CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER

Vol. 3 Issue December 2020

NEWS LETTER

In This Issue:

- INTRESTING CLINICAL CASES !
- ***Can people with heart disease exercise safely?***
- ***My Mnemonics in Cardiology***
- **APPROACH TO MANAGEMENT OF (ACHD)**
- **Digoxin , the "King" in the management of Heart Failure over 100 yrs**
- ***Coronary Artery Dissection leading to Myocardial Infarction following Blunt Chest Trauma***
- ***Iron deficiency in heart failure***
- *NOACs REVISITED*

Vol. 3 Issue December 2020

CCDSI - Clinical Cardio -Diabetic Society of India (Bihar -Jharkhand)

Message from Editor- in - Chief

Dr. Ajay Kumar Sinha

This is my proud privilege to bring out The 4th issue of CCDSI Newsletter
I am extremely thankful to my esteemed colleagues who have contributed in this very prestigious journal.
The drive and inspiration of Prof Dr. A.N Rai is phenomenal. Past and present presidents, Secretaries and the entire team have done great effort
Dr.Dina Nath, associate editor has done a commendable job and needs to be congratulated.

I wish this organization a great future!

Message from The Editor's Desk

Dr. Dinanath Kumar

According to In this COVID-19 era where physical meeting is not possible, CCDSI has decided to publish E-bulletin in various specialities quarterly.

In this E-bulletin of cardiology, our eminent authors have covered the whole spectrum of cardiology from approach to a disease to recent development and interesting cases in cardiology.

In this ever changing field of cardiology, we look forward to keep getting expert comments from our eminent authors, so that we can dissipate the knowledge down to the down to the primary care physicians.

Vol. 3 Issue December 2020

CCDSI - Clinical Cardio -Diabetic Society of India (Bihar -Jharkhand)

Message from The President's Desk

Dr. D.P.Khaitan

This is indeed a pleasure moment for all of us to know that Cardiology update is being published under the editorship of Dr. Ajay Kumar Sinha and Dr. Dinanath Kumar. The topics selected are most informative to the physicians and specialists in their day to day practice. Cardiology has grown leaps and bounds in its dimension.

The Editor-in-Chief Dr. Ajay Kumar Sinha and Associate Editor Dr. Dinanath Kumar , eminent cardiologists deserve appreciation and felicitation for spending many sleepless nights during their planning with involving so many erudite faculties to contribute on the subject and finally editing the manuscript before its release. I express my appreciation and gratitude to both the editors for so excellent cardiology update.

Long live CCDSI !

Message from The Secretary's Desk

Dr. Mritunjay kumar singh

It is indeed a great pleasure to know that e-bulletin on cardiology is being published under the able guidance of Dr. Ajay Kumar Sinha and Dr. Dinanath along with a dedicated team of colleagues.

I have also come to know that the topics selected are very contemporary and useful for physicians and specialists in their day to day practice.

I wish all the best to editorial team for their great effort.

CCDSI
CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER
NEWSLETTER

INTRESTING CLINICAL CASES !

Dr A.N.Rai
MD, MRCP (U.K), FRCP (Glasgow)
FICP, FICC, FICN
Former Prof. & Head Department of Medicine and Principal, ANMCH, Gaya
Chairman of AIMS, Gaya

Case 1

- *18 years old boy was admitted with palpitation and fainting attacks since 1 hour.*
- *His pulse and BP was not recordable*
- *He gave past H/O recurrent palpitation with fainting attacks since 3 months*
- *His ECG during palpitation is given below.*

Differential Diagnosis

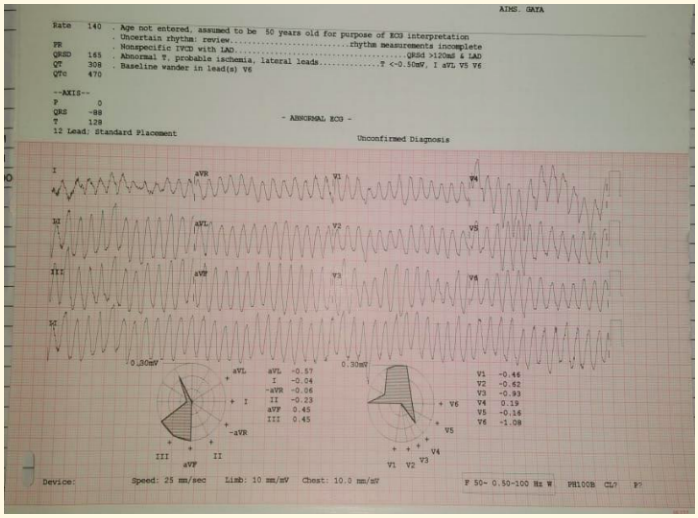
1 Polymorphic VT

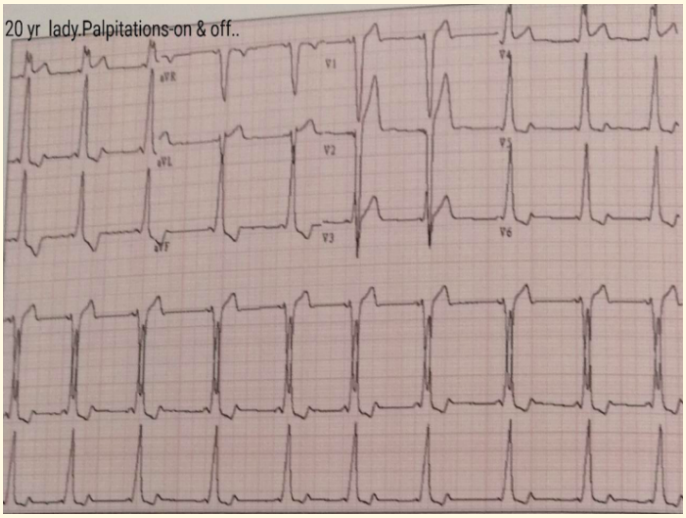
2 Fast Broad Irregular Tachycardia due to Pre excitation with AF.

3 Prolonged QT with Torsade depoint.

Management :

DC Shock , post DC shock ECG given below





Final Diagnosis Management

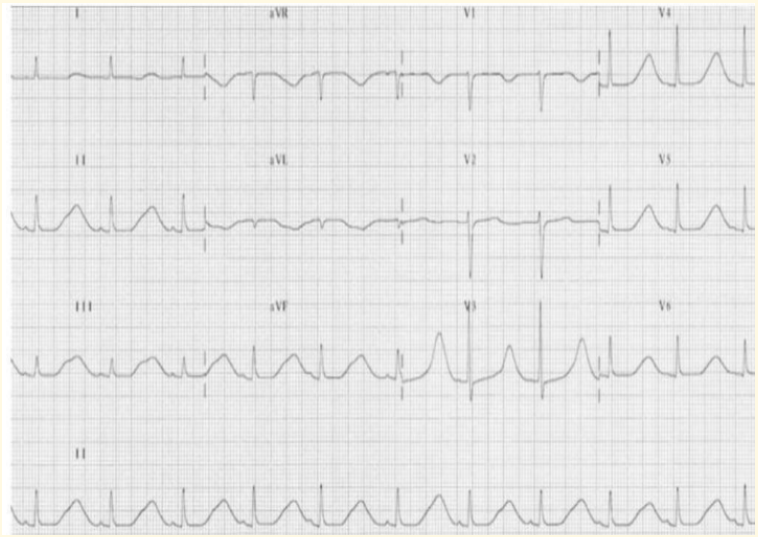
Diagnosis: *It is a case of WPW SYNDROME with AF conduction through Accessory pathway.*

Mangement : *EPS with RF catheter ablation.*

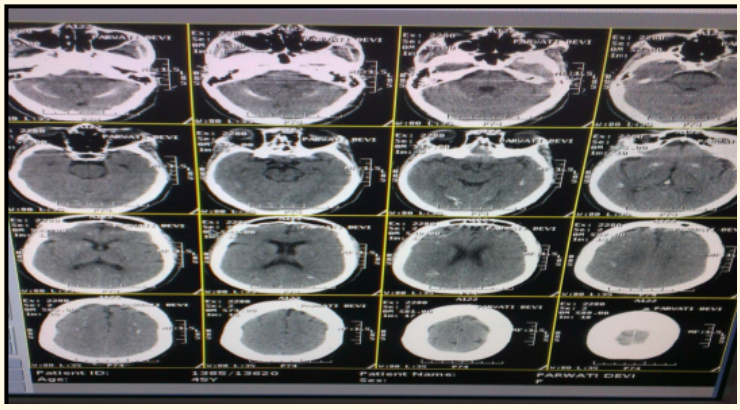
O/E

Pulse 75/ min, BP- 150/90 mmHg

RR- 18/min. No pallor/icterus/cyanosis/clubbing/ No lymphadenopathy/ oedema CVS- WNL, RS- WNL



CT Brain



Salient Features

Recurrent seizure

QT Prolongation in ECG

Bilateral basal ganglia calcification

hypocalcemic seizure

Investigation

Blood Sugar, Blood Urea Serum creatinin and Electrolyte : Normal

- Serum calcium-7.5mg/dl
- Serum albumin-4.5gm/ml
- Serum Phosphorus-8.5mg/dl
- Vitamin D-40omg/dl
- Serum Mg-1.8mg/ml
- Serum PTH-3pg/ml

Approach to Hypocalcemia

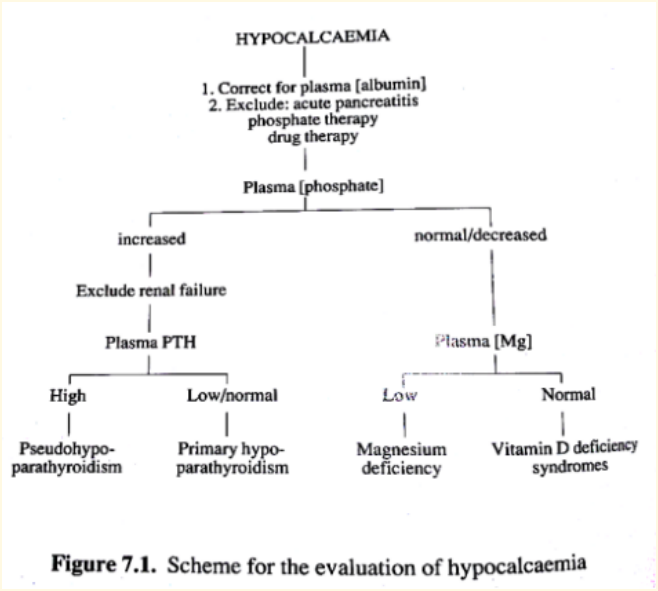


Figure 7.1. Scheme for the evaluation of hypocalcaemia

Final diagnosis

In our case primary hypoparathyroidism was diagnosed on the basis of low serum calcium, high phosphate, and low PTH in background of normal magnesium level along with radiological evidence of basal ganglia calcification.

Management

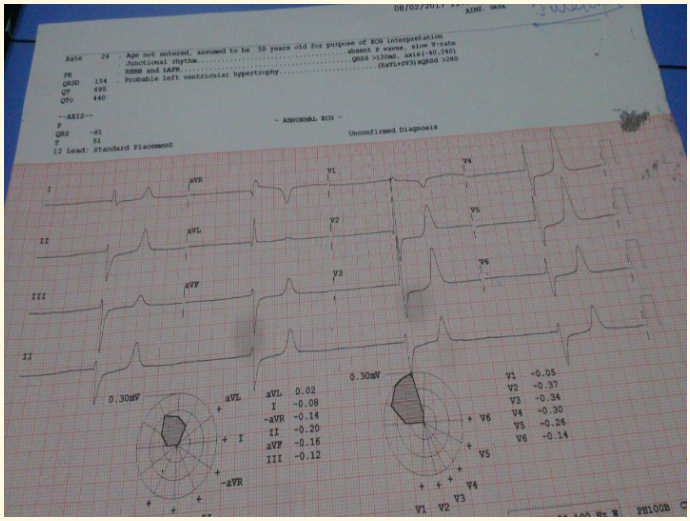
Iv calcium gluconate initially followed by calcium carbonate and vit D 60000IU once a week.Antiepileptic for symtomatic management of seizure.

