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MEDICINE UPDATE

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INTRODUCING...

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1 What is the protocol for patients using Direct acting Oral AntiCoagulants (DOAC) – who are awaiting surgery?.

DOACs have short half lives, and withholding these agents for only a few days should be possible when they require interruption of anticoagulation around the time of elective surgery.

3,007 adults with atrial fibrillation scheduled for elective surgery receiving long term DOACs were studied. The following protocol was adhered to:

1) For surgical procedures with low risk for bleeding, DOACs were **withheld for 1 day and restarted after 1 day.**

2) For surgical procedures with higher risk for bleeding, DOACs were **withheld for 2 days and restarted 2-3 days after surgery.**

The 30 day post operative outcomes were as follows.

1. Rates of major bleeding varied from 0.9% to 1.9%.
2. Rates of bleeding in surgical procedures with high bleeding risks varied from 0.9% to 3.0%
3. Rates of arterial thromboembolism (due to withdrawal of anticoagulation) varied from 0.2% to 0.6%.

Comment: These results met the predetermined goals for rates of perioperative major bleeding of <2.0% and of arterial thromboembolism of < 1.5%. In the absence of an accepted perioperative standardized protocol in the use of DOACs undergoing surgical procedures – this is an acceptable simple protocol.

Ref:Douaetis J.D. et al JAMA Intern.Med 2019 Aug 5; e pub.

2 Does the use of Aspirin increase the bleeding risk after percutaneous core biopsies?.

It is known that use of Aspirin is safe during procedures such as aspiration of joints, pleural effusions and lumbar puncture. What about image guided core needle biopsies such as the kidney, liver or the lungs?.

Mayo clinic researchers analysed the data base on Aspirin usage just prior to 30,000 percutaneous biopsies performed by Radiologists under CT or ultra sound guidance.

Bleeding complications that required transfusions or interventions (radiologic, endoscopic or surgical) occurred in 0.3% overall of patients. Number needed for harm (NNH) 330. The risk for those who stopped Aspirin 0 – 3 days before biopsy was 0.6% (NNH = 1/160) and 1.9% in patients who took Aspirin on the day of their biopsy (NNH = 51). Stopping Aspirin **4-7 days or 7-10 days** before the procedure was not associated with bleeding complications.

Comment: These data suggest the risk for important bleeding complications are uncommon but not negligible. Stopping Aspirin **about 5 days** before the procedure apparently would eliminate excess risk. The risk for breakthrough thrombotic events during the 5 days without Aspirin is difficult to quantitate.

Ref:Potretzke T.A. et al A J R Am.J.Roentgenol 2019 July; 213: 211.

3 A new procedure in Cardiology – Hand held bedside Cardiac Ultrasound.

Ultrasound examinations have rapidly grown and recently a hand held ultrasound device has been introduced. This permits extension of the physical examination of the heart enhancing diagnostic accuracy. Compared with physical examination alone incorporating this procedure has significantly increased sensitivity for detecting left ventricular dysfunction and moderate aortic or mitral valve disease.

Comment: This procedure enhances the Clinician's diagnostic capability. What we do not know for certain yet is whether it changes patient's outcomes.

Ref:Marbach J.A et al Ann.Intern.Med 2019 Aug 20; 171: 264.
Flint N. and Siegel R.J. IBID : 291.

4 In patients with Chronic Kidney Disease (CKD) and either atrial fibrillation (AF) or venous thromboembolism (VTE) – what is the safest antithrombotic agent?.
Apixaban 5mg/d

CKD (eGFR< 60ml/mt) or end stage renal disease (ESRD) – eGFR< 30ml/mt are considered prothrombotic states but are often excluded from the use of anti thrombotic agents. Investigators performed a meta analyses of 45 randomized trials,which included 34,000 patients with CKD or ESRD, to assess the efficacy and safety of direct acting oral anticoagulants (DOACs) compared with Vitamin K antagonists (VKAs) for managing AF or VTE.

