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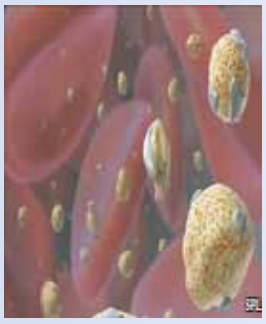

Familial Hypercholesterolemia: An Under-recognized but Significant Concern in Cardiology Practice

Introduction

Familial hypercholesterolemia (FH) is a common genetic disorder that leads to significantly increased levels of circulating atherogenic particles (or lipoproteins), including low-density lipoprotein (LDL) and lipoprotein(a) [Lp(a)]. Mutations in the LDL receptor (LDLR) gene are the most frequent cause of FH; however, mutations in other genes, such as apolipoprotein B (APOB) or proprotein convertase subtilisin/kexin type 9 (PCSK9), have been identified and may lead to a similar phenotype.

FH promotes premature coronary artery disease. Often, the initial presentation of a patient with FH is to a cardiologist at the time of a first major coronary event such as myocardial infarction (MI). Cardiologists therefore play an important role in the identification and management of this genetic disorder. However, little is known about cardiologists' knowledge, attitudes, and beliefs about FH.

In order to gauge the awareness of FH among cardiologists, an Internet-based survey was conducted among American College of Cardiology (ACC) CardioSurve members in 2011. CardioSurve is a panel of 300 to 500 cardiologists that provides in-depth perspectives of US cardiologists. Cardiologists received payment for participation in the survey. The majority of participants were male, had >10 years' experience in practice, and worked in a cardiovascular (CV) practice setting. A summary of survey results appeared in the July 2012 issue of CardioSurve Newsletter.

In the survey, only approximately 10% of cardiologists reported being very or extremely confident about their understanding of FH. Nearly 70% expressed a desire to know more about FH. Most cardiologists (~ 80%) were unaware of the true prevalence of FH (Figure 1A), and 60% did not realize that half of all first-degree relatives of a patient with FH also have the disease.

None of the cardiologists surveyed knew that individuals with FH are about 20 times more likely to develop premature coronary heart disease (CHD) (Figure 1B). Sixty-three percent believed that the risk was no greater than 10 times that of the general population. Fewer than 30% of cardiologists surveyed recognized FH when shown a National Lipid Association (NLA) case example.

This brief review is intended to provide current information about FH and increase awareness about FH among cardiologists in the hope that affected individuals can be diagnosed and properly treated earlier in the course of their disease. This review focuses on summarizing key aspects of the diagnosis and treatment goals for patients with FH (treatment of FH is not comprehensively reviewed). In particular, this paper responds to those areas of educational need identified in the ACC CardioSurve FH cardiologist and patient needs assessment survey.

Prevalence, Characteristics, and Etiology of FH

FH affects approximately 1 in every 300 to 500 individuals. An estimated 1 in every 1 million individuals has the more severe form, homozygous FH (HoFH), in which both copies of LDLR carry mutations. In the United States, more than 600 000 individuals have FH. The prevalence of FH is greatest in genetically isolated regions with founder effects, where the risk is elevated by the practice of consanguineous marriage. Founder effects for FH are seen among French Canadians, Christian Lebanese, Ashkenazi Jews, and South African Afrikaners, among whom the frequency of LDLR mutations is high.