Follow up: After 3 month

She was off the antiepileptic and doing well on oral calcium and vit D

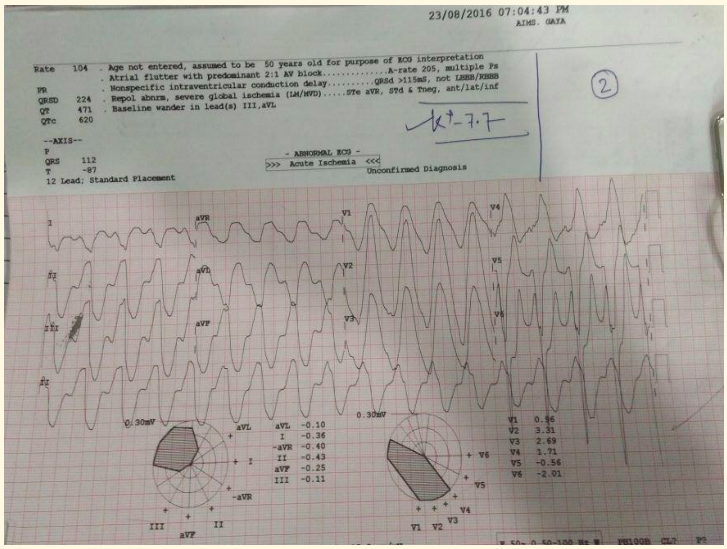
Case 2

- 35 years old Diabetic male was admitted with H/O sudden weakness and giddines since morning.
- O/E Pulse 40/min, BP 160/100



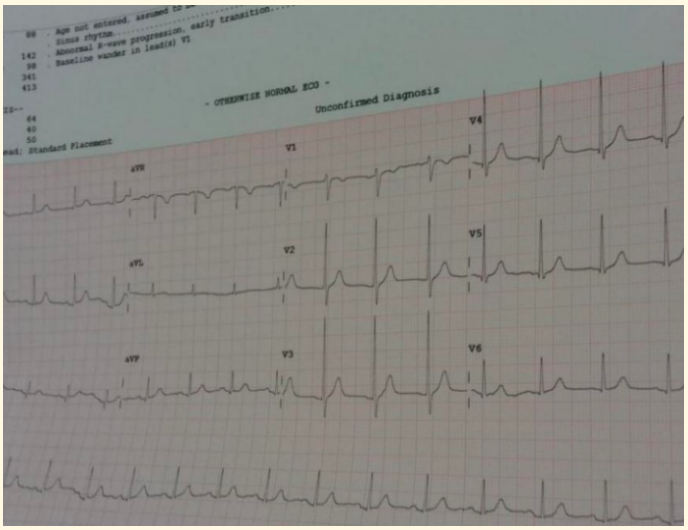
Investigations

Blood Sugar 300mg/dl
Serum Creatinine 3.5mg/dl
Serum Potassium 6.5 millieq/L
Patient was manage conservatively by giving IV calcium and insulin.
He was advise Dialysis when he did not show improvement but refused. his ECG 6hours latter given below



This is Sine wave due to merger of wide QRS with wide T wave. serum potassium 7.7 millieq/L. Patient was saved after he agreed for dialysis.

His post recovery ECG with potassium 5millieq/L



Case 3

A 45 yrs. Female presented to the emergency department with recurrent seizures since 1 day. She was diagnosed with epilepsy 6 years back and was on sodium valporate 300mg bd
No proper workup for seizures were done.

CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER

NEWSLETTER

Can people with heart disease exercise safely?

Dr. Ajay K Sinha

M.D. (PGI Chandigarh),PhD, FACC, FESC, FCSI, FICC, FAPSCC

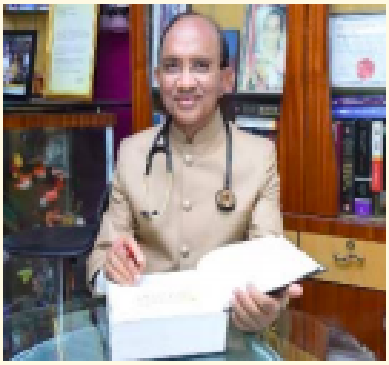
Sr Consultant Cardiologist, Medanta Hospital ,Patna

Ex-Director,Paras-HMRI,Patna,India

Ex-Associate Editor, Indian Heart Journal

Ex-President, Clinical Cardio Diabetic Society of India, Bihar and Jharkhand

Convenor, Preventive Cardiology Council , CSI



Pro. (Dr.) D. P. Singh

MD FICP FACP FIAMS FCSI FICS

FIACM FRC,Glasgow FRCP,Edinburgh

Professor of Respiratory Medicine

J L NMCH Bhagalpur

Governing body member of National API ,

President-elect CSI Bihar

ESC Guidelines on Sports Cardiology and Exercise in Patients with Cardiovascular Disease

29 Aug 2020

"With rising levels of obesity and sedentary lifestyles, promoting physical activity is more crucial now than ever before," said Professor Antonio Pelliccia, Chairperson of the guidelines Task Force and chief of cardiology, Institute of Sports Medicine and Science, Rome, Italy. "Regular exercise not only prevents heart disease, but also reduces premature death in people with established heart disease."

"The chance of exercise triggering a cardiac arrest or heart attack is extremely low," said Professor Sanjay Sharma, Chairperson of the guidelines Task Force and professor of sports cardiology and inherited cardiac diseases, St. George's, University of London, UK. "People who are completely inactive and those with advanced heart disease should consult their doctor before taking up sports."

The document covers leisure exercise and competitive sports for people with heart disease and conditions which raise the risk of heart disease such as obesity and diabetes. Advice is also given on exercise during pregnancy, or in special settings such as at high altitude, in deep sea, in polluted areas, and at extreme temperatures. The document states that traffic fumes are unlikely to lessen the benefits of physical activity to heart health.

In common with healthy adults of all ages, people with heart disease should exercise on most days, totalling at least 150 minutes per week of moderate intensity exercise. Moderate intensity means increasing your heart rate and breathing rate but still being able to hold a conversation.

For people who are obese or have high blood pressure or diabetes, the guidelines recommend strength-building exercise (for example, lifting light weights) at least three times a week plus moderate or vigorous aerobic exercise, such as cycling, running, or swimming.

Coronary artery disease is the most common type of heart disease and is caused by build-up of fatty deposits on the inner walls of the arteries. If the arteries become completely blocked this can cause a heart attack. Most people with coronary artery disease can play competitive or amateur sports

“People with long-standing coronary artery disease who wish to take up exercise for the first time should see their doctor first,” said Professor Pelliccia. “The aim is to tailor the intensity of activity according to the individual risk of causing an acute event such as a heart attack.”

Regular, moderate physical activity is recommended to prevent the most common heart rhythm disorder – called atrial fibrillation. People with atrial fibrillation who are taking anticoagulants to prevent stroke should avoid contact sports due to the risks of bleeding.

CCDSI
CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER
NEWSLETTER

My Mnemonics in Cardiology

Dr.R.RAJASEKAR, MD.
FICP,FACP(USA).
FRCP(Glasgow, Ireland & London).
Senior Consultant Physician & Diabetologist
#HEART AND DIABETES THERAPY CENTRE,
#DIABETES TRAINING CENTRE FOR DOCTORS
KUMBAKONAM .612001.Tamil Nadu.

Cardiology

C. Clinical Examination-vital,CAD/Congenital heart diseases/Cardiac Transplant as modality of treatment
A. Atherosclerosis
R. Renal involvement has impact
D. Diabetes has impact/Drugs as cause and for treatment/Device implantations have
impact as modality of treatment
I. Impact by high blood pressure/Brain->Stroke,Liver,Peripheral vascular system.Investigations-Biochemical, ECG, Echo, Imaging Studies/Interventions have
impact in diagnosis and treatment
O. Obstructive Sleep Apnoea has impact
L. Life Style modifications have impact
O. Old Age has impact
G. Genetics has impact
Y. Younger age gro

Physical findings in Cardiac Failure

C. Cool/Mottled Extremities.
A. Apical impulse sustained/displaced leftward or inferiorly.
R. Respiration - Tachypnoea.
D. Dullness & Diminished breath sounds at one or both lungs.
I. Increased JVP.. Jugular Venous Pressure.
A. Alternans Pulse / Audible or Palpable S3& or S4
C. Chronic Venous Stasis Changes.
F. Freaky Pulse--Thready pulse-Narrow pulse pressure.
A. Ascites-Anasarca.
I. Irregular Rhythm-Extrabeats.
L. Lift of Parasternum / Liver Enlargement.
U. Underlying Cardiac Diseases Physical findings--CAD,HT,CHD,RHD Cardiomyopathy,Pericarditis, Myocarditis.
R. Rales / Rhonchi or Wheezes, Regurgitation Murmurs due to MR, TR.
E. Edema--Presacral / Pedal

CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER

NEWSLETTER

Clinical manifestations- Symptoms and physical Signs of Congestive cardiac failure

C. Cardiac asthma,Confusion
O. Orthopnea
N. Nocturnal Dyspnoea-Paroxysmal, Nocturia,Neck Veins distended,
G. Gallop Rhythm --> S4(Atrial gallop)
E. Exercise Intolerance
S. Skin cold and clammy
T. Tachycardia
I. Increased Pulmonary arterial pressure -->PHT-loud P2
V. Ventricular gallop. S3
E. Edema->Peripheral
C. Cheyne Stokes Respiration
A. Anorexia
R. Rales
D. Dyspnoea, Displaced PMI
I. Increased Fluid load -> Fluid over load
A. Anorexia
C. Cardiac Cachexia
F. Fatigue, Weakness
A. Alternans Pulsus
I. Icterus
L. Lethargy
U. Urine output ->decreased
R. Retention of fluid in peritoneal cavity-Ascites
E. Enlargement -> Liver, Effusion-> Pleural,

ABC of Sinus Bradycardia

A. Athletic Heart
B. Brady Tachy Syndrome. Sinus node dysfunction..Sick Sinus Syndrome.
C. Cold..Hypothermia
D. Drugs.. Digoxin, Antiarrhythmics, Beta Blockers
E. Electrolytes.
F. Fever, Relative Bradycardia.. Enteric Fever, Fal asleep
G. Goitre.. Hypothyroidism
H. Heart Disease..

M.I.Types

M. M I - Spontaneous-Type 1
I. Ischaemic Imbalance MI-Type 2
T. Type 3 MI -->resulting in death without biomarkers-Type 3
Y. Yield of MI related to PCI-Type 4a
P. PCI Stent thrombosis Related MI-Type -4b
E. Evolving MI related to CABG

CCDSI
CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER
NEWSLETTER

Sinus Tachycardia

S. Sympathetic stimulation of SA node.
I. Intake of Stimulants Caffeine, Theophylline, Niacin / Inflammation of blood vessels of the body-Kawasaki's Disease.
N. No Hydration..Dehydration
U. Usual occurrence in Women--Post Orthostatic Tachycardia Syndrome.
S. Shock/Sepsis/Severe Bleeding
T. Tension Pneumothorax/Thromboemolism-Pulmonary Embolism.
A. Anemia/Adrenal medulla tumor-Pheochromocytoma.
C. Cardiac Tamponade
H. Hyperthyroidism / Hypoxaemia / Hypotension / Hg-Mercury Poisoning / Heart Failure.
Y. Yelping Pain.
C. Chronic Pulmonary Disease.
A. Anxiety.
R. Rate of Sinus Node 60-100 beats /minute.
D. Drugs/Over Dose.
I. Infections-Fever
A. Acute myocardial infarction.