In these patients with CKD and AF, DOACs significantly lowered the incidence of stroke or systemic embolism compared with VKAs (4% vs 5%, NNT 100) or Aspirin 2% vs 6% (NNT = 25) and conferred significantly lower risk for intracranial haemorrhage compared with VKAs (1 % vs 2% NNT =100)

In patients with ESRD no randomized trials of DOACs for managing AF or VTE has been conducted.

Comment: In patients with CKD – DOACs were superior both to prevent systemic embolism and intracranial haemorrhage compared to both VKAs and Aspirin. In patients with CKD and VTE, the use of DOACs was not superior to VKAs. In patients with ESRD – 3 on going trials will inform efficacy and safety in this high risk population.

Ref:Ha J.T et al Ann.Intern.Med 2019 Aug 6th; 171: 181.
Hildebrand A. et al IBID : 214.

5 A new treatment for Idiopathic Pulmonary Fibrosis (IPF) –

Nintedanib (ND) 150mg/d or Pirfenidone (PF) 200 - 2400mg/d

In 2014, two new drugs ND and PF were approved for IPF. Both medications slow the progression of the disease on pulmonary function tests. Neither improved the quality of life and both had substantial side effects – nausea and rash with PF, diarrhoea and abnormal liver function tests with ND. No head to head comparisons with these two agents have been done.

Using US insurance and Medicare data from 2014 – 2018, Investigators have now compared 1,255 ND or PF treated IPF patients with 1,255 propensity matched but untreated IPF patients. Most were men and average age 72. About half the patients had received Prednisolone in the preceding 6 months and nearly 60% used supplemental Oxygen. Treated patients were significantly less likely than untreated patients to have been hospitalized (47vs 62 per 100 patient years) or to have died (14 vs 16 per 100 patient years). The latter benefit was only significant during the first two years of follow up. Outcomes were similar in the ND and PF subgroups.

Comment: This observational study supports trial data that suggested mortality benefits with both agents. Either medication is reasonable for initial treatment. Choice of which agent to start with should focus on the side effect profiles, cost and availability of the two drugs.

Ref: Dempsey T.M. et al Am.J.Respir.Crit.Care Med 2019 July 15; 200:168.

6 Diagnosis of Giant cell Arteritis (Temporal Arteritis) GCA.

GCA patients present usually after the age of 50 with either jaw claudication, unilateral headache or visual symptoms.

Investigations include:

1. ESR - high.

2. Temporal artery biopsies.
3. Ultra sound of temporal artery which shows irregularity and narrowing of the lumen and thickening of the arterial walls – user dependent.
4. 18F -= FDG PET/CT to view only the head and neck, temporal, maxillary and vertebral arteries. Sensitivity of these tests was 64% for uptake in the maxillary or temporal arteries and 82% when the vertebral arteries were included. Specificity was 100%.

Comment: PET CTs are expensive but they appear to be less susceptible to reader variability than ultra sound scans. The absence of false positive results suggest that suspected GCA patients who have positive PET CT results could avoid temporal artery biopsy. When PET CT is not available, temporal artery biopsies need to be performed on the Ipsilateral side of the symptoms and if negative on the contra lateral side.

Ref: Nielsen B.D et al Eur.J.Nucl.Med.Mol Imaging 2019 Jan ; 46: 184.

7 Restarting antiplatelet therapy after an intra cerebralhaemorrhage (ICH).

Patients who are taking anti thrombotic agents occasionally develop ICH. When this happens, the Clinician faces a conundrum – should the anti thrombotic agent be restarted at some stage if there is a valid indication for it?.

To address this question, UK researchers performed a randomized trial involving 537 adults who had spontaneous ICH while **taking antiplatelet or anticoagulant drugs** for preventing occlusive vascular disease. About quarter of these patients also had atrial fibrillation. After an interval during which antithrombotic therapy was withheld averaging about **2-3 months**, paients either started **antiplatelet therapy** (Aspirin, Clopidogrel or Dipyridamole) or were instructed to avoid it.

