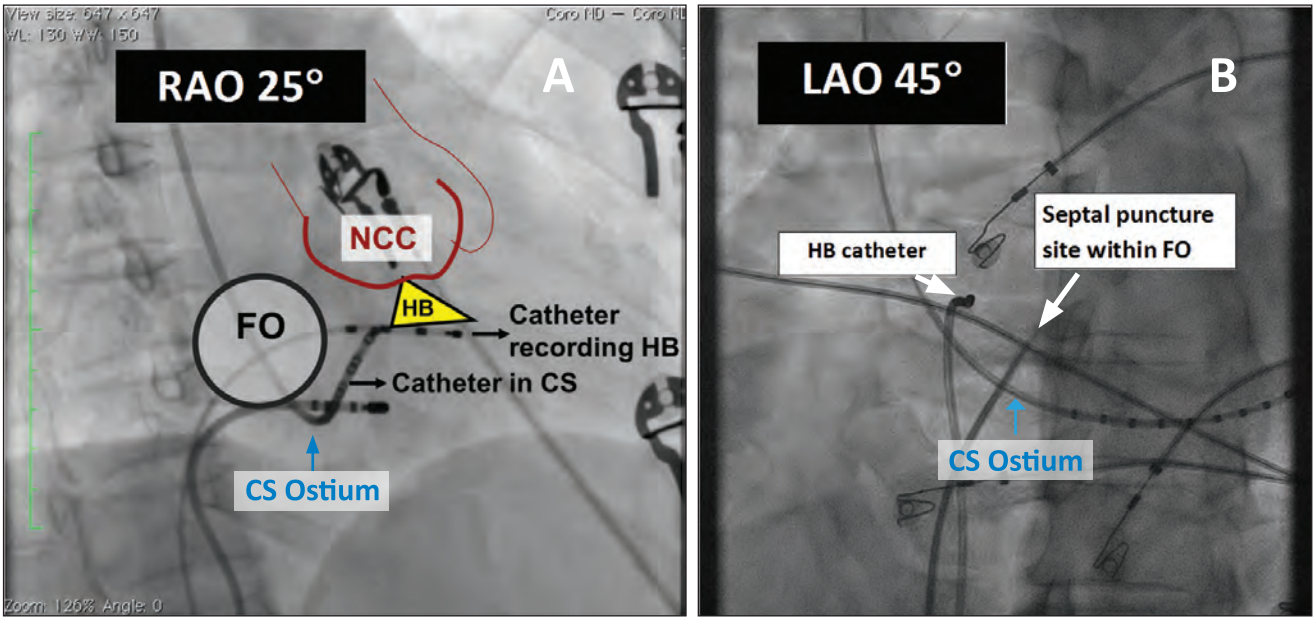

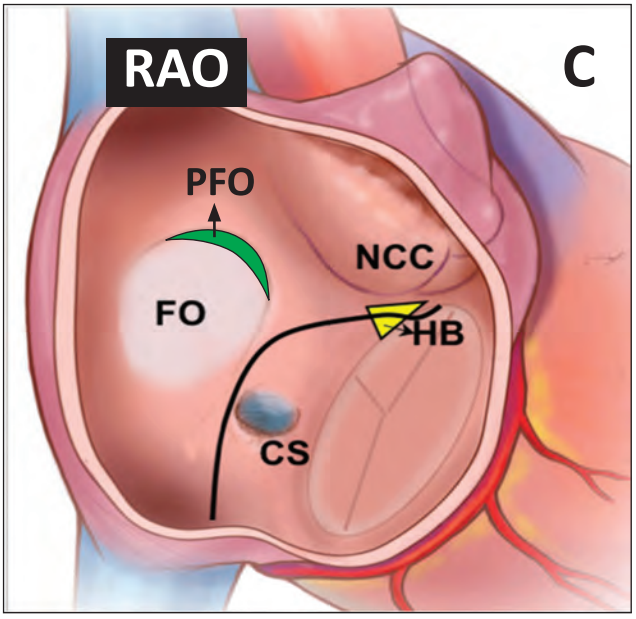

Figure 1. Use of EP catheters to guide site of septal puncture. Panel C is an illustration of the interatrial septum as seen in the right anterior oblique projection, and shows catheter positioning to record the His bundle deflection (see text for description).
RAO = Right Anterior Oblique view, LAO = Left Anterior Oblique view, FO = Fossa Ovalis, PFO = Site of patent foramen ovale, NCC = Non coronary cusp, HB = His bundle, CS = Coronary sinus

2) Procedure – specific tailoring of site of trans-septal access within the fossa ovalis

In order to facilitate maximum catheter manipulation in the target areas, trans-septal access to the mitral annulus and the left ventricle is best obtained through the mid or superior aspects of the anterior fossa ovalis, or through a patent foramen ovale. In contrast, the pulmonary veins (specifically the right inferior pulmonary vein, which is located posteroinferior to the left sided veins) are best approached though a puncture made in the lower aspect of the posterior or mid fossa ovalis (Figure 2).[1]

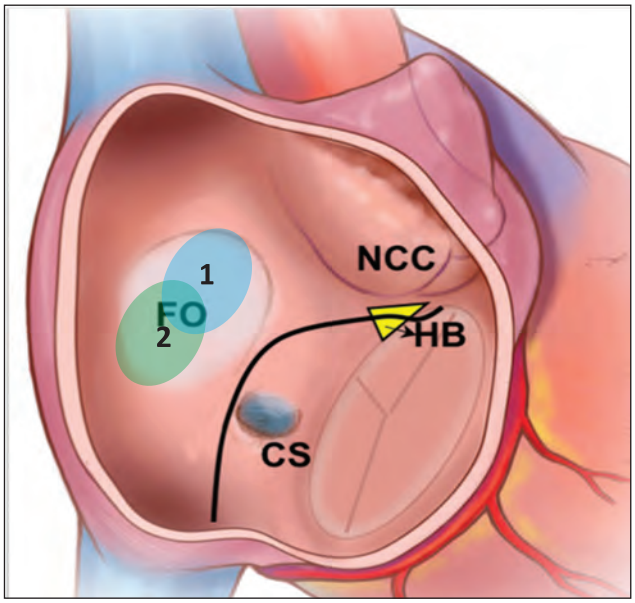

Figure 2. Procedure specific tailoring of site of septal puncture within the fossa ovalis. In this illustration of the interatrial septum as seen in the RAO projection, site 1 is preferred for access to the mitral annulus and the left ventricle, and site 2 is preferred for access to the pulmonary veins
NCC = Non coronary cusp, HB = His bundle, CS = Coronary sinus

3) Double trans-septal access

Two catheters (an ablation catheter and a spiral shaped recording catheter) are typically introduced into the left atrium via separate long sheaths to perform radiofrequency ablation for pulmonary vein isolation for the treatment of atrial fibrillation. This requires two trans-septal accesses, both through the fossa ovalis. Some operators prefer to perform two separate trans-septal punctures to obtain these accesses (Figure 3). Alternatively, after obtaining an initial access, the fossa ovalis may be probed using a deflectable catheter to obtain the second access (Figure 4).

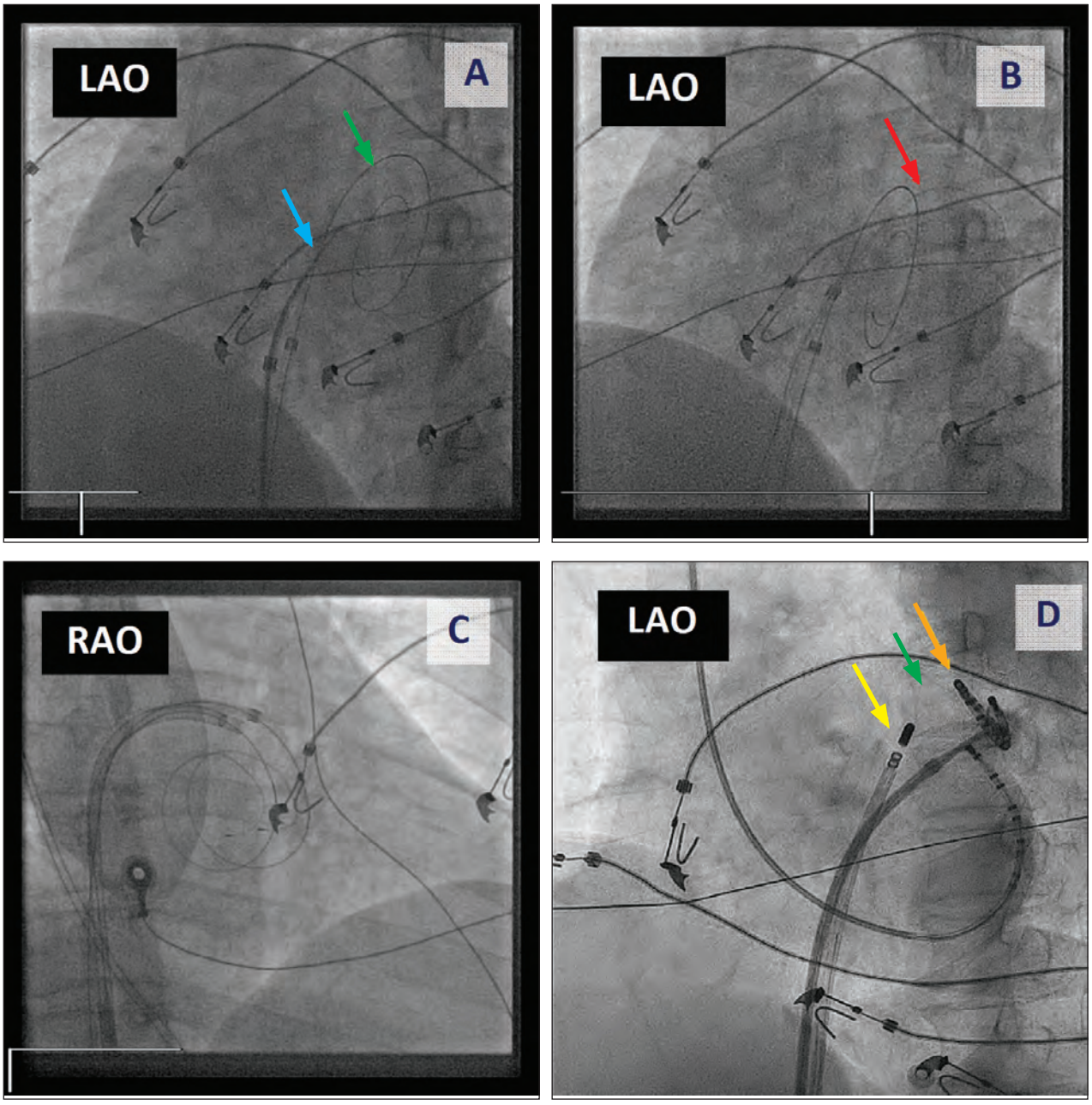

Figure 3. Dual trans-septal access obtained through two separate punctures. Panel A : A wire has been placed in the left atrium through the initial access (green arrow) , and the sheath introduced through this access has been withdrawn into the right atrium. A second trans-septal puncture is about to be made using a BRK needle introduced through another sheath (blue arrow). Panel B : The second trans-septal puncture has been made, and the sheath has been introduced into the left atrium over a wire through this puncture (red arrow). Panel C : The first sheath is re-introduced into the left atrium. Now there are two sheaths in the left atrium. Panel D : An ablation catheter is introduced into the left atrium through one of the sheaths (yellow arrow). The other sheath is used to introduce a spiral shaped catheter into the pulmonary vein (the left superior vein in this example; orange arrow)

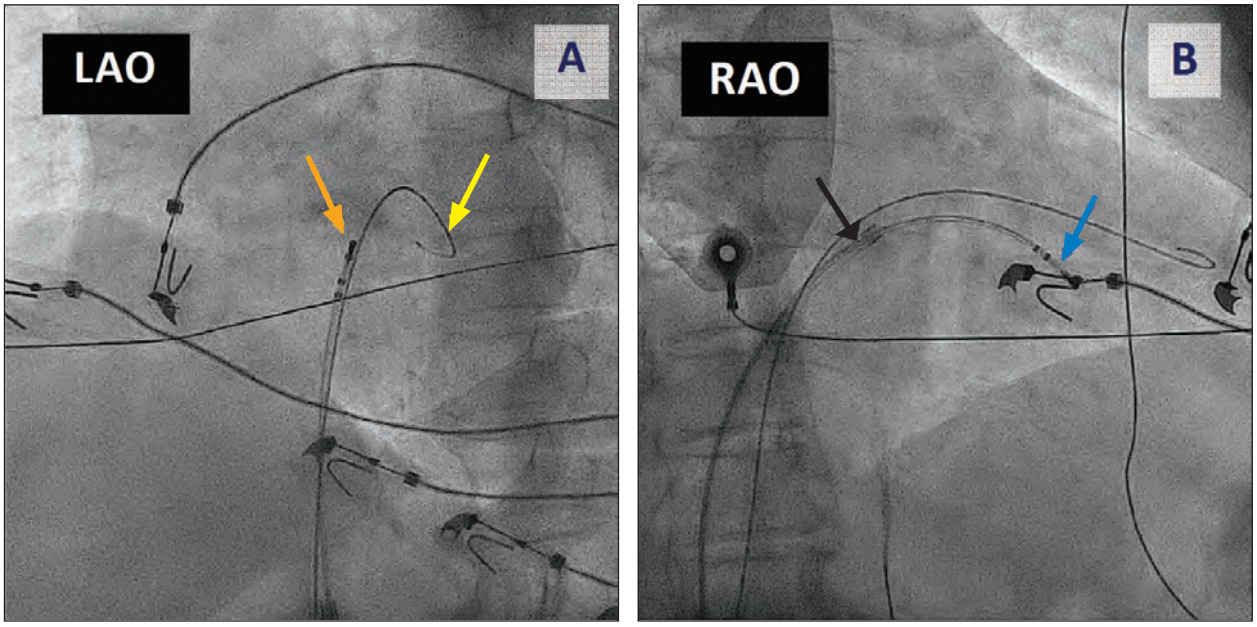

Figure 4. Dual trans-septal access obtained via probing. Panel A: A wire has been placed in the left atrium through the initial access (yellow arrow) , and the sheath introduced through this access has been withdrawn into the inferior venecava. A deflectable catheter (a 5French ablation catheter in this example; orange arrow) introduced through another sheath is being used to probe the opening created in the fossa ovalis by the initial trans-septal sheath passage. Panel B: Trans-septal access is obtained by the probing catheter through the initial puncture site. The catheter is passed trans-septally into the left ventricle (blue arrow) , and the second sheath (black arrow) is tracked into the left atrium over the catheter. Subsequently, the initial sheath is pushed back into the left atrium over the retained wire to complete dual trans-septal access.

4) Differences in trans-septal hardware for mitral commissurotomy vs electrophysiology procedures

Minor differences exist in the hardware used for trans-septal access in the electrophysiology laboratory as compared to those used for mitral commissurotomy. The trans-septal long sheaths that are most commonly used to access the left atrium are the SL 0, SL 1 and SL 3 fixed curve sheaths, and the Agilis deflectable sheath. All of them accommodate guidewires of upto 0.032" diameter. The long sheath most commonly used for trans-septal left ventricular access is a Mullin's sheath with a large curve. The Mullin's sheath accommodates guidewires of upto 0.035" diameter. Thesesheaths have varying tip shapes and curvatures that are designed for access to specific sites within the left atrium. The SL series of sheaths and the Mullin's sheath are all 61 - 63 cm long, with a 67-69 cm dilator length. Thus, the usually used 71 cm long BRK or BRK 1 or Brockenbrough needles can be used for septal puncture through the SL series sheaths, or the Mullin's sheath.The Agilis sheaths are longer (available in sheath lengths of 61 cm and 82 cm, with corresponding dilator lengths of 81 cm and 91 cm). Thus, longer septal puncture needles (long BRK or BRK-1 needles are available in 89 cm and 98 cm lengths) are required if these sheaths are used to guide the puncture. Alternatively, all punctures may be made using the Mullin's sheath, and the desired long sheath can be exchanged over the wire retained in the left atrium or left ventricle. When the sheath of one manufacturer is paired with the needle of another manufacturer, the operator should always check the relative lengths of the sheath-dilator-needle assembly before introducing it into the patient.

Most septal punctures can be made using the Brockenbrough (manufactured by Medtronic) or the BRK (manufactured by Abbott- St. Jude) needle; both of them have a 19^0 angulation of the tip. The BRK-1 needle (manufactured by Abbott- St. Jude) has a 53^0 angulation at the tip, and is typically used for septal puncture in presence of a dilated right atrium (Figure 5). The left atrial pressure among patients undergoing mitral commissurotomy is often higher than in patients undergoing radiofrequency ablation for left sided accessory pathways. This can sometimes influence the extent to which the fossa ovalis stretches into the right atrium, and consequently the amount of force required for puncture as well as the angulation at which the puncture needle engages the septum. The BRK needle may slide up the septum rather than tent the fossa ovalis due to a very tangential engagement

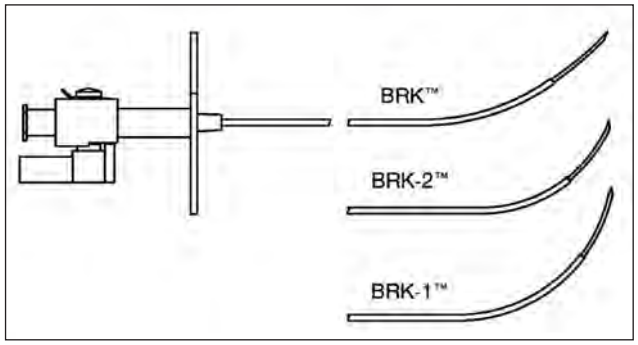

Figure 5. BRK series trans-septal access needles of varying tip angulations. BRK and BRK -2 needles are available in pediatric (56 cm) and various adult (71, 89 and 98 cm) lengths. BRK -1 needles are available in the various adult lengths.

of the fossa ovalis. In such situations, either the same needle may be rotated slightly to engage a different part of the fossa ovalis, or a needle with a greater angulation may be used to obtain a more perpendicular and less tangential engagement of the fossa ovalis. The BRK -1 needle is useful in this situation, but may be slightly difficult to manipulate in a normal sized right atrium. In this situation, many experienced operators prefer to manually increase the tip curvature of the BRK needle rather than choose the BRK-1 needle. This should be done carefully and preferably with the stylet retained inside, to prevent kinking of the needle lumen.

Radiofrequency powered trans-septal access represents a safe and effective alternative to trans-septal puncture using manual pressure as described here. For this, the NRG™ radiofrequency powered trans-septal needle (Baylis Medical, USA) is positioned at the desired site of septal puncture using conventional techniques. The needle is connected to the dedicated Baylis™ radiofrequency power generator; a few seconds of radiofrequency power delivery suffices to create a trans-septal passage. In a small randomized control trial, use of this needle was associated with faster trans-septal access and greater success at achieving trans-septal access compared to the BRK-1 needle.[2] This technique is particularly useful in thick/ fibrotic septa which cannot be punctured manually.

5) Alternatives to fluoroscopic guidance for trans-septal access

Two effective imaging modalities used as alternatives to fluoroscopy to guide trans-septal puncture are intracardiac echocardiography (ICE) and trans-esophageal echocardiography (TEE). Of these, intracardiac echocardiography is widely used, and is the easier one to use. The commonly used intracardiac echocardiography catheters are 9 french, bidirectionally steerable catheters mounted at the tip with a forward-viewing linear phased array probe capable of generating 2 dimensional ultrasound as well as conventional and colour doppler images. These catheters are introduced trans-femorally, and can be connected to selected cardiac echocardiography machines (most commonly to the Philips CX 50™, Abbott-St. Jude Zonare™ and Siemens Acuson™ machines) using dedicated connecting modules. The Carto Sound™ catheter is an intracardiac echocardiography catheter that can be integrated into a 3 dimensional electroanatomic mapping system (the Carto 3™ mapping system, Biosense Webster, Diamond Bar, CA, USA) used for electrophysiology procedures. The catheter can be left in place throughout the electrophysiology procedure, and is also used to guide catheter placement in various areas of the heart like the pulmonary veins, papillary muscles and the aortic cusps. For intracardiac echocardiography-guided septal puncture, the intracardiac echocardiography catheter is usually introduced into the right atrium through the left femoral vein. The intracardiac echocardiography catheter is initially positioned in the mid right atrium with the controls in neutral position to view the tricuspid valve and the right ventricle. This view is called the “home view” (Figure 6).

Gradual clockwise rotation from the home view allows sequential visualization of anterior to posterior structures starting with the aortic root and the pulmonary artery, followed by the mitral valve and the left atrial appendage along the anterior aspect of the fossa ovalis, and finally the pulmonary venous ostia along the posterior aspect of the fossa ovalis. Slight posterior and/or leftward deflection of the transducer tip may be required for adequate visualization of the fossa ovalis. Septal puncture must be accomplished in a plane posterior to the plane of the aortic root, at an area where there is adequate space from the interatrial septum to the posterior wall of the left atrium. The site of puncture should also be a relatively thin area of the interatrial septum. With the needle tip just inside the dilator, the appropriate site in the septum is engaged by the septal puncture assembly under intracardiac echocardiography guidance. Tenting of the septum at this area is visualized on snugly engaging the septum. Subsequently, the septum is punctured with the needle, at which point sudden loss of resistance is felt on the needle, and the tented part of the septum abruptly collapses back onto the needle. There are certain advantages to intracardiac echocardiography guided trans-septal access as compared to fluoroscopy guided trans-septal access. Intracardiac echocardiography – guided puncture allows more precise tailoring of the site of puncture within the fossa ovalis (Figure 7), though

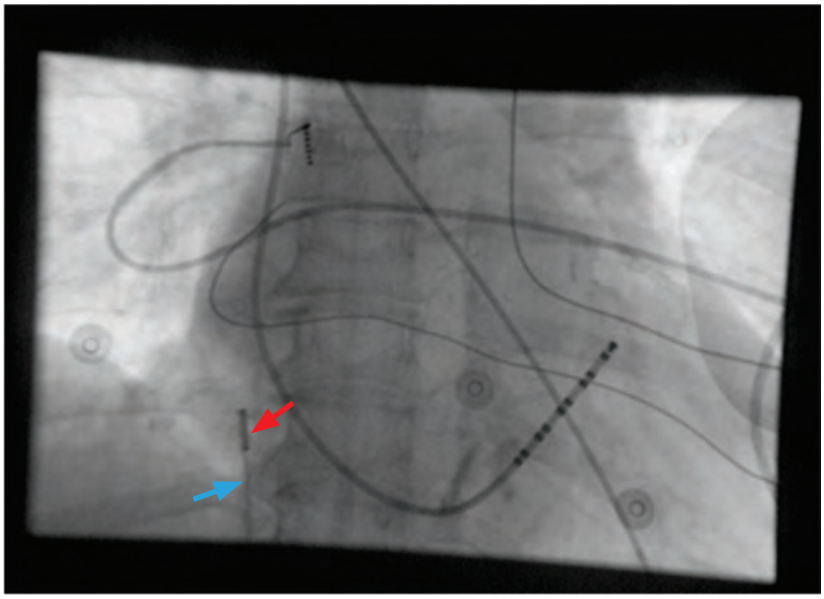

Figure 6 . Fluoroscopic orientation of the intracardiac echocardiography (ICE) catheter (shown in anteroposterior projection) to obtain the "home view". A slight tilt/ rotation (as shown in the figure) may sometimes be required to obtain an adequate home view. Blue arrow = catheter shaft; red arrow = ultrasound transducer

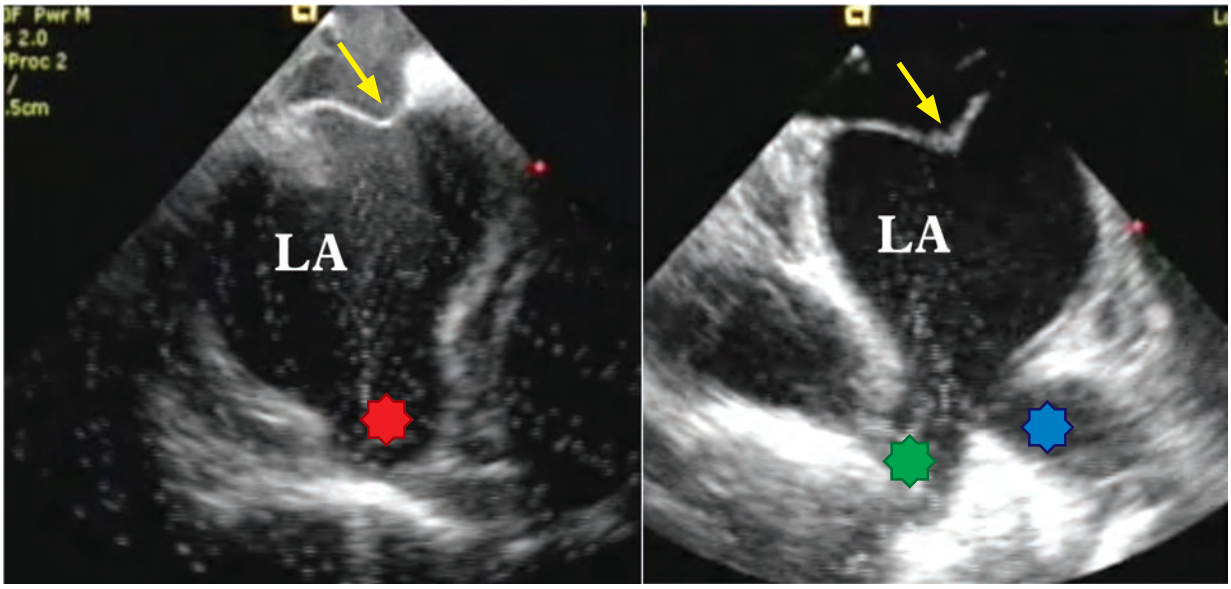

Figure 7. ICE to tailor the site of septal puncture. The left panel shows tenting of the interatrial septum (yellow arrow) in the plane of the left atrial appendage (red star). This is a very anterior plane; access to structures in the posterior left atrium can be difficult if puncture is performed in this plane. The right panel shows tenting of the interatrial septum (yellow arrow) in the plane of the left superior pulmonary vein (blue star) and the left inferior pulmonary vein (green star). This is a more posterior plane, and is the best plane to access the pulmonary veins. LA = left atrium

an experienced operator may be able to do the same without the aid of intracardiac echocardiography.

In some situations, upon attempted septal puncture, the needle slides up the fossa ovalis rather than puncturing the septum at the site of initial engagement. Too much sliding up can result in puncture beyond the fossa ovalis, and should be avoided. Sliding movement on attempted septal puncture is often due to a slightly tangential engagement of the septum by the needle. This can be readily visualized on intracardiac echocardiography. (Figure 8)

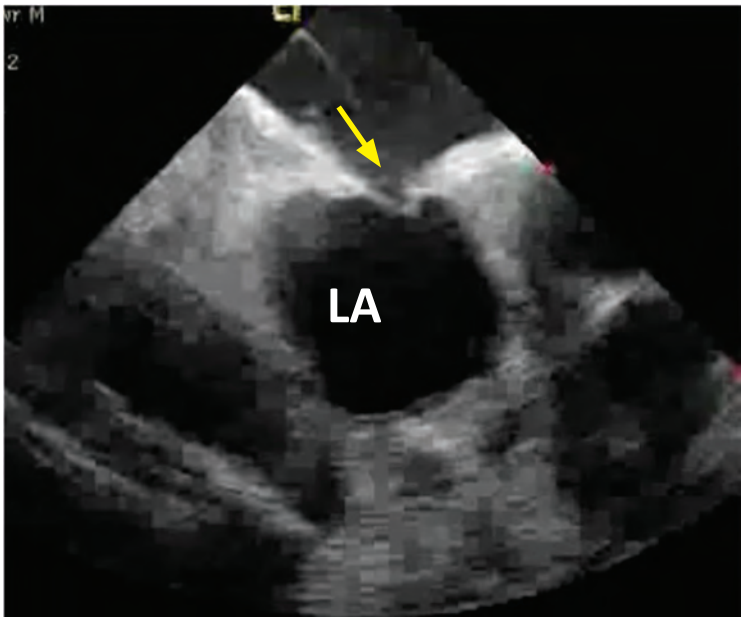

Figure 8. ICE Tangential engagement of the interatrial septum by the septal puncture needle (yellow arrow) causing the needle to slide up the fossa ovalis. Compare the angle of tenting in this figure with that in Figure 7 which shows a more perpendicular engagement of the interatrial septum. LA=left atrium.

The interatrial septum is thick in certain patients. Puncturing a thick septum may require considerably more force than the usual. Visualisation of the position of the septal puncture needle provides the operator with a greater degree of confidence while using more force against a thick interatrial septum. (Figure 9)

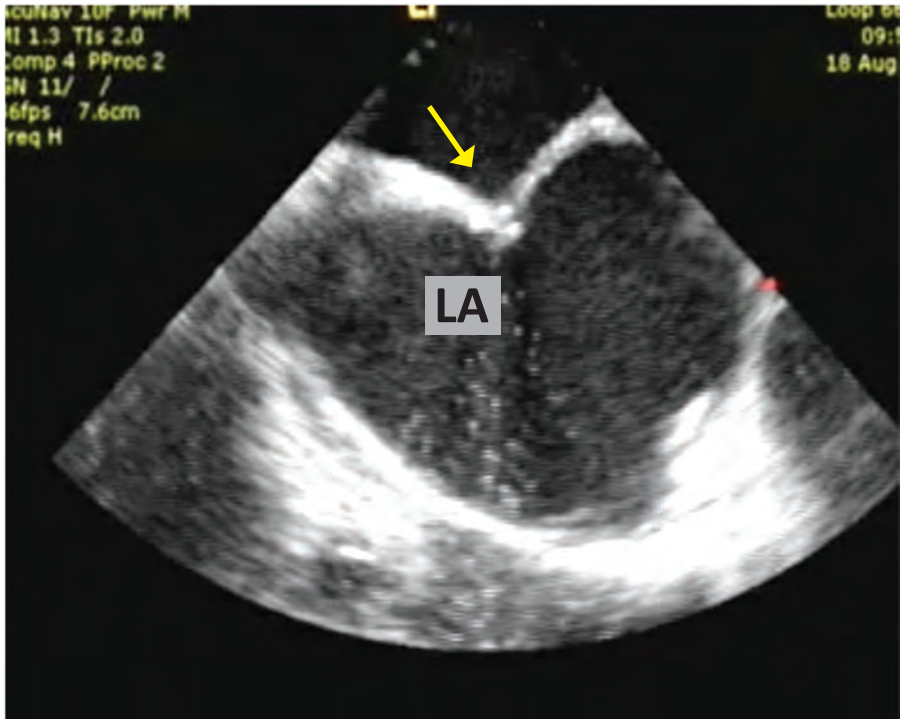

Figure 9. Intracardiac echocardiography (ICE) to visualize the septal puncture needle tenting (yellow arrow) a thick interatrial septum (compare the thickness of the interatrial septum to Figure 7)

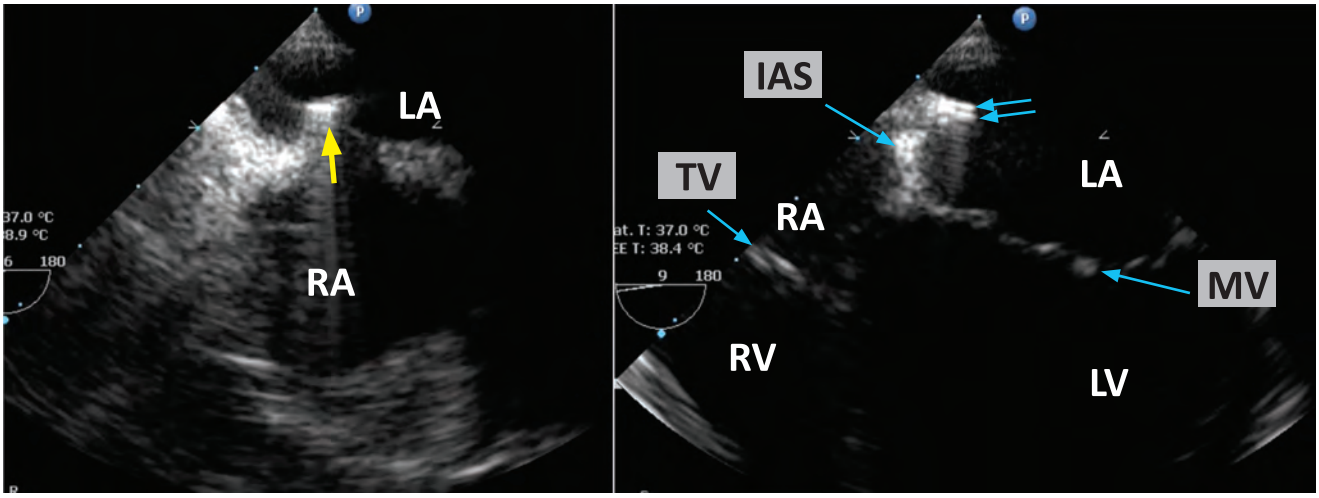

Figure 10. Images of trans-esophageal echo (TEE) to guide trans-septal access in pediatric electrophysiology. The left panel shows tenting of the interatrial septum (yellow arrow) by the trans-septal needle just before puncture. The right panel shows a Mullin's sheath (twin blue arrows) across the interatrial septum. RA = right atrium, LA = left atrium, RV = right ventricle, LV = left ventricle, TV = tricuspid valve, MV = mitral valve, IAS = intertarial septum.

Besides the above situations, intracardiac echocardiographic guidance can be useful to guide septal puncture when the anatomy of the interatrial septum is altered such that the conventional fluoroscopic landmarks are less reliable. Thus, in the electrophysiology laboratory, it is useful to have intracardiac echocardiography as a standby option to guide difficult trans-septal accesses.

Trans-esophageal echocardiography to guide trans-septal access is more cumbersome as compared to intracardiac echocardiography. One situation where it may be particularly useful is in small children in whom the operator may want to avoid the 9 french or 10 french sheath required for introduction of the intracardiac echocardiography catheter. Figure 10 provides an example of transesophageal imaging to guide a difficult trans-septal access in a 4 year old girl with tachycardiomyopathy due to an incessant atrial tachycardia ablated in the left atrial appendage.

To summarise, obtaining trans-septal access in the electrophysiology laboratory is broadly similar to obtaining access for non-electrophysiological indications. A variety of situations may arise which require slight modification of the technique and the hardware used. It is important to be aware of these situations, and the options available to tackle them.

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Trans-jugular Atrial Septal Puncture

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Editor's Note: ***This article is reviewed and edited by one of the pioneers of this technique in our country, Prof. George Joseph. KJC is proud to have this article by Dr. Dibya Ranjan Behera from CMC, Vellore.***

Introduction

Atrial septal puncture is required mainly during transvenous balloon mitral valvotomy (BMV) and in the electrophysiology laboratory for ablation at the mitral annulus or in the left ventricle. Atrial septal puncture can be done using femoral, jugular or, very rarely, hepatic venous approaches. The transfemoral route is the standard and most commonly used approach. The transjugular route is a useful alternative when transfemoral approach fails and may be the preferred approach in certain situations.

Technique[1]

Transjugular septal puncture is best done when the left atrium is large and the atrial septum bulges towards the right (Fig. 1); in this situation the transseptal needle engages the inter atrial septum (IAS) perpendicularly and will not slide down the septum. When the right atrial side of the atrial septum faces inferiorly, trans-femoral septal puncture is better, since that allows perpendicular engagement of the atrial septum.

The right internal jugular vein is cannulated percutaneously, preferably with ultrasound guidance, and a short 9F sheath is inserted. Next, a Berman catheter is advanced into the pulmonary artery (PA), passing successively through the right innominate vein, superior vena cava, right atrium, right ventricle and main PA to reach its right branch. Pulmonary angiogram is performed in right anterior oblique (RAO) 45° view. The levophase of the angiogram (Fig. 2)

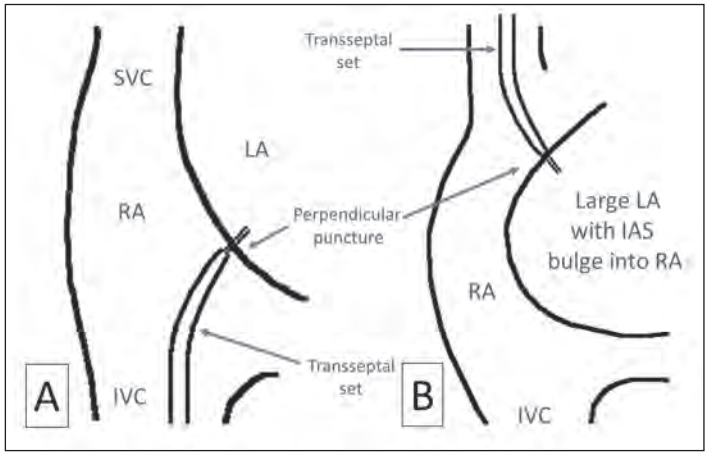

Figure 1. Cartoon showing relation between IAS anatomy and ideal route of septal puncture. If IAS is not bulged into RA and faces inferiorly, then transfemoral route for septal puncture is preferred as the puncture needle is perpendicular to it (Figure A). But, if the IAS is bulged into RA then transjugular route is preferred as the puncturing needle is perpendicular to IAS. (Figure B)

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delineates the left atrium (LA) and its upper and lower borders with the interatrial septum viewed *en face*. The RAO 45° view maximally separates the aorta anteriorly from the posterior LA border and spine posteriorly. This image is selected and displayed on the side screen for reference. Using right radial artery percutaneous access a pigtail catheter is introduced and positioned in the non-coronary sinus of the aorta. The tip of the pigtail catheter marks an important reference point in the RAO view (Fig. 2) for transjugular septal puncture

The Berman catheter is removed and a pediatric Mullins sheath is placed into inferior vena cava (IVC) over a 0.032" wire. A pediatric Brockenbrough needle is introduced through the Mullins sheath after increasing its tip curve manually so that oblique passage of the needle through the atrial septum is avoided. Then the whole assembly is withdrawn into the RA keeping the needle tip oriented towards the atrial septum (7 to 8 o'clock position). In patients with large left atrium and atrial septum bulging into the RA, the needle-sheath assembly tends to fall into the 'gutters' on either side of this bulge. By pulling higher up and rotating the assembly, correct orientation can be obtained.