AHA.Risk Enhancers.. ASCVD

My Mnemonics "A to E "
A. ASCVD (men <55 years old, women <65)--Family history of early ASCVD
Ankle-brachial index (ABI) ‹0.9
B. BMI->High->30-Metabolic Syndrome
C. Current high cholesterol (LDL-C 160-189mg/dl; non-HDL-C 190-219mg/dL)
Chronic kidney disease
Chronic inflammatory conditions (e.g., rheumatoid arthritis, psoriasis, HIV)
D. Dyslipedemia->-High Lipid Biomarkers-->Triglycerides ⩾175 mg/dL
High-sensitivity C-reactive protein ⩾2.0mg/dL
Elevated lipoprotein (a) ⩾50 mg/dL or ⩾125 nmol/L
Elevated apolipoprotein B ⩾130 mg/dL
E. Early -->menopause -History, Eclampsia-Pre -History
Ethnicity (e.g. South Asian Ancestry)--High Risk

Properly Validated Diagnostic Algorithm for Heart Failure With Preserved Ejection Fraction

H2FPEF risk score, ranging from 0 to 9 points:-
H2- Heavy (body-mass index, >30 kg/m2, 2 points)-->First H
Hypertension (=2 medications for hypertension, 1 point)-->Second H
F. Fibrillation
Atrial- (paroxysmal or persistent, 3points);
P.Pulmonary hypertension (pulmonary artery systolic pressure, >35 mm Hg by echocardiography, 1point);
E. Elder(age,>60, 1point)

CCDSI
CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER
NEWSLETTER

Cardiac Biomarkers

C. CRP.high sensitive C Reactive Protein-hs-CRP
A. Albumin --Ischemia Modified. IMA
R. Release from -->1) activated platelets--> Soluble CD40 ligand (sCD40L),2) Platelet derived Protein --> Placental growth factor--> PGF
D. Differentiation factor. Growth15 -GDF15
I. Isoenzyme BB <- Glycogen Phosporylase - GPBB
A. Atrial Natriuretic Peptides
C. Copeptin
B. Binding Protein <--Heart fatty acid --> H-FABP
I. I-T-->Treponin
O. Originate from most tissues, but localised to shoulder of plaque, leads to fibrous cap.. Matrix Metalloproteinase -9 (MMP-9),
M. Mid-regional pro adrenomedullin (MR proADM), Myoglobin,
A. Associated<--Pregnancy plasma protein..Pregnancy associated plasma protein A -- PAPP-A
R. Release from activated neutrophils and macrophages in culprit lesions--> Myeloperoxidase - MPO.
K. Kindling of Adipose Lypolysis ---> Catecholamines--> Unbound free fatty acid->FFA
E. Enzymes. Creatine Kinase - MB
R. Release from membrane phospholipids --> Choline
S. SCUBE 1

Drugs for Heart Failure A, B, C, D

A. Ace Inhibitors
Angiotensin Receptor blocker.
Angiotensin receptor-neprilysin inhibitor" (ARNi).->Sacubitril/valsartan
B. Beta blocker
C. Current->inhibitor of the "funny current" I (f) channel.->heart rate reducing agent--> Ivabradine
D. Diuretics :-Loop Diuretics->Bumetanide, Furosemide,Torsemide, Ethacrynic. acid
Thiazide Diuretics->Hydrochlorothiazide
Thiazide like Diuretic-> Metolazone,
Thiazide Diuretics Used in Combination With Loop Diuretics
Aldosterone Antagonists-> Spironolactone,Inhibitors-Gliflozins
Dilators->Vasodiators->Hydralazine,Isosorbide di nitrate

CCDSI
CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER
NEWSLETTER

Atrial Fibrillation.. (AF) Causes

A. Alcohol.. Binge drinking..Abnormalities of Electrolytes, ECG, Hypokalemia, Hyperkalemia (occasional), Hypomagnesemia,

T. Thyroid disorders.. Hyperthyroidism, Hypothyroidism-- >cardiac failure--> Predisposes--> AF

R. Rheumatic heart disease

I. Idiopathic. Lone AF

A. Amyloidosis

L. Lung Disease.. Ca lung,COPD

F. Fever, Familial,

I. Intracardiac Tumours.. Atrial Myxoma

B. Blood pressure high..HT, Pheochromocytoma.

R. Restrictive <---Cardiomyopathy-->Dilated, Obstructive.. HOCM / HCM

I. Infection, Ischemic Heart Disease Inflammation-->Pericarditis, Myocarditis,
Endocarditis..

L. Lung ..HT -->Pulmonary HT.Lung embolism--->Pulmonary embolism

L. Lasting since birth..Congenital heart disease.

A. Amyloidosis.

T. Trauma Chest

I. Induced by drugs..(mnemonics a,b,c,d,e)

a. aminophylline,.. Other Xanthines..Deriphylline, adenosine, antidepressants.. Fluoxetine, Tricyclic group, Amphetamine, anticholinergic.. atropine, antimigraine..
Sumatriptan, anaesthetic.. bupivacaine

b. Beta agonist, albuterol

c. Cocaine, Caffeine, Cytostatics, Cisplatine, Melphalan, Corticosteroid.. Methyl
Prednisolone.

d. Diet Pills, (Ephedra), Dopamine, Digoxin, Diuretic --> Thiazide --> Hypokalemia,

e. Erctile dysfunction.. Sildanafil,

O. OSA (Obstrctive Sleep Apnoea) / Obesity / Operating on chest

N. Non-Hemorragic <--Stroke--> Hemorrhagic (SAH)..

CCDSI
CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER
NEWSLETTER

Pulmonary Embolism

P. Pain in chest

U. Underlying causes like thrombophilia screening like Antiphospholipid antibody syndrome

L. Low oxygen level in blood

M. Malignancy--due to secretion of procoagulant

O. Oestrogen containing hormonal contraceptions - cause

A. Acquired thrombophilia - cause

R. Rapid breathing, Rapid heart rate

Y. Yield better outcome by combination of standardized clinical prediction rules, D-dimer testing, and high-accuracy multidetector CT angiography - Proper management by anticoagulation.

E. Embolistion of air, fat,amniotic fluid

M. Mild fever

B. Blood coughing out-Hemoptysis

O. Obstruction of pulmonary vascular bed by large emboli --> Hypotension, Right Ventricular dysfunction.

L. Low BP, Leg warm, Swollen, Painful

I. Imaging tests-CT Pulmonary Angiogram, Ventilation / Perfusion Scan, Imaging tests of less probability values-->Xray chest,USG of legs,ECG-S1Q3T3 pattern,Echo-McConnel's Sign (akinesia mid free wall but a normal motion of apex) S.Sudden death/Scoring system to predict outcome--Well's Score M.Management by anticoagulation, Thrombolysis --> Catheter directed thrombolysis, Inferior vena cava Dec filters, Pulmonary thrombetomy / Pulmonary thromboendarterectomy

CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER

NEWSLETTER

APPROACH TO MANAGEMENT OF ACYANOTIC CONGENITAL HEART DISEASE (ACHD)

DR. ABHINAV BHAGAT
MBBS, MD (MEDICINE)
DNB (Cardiology), FACC, FSCAI
SENIOR CONSULTANT CARDIOLOGIST,
HEART HOSPITAL, PATNA

APPROACH TO ACYANOTIC CONGENITAL HEART DISEASE (ACHD)

- ACHD produce a left to right shunt implying recirculation of oxygenated blood back to the lung.
- The clinical manifestations occur due to
  - (i) Excessive pulmonary blood flow. (PBF)
  - (ii) Systemic steal of blood

CLASSIFICATION :

Left to Right Shunts can be classified into Pretricuspid and Post tricuspid shunts. The hemodynamics and thus the presentation and natural history are different for the two groups.

(A) PRETRICUSPID SHUNTS:

- Occur at the level of atria and include:
  - **(i) Atrial Septal defect-**
    - Ostium Secundum ASD-> most common / 50-70% of all ASD.
    - Ostium Primum ASD
    - Sinus Venosus ASD
    - Coronary Sinus type of ASD
  - **(ii) Partial anomalous pulmonary venous drainage**

Features : -

- Pre tricuspid shunts- generally do not present during 1st few months of life. Over time as the PBF increase, RV enlarges and the pulmonary vasulature become more capacious to accommodate the ↑ Pulmonary Blood Flow.
- PAH is absent or mild. But in some cases PAH even if moderate is worrisome and may even suggest irreversible PAH.
- PAH/CHF -> generally develop during 3rd / 4th decade of life.

(B) POST TRICUSPID SHUNTS:-

Features : -

- Occur at the level of ventricles or the great arteries.

- There is direct transmission of pressure from systemic to pulmonary circuit at either the ventricular or great artery level.
- Produces diastolic volume overload of LV
- Relatively early presentation, in early infancy in the presence of large shunts.
- PAH is early and often irreversible.

Post Tricuspid Shunts Include :

(i) Ventricular Septal Defects (VSD) -> can be classified as : -
   a. Peri Membranous – most common
   b. Outlet VSD – Aortic Valve Prolapse / AR, can occur (2 -7% of all VSD's, part of rim formed by aortic and Pulmonary annulus.
   c. Inlet VSD – 5 – 8%
   d. Muscular VSD – 20% of VSD's

(ii) Endocardial cushion defect — Two types- (1) Complete (2) Partial.

(iii) Patent Ductus Arteriosus (PDA)

(iv) Aortopulmonary Window (APW)

(v) RSOV aneurysm

FACTORS DETERMINING THE MAGNITUDE OF LEFT TO RIGHT SHUNTS:-

(i) Defect Size

(ii) Systemic Vascular Resistance /Pulmonary Vascular Resistance Ratio
   ↓ PVR → ↑ Left -> Right SHUNT
   ↑ PVR → ↓ Left -> Right SHUNT

(iii) Relative compliance of the two ventricles → for ASD

PATHOPHYSIOLOGY : - 2 PHENOMENON OCCUR :->

(a) ↑ Left to Right Flow
↓
↑ PBF
↓
↑ Pulmonary Hydrostatic Pressure
↓
↑ LA Pressure / LV end diastolic pressure

↑ Pul. Congestion → ↑ stiffness of lungs.

(b) Systemic Steal

↑ System Vascular Resistance → Low cardiac output

↓ ↓
Symptomatic stimulation RAAS activation
↓
Salt / Water retention
Shock (non compensated)

CLINICAL FEATURES:

(1)**Symptoms** :-

Large shunts become symptomatic within the first 6/8 weeks of life.

- ⇨ Breathlessness, esp on feading is the 1st symptom
- ⇨ Increased sweating / poor feed.
- ⇨ Recurrent LRTI
- ⇨ Failure to thrive / failure to weight gain → often the only presenting complaint.

(2) **Signs:-**

(A) **Systemic exam : -**

a. Poor growth percentiles
b. Tachypnea
c. Intercostal / subcostal retractions, nasal floring, grunty respiration.
d. Tachycardia / cold extermites
e. Crepts / edema generally absent, hematomegaly more common in children.
f. Low oxygen saturation.

(B) **CVS Exam:-**

a. Increase precordial activity \ bulge.
b. Increase intensity of P2 / S3+
c. Murmurs are often masked or lack their typical quality in infants.

CVS Findings in specific Left to Right Shunts

1) ASD

- ➢ S2 split (wide/fixed) -> Hallmark of ASD
- ➢ No shunt murmur / only flow murmurs exist
- ➢ ESM AT Left Sternal Edge / MDM at tricuspid area.

Pearls : -

- ⇨ In ASD with CHF in early infancy, always try to look out for PAPVR or associated Mitral Valve Disease.
- ⇨ Untreated large left to right shunts lead to compensatory changes aimed at decreasing PBF, by producing proliferative changes in the pulmonary vasculature. Spontaneous improvement in signs and symptoms or the need for low CHF medications is highly suggestive of increased PVR. If not detected at any early stage these changes could lead to irreversible PAH and an inoperable child.

2) VSD :

- ➢ Systolic thrill / Harsh PSM AT Left Sternal Edge.
- ➢ MDM at apex (Large shunts) → denotes ↑ flow across the mitral valve.P2 Loud in large shunts
- ➢ EDM of AR in outlet / perimembranous VSD

3) PDA

- ➢ Wide pulse pressure
- ➢ Continuous murmur at Left Upper Sternal Edge / Infraclavicular area.
- ➢ MDM at Mitral Area. (↑ flow across mv)
- ➢ Differential cyanosis ((when reversal of flow occurs with SEVERE PAH)

DIAGNOSTIC TESTS:

1) Routine Blood Chemistries / ABG
2) ECG
3) CXR
4) Echocardiography – for precise anatomic diagnosis / flow characteristics / associated lesion / chamber size & functions.
5) Cardiac catheterization for hemodynamic assessment of a defect, PVR, ratio of pulmonary / systemic blood flow ratio etc.

MANAGEMENT PRINCIPLES OF A CHILD WITH LEFT TO RIGHT SHUNT : -

A. **GENERAL PRINCIPLES:-**

a. Early surgery for most symptomatic large post tricuspid shunts.
b. Pretricuspid shunts rarely need surgery in early infancy.

1) NUTRITION:

a. Decrease fluid intake
b. Increase caloric density
c. Gavage feeds
d. Correction of Anaemia

2) INFECTIONS:

a. Prompt treatment with antibiotics for LRTI

b. Vaccination against common respiratory pathogens.

3) MEDICAL THERAPY

a. DIURETICS
   i. Use judiciously to improve symptoms
   ii. Watch for electrolyte imbalance
   iii. Loop diuretics preferred
b. ACEI INHIBITORS -> dubious ? role in children.
c. IONOTROPES
   i. In patients with shock, IV ionotropes to be used in hospitalized children.
d. OXYGEN

Allow permissive hypoxia (keep SPO_2 -> 88 – 92%) as oxygen is a potent pulmonary vasodilator, and can increase the left to right shunt and system steal, detrimental to the patients.