During a median follow up of 2 years, the incidence of recurrent ICH was slightly **lower** in the antiplatelet therapy group compared to the control group (4% vs 9%; P = 0.06). A secondary end point (a composite of non fatal MI, non fatalstroke or vascular death occurred with significantly **lower** frequency in the antiplatelet group (17% vs 24%; P = 0.03).

Comment: This trial suggest that restarting clinically indicated antiplatelet therapy, 2-3 months after an episode of ICH is safe. The incidence of recurrent ICH was lower in the antiplatelet group although it did not reach statistical significance. The secondary end point however of vascular disease or death was lower and statistically significant in the anti platelet treatment group. No mention is made regarding restarting anticoagulants.

Ref: RESTART Collaboration Lancet 2019 June 29; 393: 2613.

Ziai W.C. and Tsiskaridze A. IBID 2567.

8 A technique to decrease intake of sugar sweetened beverages - drink plenty of water.

Sugar sweetened beverages include soda, fruit drinks, sports and energy drinks, sweetened coffee and tea. Efforts to reduce intake of these have been emphasized in order to decrease calorie intake, especially in children. These have replaced intake of water.

Researchers have analysed 24 hour dietary recall data from 8,400 US children. They compared sugar sweetened calorie intake between children who drank any water and those who had none. It was found that no water intake was associated with higher total sugar sweetened beverage calorie and percentage of total calories from sugar sweetened beverages. Approximately twice the sugar sweetened beverage calories were consumed among those with no water intake compared with those who drank water.

Comment: This study supports the American Academy of Paediatrics recent call to lower intake of sweetened drinks and champion water consumption. Water should be the primary drink for all children, adolescents and young adults.

Ref:Rosinger A.Y et al JAMA Paediatr.2019 April22; e pub.

9 A new treatment for Membranous Nephropathy (MN) – Rituximab.

MN is a common cause of nephrotic syndrome in adults. Many patients can be observed without initiating immunosuppressive treatment. On monitoring, if the albuminuria continues to rise, then therapeutic intervention is necessary. Common regimes are either Cyclophosphamide + steroids or Cyclosporine + steroids.

130 adults with MN who exhibited progression were randomized to either Cyclosporine or Rituximab (a CD20 monoclonal antibody). At 24 months, the incidence of complete remission (< 300mg proteinuria /24 hours) or partial remission (proteinuria between 300 – 3,500mg/24 hrs or >50% reduction in proteinuria) was significantly higher with Rituximab (60%) than Cyclosporine (20%). The incidence of serious adverse events was somewhat higher with Cyclosporine than with Rituximab (31 % and 17% resp).

Comment: Currently, Rituximab is reserved for patients with MN whose disease has been resistant to standard therapies that include steroids, cyclophosphamides or Cyclosporine. The results of this study suggest that Rituximab might become a first line treatment option in selected patients. The dose of Rituximab was 500mg iv weekly or 1 gm iv fortnightly.

Ref:Fervenza F.C. et.al NEJ Med 2019 July 4; 381`: 36
Ruggenenti P. and Remuzzi G. IBID: 86.

10 Use of Troponin I estimations in Diabetes with Myocardial Infarction (MI).

Troponin I levels are normally increased in patients with diabetes, obesity , chronic kidney disease, elderly, and microvascular disease at presentation. Troponin I levels are measured at admission and at 3 hours after admission. If levels are normal at presentation, MI can be ruled

out. If the 3 hour levels are increased or if the increment between presentation and 3 hour values increases by 20 – 50% - then MI is ruled in. If patients have increased levels at presentation but no increase in 3 hours – it is best to observe the patient.

Ref:Haller P.M. et al Diabetes Care 2020 Feb ; 43: 460 – 467.

11 What is the mechanism for the Cardio Renal protective effects of SGLT2 Inhibitors (SGLT2Is)?.

SGLT2Is are known to have cardio renal protective effects. These have been attributed to the following:

a) Removal of glucose in the urine which decreases the blood sugar, which prevents toxicity to the renal and myocardial cells.(The blood sugar threshold for glycosuria falls from 180mg /dl to about 40mg/dl).
b) Direct renal protection by increased afferent glomerular artery constriction which leads to decreased intraglomerular hypertension.
c) Increased haematocrit.
d) Decreased Sodium in cardiac myocytes resulting from Natriuresis.
e) Decreased serum uric acid, blood pressure, weight and visceral fat.