The ideal site for transjugular atrial septal puncture is at a point 2 cm (one vertebral body height) below the upper LA border, and mid-way between the aorta (marked by the pigtail catheter tip) and the anterior border of spine (Fig. 2). This site is usually above the fossa ovalis and so the 'catch' of the limbic ledge, which is experienced during transfemoral septal puncture, is not felt here. Transjugular septal puncture is easiest when the atrial septum bulges into the RA as this allows perpendicular engagement of the septum by the needle tip. The external needle indicator is usually kept between 7 and 8 o'clock position (viewed from the head end of the patient) during septal puncture. LA entry is confirmed by, pressure tracings and contrast injection that typically outlines the inferior margin of the LA (Fig. 3C).

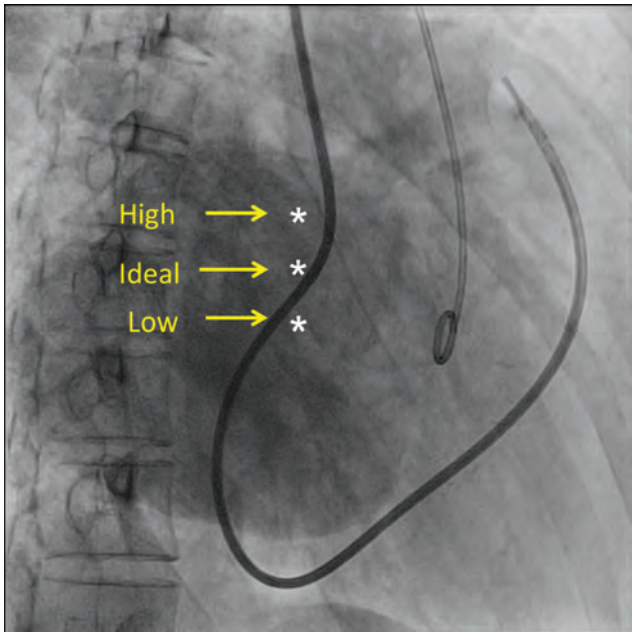

Figure 2. Levophase of pulmonary angiogram in RAO 45' view showing LA. The possible sites of punctures are very high (1cm below LA roof), ideal (2cm or 1 vertebral body height below LA roof), and low puncture. Pigtail catheter is placed in right coronary cusp to mark the aorta anteriorly.

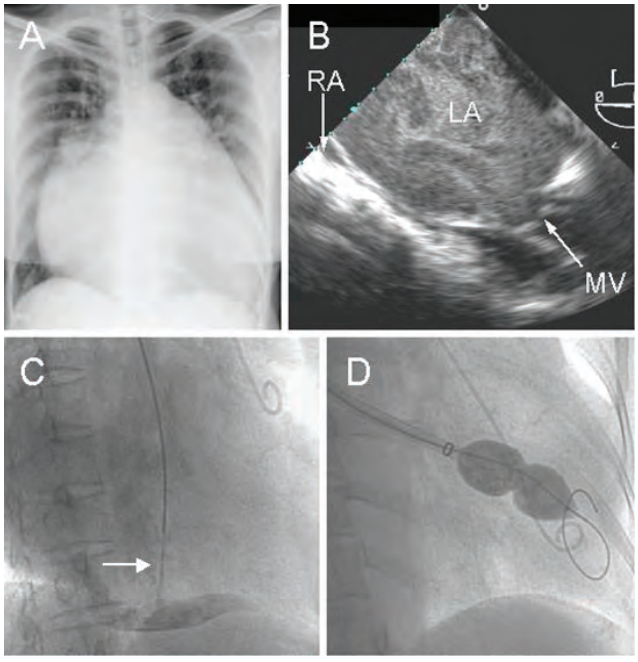

Figure 3. A 54-year-old lady presented with severe rheumatic mitral valve stenosis, atrial fibrillation and class III NYHA dyspnea. Chest X-ray (Panel A) showed gross cardiac enlargement (91% cardio-thoracic ratio). Transoesophageal echocardiography (Panel B) revealed a giant (95 x 100 mm) left atrium (LA) with spontaneous contrast within, slit-like right atrium (RA), and severely stenosed but pliable mitral valve (MV). The marked cardiac anatomic distortion predicted significant technical difficulty in performing conventional transfemoral mitral balloon valvuloplasty; hence a transjugular approach was used electively. The rightward bulging atrial septum was punctured (Panel C) midway between the ascending aorta (with pigtail catheter within) and the thoracic spine, in right anterior oblique view; contrast injection (arrow) through the transseptal needle delineated the left atrial floor and confirmed left atrial entry. Mitral valvuloplasty was performed using a 26mm cylindrical balloon that was introduced through an angled 14F left atrial sheath over a 0.035" guidewire (Panel D); orientation of the sheath, balloon and guidewire in a straight line, co-axial with the mitral valve, facilitated the procedure; the mid-balloon waist produced by the stenotic mitral valve was abolished. Mitral valve area increased from 0.6 cm2 to 2.3 cm2, though mitral regurgitation increased from trivial to moderate.

Advantages of transjugular over transfemoral approach of septal puncture

A) **If Balloon mitral valvotomy (BMV) is planned:**

1. The BMV balloon catheter undergoes a 180^0 turn during LV entry which poses procedural difficulty sometimes. Whereas in transjugular approach no such catheter turning or bend is present and it provides more direct route for mitral valve entry which makes the procedure easy.
2. Transseptal puncture is done at fossa ovalis in transfemoral route while it is done above fossa ovalis in transjugular route. Avoiding fossa ovalis for puncture site results in less residual left to right shunt.
3. Traction in atrial septum is more during BMV by tranfemoral route whereas it is less during transjuglar approach.

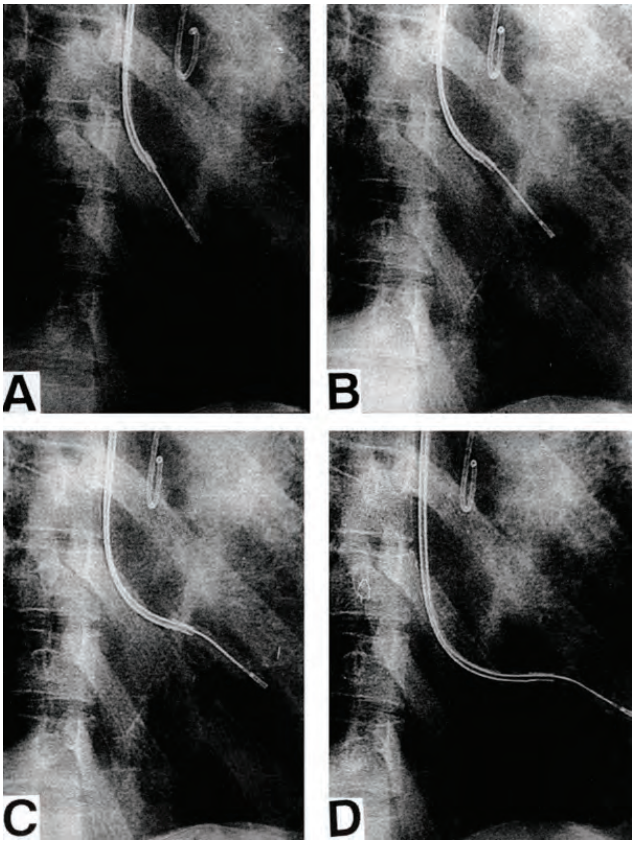

Figure 4. LV entry in RAO 30' view. Inoue-balloon catheter with deflecting stylet advanced to the tip was positioned at mitral valve level. Its to-and-fro movement between the positions A and B indicates proximity to and coaxial alignment with the mitral valve. Its advancement (the catheter and stylet as a unit) in diastole (position B) will cause it to cross the mitral valve and enter the left ventricle. (C,D) *(with permission from Joseph G et al. Preliminary reports … works in progress: Transjugular approach to transseptal balloon mitral valvuloplasty. Cathet Cardiovasc Diagn. 42(2):219–26)*

4. Inadvertent catheter entry into left atrial appendage and dislodgement of clot is more likely in transfemoral approach, whereas it is less likely in transjugular approach as septum is transversed in superinferior direction.

B) **For electrophysiology study and catheter ablation:**

1. More direct approach to mitral annulus, inferior LA and LV than the transfemoral approach.

C) **Other general advantages:**

1. All complication of femoral puncture are absent in transjugular route. Patient can be ambulatory short time after the procedure and can be discharged on the same day.
2. In pregnant patients transjugular BMV leads to less radiation exposure than the transfemoral route.

Disadvantages

Operator learning curve is high as it is not widely practiced. Radiation exposure to the operator may be high as he operates close to the X-ray source, but it is compensated by shorter procedure time than the transfemoral route. Cardiac tamponade may be produced particularly when puncture is high, though it is rare. Complication of IJV puncture though rare can happen. Pneumothorax, hydrothorax, thoracic duct injury, vagus, phrenic and other nerve injuries, laryngeal edema are described in literature. So, meticulous attention and ideally ultrasound guided IJV puncture should be performed.

Limitations

1. Difficulty in puncturing the interatrial septum when the LA size is small as here the IAS looks inferiorly and the puncture needle tends to slide inferiorly without puncturing it.
2. The commonly used hardwires need some modification for this approach. Shorter sheath is required. The usual Brokenbrugh needle's curve has to be made more acute. Alternatively, other hardwires as previously described are not widely available.
3. Most of the operators are unfamiliar with this approach.

The CMC, Vellore experience

In a large series published from CMC, Vellore, Joseph et al[5] compared BMV results done through different techniques, in which 130 patients underwent transjugular BMV. BMV outcome was similar in both

Table1. Comparison of transjugular versus transfemoral BMV in CMC, Vellore (from Joseph et al[3])

	Transjugular BMV (n=130)	Transfemoral BMV (n=1227)	P value
Outcome*			
Optimal	86.9%	91.4%	0.016
Suboptimal	5.4%	5.2%	0.832
Incomplete	0.8%	0.1%	0.171
Major complications	6.9%	3.4%	0.049
In hospital death	0	0.5%	-
Cardiac perforation	2.3%	0.6%	0.057
LV perforation	0	0.2%	-
Access site complication	0	0.3%	-
Systemic embolization/TIA	0.8%	0.2%	0.250
Fluoroscopy time (min)	9.0 ±4.2	12.8±7.0	0.000
Right heart O2 stepup >10%	3.5%	4.9%	0.516

*: optimal (post-BMV mitral valve area >= 1.5 cm^2); suboptimal (valve area 2cm^2); incomplete procedure; and 4) major complication (irrespective of valve area)

transfemoral vs. transjugular approach while mildly increased complications found in transjugular approach. (Table 1)

The jugular approach has relatively lesser optimal outcomes compared to the femoral approach and also relatively higher complications particularly cardiac perforations. But with the evolution of this approach the avoidance of very high septal puncture led to decreased incidence of this complication. But other outcomes such as access site complications, LV perforations were less compared to the femoral approach. Fluoroscopy time was also significantly lesser and also lesser incidence of right heart O_2 step up with jugular approach.

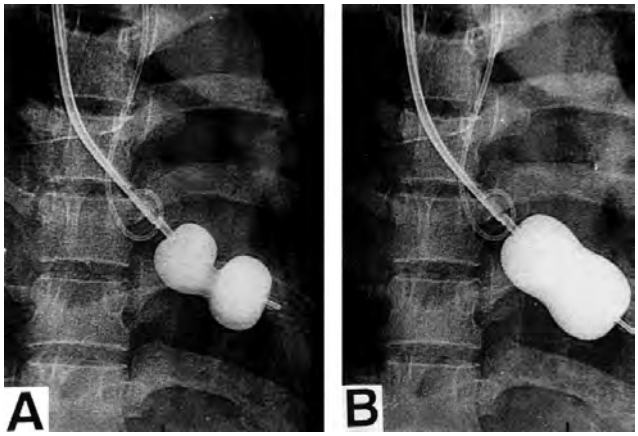

Figure 5. Mitral valve dilation by inoue-balloon by transjugular transseptal approach (straight anteroposterior projection). A: Waist on balloon produced by the stenotic valve. B: Full expansion of the balloon. *(with permission from Joseph G et al. Preliminary reports … works in progress: Transjugular approach to transseptal balloon mitral valvuloplasty. Cathet Cardiovasc Diagn. 42(2):219–26)*

Special case scenarios for transjugular septal puncture

The most common scenario where transjugular BMV can be offered is when it is not successful by transfemoral approach[4]. Other special case scenarios are described below.

1) Dextrocardia: In situs inversus dextrocardia, Left IJV access to be taken and septal puncture done with needle index at 5 o' clock position. In situs solitus dextrocardia right IJV access to be taken and septal puncture done with the needle index at 7 o' to 8 o' clock position[5]
2) Inferior venacaval anomalies: IVC interruption with azygous communication[6]
3) Mitral paraprostheic leak closure[7]
4) Severe kyphoscoliosis[2]

Conclusion

Transjugular septal puncture is an effective alternative in patients with various conditions when transfemoral method is ineffective or cannot be performed. It also provides more direct appproch for LV entry and BMV. Knowledge and familiarity with transjugular septal puncture will be of great help whenever anatomical limitations make transfemoral septal puncture difficult.

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Anatomy and Embryology of Inter-atrial Septum

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Editor's Note: ***Pictures drawn by author herself....***
Remembering drawing these in our 1st MBBS days....?!!

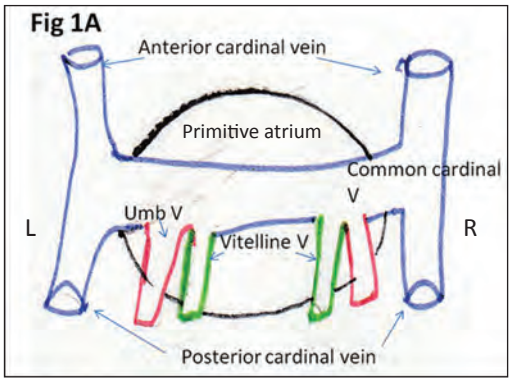
Introduction

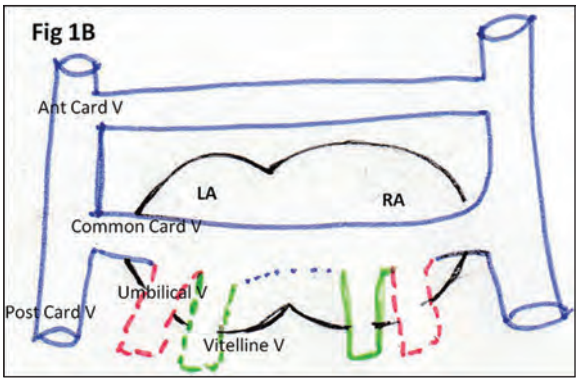
A thorough knowledge of the anatomy of the inter-atrial septum is necessary for the interventional cardiologist to perform procedures on the atrial septum safely and accurately. The acquisition of knowledge of anatomy of any structure begins its way from a good grasp of embryological development. This is especially true of the interatrial septum, where the development of the septum provides sharp insight into the anatomy as well as the clinical implications of the various structures related to the septum. As more and more procedures are being performed via trans-septal route, the interventional cardiologist has to be well-versed in its anatomy.

Embryology of the inter-atrial septum

In the early stages of cardiac development, the primitive heart tube is initially short, straight and suspended along its length by the dorsal mesocardium. It then undergoes remarkable growth and the ventricular component liberates itself from the body wall by a process called looping. The caudal inlet part begins to expand and forms the primitive atrium. The systemic venous tributaries which carry blood from both sides of the body are directly connected with the primitive atrium from the outset. The umbilical veins from the placenta,the vitelline veins from the yolk sac and the common cardinal veins (Ducts of Cuvier) drain into the sinus venosus (Fig 1A). The paired sinus venosi fuse to form a transverse sinus with right and left "horns". A pronounced asymmetry develops early in the connections of the right and left sided venous channels to the heart. The right horn of sinus venosus continues to grow and the sinus venosus is shifted to the right of the developing atrial mass. This stage of development is reached when the entire embryo is less than 5 mm long, in the sixth week of development. At this stage, the lung buds are just growing and the pulmonary veins are yet to appear.

The right vitelline and umbilical veins disappear (Fig 1B). The left vitelline and umbilical veins become a single vessel, the inferior caval vein (inferior vena cava). Thus, the venous component, which includes the entrances of three veins, namely the inferior caval vein and the right and left common cardinal veins, opens into the posterior





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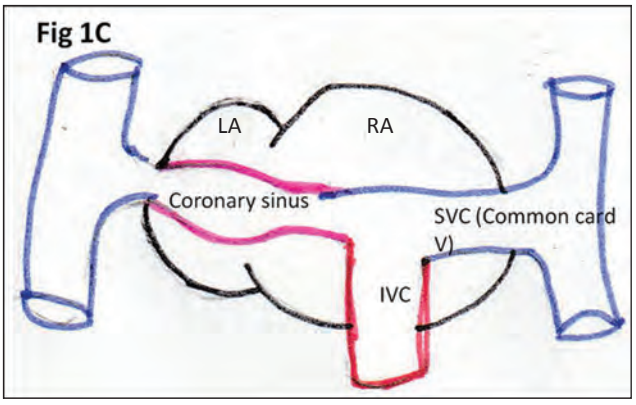
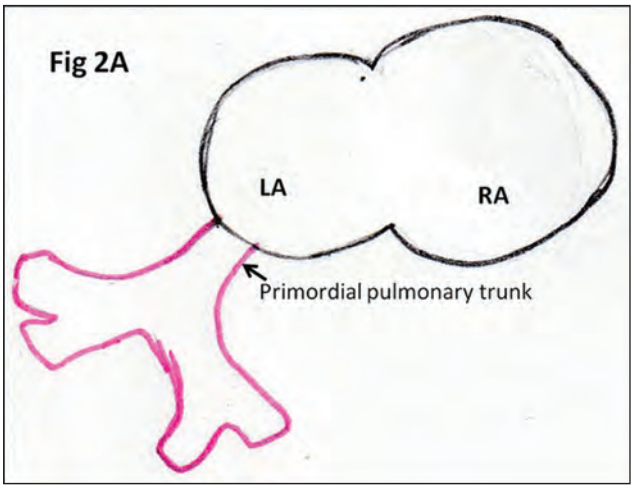
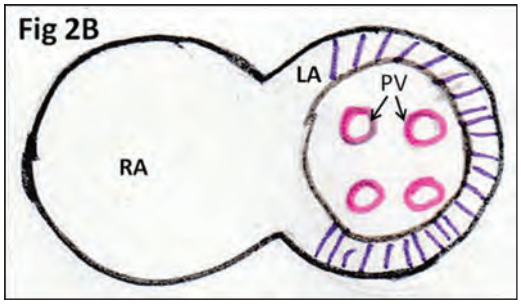






aspect of the primitive right atrium. The left horn, which ultimately receives only the left common cardinal vein, persists as the coronary sinus (Fig 1C).

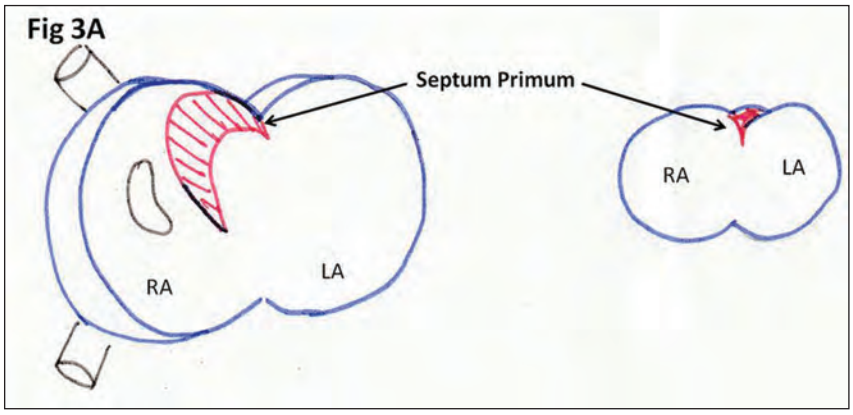
Valve like structures develop on either side of the sinus venosus and these fuse superiorly and inferiorly. These valves demarcate the boundary of the true sinus venosus from the rest of the atrium. The postero-superior part of the right venous valve continues into the wall of the atrium, forming the septum spurium, which later becomes the sagittal bundle in the formed heart. The posteroinferior wall of the sinus venosus folds inward and divides the right venous valve into two. The inferior part of the sinus venous valve becomes the Eustachian ridge and the thebesian valve. The tendinous commissure between the two venous valves later becomes the antero-inferior rim of the foramen ovale and a border of the triangle of Koch (Tendon of Todaro). The right atrium is separated from the sinus venosus by the "crista terminalis" (terminal crest). Expansions to the right and left in the primary atrium have by now resulted in the development of atrial appendages.

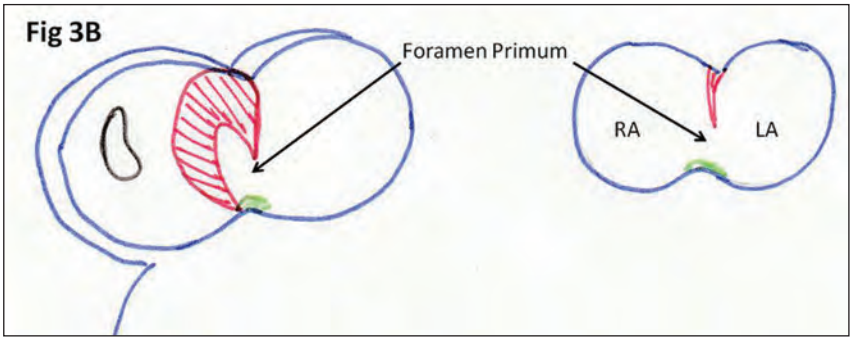
Lungs develop in the body wall behind the heart and the common pulmonary vein canalises within the dorsal mesocardium. This canalisation brings the common pulmonary vein into continuity with the cavity of the left atrium (Fig 2A). The entry of the common pulmonary vein into the left atrium is bounded by two ridges ; the right sided ridge becomes more prominent and is called the " spina vestibuli"or vestibular spine. At the 8th week of development, the common pulmonary vein starts getting incorporated into the left atrium (Fig 2B). The right upper pulmonary vein separately drains into the left atrium by the 12th week.

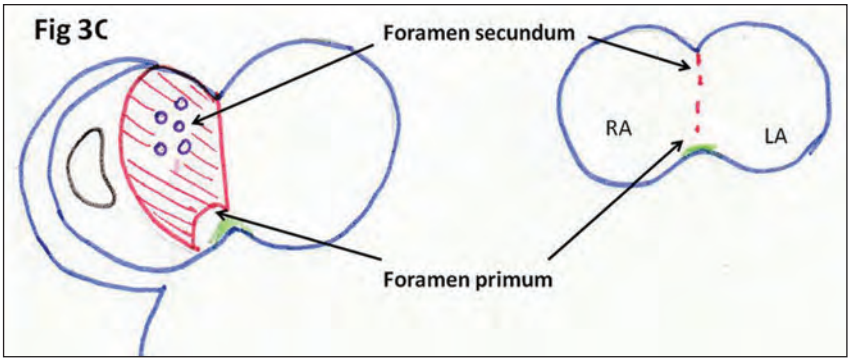
Atrial septation starts with the formation of a primary septum (septum primum) as a crescent shaped structure in the atrial roof (Fig 3A). The primary atrial septum (septum primum) is continuous inferiorly with the spina vestibule and is covered by a mesenchymal cap on its leading edge. The septum primum moves towards the developing endocardial cushions and the space between the septum primum and the endocardial cushions is the foramen pimum or the primary atrial foramen (Fig 3 B). The endocardial canal also expands rightward and connects the right atrium to the looping heart tube, which is the future right ventricle. As the septum primum fuses with the endocardial cushions, it divides the right-sided venous component from the orifice of the common pulmonary vein. Before the septum primum totally fuses with the endocardial cushions, it breaks down at the superior end to form the foramen secundum or the secondary atrial foramen (Fig 3 C). The thinner upper margin of the septum primum is the flap of the oval foramen.

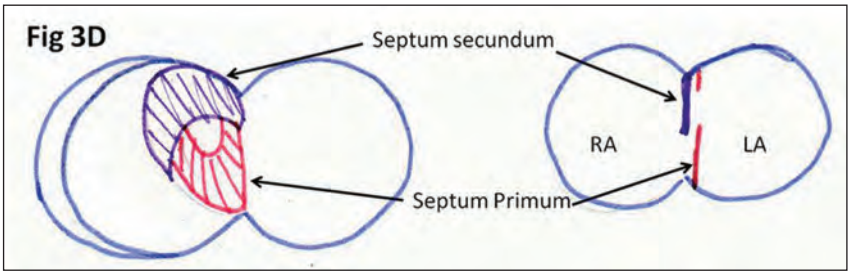
Subsequently an infolding develops adjacent to the superior venacava and grows downwards to form the antero-superior border of the oval foramen. This infolding to the right of the septum primum is the septum secundum (Fig 3D). At the end of atrial septation, each atrium has a venous component, a part of the body of the primary atrium, a vestibule, and an appendage.

The septum primum acts as a one-way valve allowing blood to pass from right atrium to left atrium in fetal life. After birth, when left atrial pressure increases, the septum primum closes off against the septum





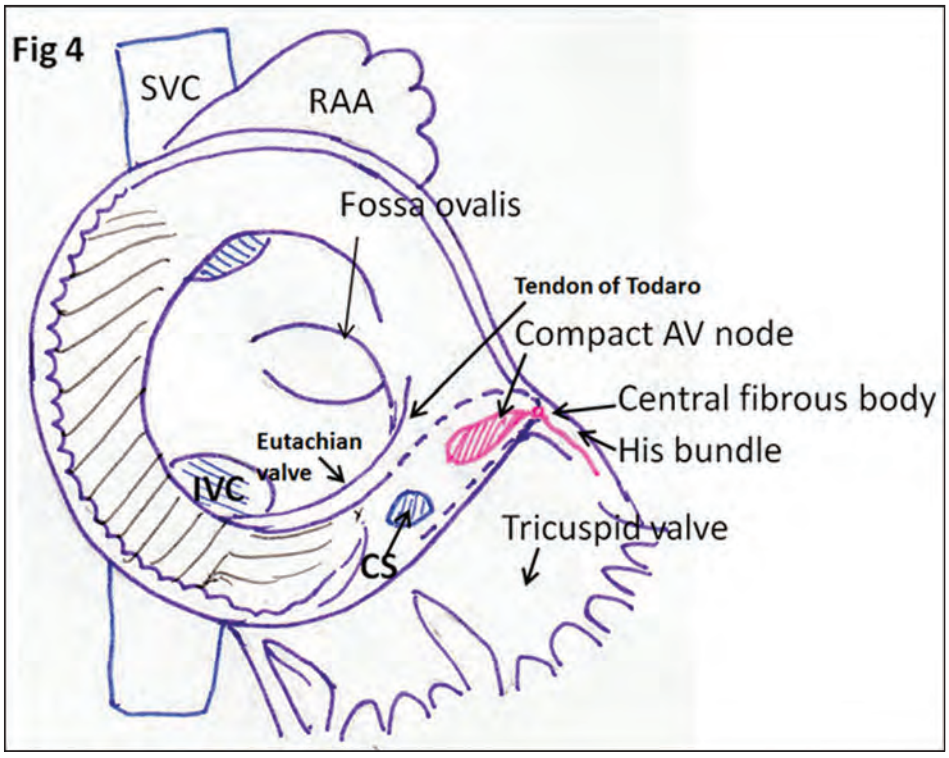




secundum. Anatomical closure occurs later by fibrosis of the margins of the muscular rim. The anterosperior margin may still remain patent ("probe-patent foramen ovale") leaving potential for right to left shunting.

Anatomy of the atrial septum

The true atrial septum (Fig.4) is that which, when opened, will provide communication between right and left atria and that which can be removed without exiting the cavities of the atria. Thus the true septum is confined to a small area between the floor of the fossa ovalis (septum primum), the flap valve and the antero-inferior part of the fossa (embryologically, the spina vestibuli) which reaches the vestibule of the tricuspid valve. The septum secundum or the area between the superior venacava and the superior margin of the fossa ovalis is actually a deep infolding of the atrial wall.



The valve of the floor of the fossa ovalis is thin and sometimes maybe aneurysmal with excursions into the left atrium.The size and location of the fossa also varies. The size may range from 10-30 mm in the supero-inferior dimension and 5-15 mm in the antero-posterior dimension. The muscular rim around the fossa may be very prominent (which will make the interventionist feel a "jump" as the catheter falls from the muscular rim into the fossa) or may have gradual thinning towards the fossa ovalis. The fossa may be located superiorly, with risk of injury to aortic root while attemptimg septal puncture, or it may be located posteriorly with risk of perforation to the pericardial space.

Antero-superior to the oval fossa lies the right atrial wall overlying the aorta and this extensive area should not be mistaken for the atrial septum. Accidental puncture in this area can cause trauma to the aortic root and can be avoided by keeping a catheter in the aortic root as a marker.

The superior part of the fossa is formed by the septum secundum and as mentioned earlier, it is actually the infolding of the right atrial wall between the superior venacaval entry and the right upper pulmonary vein orifice. This infolding seen in the epicardial surface is called the Waterston groove which is used by the cardiac surgeons to access the left atrium without entering the right atrium. Postero-inferiorly the groove is continuous with the wall of the inferior venacava. The antero-superior part of the groove contains the sinus node artery.

The antero-inferior part of the septum is continuous with the eustachian ridge and the vestibule of the tricuspid valve. This part separates the right atrium from the left ventricle and is comprised of the right atrial wall, fatty tissue and left ventricular wall. The atrial part of this septum contains the atrio-ventricular node very close to the endocardial surface. The node lies in the apex of the triangle of Koch which is bounded posteriorly by the tendon of Todaro, anteriorly by the septal leaflet of the tricuspid valve and inferiorly by the orifice of the coronary sinus (Fig 4). The artery to the atrioventricular node passes through the fatty tissue. The area between the orifice of coronary sinus and vestibule of tricuspid valve is the target of ablation of slow pathway in atrioventricular nodal re-entrant tachycardia.

Conclusion

A thorough knowledge of the structure of the atrial septum is essential for the interventional cardiologist to avoid injury to adjacent structures like aorta and atrioventriuclar node during procedures such as inter-atrial septal puncture, radiofrequency ablation etc. Anatomical and radiological landmarks are important to plan procedures and proper imaging must be done to avoid complications.

Invasive Hemodynamic Assessment of Cardiac Shunt Lesions

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Editor's Note: ***This review focuses not just on shunt lesions at atrial level. It's a compact synopsis direct from the Master covering all the common cardiac shunt lesions residents can come across.***

Hemodynamic data is an integral part of all cardiovascular observations. With improvement in 2D and Doppler echocardiographic techniques, most of these data are available non-invasively. CT and MRI have almost eliminated the need for a diagnostic cardiac catheterization. However, there is a subset of patients in whom non-invasive examination would be suboptimal and would need invasive hemodynamic assessment, especially to assess the pulmonary vascular resistance.

Cardiac catheterization is mostly the final investigation done in any clinical situation. However, it should not be considered as the final decision making investigation. A well done hemodynamic study should be read along with appropriate history, clinical examination, chest X ray and echocardiographic findings to arrive at a reasonable conclusion. There are two components of hemodynamic study: oximetry and pressure measurement/recording. Both are performed simultaneously .

Definitions

Qp: Blood flowing through the pulmonary capillary bed (PBF)

Qs: Blood flowing through the systemic capillary bed (SBF)

Qep: It refers to the mixed venous blood (deoxygenated) that gets oxygenated at the pulmonary capillary bed. It is also referred as effective pulmonary blood flow.

Qes: It refers to the oxygenated blood from the lungs reaching the systemic vascular bed.

Normally, **Qp = Qep = Qes = Qs.**

The systemic blood flow (Qs) returns to the right atrium via venae cavae. Hence systemic venous return is equivalent to Qs. Similarly the pulmonary blood flow (Qp) returns to left atrium via pulmonary veins. Hence pulmonary venous return is equivalent to Qp. The amount of oxygenated blood reaching the left atrium and hence, the systemic circulation depends on the effective pulmonary blood flow (Qep), not just Qp. For example, in a patient with lobar pneumonia, Qp would be normal. However, the blood flowing into the consolidation would not be oxygenated. That would constitute intra pulmonary R-L shunt and hence Qep would be reduced.

Pathophysiology in common congenital cardiac conditions

1. **Simple post tricuspid shunts** e.g., ventricular septal defect (VSD). Here Qp is increased, Qs is normal. The entire venous return (Qs) enters the lungs and gets oxygenated. Thus Qs=Qep. In addition, the left to right shunted blood also enters the lungs causing increased PBF. Thus Qp = Qs + L-R shunt and L-R shunt = Qp – Qs.

2. **Tetralogy of Fallot (TOF).** The systemic venous return (Qs) partly enters the lungs as Qp. whatever enters the lungs would be oxygenated and hence Qp=Qes. Part of the systemic venous return is directly shunted to systemic circulation from right ventricle (RV) to aorta causing R-L shunt. Thus Qs = Qp + R-L shunt and R-L shunt = Qs-Qp

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3. **Admixture physiology.** Qp is increased which is a mixture of a portion of systemic venous return (Qep) and L-R shunt. Hence L-R shunt = Qp – Qep. Systemic blood flow (Qs) consists of a portion of pulmonary venous return (Qes) and R-L shunt. Hence R-L shunt = Qs – Qes.

4. **Transposition physiology.** There are two parallel wasted circulations in this situation. The entire systemic venous return goes back as Qs (very large R-L shunt) and the entire pulmonary venous returns flows back into the lungs as Qp (very large L-R shunt). That portion of systemic venous blood entering the lungs via an atrial septal defect (ASD), VSD or patent ductus arteriosus (PDA) would get oxygenated constituting the Qep. As in any condition, the systemic saturation depends on this Qep.

Cardiac catheterization for hemodynamic assessment is relatively commonly done for post tricuspid L-R shunts and less commonly in some conditions with admixture physiology. It is very rarely needed in TOF or transposition physiologies.

Standard sites for vascular access

Femoral artery and vein are the usual sites chosen for vascular access. Presence of a patent foramen ovale (PFO) would aid in reaching pulmonary veins. In its absence, pulmonary venous saturations are assumed to be 99% and the pulmonary capillary wedge pressure is substituted for the pulmonary venous pressure. Rarely trans-septal puncture is needed for accurate assessment of the left atrial or pulmonary veins pressures and saturations.

Commonly used hardwares

Cournand, GL (Goodale-lubin) and Swan Ganz catheters are used to record pressures in the right heart chambers. The latter is especially useful to measure the pulmonary capillary wedge pressure. Multipurpose or Judkin's right catheters are commonly used for recording the pressures both in right and left heart chambers. Burman or NIH catheter is used for performing RV angiogram while pigtail catheter is used for LV angiogram.

Accurate measurement of the pressures

Proper calibration is a very basic requisite for pressure recordings. The accuracy of pressure measurement requires a fixed reference point. Mid chest level is used widely as zero reference and zeroing is done at this level. Hence the level of transducer should be raised in an obese individual and should be lowered in children.

Underdamping and overdamping would result in overestimation and underestimation of systolic pressures respectively, though mean pressures are not affected. Loose connections and excessively complaint tubing causes underdamping while air bubble or blood / clot in the line would result in overdamping.

Appropriate scale and speed have to be used while recording pressures. Atrial pressures and ventricular end diastolic pressures are recorded on a scale of 20mmHg and at a faster paper speed of 50mm/sec. Ventricular pressures are recorded on a scale of 100 or 200mmHg at the usual speed of 25mm/sec. The monitor automatically displays the maximum, minimum and mean pressures. The maximum and minimum pressures would correspond to the systolic and diastolic pressures respectively. However, in pulmonary veins or atria, one has to read the 'a' and 'v' waves directly from the tracings as the machine does not automatically give these numbers.

In the absence of ASD or PFO, pulmonary capillary wedge pressure is substituted for PV pressure. In the event of poor wedging, left ventricular end diastolic pressure could be taken to represent PV pressure in the absence of mitral valvular disease.