All individuals with FH have increased levels of low-density lipoprotein cholesterol (LDL-C) from

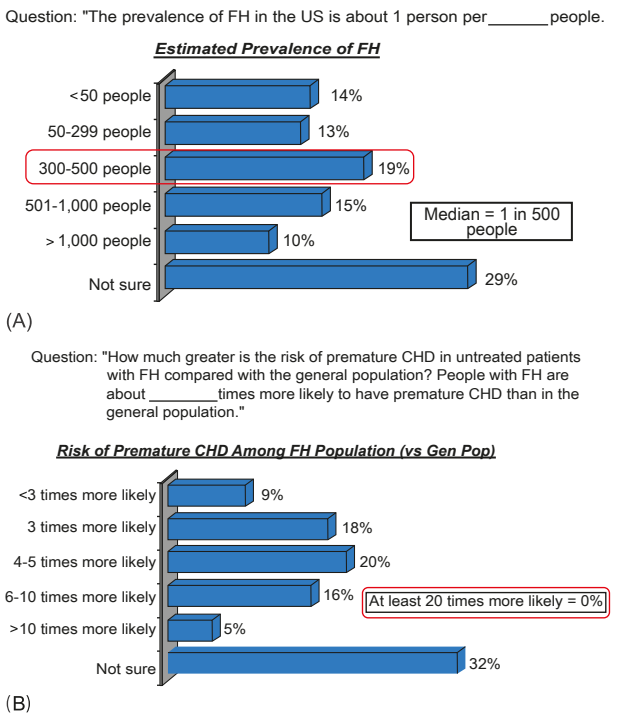

Figure 1. Selected questions and responses from the American College of Cardiology CardioSurve Familial Hyper - cholesterolemia Survey. Correct answers are circled in red. Percentages indicate the responses (N = 152). The survey was conducted in November 2011.
Abbreviations: CHD, coronary heart disease; FH, familial hypercholesterolemia; Gen Pop, general population.

birth. As a result of this chronic, lifelong exposure to elevated LDL-C concentrations, the risk of atherosclerosis and CHD is increased by about 20-fold in these patients if these high levels of lipoproteins are left untreated. The likelihood of FH is greater in patients with a family history of hypercholesterolemia or of premature CHD (with the latter defined as onset at age <55 years in men and at age <65 years in women). The severity of FH ranges widely among patients, particularly among those with heterozygous FH (HeFH), with some individuals having greater elevations in LDL-C levels than others, presenting with more signs and symptoms of disease, or being more refractory to statin therapy. HoFH is considered the most severe form of FH and is associated with the early onset of atherosclerosis; however, some patients with HeFH may present with high cholesterol levels even after maximal lipid-lowering therapy.

FH is most commonly caused by a mutation of either 1 (heterozygous) or both (homozygous) alleles of LDLR. The term severe familial hypercholesterolemia encompasses disease in individuals exhibiting more grave elevations in LDL-C levels and who may be refractory to medical therapy, regardless of hetero- or homo- zygosity. More than 1600 mutations of the LDLR gene have been identified. The mutations cause a varying extent of dysfunction of the LDLR gene, ranging from partial receptor dysfunction to complete absence of receptor synthesis. The underlying mutation is related to the phenotypic expression and severity of symptoms. Mutations in 3 other genes associated with plasma LDL-C levels have been identified that may have an impact on the phenotype or cause similar symptoms—namely, PCSK9, APOB, and more rarely, the autosomal recessive hypercholesterolemia adaptor protein.

These mutations affect the rate of LDL clearance from the blood, resulting in LDL levels >220 mg/dL in untreated patients. However, despite the genetic basis of FH, genetic testing is usually not needed for diagnosis or clinical management.

Cardiovascular Risk in FH

The risk of CV events is about 20-fold greater in untreated individuals with FH. Elevated levels of LDL-C (and other apo B-containing lipoproteins) are known to increase the risk of CHD. Although less well recognized, an elevated Lp(a) level (>30 mg/dL) has also been shown to independently predict cardiovascular disease (CVD) risk in patients with FH. Patients with FH who are at even greater risk for CVD include those with diabetes, a family history of very early CHD (age <45 years in men and <55 years in women), and the presence of 2 or more CVD risk factors, including smoking.