B. SURGICAL / CATHETER INTERVENTION:

- Corrective surgery for most of the left to right shunt is safe and can be taken as early as a first few months, in experienced hands
- Unwise to make sick patients wait to achieve a certain weight threshold to proceed with surgery.

Early surgery indicated for : -

I. Refractory CHF
II. Evidence of PAH that is reversible
III. Failure to gain weight / thrive, despite optimised medical treatment.
IV. Recurrent LRTI

TIMING OF SURGERY / CATHETER INTERVENTION

- The most critical decision in the management of such children.
- We need to balance the result of the procedure with the natural history of the defect.
- Need to individualize each child.
- Remember procedural outcomes vary from one institution to another.
- Not all Defects need closure.

1) ASD CLOSURE :

a) Natural History

a. Earlier reports: - 40% close by 4 years.
b. Recent reports -> ASD <3mm diagnosed before 3 months -> 100% close by 1½ year of age; rarely close after 2 years.
c. Large defect → CHF / PAH by 3rd decade of life.
d. AF in 13-15% of adult.
e. Infective endocarditis rare.

b) Indication of closure -
All "Significant ASD's" need closure and they are defined as those having : -
a. Qp /Qs > 1.5
b. ASD's associated with RV volume overload
c. For ASD with PAH (PASP > 2/3RD of SBP) closure can be done if there is a net Left to Right Shunt of at least 1.5 : 1 or evidence of "Reversibility" of PA pressure when challenged with a vasodilator

c) Timing of closure: -
Elective closure of an ASD should be done between 2 – 5 years of age (preschool).

Pearls:-
Ostium Secundum ASD's can be closed percutaneously with Device Closure, if rims are adequate.
Sinus venosus, ostium primum and coronary sinus ASD can only be closed by SURGERY and must be done between age of 3 – 4 years of age

.

2) VSD CLOSURE

I. Natural history : Spontaneous closure of small to moderate muscular & perimembranous VSD's occur.
   i. 60% muscular VSD Close by 8 years of age.
   ii. 30-35% of perimembranous VSD close by 5 years age,
   iii. PVOD may begin to develop as early as 12 months of age in large VSD's.

II. Indication / Timing of VSD Closure

(a)Large VSD :
Defined as having any of the following:-
   i. Diameter of defect = aortic root size.
   ii. PAH present. (PASP >2/3rd SBP)
   iii. QP / QS > 2
   iv. LV dilatation or dysfunction present

TIMING OF CLOSURE - 3 – 6 months (or even early)

(b)Moderate size VSD's

   i. Defect diameter less then aorta root size
   ii. QP / QS > 2:1
   iii. PASP between 1/2 to 2/3 rd of systemic blood pressure.

Timing of Closure - 1 – 2 years of age

(c) Small VSD's –
QP / QS < 2

Close if (a) Recurrent I.E. (b) Aortic valve prolapse with significant AR

(d) VSD WITH AR:-
Occur in 2 – 7 % of VSD's

i. More common with doubly committed VSD and perimembranous VSD
   a. No AVP – follow up early 6 / 12 months.
   b. AVP + ANY degree of AR – early surgery.

ii. Perimenbranous VSD + AR -> Close If AR more than Mild AR

VSD closure can be done by either:-

I. SURGICAL CLOSURE

II. DEVICE CLOSURE -> FOR MUSCULAR VSD and some perimembranous VSD's (> 15 kg children).

3) **PDA CLOSURE:** All audible PDA's need closure.
PDA is classified as ->
   i. Small -> Qp / Qs <1.5 / 1
   ii. Moderate – Qp / Qs > 1.5 to 2.2
   iii. Large -> Qp / Qs > 2.2 / 1 or evidence of LV Dilatation Dysfunction.

TIMING i. ALL LARGE PDA's with CHF should be closed within 1 – 3 months of life

ii Small / moderate sized PDA - after 1 year

Transcatheter Device closure is treatment of choice for PDA Closure.

4) **AV CANAL DEFECT CLOSURE :**
   i. COMPLETE AV CANAL DEFECT

      i. Early surgery needed to present development of irreversible PVOD – Close between 12 – 24 weeks of age.
   ii. PARTIAL AV CANAL DEFECT
      i. 2 – 3 years of age.

5) **AP WINDOW CLOSURE:**
Presents in early infancy with CHF / PAH.
Surgery at 8 weeks needed.

BIBLIOGRAPHY

i) Braunwald's text book of cardiology
ii) Srivastava's timing of intervention in common congenital defects. Indian journal of pediatrics 2000. 67 :273-77
iii) Dooely KJ. Medical management of the cardiac infants. Critical care nurses cp 2002 / 98-104
iv) Cardiology update CSJ, 2017. YOGESH SATHI, MUNISH TOMAR, 87/ 717-724.
v) IAP series on pediatric cardiology second edition, R. Krishna Kumar, Abhay, 13 , 168-175.
vi) Wiley J (2003) – treatment of patent ductus arteriosus NEONATOLOGY 8, 425-432.
vii) BRAWN W. J (1991) Surgical treatment and outline of congenital heart disease. Current pediatrics 1 (2) 73-78)
viii) Working group on management of CHD IN India (2008), Indian pediatrics 45 (2) , 117- 126)
ix) Sethia , B (1992) current status of definitive surgery for congenital Heart disease. Arhieves of disease in childhood, 67 (8)) 981-982.
x) Kostolny M, Schreiber (2006), timing of repair in VSD WITH aortic insufficiency. Thoracic and Cardiovascular Surgeon 54/8), 512-512.

CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER

NEWSLETTER

Digoxin , the "King" in the management of Heart Failure over 100 yrs

DR. HEM SHANKER SHARMA,
MD, FICP, MACP
ASSOCIATE PROFESOR OF
MEDICINE, JLNMCH BHAGALPUR

After 230 yrs of use , digitalis remains an important and useful therapy for patients with atrial fibrillation and heart failure in 30 -50 % of patients.

Digoxin is the oldest known treatment of heart failure and has been demonstrated to reduce admissions for worsening heart failure in large randomized trial recruiting patients in sinus rhythm with heart failure and ejection fraction less than 45%. Digoxin therapy has no effect on mortality in heart failure. It may be useful for maintaining clinical stability and exercise capacity in with symptomatic heart failure.

Digoxin should be used as a 2nd line drug after diuretics , ACE Inhibitors and B blockers in patients with congestive heart failure who are in sinus rhythm . Digoxin should be used as a 1st line drug in patients with congestive heart failure who are in atrial fibrillation .

Digoxin has a limited but useful role either alone or in combination with other agents such as beta b blockers , calcium channel blockers (diltiazem or verapamil) in achieving satisfactory resting ventricular rate control in patients with chronic Atrial Fibrillation .

Digoxin is the most frequently used cardiac glycosides . The combination of positive inotropic activity with negative chronotropic effect has been shown to reduce hospital admissions in heart failure. Digoxin exerts its effects by inhibiting the Na- K-ATPase pump in cell membranes , including the sarcolemmal pump of cardiac myocytes .Inhibition of Na-K –ATPase pump results in increased intracellular calcium and thus increased cardiac contractility ,which lead to the suggestion that beneficial effects of digoxin were secondary to its inotropic properties . However the more likely mechanism of Digoxin in Heart Failure patients is to sensitize Na-K-ATPase activity in vagal afferent nerves , leading to an increased vagal tone that counterbalances the increased activation of adrenergic system in Advanced Heart Failure. Digoxin also inhibits Na-K-ATPase activity in the Kidney and therefore may blunt renal tubular resorption of Sodium .

Therapy with Digoxin is usually initiated and maintained at a dose of 0.125- 0.25 mg daily . For the great majority of patients , the dose should be 0.125 mg/day and the serum digoxin level < 1.0 ng/ml , especially in elderly patients , patients with impaired renal function and patients with a low lean body mass .

Although clinicians have used cardiac glycosides to treat patients with chronic heart failure for more than 200 yrs , there is still considerable debate regarding the effectiveness of the cardiac glycosides in heart failure patients . Wheras small and medium sized Trials conducted in 1970s and 1980s yielded equivocal result , 2 relatively large digoxin withdrawal studies in the early 1990s , the RADIANCE and PROVED trial provided strong support for clinical benefit from Digoxin. In these studies worsening heart Failure and Heart Failure hospitalizations developed in more patients who were withdrawn from digoxin than in patients who were maintained on Digoxin therapy.

Digoxin is approved by the US Food and Drug Administration for the treatment of mild to moderate Heart Failure to reduce the risk of heart failure related hospitalizations and emergency case. According to American College of Cardiology Foundation / American Heart Association Heart Failure Guidelines , Digoxin may be used unless contraindicated to decrease hospitalizations due to worsening heart Failure in patients with HFrEF .

In DIG(Digitalis Investigation Group) trial , the largest Randomized Controlled Trial of Digoxin in Heart Failure , digoxin reduced the risk of all cause and Heart Failure hospitalizations in patients with HFrEF but had no effect on all cause mortality . The lack of mortality benefit of digoxin in the DIG trial with the emergence of other evidence based guideline directed medical therapies (GDMT) with proven efficacy and effectiveness in lowering the risks of both all cause mortality and hospitalization, has lead to dramatic decline in the use of digoxin in patients with HFrEF. One of the most important findings to emerge from the DIG trial was that mortality was directly related to the digoxin serum level. In men trough levels between 0.6- 0.8 ng / ml were associated with decreased mortality suggesting that trough levels should be maintained between 0.5 -1 ng / ml .

Findings from RADIANCE (Randomized Assessment of the Effect of Digoxin on Inhibitors of the Angiotensin Converting Enzyme) and PROVED (Prospective Randomised Study of Ventricular Failure and the Efficacy of Digoxin) trials suggest that discontinuation of Digoxin therapy increased the risk of Adverse outcomes in ambulatory patients with chronic HFrEF.

A posthoc analysis of the DIG trial demonstrated that discontinuation of digoxin is associated with poor outcomes in ambulatory patients with chronic HFrEF .

Digoxin is an inexpensive and relatively safe drug at low doses and is recommended for patients with HFrEF who remain symptomatic despite optimal GDMT (Guideline Directed Medical Therapies) Use of these agents in clinical practice should take account of appropriate dose, serum concentration , drug interactions and potential side effects.

In patients with heart failure , overt digitalis toxicity tends to occur at serum concentration > 2 ng/ ml however digitalis toxicity may occur with lower digoxin levels particularly if hypokalemia or hypomagnesemia co- exist. Oral potassium administration is often useful atrial , atrio- ventricular (AV Junctional) or ventricular ectopic rhythm , even when the serum potassium level is in the normal range ,unless high grade AV block is present . However serum K levels must be monitored
carefully to avoid hyperkalemia especially in patients with renal failure or those taking aldosterone receptor antagonists . The concomitant use of Quinidine, Verapamil, Spironolactone, Flecainide , propafenone and amiodarone can increase serum digoxin levels and may increase the risk of adverse reactions . Patients with advanced heart block should not receive the digitalis unless the pacemaker is in place.

CCDSI
CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER
NEWSLETTER

Coronary Artery Dissection leading to Myocardial Infarction following Blunt Chest Trauma

Dr. Shamshad Alam, Dr.Vipin Kumar
Department of Cardiology, Ruban Memorial Hospital, Patna 800001, India

ABSTRACT:

Coronary artery dissection following a blunt chest trauma leading to myocardial infarction is a rare complication. The culprit lesion may be atherosclerotic or non atherosclerotic coronary artery segment which is an harbinger of dissection. There are a multiple mechanisms leading to coronary injury after chest trauma, most notably are vascular spasm, coronary dissection with intimal tear or rupture of any existing atheromatous plaque or thrombus. Often myocardial infarction is masked by chest pain due to multiple injuries on chest wall.

Current case report is based upon a 24 years old male without any significant past medical history as well as any risk factors for coronary artery disease was admitted to our hospital with blunt chest trauma with rib fractures and hemothorax. He was managed for his injuries and hemothorax and in hospital 2D echocardiography was done as a routine protocol for chest trauma which revealed LAD territory hypokinesia alongwith ecg changes. Then he went coronary angiography which revealed dissection with dissection flap leading to luminal narrowing of proximal left anterior descending artery.