Accurate measurement of oxygen saturations (SO2)

Blood sampling: While withdrawing the blood in a syringe, it is not uncommon to have got a small air bubble. In order to purge it out, it is a common practice to suck in some additional air. This results in mixing up of room air that would increase the oxygen content of the sample. Rather, one should withdraw adequate volume of blood, say 3-4ml and discard 1-2ml by holding the syringe vertically to make the sample air bubble free.

Measurement of SO2: Ideally spectrophotometry should be used to measure SO2. However, due to rarity of the need and difficulty in maintaining the apparatus, it is not available in most of the centers. Blood gas analysis is done instead and the SO2 is derived using the oxy-hemoglobin dissociation curve. Additional details like PCO2 and oxygen content are available by using this method. The blood gas machine and the laboratory personal should be alerted before starting the study and the time gap between collection of the sample and blood gas analysis should be kept bare minimum.

Sites of sampling: Conventionally, standard books mention to collect two samples from superior vena cava (high and low), three from right atrium (high, mid and low) etc. This kind of collecting samples from multiple

sites of the same chamber was done in olden days to diagnose the level of L-R shunt. As anatomical details are readily available with echocardiography and other non-invasive imaging, multiple sampling is not needed currently.

The degree of L-R shunt is calculated by measuring the difference in the oxygen content of the blood drawn from the chamber prior and after the level of shunt. For example, for VSD, samples from right atrium and main pulmonary artery are taken. For PDA, we don't have a chamber beyond the level of shunt. Sampling from left pulmonary artery alone would result in over estimation of shunt as the duct is commonly connected to its origin. For the same reason, sampling from right pulmonary artery would result in underestimation of the shunt. Hence, an average of the SO2 from both branches is taken for shunt calculation. For ASD, we don't have a chamber prior to the level of shunt to assess the venous oxygen saturation. Various authors have proposed various methods to calculate the mixed venous oxygen. For example, formulae like (3xSVC+IVC)/4 or (2xSVC+IVC)/3 or simply SVC is taken to represent mixed venous oxygen. One would use the formula as per the practice in their institution. Thus the sites for oximetry sampling for various lesions are:

ASD: SVC (±IVC), PA, PV and Aorta (any arterial blood, even a femoral or radial arterial sample).
VSD: SVC (±IVC), PA and Aorta. PV is assumed.
PDA: SVC (±IVC), both branch pulmonary arteries and descending aorta or femoral artery. Ascending aortic blood should not be used for calculation. In the presence of lower limb desaturation suggestive of R-L shunt across PDA, one should take ascending aortic sample also, to record the change in the SO2.

Table 1: Understanding various congenital heart physiologies could be simplified by analyzing the aortic and pulmonary artery SO2 as given below.

Ao SO2	PA SO2	CHD physiology	Example
Normal	Normal	No shunt	
Normal	Increased	L-R shunt	ASD
Decreased	Normal	R-L shunt	TOF
Decreased	Increased (but lesser than aorta)	Both R-L and L-R shunts	TOF with BT shunt
Decreased	Increased and nearly same as aorta	Admixture physiology	Single ventricle
Decreased	Increased, more than aorta	Transposition physiology	D-TGA

Table 2: Typical findings in common left to right shunts are given below.

	ASD		VSD		PDA	
	SO2	Pressure	SO2	Pressure	SO2	Pressure
SVC	72		72		72	
RA	88	3	70	3	70	3
RV	86	28	86	110	70	90
PA	86	20/12	86	110/26	86	90/26
LA	99	4	99	4	99	4
LV	99	110	99	110	99	110
Aorta	99	110/70	99	110/70	99	110/50

In VSD and PDA, the RV pressure is elevated to near systemic levels if the defect is unrestrictive and hence pulmonary hypertension is an inherent component of any large post tricuspid shunt. However, the PA diastolic pressure remains low due to low pulmonary vascular resistance. This results in large left to right shunt. Note the step up at the level of RA, RV and PA in ASD, VSD and PDA correspondingly. With progressive increase in PVR, the PA diastolic pressure gradually increases, thus reducing the PBF correspondingly.

Table 3: Typical findings in various L-R shunt lesions with Eisenmenger status.

	ASD		VSD		PDA	
	SO2	Pressure	SO2	Pressure	SO2	Pressure
SVC	68		68		68	
RA	74	10	70	8	70	8
RV	72	110	74	110	70	110
PA	72	110/62	74	110/62	70	110/62
LA	90	10	99	9	99	9
LV	88	110	88	110	98	110
Asc aorta	88	110/70	88	110/70	98	110/70
Des aorta					86	110/70

Note the step down at the level of LA, LV and descending aorta in ASD, VSD and PDA correspondingly. In pre-tricuspid shunts like ASD, PA pressure gradually increases with progressive increase in PVR. It could reach even suprasystemic levels. In post tricuspid shunts, the RV or PA pressure cannot raise above the systemic pressure because of the equalization caused by the large defect. With progressive increase in PVR, there is gradual increase in the PA diasolic pressures resulting in reversal of shunt.

Table 4: Examples of admixture lesions.

	TAPVC		Single ventricle (Operable)		Single ventricle (Eisenmenger status)	
	SO2	Pressure	SO2	Pressure	SO2	Pressure
SVC	66		66		66	
RA	90	12	68	4	68	4
RV	88	48	92	90	78	90
PA	90	48/22	92	90/34	74	90/62
LA	90	12	99	5	99	5
LV	91	92	90	90	76	90
Aorta	90	86/60	90	90/60	76	90/66

Note that the PA and aortic saturations are nearly identical suggestive of admixture physiology. Total anomalous pulmonary venous drainage (TAPVC) being a pre-tricuspid shunt could have any degree of pulmonary hypertension from mild to suprasystemic levels. In single ventricle, the PA pressure behaves as in any large post tricuspid L-R shunt like VSD.

Performing a hemodynamic study

Patient should be in a normal conscious state and the study is done preferentially under local anesthesia and on room air breathing. In children, the sedation should be minimal to avoid hypoventilation, CO2 accumulation and its effect on pulmonary vasculature. The hemodynamics should be steady and stable with no undue tachycardia or bradycardia.

The time gap between the samples should be minimal. Conventionally, sampling is started in the vena cavae. At times, guiding the catheter into the right ventricle and or pulmonary artery could be difficult, especially in the presence of a large ASD. The time delay could be significant and calculations based on this delayed pulmonary artery sampling could be fallacious. Hence, the following order is followed.

1. Place a MPA or JR catheter in the pulmonary artery and a pigtail catheter in the aorta. Record both pressures and collect samples.
2. Pull back the venous catheter to RV, record if any gradient at the right ventricular outflow tract. Lower the scales and record the RV EDP.
3. Pull back further to RA, record the atrial pressures.
4. Guide the catheter into superior vena cava, collect a blood sample.
5. Pull back the catheter into inferior vena cava, collect a blood sample

Between each sampling, 3-5 ml of blood should be withdrawn and discarded. After the completion of this step, one should wait for the reports. The values have to be checked for their appropriateness. For example, in the absence of clinical systemic desaturation, if the arterial sample shows a saturation <95%, it could either mean hypoventilation or a sampling error. SVC saturation is expected to be around 70%. A value <65% or >75% would strongly influence the shunt calculation. Hence, if warranted, one should resort to repeat the entire basal study.

If the pressures and the simple shunt calculation using the SO2 are acceptable and compliment the clinical assessment, one can terminate the study. If there is severe pulmonary hypertension and borderline shunt, one can repeat the study by administering oxygen and/or nitric oxide. Traditionally 100% oxygen is recommended which is possible only with endotracheal intubation and mechanical ventilation. A pulmonary venous pO2 of >200mmHg is good enough to tide over the hypoxia induced vasoconstriction or to cause hyperoxia induced pulmonary vasodilatation. This could easily be achieved through a tight oxygen mask with the oxygen flow at the rate of 10L/min and hence mechanical ventilation is not needed.

The formulae for calculating pulmonary and systemic blood flow are as follows:

$$Qp = \frac{\text{O2 consumption (VO2)}}{\text{PV O2 content} - \text{PA O2 content}}$$

$$Qs = \frac{\text{O2 consumption (VO2)}}{\text{Ao O2 content} - \text{MV O2 content}}$$

O2 content = Total oxygen carrying capacity + dissolved oxygen
Total oxygen carrying capacity = 1.36ml x Hb (g/dl) x 10 x SO2
Dissolved oxygen = 0.03ml x pO2

Including these variables, the formulae could be rewritten as follows:

$$Qp = \frac{\text{Oxygen consumption (VO2)}}{\text{(PV SO2-PA SO2) x Hb x 1.36 x 10}}$$

$$Qs = \frac{\text{Oxygen consumption (VO2)}}{\text{(Ao SO2- MV SO2) x Hb x 1.36 x 10}}$$

So,

$$\frac{Qp}{Qs} = \frac{\text{Ao SO2} - \text{MV SO2}}{\text{PVSO2} - \text{PA SO2}}$$

Measurement of oxygen consumption is laborious and difficult, done using a Douglas bag. Commonly charts based on Laferge and Meitinnen's formula adjusted for the variables like gender, age and heart rate are available and are used for the calculations. The simple equation Qp/Qs is independent of Hb and VO2 and hence considered the most important component of the invasive hemodynamic study.

Pulmonary vascular resistance (PVR) and systemic vascular resistance (SVR) are calculated using the following formula and expressed in Woods units (Wu).

$$PVR = \frac{\text{mean PA pressure} - \text{mean LA pressure}}{Qp}$$

$$SVR = \frac{\text{mean Ao pressure} - \text{mean RA pressure}}{Qs}$$

Role of Oxygen and Nitric oxide for reversibility testing

The demonstration of a good basal shunt is the most important decision make in the hemodynamic study. As one can easily understand, this is the only component addressed by closure of the defect surgically or by transcatheter means. Even with a relatively high calculated PVR, if the basal shunt is good, closure of the defect can be considered. On the other hand, if the basal Qp:Qs is <1.5, surgery should be deferred even if the calculated PVR is in the acceptable range.

Though conventionally oxygen and nitric oxide have been used to test 'reversibility', the repeat study with these agents have not been useful in predicting the outcome of the lesions. The oxygen content and the hemodynamic calculations become inaccurate in patients breathing high FiO2. Similarly, the concentration and duration of administration of nitric oxide have not been standardized and long term outcome data are not available. Thus the entire emphasis is on the basal study on room air though a repeat study on high oxygen flow is often done in patients with severe pulmonary hypertension.

Role of temporary balloon occlusion

In post-tricuspid shunts, there is direct transmission of pressure from the left heart to the pulmonary circuit. Occluding the defect temporarily with a balloon would eliminate the left to right shunt as well as the influence of the systemic pressures on the pulmonary system. This also could represent the hemodynamic status following permanent closure. In VSD, achieving a total occlusion of the defect without compromising the ventricular inflow or outflow is impossible and hence balloon occlusion study is not performed. This could be quite successful with PDA. Absence of fall in the PA pressure or fall in systemic pressures would clearly indicate inoperability. If there is a reduction in the PA pressure following balloon occlusion, there are no standardized criteria based on which operability could be defined. A post occlusion fall of > 20mmHg or >25% reduction from the basal pressure is considered appropriate for closure of PDA.

In pre-tricuspid shunt (ASD), flow related pulmonary hypertension is quite rare and there is no influence of the systemic pressure on the pulmonary circuit. Balloon occlusion to block the flow across ASD would have no acute effect on the PA pressure and hence it is not done. However, in older individuals, balloon occlusion of the ASD is helpful to assess the raise in the LA pressure following ASD closure.

Conclusion

In L-R shunt with pulmonary hypertension, a comprehensive assessment of clinical status, Chest-X-ray, ECG and echocardiographic findings are often enough to conclude regarding the operability in most of the patients. However, a small percentage of them would need hemodynamic assessment by invasive cardiac catheterization. A good planning and careful attention to collect accurate details are very essential to have a meaningful data which would further assist in decision making. Basal study and the basal shunt would be the most important decision making factor. The role of reversibility studies with oxygen or nitric oxide is controversial. Balloon occlusion could be attempted to assess the pulmonary vasculature in PDA.

Atrial Septal Defect: Step-by-step Approach to Device Closure

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Editor's Note: ***A picture can speak a thousand words.... This article attempts to do that with sixty one figures.... No wonder, a master with experience of thousands of ASD closures opted for more pictures than words....! Readers are advised to refer KJC 1, September 2017, 1:1:61-68, for a detailed discussion on systematic assessment prior to ASD device closure by Dr. Arun Gopalakrishnan.***

Introduction

Transcatheter device closure of atrial septal defect (ASD) is associated with low complication rates and short anaesthetic and hospital duration. It is the treatment of choice with proper patient selection and techniques. Closure rate is >96%, with <1% complications.

Indications of percutaneous closure

Anatomy should be suitable* along with the following:

- Right cardiac chamber enlargement with or without symptoms
- Paradoxic embolism
- Exercise-related cyanosis
- Orthodeoxia-platypnea syndrome
- Left-to-right shunt with pulmonary arterial (PA) hypertension responsive to pulmonary vasodilator therapy and tolerating a balloon occlusion test

***Anatomy that is not suitable** includes defect >36 mm, device is large for the patient, inadequate rims or ASD is close to other cardiac structures

Contraindications of percutaneous Closure

- Eisenmenger syndrome with severe PA hypertension unresponsive to vasodilator therapy
- Intracardiac thrombus
- Contraindication to antiplatelet agents
- Other defects requiring surgery
- Recent or active infection
- Femoral veins too small to allow access

In pregnant women diagnosed with an ASD during pregnancy, closure can be deferred for ~6 months after delivery.

Important steps in a successful procedure

- Careful case selection
- Sizing of defect & device
- Proper hardware and technique
- Ensuring stability
- Early detection of complications
- Prompt remedial action to minimise risk

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Timing of closure

A haemodynamically significant ASD should be closed electively once the diagnosis is confirmed. Although there is no lower limit of age for defect closure, many clinicians choose to refer asymptomatic children for the procedure to the age of 3-5 years. At the other end of the age spectrum, defect closure is safe and effective in improving symptoms, even in elderly patients.

Imaging

Accurate imaging is critical for case selection, planning, and intraprocedural guidance. The operator should identify the number of defects, size, location, morphology, and the surrounding tissue to determine whether the defect is amenable to transcatheter closure or not. Baseline assessment of cardiac structures that may be affected by the procedure should also be carried out.

Two-dimensional (2D) and color Doppler transthoracic echocardiography (TTE) can adequately demonstrate the anatomy and haemodynamics. Subcostal and parasternal short axis as well as long axis should be done. (Fig 1 shows subcoastal TTE short axis and Fig 2 the long axis view. Fig 3 and Fig 4 are parasternal short axis and apical 4 chamber views). 2D TTE has limited ability to visualize ASD in adults, obese, those with large body habitus and previous thoracic surgery. Evaluation using transoesophageal echocardiography (TEE) is necessary in them. In TEE, through a midesophageal view, a sweep must be performed from 0° to 150° (4-chamber plane: 0°, 30°; aortic short-axis plane: 45°; vena cavae plane: 90°; long-axis plane: 120°, 150°). Fig 5 shows the 0° and fig 6 a 90° view during TEE. 3D echocardiography provides better spatial visualization and 3D TEE can delineate the 3D structure with high-resolution images. Real-time 3D TEE allows for evaluation of various shapes of ASD especially in patients with complex-shaped ASD ssuch as multiple ASDs (fig 7). Disadvantages of 3DE are dependence on the skill of the operator, restrictive echo window especially in elderly patients, echo dropout in the region of the mid portion which can lead to false diagnoses of large defects, and lower both temporal and spatial resolutions compared to 2D TTE.

The haemodynamic burden associated with the defect is determined by assessments of right atrial (RA), right ventricular (RV), and PA size. RV and PA pressures can be estimated by Doppler determination of the velocities of the tricuspid and pulmonary valve regurgitation jets. The former estimates the peak systolic pressure difference between RV and RA whereas the latter estimates the early and late pressure differences between the main PA and RV, which correlate with the mean and diastolic PA pressures.

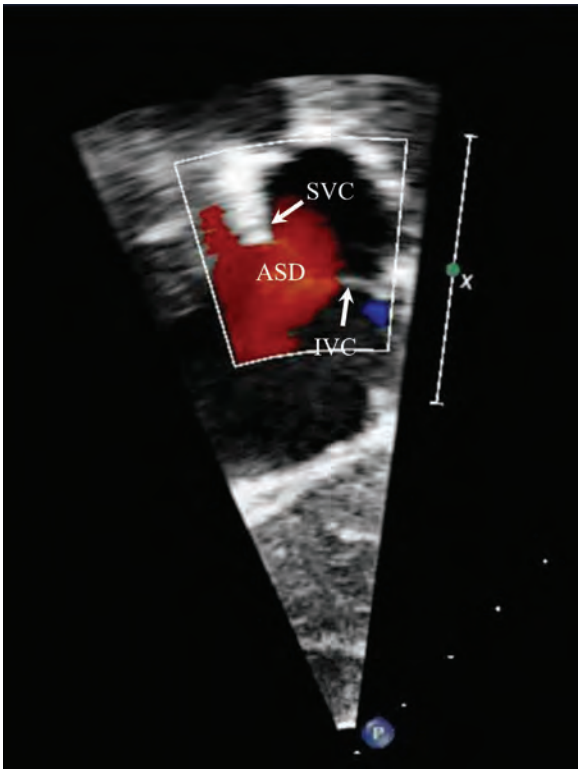

Fig 1. TTE: subcostal short axis view; ASD=atrial septal defect; SVC=superior vena caval rim; IVC=inferior vena caval rim

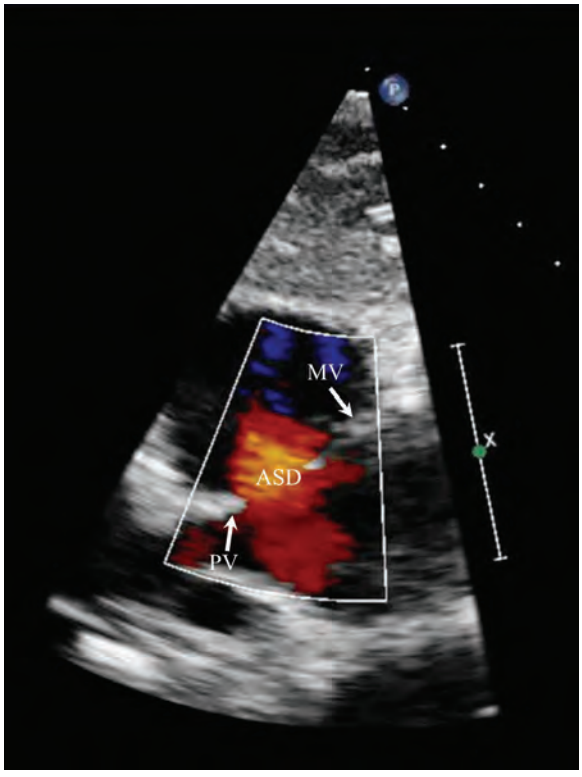

Fig 2. TTE: apical four chamber view; ASD=atrial septal defect; MV=mitral rim; PV=pulmonary vein rim

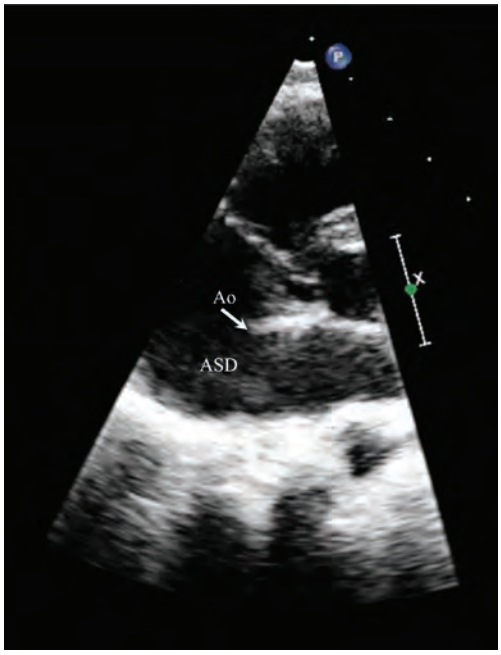

Fig 3. TTE: parasternal short axis view; ASD=atrial septal defect; Ao=aortic rim

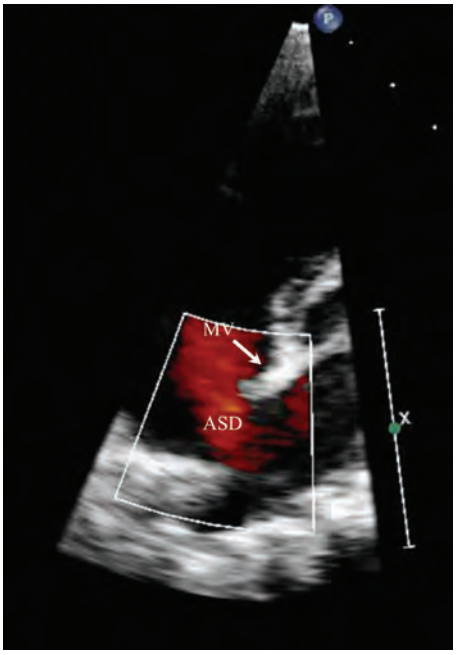

Fig 4. TTE: Apical four chamber view; ASD=atrial septal defect; MV=mitral rim

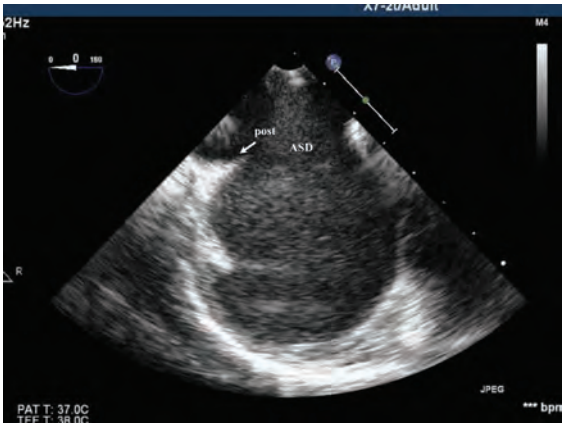

Fig 5. TEE: 0^0 degree view (four chamber view); ASD=atrial septal defect; post=posterior rim

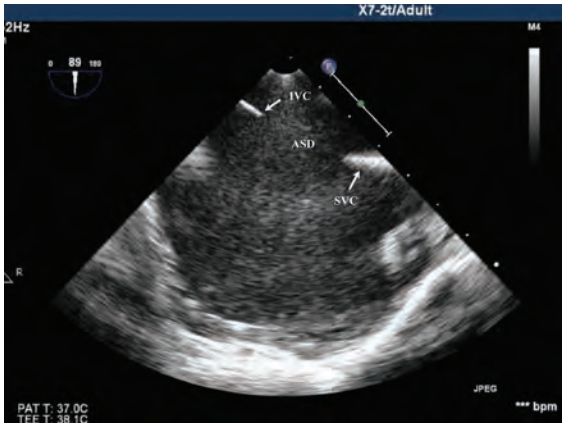

Fig 6. TEE: 90^0 degree view (bicaval view); ASD=atrial septal defect; SVC=superior vena caval rim; IVC=inferior vena caval rim

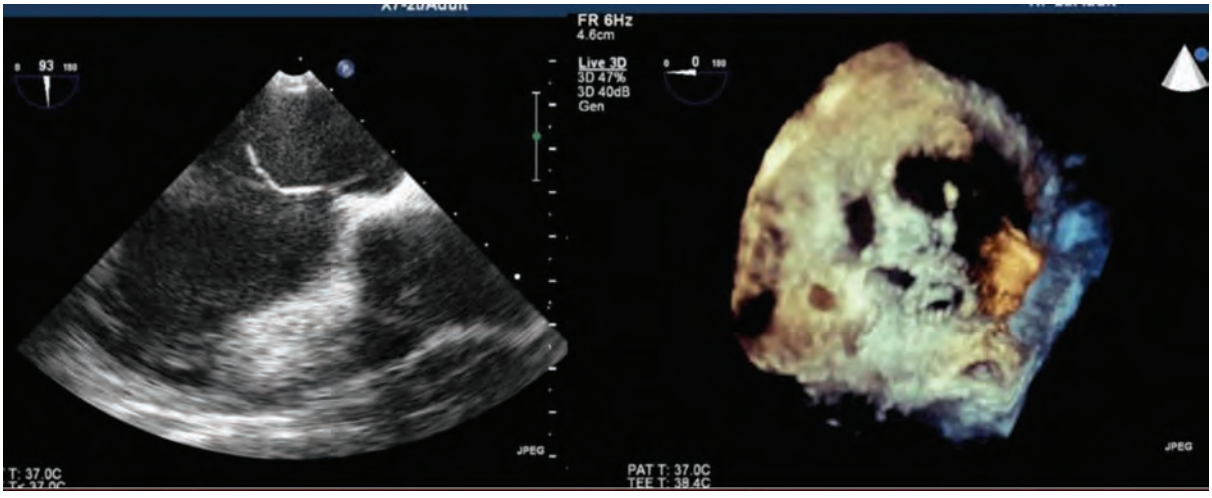

Fig 7. 2D and 3D TEE of multiple ASD

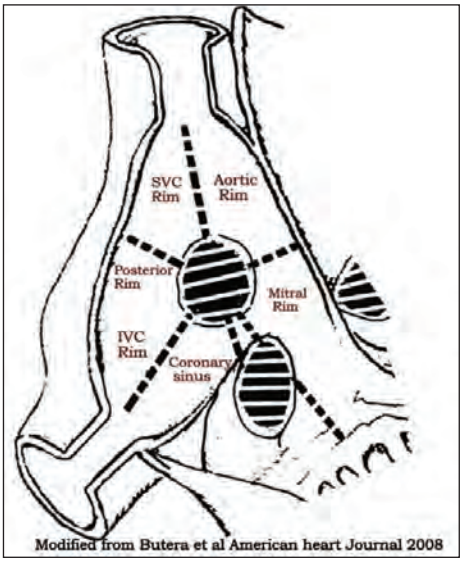

Fig 8. Schematic diagram of rims

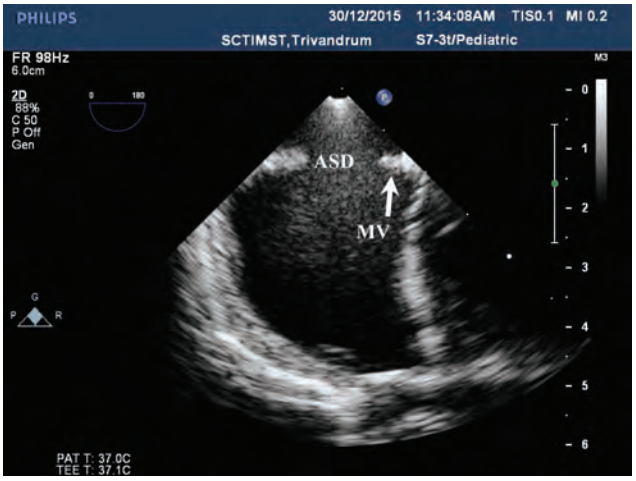

Fig 10. TEE: 0^0 four chamber view showing poor mitral rim; ASD=atrial septal defect; MV=mitral rim

Rims

Distances from ASD to aorta (antero-superior rim), superior vena cava (SVC) (postero-superior rim), right upper pulmonary vein (PV) (posterior rim), inferior vena cava (IVC) (postero-inferior rim), coronary sinus, and atrioventricular valve (antero-inferior rim or mitral) are assessed. Fig 8 shows the rims of an ASD. A rim is considered deficient if its length is <5 mm. examples of deficient rims are shown in fig 9 (IVC), fig 10 (mitral) and fig 11 (posterior). Here, device closure is not an option. Absence of aortic rim (fig 12) is not a contraindication, but may require oversizing of the device so as to straddle the aorta. With experience, operators have been able to close a range of challenging defects, including defects with deficient posterior rim, SVC rim, and even IVC rims.

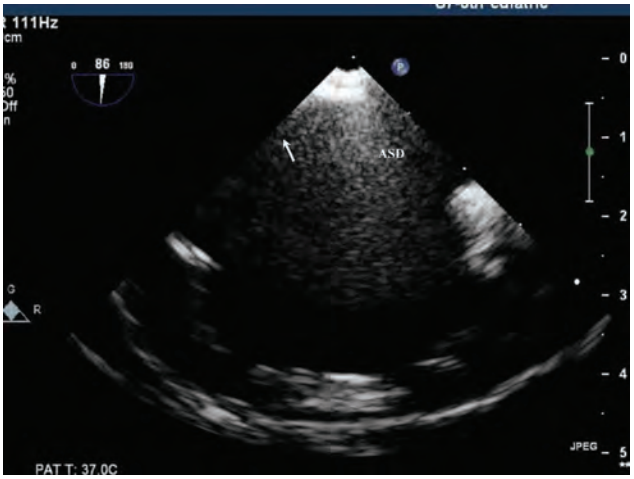

Fig 9. TEE: bicaval view showing poor IVC rim (arrow); ASD=atrial septal defect

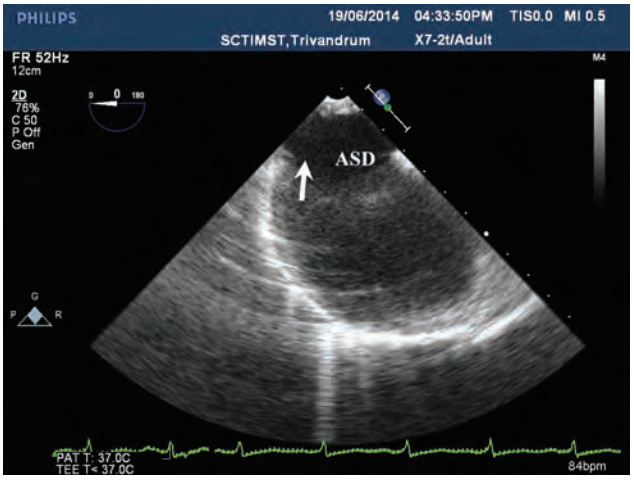

Fig 11. TEE: 0^0 four chamber view showing poor posterior rim (arrow); ASD=atrial septal defect

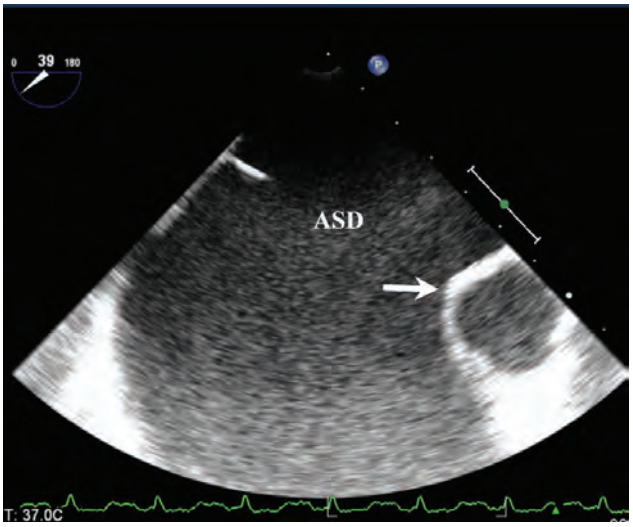

Fig 12. TEE: 45^0 view showing absent aortic rim (arrow); ASD=atrial septal defect

Specific features that should be routinely reported

ASD size-maximal and minimal diameters (optimally measured from 3D volume data sets), measurement of all rims, PV drainage and Doppler flow are essential. Fig 13 shows left upper PV drainage to innominate vein. Fig 14 and Fig 15 show right upper and lower pulmonary veins draining to RA. Presence or absence of atrial septal aneurysm (ASA), Eustachian valve, Chiari network, and multiple fenestrations should be looked for (*see below*). Normal origin of coronary arteries should be ensured. Left circumflex may take origin from right coronary and pass posterior to aorta (fig 16). A device will compromise the circumflex artery here.

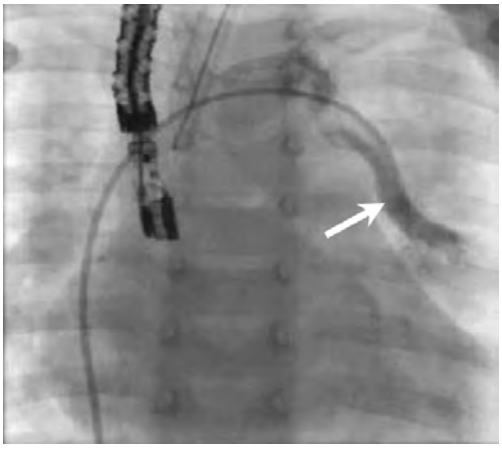

Fig 13. Angiogram: left upper PV drainage to innominate vein (arrow)

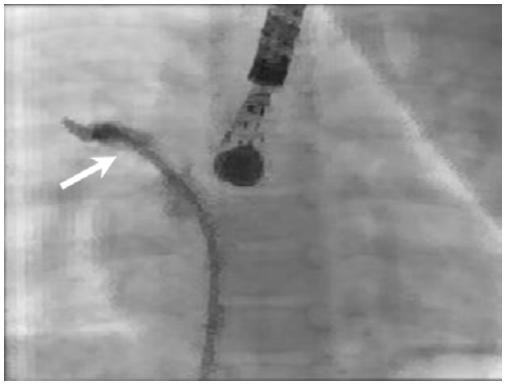

Fig 14. Angiogram: right upper PV drainage to RA (arrow)

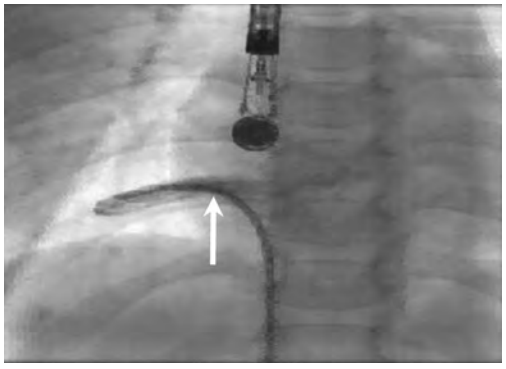

Fig 15. Angiogram: right lower PV drainage to RA (arrow)

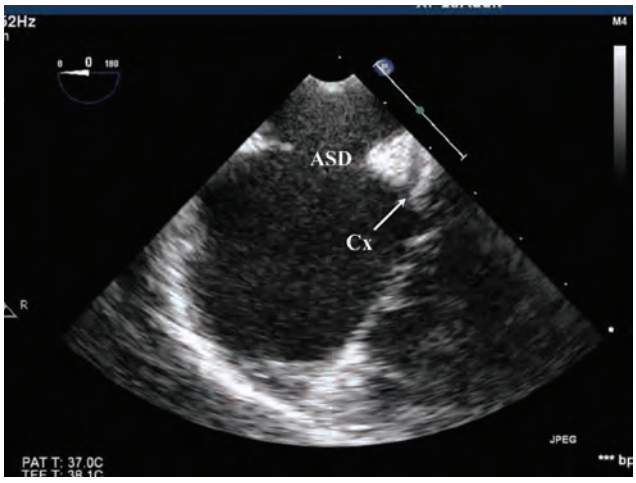

Fig 16. TEE: circumflex artery (Cx) arises from right coronary and passes behind aorta; ASD=atrial septal defect

Devices

Amplatzer septal occluder (ASO), AGA (St. Jude Medical, St. Paul, MN, USA), Occlutech (Helsingborg, Sweden), Lifetech Cera (Shenzhen, China) are the commonly available devices (fig 17). These are self-expanding, self-centering, fully retrievable, and can be repositioned. They are made of nitinol (nickel-titanium alloy) mesh and polyester fabric sewn into the wire mesh (to facilitate thrombosis and total occlusion), and consists of 2 disks linked through a central 3-4 mm long connecting waist. The waist centers the device in the defect and occludes it; the retaining discs provide stability on either sides of the defect. The diameter of waist corresponds to the device size (ranges from 4 to 40 mm, with 1 mm increments from 4 mm to 20 mm and then 2 mm increments from 20 mm to 40 mm). The size of the device is known by the diameter of the waist. The left atrial (LA) disk exceeds the connecting waist diameter by 12 to 16 mm, whereas the RA disk exceeds the connecting waist by 8 to 10 mm (depending on the size). This is to help retention and stability. The delivery system varies depending on the device size: 6-12 Fr with a length of 60-80 cm. We generally use one Fr size higher than the recommended size for ease of manipulation (if body size allows). This is particularly useful if retrieval of device becomes necessary. These devices are MRI compatible.

An extra 1-2 mm should be added to the maximum diameter found in the defect. Device size used is generally less than 1.5 times body weight, particularly in children.

Fig 17. Amplatzer type device

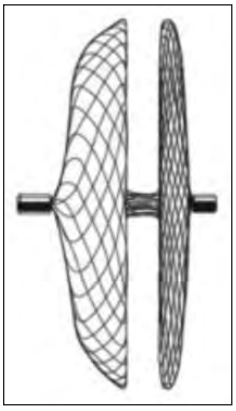

Fig 18. Cribriform device

If the aortic rim is deficient, oversize by 4 mm, so that the rims splay at the aorta. Smaller devices predispose to embolization while larger ones cause perforations and damage to adjacent structures.