Because of their exposure to elevated levels of LDL-C from birth, patients with FH, particularly those with severe HeFH or HoFH, may experience CV events as early as the first decade of life. Treatment with statins should be considered beginning at age 8 years, after diet and exercise management have been started, with statin treatment beginning at possibly even younger ages in patients with HoFH. Cardiovascular events are probable within the first 3 decades of life in patients with untreated severe FH. Severe coronary atherosclerosis and aortic stenosis are the key life-threatening complications associated with FH. Although the onset of CHD varies among individuals with FH, approximately 50% of men and at least 30% of women with this disorder will have CHD by age 50 and 60 years, respectively.

Identifying the Individual With FH

Given the association of FH with CHD and the fact that many patients are not aware that they have FH until a CV event occurs, cardiologists are in an ideal position to identify individuals who have not yet been diagnosed with the disease. In addition, following a diagnosis of FH with cascade screening in relatives of newly diagnosed patients can help identify additional patients with FH before they have a CV event or develop severe CHD.

Screening

Diagnosis of FH often begins by screening the individual based on NLA-recommended guidelines (Table 1). These guidelines provide target cholesterol levels (LDL-C and non–high-density lipoprotein cholesterol [non–HDL-C]) for adults and children, as well as other criteria, such as family history of high cholesterol levels and CHD and physical findings (eg, xanthomas). Among the general population, the likelihood that an individual has FH is approximately 80% with the following LDL-C levels: ≥250 mg/dL (in patients age ≥30 years), ≥220 mg/dL (in patients age 20–29 years), or ≥190 mg/dL (in patients age <20 years). Given that FH is an inherited disease, the likelihood of FH is greater when the patient has a close relative who has been diagnosed with FH.

Physical signs of elevated lipid levels are strongly suggestive of FH and are more likely to be seen in individuals with severe FH. Patients with such high plasma lipid levels often accumulate cholesterol deposits in the skin, resulting in xanthomas (commonly tendinous xanthomas of the Achilles tendon and finger extensor, but can also occur in the patellar and triceps tendons) and corneal arcus. Both xanthomas and corneal arcus are pathognomonic for HoFH and HeFH. It was shown that the presence of xanthoma and corneal arcus is associated with a 3-fold greater risk of CVD development in patients with FH. Tuberous xanthoma or xanthelasma in patients younger than 25 years greatly raises the probability of FH. In patients with HoFH, xanthomas may be observed at birth or develop during early childhood, along with other severe and early signs and symptoms.

Diagnosis

Screening criteria are most often applied initially to identify patients with FH in the general population, followed by the application of diagnostic criteria. However, applying diagnostic criteria initially may be prudent for patients who have, or are closely related to someone who has, premature onset of CHD. Several validated criteria recommended by the NLA are available that can help a clinician definitively diagnose FH. These include the US Make Early Diagnosis Prevent Early Death (US MEDPED) Program Diagnostic Criteria, the Simon Broome Register Diagnostic Criteria for FH, and the Dutch Lipid Clinic Network (Dutch MEDPED) program. We have included the Dutch MEDPED criteria in this review (Table 2). All of the

Table 1. National Lipid Association Screening Recommendations

Universal screening for elevated serum cholesterol is recommended. FH should be suspected when untreated fasting LDL-C or non–HDL-C levels are at or above the following:

Adults (age ≥20 years): LDL-C ≥190 mg/dL, or non–HDL-C ≥220 mg/dL

Children, adolescents, and young adults (age <20 years): LDL-C ≥160 mg/dL, or non–HDL-C ≥190 mg/dL

For all individuals with these levels, a family history of high cholesterol and heart disease in first-degree relatives should be collected. The likelihood of FH is higher in individuals with a positive family history of hypercholesterolemia or of premature CHD (onset in men age

<55 years and women age<65 years).

Cholesterol screening should be considered beginning at age 2 years for children with a family history of premature CVD or elevated cholesterol levels.

All individuals should be screened by age<20 years.