A new explanation is that SGLT2Is induce a dormancy at the cellular level, leading to decreased inflammation, anabolic metabolism and adipocity similar to the " hibernation effects" seen in animals and protects against the environment.

Comment: SGLT2Is should be considered to be " organ preserving agents" and not as presently as " blood sugar lowering agents".

Ref:Aragerro A. et al Diabetes Care 2020 March ; 43: 501 – 507.

12 Prevention of Spontaneous Bacterial Peritonitis (SBP) recurrence.

SBP is a complication of ascites due to cirrhosis. The current practice is to start **daily** antibiotics after the 1st episode of SBP to prevent recurrence. Norfloxacin and Ciprofloxacin have been used **daily** (400mg and 750mg resp) for this purpose. Now Researchers undertook an open label 12 month trial of 124 patients with SBP who were randomized to **daily** Norfloxacin 400mg or **weekly** Ciprofloxacin 750mg. No significant difference in SBP recurrence rates were seen between theNorfloxacin and Cipro groups (7% and 5% resp). Infectious and liver related complications and one year transplant free survival rates were similar.

Comment: In this head to head study, **weekly** Ciprofloxacin and **daily** Norfloxacin were equally effective in preventing SBP in high risk patients with cirrhosis and ascites. Whether intermittent antibiotic dosing might select for resistant flora is a real concern.

Ref:Yim H.J. et al Am.J.Gastroenterol 2018 Aug; 113: 1167.

13 A new treatment for Mitral regurgitation – Transcatheter Mitral valve repair (TMVR).

Transarterial aortic valve repair (TAVR) is now established as a procedure for aortic stenosis or regurgitation. A similar procedure has now been introduced for repair of mitral regurgitation especially for patients with heart failure, frequent hospitalization and poor prognosis.

In the manufacturer funded COAPT trial, investigators compared standard medical therapy alone vs TMVR + standard medical therapy in 614 patients with severe MR who were not suitable for open valve surgery. Patients were included only if they had remained symptomatic despite previous standard medical therapy. Follow up was for 24 months. The results were as follows:

1. Heart failure hospitalization was fewer in the device group than in the standard treatment group (36% vs 68% resp).
2. All cause mortality was 29% in the device group and 46% in the standard therapy group.
3. Device therapy also improved symptoms and quality of life and it better preserved functional capacity (6 minute walking distance).
4. At 30 days, mitral regurgitation grade 2 was seen in 90% of the device group and was sustained for 2 years.
5. Rate of freedom from device related complications was 97% at 1 year.

Comment: This is the 1st therapy demonstrating improved prognosis in patients with heart failure and severe secondary MR, despite standard medical therapy. The remarkable difference between the two therapies can be attributed to some extent by the deterioration in the control group and stabilization in the device group. This study provides another option for our patients with heart failure and severe MR.

Ref: Stone G.W et al NEJ Med 2018 Sept 23; e pub.

14 A new drug for Plasmodium vivax malaria - Tafenoquine (TQ) 300mg (O) stat.

Primaquine has been the drug of choice to treat P.vivax malaria in order to decrease relapses due to hepatic hypnozoites. It is given as 15mg once daily for 14 days. TQ is a new addition , given orally in a **single dose**. It is not indicated during pregnancy, lactation or in patients younger than 16 years. Both Primaquine and TQ may cause haemolysis in G6PD deficient patients. Therefore G6PD deficiency needs to be excluded by the NADPH fluorescent spot test before these drugs

are administered. Haemolysis occurs when G6PD levels are <40% of normal. This requires a quantitative G6PD analysis also.

TQ is more convenient than Primaquine as it requires only a single dose, but its half life is 15 days compared to 5 hours only for Primaquine. Therefore the advantage of TQ is lost if there is haemolysis, as the duration would last for 15 days or more, whereas Primaquine administration results in haemolysis only for a day or two. Break through relapses can occur up to one year after treatment. However differentiation of relapses due to activation of hypnozoites has to be distinguished from recurrences.