The cribriform device (fig 18) is of a similar design as the standard Amplatzer device but with a narrow waist that facilitates the occlusion of multiple defects or fenestrations in close proximity to one another. In addition the LA and RA discs are of equal size.

The Helex occluder is made of a 0.012-inch nitinol wire covered with an ultra-thin expanded polytetrafluoro-ethylene membrane. Once deployed, the device forms 2 round flexible disks on either side of ASD.

Patient preparation

Although closure of small-to-moderate sized defects with good rims is frequently straightforward, it should be performed only in laboratories and by experienced operators equipped to deal with complications and unexpected challenges of the procedure. Surgical back-up should be available. Blood and retrieval materials should be ready. Contraindication to nickel, antiplatelets, anticoagulants, anaesthetic drugs, and antibiotic agents should be used. In addition thrombotic and bleeding risks should be assessed. Informed consent is necessary. Cardiopulmonary, peripheral vascular and neurologic examination should be done. The anesthesiologist should be consulted when general anesthesia is planned (pediatric and all TEE based procedures). Vital signs, pulse oxymetry, and electrocardiogram should be monitored throughout the procedure.

Before the procedure, aspirin therapy (3-5 mg/kg/day and continued for 6 months) is prescribed. We generally administer clopidogrel 2 mg/kg/day additionally. Intravenous heparin is given to keep activated clotting time >200 seconds throughout the procedure. Antibiotic is administered 30 minutes before the procedure followed by 2 more doses over the next 12 hours.

Procedure

Uninterrupted TEE is recommended. Prolonged TEE monitoring under conscious sedation is associated with risk of aspiration. From the current perspective, conventional TEE has historically improved the results of the ASD closure. Short-axis, bicaval, and four-chamber TEE views are used to verify the proper placement of sheaths in the LA, and to monitor device deployment and its release from the delivery system. The size of ASD is measured again during the procedure. The defect diameters can be directly measured with 3D TEE, which permits an en face view.

A right femoral venous access is taken. Generous soft tissue predilatation is advised as a preparation for a sheath exchange later. A second contra-lateral venous sheath is needed if dilator or balloon support (see below) is required. Arterial access is optional. In cases of IVC drainage to azygos system, a jugular approach may be indicated (fig 19). We have had to use the jugular approach for balloon support in a patient with deep vein thrombosis in left iliac vein (fig 20).

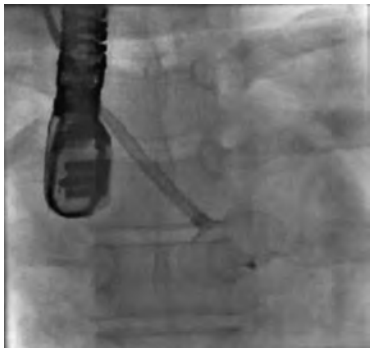

Fig 19. Fluoroscopy: device deployment by jugular approach

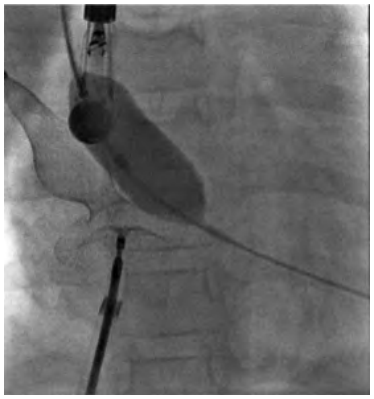

Fig 20. Fluoroscopy: balloon support by jugular approach

An end hole catheter is used with an exchange length wire to cross the defect. The catheter is advanced across the defect and into the left upper PV under fluoroscopy. Feeling of resistance before advancement beyond fluoroscopic left main bronchus / LA border or appearance of premature atrial contractions suggests that the wire/catheter is at atrial appendage position and the assembly should be withdrawn. The delivery system is introduced through the venous sheath and advanced into the left upper PV over the wire. The wire and the dilator are then slowly withdrawn and the sheath held below the level of the heart to allow back-bleed to prevent air embolism. This is better done under water (see below).

The device is screwed onto the delivery cable and loaded by drawing into the loader sheath under saline. It is introduced through the sheath and advanced. The device is pulled back a short distance to document device-delivery lock before LA advancement and then advanced to LA.

The operator fixes the cable and retracts the sheath, thus deploying the LA disc (fig 21). The LA disc should be away from the PV or LA appendage. Once the LA disc is within a few millimetres from the septum, the connecting waist is deployed partially in the LA with continuous traction toward the defect. The objective is to

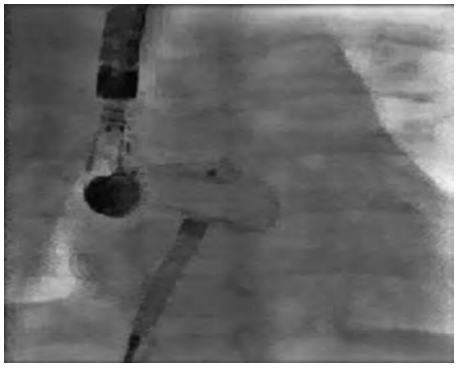

Fig 21. Fluoroscopy: LA disc deployment

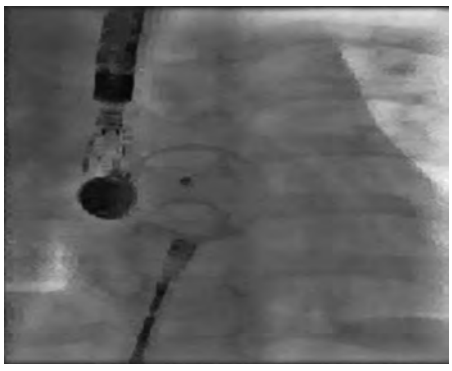

Fig 22. Fluoroscopy: RA disc deployment

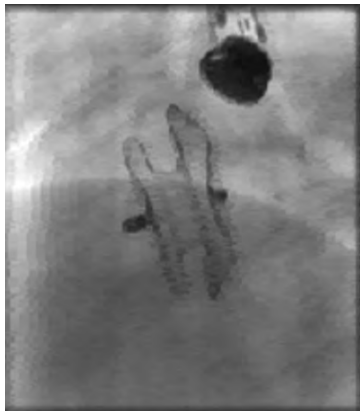

Fig 23. Fluoroscopy: left anterior oblique view of device in situ

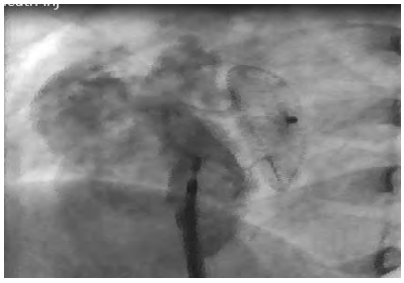

Fig 24. IVC injection showing IVC rims

''stent'' the defect with the waist. Complete apposition of the distal component to the LA side of the septum before proximal component deployment is essential to avoid prolapse. Next, with continuous traction towards the RA, the RA disc is deployed (fig 22). Once the entire disc is free of the sheath, the delivery cable is advanced toward the septum to bring the two discs into approximation. A complete assessment of the device, atrial septum and surrounding structures is performed. On fluoroscopy, both the discs will be parallel in LAO view (fig 23), but not in AP view (fig 22). A "Minnesota" wiggle is rarely required. In difficult cases, a contrast injection into RA may be done to show the device position, with both discs on either side of the IVC rim (fig 24). Then the device is unscrewed and released. Rhythm should be watched. Cough should be avoided during extubation to prevent embolization. TTE should be done before shifting out.

Balloon sizing/testing

A stop-flow diameter by inflating the balloon is not performed by most centres now. It is reserved for extremely floppy rims or multiple ASDs when single device occlusion is planned. Temporary balloon occlusion allows assessment of preload changes on cardiac output, atrial pressure, and PA pressure before definitive closure, and should be performed in patients with left-to-right shunt and decreased left-sided compliance (see below). Patients with bidirectional shunt and reduced

RV compliance or Eisenmenger syndrome responsive to pulmonary vasodilator therapy should also be tested before closure.

Complex ASDs

Morphological features of difficult ASDs are **(1)** large size (>30 mm, fig 25), **(2)** rim deficiency (fig 9: IVC rim, fig 10: mitral rim and fig 11: posterior rim), **(3)** multiple defects (fig 7), **(4)** malaligned ASD (fig 26) and **(5)** floppy rim (fig 27). Hemodynamic features of difficult ASDs are (1) severe PA hypertension, (2) ventricular dysfunction, and (3) left ventricular (LV) diastolic dysfunction after closure.

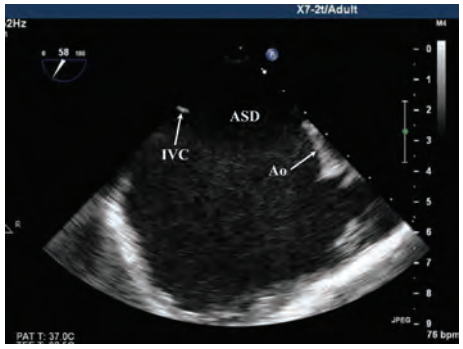

Fig 25. TEE: Large ASD; ASD=atrial septal defect; Ao=aorta; IVC=inferior vena caval rim

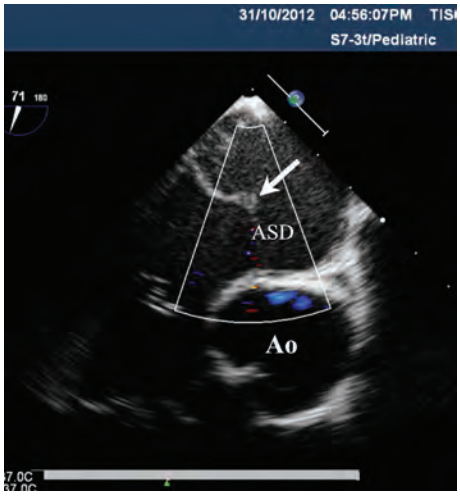

Fig 26. TEE: malaligned ASD; ASD=atrial septal defect; Ao=aorta

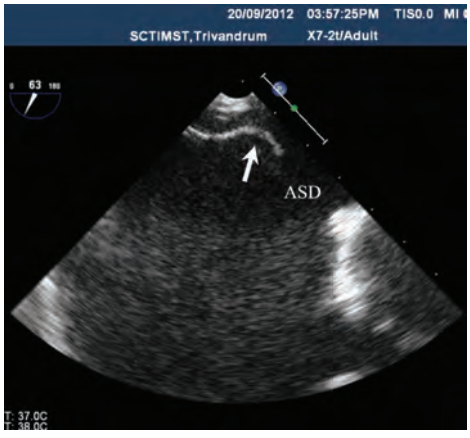

Fig 27. TEE: ASD with floppy rims (arrow); ASD=atrial septal defect

Prolapse

Difficulty in deploying the device in patients with a deficient anterosuperior rim is that the LA disc tends to become perpendicular to the atrial septum, leading to prolapse of the disc into the RA and prevent proper alignment (fig 28).

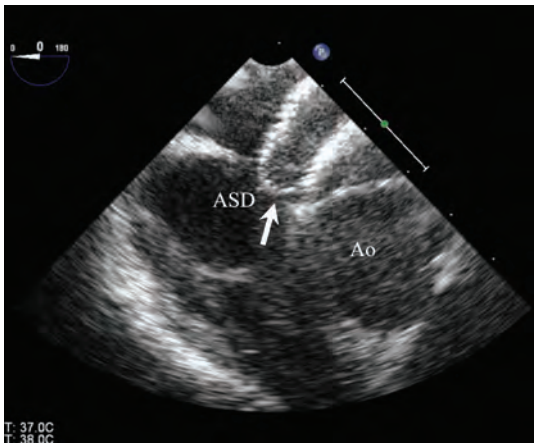

Fig 28. TEE: prolapse of device (arrow); ASD=atrial septal defect; Ao=aorta

Modifications to prevent prolapse

(1) Modification of delivery sheath: exit orifice on the side of the distal portion of the sheath - ie. a straight, side-hole delivery sheath, **(2)** Rotation of delivery sheath, **(3)** Increasing the curvature of the sheath by remoulding outside the body, **(4)** Specially designed sheaths (Hausdorf sheath, Cook, Bloomington, IN, USA) with two curves at the end to help align the LA disc parallel to the septum. Disadvantages are: need for additional hardware and manipulation (with risk of perforation), and chances of embolization, **(5)** Partial deployment of the distal component into the LA roof leads to component jump parallel to the atrial septum, which is followed by quick deployment of the proximal component before the sheath recoils out of position (fig 29), **(6)** Deployment of the LA disk in the right (fig 30) or left upper PV (fig 31) followed by pulling of the sheath into the RA to improve the approach to the atrial septum, **(7)** Supporting/holding the LA disc with the tip of a dilator (fig 32) or additional material (balloon, fig 33). A second operator uses a dilator or balloon to hold the superior anterior part of the distal component, preventing prolapse

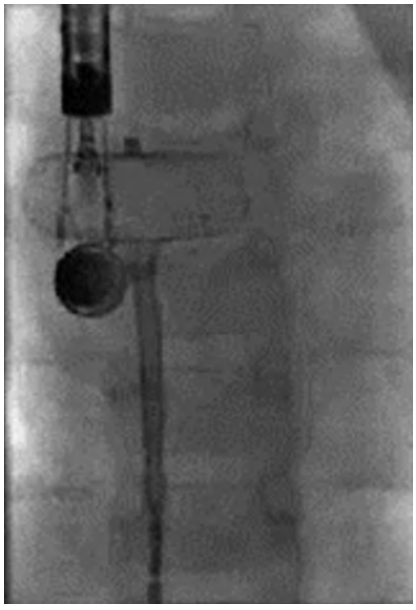

Fig 29. Fluoroscopy: LA roof deployment

Fig 30. Fluoroscopy: right upper PV deployment

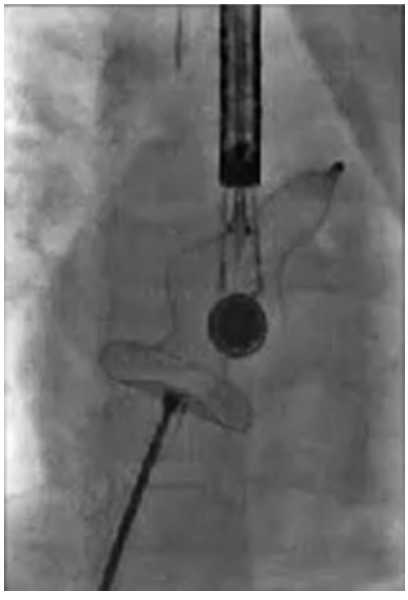

Fig 31. Fluoroscopy: left upper PV deployment

across the ASD, whereas the primary operator deploys the proximal component. Disadvantages are: need for additional hardware, venous access, time, fluoroscopy and personnel. Concerns of injury to PV exist with the PV technique.

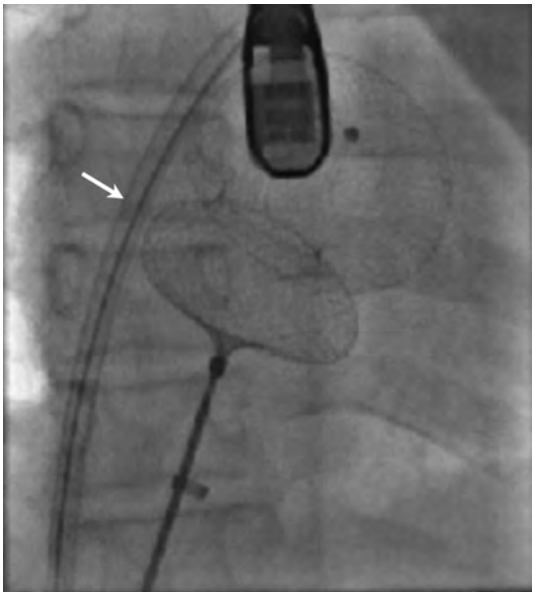

Fig 32. Fluoroscopy: deployment with dilator (arrow) support

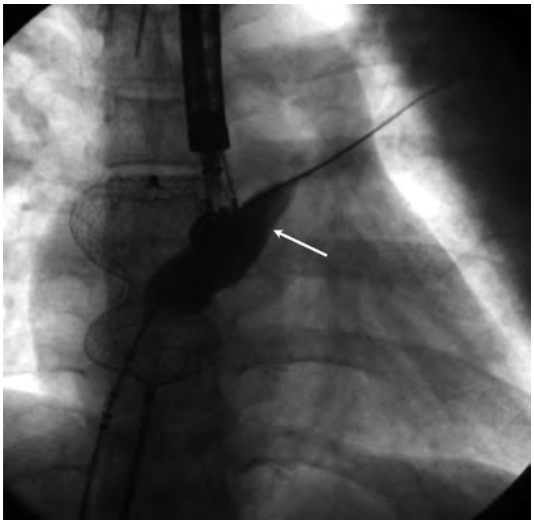

Fig 33. Fluoroscopy: deployment with balloon (arrow) support

Deficient posteroinferior rim

Closure of a large ASD with a deficient or absent postero-inferior (defined as rim measuring <3 mm) is a real challenge (fig 9: deficient IVC rim, fig 11: deficient posterior rim). They tend to be larger in diameter. The number of cases taken up for device closure is too

small, however, to make a generalized conclusion. As the difference in radius measurement between RA and LA discs is 2–3 mm, a rim <3 mm will not allow both discs to hang on both sides of the rim. Although stable deployment is possible, these defects are more likely to have complications such as PV or IVC obstruction, encroachment onto the anterior mitral leaflet, or frank embolization.

Atrial septal aneurysm (ASA)

This is a sac-like redundancy of IAS associated with increased mobility (fig 34). This is defined as a protrusion of septal tissue of the fossa ovalis >10 mm from the atrial septal plane in the direction of RA or LA, or a combined total protrusion from one side to the other measuring ≥15 mm. ASA can be associated with multiple ASDs or fenestrations, and should be evaluated using color doppler imaging. ASA with single or multiple defects represent a different kind of complex anatomy of ASD. Such anatomy is better treated with devices that do not rely on a stenting mechanism within the defect to achieve stabilization in the septum. Cribriform device may be appropriate. Such a defect before (fig 35) and after (fig 36) closure with cribriform device is shown. A large defect within an aneurysmal septum may, however, require a large device or may not be amenable to device closure. Closing two small but distant defects within an aneurysmal atrial septum may effectively close both defects, but carries a higher risk of development of thrombus formation later.

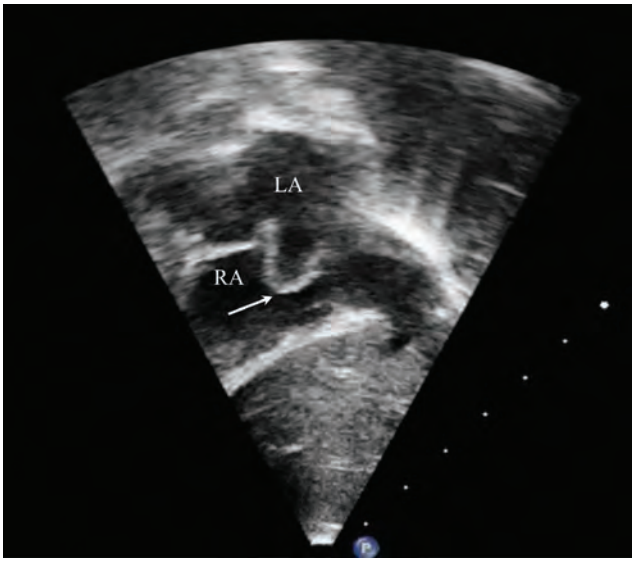

Fig 34. TTE: atrial septal aneurysm (arrow); RA=right atrium; LA=left atrium

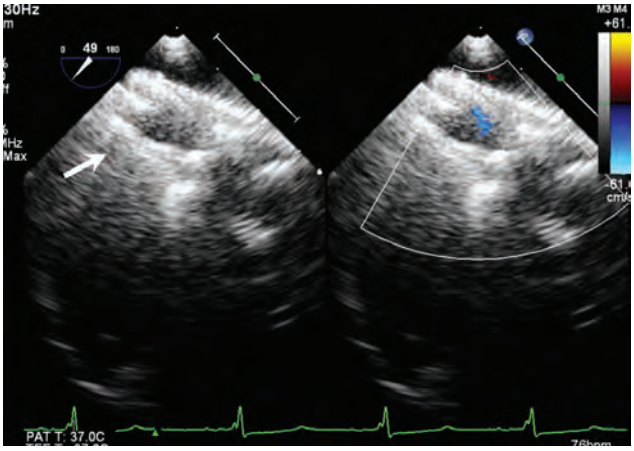

Fig 36. TEE: atrial septal aneurysm after closure with cribriform device (arrow)

Eustachian valve and Chiari network

The Eustachian valve is a remnant of the valve of the IVC that, during fetal life, directs IVC flow across the fossa

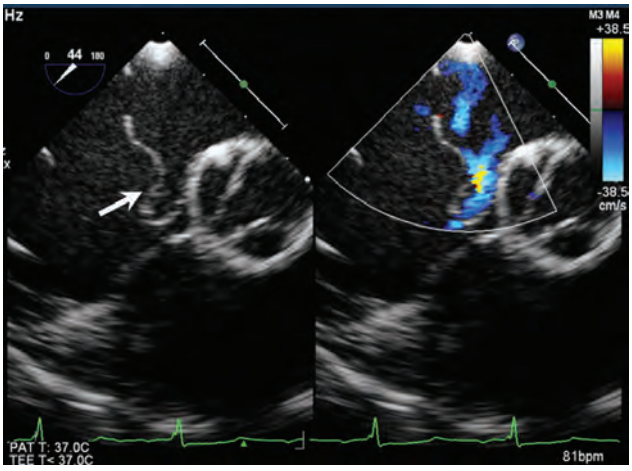

Fig 35. TEE: atrial septal aneurysm (arrow) before closure with cribriform device

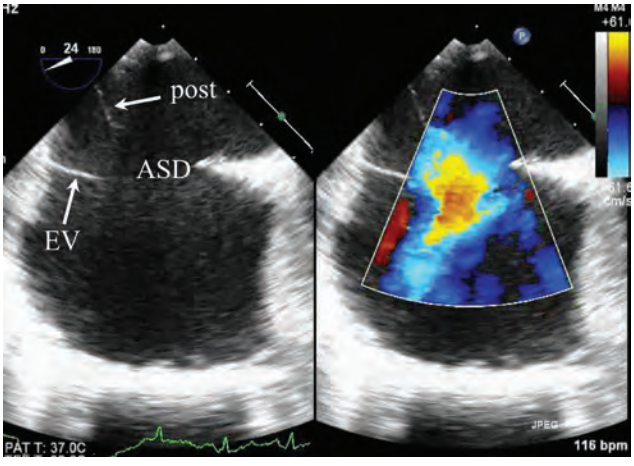

Fig 37. TEE: EV=Eustachian valve; post=posterior rim; ASD=atrial septal defect

ovalis. It extends anterior from the IVC-RA junction. One should not mistake it for a posterior rim (fig 37). A Chiari network is a remnant of the right valve of the sinus venosus and appears as a filamentous structure in various places in the RA, including near the entry of the IVC and coronary sinus into the RA. It is present in 2-3% of the general population and is associated with the presence of ASA. Reduction of Chiari network herniation across the ASD requires sheath retraction and repositioning. Redundant Eustachian valve interfering with deployment may be deflected with a steerable radiofrequency ablation catheter during device passage. The key component is recognition of these entities.

Fenestrated defects (Multiple ASDs)

Fenestrated defects (fig 7) may be successfully closed using different techniques or devices. Use of balloon atrial septostomy to create a single large defect that could be closed with a single large device is described. We generally use a single device deployed in the larger defect to occlude two or more smaller defects. A smaller defect <7 mm distance from the larger defect

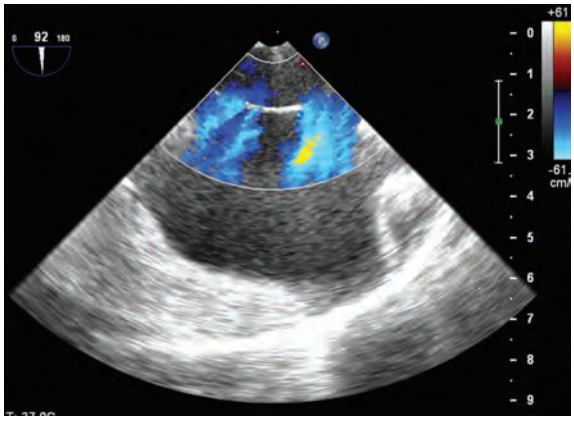

Fig 38. TEE: multiple defect before closure with a cribriform device

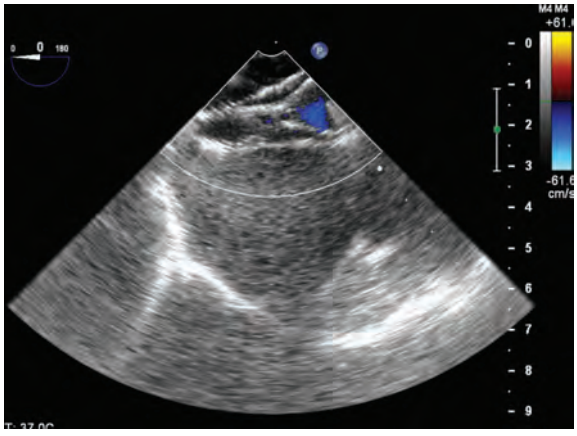

Fig 39. TEE: multiple defect after closure with a cribriform device

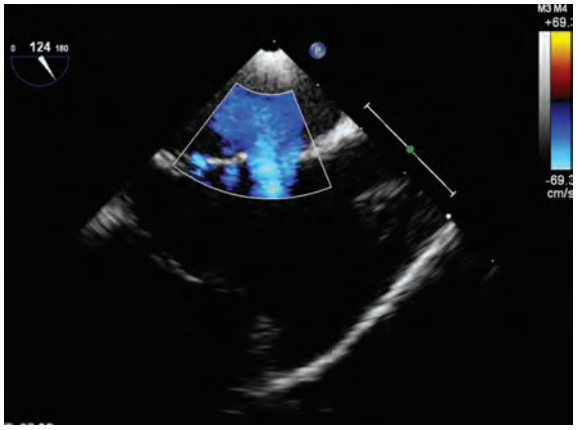

Fig 40. TEE: multiple defect before closure with a single Amplatzer type device

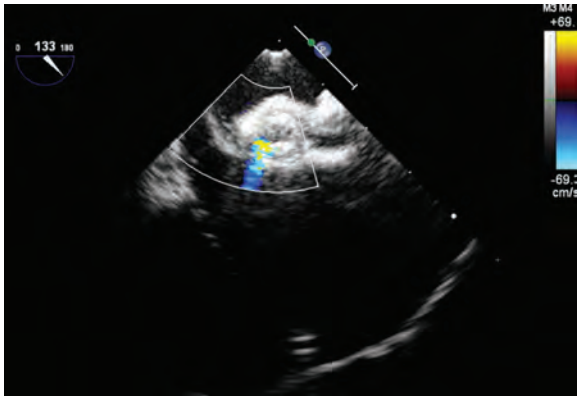

Fig 41. TEE: multiple ASD after before closure with a single Amplatzer type device

has a 100% closure rate at follow up. Deploying the device in the larger defect may decrease the distance between the two defects, or even compress the smaller defect. If the distance between the two defects is >7 mm, a residual left-to-right shunt may persist. The device waist crosses the largest defect, and the large components occlude the remaining defects. If the smaller defect is hemodynamically significant, and is far from the other defect (>7 mm), two devices should be used. The first device is deployed without release across the smaller defect, followed by deployment in the larger defect, aiming to overlap devices. After verifying good positioning of both devices, the smaller device is released first, then the larger device. Fig 38 shows multiple defects before closure and Fig 39 shows after closure with a cribriform device. A similar defect is seen before (fig 40) and after (fig 41) closure with a single Amplatzer type device, in next images.

Elderly

Elderly patients have PA hypertension, atrial arrhythmias, and valvular regurgitation, and may

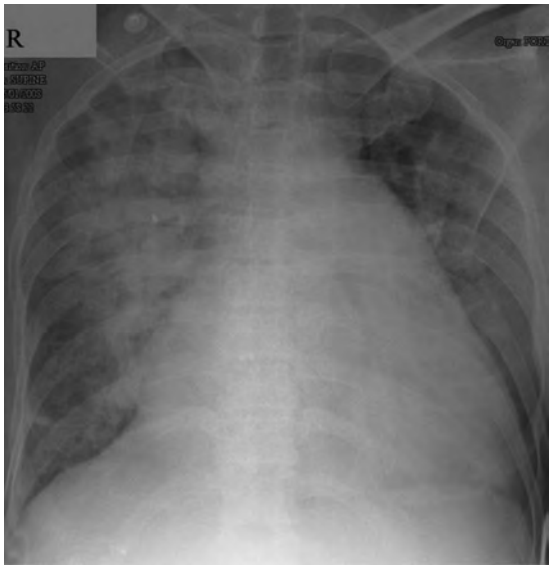

Fig 42. Xray chest: pulmonary oedema after device closure

present with congestive heart failure. Comorbidities such as systemic hypertension, chronic obstructive pulmonary disease, coronary artery disease, chronic kidney disease, and LV diastolic dysfunction complicate the clinical picture. Congestive heart failure may occur due to abrupt elevation in LV preload following device closure, especially in elderly patients with impaired LV systolic or diastolic function. This may progress to pulmonary oedema (fig 42). It is recommended to monitor pulmonary capillary wedge (PCWP) or LV diastolic pressure during the procedure. If mean PCWP increases >10 mmHg from the baseline value during balloon occlusion of the defect (test balloon occlusion), or PCWP increases to >20 mmHg, it is preferable not to close ASD at that point of time. They may be pre-treated with intravenous diuretics, nitroglycerin or inotropic agents to lower LA pressure. Some of them may require supplemental respiratory support, requiring intensive care unit admission and longer hospitalization. Alternatively, a perforated device to avoid the abrupt hemodynamic change can be used. This allows for atrial decompression in the acute phase with improvements in hemodynamics and symptoms.

Fenestrated device

Patients with LV diastolic dysfunction or RV dysfunction and/or PA hypertension may have haemodynamic deterioration after closure of ASD. Fenestrated device (either commercially available or custom made on table, fig 43) is as an alternative in such cases, although supporting data are meagre. It serves to alleviate volume overload and preserve a minor shunt across the atrial septum to serve as an acute and short-term pop-off that prevents right or left sided pressure elevation.

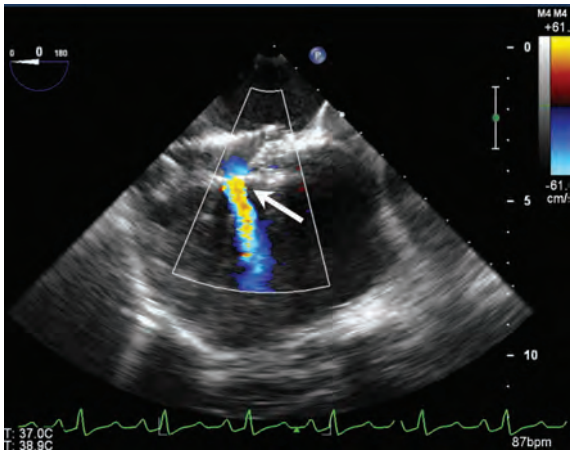

Fig 43. TEE: fenestrated device in situ. Arrow=fenestration

ACUTE AND CHRONIC COMPLICATIONS OF PERCUTANEOUS CLOSURE

- Cardiac perforation causing pericardial effusion and tamponade
- Erosion
- Compromise to neighbouring structures: mitral valve, vena cavae
- Device embolization requiring percutaneous or surgical removal
- Pulmonary embolism
- Air embolism
- Vascular access site complications
- Hemorrhage
- Arrhythmias
- Device thrombosis
- Infective endocarditis
- Cerebrovascular accidents
- Nickel allergy
- Deformity
- Tearing of rims
- Residual defects

Erosion

Devices with higher risk are those with protruding LA disk into the aortic root and may have motion relative to adjacent heart structures. However, a large number of cases with an aortic rim deficiency have undergone successful deployment without erosion. Symptoms include chest pain, dizziness, shortness of breath, hemodynamic collapse, or sudden death, but patients can also be totally asymptomatic. Pericardial effusion/tamponade, hemopericardium, and aortic to atrial fistula have been associated with erosion. An expert panel reviewed 28 cases cases of hemodynamic compromise with Amplatzer device between 1998 and 2004. They determined the erosion rate to be 0.1%. In 25 patients, the aortic rim was deficient and/or the ASD was

described as "high" suggesting deficient superior rim. 19 had symptoms develop within 72 h. In 8 patients, diagnosis was made between 5 days and 8 months, and in 1 patient, pericardial effusion developed after 3 years. 21 patients required surgery. In 7 of 28 cases with hemodynamic compromise, the patients were managed medically with pericardiocentesis and/or observation.

Risk factors for erosion

- Aortic rim deficiency in several views (''bald aorta'')
- Superior rim deficiency in multiple views
- High location of ASD
- Oversized ASD device (device diameter >1.5 times static stop-flow diameter)
- Device measuring >26 mm.
- Dynamic ASD (50% change in size of ASD)
- Poor alignment between the discs and the defect (contact by the edge of the device with the atrial wall causing protrusion of the device into wall and into adjacent structures such as the aorta OR splaying or flaring of the device around the aortic root following implantation).
- Tenting of the atrial free wall after device implantation
- Pericardial effusion after device implantation
- Atrial septal malalignment
- Deformation of device at aortic root
- Thicker device profile at the time of deployment.

Compromise to neighbouring structures

Damage to mitral valve

One patient had perforation of anterior mitral leaflet by a cribriform device (fig 44). She was asymptomatic and underwent elective valve repair, removal of device and closure of ASD.

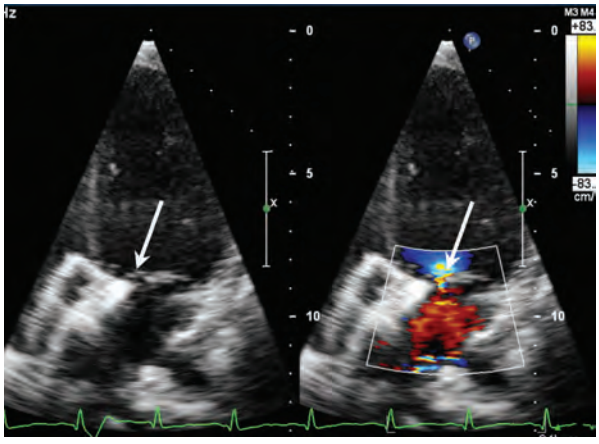

Fig 44. TTE: mitral valve perforation by cribriform device; Arrow suggests perforation

Osbtruction to vena cavae

Very rarely, obstruction to superior vena cava (fig 45) and to IVC (fig 46) can occur with a large device which may have to be retrieved.

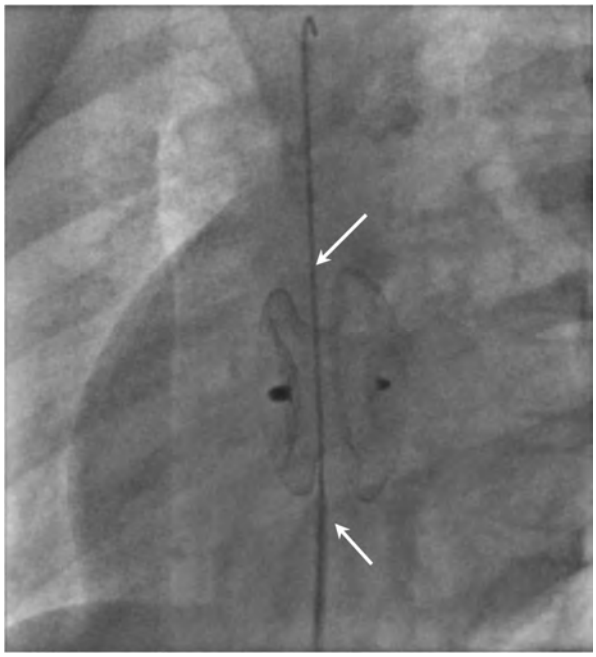

Fig 45. Fluoroscopy: superior vena caval obstruction; arrow depicts the path course of catheter and wire through the superior vena cava, overlapping the device

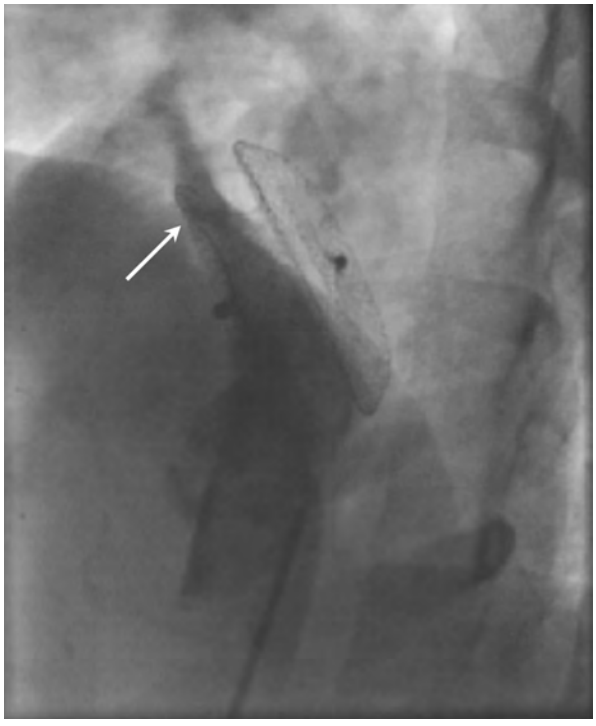

Fig 46. Fluoroscopy: IVC obstruction; arrow depicts the narrow drainage into right atrium

Compromise to LA

In small children, when a large device is used, the small LA may appear compromised (fig 47). Retrieval may be needed.