So apart from major structural cardiac injuries, coronary artery injuries should also be kept in mind following blunt chest trauma. Diagnosis of myocardial infarction may be difficult as chest pain may be interpreted as secondary to chest wall injuries. So an ECG and 2D Echocardiography is mandatory to screen for regional wall motion abnormalities following any coronary artery injury.

INTRODUCTION :

Dissection of a coronary artery is a rare and life-threatening condition. It can result in thrombus formation and coronary occlusion with subsequent acute coronary syndrome, ventricular arrhythmia, and death. Known etiologies include atherosclerosis, trauma, and iatrogenic causes . It may also occur spontaneously with no identifiable cause. Traumatic coronary artery dissection is an especially rare type of dissection and generally happens in the setting of a high-speed motor vehicle collision . Delayed diagnosis of this condition can lead to catastrophic outcomes. Here we discuss a case of traumatic coronary artery dissection.

CCDSI
CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER
NEWSLETTER

CASE REPORT:

A 24 year old male without any significant past medical history and without any risk factors for coronary artery disease met with a road traffic accident leading to multiple injuries which included chest injuries and forearm radius fracture. Due to chest trauma he had rib fracture and had developed hemothorax and was managed by intercostals chest tube drainage with stable vitals. His forearm fracture was managed by metallic plate insertion. In hospital he underwent ECG which revealed changes suggestive of anterior wall myocardial infarction. On 2D Echocardiography to rule out any major cardiac injury it was found that there was LAD territory hypokinesia with an Ejection Fraction of 44%.

Then he underwent coronary angiography [Figure 1 and 2] which revealed dissected segment in proximal portion of LAD alongwith a dissection flap leading to luminal narrowing with TIMI 2 flow. Left main, left circumflex and right coronary artery were nearly normal with TIMI 3 flow.

Meanwhile after discussion decision for PCI to LAD was taken. PCI to LAD was done after wiring LAD with whisper wire. Ostial LAD placement[Figure 3] of 3.5 x 18 mm Everolimus Eluting Stent was done @ 16 atm. Post stenting good results [Figure 4 and 5] were obtained with TIMI 3 flow, without any residual dissection or dissection flap.

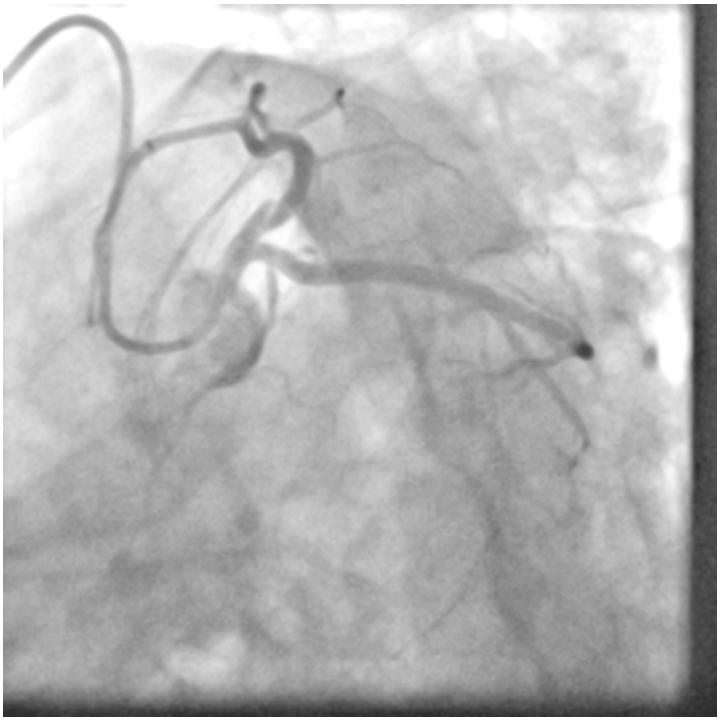


Figure 1. Coronary angiography, LAO caudal view, a significant dissection in proximal LAD segment with dissection flap leading to luminal narrowing.

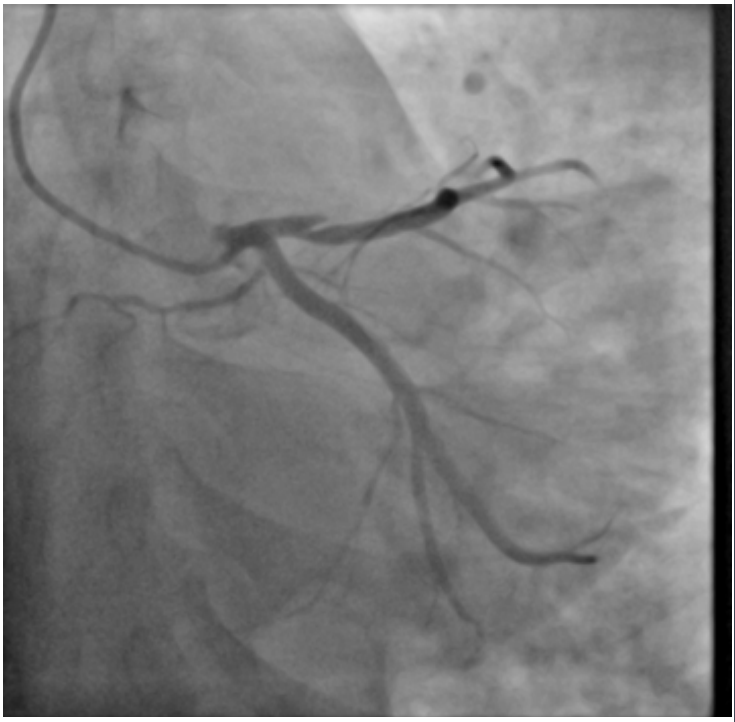


Figure 2. Coronary angiography, AP caudal view, a significant dissection in proximal LAD segment with dissection flap leading to luminal narrowing.

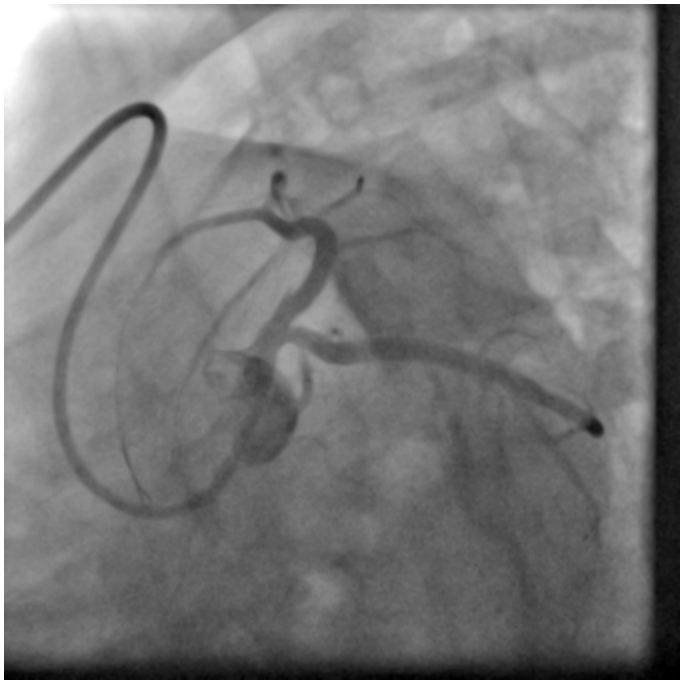


Figure 3. Coronary angiography, LAO caudal view , after successful stenting the dissection and the dissection flap were sealed off.

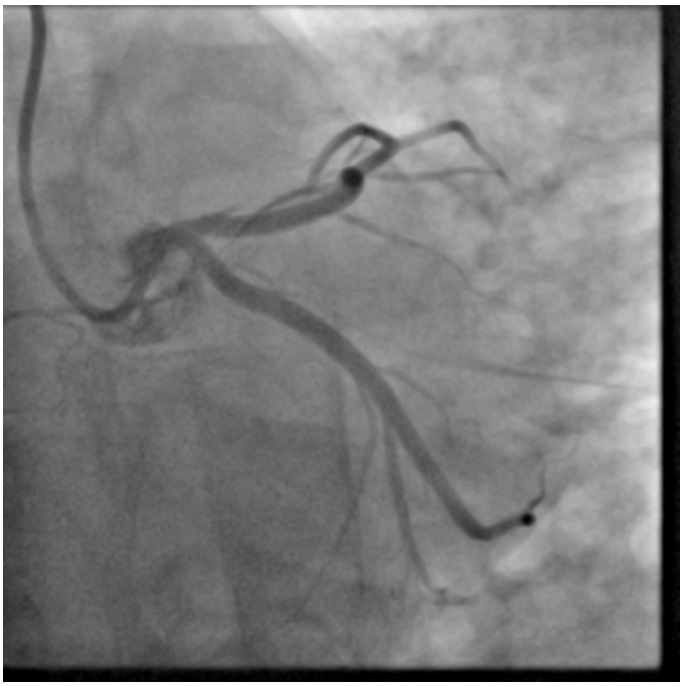


Figure 4. Coronary angiography, AP caudal view , after successful stenting the dissection and the dissection flap were sealed off.

DISCUSSION :

Traumatic coronary artery dissection due to blunt trauma is an extremely rare condition [1]; however, it has been more frequently described in recent literature [2]. This might indicate that this condition has been previously under-diagnosed. It was first described by Kohli et al. in 1988 [3].Mostly patients who have blunt chest trauma present with complaints of dyspnoea or chest pain. Also, in most of these patients it is mostly the minor injuries that cause the pain, some would have serious underlying conditions that would need specific therapies. Majority of blunt cardiac injuries are as a result of rapid deceleration and trauma caused by high speed motor vehicle accidents [4-7]. One of the most common scenarios is chest damage by the steering wheel axis when the car comes to a sudden stop for an unrestrained driver in a high speed motor vehicle collision. Less common causes include a direct blow to the anterior chest, falls from a height and sport related accidents [7,8]. In some cases direct abdominal trauma have been found to generate enough upward force into the chest cavity to cause blunt cardiac injury [8,9]. There have been several recent reports describing coronary artery dissection following blunt chest trauma which shows the previous underestimation of this sequele [4-13]. In a case described, anterior chest wall blunt trauma has led to damage to both LAD and left circumflex artery (LCx) and the patient was treated by surgery [4]. In another case, a patient had occlusion at the mid part of both LAD and LCx arteries after a motorcycle accident and polytrauma, was treated by PCI [5].

Left main coronary artery dissection following blunt chest trauma is also a rare condition which has been reported as a case and has led to patient's mortality [13]. The pain may be masked by different injuries so a high clinical suspicion is required. Although fibrinolytic therapy has been given to certain patients after mild trauma, it is better not to use such a strategy in patients for potential bleeding risk [11]. The most commonly affected artery is the LAD because of its anatomical relationship. The higher incidence of dissection in LAD artery may be due to its proximity to the chest wall. Relative weakness to acceleration/ deceleration forces at the junction of proximal and middle part of the LAD can also explain the higher incidence of injuries to the vessel. The second most affected artery is the RCA [6,14]. It was even reported that cardiopulmonary resuscitation (CPR) can lead to coronary dissection[15].

While the definitive diagnosis is most commonly established through cardiac catheterization, it is usually a challenge for physicians to promptly suspect coronary artery dissection because patients may not develop any symptoms until ischemia or infarction develops and also because of its rare occurrence which makes it a distant diagnosis in any clinicians' mind. A combination of normal ECG and troponin-I at admission and at eight hours has a 100% negative predictive value for significant cardiac injury [16]. Typically, coronary artery dissection would manifest on ECG as hyperacute T waves, which subsequently evolves into ST segment elevations, and eventually formation of Q waves.

CONCLUSION :

It is important to have in mind the possibility of injury of the coronary artery after blunt trauma of the chest. Sometimes the condition is underdiagnosed. As chest pain can be interpreted as being secondary to chest wall contusion or it may be overshadowed by other injuries, the diagnosis may be difficult. After chest trauma, high clinical suspicion and systematic evaluation of the patient is needed for the diagnosis of coronary artery dissection. As the clinical findings may be misleading, Electrocardiography (ECG) should be done in every patient with thoracic trauma. Echocardiography is necessary in patients with hemodynamic compromise to rule out mechanical complications such as new valve regurgitation, ventricular wall rupture or cardiac tamponade. An abnormal cardiac enzymes and or ECG show the need for further investigation. Both coronary angiography and echocardiography should be used when needed. It is needed to make the time span between coronary artery occlusion and revascularization short as to avoid acute myocardial infarction.

ACKNOWLEDGEMENTS :

We would like to thank the patient for giving his consent for this publication and our cathlab team for a successful procedure.