Ref: Lacerda M.V.G et al NEJ Med 2019 Jan 17; 380:215 – 228.
Llanos – Cuentas A. et al IBID : 229 -241.

15 Can the complication of bleeding by use of Factor X A inhibitors be reversed?.

Bleeding due to Factor X inhibitors such as Apixaban, Rivaroxaban and Edoxaban can occur due to prevention of clotting. Bleeding can be severe and may occur in vital organs such as the brain. Unlike Warfarin, hitherto there has been no known antidote. Now, the bleeding can be decreased or abolished by either

a) **Prothrombin concentrates.**
b) **Andexanet–** a factor XA inhibitor antagonist.

The dose of Andexanet depends on whether the last dose of the inhibitor was given within 7 hours or more. For those whose onset is within 7 hours, the bolus dose is 400 mg and for more than 7 hours 800mg iv over 15 – 30 minutes. This is followed as an iv infusion over 2 hours in a dose of 480mg or 960mg for onset < 7 hours and > 7hours respectively.

Thereafter, it is important to measure the Factor XA inhibitor level at 4, 8 and 12 hours. The volume of bleeding in internal organs or cavities can be assessed by estimation of Hb percent, fall of BP and by imaging modalities such as CT and MRI. Blood transfusion may be required in cases of shock. Haemostatic efficacy at 12 hours is 82% for Andexanet and 72% for Prothrombin concentrate. After reversal of the bleeding, Factor XA inhibitors need to be restarted at a lower dose to prevent clotting in the vascular system.

Ref: Connolly S.D t al NEJ Med 2019 April 4; 180: 1326 – 1335.

16 Iron Chelation therapy.

Iron chelators remove Iron from the body and are useful in conditions in which Iron accumulation results in destruction of parenchymal cells.

Indications :

1. Haemochromatosis (genetic).
2. Thalassaemia major.
3. Sickle cell anaemia.
4. Myelodysplastic syndrome.
5. Aplastic anaemia.
6. Congenital sideroblastic anaemia.
7. Myelofibrosis.

In the majority of the above conditions, recurrent blood transfusions are required and this accumulates Iron in the organs. Some neurodegenerative diseases such as **Parkinsonism** and **dementia** may also accumulate Iron in the brain which is detectable by diffusion weighted MRI scans of the brain. They also may benefit from Iron chelation therapy. Iron chelators are used when the **serum ferritin exceed 800 mg/ml** (normal < 100mg/ml) or **transferrin saturation exceeds 70%** (normal 33%).

Drugs: Drugs available are

1. Deferroxamine – given sc or iv over 12 hours, 2-5 times a week.
2. Deferiprone - oral given as 100mg/d,increased gradually to a maximum of 7,000mg/d.
3. Deferasirox – oral 60mg/Kg/day.
4. Combination of Deferiprone + Deferroxamine – removes Iron better than either alone.

Benefits:

1 Prolongs life and decreases complications such as heart failure, arrhythmias and liver disease.

2 Decreases hormonal deficiencies that occur due to Iron deposition in the pituitary, thyroid, parathyroid, adrenals, pancreas and gonads.

Side effects: The most important side effect is agranulocytosis. Others include abdominal pain, vomiting, transient increases in liver enzymes, arthropathy, neutropaenia and Zinc deficiency mainly in diabetics.

Comment: Monitoring for side effects include full blood counts, serum ferritin, serum Iron and TIBC, Liver function tests and ECG. In neurological diseases assessment of brain iron by MRI brain is useful.

Ref: Hider R. and Hoffbrand A. NEJ Med 2018 Nov 29; 379: 2140 – 2150.

17 Elimination of chronic viral hepatitis (CVH).

Death due to combined hepatitis B and Hepatitis C exceed the deaths due to combined TB + malaria + HIV in the world. A vaccine is available for Hepatitis B but not for Hep C. Curative treatment is available for HepC but not for HepB.