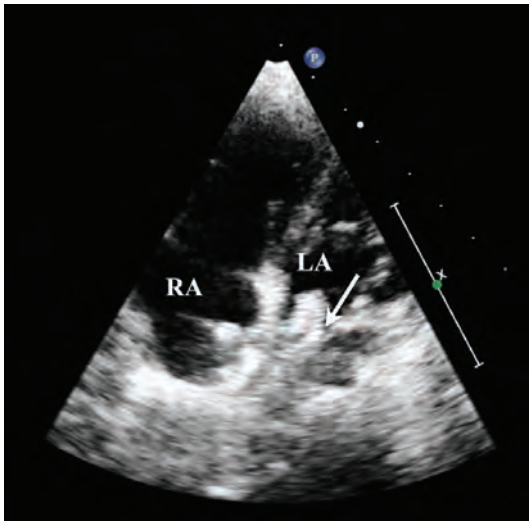

Fig 47. TTE showing compromise of left atrium (arrow); RA=right atrium; LA=left atrium

Embolisation

Device embolization is a potential complication, and the causative factors can be undersized device, inadequate or floppy rim, operator related technical issues such as malposition during the "push-pull" manoeuvre.

Risk factors for embolization

- Large defect
- Large device: >90% across septum
- Undersizing of device relative to the defect
- Thin rim
- Mobility of device post-implantation
- Mobility of rim post-implantation
- Valsalva manoeuvre
- Tension on cable during deployment
- Excessive wiggle

Examples of device embolization are shown in Fig 48 (RA), Fig 49 (RV), Fig 50 (RV outflow tract), Fig 51 (LV). Embolization to LV can have disastrous acute mitral regurgitation due to prevention of valve closure (fig 52). Rarely, especially the smaller devices can migrate to aorta (fig 53).

Device embolization can be minimized by recognizing deficient rims, confirming delivery system to device lock, avoiding device undersizing and aggressive catheter

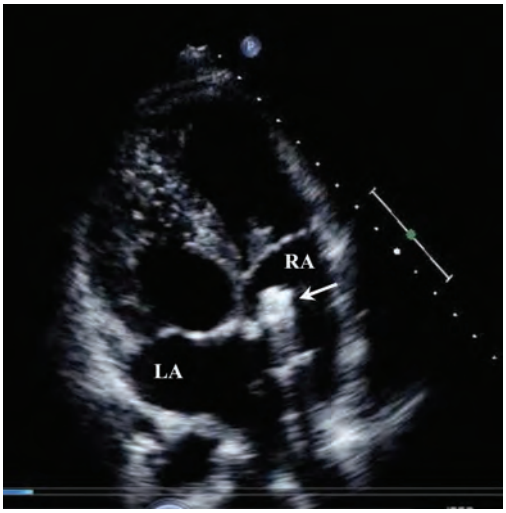

Fig 48. Fluoroscopy: RA embolization (arrow); RA=right atrium; LA=left atrium

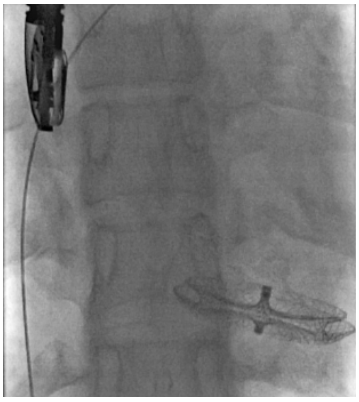

Fig 49. Fluoroscopy: RV embolisation

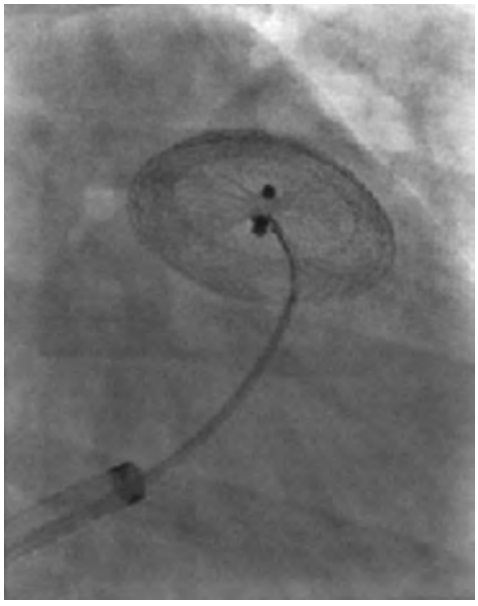

Fig 50. Fluoroscopy: RV outflow tract embolisation

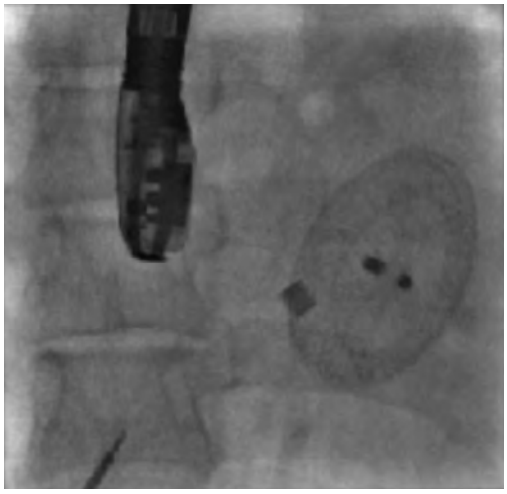

Fig 51. Fluoroscopy: LV embolisation

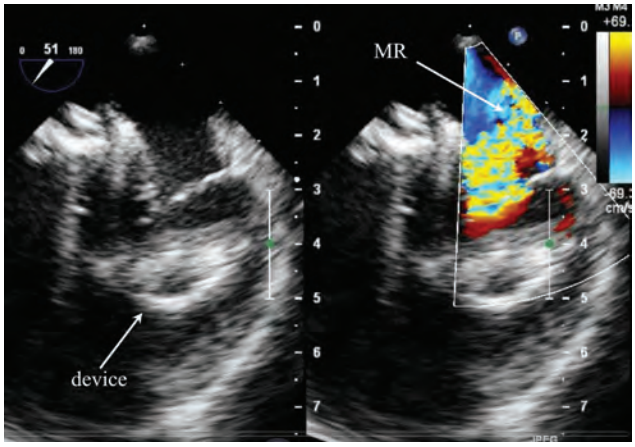

Fig 52. Fluoroscopy: LV embolization with mitral regurgitation (MR)

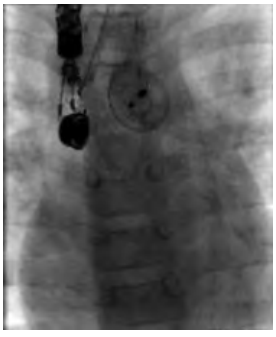

Fig 53. Fluoroscopy: arch embolisation

motion, retrieving and redeploying devices nonparallel to the septum, and confirming stable position with a pre-deployment wiggle test. Fig 54 shows a device unscrewed within the delivery sheath before deployment across ASD. This happens when the cable is vigorously manipulated particularly in difficult procedures requiring PV deployment. Hence it should be remembered not to manipulate the cable, but only the sheath during these processes.

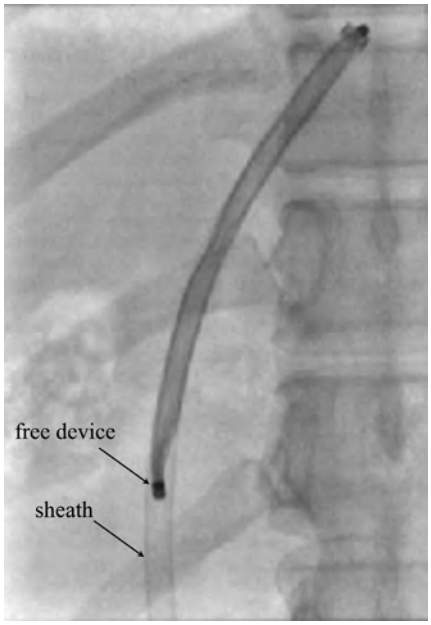

Fig 54. Fluoroscopy: unscrewing of device inside sheath

Experienced operators can successfully retrieve the embolized device using a transcatheter approach. After device embolization, the first objective is simply to get the device into the safest position, avoiding ventricular migration. The device may then be stabilized and moved or removed from the body. A wire, snare, or bioptome can be used for stabilization. One or 2 loop snares are used to pull embolized device towards the IVC, into a stiff sheath, at least 2-Fr sizes larger than the implanting sheath. Retrieval requires snaring the microscrew on the proximal component. If needed, a bioptome from an internal jugular access may better orient, elongate, and place tension from above on the distal component of the device, assisting snare retrieval toward the IVC. If retrieval into a sheath is difficult, device migration can be avoided by crossing it with a stiff wire in the infrarenal vena cava and advancing the wire tip into the SVC for stabilization. Bare vein retrieval carries high risk for vascular complications, and surgical venous cut-down is preferred and avoids intrathoracic retrieval. Crossing the AV valve with the device should be avoided. The device can often be repositioned and redeployed. If these fail, emergency surgery may be required.

Air embolism

Removal of dilator creates vacuum in a large sheath and sucks air to the low pressure venous system. Air embolism can be prevented by preprocedure hydration, preemptive use of positive pressure ventilation in patients with airway or pulmonary disease that is likely to produce wide negative intrathoracic pressure swings during sedation, maintenance of catheters below atrial level, delivery sheath flushing during slow withdrawal

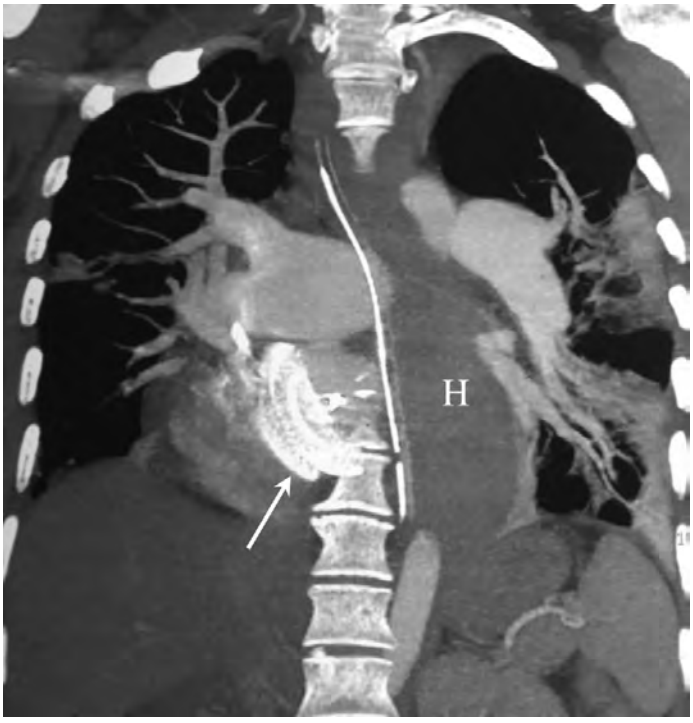

Fig 55. CT: retro-oesophageal haematoma (H); arrow=device

of the dilator and wire with subsequent sheath back bleeding, and prompt identification of air bubbles during fluoroscopy-assisted flushing. Use as small sheath as possible, remove the dilator slowly, use under water de-airing and de-air during prolonged manipulation. Cases should be scheduled earlier in the day to avoid dehydration.

The right coronary artery is commonly affected because of its anterior position in a supine patient. Changes in mentation, focal neurologic deficits, chest discomfort, ST segment changes and arrhythmias are usually transient, but can be life threatening and should be treated supportively with supplemental oxygen, analgesia, volume expansion, and standard arrhythmia therapy. Occasionally, coronary air embolism extraction may be necessary.

Hemorrhage

Retro-oesophageal hemorrhage due to access complication can occur (fig 55) We have seen one large retro-oesophageal haematoma that required only conservative management.

Arrhythmias

Transient arhythmias like ectopics, supraventricular tachycardia and atrial fibrillatioin are not uncommon.

Fig 56. Complete heart block after device closure

Large devices can predispose to complete heart block (fig 56) that may require either steroids or surgical removal if not improved with conservative management.

Thrombus formation

This occurs in ~2% of device closure procedures (fig 57). Proper heparinisation, especially when the procedure is prolonged, should be done. Prothrombotic disorders, postprocedure atrial fibrillation, and persistent atrial septal aneurysm are predictors for thrombus formation. Thrombus tends to resolve with heparin or warfarin and rarely requires thrombolysis or surgical removal.

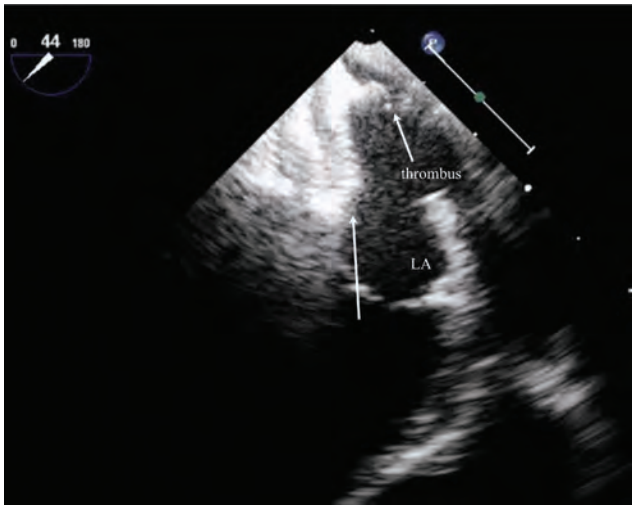

Fig 57. TEE: thrombus on LA aspect of device; arrow=device

Infective endocarditis

Endocarditis is very rare, but cases have been reported weeks after the procedure. Antibiotic prophylaxis against infective endocarditis is recommended for at least 6 months.

Nickel allergy

About 8% of women and 2% of men are sensitized to nickel. A rise in serum nickel concentrations after Amplatzer device delivery has been demonstrated. It presents with dermatitis, pericardial effusion, or severe bronchospasm. There have been reports of devices having to be removed secondary to nickel allergy and one report of treatment with prednisone until the device had endothelialized. History of nickel contact allergy must be elicited before device selection.

Deformity

During deployment, the device components rotate as they exit the sheath and return to their inherent shape. Commonest twist obstruction results in a cobra head malformation (fig 58), which should prompt device withdrawal and redeployment. A tulip deformity (fig 59) may require slenderising the LA disk from a jugular approach before being able to retrieve the RA disc from femoral site. If withdrawal is unsuccessful, exchange to a larger sheath over the delivery cable ensures capture.

Tearing of rims

This usually occurs with large ASD with floppy rims that require repeated and prolonged manipulation (fig 60). Surgical closure may be required. Systemic embolization can occur.

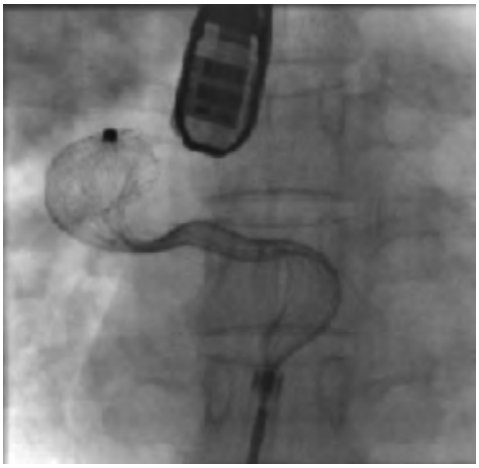

Fig 58. Fluoroscopy: cobra head deformity

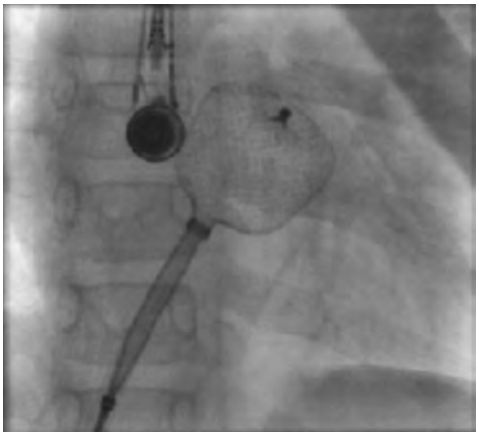

Fig 59. Fluoroscopy: tulip deformity

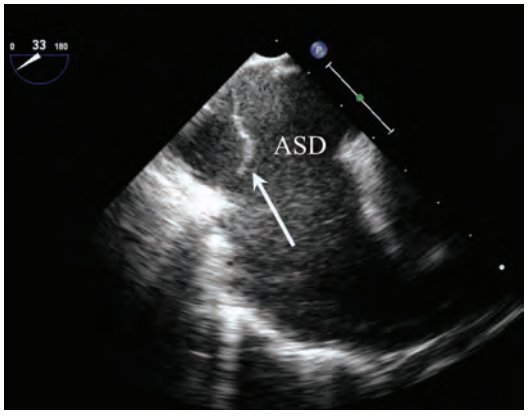

Fig 60. TEE: torn posterior rim (arrow); ASD=atrial septal defect

Residual defects

Residual defects are more common in multiple ASDs. If the shunt is not significant, they may be left alone (fig 61). Rarely, additional device or surgical closure may be required.

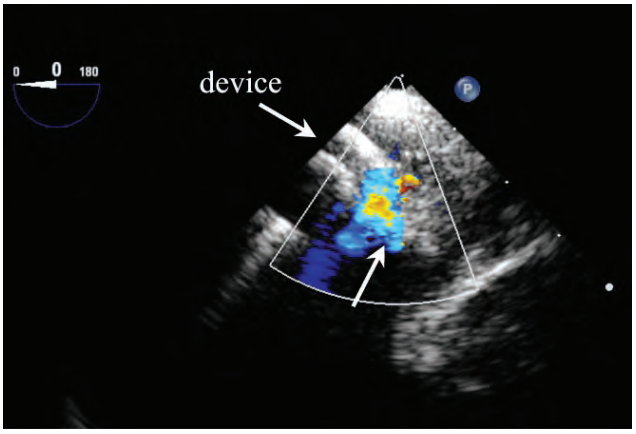

Fig 61. TEE: residual shunt after device closure (arrow); arrow=device

Follow up

A TTE study should be performed before hospital discharge (and repeated in 1 week when Amplatzer device has been used). Attention should be given to the device position, any residual shunt, and any evidence of erosion, device instability, or deformation of the surrounding structures. The presence of a pericardial effusion of even modest size could be an indication of device erosion. A 12-lead electrocardiography study should also be performed because rare cases of heart block have been reported with large devices. Follow-up evaluations, including TTE, should be performed at 1, 6, and 12 months after the procedure, with a subsequent evaluation every 1-2 years. Endocarditis prophylaxis is required during the first 6 months after device closure, as is antiplatelet therapy. Restriction from high-intensity physical activity for 3 months is recommended.

Atrial Septal Defect - Accesses for Surgical Closure

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INTRODUCTION

Atrial septal defect (ASD) is one of the most common congenital heart disease (CHD)[1], and accounts for 6 to 10 % of all CHDs. The procedural success in the transcatheter approach for closure of ASD depends on the size and shape of the defect, and mostly reserved to ostium secundum type of ASDs. The failure rate of transcatheter closure increases with large ASDs with insufficient rims or with fenestrated or aneurysmal interatrial septum.[2,3] In addition, potential complications include cerebral microembolism during the procedure, postprocedural thromboembolic risk, intracardiac shunt recurrence, injury to intracardiac structures, device dislocation, and subsequent peripheral embolization.[4-6] Therefore, surgery undoubtedly will continue to keep its place in the treatment of ASD along other existing percutaneous treatment options. The less invasive approaches decrease operative trauma and reduce hospital stay, although they are associated with occasional major complications.[4] However, full sternotomy has been gradually replaced by different minimally invasive techniques that guarantee a safe procedure, shorter hospital stay, good cosmesis, and a durable correction.[7-9]

STANDARD TECHNIQUE: MEDIAN STERNOTOMY, AORTIC AND CENTRAL VENOUS CANNULATION

This is the standard technique for closure of ASD in all patient populations. It is the time tested and the safest one with mortality rate close to zero.[10] The projected disadvantage is complete splitting of sternum to repair a defect in the atrial septum causing higher morbidity post operatively. Nevertheless, it is the best in certain subsets of patients like those with massive cardiomegaly or associated defects like anomalous pulmonary or systemic venous drainage. The operation is performed usually under general anaesthesia (although there are reports of awake surgery with thoracic epidural regional anaesthesia). A full median sternotomy (Fig 1) is performed with an electrically operated saw. An inverted T shaped pericardiotomy is performed. Standard aortic and bicaval cannulation with snares around the cavae will help establish CPB after full systemic heparinisation. If there is a persistant left SVC then it could be separately cannulated or venous return sucked by pump suckers from right atrium. An ACT (activated clotting time) is monitored for adequacy of heparinisation. The temperature is usually kept normothermic or mildly hypothermic (>34<36 C).

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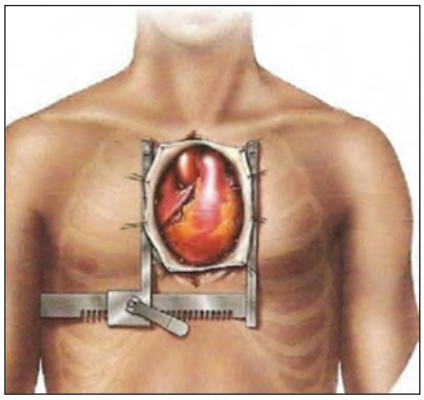

Fig 1: Schematic drawing of full sternotomy to ASD closure

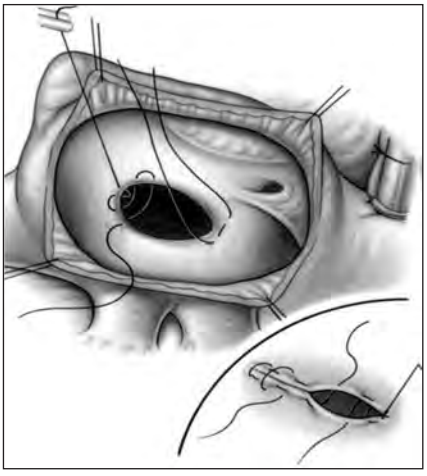

Fig.2: Direct closure of Secondum ASD (Surgery for congenital heart defects 3rd edition- J Stark, M de Leval, VT Tsang)

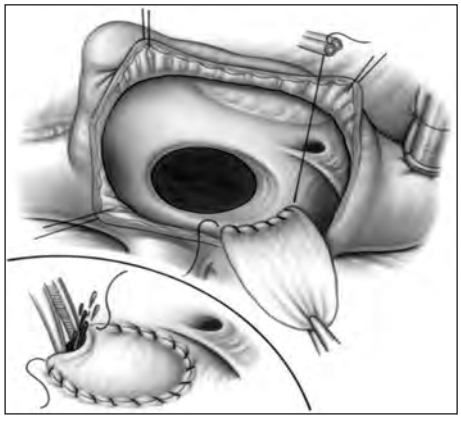

Fig 3: Patch closure of Secondum ASD (Surgery for congenital heart defects 3rd edition- J Stark, M de Leval, VT Tsang)

The approach to the septum is through right atrial free wall with varying incisions planned for different types of ASDs. The atriotomy is performed with cardioplegia electrical quiescence or induced ventricular fibrillation with or without aortic cross clamping. The septal defect is identified and margins defined. Care should be taken to identify the pulmonary veins draining into the left atrium, mitral valve morphology, coronary sinus opening and SVC and IVC drainage to right atrium. Small defects with adequate margins may be closed directly (Fig 2) with polypropelene but larger ones and those without margins all around are best closed using a patch (Fig 3). Autologous pericardium - glutaraldehyde treated or untreated, bovine pericardium, dacron or PTFE patch are used for this purpose.

LESS INVASIVE TECHNIQUES

The minimally invasive approaches in cardiac surgery aim to reduce surgical trauma and achieve faster postoperative convalescence and better cosmetic results compared with the conventional full sternotomy approach. A sternotomy has a negative effect on post operative respiratory efforts as the "pump-handle" movement which aids deep breathing is impaired leading to atelectasis. The last decade has seen a leap in this field as a result of technical innovation in peripheral CPB technology combined with the possibility of endoaortic clamping and remote cardiac arrest. Advent of Video Assisted Thoracoscopy (VATS) and robotic telemanipulation into cardiac surgery has even increased surgical dexterity and enabled surgeons to perform totally closed-chest intracardiac procedures.[11] However, it hasto be noted that the CPB time, aortic cross clamp time and overall operative time were significantly higher in the minimally invasive approaches.[9] Potential complications related to minimal access CPB are air embolization and peripheral cannulation issues, such as retrograde aortic dissection, limb ischemia, or delayed wound healing at the femoral region.

In general, the complications resulting from systemic atherosclerosis are uncommon in ASD surgery due to younger age of patients However, the presence of atherosclerotic iliofemoral arterial disease and small vessel size may complicate the peripheral access to place the patient on heart-lung machine. General anesthesia with a double lumen tube for single lung ventilation is preferred. There are several reasons why this is preferred (1) ease of central arterial cannulation (2) less risk of injuries to the right lung during the dissection phase and easier preparation of the patient; (3) reduced dependency for cardiopulmonary bypass (CPB) in case of adhesions; (4) minimization of the time of deflation of both lungs (before and after CPB); (5) easier control of possible bleeding (from the heart or the thoracic wall) at the end of CPB.[12]

Technique 1

Lower partial Sternotomy, aortic and central/ peripheral venous cannulation

This technique involves partial median sternotomy of the lower part usually terminating into a horizontal cut into the 3rd or 4th right intercostal space. (Fig 4) The pericardiotomy and cannulation is just the same as in the standard approach as above. Aortic cannulation and SVC cannulation requires manipulation of these vessels to allow adequate exposure. Special sternal retractor devices also aid in safe aortic cannulation. Encircling the SVC is also tricky with this approach. Cannulating the IVC is straight forward. Alternatively femoral vessel cannulation (Fig 5) may be done to reduce the extent of sternal split and retraction. The rest of the procedure is similar to the standard technique. There is no need for specially designed instruments, and resource use is not too high. This approach yields higher cosmetic acceptance in male patients.[9]

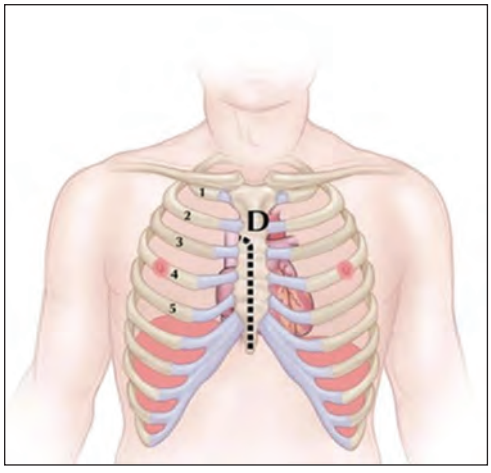

Fig 4: Lower partial sternotomy

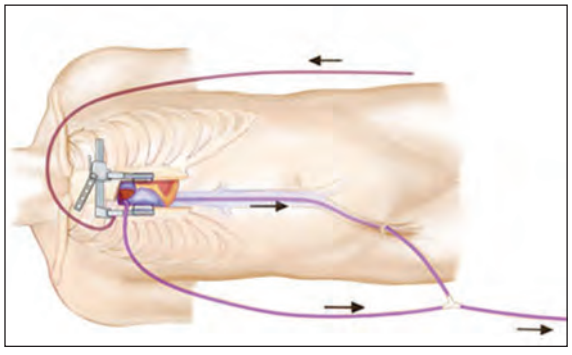

Fig 5: Cannulation for CPB in lower partial sternotomy

Technique 2

Right parasternal mini-incision, aortic and central venous cannulation

Thoracic access is achieved by a right parasternal incision above the third and fourth ribs (Fig 6). A small cartilaginous part of one or two ribs can be removed before inserting the retractor to improve exposure. Ligation of the right internal mammary artery is not necessary. The exposure is improved by longitudinal incision of the pericardium, pledgeted traction sutures to displace intrapericardial structures more anteriorly and laterally, thus allowing better access to the aorta and right atrium. The inferior vena cava (IVC) and superior vena cava (SVC), are encircled and looped. Full heparinized cardiopulmonary bypass is instituted by direct cannulation of the aorta and the venacavae (size depends on CPB flow and BSA). The IVC cannula is usually guided through a separate lateral incision, which will be used later for placement of a single drainage tube at the end of procedure. This allows better operative space. On total bypass, the right atrium is entered through a conventional incision, and direct or patch closure is performed with over-and-over (polypropylene) sutures with suction through the defect and coronary sinus. The lungs can be left nonventilated to decrease the left atrial inflow. If cardioplegia is given, the field will be blood free and closure is less cumbersome. Before tying the suture, deairing of the left atrium is performed. After full deairing, the CPB is terminated and decannulation is performed after defibrillation using either external or internal pediatric pads. The pericardial edges are then reapproximated. In cases without removal of the cartilaginous parts, the ribs are repositioned with absorbable sutures before regular wound closure. The closure is a bit cumbersome but sternotomy can be avoided when this technique is being followed.

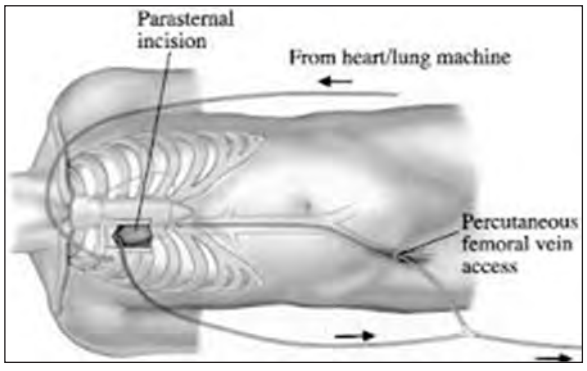

Fig 6: Right Parasterna incision and cannulation

Technique 3

Right submammary mini-incision, femoral arterial cannulation, and central venous cannulation

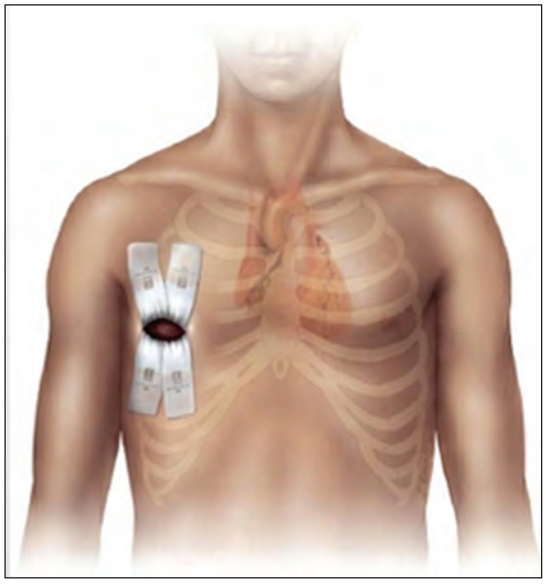

Fig 7: Right anterior thoracotomy (submammary incision)

The approach to the right atrium is through an anterior right submammary 6-to 8-cm-long incision through the fourth interspace (Fig 7). An oblique or longitudinal 2-3 cm groin incision is made within the inguinal fold for adequate exposure and subsequent cannulation of the common femoral artery. The pericardium is opened longitudinally (about 3 cm above the phrenic nerve) and retracted using stay sutures. The SVC is encircled, which may be difficult at times. In contrast, encircling of the IVC is usually easy in this approach. Both venacavae are cannulated through the right atrium best using right angled cannula, the IVC cannula going in through the chest drain port to allow better space in the operating field. Closure of the ASD, removal of air, and decannulation are similar to any other access techniques. In female patients, this approach, either transthoracic or endoclamping for aortic occlusion has a high cosmetic acceptance and is referred to as the "bikini" line incision.[7,8] Some have questioned this approach in young females citing impaired breast development on the side of incision. Damage to phrenic nerve is a potential complication in this approach as the nerve is close to the surgical sites of pericardiotomy, IVC looping and cannulation, topical cooling and pericardial stay sutures.[13] The routine intraoperative use of intercostal nerve blockage, cryoablation, or soft tissue retractors may help to minimize the degree of postoperative pain in patients undergoing closure using this approach.[14,15]

Technique 4

Right submammary mini-incision, femoral arterial cannulation, right atrial-IVC/ femoral venous cannulation, and percutaneous jugular vein cannulation

The aim here is to create better access through a smaller incision by reducing the number of cannula entering through the incision. It also shortens time to place patient on CPB as the cannulation are done via easier vascular access sites. The tedious manoeuvres required to cannulate intrapericardial vessels are also avoided saving time and decreasing risks of catastrophic events. The thoracic and inguinal incisions are the same as in technique 3. In contrast, a previously placed central venous catheter through the right jugular vein is used to cannulate the SVC by the Seldinger technique. Here encircling the SVC is avoided, and instead a vascular clamp can be safely placed when going on total bypass. To improve venous return from the small SVC cannula, an additional centrifugal pump which creates suction venous drainage, is usually added to the heart-lung machine. IVC drainage can be attained through femoral venous cannulation or direct cannulation as in technique 1 or 2. Atrial incision and ASD closure are similar to technique 1. The jugular vein can be safely decannulated after heparin reversal, and local compression is applied until the bleeding stopped. Wound closure is similar to any thoracotomy approach. Even though the thoracotomy is limited, there is still a rib-spreading process and consequent intercostal nerve damage in this technique. Walther and colleagues[14] showed that among cardiac operations, whether minimal access (partial sternotomy or mini-thoracotomy) or conventional approach, overall postoperative pain levels are low. It is also observed that lateral mini-thoracotomy approach is associated with slightly higher pain levels during the first 2 postoperative days.

Technique 5

Right mini thoracotomy - femoral arterial and venous cannulation

Again, the aim here is to create better access through a smaller incision by reducing the number of cannulae entering through the incision. The arterial inflow is via a femoral arterial cannula and venous drainage via long femoral cannula which has a perforated end segment and lies in the SVC followed by a non-perforated solid tube which lies in right atrium and then further down perforated all along to gather IVC blood (Fig 8). The cannula is placed over a wire with TEE guidance. Palpation of the cannula can also be a very good guide to ascertain the position of the cannula. This method avoids major manipulations of neck vessels.