REFERENCES :

[1] Marcum JL, Booth DC, Sapin PM: Acute myocardial infarction caused by blunt chest trauma: successful treatment by direct coronary angioplasty. Am Heart J. 1996, 132:1275-1277. 10.1016/S0002-8703(96)90475-5

[2] Bjørnstad JL, Pillgram-Larsen J, Tønnessen T: Coronary artery dissection and acute myocardial infarction following blunt chest trauma. World J Emerg Surg. 2009, 4:14. 10.1186/1749-7922-4-14

[3] Kohli S, Saperia GM, Waksmonski CA, Pezzella S, Singh JB: Coronary artery dissection secondary to blunt chest trauma. Catheter Cardiovasc Interv. 1988, 15:179-183. 10.1002/ccd.1810150310

[4] Lai CH, Ma T, Chang TC, Chang MH, Chou P, Jong GP. A case of blunt chest trauma induced acute myocardial infarction involving two vessels. Int Heart J. 2006;47(4):639-43.

[5] Mauser M, Schwenk M, Schmelzeisen H, Fleischmann D, Fösel T. Acute myocardial infarction after blunt polytrauma--successful coronary intervention. Anasthesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie: AINS. 2003;38(2):102-06.

[6] Morin J, Bogaty PM, Roy L, Poirier P. Trauma-induced occlusion of the left anterior descending artery following a snowmobile accident in a man without prior coronary artery disease. Can J Cardiol. 2003;19(5):565-68.

[7] Vasudevan AR, Kabinoff GS, Keltz TN, Gitler B. Blunt chest trauma producing acute myocardial infarction in a rugby player. The Lancet. 2003;362(9381):370.

[8] Goktekin O, Unalir A, Gorenek B, Kudaiberdieva G, Cavusoglu Y, Melek M, et al. Traumatic total occlusion of left main coronary artery caused by blunt chest trauma. J Invasive Cardio. 2002;14(8):463-65.

[9] Marcum JL, Booth DC, Sapin PM. Acute myocardial infarction caused by blunt chest trauma: successful treatment by direct coronary angioplasty. Am Heart J. 1996;132(6):1275-77.

[10] Pringle S, Davidson K. Myocardial infarction caused by coronary artery damage from blunt chest injury. Br Heart J. 1987;57(4):375-76.

[11] Christensen MD, Nielsen PE, Sleight P. Prior blunt chest trauma may be a cause of single vessel coronary disease; hypothesis and review. Int J Cardiol. 2006;108(1):1-5.

[12] Aoyagi S, Okazaki T, Fukunaga S, Ueda T. Concomitant traumatic aortic valve and coronary artery injury. Ann Thorac Surg. 2007;83(1):289-91.

[13] Li CH, Chiu TF, Chen JC. Extensive anterolateral myocardial infarction caused by left main coronary artery dissection after blunt chest trauma: a case report. Am J Emerg Med. 2007;25(7):858. e3-. e5.

[14] Lobay KW, MacGougan CK. Traumatic coronary artery dissection: a case report and literature review. J Emerg Med. 2012;43(4):e239-e43.

[15] Kapłon-Cieślicka A, Kosior DA, Grabowski M, Rdzanek A, Huczek Z, Opolski G: Coronary artery dissection, traumatic liver and spleen injury after cardiopulmonary resuscitation – a case report and review of the literature. Arch Med Sci. 2013, 9:1158-1161. 10.5114/aoms.2013.39235

[16] Velmahos GC, Karaiskakis M, Salim A, Toutouzas KG, Murray J, Asensio J, Demetriades D: Normal electrocardiography and serum troponin I levels preclude the presence of clinically significant blunt cardiac injury. J Trauma Acute Care Surg. 2003, 54:45-50. 10.1097/01.TA.0000046315.73441.D8

CCDSI
CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER
NEWSLETTER

Iron deficiency in heart failure

Dr. RAVI VISHNU PRASAD
MD (MEDICINE), DM (CARDIOLOGY), ADDITIONAL PROFESSOR,

Dr. NIRAV KUMAR
DNB (CARDIOLOGY), ADDITIONAL PROFESSOR,

Dr.B P SINGH
MD (MEDICINE), DM (CARDIOLOGY), PROFESSOR AND HEAD,

Dr. GOUTAM KUMAR
MD (MEDICINE), DM (CARDIOLOGY) ASSISTANT PROFESSOR,

DEPARTMENT OF CARDIOLOGY, IGIMS, PATNA

ABSTRACT

The role of iron deficiency anemia has long been a part of assessing reversible and treatable contributors to patients symptoms in heart failure. Recent studies have demonstrated how vital identifying not only anaemic patients but those who are iron deficient without anemia, may allow clinicians to impact their quality of life by several different measures. The latter appears to be the case not only for reduced ejection fraction but also impacts patients with preserved ejection fraction who have very few other modalities which improve symptoms. With improvements in diagnosis and management, it has led to a better understanding of the importance of iron deficiency in cardiac failure and function.

Keywords : Ferric carboxylates, heart failure, intravenous iron, iron deficiency, treatment

INTRODUCTION

Iron deficiency has previously been considered clinically significant only in the setting of anemia in patients with heart failure. Treating the cause of anemia was the strategy to improve the hemoglobin and therefore improve the exercise capacity, ejection fraction, and symptoms [1]. Recent literature has illuminated the fact that iron deficiency, even in the setting of normal hemoglobin, has a high impact on a heart failure patient's symptoms and outcomes.

Definition of iron deficiency in heart failure

The definition of iron deficiency in heart failure differs from that of the general population because heart failure is a chronic inflammatory disease. Iron deficiency in heart failure is defined as a ferritin level less than 100ng/ml (absolute iron deficiency) or between 100 and 299 ng/ml and a transferrin saturation (TSAT) of less than 20% (functional iron deficiency) [2]. Definitive testing should currently be avoided in the setting of an acute heart failure exacerbation because of the variation of ferritin and TSAT [3]. Absolute iron deficiency is reduced or absent storage of iron in the bone marrow, liver, and spleen. Functional iron deficiency is normal or increased total body iron stores which are unavailable for incorporation into erythroid precursors for erythropoiesis [4].

Iron physiology and clinical effects in heart failure

Iron has an essential role in cardiac physiological processes, including oxygen transport, oxygen storage, oxidative metabolism, lipid, DNA, and RNA metabolism, as well as muscular oxidative metabolism [5]. The hepcidin/ferroportin axis controls systemic iron homeostasis. Hepcidin is the hormone that controls systemic iron availability through the binding of ferroportin. Ferroportin is an iron export protein that releases iron into the circulation from its storage [6]. Hepcidin production is stimulated in inflammation and suppressed by hypoxia. Hepcidin levels, as well as serum soluble transferrin receptor level, have also been proposed as possible markers of iron deficiency and the later has also been found to have prognostic value in chronic heart failure [7]. The cause of iron deficiency likely stems from this in combination to those absolute causes such as gastrointestinal losses, poor nutrition, and malabsorption [8]. Iron deficiency had previously been thought to have clinical consequences only in the setting of *anemia. Iron deficiency without anemia, however, is a significant contributor to increased mortality and hospitalization for heart failure. Despite this, iron deficiency is often underdiagnosed and under- treated. Iron deficiency has an estimated prevalence of 30 – 79%, but patients are commonly overlooked even to undergo screening [9]. Iron deficiency in heart failure with reduced ejection fraction (HFrEF) has been more extensively studied and is more prevalent in women in those with advanced NYHA class, in those with a higher plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP) and higher serum have C-reactive protein (CRP) [10]. Heart failure with preserved ejection fraction (HFpEF) has a prevalence of iron deficiency of 59%, and those patients are associated with a lower VO2max, worse health-related QoL and 6- min walk test [11]. It has also been shown to increase the risk of mortality by 40–60% [12].*

Non-anemic iron-deficient patients have worse clinical outcomes than anemic iron-replaced patients suggesting iron deficiency affects the heart directly and distinctly different than anemia alone. Recent work from Rineau et al. [14] demonstrated that iron deficiency without anemia was associated with decreased exercise capacity and reduced left ventricular ejection fraction in mice as well as reducing mitochondrial complex I. These abnormalities are reversed when iron is replaced intravenously, which is a theory that may explain why treatment is beneficial. Trials investigating skeletal muscle energetics such as FERRIC-HF II have shown that a total repletion dose of iron isomaltoside given at a single sitting was associated with faster skeletal muscle demonstrating better mitochondrial function. These underline the possible importance of skeletal changes despite very little change in haemoglobin. [15].

Iron in the myocardium has also been noted on T2 cardiac magnetic resonance imaging (CMR) (16).

Iron treatment in heart failure

Treatment of heart failure has remained complex and focused on improving both the morbidity and mortality of this common chronic disease. Initially, research began with erythropoietin because of the chronic inflammatory disease, which was not beneficial and had been linked to increased thromboembolic events [17]. There has also been evidence to prove little benefit with oral iron in the setting of iron deficiency in heart failure. The latter is likely because of poor absorption, low rates of adherence, and gastrointestinal side-effects and has not been shown to replete iron stores [18]. In the IRONOUT HF trial, the results did not support the use of oral iron in HFrEF with iron deficiency. There were no significant differences detected in natriuretic peptides, pVO2, 6MWT, or KCCQ scores [19]. Even posthoc analysis failed to identify any responders who might derive a benefit from oral iron therapy; therefore, we should not use it routinely in symptomatic HFrEF and iron deficiency [20].

Intravenous iron treatment has shown much more promise in modifying the risks of iron defi- ciency. The two preparations most studied and sup- ported by heart failure trials include ferric carboxymaltose (FCM) and iron sucrose [21].

In the FAIR-HF trial, 459 patients with heart failure and ejection fraction less than 40 – 45%, NYHA class II or III and iron deficiency and a con- centration of Hgb 95 – 135 g/l were assigned 2:1 FMC 200mg IV versus saline [22]. It was given weekly until iron repletion (correction phase) and then every four weeks starting week 8 or 12 (maintenance phase). Those receiving FMC reported 50% versus 28% improvement in the Patient Global Assessment [OR 2.51; 95% confidence interval (CI) 1.75 – 3.61]. Improvement of NYHA to class I or II at week 24 was 47 versus 30% (OR 2.40; 95% CI 1.55 – 3.71). The secondary endpoint of distance on the 6-min walk test and in the QoL EQ-5D score and Kansas City Cardiomyopathy score also showed significant improvements. The results were independent of the presence of anemia, demonstrating that the iron deficiency appeared to be the more critical factor. There were no statistically significant differences in the rates of adverse events, serious adverse events, or death.

The CONFIRM-HF trial looked at a similar pop- ulation of symptomatic patients with an ejection fraction less than 45% and iron deficiency random- ized 1:1 FMC versus saline for 52 weeks. The latter improved the 6MWD test at week 24 and continued consistently to the end of the trial (difference 36 þ 11 min; P < 0.001). This was associated with improvements in NYHA class and QoL measures. This was also the first trial to show a drop in the risk of hospitalization for worsening heart failure (HR 0.39; 95% CI 0.19 – 0.82, P 1⁄4 0.009) [23].

There have been several meta-analyses of IV iron in HFrEF. The most recent from Zhou et al. [24&&] which demonstrated iron supplementation significantly reduced hospitalization for worsening heart failure (OR 0.39; 95% CI 0.19 – 0.80) and also the combined endpoint of death and heart failure hospitalization (OR 0.47; 95% CI 0.32 – 0.69). They again saw improvements in 6MWT, LVEF, pVO2max, KCCQ score, European Quality of Life-5 Dimensions score, and Minnesota Living with Heart Failure Questionnaire score. They also had definitive improvements in CRP and NT-proBNP. More work is underway in trying to further understand iron deficiency in both HFrEF and HFpEF.

Treatment of iron deficiency in heart failure: guidelines

The 2017 AHA/ACC Guidelines have made recommendations about iron deficiency for the very first time and created a class IIb recommendation to use IV iron to treat those patients with class II and III heart failure with iron deficiency and do not specify which agent to utilize for therapy [25]. The ESC guidelines have been early adopters and also only advocate for the use of ferric carboxymaltose because of evidence that has come with the drug and safety has been demonstrated [26]. The ESC recommends that all patients should undergo iron deficiency testing initially and then yearly to ensure proper replacement and management (Fig. 1).