Prevention of Hep C:

1. Prevent reuse of syringes and needles.
2. Avoid tattooing ,scarifications .
3. Screen blood for Hep C before transfusion by looking for Hep C antibodies and RNA.
4. Avoid opioid use.
5. Avoid perinatal transfusion by measuring Hep C antibodies, Hep C RNA and core antigen in the mothers – which are now available by finger stick methods.
6. Avoid men having sex with men.

Hep C infections are usually asymptomatic. Treatment for 8 – 12 weeks with antiviral drugs can eliminate the virus in 95% of patients. The price of a complete 12 week course is now available for US$ 100 (SL Rs.19,000). When treatment is given before cirrhosis occurs, both cirrhosis as well as future cancer is prevented. However, if cirrhosis is present before initiation of treatment, then cancer of the liver incidence will be decreased but not eliminated.

Prevention of Hepatitis B:

Hep B infection mostly starts in the mother and is transmitted to the infant during delivery or in early childhood. Onset in adult life is much less frequent.

Preventive measures:

1. Administration of Hep B vaccine in 3 doses alone or as a pentavalent vaccine incorporated with diphtheria, tetanus, pertussis and haemophilus influenza. It is ideally given shortly after birth, preferably in the first 24 hours.
2. Children of Pregnant women with Hep B > 200,000 units /ml should be given Hep B immunoglobulin.
3. Avoid sex with multiple partners.
4. Avoid sharing syringes and needles and drug use.

Blood test required include Hep B surface antigen, Hep B DNA, Hep B e antigen, liver enzymes and full blood count. Treatment for Hep B is prolonged as cure is unlikely but the level of Hep B virus is kept at a minimum.

Ref: Thomas D.L. NEJ Med 2019 May 23rd; 380: 2041 – 2050.

18 Are statins indicated for primary prevention in the very elderly(>75 yrs)?.

Guidelines classify most elders >75 yrs as eligible for statin therapy because CVD risk is highly associated with age. There is little evidence to support primary prevention in this category of patients. To address this question, Researchers in Spain determined whether initiating statins (for primary prevention lowers risk for CV disease and all cause death) was useful in 47,000 elders over the age of 75 without prior CVD. 16% of these were on statins and 84% without statins. After multivariable adjustments, statins **did not** lower CVD or all cause death in non diabetics. Among **diabetics**, statins significantly **lowered** risks for CVD and all cause death. However, in diabetics over 85, statins did not lower risks for CVD and all cause death.

Comment: In non diabetics, statins did not reduce CVD above the age of 75, in those who had no prior CVD. Statins was useful for primary prevention in diabetics between the ages of 75 – 85 but not above 85 years.

Ref: Ramos R. et al BMJ 2018 Sept 5; 362: k3359.

19 Should uncomplicated acute appendicitis be treated with antibiotics or by surgery?.

Studies have shown that most patients with uncomplicated acute appendicitis can be treated successfully in the short term with antibiotics. However, many patients undergo surgery in the 1st instance because long term recurrence rates are unknown. Finnish researchers conducted a one year study in which antibiotic therapy was compared with appendicectomy to determine 5 year recurrence among 530 adults (mean age 35) with uncomplicated acute appendicitis which was confirmed by a CT abdominal scan. The antibiotic group received **Ertapenem** 1g iv daily for 3 days followed by oral **Levofloxacin** and **Metronidazole** for 7 days.

At 5 years, 39% in the antibiotic group experienced recurrences, underwent surgery (27% within 1 year and 12% in years 2-5). In the surgery group, 24% had complications – mostly superficial wound infection, incisional pain and hernias. In the original antibiotic group 6% experienced complications.

Comment: 60% of patients with uncomplicated acute appendicitis who received antibiotics instead of immediate surgery experienced no recurrence in the subsequent 5 years. Recurrences, if they occurred, was usually within 1 year. Giving the patient a choice of either surgery or medical treatment for uncomplicated CT diagnosed acute appendicitis seems reasonable.