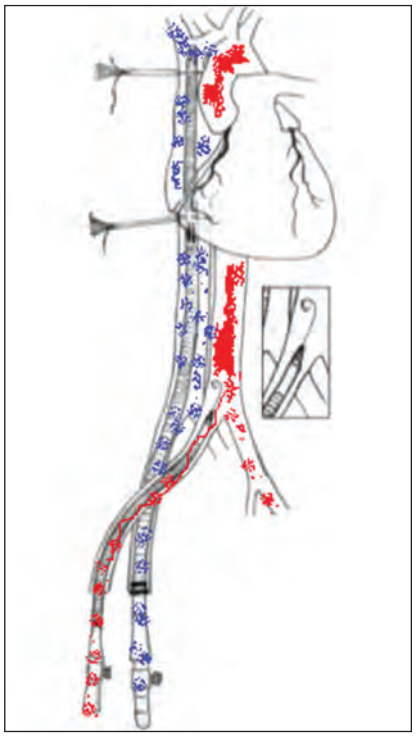

Fig 8: Two stage femoral venous cannula inserted through femoral vein into IVC and to the SVC

Technique 6

Totally Endoscopic Atrial Septal Repair (TEASR)-femoral arterial and venous cannulation with percutaneous jugular vein cannulation

TEASR is performed in a similar method with the patient positioned on the operating table with the right side elevated by 40°. (Fig 9). After right lung deflation and insufflation of the thorax with carbon dioxide, a stereo– endoscope is inserted into the right fourth ICS between the midaxillary and anterior axillary line. The robotic arms are inserted through the third and sixth ICSs in the anterior axillary line. An additional 8-mm stab incision is necessary in the fifth ICS in the midaxillary line for transthoracic instrumentation. CPB is instituted via femoro–femoral cannulation. After transthoracic Chitwood aortic clamping or endoaortic balloon clamping and cardioplegia, a standard right atriotomy was performed to repair the defect either directly or with a patch by the da Vinci Surgical system. The procedure is performed at mild (34 degree Celsius) or moderate (28 degrees) systemic hypothermia. TEASR is a recent step in the surgical evolution of ASD repair. It is a standardized and reproducible totally endoscopic cardiac procedure.[9] The results from literature showed that TEASR is superior to the other minimally invasive approaches in terms of the degree of invasiveness, patient satisfaction, and cosmesis.[11]

The apparent limitations, despite some indisputable advantages over other surgical techniques in ASD repair that TEASR has, are being ironed out as technology evolves. It is technically demanding and necessitates great expertise in both robotic and port-access perfusion surgical technology. Hence a steep learning curve is involved in reproducing excellent results. The other significant limitation is exorbitantly high costs for robotic surgery. The overall costs could be levelled when benefits in early postoperative recovery and expeditious return to work, were converted into productive days.[16] Third, it remains a time-consuming procedure. Most studies showed that longer crossclamp, CPB, and operative times are still hurdles to overcome.[9]

However, longer operation times do not appear to cause additional complications after TEASR, which may be attributed to the relatively younger age and lower incidence of comorbidities in this patient cohort. It is to be noted that, there is no tactile feedback in robotic telemanipulation. Therefore, it may be difficult to estimate the tension over the suture line in the direct suturing technique in TEASR. This may result in residual shunting early or late in the postoperative phase.[17]

Studies have shown that minimally invasive access provides additional advantages of shorter hospital stay, earlier return to normal activity, and better wound healing compared with the conventional sternotomy methods.[16] These achievements may be related to limited surgical trauma and better stability of the bony thorax. TEASR provides less postoperative pain and better quality of life than does the mini thoracotomy or complete sternotomy.[14] However, pain perception and, to a lesser extent, quality of life are subjective issues

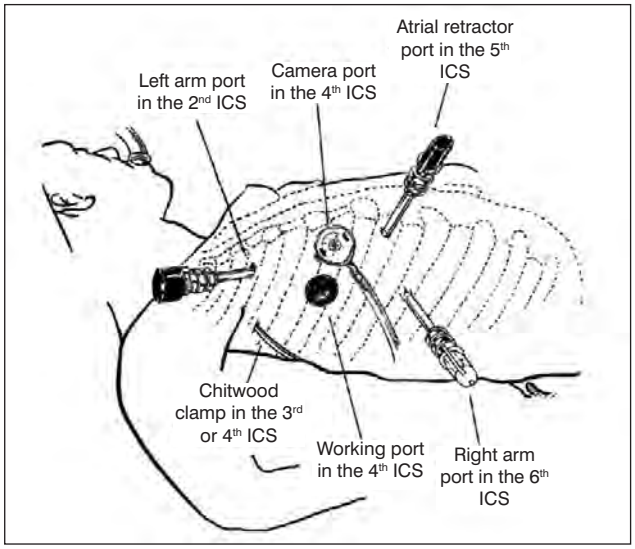

Fig 9: Schematic diagram showing position of patient, port placement and mini incision for TEASR

rather than standardized. They may vary according to socioeconomic status, difference in sex and race, mental preparation of the patient for such surgical intervention preoperatively, and confidence of the patient in the procedure (especially in robotic procedures).

In conclusion, surgical closure of ASD is a time tested and safe method to treat this congenital defect. The advent of new minimally invasive approaches and the improved safety outcomes of these procedures make it the standard of care to those patients not suitable for transcatheter ASD device closure.

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KJC Pearls

An Update on STEMI Management

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Editor's Note: ***'Pearls' section carries topics unrelated to the focused topic of 'Diamonds'. In this edition of Pearls, we have an update on STEMI management- a comprehensive one, direct from the master.***

The ACCF / AHA guidelines define ST Elevation Myocardial Infarction (STEMI) as "a clinical syndrome with characteristic symptoms of myocardial infarction in association with persistent electrocardiographic (ECG) ST elevation and subsequent release of biomarkers of myocardial necrosis"[1,3,4]. New-onset LBBB is considered to be a STEMI equivalent.[5] These ECG changes are surrogates for acute occlusion of an epicardial coronary artery. It has been established that immediate treatment aimed at re-establishing patency of the artery is of utmost importance. Such definitive treatment strategies depend on ECG criteria for initiation of therapy. Other ECG abnormalities that indicate probable coronary occlusion are multilead ST depression with co-existent ST elevation in lead AVR, hyperacute T waves in V1, V2 and deep T inversions in chest leads.

Because of the urgency in initiating treatment, risk stratification and triaging for therapy are started before the patient reaches the hospital, preferably at the point of first medical contact. Therefore, in the majority of cases, "ICU management" is initiated in the pre-hospital setting and continued through the Emergency Room(ER), Cardiac Catheterization Laboratory(Cath Lab) and the Intensive Cardiac Care Unit(ICCU). From the ER, the patient may either be taken directly to the Cath Lab or admitted to the ICCU for continuing the treatment initiated in the ER.

Prehospital care involves a highly integrated strategy aiming at restoration of flow in the infarct artery as early as possible[6,7]. Delays in this process may be caused by 1) the time for the patient to recognize his symptom as cardiac, 2)the time taken for prehospital evaluation, treatment and transportation, 3)the time taken in the hospital for diagnostic tests and initiation of treatment – "door-to-needle time" for patients triaged to receive a fibrinolytic agent and "door-to balloon" time for patients undergoing catheter-based reperfusion and 4) the time from initiation of treatment to restoration of flow.

The two treatment strategies for achieving reperfusion of the infarct artery are 1) Fibrinolysis and 2) Primary percutaneous coronary intervention (PCI). PCI is the preferred option[8]. A meta-analysis of 23 trials has demonstrated the superiority of PCI, showing a lower mortality rate(7% vs 9%), less re-infarction (3% vs 7%) and fewer strokes (1% vs 2%) when compared with fibrinolysis[9]. The disadvantage of PCI lies in the inherent delay in organizing and executing this treatment strategy. It is extremely important to achieve reperfusion in the shortest possible time. A large meta-analysis involving 7739 patients showed that the mortality advantage of primary PCI is lost if the door-to-balloon time is 60 minutes greater than the door-to-needle time for fibrinolytic therapy.

Several interventions have been devised for improving door-to-device time[10]. These include:

1. The prehospital ECG is used to activate the PCI team while the patient is being transported to the hospital.
2. Emergency room physicians activate the PCI team.
3. A single call to a central page operator activates the PCI team.
4. A goal is set for the PCI team to arrive at the catheterization laboratory within 20 min after being paged.

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5. Timely data feedback and analysis provided to the STEMI care team.

Choice of the ideal reperfusion strategy for individual patients remains complex; the duration of symptoms and time to treatment play a crucial role. STEMI patients presenting to PCI capable hospitals should undergo primary PCI with a target door-to-balloon time of less than 90 min. If the hospital does not have PCI capability, the clinician should rapidly determine whether the patient is eligible for fibrinolytic therapy. Patients who are ineligible for fibrinolysis should be transferred for primary PCI. If the patient is eligible for fibrinolysis, the clinician should consider two important factors: the duration from the onset of symptoms ("fixed" ischemia time) and transport time to the nearest PCI facility ("incurred" ischemia time)[10]. Patients facing a transport time of less than 30 minutes should be transferred for primary PCI. Fibrinolytic-eligible patients who present less than 2 to 3 hours from the onset of symptoms and have a transport time precluding primary PCI within 120 minutes of the first medical contact should receive fibrinolytic therapy. Patients presenting more than 2 to 3 hours after the onset of chest pain and have a transport time of less than 60 minutes should be promptly transferred for primary PCI. If the transport time is more than 60 minutes and the anticipated time from medical contact to reperfusion is 120 minutes, then the patient can be treated with either fibrinolytic therapy or primary PCI.

The data from CAPTIM and PRAGUE trials suggest that duration of symptoms should be a major consideration in the selection of fibrinolytic versus primary PCI therapy for STEMI. Barring exclusion criteria, in patients presenting within 2 to 3 hours of the onset of symptoms, prehospital fibrinolytic therapy is a viable option if the anticipated transport time is more than 60 minutes.

EVALUATION OF THE PATIENT AND TRIAGING FOR MANAGEMENT

A rapid and accurate evaluation of the patient is the cornerstone of STEMI therapy[8,10]. A focused history is obtained to assess the patient's clinical status. Special attention is given to the exact duration of symptoms and the presence of symptoms of cardiac failure. Approximately 20% of patients may have atypical symptoms or may be asymptomatic. Painless myocardial infarction occurs more commonly in the elderly, women, diabetics and postoperative patients. These patients may have dyspnea or congestive heart failure as their initial symptom. A careful search is also made for any contraindication to fibrinolytic therapy and anticoagulant therapy.

Physical examination is also performed in a targeted manner. Left ventricular dysfunction is indicated by the finding of tachypnea, tachycardia, pulmonary rales and a third heart sound. The presence of a murmur may suggest ischemic dysfunction of the mitral valve or ventricular septal rupture, and should be differentiated from a pericardial rub. In patients with right ventricular infarction, elevated jugular venous pressure and Kussmaul's sign may be noted. These patients usually have inferior wall infarction and are exceedingly prone to develop hypotension with exposure to nitrates and with hypovolemia. Shock is associated with cool skin and extremities, hypotension, diaphoresis, oliguria and possible altered mental status.

Physical examination provides a means for risk stratification and prediction of outcome based on the Killip classification, which has stood the test of time. In addition, a limited, focused neurologic examination to look for prior strokes or cognitive defects is needed in patients triaged to receive fibrinolytic therapy.

An ECG is obtained within 10 minutes of arrival in the ER. If the initial ECG is not diagnostic and there is a strong clinical suspicion, serial ECGs at 5 to 10 minute intervals or continuous ST segment monitoring should be performed to detect the potential development of ST segment elevation. Patients with inferior wall infarction should have right sided chest leads to look for right ventricular infarction. In patients who exhibit ST depression in the anterior chest leads, leads V7, V8 and V9 may bring out ST elevation due to a posterior wall infarct.

The initial diagnostic assessment should be brief as the goal for STEMI is to reduce the time to reperfusion. Accordingly, the current guidelines do not include echocardiography as a diagnostic test. However, the echocardiogram can provide extremely important information regarding the presence of aortic dissection, pericarditis and several types of abnormalities that can result in coronary embolism. A brief, focused echo study may be in order, although there is no firm recommendation regarding this at the present time.

GENERAL TREATMENT MEASURES IN THE EMERGENCY ROOM

Oxygen

Oxygen delivered by nasal cannula was previously a routine recommendation for patients with acute myocardial infarction, despite the fact that hard

evidence to support the use of supplemental oxygen was lacking. A Cochrane analysis that pooled the results of three trials found a three-fold increase in mortality in patients receiving oxygen compared to patients on room air[11]. Oxygen has also been found to increase coronary vascular resistance. Oxygen is currently not recommended for routine use in STEMI. It may be used if a patient has clinically significant hypoxemia or heart failure. Hypoxemia may occur as a result of ventilation-perfusion abnormalities due to left ventricular failure or concomitant intrinsic pulmonary disease.

Aspirin

Aspirin has been shown to reduce mortality in myocardial infarction and should be administered as early as possible and continued indefinitely in patients with ACS[12]. In patients with aspirin allergy or major intolerance, clopidogrel may be substituted. A dose of 162-325 mg of chewable aspirin is given so that buccal absorption is facilitated rather than absorption through gastric mucosa. The clinical practice guidelines make the following recommendation:

Class I

1. Aspirin 162 – 325 mg should be given before primary PCI. (Level of Evidence B)
2. Aspirin 162 – 325 mg should be given before fibrinolysis. (Level of Evidence B)
3. Aspirin should be continued indefinitely. (Level of Evidence A)

Class II a

1. It is preferable to use 81 mg aspirin per day in preference to higher maintenance doses after primary PCI. (Level of EvidenceB)
2. It is preferable to use 81 mg aspirin per day in preference to higher maintenance doses after fibrinolysis. (Level of Evidence B)

P2Y12 Inhibitors

Thienopyridines (clopidogrel and prasugrel) and the direct P2Y12 inhibitor ticagrelor are oral antiplatelet agents that inhibit platelet activation through the adenosine diphosphate (ADP) dependent pathway. They should be administered early, generally at presentation. The choice of these antiplatelet agents and their dosage depend on what type of reperfusion is subsequently planned. Clopidogrel remains the choice for patients treated with fibrinolysis; even though data with ticagrelor is emeging. For patients treated with primary PCI; ticagrelor, prasugrel or clopidogrel may be used (Class I recommendation); but recent guidelines prefer ticagrelor or prasugrel over clopidogrel in such a scenario (Class II a).

Analgesia

The initial management should target the relief of pain and the heightened sympathetic activity associated with pain. Morphine is the preferred agent and is given in bolus doses of 1 to 2 mg intravenously, carefully watching the patient's pain status and haemodynamic condition and looking for side-effects like hypotension, bradycardia and vomiting. An anti-emetic agent is given concomitantly, and atropine should be ready at hand. Over-sedation and respiratory depression should be avoided. The maximum dose for an adult patient is 10-15 mg.

Morphine helps to alleviate the patient's restlessness and anxiety. It has a beneficial effect in patients with pulmonary oedema by virtue of peripheral arterial and venous dilation, particularly in patients with excessive sympatho-adrenal activity. Work of breathing and heart rate are reduced, by a combined effect of reducing sympathetic tone and increasing vagal activity.

Morphine should be used with caution in patients with haemodynamic instability as it results in a reduction of cardiac preload. In patients with inferior wall infarction and right ventricular infarction, this preload reduction may be poorly tolerated. In patients who are already volume depleted because of poor intake, vomiting, diaphoresis and older age, drugs like morphine and nitrates should be used with extreme caution.

Non-steroidal anti-inflammatory agents and cyclo-oxygenase-2 inhibitors should not be used for pain relief in STEMI patients. Several studies have demonstrated an increased risk of adverse cardiovascular events associated with these agents[13].

Beta-Adrenergic Blockers

Several early clinical trials investigating the use of beta-blockers in myocardial infarction have documented a decrease in early and late mortality. In a meta-analysis of 82 randomized trials of beta-blockers, there was a significant reduction in long term, but not short term, mortality. Traditionally, metoprolol has been the drug of choice, initially administered intravenously and later given in oral doses. Data from the COMMIT (Clopidogrel and Metoprolol in Myocardial Infarction Trial) showed a 15% to 20% relative risk reduction in the rate of recurrent infarctions with IV beta blockers. However, the study also showed a 30% relative increase in the risk of cardiogenic shock. Therefore, the routine initial use of intravenous beta-blockers is no longer considered standard therapy. It is important to avoid them in patients with Killip class II or greater. The benefits of β-blockers in patients undergoing primary PCI are not clear as there has have been no randomized prospective studies addressing this issue.

Oral beta-blocker therapy is recommended for STEMI patients, irrespective of the administration of fibrinolytic agents or the performance of primary PCI. They are especially helpful in patients with significant residual unrevascularized segments and evidence of recurrent ischemia or tachyarrhythmias early after the onset of infarction. They should be withheld in patients who have heart failure or heart block. The beta-blockers with reported favourable effects include metoprolol, atenolol, carvedilol, timolol and alprenolol. Agents with intrinsic sympathomimetic activity (pindolol and oxprenolol) are not recommended in the treatment of STEMI. The CAPRICORN (Carvedilol PostinfaRction survival COntRol in left ventricular dysfunction) study revealed a significant reduction of all-cause mortality in patients receiving carvedilol over a mean follow-up of 1.3 years.[14]

In patients who have heart failure or shock, beta blocker therapy is delayed until the patient becomes hemodynamically stable.

Clinical Practice Guidelines

Class I

1. Patients receiving beta blockers within the first 24 hours of STEMI without adverse effects should continue to receive them in the early convalescent phase of STEMI. (Level of Evidence A)
2. Patients without contraindications to beta blockers who did not receive them within the first 24 hours after STEMI should have them started in the early convalescent phase. (Level of Evidence A)
3. Patients with early contraindications within the first 24 hours of STEMI should be re-evaluated for candidacy for beta blocker therapy.(Level of Evidence C)

Nitrates

Nitrates have the ability to enhance coronary blood flow by non-endothelium-dependent coronary vasodilatation and also to reduce cardiac preload[15]. Sublingual administration of nitrates is indicated in most patients with ACS. It is important to avoid them in patients who are hypotensive and in patients who are suspected to have right ventricular infarction. Long-acting oral nitrate preparations are to be avoided, in view of the frequently changing haemodynamic status.

In symptomatic patients, intravenous nitroglycerin may be initiated at a dose of 5 to 10 μg / min and gradually increased with a goal of 10% to 30% reduction in systolic blood pressure and symptomatic relief.

Approximately 40% of patients with inferior wall infarction are associated with right ventricular infarction. Nitrates should be used with extreme caution in these patients, to avoid profound hypotension. Caution is advised also in patients with aortic stenosis and also in the elderly age group, particularly in the setting of volume depletion. The combination of hypotension and bradycardia may be a manifestation of the von Bezold Jarisch reflex, especially in patients with RV infarction. Nitrates are contraindicated if there is a history of recent sildenafil use.

ACE Inhibitors and ARBs

ACE Inhibitors are clearly indicated for patients with anterior infarction, post MI LV dysfunction or heart failure. They may be given routinely to all patients without contra-indications[16]. Lisinopril, Captopril, Ramipril, Trandolapril and Perindopril have been used. Treatment is initiated in small doses and stepped up gradually to a tolerated higher dosage.

Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers: Five trials have studied the use of ACE inhibitors after acute myocardial infarction. Patients were selected on the basis of LV dysfunction indicated by LV ejection fraction less than 40%, or the occurrence of transient heart failure. Clinically and statistically significant mortality reduction of 40 to 70 lives saved per 1000 patients treated was documented in four of these five trials. Given the results of these trials, it is reasonable to initiate therapy within the first 24 hours, as long as no contraindications exist and the patient is hemodynamically stable. Patients with an ejection fraction greater than 45% and no evidence of significant heart failure, mitral regurgitation or hypertension may have the therapy discontinued while still hospitalized.

Additional blockade of the renin-angiotensin system with the angiotensin receptor blocker valsartan was studied in the VALIANT trial. Valsartan was as effective as captopril in the management of AMI patients with LV dysfunction. However, the combination group had a significantly greater amount of hypotension and renal dysfunction. The combination of ACE inhibitor and ARB is to be avoided. The OPTIMAAL study which compared captopril and losartan, suggested that ACE inhibitors should be used as primary therapy and ARBs should be used in those who cannot tolerate ACE inhibitors.

Aldosterone Antagonists: The use of an aldosterone antagonist in patients with AMI complicated by LV dysfunction was studied in the EPHESUS trial. After a mean follow-up of 16 months, the primary endpoint of death occurred in 14.4% of treated patients and 16.7% in the placebo group. Predictably, eplerenone was

associated was associated with a greater amount of hyperkalemia and less of hypokalemia. It is reasonable to use an aldosterone antagonist in conjunction with beta blockade and ACE inhibition in patients with AMI and LV dysfunction (ejection fraction less than 0.4), with diligent monitoring of serum potassium. These drugs are either avoided or used with caution in patients who have hypotension, renal failure or hypokalemia.

Statins

Statins are given to all STEMI patients without contraindications. High intensity statin therapy is initiated early in the course of STEMI management. Atorvastatin 80 mg / day was compared with moderate lipid lowering therapy with pravastatin in the PROVE-IT trial. Four more similar trials and a meta-analysis have established high dose statin as a useful therapeutic option[17]. The National Cholesterol Education Programme (NCEP) has recommended a therapeutic goal of LDL less than 70 mg/dL. Of note, no adverse effects of ultra-low LDL levels (40-50 mg/d L) have emerged. In addition to blocking the synthesis of cholesterol, statins interfere with the synthesis of lipid intermediaries with important biologic effects. They also have important anti-inflammatory effects, and decrease the inflammatory component of atheromatous plaque.

ANTICOAGULANT THERAPY

Heparins

The rationale for administering anticoagulant therapy to patients with STEMI includes establishing and maintaining patency of the infarct-related artery, and preventing deep venous thrombosis, pulmonary embolism, ventricular thrombus formation and systemic embolization.

Unfractionated heparin (UFH): When bound to antithrombin III, UFH inactivates factor Xa and thrombin. In the pre-fibrinolytic era, randomized trials showed a lower risk of re-infarction, pulmonary embolism and stroke in those treated with intravenous heparin. However, with the publication of ISIS-2 (International Study of Infarct Survival-2) trial, an increase in bleeding risk was shown to be associated with the reduction in deaths and recurrent infarctions. Although the evidence favouring the use of heparin for improving the patency of infarct-related artery when a fibrin-specific lytic agent is[1]used is not conclusive, the suggestion of a mortality benefit and amelioration of left ventricular thrombi after STEMI indicates that the use of heparin for at least 48 hours after fibrinolysis is prudent. UFH is also a Class I indication for patients undergoing primary angioplasty.

UFH is administered as an initial bolus of 60U/kg (maximum 4000U) and an infusion at a rate of 12U/kg/h, maintaining an activated partial thromboplastin time of 1.5 to 2.0 times the control. The anticoagulant effects of UFH may be unpredictable because of unpredictable protein binding.

Low Molecular Weight Heparin (LMWH): These are glycosaminoglycans with a more predictable anticoagulant effect by virtue of longer half-life, better bio-availability and dose-dependent clearance. They have a greater activity against Factor Xa than against thrombin. In combination with fibrinolytic agents, the effectiveness of enoxaparin has been compared with that of UFH in the ASSENT (Assessment of the Safety and Efficacy of a New Thrombolytic) 3 trial and in the TIMI-25 EXTRACT (Enoxaparin and Thrombolysis Reperfusion for Acute Myocardial Infarction Treatment) trials. The combined primary endpoint of death and recurrent myocardial infarction were significantly less (11.4% vs 15.4% and 9.9% vs 12%) in the enoxaparin group[18]. Because of the delay in effect after subcutaneous administration, initial intravenous loading dose of 30 mg followed by 1mg/kg subcutaneously every 12 hrs was used in both trials. An increased risk of major and minor bleeding was found to be associated with LMWH in both trials.

Direct Thrombin Inhibitors: Direct thrombin inhibitors bind directly to thrombin and have been used as an alternative to heparin in patients with heparin-induced thrombocytopenia. Several studies have looked into their use in STEMI patients. The Hirluog Early Reperfusion and Occlusion (HERO) trial compared bivalirudin with UFH found a reduction in the incidence of re-infarction at the cost of an increase in bleeding rates. In patients undergoing fibrinolysis, hirudin and bivalirudin were found to reduce reinfarction rates but result in higher rate of major bleeding[19]. In contrast, bivalirudin has been used as an adjunct in primary PCI with reduction in major bleeding compared to heparin plus glycoprotein IIb/ IIIa inhibitors. However, an increase in acute stent thrombosis rate was reported in the HEAT PPCI trial. The BRIGHT trial found a clinical benefit from the use of bivalirudin; the EUROMAX trial reported no benefit from prolonged bivalirudin infusion but found a reduction in bleeding rate.

Factor Xa Inhibitors: The factor Xa antagonist Fondaprinux was evaluated in the OASIS (Organization for the Assessment of Strategies for Ischemic Syndromes)-6 trial against placebo and shown to be superior. The primary endpoint of death /myocardial infarction was reduced with Fondaparinux (9.75 vs 12.4%). When combined with fibrinolytic therapy, it does not cause a significant increase in the risk of bleeding.

In patients undergoing PCI, the use of Fondaparinux resulted in an increased incidence of catheter thrombosis. This trend was reversed when additional UFH was used at the time of PCI.

Clinical Practice Guidelines for Antithrombotic therapy

Class I

1. Patients undergoing reperfusion with fibrinolytics should receive anticoagulant therapy for a minimum of 48 hours (Level of Evidence C) and preferably for the index hospitalization. Regimens other than UFH are recommended when anticoagulation is given for more than 48 hours. Anticoagulants with established efficacy include:
   a. UFH 60 U/kg, maximum 4000U bolus, followed by infusion 12U/kg/h.
   b. Enoxaparin (provided s. creatinine is < 2.5 mg/dl in men and 2.0 mg/dl in women) for patients less than 75 years age, an initial 30 mg bolus followed 30 min later by subcutaneous 1mg/kg every 12 hours. For patients older than 75 years, the intravenous dose is eliminated and subcutaneous dose is reduced to 0.75 mg / kg. If creatinine clearance is less than 30 ml/min, the subcutaneous dose is 1 mg/kg in 24 hours.
2. Patients Undergoing PCI:

Class I

For patients with STEMI undergoing PCI, the following supportive anticoagulant regimens are recommended:

a. UFH, with additional boluses as required to maintain activated clotting time at therapeutic levels (between 250 - 300 sec.), taking into account whether a glycoprotein IIb/IIIa receptor antagonist has been administered (between 200 - 250 sec.).
b. Bivalirudin with or without prior UFH.

Class II a

In STEMI patients undergoing PCI who are at a high risk for bleeding, it is reasonable to use bivalirudin monotherapy in preference to a combination of UFH and glycoprotein IIb/IIIa receptor antagonist.

Class III: Harm

Fondaparinux should not be used as the sole anticoagulant in support of primary PCI because of the risk of catheter thrombosis.

REPERFUSION THERAPY

Timely restoration of flow in the infarct-related artery is the most effective way of salvaging myocardium and reducing infarct size[20]. Myocardial salvage is critically dependent on the time elapsed before reperfusion, irrespective of the strategy utilized. The benefit is greatest in the first 2 to 3 hours after the onset of symptoms. The exact duration of this critical period is modified by several factors. These include:

1. The presence of functioning coronary collaterals
2. Ischemic preconditioning
3. Myocardial oxygen demand
4. The duration of sustained ischemia.

After about 4 hours, depending on the factors mentioned, the benefits of reperfusion diminish progressively. Each 30-minute delay from symptom onset to PCI increases the relative risk for 1 year mortality by 8%. The efficacy of fibrinolytic agents decreases as coronary thrombi mature over time.

Currently, there are three strategies available for reperfusion:

1. Fibrinolysis
2. Primary PCI
3. Pharmaco – invasive therapy.

1. Fibrinolytic therapy

The advantages of fibrinolytic therapy are that it is widely available, easily administered, and relatively inexpensive. However, about 40% of patients may be considered ineligible for this treatment because of contra-indicating factors. Another disadvantage is the fact that only about 60% of treated patients achieve complete reperfusion (TIMI grade 3 flow). In addition, about 20% of patients will experience re-occlusion and 1% may develop stroke from intracranial haemorrhage. The Clinical Practice Guidelines focus on getting primary PCI as the preferred mode of perfusion within 120 minutes, and recommend fibrinolysis when the anticipated delay is more than 120 minutes.

The Clinical Practice Guidelines are as follows:

Class I

In the absence of contraindications, fibrinolytic therapy should be administered to STEMI patients with symptom onset within the prior 12 hours when it is anticipated that primary PCI cannot be performed within 120 minutes of First Medical Contact (Level of Evidence A).

Class II a

In the absence of contraindications and when PCI is not available, fibrinolytic therapy is reasonable for patients with STEMI if there is clinical and/or ECG evidence of ongoing ischemia within 12-24 hours of

symptom onset and a large area of myocardium at risk or haemodynamic instability. (Level of Evidence C)

Class III

Fibrinolytic therapy should not be administered to patients with ST depression except when a true posterior (inferobasal) myocardial infarction is suspected or when associated with ST elevation in lead AVR. (Level of Evidence B)

Fibrinolytic therapy is most effective when administered within 3 hours of the onset of symptoms, the greatest benefit noted in the first two hours. Data from the LATE and EMERAS trials indicate that there is hardly any benefit if fibrinolysis is undertaken more than 12 hours later. The window of treatment was extended to 12 hours based on data from the same trials.

Contraindications to Fibrinolytic Therapy

A limitation of fibrinolytic therapy is that about 40%of patients with STEMI may have contraindications to this form of treatment. These have been classified as major and relative contraindications. The presence of one major contraindication would generally preclude thrombolysis, as the complications related to this therapy may be catastrophic. On the other hand, if the patient has only a relative contraindication, the situation needs to be studied and discussed in detail before delivering or denying the therapy. A targeted history-taking and physical examination are extremely important in a STEMI patient, in order to determine the presence or absence of contraindications to fibrinolytic therapy.

Fibrinolytic Agents

All fibrinolytic agents convert plasminogen to the active enzyme, plasmin, which in turn cleaves fibrin to soluble degradation products. Streptokinase was the first fibrinolytic agent to be used, and continues to be the most widely used worldwide. It is a bacterial protein that contains three plasminogen-binding domains. The action of streptokinase is not fibrin-specific; it leads to proteolysis of fibrinogen and coagulation factors, inducing a systemic lytic state. With intravenous administration, its peak plasma levels are reached rapidly and the maximal fibrinolytic effect is reached in about 30 minutes. It is highly immunogenic, and the formation of a neutralising antibody generally precludes re-administration. The plasma half-life is 30 to 40 minutes, with hepatic – mediated clearance. Streptokinase is administered as an intravenous infusion, 1.5 million units given over 30-60 min.

Tissue plasminogen activator is a fibrin-specific agent. It is a 70 k-Da serine protease with five key active domains. It is administered as intravenous infusion. Following a 15 mg bolus dose, infusion of 0.75 mg/kg (maximum 50 mg) in 30 minutes and then 0.5 mg/kg for 60 min (maximum 35 mg). The total dose is given over a period of 90 minutes and does not exceed 100 mg.

Second generation agents were designed for bolus administration, enhanced potency, enhanced fibrin specificity and PAI resistance. Three such agents are available. Reteplase (r-PA) is the smallest derivative, containing two of the five domains. It is administered as a fixed double dose of 10 units each, given 30 minutes apart. Excretion of r-PA is by both renal and hepatic elimination. Lanoteplase (n-PA) is derived from t PA by deleting two domains. It is administered as a single, weight-adjusted dose and is eliminated entirely by the liver. Tenecteplase is an analogue of t PA with several modifications designed to increase fibrin specificity, endow PAI resistance and reduce plasma clearance. All 5 domains of the parent t PA remain, so that the molecular weight is not altered. TNK is administered as a weight-adjusted single bolus dose, and is cleared by the liver.

Patency rate for the infarct-related artery at 90 min has been estimated as 60-68% for streptokinase, 73-84% for t PA, 84% for Reteplase and 85% for Tenecteplase.

Adjuvant therapy in patients receiving fibrinolytics

Anticoagulation: Given the pivotal role of thrombin in the pathogenesis of MI, antithrombotic therapy remains an important intervention. A regimen of intravenous unfractionated heparin in bolus of 60 units/kg to a maximum of 4000 units, followed by infusion at 12 units/kg/hour is effective in patients receiving thrombolytic therapy. However, because infusions of heparin may be cumbersome to administer and because prolonged administration carries a risk of heparin-induced thrombocytopenia, alternative anticoagulant regimens using enoxaparin or fondaparinux may be preferred. Both the ExTRACT TIMI 25 and OASIS-6 trials indicated that prolonged administration of an anticoagulant for the duration of hospitalization is beneficial in STEMI patients treated with fibrinolytics. Enoxaparin should be administered according to age, weight and creatinine clearance, with an initial intravenous bolus followed 15 min later by subcutaneous injections. Fondaparinux is administered as an initial intravenous dose followed in 24 hours by daily subcutaneous injections. If PCI is performed on a patient treated with fondaparinux, an additional anticoagulant will be necessary.

Antiplatelet therapy: Obstructive platelet-rich arterial thrombi resist fibrinolysis and tend to cause re-

occlusion after initial successful reperfusion in STEMI patients. Despite inhibition of cyclooxygenase by aspirin, platelet activation leading to platelet aggregation and thrombin formation continues through other pathways. An ADP receptor antagonist is beneficial in this setting. CLARITY-TIMI and COMMIT trials have demonstrated that the addition of clopidogrel is highly effective in preventing re-occlusion in a reperfused infarct artery.

Initial studies evaluating the use of GP IIb/IIIa inhibitors along with fibrinolytic agents showed improvement in reperfusion rates. However, large outcomes trials showed no benefit in survival and demonstrated a significant increase in bleeding. Therefore, the combination of a GP IIb/IIIa inhibitor and a fibrinolytic agent is not recommended.

Complications of Fibrinolytic Therapy

Bleeding is the most common and intracranial haemorrhage is the most serious complication of fibrinolytic therapy. Its frequency is generally about 1%, but varies with the clinical setting. The common risk factors for this complication are elderly age, low body weight and hypertension on admission. Intracranial bleeding in the setting of fibrinolysis for STEMI has a high case fatality rate. Non-intracranial bleeding also can result in increased morbidity.

An "early hazard' has been recognized in patients undergoing fibrinolysis for STEMI, which refers to an increase in mortality in the first 24 hours, compared with control subjects. This has been most evident in elderly patients treated more than 12 hours after symptom onset. This excess early mortality is more than offset by the prevention of deaths beyond the first day, with an average 18% reduction in mortality by 35 days compared with not offering reperfusion. The mechanisms responsible for this early hazard are not clear, but may include an increased risk for myocardial rupture, fatal intracranial haemorrhage and possible myocardial reperfusion injury.

Recent exposure to streptococcus or streptokinase produces some kind of antibody-mediated resistance to streptokinase. Such resistance is usually not clinically relevant. However, patients should not be given streptokinase if they have received a streptokinase product within the past 6 months.

2. Primary Percutaneous Coronary Intervention (PCI)

The advantages of primary PCI are:

1. Approximately 95% of patients undergoing primary PCI achieve complete reperfusion, versus 50 -60% of patients receiving fibrinolytic therapy.
2. Primary PCI is associated with a lower risk of stroke than fibrinolysis.
3. The study quickly defines coronary anatomy, LV function and mechanical complications.

The disadvantage of this strategy is its limited availability. As mentioned earlier, the mortality advantage of PCI is lost if the door-to-balloon time is 60 minutes greater than the door-to-needle time for fibrinolysis. If the patient presents to a hospital without PCI capability, a choice needs to be made between fibrinolysis and transfer to a PCI capable facility. Three large trials compared these two strategies and demonstrated that transferring for PCI is associated with significant benefits in terms of death, re-infarction and disabling stroke. However, the transfer times were rather short in these studies (mean 32 min). It is noted that fibrinolysis has a critically important role in the "golden hour".

The clinical practice guidelines recommend the following:

Class I

1. Primary PCI should be performed in patients with STEMI and ischemic symptoms of less than 12 hours' duration, (Level of Evidence A).
2. Primary PCI should be performed in patients with STEMI and ischemic symptoms of less than 12 hours' duration who have contraindications to fibrinolytic therapy, irrespective of the time delay from FMC. (Level of Evidence B).
3. Primary PCI should be performed in patients with STEMI and cardiogenic shock or acute severe heart failure irrespective of time delay from MI onset, (Level of Evidence B).

Class II a

Primary PCI is reasonable in patients with STEMI if there is clinical and/or ECG evidence of ongoing ischemia between 12 and 24 hours after symptom onset, (Level of Evidence B).

Management in the Cath. Lab

The most important factors in primary PCI are the speed and efficiency with which the procedure can be accomplished. A protocol to standardize the care of STEMI patients should be developed by hospitals based on available facilities and logistics. By using a systematic protocol, the Mayo Clinic was able to reduce door-to-balloon time from 202 to 107 minutes; even further improvements may be possible. It is recommended that primary PCI should be done by operators who perform at least 75 PCIs per year, 36 of which are primary PCI

for STEMI patients, in a catheterization laboratory that performs at least 200 PCIs per year.

Management of thrombus load: Presence of thrombus in the coronary arteries and distal embolization of this thrombus resulting in occlusion of the distal vascular bed have been major problems in STEMI management. Several approaches have been made to this problem. Distal protection devices like Guardwire and filter devices were tried and evaluated in randomized trials, and were not found to be clinically useful. The Angiojet rheolytic thrombectomy system was also tried and found to be of no significant benefit. Manual aspiration of thrombus using aspiration catheters was investigated in the TAPAS study and was shown to be beneficial[21]. The procedure is simple and easily available, and has become popular. However, recently published TASTE and TOTAL trials failed to show any significant benefit and showed minor increase in the incidence of stroke. The current recommendations are:

Class II b

The usefulness of selective and bailout aspiration thrombectomy in patients undergoing primary PCI is not well established. (Level of Evidence C)

Class III: No benefit

Routine aspiration thrombectomy before primary PCI is not useful. (Level of Evidence A)

Despite these recommendations, patients are often treated by manual thrombus aspiration on an individual basis, depending on the angiographic findings.

Treatment of Non-infarct-related arteries

Older versions of STEMI guidelines had advised against performing PCI of non-infarct-related arteries along with revascularization of the infarct artery[22]. This was based on the concern that the pro-thrombotic conditions prevailing in these patients may adversely affect the outcome in these arteries. However, 3 recent clinical trials (PRAMI, CvLPRIT and DANAMI-PREMULTI) have demonstrated that treatment of significant lesions in non-infarct-related arteries is beneficial and may reduce the need for urgent revascularization[23]. This has led to a change to Class II b recommendation and ongoing studies.

3. Fibrinolytic-facilitated PCI:

This term refers to the pre-treatment with fibrinolysis in STEMI patients as a bridge to intended routine primary PCI, as a method to initiate earlier reperfusion and reduce infarct size[21,22]. However, this strategy exposes the patient to higher risk of bleeding, especially intracranial haemorrhage, and increases 30-day mortality. Based on the results of ASSENT-4 and FINESSE trials, data do not support the use of facilitated PCI as a routine reperfusion strategy.