CONCLUSION

Iron deficiency in heart failure has been increasingly studied and is seen in 50% of heart failure patients. Iron deficiency in heart failure has a modified defi- nition because of the role of inflammation and an increase in the functional iron deficiency given the underlying pathophysiology. Iron deficiency on its own appears to have prognostic importance as dem- onstrated in a decrease in QoL, pVO2, 6MWT, and NYHA class. Patients with iron deficiency, an ejection fraction less than 45% and FC II–III benefit from IV iron therapy with iron sucrose or FCM and do not appear to benefit from oral therapy. IV iron therapy has also been shown to decrease the composite endpoint of hospitalization for heart failure and all-cause mortality. Iron deficiency certainly appears to be one modality to help improve patient QoL, outcomes as well as potentially help decrease overall costs associated with heart failure management.

CCDSI
CLINICAL CARDIO-DIABETIC SOCIETY OF INDIA
BIHAR-JHARKHAND CHAPTER
NEWSLETTER

NOACs REVISITED

Dr. Gautam Kumar, Dr. Ravi Vishnu Prasad**, Dr. Nirav Kumar**, Dr. B. P. Singh ***, Dr. Rahul M Gutte*****

(- Assistant Professor, Department Of Cardiology IGIMS, Patna.,*

***- Additional Professor, Department Of Cardiology IGIMS, Patna.,*

****- Professor & HOD, Department Of Cardiology IGIMS, Patna.,*

*****- DM Senior Resident, Department Of Cardiology IGIMS, Patna.,)*

ABSTRACT:

The non-vitamin K antagonist oral anticoagulants (NOACs) or direct-acting oral anticoagulants are a novel class of anticoagulants developed to offer more predictable pharmacodynamic and pharmacokinetic properties compared to vitamin K antagonists (VKAs). Currently, four NOACs are approved by the US Food and Drug Administration (FDA), i.e., Dabigatran [direct thrombin inhibitor (DTI)], apixaban, edoxaban, and rivaroxaban (factor-Xa inhibitors). In phase III randomized trials that included over 100,000 patients, these agents have proven to be at least as effective as vitamin K antagonist for prevention of stroke in patients with non-valvular atrial fibrillation and treatment of venous thromboembolism, and to produce less bleeding, particularly less intracranial bleeding. The article addresses some crucial aspects of NOAC therapy such as measurement of anticoagulant effects, transition between different agents, ensuring drug intake compliance, dealing with dosing errors, management of bleeding complications etc based on the guidance offered by the European Heart Rhythm Association in 2018.

INTRODUCTION:

Until 2010, the VKAs such as warfarin were the only available oral anticoagulants to protect against stroke in patients with AF. Slow drug onset, drug–drug and drug–food interactions, genetic polymorphisms in CYP2C91 & the vitamin K epoxide reductase complex subunit2 and patient factors including co morbidities all affect the pharmacokinetic properties, dosing requirements and anticoagulant effect of warfarin, making it an unpredictable drug requiring regular monitoring.

The NOACs (previously referred to as new or novel oral anticoagulants3) were developed to provide efficacious anticoagulant drugs with rapid onset, a favourable side effect profile and predictable pharmacokinetic properties obviating the need for therapeutic drug monitoring.4

Currently, four NOACs are approved by the US Food and Drug Administration (FDA), i.e., Dabigatran [direct thrombin inhibitor (DTI)], apixaban, edoxaban, and rivaroxaban (factor-Xa inhibitors).

ELIGIBILITY FOR NOACs:

NOACs are approved for stroke prevention in non-valvular atrial fibrillation (AF) . Strictly, the term 'non valvular AF' refers to AF in the absence of a mechanical prosthetic heart valve or moderate to severe mitral stenosis (usually of rheumatic origin).

Table1 Indications and contraindications for NOAC therapy in AF patients

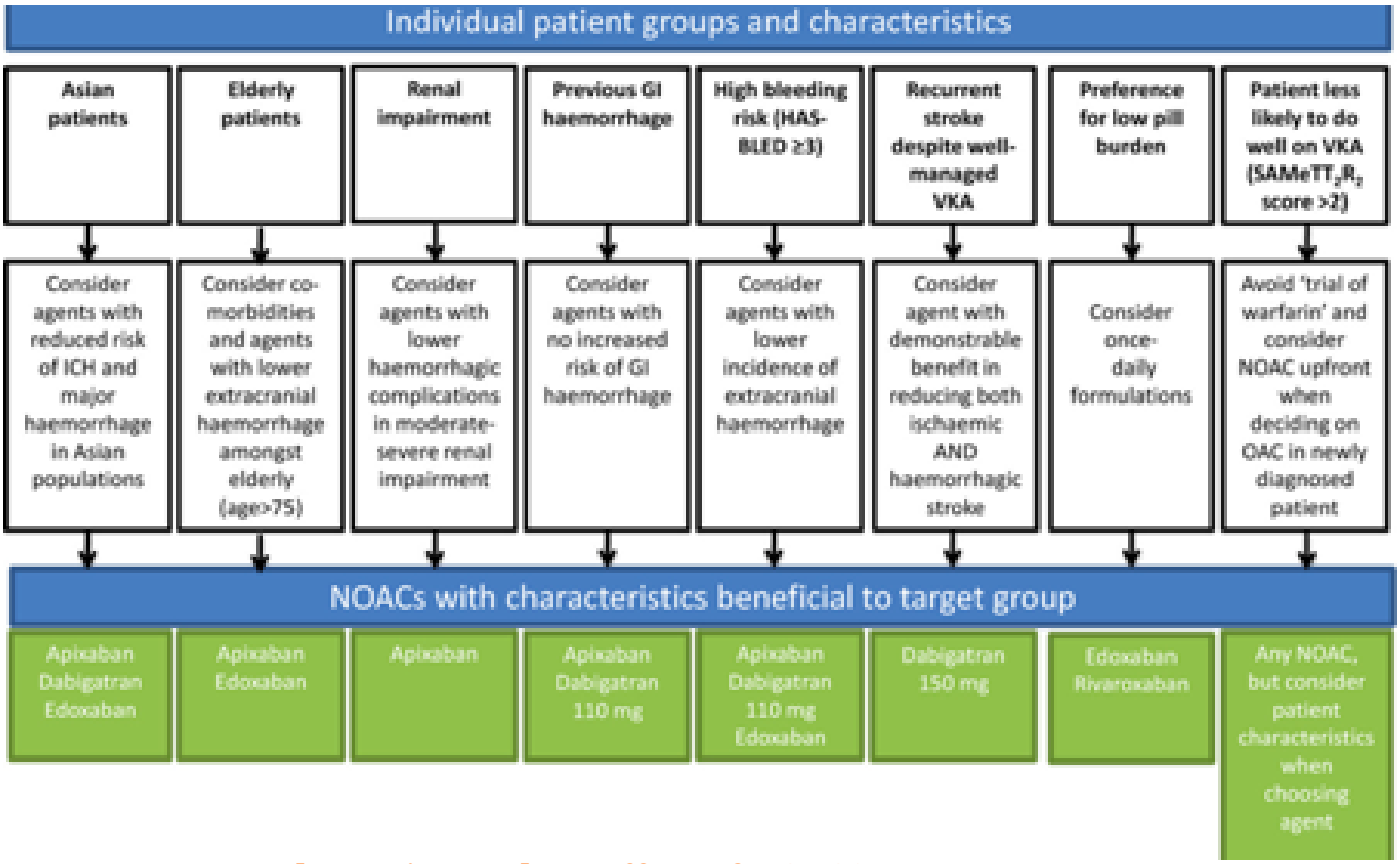
Condition	Eligibility for NOAC therapy
Mechanical prosthetic valve	Contraindicated
Moderate to severe mitral stenosis (usually of rheumatic origin)	Contraindicated
Mild to moderate other native valvular disease (e.g., mild-moderate aortic stenosis or regurgitation, degenerative mitral regurgitation etc.)	Included in NOAC trials
Severe aortic stenosis	Limited data (excluded in RE-LY) Most will undergo intervention
Bioprosthetic valve (after > 3 months post operatively)	Not advised if for rheumatic mitral stenosis
	Acceptable if for degenerative mitral regurgitation or in the aortic position
Mitral valve repair (after > 3 months post operatively)	Some patients included in some NOAC trials
PTAV and TAVI	No prospective data yet May require combination with single or dual antiplatelet therapy
Hypertrophic cardiomyopathy	Few data, but patients may be eligible for NOACs

PRACTICAL ISSUES ASSOCIATED WITH USE OF NOACS:

Clinicians in India though eager to switch to NOAC, have approached these drugs with caution because of lack of knowledge on their proper use. Dr. Sachdeva, in his report states that shorter half-life of dabigatran may have implications in AF patients with poor compliance; with no INR guide and lack of antidotes for these drugs, reversal may be a big issue. Dose adjustment in hepatic and renal dysfunction and higher cost of these drugs compared to warfarin are of concern.5 European Heart Rhythm Association (EHRA) has tried to address these issues to provide a coordinated guidance to physicians.6

Which NOACS to use?

Following figure summarizes individual patient group in which one NOACs can be used preferably over on the basis of multiple subgroups and post hoc analysis, and metanalysis.



How to measure the anticoagulant effect of NOAC?

NOACs do not require routine monitoring or dose adjustment except in emergency where the drug exposure assessment is required. The activated partial thromboplastin time (aPTT) shows a curvilinear response to dabigatran concentration and becomes incoagulable at higher concentrations. Similarly, prothrombin time (PT) provides information on presence of factor Xa inhibitors. Quantitative tests for DTI and FXa inhibitors [thrombin clotting time (TT), activated clotting time (ACT)] are sensitive tests to evaluate the anticoagulant effects of dabigatran.6,7

Switching between anticoagulant regimens

Switching from VKAs to NOAC can be immediate if the INR is < 2.0. However, while switching from NOAC to warfarin, both should be administered concomitantly until the INR is in the desired range

(about 5-10 days due to the slow onset of action of warfarin). Since NOACs may have an additional influence on INR during the overlap phase, INR should be measured just before the NOAC dosing and re-tested 24 hours after the last NOAC dose (i.e. sole warfarin therapy) to assure adequate anticoagulation. It is also recommended to closely monitor INR within the first month until stable values are attained (i.e. three consecutive measurements between 2 and 3)7

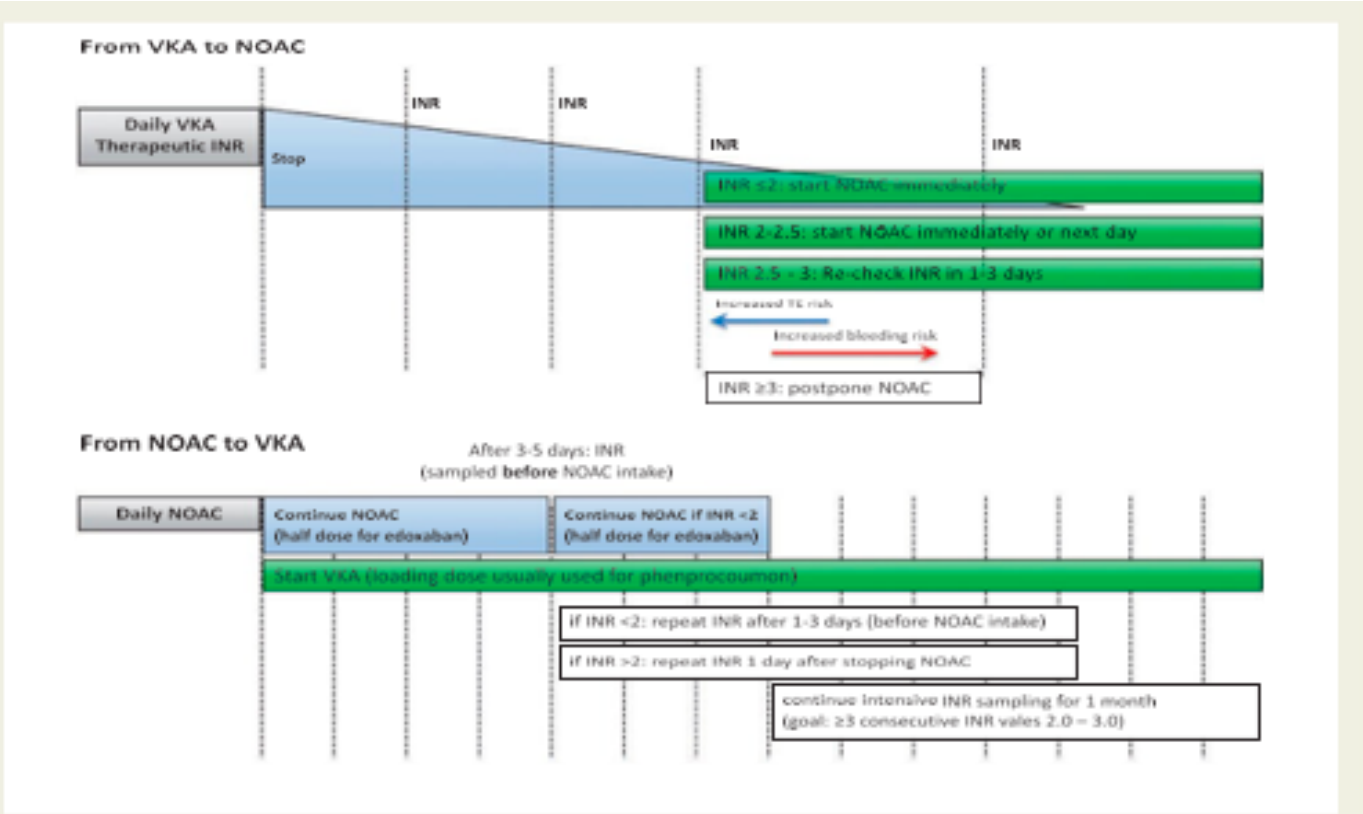


Figure2 Switching between vitamin K antagonists and non-vitamin K antagonist oral anticoagulants and vice versa. TE, thromboembolic.