Ref:Salminen P et al JAMA 2018 Sept25; 320: 1259.
Livingston E.H. IBID : 1245.

20 What do we know of "Clinician burn out"?.

Half of all clinicians are said to suffer from burn out. Investigators addressed this issue in a systematic review and in a new prospective study. The following questions were asked from the participants.

1. Are you emotionally exhausted (emotional exhaustion)?.
2. Do you feel unreal (depersonalization) ?.
3. Do you have a diminished sense of personal accomplishment?.
4. Do you feel anxious?.
5. Do you feel empathy for your patients (identifying yourself with the patient's illness)?.

A prospective study of 3,588 participants who were medical students and thereafter when they were 2nd year residents was performed. 45% were assessed to have burn out and it was more common among females. Residents in neurology, Urology, emergency medicine and General surgery were specialities where burn out was common. It was least in Dermatology and Pathology. Physicians do not seem to be affected.

Comment: Causes for burn out include, burdensome electronic health records, administrative and clerical functions and productivity demands. Medical personnel should consult Psychologists/ Psychiatrists to help them get over this problem.

Ref:Rotenstein L.S et al JAMA 2018 Sept 18; 320: 1131.
Dyrdye L.N. et al IBID: 1114.

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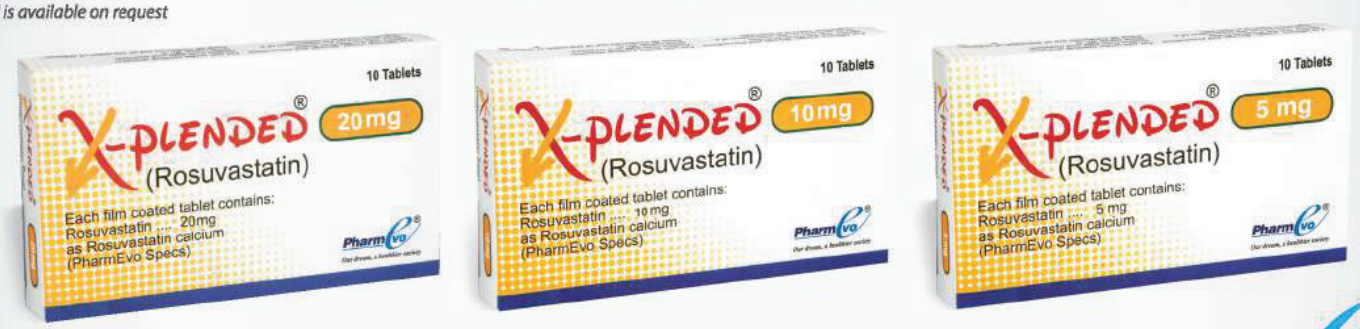
EVALUATE

Clinical ASCVD

- **Y** → **Secondary prevention (age18+)**
  - **History of multiple major ASCVD events or 1 major ASCVD event + multiple high-risk conditions**
    - **Y** → **Very high risk ASCVD** → **Maximum tolerated statin**
    - **N** → **Stable ASCVD** → **High- or moderate-intensity statin**
- **N** → **Primary prevention (age 40-75y)**
  - **LDL-c >190 mg/dl** → **Maximum tolerated statin**
  - **LDL-c 70-189 mg/dL** → **Diabetes**
    - **Y** → **Moderate-intensity statin**
    - **N** → **Assess 10-year ASCVD Risk**
      - **>20% High Risk** → **High-intensity statin**
      - **>7.5 to<20% Intermediate Risk** → **Evaluate risk enhancers and coronary artery calcium score if uncertain** → **Moderate-intensity statin**
      - **5 to < 7.5% Borderline Risk** → **Risk discussion for statin benefit; use risk enhancers** → **Lifestyle; selective moderate statin**
      - **<5% Low Risk** → **Lifestyle; and risk discussion**
  - **LDL-c <70 mg/dL** → **Assess lifetime risk**

THERAPY

Detailed PI is available on request



2018 ACC/AHA/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol. http://www.onlinejacc.org/guidelines/cholesterol

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