Pharmacoinvasive Strategy: Unlike facilitated PCI where PCI is performed immediately after fibrinolysis, pharmacoinvasive strategy refers to PCI that is routinely performed between 3 and 24 hours after fibrinbolysis in hemodynamically stable patients[23]. This strategy is different from "rescue PCI", where PCI is performed in patients who have failed fibrinolysis with absence of ST resolution, ongoing symptoms or hemodynamic instability. Five randomized trials, especially the large TRANSFER-AMI trial, have established the pharmacoinvasive method as a useful routine strategy. The current guidelines recommend the following:

Class I

Immediate transfer to a PCI capable hospital for coronary angiography is recommended for suitable patients with STEMI who develop cardiogenic shock or acute severe heart failure, irrespective of the delay from MI onset (Level of Evidence B).

Class II a

Transfer to a PCI-capable hospital for coronary angiography is reasonable for patients with STEMI who have received fibrinolytic therapy even if they are hemodynamically stable and have evidence of successful reperfusion. Angiography can be performed as soon as logistically feasible and ideally within 24 hours, but should not be performed within the first 2 to 3 hours after administration of fibrinolytic therapy.

RESCUE PCI

About 40% to 50% of patients who undergo fibrinolysis fail to achieve optimal reperfusion, and about 20% suffer re-infarction within the first 12 hours. The REACT (Rescue Angioplasty versus Conservative Treatment or Repeat Thrombolysis Trial) study demonstrates that rescue angioplasty is a superior strategy, both in terms of short-term and long-term outcomes[25]. The clinical practice guidelines are as follows:

Class I

1. Cardiac catheterization and angiography with intent to perform revascularization should be performed in patients after STEMI in patients with any of the following:
   a) Cardiogenic shock or acute severe HF that develops after the initial presentation(Level of Evidence B)
   b) Intermediate or high risk findings on pre-discharge non-invasive ischemia testing(Level

of Evidence B)

c) Myocardial ischemia that is spontaneous or provoked by minimal exertion (Level of Evidence C)

Class II a

Coronary angiography with intent to perform revascularization is reasonable in patients with evidence of failed reperfusion or re-occlusion after fibrinolytic therapy. Angiography can be performed as soon as logistically feasible. (Level of Evidence B)

ADJUVANT ANTIPLATELETS FOR PCI IN STEMI

Clopidogrel: Clopidogrel is a thienopyridine prodrug whose active metabolite inhibits the activation of platelets by ADP. Its effectiveness and superiority of clopidogrel over aspirin were proven in the CLARITY-TIMI 28 trial and in in the COMMIT trial. The PCI-CURE trial demonstrated that pre-treatment with clopidogrel followed by long term therapy was beneficial in patients with non ST Elevation ACS who eventually undergo PCI. Extrapolation of these data led to the recommendation for oral clopidogrel at the time of STEMI presentation and long term maintenance therapy.

Prasugrel: Prasugrel is novel thienopyridine with potent P2Y12 receptor blocking property and has been studied in several trials. The largest study[29] was TRITTON TIMI-38, which demonstrated significantly reduced primary ischemic events and stent thrombosis compared to clopidogrel. However, a higher risk of bleeding was noted; patients older than 75 years and those weighing less than 60 kg were identified as vulnerable subgroups. A significantly higher risk was also noted in patients who have STEMI and require bypass surgery as well as in patients with a history of CVA.

Ticagrelor: Ticagrelor is a non – thienopyridine P2Y12 receptor antagonist that does not require metabolic conversion to active drug[30]. Comparison with clopidogrel was made in the PLATO study. 35% of the 18,264 patients evaluated had STEMI, and showed reduced stent thrombosis and ischemic events. Prespecified subgroup analysis showed a reduced effectiveness in the U.S. arm of the study; this was attributed to a larger dose of aspirin (>100 mg) than in other countries.

Clinical practice guidelines for P2Y12 antagonists are as follows:

Class I

1. A loading dose of a P2Y12 receptor inhibitor should be given as early as possible or at the time of primary PCI to patients with STEMI. Options include:
   a. Clopidogrel 600 mg (Level of Evidence B)
   b. Prasugrel 60 mg (Level of Evidence B)
   c. Ticagrelor 180 mg (Level of evidence)

2. P2Y12 inhibitor therapy should be given for 1 year to patients with STEMI who receive a stent(BMS or DES) during primary PCI using the following maintenance doses:
   a. Clopidogrel 75 mg daily, or
   b. Prasugrel 10 mg daily, or
   c. Ticagrelor 90 mg twice daily

Class III

Prasugrel should not be administered to patients with a history of prior stroke or transient ischemic attack (Level of evidence B).

Glycoprotein IIb/IIIa inhibitors

Glycoprotein IIb/IIIa inhibitors are potent antiplatelet agents that inhibit the final common pathway of platelet aggregation[31]. Currently there are 3 agents in this group, abciximab, eptifibatide and tirofiban. There were initial studies on the use of these agents in combination with fibrinolytic therapy in order to improve the coronary artery patency rate. This strategy was found to be associated with a high risk of major bleeding. In view of the increased bleeding risk and lack of survival benefit, Glycoprotein IIb/IIIa inhibitors should not be used in combination with fibrinolytic therapy.

In patients undergoing primary PCI, the administration of GP IIb/IIIa inhibitors has been found to be useful, with a greater prevalence of TIMI grade 2 or 3 flow in the treated patients. Initial studies showing such benefit had used abciximab. Subsequently, a meta-analysis of 6 trials using abciximab and the smaller molecules eptifibatide and tirofiban has shown similar outcomes with all 3 agents in terms of clinical efficiency and bleeding risk. However, with the availability of newer anti platelet drugs, role of GP IIb/IIIa inhibitors in primary PCI has come down to selected cases only.

MANAGEMENT OF COMPLICATIONS OF STEMI

1. Left Ventricular Failure

Left ventricular dysfunction is the single most important predictor of mortality following STEMI. Either systolic dysfunction alone or a combination of systolic and diastolic dysfunction can occur. Diastolic dysfunction leads to pulmonary venous hypertension and pulmonary congestion. The most important determinant is the size of the infarct; other factors

include advanced age and diabetes. Classification of STEMI by hemodynamic subsets is therapeutically relevant, and invasive monitoring can help guide therapy. A pulmonary capillary wedge pressure >18 mmHg and a cardiac index < 2.2 L/min/sq m indicate significant left ventricular failure. The four modifiable factors (targets of therapy) are (1) preload, (2) afterload, (3) disturbances of rate and rhythm and (4) cardiac contractility. Although positive inotropic agents can be useful, heart failure is most effectively managed by reducing preload and then, if possible, by lowering afterload. Correction of arrhythmias is of paramount importance.

Hypoxemia

STEMI patients who develop cardiac failure, pulmonary venous engorgement and interstitial oedema can lead to hypoxemia. Respiratory depression from narcotic analgesia also may be a contributory factor. Increasing inspired oxygen (FIO2) via facemask may be useful. If oxygen saturation cannot be maintained above 85 to 90% with 100% FIO2, strong consideration should be given to endotracheal intubation and positive pressure ventilation. Positive end-expiratory pressure helps to alleviate pulmonary oedema, but may result in decreased venous return and reduced filling pressure. A careful adjustment of the degree of end-expiratory pressure, rate of fluid infusion and vasodilator drugs will be needed in this setting. As already noted, routine administration of oxygen to STEMI patients without hypoxemia is not recommended.

Diuretics

Mild heart failure in patients with STEMI responds well to diuretics like furosemide 10 to 40 mg bolus doses, repeated at 3 to 4 hour intervals. The resultant decrease in pulmonary capillary pressure reduces dyspnoea, and the reduction in ventricular diastolic volume and wall tension helps to improve coronary perfusion. These effects occur within 15 minutes of intravenous administration, before renal excretion of sodium and water has occurred. However, excessive lowering of left ventricular filling pressure may lead to a reduction in cardiac output, resulting in hypotension. Excessive diuresis may also cause hypokalaemia.

Afterload reduction

Left ventricular wall stress, which determines myocardial oxygen requirement, is dependent on systolic ventricular pressure, volume and wall thickness. Intravenous vasodilator therapy to reduce afterload may be considered in STEMI patients who have (1) heart failure not relieved by diuretics, (2) hypertension, (3) mitral regurgitation and (4) ventricular septal defect. Improvement in stroke volume and decrease in myocardial oxygen requirement are expected. As it is essential to avoid excessive systemic arterial hypotension and excessive reduction in ventricular filling pressure, hemodynamic monitoring is generally indicated.

Vasodilator therapy is particularly useful in patients who develop mitral regurgitation or ventricular septal rupture. Vasodilators alone or in combination with intra-aortic balloon counterpulsation may be helpful in stabilizing the patient and arranging for angiography and definitive intervention.

Nitroglycerin may be a particularly useful vasodilator in patients with STEMI who develop left ventricular failure. A dosage of 10 to 15 mg/min is infused, and the infusion rate is increased by 10 mg/min every 5 minutes, until the desired effect is reached, or a decline in blood pressure to 90 mmHg has occurred. Improvement in hemodynamics and relief of ischemic pain are often noted.

Inotropic Agents

When left ventricular failure is severe with decreased cardiac index and normal or excessive pulmonary capillary wedge pressure despite the use of diuretics, treatment with beta-adrenergic agonists is indicated. Dopamine and dobutamine are useful in patients with STEMI and reduced cardiac output, increased left ventricular filling pressure, pulmonary congestion and hypotension. Fortunately, the potentially deleterious alpha-adrenergic actions of dopamine occur only at doses higher than those required to increase contractility. The vasodilating actions of dopamine on renal and splanchnic vessels and its positive inotropic effects generally improve haemodynamics and renal function. Dopamine is started at a dose of 3 mcg/kg/min and increased stepwise to 10 mcg/kg/min.

Dobutamine has a positive inotropic action similar to that of dopamine with slightly less chronotropic effect and less vasoconstrictor activity. It may be started at a dose of 2 mcg/kg/min and increased stepwise to a maximum of 30 mcg/kg/min. Both dopamine and dobutamine should be administered cautiously, with monitoring of ECG, arterial pressure and preferably pulmonary arterial pressure as well.

Norepinephrine increases myocardial consumption because of its positive inotropic and vasoconstrictor effects; there has been some hesitation in using it in the setting of STEMI with heart failure. A recent randomized trial has shown that it confers hemodynamic benefits similar to or greater than dopamine, with fewer adverse effects. As a result, there has been a resurgence of its use in STEMI patients with left ventricular failure.

Isoproterenol is not recommended in STEMI patients

in view of its potential to cause tachycardia, increased myocardial oxygen consumption and systemic vasodilation.

2. Cardiogenic Shock

Cardiogenic shock as a result of severe LV dysfunction occurs in 7% of patients with myocardial infarction and has a historic mortality of 80%. With the availability of reperfusion technologies, this mortality figure has improved to some extent. The SHOCK II trial reported a mortality rate of 50%. The aims of treatment are two-fold. The first is to achieve hemodynamic stabilization to ensure adequate oxygenation, acid-base balance and tissue perfusion. The second goal is to investigate rapidly for any potentially reversible factors. Hypovolemia must be corrected. Forrester and his colleagues[32] described treatment of patients on the basis of hemodynamic subsets related to pulmonary capillary wedge pressure and cardiac output. The basic goals include adjustment of intravascular volume status to bring the pulmonary artery wedge pressure to 18-20 mmHg and optimization of cardiac output with inotropic and vasodilating agents. Severely hypotensive patients can be temporarily helped by intra-aortic balloon pump or a ventricular assist device.

Many observational studies have indicated that the reperfusion therapy, especially primary PCI, can reduce the incidence of cardiogenic shock[33]. The SHOCK trial evaluated the effect of early revascularization in AMI complicated by cardiogenic shock. A 20% relative mortality reduction was demonstrated.

The SHOCK II trial randomized patients to planned intra-aortic balloon pump with PCI, with PCI alone. It was found that there was no mortality reduction with IABP use. This has led to a change in guideline recommendations.

The clinical practice guidelines recommend:

Class I

1. Emergency revascularization with either PCI or CABG is recommended in suitable patients with cardiogenic shock due to pump failure after STEMI irrespective of the time delay from MI onset.(Level of Evidence B)
2. In the absence of contraindications, fibrinolytic therapy should be administered to patients with STEMI and cardiogenic shock who are unsuitable candidates for either PCI or CABG.(Level of Evidence B)

Class II a

The use of intra-aortic balloon pump can be useful for patients with cardiogenic shock after STEMI who do not quickly stabilize with pharmacological therapy. (Level of Evidence B)

Class II b

Alternative LV assist devices for circulatory support may be considered in patients with refractory cardiogenic shock. (Level of Evidence C)

3. Right Ventricular Infarction

The clinical triad of hypotension, increased jugular venous pressure and clear lung fields in a patient with inferior wall infarction indicates the possibility of right ventricular myocardial infarction[34]. The finding of ST segment elevation in right-sided chest leads and the presence of RV wall motion abnormality and RV dilatation on echocardiography would support the diagnosis. Right atrial pressures are elevated; this may lead to the opening up of a patent foramen ovale and a decrease in arterial saturation. Bradycardia is common and is detrimental because an increased heart rate is required to maintain cardiac output. High grade atrioventricular block may result in loss of atrioventricular synchrony and further compromise cardiac output.

Treatment of RV infarction requires infusion of fluid to maintain pulmonary capillary pressure at 18-20 mmHg. Patients who have A-V block benefit from atrioventricular pacing rather than single chamber RV pacing. The clinical practice guidelines recommend the following:

Class I

1. Patients with inferior STEMI and hemodynamic compromise should be assessed with a right precordial V4R lead to detect ST segment elevation and an echocardiogram to screen for RV infarction. (Level of Evidence B)
2. The following principles apply to therapy for patients with STEMI and RV infarction:
   a. Early reperfusion should be achieved if possible.
   b. Atrioventricular synchrony should be achieved, and bradycardia should be corrected.
   c. RV preload must be optimized, which usually requires early volume challenge.
   d. RV afterload should be optimized, which usually requires therapy for concomitant LV dysfunction.
   e. Inotropic support should be used for hemodynamic instability not responsive to volume challenge.

4. Acute Mitral Regurgitation

Severe mitral regurgitation caused by papillary muscle rupture is responsible for about 5% of

deaths in AMI patients. Rupture usually involves the posteromedial papillary muscle which is solely supplied by the posterior descending artery, in contrast to the anterolateral papillary muscle which derives a dual arterial supply from LAD and circumflex arteries. The clinical presentation is in the form of acute pulmonary oedema, usually within 2 to 7 days after inferior wall infarction. The length and character of murmur are highly variable and a high index of suspicion is necessary for diagnosis. Echocardiography demonstrates a flail mitral valve and a partially or completely severed papillary muscle head.

The cornerstone of therapy is prompt diagnosis and early surgery. Placement of IABP and pharmacologic control of blood pressure may be beneficial. The clinical practice guidelines are:

Class I

1. Patients with acute papillary muscle rupture should be considered for urgent cardiac surgical repair unless further support is considered futile because of the patient's wishes or contraindications / unsuitability for further invasive care.
2. Coronary artery bypass must be performed at the same time as valve repair.

5. Ventricular Septal Rupture

The incidence of ventricular septal rupture was 1-3% and caused about 5% of peri-infarction deaths in the pre-fibrinolytic era. This was reduced to 0.2% after reperfusion strategies became available. Typically, VSDs associated with anterior infarction are located in the apical septum and those associated with inferior infarction are located in the basal inferior septum. The prevalence of anterior and inferior infarctions is equal, unlike papillary muscle rupture.

As with other cardiac ruptures, surgical management is advocated for VSR. The outcome is not as gratifying as in mitral regurgitation, because the extent of myocardial necrosis is generally larger. Advanced age, cardiogenic shock and long delay between septal rupture and surgery are correlated with adverse outcome.

Percutaneous closure using occluding devices has been performed in non-surgical candidates, with variable results.

The clinical practice guidelines state:

Class I

1. Patients with STEMI complicated by the development of VSR should be considered for urgent cardiac surgical repair unless further support is considered futile.
2. Coronary artery bypass should be undertaken at the same time as the repair of VSR.

6. Cardiac Arrhythmias in STEMI

Bradyarrhythmias

These usually result from ischemic injury to the sinus node or conduction system. The blood supply to the sinus node is derived from the proximal right coronary artery in 55% of cases and from the proximal left circumflex in the remainder. The blood supply to the atrioventricular node is from the distal right coronary artery in 90% cases and from the distal left circumflex in the remaining 10%. The right bundle branch and the anterior division of the left bundle are supplied by the left anterior descending artery; the main left bundle branch has a dual supply from distal right coronary and proximal circumflex. In general, conduction disturbances associated with inferoposterior infarction are related to enhanced vagal activity, tend to be transient and have a more benign outcome. Conduction disturbances associated with anterior infarction imply extensive septal necrosis and more significant LV dysfunction.

Sinus bradycardia

Sinus bradycardia and sinus pauses are usually benign.

First degree atrioventricular block

This mandates observation and avoidance of any medications that might prolong A-V conduction.

Second degree A-V block

This develops within the first 24 hours in 3to 10% of individuals. With type I second degree A-V block, progressive PR prolongation may be noted. This is usually associated with inferior MI and responds to atropine. Temporary pacing is usually not needed. Type II A-V block is identified by intermittent dropped beats in the absence of P-R prolongation. This signifies more extensive injury and progresses to complete heart block in about one third of cases[35]. Most patients with anterior infarction and type II second degree block will require pacing.

Complete heart block

This occurs in 3% to 12% of AMI s. In general, patients with inferior infarction develop second degree block and then progress to complete heart block. A stable junctional escape rhythm is present and responsiveness to atropine is present. Recovery occurs usually in 3 to 7 days. In contrast, CHB in patients with anterior infarction indicates extensive myocardial necrosis and has a poor prognosis.

The clinical practice guidelines recommend:

Class I

1. Permanent ventricular pacing is indicated for persistent second degree atrioventricular block in the His Purkinje system with bilateral bundle branch block or third degree atrioventricular block within the His-Purkinje system after STEMI.(Level of Evidence B)
2. Permanent ventricular pacing is indicated for transient advanced second degree or third degree infranodal block and associated bundle branch block. (Level of Evidence B)
3. Permanent ventricular pacing is indicated for persistent second or third degree atrioventricular block. (Level of Evidence C)

Class IIb

Permanent ventricular pacing may be considered for persistent second or third degree atrioventricular block at the A-V node level. (Level of Evidence B)

Class III

1. Permanent ventricular pacing is not recommended for transient atrioventricular block in the absence of intraventricular conduction defects.
2. Permanent ventricular pacing is not recommended for transient atrioventricular block in the presence of isolated left anterior fascicular block.
3. Permanent ventricular pacing is not recommended for persistent first degree atrioventricular block in the presence of bundle branch block that is old.

Tachyarrhythmias

Tachyarrhythmias in STEMI are caused by a combination of factors, which include ionic changes, alteration in sympathetic and vagal tone, slowing of conduction and prolonged refractoriness. The presence of injury currents and myocardial fibre stretch are also contributing factors.

Supraventricular arrhythmias

Sinus tachycardia may be related to pain, anxiety and sometimes hypovolemia. Persistent sinus tachycardia may also be a marker of severe LV dysfunction. Atrial fibrillation occurs in 6% to 21%patients with acute infarction. Risk factors include advanced age, heart failure symptoms, LV dysfunction and tachycardia on admission. Early atrial fibrillation may y be due to atrial ischemia; later occurrence is generally a manifestation of LV dysfunction. Symptomatic atrial fibrillation with rapid ventricular rates causing ischemia should be treated by immediate cardioversion. If the ventricular rate is only moderate and the patient is asymptomatic, rate control with esmolol or diltiazem may be attempted. Recurrent episodes of atrial fibrillation should be suppressed by an antiarrhythmic agent like amiodarone. The therapy guidelines are:

Class I

1. Sustained atrial fibrillation or atrial flutter in patients with hemodynamic compromise should be treated with one or more of the following[36]:
   a) Synchronized cardioversion with an initial monophasic shock of 200 J for atrial fibrillation and 50J for atrial flutter, preceded by brief general anaesthesia or conscious sedation.
   b) For atrial fibrillation that does not respond to cardioversion or recur after a brief period, antiarrhythmic therapy aimed at slowing the ventricular rate is indicated. One or more of the following may be used:
      a. Intravenous amiodarone (Level of Evidence C)
      b. Intravenous digoxin for rate control, principally for patients with severe LV dysfunction and heart failure (Level of Evidence C)
2. Sustained atrial fibrillation or flutter in patients with ongoing ischemia without hemodynamic compromise should be treated with one of these:
   a) Beta-adrenergic blockade, unless contraindicated.
   b) Intravenous diltiazem or verapamil
   c) Synchronized cardioversion.
3. For episodes of sustained atrial fibrillation without hemodynamic compromise or ischemia, rate control is indicated. In addition, they should be given anticoagulant therapy. In patients without a history of atrial fibrillation or flutter before STEMI, conversion to sinus rhythm may be considered.
4. Re-entrant paroxysmal supraventricular tachycardia should be treated by the following sequence:
   a. Carotid sinus massage(Level of Evidence C)
   b. Intravenous adenosine 6mg IV over 1-2 sec; if no response, 12 mg IV after 1-2 min.
   c. Intravenous beta blockade; metoprolol 2.5 to 5 mg every 2-5 min, to a total of 15 mg over 10-15 min.
   d. Intravenous digoxin, recognizing that there may be a delay of at least 1 hour before effects appear. (8-15 mcg/kg)

Class III

1. Treatment of atrial premature beats is not indicated.

Ventricular arrhythmias

Accelerated idioventricular rhythm is common and may be a marker of reperfusion. This generally considered benign and does not require any treatment.

Ventricular tachycardia occurs in about 15% patients during acute MI. The rate is usually between 140 and 200 per min., and this may degenerate into ventricular fibrillation. It usually responds to lidocaine given intravenously. However, for resistant cases, procaineamide, bretylium, cardioversion, ventricular overdrive pacing or amiodarone may become necessary. Prophylactic use of lidocaine is not recommended.

Ventricular fibrillation is seen in about 8% of patients. It is more common with large infarcts and may occur without warning symptoms. Early occurrence of ventricular fibrillation, in the first 24 hours, may not contribute to long term risk significantly; however, occurrence of these arrhythmias later in the hospital may be related to severe LV dysfunction and pump failure, indicating a poor prognosis. Sustained monomorphic VT occurring early or late may indicate an arrhythmogenic substrate with a tendency to recur after discharge.

The clinical practice guidelines recommend:

Class I

1. Sustained polymorphic VT should be treated with an unsynchronized electric shock with initial monophasic shock energy 200J; if unsuccessful, a second shock of 200-360 J should be given; if necessary a third shock of 360 J.
2. Episodes of sustained monomorphic VT associated with angina, pulmonary oedema or hypotension should be treated with synchronized shock of 100J; increased energy for repeat shocks if required.
3. Sustained monomorphic VT without angina , pulmonary oedema or hypotension should be treated with:
   a) Amiodarone infusion: 150 mg over 10 minutes; 360 mg over 6 hours and 540 mg over 18 hours; the total cumulative dose in 24 hours should not exceed 2.2 g.
   b) Synchronized electrical cardioversion starting at monophasic energy of 50 J.

Class II a

1. It is reasonable to manage refractory polymorphic VT by:
   a. Aggressive attempts to reduce myocardial ischemia and adrenergic stimulation, including therapies such as beta-adrenoceptor blockade, intra-aortic balloon pump, consideration of emergency PCI / CABG
   b. Aggressive normalization of serum potassium to >4.0 m Eq / L and serum magnesium to > 2.0 mg / d L.
   c. If the patient has bradycardia at rate <60/ min, temporary pacing at a higher rate may be instituted.

Class III

1. The routine use of prophylactic antiarrhythmic drugs (eg. Lidocaine) is not indicated for prevention of premature beats, couplets or non-sustained VT.
2. Treatment of isolated ventricular premature beats, couplets and non-sustained VT is not recommended.

Implantable Cardiac Defibrillator

AMI patients with LV dysfunction should not receive an ICD during the early period for prophylactic indications. ICD therapy is recommended in those who have recurrent episodes of sustained VT during the post-infarction period. A repeat assessment of LV function should be performed 30-40 days after the acute event; those with an ejection fraction less than 35% should receive ICD. STEMI patients with abnormal LV function who are not candidates for ICD remain at risk for sudden cardiac death; this group of patients may be considered for wearable defibrillators[37].

Clinical practice guidelines recommend the following:

Implantable cardioverter-defibrillator therapy before discharge

Class I

1. Implantable cardioverter-defibrillator is indicated before discharge in patients who develop sustained VT/VF more than 48 hours after STEMI, provided the arrhythmia is not due to transient reversible ischemia, re-infarction or metabolic abnormalities. (Level of Evidence B)

Assessment of risk for SCD: Recommendation

Class I

1. Patients with reduced LVEF who are possible candidates for ICD therapy should undergo re-evaluation of LVEF 40 or more days after discharge (Level of Evidence B)

ICCU MANAGEMENT OF STEMI AFTER REPERFUSION

The ICCU has a central role in the management of patients with myocardial infarction. A dedicated ICCU is the environment most often used to provide care for patients with STEMI, and it plays a pivotal role in the management of major complications of STEMI[32]. A calm, quiet atmosphere can allay anxiety and reduce sympathetic tone, thereby potentially reducing hypertension, tachycardia and arrhythmias. Anxiolytic medication may be appropriate in some cases. In order to reduce the risk of nausea and vomiting early after infarction, and to reduce the risk of aspiration, patients

should receive either nothing by mouth or a clear liquid diet during the first 4-12 hours after admission. Thereafter, dietary intervention is an important component of the overall strategy for secondary prevention.

The results of laboratory tests should be scrutinized for any derangements that could contribute to cardiac arrhythmia. Delirium can be provoked by many medications; potentially offending agents should be discontinued if the patient has abnormal mental status. Haloperidol can be used safely in STEMI patients. Stool softeners should be considered to prevent constipation and straining.

Physical activity: In the absence of complications, stable patients with STEMI need not be confined to bed for more than 12 hours after admission, and unless they are hemodynamically compromised, they may use a bedside commode shortly after admission. Early mobilization of these patients does not usually cause important changes in heart rate, blood pressure and pulmonary wedge pressure. As long as blood pressure and heart rate are monitored, early mobilization offers psychological and physical benefit without any clear medical risk.

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Medical Management of Valvular Heart Diseases

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There is a growing population of elderly patients in India with degenerative valvular heart disease (V.H.D), who choose not to have surgery or may not be surgical candidates due to comorbidities. Optimizing medical management improves symptoms of heart failure, minimizes complications like pulmonary hypertension, stroke, atrial fibrillation and may prolong survival. Initiating treatment at the right time, often when asymptomatic, is crucial to prevent the onset of irreversible ventricular dysfunction. There is limited data regarding medical management of valvular heart disease in literature. In this article, medical management of four major valvular heart lesions based on available data is being discussed.

AORTIC REGURGITATION

The most common causes of chronic aortic regurgitation (AR) are calcific valve disease, bicuspid aortic valve, rheumatic heart disease and diseases causing dilation of the ascending aorta or the sinuses of Valsalva.

Aortic regurgitation imposes volume overload on left ventricle. In slowly progressive chronic aortic regurgitations adaptive remodelling processes, including left ventricular dilatation and eccentric hypertrophy (replication of sarcomeres in series and elongation of myocardial fibres) can accommodate large volumes of regurgitant flow for many years with little or no change in filling pressures or cardiac output. When these adaptive processes fail myocardial dysfunction ensues[1].

The regurgitant orificearea, the duration of diastole (a function of the heart rate), and the diastolic transvalvar pressure gradient (aortic diastolic minus left ventricular end diastolic pressure) are the main determinants of regurgitant volume. Bradycardia and hypertension are therefore not well tolerated.

Vasodilator Therapy

The hemodynamic effects of arterial vasodilators[2] include redistribution of left ventricular stroke volume by increasing forward flow and reducing regurgitant volume. Venodilators and diuretics diminish preload and will reduce both left ventricular end diastolic volume and pressure which helps to manage patients in LV failure. These drugs are therefore useful to alleviate the symptoms of heart failure and to preserve left ventricular function by reducing wall stress.

Many studies have tested the hypothesis that vasodilators given on long term basis to asymptomatic patients with severe aortic regurgitation to reduce

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systolic blood pressure and afterload mismatch, and preserve left ventricular function, prevent heart failure, and delay the need for aortic valve replacement. Short term studies (6 months- 2 years) have shown beneficial effects of oral hydralazine, nifidepine, felodipine, and ACE inhibitors in patients with chronic severe aortic regurgitation with volume overload. One randomised study comparing effects of long acting nifidepine(20 mg twice daily) and digoxin on LV function in asymptomatic AR showed a delay in the need for surgery among patients in the nifidipine group at 6 years[3]. However another randomised data comparing nifidipine and ACE inhibitors with placebo revealed no delay in the onset of symptoms or LV dysfunction.

Diuretics and vasodilators remain the drugs of choice for the relief of symptoms in patients with aortic regurgitation who are considered unfit for aortic valve replacement due to comorbidities. Short term vasodilator treatment can be given to patients with severe heart failure and severe left ventricular dysfunction to improve their clinical condition before aortic valve replacement. Betablockers are used with great caution since bradycardia increases regurgitation.

The goal of protecting the left ventricle in severe aortic regurgitation depends on reducing afterload mismatch by lowering systolic blood pressure. It is rarely possible to reduce systolic blood pressure to normal because of the high stroke volume which is characteristic of severe aortic regurgitation. The positive effects of vasodilators on left ventricular remodelling are greatest in patients with largest LV.

- It is preferable to treat hypertension (systolic BP > 140 mmHg) in chronic Aortic regurgitation (stage B and C) with dihydropyridine calcium channel blockers or angiotensin convertase enzyme inhibitor (ACE inhibitors)/ angiotensin receptor blocker (ARB) (level of evidence B: Class 1)[4,5].
- Medical therapy with ACE inhibitors/ARBs and beta blockers is reasonable in patients with severe AR who have symptoms and/or LV dysfunction (stages C2 and D) when surgery is not performed because of comorbidities. (Level of Evidence: B)[4,5]. However, as already mentioned, beta blockers are to be used with caution.

AORTIC STENOSIS

Progressive calcification of a congenitally bicuspid valve, usually presents in the fourth and fifth decades of life while calcification and stenosis of a trileaflet valve present later in life. The risk factors for the development of calcific aortic stenosis are similar to those for vascular atherosclerosis. Significant coronary artery disease is present in approximately 50% of patients with calcific aortic stenosis. Rheumatic disease of the aortic valve usually causes mixed stenotic and regurgitant lesions and is commonly associated with mitral valve disease.

Acquired aortic stenosis develops slowly and the cardiac output is initially maintained with a steadily increasing gradient across the aortic valve. Chronic pressure overload typically results in concentric LV hypertrophy with increased wall thickness and normal chambers size. Once left ventricle becomes hypertrophied, coronary blood flow may become inadequate, even in the absence of obstructive coronary artery disease and patients may develop angina. The fixed outflow obstruction limits the increase in cardiac output required on exercise and manifesting as exertional syncope. Eventually left ventricular failure supervenes. Patients with aortic stenosis typically remain asymptomatic for many years but once symptoms develop the average survival is 1 – 3 years.

Symptom control

The treatment of choice for symptomatic aortic stenosis is aortic valve replacement. Medical management of patients not suitable for aortic valve replacement is challenging. Patients with severe aortic stenosis should be asked to avoid vigorous physical activity. The cautious use of β blockers and nitrates may control angina. It is to be noted that β blockers may decompensate patients with low cardiac output who maintain cardiac output by increased heart rate. Nitrates may cause symptomatic hypotension, especially if they are used shortly after exertion. Diuretics are used to relieve symptoms of pulmonary congestion. Severe aortic stenosis is dependent on adequate filling pressures and excessive diuretic treatment may cause hypotension. Atrial fibrillation is often poorly tolerated and attempts to restore sinus rhythm by means of early DC cardioversion, or antiarrhythmic treatment with amiodarone, should be considered. Digoxin may be used in patients with atrial fibrillation or reduced LV systolic function. ACE inhibitors should be used with caution but are useful in treating patients with symptomatic LV systolic dysfunction. They should be started at low doses to avoid hypotension.

Secondary prevention

Natural history studies have shown that the annual reduction in valve area in aortic stenosis is approximately 0.1 cm2/year, with an average increase in Doppler jet velocity of approximately 0.3 m/s/year (equivalent to an increase in gradient of 7 mm Hg/year)[6]. Progression could be faster in the elderly, those with heavy aortic valve calcification, and, in patients with hyperlipidaemia.

Statins have been the most extensively studied medical treatment in Aortic Stenosis. SALTIRE trial (atorvastatin), SEAS trial (simvastatin), TASS trial (atorvastatin), ASTRONOMER trial (rosuvastatin)and PROCAS trial (rosuvastatin in congenital AS) were the trials which studied the use of statins in the progression of aortic stenosis. Unfortunately, none of these trials were able to demonstrate reduction in hemodynamic progression, aortic valve calcification, or improved clinical outcomes despite successfully decreasing serum LDL concentrations. Except for the SEAS trial none of these trials were powered to detect significant clinical benefits.

- Hypertension in patients at risk for developing AS (stage A) and in patients with asymptomatic AS (stages B and C) should be treated according to standard GDMT(Guideline Directed Medical Treatment), started at a low dose, and gradually titrated upward as needed with frequent clinical monitoring . (Level of Evidence: B, class I)[4,5]
- Vasodilator therapy may be reasonable if used with invasive hemodynamic monitoring in the acute management of patients with severe decompensated AS (stage D) with New York Heart Association class IV heart failure symptoms. (Level of Evidence: C, class IIb)[4,5]
- Statin therapy is not indicated for prevention of hemodynamic progression of AS in patients with mild-to-moderate calcific valve disease (class III)[4,5]

MITRAL REGURGITATION

The major causes of mitral regurgitation include mitral valve prolapse, rheumatic heart disease, infective endocarditis, annular calcification, cardiomyopathy and ischemic heart disease.Medical management of patients with severe mitral regurgitation is poor with mortality due to deteriorating left ventricular function and heart failure.

Chronic Mitral regurgitation causes left ventricular volume overload, compensatory eccentric left ventricular hypertrophy (new sarcomeres laid down in parallel) and dilatation, and progressive left ventricular failure. In patients with mitral regurgitation the afterload is typically reduced since ejection is both into left atrium and aorta (bidirectional) compared to aortic regurgitation where it is unidirectional. The size of the regurgitant mitral orifice is often dynamic and critically dependent on ventricular dimensions[7]. The reduction in preload or an increase in contractility will reduce the regurgitant volume when mitral regurgitation is caused by left ventricular dilatation in ischaemic heart disease, or dilated cardiomyopathy, whereas a fall in preload may produce a deleterious increase in the mitral regurgitant volume in patients with hypertrophic cardiomyopathy or mitral valve prolapse. In rheumatic heart disease the mitral orifice is usually rigid or fixed and the degree of regurgitation is not influenced by preload.

Mitral valve repair or replacement is indicated in symptomatic severe mitral regurgitation. The role of pharmacological therapy for Mitral regurgitation is an area of debate. Medical treatment can be used to reduce symptoms if surgery is contraindicated by serious comorbidity or due to very poor left ventricular function. In patients with signs and symptoms of pulmonary congestion venodilators like nitrates and diuretics are useful.Venodilators are particularly beneficial in patients with preload dependent mitral regurgitation especially functional mitral regurgitation.

Afterload reduction therapy is lifesaving in patients with acute severe Mitral regurgitation. The indication for such therapy in chronic mitral regurgitation is not clear. The afterload is not increased in most patients with chronic mitral regurgitation. Short term haemodynamic studies have demonstrated that hydralazine and ACE inhibitors reduce the degree of mitral regurgitation, and increase forward flow with little or no change in ejection fraction. Long term treatment with quinalapril has been reported to improve functional class and reduce left ventricular volume and mass in a very small study of selected patients with chronic mitral regurgitation. ACE inhibitors and betablockers should be used in patients with mitral regurgitation and heart failure.

- Medical therapy for systolic dysfunction is reasonable in symptomatic patients with chronic primary MR (stage D) and LVEF less than 60% in whom surgery is not contemplated.(Level of Evidence: B class IIa)[4,5]
- Vasodilator therapy is not indicated for normotensive asymptomatic patients with chronic primary MR (stages B and C1) and normal systolic LV function. (Level of Evidence: B class III)[4,5]

MITRAL STENOSIS

Mitral stenosis is almost always rheumatic in origin. Rheumatic fever leads to thickening at the mitral leaflet edges, fusion of commissures, and chordal shortening and fusion. The flow of blood from the left atrium to the left ventricle is restricted and left atrial pressure rises, leading to pulmonary venous congestion and breathlessness. There is dilatation and hypertrophy of the left atrium and left ventricular filling becomes more dependent on left atrial contraction. Whenever the heart rate increases, there is shortening of diastole and rise in left atrial pressure. Anemia, infections, hyperthyroidism, exercise and pregnancy are situations that demand an

increase in cardiac output, resulting in tachycardia and increase in left atrial pressure. Exercise and pregnancy are therefore poorly tolerated by patients with severe mitral stenosis.

Initially symptoms occur only on exercise. Once the stenosis becomes severe and the left atrial pressure is permanently elevated, the patient can become symptomatic at rest. Reduced lung compliance, caused by chronic pulmonary venous congestion in patients with severe mitral stenosis contributes to breathlessness. A low cardiac output causes fatigue.Atrial fibrillation caused by progressive dilatation of the left atrium is very common. A minority of patients (less than 20%) remain in sinus rhythm; many of these individuals have a small fibrotic left atrium and severe pulmonary hypertension.