Ensuring compliance with NOAC intake

Ensuring compliance with NOAC intake is vital because the anticoagulant effect drops rapidly after 12–24 hours. Physicians should develop ways to optimize compliance which is known to be ⩽80% for most drugs in daily practice. If low compliance persists, switch to VKAs may be appropriate.

How to deal with dosing errors?

In case of a missed dose, the forgotten dose can be taken up to 6 hours or upto 12 hours after the scheduled intake for a BID or QD regimen respectively. If this is not possible, the dose should be skipped and the next scheduled dose taken. Incase of a double dose on a BID regimen, next planned dose can be skipped and restarted BID after 24 hours while in OD dosing, normal regimen can be continued. In case of overdose, dialysis removes dabigatran. Rivaroxaban and apixaban are not dialyzable.8

NOAC use in chronic kidney disease (CKD)

Approximately 80%, 33%, and 25% of dabigatran, rivaroxaban, and apixaban, respectively, are eliminated renally. NOACs may be used in AF patients with mild or moderate CKD. Dose reductions are indicated in patients with CrCl< 30 mL/min), and the current ESC guidelines recommend against their use in such patients although USFDA allows reduced doses of all three NOACs (CrCl: 15 to 29 mL/min: dabigatran: 75 mg BID, rivaroxaban 15 mg QD; apixaban: 2.5 mg BID). NOACs (except apixaban) should be avoided in AF patients with haemodialysis.

Management of bleeding complications

Bleeding rates with NOACs are generally equal to or less than warfarin bleeding rates.9,10 There is no specific antidote for NOACs; in case of bleeding NOACs should be discontinued and assessment of severity of bleeding should be done. Minor bleeding can be managed with simple delaying of the next dose. Moderate bleeding such as upper/lower GI can be managed by treating the bleeding source. Adequate diuresis is recommended for all NOACs, but particularly in case of dabigatran. In addition, dialysis may be an option for non life-threatening, severe bleeding with dabigatran in cases of severe renal failure if idarucizumab is not available.11,12 Incontrast, dialysis has no significant impact in patients treated with any of the FXa inhibitors.13,14 The use of antifibrinolytics, especially in special situations with associated coagulopathy or thrombopathy – may be considered. Adequate diuresis, RBC transfusion, platelet substitution, FFPas plasma expander (not as reversal agent) and dialysis may be considered if required. For major life-threatening bleeding, in addition to above measures, prothrombin complex concentrate (PCC) may be used.

When to stop and reinitiation

NOACs in patients undergoing common surgical interventions with no clinically important bleeding risk can be performed at trough NOAC concentration (i.e. 12 or 24 hours after the last intake, depending on BID or QD regimen. Peri-operative NOAC interruption for dabigatran [1-2 days and 2-4 days depending upon CrCl in low and high bleeding risk respectively] is more than rivaroxaban/ apixaban [1 and 2 days respectively for low and high bleeding risk]. Resumption of NOACs could be recommenced as early as 12-24 hours (low bleeding risk and high thromboembolic risk) to >72 hours (high bleeding risk and low thromboembolic risk) post-surgery upon ensuring haemostasis .

How to manage a patient with AF and Coronary Artery Disease (CAD)

In patients presenting with both AF and CAD, dual therapy [OAC (NOAC or a VKA) + clopidogrel] for 4 weeks after PCI followed by dual therapy (OAC + clopidogrel or alternatively, aspirin) up to 12 months. Long term antithrombotic therapy with OAC (i.e. whether NOAC or a VKA) (beyond 12 months) is recommended in all patients.

How to manage patients presenting with acute ICH or ischemic stroke while on NOAC?

Limited data is available regarding NOAC use in AF patients presenting with acute ICH or ischemic stroke. The coagulation status of patients under NOAC who have acute ICH should be corrected rapidly and NOAC should be discontinued. For ischemic stroke, thrombolytic therapy with recombinant tissue plasminogen activator is not recommended in patients taking NOACs because of increased bleeding risk within 48 h of last NOAC dose.

Management of bleeding complications

Bleeding rates with NOACs are generally equal to or less than warfarin bleeding rates.9,10 There is no specific antidote for NOACs; in case of bleeding NOACs should be discontinued and assessment of severity of bleeding should be done. Minor bleeding can be managed with simple delaying of the next dose. Moderate bleeding such as upper/lower GI can be managed by treating the bleeding source. Adequate diuresis is recommended for all NOACs, but particularly in case of dabigatran. In addition, dialysis may be an option for non life-threatening, severe bleeding with dabigatran in cases of severe renal failure if idarucizumab is not available.11,12 Incontrast, dialysis has no significant impact in patients treated with any of the FXa inhibitors.13,14 The use of antifibrinolytics, especially in special situations with associated coagulopathy or thrombopathy – may be considered. Adequate diuresis, RBC transfusion, platelet substitution, FFPas plasma expander (not as reversal agent) and dialysis may be considered if required. For major life-threatening bleeding, in addition to above measures, prothrombin complex concentrate (PCC) may be used.

When to stop and reinitiation

NOACs in patients undergoing common surgical interventions with no clinically important bleeding risk can be performed at trough NOAC concentration (i.e. 12 or 24 hours after the last intake, depending on BID or QD regimen. Peri-operative NOAC interruption for dabigatran [1-2 days and 2-4 days depending upon CrCl in low and high bleeding risk respectively] is more than rivaroxaban/ apixaban [1 and 2 days respectively for low and high bleeding risk]. Resumption of NOACs could be recommenced as early as 12-24 hours (low bleeding risk and high thromboembolic risk) to >72 hours (high bleeding risk and low thromboembolic risk) post-surgery upon ensuring haemostasis .

How to manage a patient with AF and Coronary Artery Disease (CAD)

In patients presenting with both AF and CAD, dual therapy [OAC (NOAC or a VKA) + clopidogrel] for 4 weeks after PCI followed by dual therapy (OAC + clopidogrel or alternatively, aspirin) up to 12 months. Long term antithrombotic therapy with OAC (i.e. whether NOAC or a VKA) (beyond 12 months) is recommended in all patients.

How to manage patients presenting with acute ICH or ischemic stroke while on NOAC?

Limited data is available regarding NOAC use in AF patients presenting with acute ICH or ischemic stroke. The coagulation status of patients under NOAC who have acute ICH should be corrected rapidly and NOAC should be discontinued. For ischemic stroke, thrombolytic therapy with recombinant tissue plasminogen activator is not recommended in patients taking NOACs because of increased bleeding risk within 48 h of last NOAC dose.

In case of uncertainty concering last NOAC administration, prolonged aPTT (for dabigatran) or PT (for FXa inhibitors) indicates anticoagulation status. Continuation of NOACs after ischemic stroke depends on the infarct size; as a rough guide the 1-3-6-12 day rule i.e., reinstitution of anticoagulation in patients with transient ischemic attack after 1 day, with small infarct after 3 days, with a moderate stroke after 6 days, while large infarcts not before 2 (or even 3) weeks. NOACs may be restarted 10–14 days after ICH if cardio embolic risk is high and the risk of new intra cerebral haemorrhage is estimated to be low.

CONCLUSION

NOACs offer greater patient compliance, easier management, and improved thromboprophylaxis over traditional anticoagulants. Physicians across India are keen to use NOACs yet hesitant in view of some unanswered questions around them. Safety of NOACs in subjects with renal impairment, in those needing surgery or those presenting with bleeding complications or stroke while on NOACs need more clarity. Though ESC/EHRA offer very useful guidance to physicians across the globe pertaining to these issues, more consolidated opinions from physicians across India based on their experience with these drugs is much needed.

REFERENCES

1. Aithal GP, Day CP, Kesteven PJ et al. Association of polymorphisms in the cytochrome P450 CYP2C9 with warfarin dose requirement and risk of bleeding complications. Lancet 1999; 353: 717– 9.
2. D'Andrea G, D'Ambrosio RL, Di Perna P et al. A polymorphism in the VKORC1 gene is associated with an interindividual variability in the dose-anticoagulant effect of warfarin. Blood 2005; 105: 645– 9.
3. Husted S, de Caterina R, Andreotti F et al. Non-vitamin K antagonist oral anticoagulants (NOACs): no longer new or novel. ThrombHaemost 2014; 111: 781– 2.
4. Yeh CH, Fredenburgh JC, Weitz JI. Oral direct factor Xa inhibitors. Circ Res 2012; 111: 1069– 78.
5. Sachdeva A, Biswajit P. Direct Thrombin Inhibitors versus Warfarin in Non- Valvular Atrial Fibrillation. Journal of the Association of Physicians of India 2014; 62:361-2
6. Heidbuchel H, Verhamme P, Alings M, Antz M, Hacke W, Oldgren J, et al. EHRA practical guide on the use of new oral anticoagulants in patients with nonvalvular atrial fibrillation: Executive summary. Eur Heart J 2013; 34:2094-106
7. Shulman S and Crowther MA. How I treat with anticoagulants in 2012: new and old anticoagulants, and when and how to switch. Blood 2012; 119:13.
8. Van Ryn J, Stangier J, Haertter S, Liesenfeld K, Wienen W, Feuring M, et al. Dabigatran etexilate – a novel, reversible, oral direct thrombin inhibitor: interpretation of coagulation assays and reversal of anticoagulant activity. ThrombHaemost 2010; 103:1116–1127
9. Eikelboom J, Wallentin L, Connolly S, Ezekowitz M, Healey J, Oldgren J, et al. Risk of bleeding with 2 doses of dabigatran compared with warfarin in older and younger patients with atrial fibrillation: an analysis of the randomized evaluation of long-term anticoagulant therapy (RE-LY) trial. Circulation 2011; 123:2363–2372.
10. Lip GY, Andreotti F, Fauchier L, Huber K, Hylek E, Knight E, et al. European Heart Rhythm Association. Bleeding risk assessment and management in atrial fibrillation patients. Executive summary of a position document from the european Heart Rhythm Association [EHRA], endorsed by the European Society of Cardiology [ESC] working group on
11. Stangier J, Rathgen K, Stahle H, Mazur D. Influence of renal impairment on the pharmacokinetics and pharmacodynamics of oral dabigatran etexilate: an openlabel, parallel-group, single-centre study. Clin Pharmacokinet2010;49:259–268.
12. Getta B, Muller N, Motum P, Hsu D, Zebeljan D, Rosenfeld D. Intermittent haemodialysis and continuous veno-venous dialysis are effective in mitigating major bleeding due to dabigatran. Br J Haematol2015;169:603–604
13. Parasrampuria DA, Marbury T, Matsushima N, Chen S, Wickremasingha PK, He L, Dishy V, Brown KS. Pharmacokinetics, safety, and tolerability of edoxaban in end-stage renal disease subjects undergoing haemodialysis. ThrombHaemost2015;113:719–727.
14. Wang X, Tirucherai G, Marbury TC, Wang J, Chang M, Zhang D, Song Y, Pursley J, Boyd RA, Frost C. Pharmacokinetics, pharmacodynamics, and safety of apixaban in subjects with end-stage renal disease on hemodialysis. J Clin Pharmacol2016;56:628–636.nt haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet 2010;376:23–32.