Medical treatment is a reasonable option for patients with mild symptoms, but mechanical relief of the obstruction, by balloon valvuloplasty or surgery, should always be considered in patients with more severe symptoms, those with new onset atrial fibrillation, and those with evidence of moderate or severe pulmonary hypertension.

- Diuretics will usually reduce left atrial pressure and the symptoms of pulmonary congestion (breathlessness, haemoptysis); however, they may also reduce cardiac output and worsen fatigue.
- Beta Blockers(atenolol and metoprolol) and rate limiting calcium antagonists (diltiazem, verapamil) slow the heart rate at rest and during exercise, and may improve left ventricular filling by prolonging diastole.[8,9] They relieve effort related symptoms and are effective in patients with sinus tachycardia, atrial fibrillation, and other tachyarrhythmias.

ATRIAL FIBRILLATION

Atrial fibrillation is a common complication of mitral stenosis and is associated with a high risk of arterial embolism, especially stroke. The indications for anticoagulation are discussed in the section - anticoagulation for atrial fibrillation in patients with VHD.

The onset of atrial fibrillation is often accompanied by pronounced haemodynamic deterioration, precipitated by a dramatic reduction in left ventricular filling caused by the effects of tachycardia and the loss of atrial contraction. Good rate control is essential to relieve symptoms. Digoxin, β blockers, and rate limiting calcium antagonists can be used to control heart rate at rest and during exercise.However, digoxin has a narrow therapeutic index, and is inferior to β blockade in terms of preventing paroxysms of atrial fibrillation, and controlling the heart rate at the onset of atrial fibrillation and during exercise or other forms of stress. Combination drug treatment is often necessary and a few patients require atrioventricular node ablation and pacing.

Paroxysmal atrial fibrillation may respond to treatment with amiodarone, but usually gives way to permanent atrial fibrillation. Chemical or electrical cardioversion may have a limited role in the management of persistent atrial fibrillation which invariably recurs unless mitral stenosis is relieved.

- Heart rate control can be beneficial in patients with MS and AF and fast ventricular response. (class IIa, Level of Evidence: C)
- Heart rate control may be considered for patients with MS in normal sinus rhythm and symptoms associated with exercise. (class IIb, Level of Evidence: B)

SECONDARY PREVENTION OF RHEUMATIC FEVER

Rheumatic fever is an important cause of VHD in India. Recurrent rheumatic fever is associated with a worsening of the severity of rheumatic heart disease. Infection with group A Streptococcus does not have to be symptomatic to trigger a recurrence; also note that rheumatic fever can recur even when the symptomatic infection is being treated. Prevention of recurrent rheumatic fever requires continuous antimicrobial prophylaxis rather than recognition and treatment of symptomatic episodes of group A Streptococcal pharyngitis.

Continuous prophylaxis is indicated in patients with well documented history of rheumatic fever and with definite evidence of rheumatic heart disease (class I, level of evidence of A).

Agent Dosage

- Benzathine penicillin G 12 lakh units (>27 kg)/6 lakh units (< 27 kg) IM every 4 weeks is the recommended regimen. The serum levels of penicillin may fall below protective levels before the fourth week after IM penicillin. Hence administration every 3 weeks is recommended in populations with high incidence of rheumatic fever and if patients on every 4 week regimen develop recurrence of rheumatic fever.
- Penicillin V (phenoxymethy penicillin) 250 mg orally BID.
- Sulfadiazine 1 g orally once daily for patients >27 kg and 0.5 g once daily for patients <27kg
- Macrolide or azilide antibiotic (for patients allergic to penicillin and sulfadiazine).

Benzathine penicillin is the most effective drug to prevent recurrence followed by oral sulphonamide and oral penicillin, in that order (Irvington House studies). There are no published data on the use of other penicillins like penicillin G (400mg BID), macrolides or cephalosporins for secondary prophylaxis. Incidence of allergic reactions with benzathine penicillin is 3.2 %, anaphylaxis is 0.2% and death is 0.05%.

Duration of Secondary Prophylaxis*

- Rheumatic fever with carditis and residual heart disease - 10 years or until patient is 40 years of age (whichever is longer)
- Rheumatic fever with carditis but no residual heart disease- 10 years or until patient is 21 years of age (whichever is longer)
- Rheumatic fever without carditis - 5 years or until patient is 21 years of age (whichever is longer)

* *Duration varies in different guidelines.*

INFECTIVE ENDOCARDITIS PROPHYLAXIS

The role of antibiotic prophylaxis in the prevention of infective endocarditis (IE) even in high risk subsets has been questioned due to lack of published data. Antibiotic prophylaxis is now indicated only for a subset of patients who are at high risk for developing IE and at highest risk for an adverse outcome if it occurs.

Lack of adequate evidence, increasing bacterial resistance and risks of adverse drug events have led to significant modifications in IE prophylaxis guidelines. Transient bacteremia is more common during routine activities such as brushing of teeth or while chewing food. Gastrointestinal procedures, such as esophageal dilation, sclerotherapy, and endoscopic retrograde cholangiopancreatography have higher rates of bacteremia than simple endoscopy. However, no studies showed a reduction in rates of IE with antibiotic prophylaxis. Surgery, instrumentation, or diagnostic procedures that involve the genitourinary tract may cause bacteremia. The rate of bacteremia following urinary tract procedure is higher in the presence of urinary tract infection. Sterilization of the urinary tract with antimicrobial therapy in patients with bacteriuria should be attempted before elective procedures, including lithotripsy.

1. Prophylaxis against IE is reasonable for the following patients (at highest risk for adverse outcomes from IE - *see below*) before dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa (Class IIa, Level of Evidence: B).
2. Prophylaxis against IE is not recommended in patients with VHD who are at risk of IE for nondental procedures (e.g. TEE, esophagogastroduodenoscopy, colonoscopy, or cystoscopy) in the absence of active infection. (Class III. Level of Evidence: B).[4,11]

Patients at highest risk for IE are

- Patients with Prosthetic cardiac valves (including Trans catheter-implanted prostheses and homograft) and prosthetic material used for cardiac valve repair, including annuloplasty rings and chords.
- Patients with previous IE
- Cardiac transplant recipients with valve regurgitation due to a structurally abnormal valve

ANTICOAGULATION FOR ATRIAL FIBRILLATION IN PATIENTS WITH VHD

Atrial fibrillation is a common complication of VHD and is associated with a high risk of systemic embolism, especially stroke. Although no randomised controlled trials have specifically examined the efficacy of anticoagulant treatment in mitral stenosis, there is compelling evidence to support the use of anticoagulants (target international normalised ratio (INR) 2–3) in those with all forms of atrial fibrillation and in those who have already suffered an embolic event (NASPEAF (National Study for Prevention of Embolism in Atrial Fibrillation) trial).[8,9]

Oral anticoagulant- vitamin K antagonist (VKA) is indicated in patients with 1) MS and AF (paroxysmal, persistent, or permanent), or 2) MS and a prior embolic event, or 3) MS and a left atrial thrombus (irrespective of CHA2DS2-VASc score). Long term anticoagulation in patients with MS in normal sinus rhythm on the basis of left atrial enlargement or spontaneous contrast on TEE is controversial. It is recommended to use anticoagulation in patients with VHD and AF when their CHA2DS2-VASc score is 2 or greater (excluding patients with rheumatic MS). Patients with a bioprosthetic valve or mitral repair and AF are at higher risk for embolic events and should undergo anticoagulation irrespective of the CHA2DS2-VASc score.

A retrospective analysis of databases showed no difference in the incidence of stroke or major bleeding in patients with rheumatic and non-rheumatic MS when treated with NOAC (Newer Oral Anticoagulants) or warfarin. However, it is recommended to use VKA for patients with rheumatic MS until further evidence emerges on the efficacy of NOAC in this population. NOACs appear to be as effective and safe in patients with VHD as they are in those without VHD. In the ROCKET-AF

(Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared With Vitamin K Antagonist for Prevention of Stroke and Embolism Trial in Atrial Fibrillation), ARISTOTLE (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation), and RE-LY (Randomized Evaluation of Long-Term Anticoagulant Therapy) trials, 2,003, 4,808, and 3,950 patients, respectively, had significant VHD(MR, mild MS, aortic regurgitation, aortic stenosis (AS), and tricuspid regurgitation). These trials consistently showed that NOACs were at least equivalent to warfarin in reducing stroke and systemic embolism. The rate of intracranial hemorrhage was lower among patients randomized to dabigatran, rivaroxaban, or apixaban than among those randomized to warfarin, regardless of the presence of VHD. There is an increased risk of bleeding in patients with VHD versus those without VHD, irrespective of the choice of the anticoagulant.

- Anticoagulation with a vitamin K antagonist (VKA) is indicated for patients with rheumatic mitral stenosis (MS) and atrial fibrillation (class I, level of evidence B).[4,5]
- Anticoagulation is indicated in patients with AF and a CHA2DS2-VASc score of 2 or greater with native aortic valve disease, tricuspid valve disease, or MR (class I, level of evidence C)
- It is reasonable to use a NOAC as an alternative to a VKA in patients with AF and native aortic valve disease, tricuspid valve disease, or MR and a CHA2DS2VASc score of 2 or greater (class IIa, level of evidence C).

Conclusion

The risk factors for atherosclerotic cardiovascular disease like systemic hypertension, diabetes mellitus and hyperlipidemia should also undergo GDMT (Guideline Directed Medical Treatment) in patients with VHD . Most patients with LV systolic dysfunction and severe VHD should undergo intervention for the valve. However, if medical management is the only option, patients should receive GDMT drug therapy for LV systolic dysfunction, including angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) and beta-adrenergic blockers. Understanding the hemodynamics in each valve lesion helps to tailor therapy, while minimizing side effects.

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Subcutaneous Implantable Cardioverter-Defibrillator (S-ICD)

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INTRODUCTION

The implantable cardioverter-defibrillator (ICD) has been the gold standard for prevention of Sudden Cardiac Death (SCD), with extensive evidence supporting its use[1]. The ICD has been consistently found superior to best available drug therapy for the prevention of sudden cardiac death in patients with previous cardiac arrest (secondary prevention) and in high-risk patients with depressed left ventricular function or arrhythmogenic substrates (primary prevention). ICD technology has evolved from devices that delivered therapy through epicardial patch electrodes introduced by thoracotomy to those using transvenous leads for detection and treatment of tachyarrhythmia[2]. The transvenous ICD (TV-ICD) reduced the morbidity and risk associated with thoracotomy implants. However, use of transvenous leads involves potential complications including hemopericardium, hemothorax, pneumothorax, lead dislodgement, lead malfunction, device-related infection, and venous occlusion.[3]

Transvenous leads are the "Achilles heel" in ICD therapy and their performance over time is a serious concern, with some leads showing reduced survival that has led to recalls and withdrawal from the market. The potential for serious adverse events with transvenous lead system is substantial: lead failure has been estimated 0.58%/year and up to 20% at 10 years [4]. When lead failures occur, transvenous lead extraction may be necessary: this procedure is highly challenging with major complications rates of about 1% and a mortality risk of 0.3% even in experienced centres[4,5].

The need to completely avoid venous access issues, endovascular mechanical stress producing lead malfunction, and extraction associated risks led to the development of the entirely subcutaneous ICD (S-ICD). Its unique design avoids endovascular leads, thus eliminating many of the complications associated with the traditional TV-ICD. The novel device, developed and tested over the past decade, has gained approval as an accepted therapy for detection and termination of ventricular arrhythmias. The European Union approved its use in 2009; the U.S. Food and Drug Administration approved it in 2012.

S-ICD THE DEVICE

S-ICD system consists of a 3-mm tripolar parasternal lead (12 French, 45 cm length) which is connected to an electrically active pulse generator. The lead is vertically positioned in the subcutaneous tissue of the chest, parallel to and 1-2 cm to the left sternal midline and then makes a curve followed by a horizontal segment, at the level of the 6th rib, until it reaches the left anterior axillary line (Fig.1). The electrode has a 8-cm shock coil, flanked by two sensing electrodes: the distal sensing electrode is positioned adjacent to manubrio sternal junction and the proximal sensing electrode is adjacent

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to the xiphoid process. The pulse generator is bigger (about double in size) than "traditional" ICD: 78x 65x 15 mm with a volume of 69 cc and a mass of 145 grams. The generator is positioned in the subcutaneous tissue of the chest over the 6th rib between the left midaxillary and left anterior axillary lines[6].

The S-ICD is equipped with an extracardiac, extrathoracic, subcutaneous electrode. The defibrillation coil (8 cm long) lies directly between two sensing electrodes and the S-ICD generator acts as the 3rd electrode, used for sensing and defibrillation. The pulse generator serves as a mandatory component of the defibrillation pathway and as an optional electrode for sensing. Two electrodes alongside the sternum and the S-ICD generator provide three possible sensing vectors (Fig.1). In contrast to the electrograms acquired with closely spaced endocardial electrodes, the S-ICD recording has a lower amplitude and frequency content and is more susceptible to postural variation. It resembles that of the precordial surface electrocardiogram (ECG) with distinct P-wave, QRS, and T-wave morphology, and the device software/algorithms must process the waveform to identify the QRS as distinct from the T wave and P wave. After S-ICD implant, the device will automatically choose the optimal vector to distinguish the QRS from the T wave—specifically to avoid double counting of each cardiac event. A baseline template is also stored using the optimal vector. The optimal vector can also be selected manually by the operator if so desired[7].

The original estimated longevity of the S-ICD was 5years. A second generation device (the EMBLEM TM S-ICD System) is 20% thinner than its predecessor and is projected to last 40% longer than the previous S –ICD system. The estimated longevity has been extended from 5 to 7.3 years[8].An important limitation of the device remains the cost. An important potential advantage of a device that does not have contact with cardiac tissue is magnetic resonance imaging (MRI) safety. Magnetic resonance imaging scanning with the S-ICD does appear feasible, but larger studies are necessary to confirm this.

SICD- HOW IT WORKS

Sensing and detection involve three steps. First, the sensed event detection phase identifies a QRS event and applies blanking and signal decay in an effort to avoid T-wave over sensing, in a process analogous to that used in TV-ICDs. It additionally includes filtering with a band pass and notch filter. The notch filter is specific to geography (since different countries use either 50 or 60 Hz current) and is programmed based on the time zone selected in the programmer. Second, a certification phase employs algorithms that distinguish QRS electrograms from electromagnetic interference, myopotentials, T waves, and R-wave double counting. Lastly, during the rhythm decision phase, classification occurs using only on the corrected rate and duration [ventricular fibrillation (VF) zone] or the rate, duration, and morphology and QRS width compared with a baseline normal template (conditional zone). The conditional zone also uses a

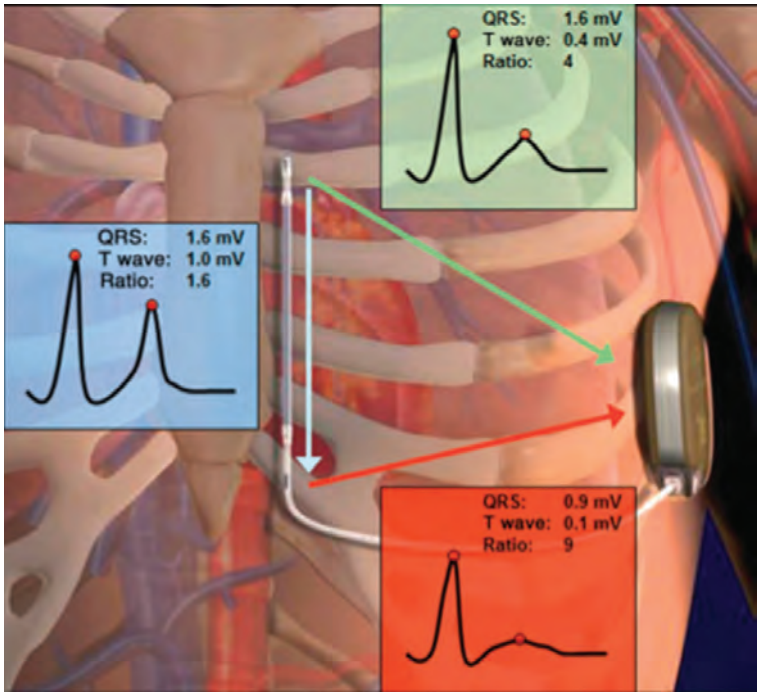

Figure 1 SICD- Diagram showing the positions of the sensing electrodes and pulsegenerator, which serve to create the vector for sensing of arrhythmia.

dynamic beat to beat analysis. With simulation-based assessment, the S-ICD's specificity for supraventricular arrhythmia discrimination is superior than that of the single- and dual-chamber TV-ICDs. In practice, however, the inappropriate shock rate of the S-ICD is approximately twice that of the TV-ICD, predominantly due to T-wave oversensing. This rate has progressively declined with software refinements and systematic use of the conditional zone[9].

During initial clinical testing, the S-ICD defibrillation threshold was confirmed to be significantly higher than TV-ICD (around 36 J compared with 11 J). In light of this, the default shock delivered is 80 J, the maximum output. Polarity is programmable but will automatically reverse upon shock failure. At implant, VF is typically induced and a shock of 65 J delivered, thereby establishing a safety margin for defibrillation of 15 J. The average time from initial detection to an 80 J shock delivery is about 15 s. Transthoracic antibradycardia ventricular pacing can be provided for up to 30 s after a shock if bradycardia is present[10].

INDICATIONS OF SICD

In a nut shell – the optimal SICD candidate would be a young patient, those needing ICD for primary prevention, patients with poor vascular access, previous ICD infections, and those at risk of infection especially patients with diabetics, renal dysfunction and mechanical valves (table 1). Primary prevention patients may benefit more from the S-ICD, based on the potential for less vascular and bloodstream complications whereas patients who require chronic pacing should not be considered for the S-ICD. While clinical experience is extremely limited, should an indication for right ventricular pacing develop post-S-ICD implant, a transvenous or leadless pacemaker may be implanted. Those who fail the screening test should not be considered for the device as risk of inappropriate shock is very high.

The importance of anti-tachycardia pacing (ATP) as an indication for a transvenous ICD remains controversial. Utilizing data from SCD-HeFT,[11] ATP-terminated monomorphic ventricular tachycardia was found to be rare occurring, 2% per annum which is interestingly less than the rate of failure of a transvenous lead. Altitude Study Investigators using data from the Altitude remote monitoring database recently provided concerning data that higher mortality was associated with ATP-treated ventricular tachycardia (VT) which accelerated the presenting ventricular arrhythmia.[12] Furthermore, one can argue that in the more recent era of higher detection rate programming for ICDs, and based on the results

Table 1. The choice of the candidates for a S-ICD.

S-ICD as a first choice • Pediatric or GUCH patients with no venous access. • Acquired stenosis or obstruction of central veins. • Previous endocarditis or device infection. • Patients at very high risk of infection of endovascular leads: dialysis, immunodeficiencies, cancer, need of a chronic indwelling catheter. • Candidates for cardiac transplantation.
S-ICD as a reasonable choice • Young patients with an active lifestyle and a long life expectancy. • Inherited genetic arrhythmogenic syndromes (Brugada, Long and Short QT, Early Repolarization). • Hypertrophic cardiomyopathy. • Prosthetic heart valves (infection risk). • Women ("cosmetic" issue). • Primary prevention patients with ischemic/non ischemic dilated cardiomyopathy. • Secondary prevention - survivors of out-of-hospital VF.
When to avoid the S-ICD • Failed pre-implant screening (up to 7% of cases). • Symptomatic bradycardia requiring permanent pacing. • Previously implanted unipolar pacemaker (sensing/detection pitfalls). • Systolic heart failure and left bundle branch block indicated for CRT. • Recurrent sustained monomorphic VT treatable with ATP. • Anatomic characteristics: thin patients with poor subcutaneous tissue, pectus excavatum.

of the MADIT-RIT study,[13] less ATP was utilized in the groups with the higher rate detection zones. But still the main indications for SICD are patients with prior ICD system infections, vascular access problems or anatomy with arteriovenous mixing placing the patient at risk for thromboembolic stroke from lead thrombosis.

Pre-implant screening utilizing surface electrodes prior to device implantation is a crucial step in patient selection for the S-ICD (Fig.2). Due to the high risk of inappropriate shock from T-wave oversensing, patients who fail the screening are not implanted with the S-ICD. On screening 7 -10% of patients fail, with a trend towards more ineligible patients with hypertrophic cardiomyopathy (HCM) or congenital heart disease. Screening at rest as well as during exercise testing has been proposed to avoid over sensing of the T wave[14]. It is better to do an exercise screening test for patients at high risk of T-wave oversensing (right bundle branch block, digoxin use, and abnormal repolarization).

Programming the S-ICD is simple as it was designed to be highly automated. In contrast to TV-ICDs (table 2), which typically have over 100 programmable parameters, the S-ICD has under 10. These include sensing vector, detection rate for each of two zones, and post shock pacing (on or off). Polarity of next shock and time delay to shock (smart charge) can be manually reset but will automatically adjust during operation. Analysis of the IDE trial data supports the important role of dual-zone programming, which resulted in a 70% reduction in inappropriate shocks for SVT compared with single zone programming[15]. A conditional detection zone at 200 b.p.m. and a nonconditional zone at 220 or 230 b.p.m. should be recommended. Interventions to prevent recurrent inappropriate shocks involve optimizing the sensing vector, adding a conditional zone if not present, modifying the detection rate, storing a baseline template during exercise testing, and addition of antiarrhythmic drugs and occasionally, ablation.

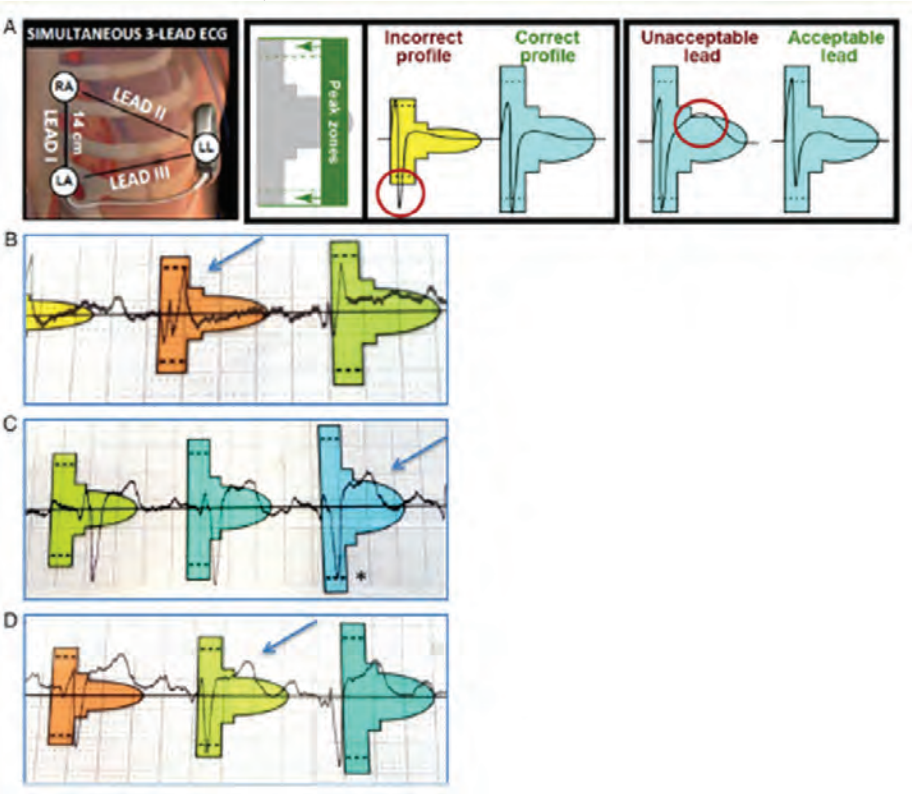

Figure 2 - SICD implant screening. Electrocardiogram leads are placed: 1 cm lateral to the xiphoid process, 14 cm cranial to the xiphoid process, and either the fifth or sixth intercostal space on the left mid-axillary line. A ground electrode is also placed. The electrode configuration is designed to mimic the sensing vectors of the subcutaneous implantable cardioverter defibrillator. The screening electrograms are obtained in the supine and upright positions at gains of 5, 10, and 20 mV for a period of 10 s, and utilizing a template tool provided by the manufacturer, the waveforms are analysed—passing if only a single lead consistently falls within the designated area throughout a 10 s period (in both positions). (A) The position of the electrocardiogram leads during the screening process mimics the position of the defibrillator lead electrodes and generator. A far field electrocardiogram type waveform is generated and this is analysed with the use of the template tool provided by the company—to determine whether the sensing algorithm reliably detects QRS waveforms vs. P or T wave. (B) An example of a waveform which is acceptable, compared with (C) or (D) that show failure of screening based on the amplitude of T wave. The arrow indicates the complex being evaluated. In each case, note that the QRS complex amplitude fits between the dashed line and top or bottom of the template, asterisk in Figure C.

Table 2 Head-to-head comparison of S-ICD versus transvenous (TV) ICD.

	S-ICD	TV-ICD
Leads within heart and vessels	NO	YES
Implant complications	Low/Negligible	Significant
X-Ray exposure	NO	YES
Infections	Lower risk More simple to manage	Higher risk Difficult to manage
Shock induced myocardial damage	Negligible	Significant
Patients suitable for implant	About 90%	Virtually all
Inappropriate shocks	4-25% (TWOS or external noise)	20-30% (supraventricular tachycardia)
Time to shock delivery	14-20"	7-9"
Pacing capability	NO	YES
Antitachycardia pacing	NO	YES
Pulse generator size	69 cc/145 grams	30 cc/70 grams
Battery life span	Up to 5 years	Up to 10 years
Costs	High	Medium/Low
Home Monitoring	NO	YES
Atrial arrhythmias monitoring	NO	YES

* TWOS: T Wave Over Sensing

SICD IMPLANTATION PROCEDURE

It is performed using a two or three incision approach. The initial incision is performed laterally, adjacent to the inframammary crease, between the anterior and mid-axillary lines at the level of the fifth or sixth intercostal space and is utilized to create the generator pocket. A second 1-1.5 cm incision is placed horizontally starting at the xiphoid at the midline, directed leftwards. A proprietary tool is employed to tunnel the lead from the device pocket to the xiphisternal incision. The electrode is secured at the xiphisternal incision with a suture sleeve. A similar process is then used to deliver the lead cephalad via a second tunneling procedure parallel to the sternum, exiting out of a third superior incision (placed at the sterno manubrial junction). The lead is thus anchored at all three incision sites. A two-incision technique avoids the superior parasternal incision but instead utilizes a standard 11Fr peel-away sheath to deliver the lead from the xiphoid incision in a cephalad direction parallel to the sternum. By avoiding the superior chest incision, the risk of infection and pain associated with it are eliminated, but potentially at the cost of increased dislodgement. The two incision technique is cosmetically more appealing for patients. infection is the most common complication, although bacteraemia is rare. Infection requiring surgical revision occurred in almost 2% of patients, and inadequate or prolonged healing or incisional, superficial infection occurred in another 0.6% of patients[16]. Other acute major complications such as haematoma appear similar to that of the TV-ICD.

CLINICAL EVIDENCE FOR SICD

The ability of the device algorithm to recognize ventricular arrhythmias appropriately has been tested in a simulated environment against conventional single- and dual-chamber TV-ICDs in the START study. Appropriate detection of ventricular tachyarrhythmias occurred in 100% of S-ICD cases compared with 99% for the various TV-ICD devices[9]. The initial clinical investigation evaluated the defibrillation efficacy of various device configurations in 78 patients compared with a standard TV-ICD system to identify the optimal lead position for subcutaneous defibrillation. This study found that the S-ICD could reliably terminate induced and spontaneous VF, but that it required significantly more energy (36+19 vs. 11+9 J) than a TV-ICD (11.1+8.5 J)[10]. In the prospective multi-centre US IDE trial,S-ICD implantation was attempted in 321 patients and successful in 314. Patients were followed up for a mean duration of 11 months. The 180-day system complication-free rate was 99% and induced VF was successfully terminated in all patients. All spontaneous ventricular arrhythmias were successfully converted; 13% of patients received an inappropriate shock.[17]

The 2-year results from the worldwide EFFORTLESS S-ICD Registry pooled together with the US IDE study was recently published[16].This report provides comprehensive data of almost 900 patients. Spontaneous ventricular tachyarrhythmias were treated during 111 events, successfully in 98.2%, with a minority requiring more than a single shock. The estimated 3-year inappropriate

shock rate was 13% with the majority occurring for T-wave oversensing (39%) or supraventricular tachycardia (24%). Device-related complications occurred in 11% of patients at 3 years, with no electrode failures and no systemic S-ICD-related infections. More specifically, this registry data provided the most complete description of real-world complications. Infection, without bacteraemia, appears to be the most common complication, while more experience with implantation and technique improvements were associated with reduced rates. Importantly, the major complication rates (haematoma, lead/device malposition/displacement) occurred in only 2% of patients—half of what is seen in some of the single- and dual-chamber ICD registries[16]. An ongoing randomized, multi-centre, prospective two-arm trial (PRAETORIAN)[18] is aimed at comparing the S-ICD with the TV-ICD with respect to inappropriate shocks and ICD-related complications, with the secondary endpoints of shock efficacy and patient mortality.

Despite the large generator size, the S-ICD has been placed in numerous children with channelopathies, cardiomyopathies, and congenital heart disease. On balance, the device implantation/operative complications appear to be fairly similar compared with other age groups[19].

CONCLUSION

The S-ICD represents a major advancement in ICD technology. The exclusive use of a subcutaneous lead for sensing and defibrillation represents the greatest advantage of this novel technology; the S-ICD eliminates the drawbacks associated with endovascular electrodes. However, the lack of demand bradycardia or anti-tachycardia pacing limits its utility in patients with conduction system disease or pace-terminable VT. Ideal candidates are younger patients (i.e., age <40 years), those at increased risk for bacteremia, patients with indwelling intravascular hardware at risk for endovascular infection, or in patients with compromised venous access. Technical refinements including size reduction, increased battery longevity, incorporating monitor zone, which can provide insight into slower ventricular or atrial arrhythmias and also chronotropy and improved T-wave rejection will enhance its clinical utility. S-ICD could serve as a remote monitoring hub to leverage emerging technologies to identify atrial fibrillation, and acute ischaemia. Cost is a concern, however, with increased utilization, production volumes, and competition , cost will likely decline and functionality increase. In future it is likely that a subcutaneous-based defibrillator will eliminate the system failures and medical problems currently associated with transvenous leads while offering the full complement of sudden death protection, resynchronization, anti-bradycardia pacing, and enhanced diagnostics for remote monitoring to transform the S-ICD into an integrated hub for health delivery that can be used for the long term after the SICD proves its role in larger clinical trials and registries.

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Atrial Septal Defect - Clinics

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Since the focus of this issue of KJC is the interatrial septum (IAS), let us discuss some FAQs regarding clinical aspects of the quintessential abnormality of the IAS - the Atrial Septal Defect (ASD).

1. What is 'hangout interval' ?

The 'incisura' in the great arterial pressure tracing represents the peak deceleration of the blood mass and is immediately followed by a pressure rebound.[1] A2 and P2 coincide with the incisura in the aortic (Ao) and pulmonary artery (PA) pressure tracings respectively. The distance (in time) between ventricular pressure and its great vessel at the level of the incisura was termed the 'hangout interval' by Shaver et al and relates to the temporal delay in closure of the valve after pressure crossover.[2] (In simple terms, it is the time taken for the valves to close after pressure crossover has happened between ventricles and great vessels.)

Normally, A2 occurs with aortic valve closure once the LV-Aorta pressure crossover happens (close to the end of LV ejection) and P2 occurs with pulmonary valve closure slightly after the RV-PA pressure crossover happens (a delay after the end of RV ejection). The PA hangout interval is normally 2 – 5 times longer than the Ao hangout interval. This is due to the differences in the characteristics of the vascular bed (high resistance, low compliance and brisk recoil in aorta vs the low resistance, high distensibility and late recoil in PA).

2. What is the reason for the wide split of the second heart sound (S2) in ASD ?

The normal inspiratory splitting of S2 was first described by Potain in 1866.[3] The relative contribution of various components to the physiologic inspiratory widening of S2 split is as follows : **A. Delay in P2** : Increased PA hangout interval (73%), Increased RV ejection time (45%) and **B. Earlier A2** : 27%.[1]

In ASD, the dilated pulmonary artery has a lower impedance, and the pulmonary arterial bed has increased capacitance and a longer hangout interval. The combined effect of this along with the increased right ventricular (RV) stroke volume and the consequent prolonged RV ejection time leads to a further delay in P2. Thus the split of S2 is wider and persists in both inspiration and expiration.

3. What is the reason for the fixed split of S2 in ASD ?

In a patient with ASD, the normal differences in the degree of RV and LV filling with respiration is balanced by reciprocal changes in the left to right shunting across the defect. The inspiratory increase in venous return to RV is more or less offset by a reduction in left to right shunt across the ASD. Thus during inspiration, RV filling remains the same or increases only mildly and LV filling

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remains the same or increases mildly. A constant relation between A2 and P2 is thereby maintained.

4. What is the effect of Valsalva maneuvre on the split of S2 in ASD ?

In a normal person, A2 and P2 come closer and 'fuse' during the strain phase of Valsalva (both RV and LV filling decreases). During the release phase, RV filling recovers faster and the S2 becomes prominently split in the next few beats (6-8 beats) as P2 is delayed. By this time, the LV filling will also increase and the LV systole is prolonged, leading to a narrowing of the S2 split (delay in A2).

In a patient with ASD, during the strain phase, the left to right shunt increases and the S2 split widens. After the release, the expected increase in A2-P2 split does not happen.[1]

5. What is the effect of atrial fibrillation (AF) on the S2 split in ASD ?

In an AF patient without ASD, S2 split is wider after shorter cycle lengths. But in ASD with AF, the opposite is seen – the split is wider after long cycle lengths as left to right shunt is more during long diastoles.

6. What happens to the intensity of P2 in ASD ?

P2 can be loud in ASD even in the absence of pulmonary artery hypertension (PAH). P2 may be loudly audible at the apex if the RV is enlarged. There is increased volume and velocity of blood flow in the PA. In addition, pulmonary dilatation itself increases the intensity of P2 (as in a patient with idiopathic dilatation of the pulmonary artery).[4] Therefore, it is important to look for other features of PAH before diagnosing PAH clinically in someone with ASD. A unexpectedly louder P2 or an increase in its loudness after even mild exercise can be suggestive of PAH.

7. What are the possibilities if a patient with ASD has a loud first heart sound (S1) ?

Of course, a careful examination for mitral stenosis must be done to rule out Lutembacher syndrome. Another possibility is an associated mitral valve prolapse (MVP) – either due to a structural or functional cause.[5]

However, an ASD patient can even otherwise have a loud S1 due to a loud T1 component. There are two proposed theories behind this : a) rapid and forceful tricuspid valve (TV) closure and b) a pulmonary artery ejection sound at the onset of pressure rise in the PA may be actually leading to this 'apparent' loudness.[1]

8. What are the possibilities if a patient with ASD has a palpable thrill in the pulmonary area ?

Two possibilities must be considered if a grade 4 murmur is heard. The ASD could be large with a hemodynamically significant left to right shunt. Secondly, there could be additional pulmonary valve stenosis (so auscultate carefully for a pulmonary valvular ejection click).

9. What are the clinical findings that suggest a 'hemodynamically significant' ASD ?

Cardiomegaly, right ventricular third heart sound (RV S3), tricuspid MDM (mid diastolic murmur), thrill in pulmonary area and development of pulmonary arterial hypertension (PAH).

10. When can a patient with ASD have a continuous murmur ?

In Lutembacher syndrome , when there is severe mitral stenosis (MS) along with a small restrictive ASD. This can also happen after balloon mitral valvotomy (BMV) in a patient with rheumatic MS due to a small residual 'defect' after atrial septal puncture.[6]

11. What is 'left – atrialisation' of JVP ?

In a normal person, the right atrial (RA) a wave is more prominent than the v wave and the left atrial (LA) v wave is more prominent than the a wave. In a patient with a large ASD, the large LA v wave is transmitted to the RA, thus making the RA v wave equal or more than the height of the RA a wave.

12. Can an opening snap (OS) occur in ASD ?

Yes, it can. But phonocardiogram will be usually required to record it. It occurs 30-70 msec after P2 or 110-120 msec after A2.1 The timing corresponds to the

maximum opening of the TV leaflets with increased flow during diastole.[7] The differences between this OS and the classical OS of MS are : the OS of ASD is heard at the lower left sternal border and is softer and lower pitched and increases in intensity with inspiration.

13. What can happen to sinus arrhythmia in the setting of a large ASD ?

The physiologic sinus arrhythmia in children is related to normal autonomic control mechanisms as well as the separation of the systemic and pulmonary venous returns. Inspiratory increase in venous return causing RA stretch and inhibition of carotid sinus reflex are involved. A dampening of this respiratory variation in RA volume occurs in ASD. In most patients with ASDs, sinus arrhythmia is preserved, but it can be blunted (high frequency vagally mediated component of variability has been found to be lower in unoperated children with ASDs).[8]

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The Official journal of Indian College of Cardiology, Kerala Chapter