Although not present in many individuals with FH, the following physical findings should prompt the clinician to strongly suspect FH and obtain necessary lipid measurements, if not already available:

Tendon xanthomas at any age (most common in Achilles tendon and finger extensor tendons, but can also occur in patellar and triceps tendons)

Arcus corneae in patients age <45 years

Tuberous xanthomas or xanthelasma in patients age <20 years

At the LDL-C levels listed below, the probability of FH is approximately 80% in the setting of general population screening. These LDL-C levels should prompt the clinician to strongly consider a diagnosis of FH and obtain further family information:

LDL-C ≥250 mg/dL in patients age ≥30 years

LDL-C ≥220 mg/dL in patients age 20 to 29 years

LDL-C ≥190 mg/dL in patients age <20 years

Abbreviations: CHD, coronary heart disease; CVD, cardiovascular disease; FH, familial hypercholesterolemia; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Table 2. Dutch Make Early Diagnosis Prevent Early Death Diagnostic Screening Criteria

Criteria	Score[a]
Family history	
I. First-degree relative with known premature coronary and vascular disease	1
II. First-degree relative with known LDL-C 95th percentile	1
III. First-degree relative with tendon xanthomata and/or arcus cornealis	2
IV. Children age <18 years with LDL-C >95th percentile	2
Clinical history	
I. Patient has premature (age <55 years in men; <60 years in women) coronary artery disease	2
II. Patient has premature (age <55 years in men; <60 years in women) cerebral or peripheral vascular disease	1
Physical signs	
I. Tendon xanthomata	6
II. Arcus cornealis in patient <45 years	4
Laboratory analysis[b]	
I. LDL-C >8.5 mmol/L, >330 mg/dL	8
II. LDL-C 6.5 to 8.4 mmol/L, 250 to 329 mg/dL	5
III. LDL-C 5.0 to 6.4 mmol/L, 190 to 249 mg/dL	3
IV. LDL-C 4.0 to 4.9 mmol/L, 155 to 189 mg/dL	1
DNA analysis	
Functional mutation in the LDL receptor present	8

Abbreviations: LDL, low-density lipoprotein; LDL-C, low-density lipoprotein cholesterol.

[a] A diagnosis is considered certain if the score is ≥8, considered probable if the score is 6 to 8 points, and considered possible when the score is 3 to 5 points. If the score is <3 points, a diagnosis is not made.

[b] High-density lipoprotein cholesterol and triglycerides are <200 mg/dL, 203 mmol/L.

diagnostic criteria mentioned are based on the key characteristics of FH, including cholesterol levels, family history, and physical signs of disease; however, characteristics may be weighted differently depending on the criteria used. The US MEDPED diagnostic criteria focus on cholesterol levels as diagnostic thresholds. These thresholds vary based on the relatedness to a confirmed case of FH, reflecting that closer relatives have a higher probability of having FH. The criteria also provide some guidance regarding clinical symptoms and sibship analysis in the diagnostic process. The Simon Broome Register diagnostic criteria include LDL-C and total cholesterol guidance for pediatric and adult patients but also incorporate clinical characteristics, molecular diagnosis, and family history. The Simon Broome Register criteria require that tendon xanthomas must be present in either the tested individual or a relative to make a definitive diagnosis. The Dutch MEDPED criteria employ a point system to weigh all evidence and classify a diagnosis as certain, probable, possible, or negative. The Dutch MEDPED, in distinction to the Simon Broome Register criteria, assign a diagnosis of probable FH to LDL-C levels >330 mg/dL, regardless of the presence of any other criterion. All of these diagnostic criteria are acceptable tools to aid in the diagnosis of FH in newly suspected cases. In most cases, genetic testing is not necessary for diagnosis, but it may be useful to confirm an uncertain diagnosis.

Cascade Screening

Cascade screening may be particularly important in the cardiology setting. As primary patients are diagnosed with FH, their relatives should be screened in a process referred to as cascade screening. This process involves applying a systematic approach to screening relatives of individuals who have been diagnosed with FH that is more cost-effective than screening in the general population. The initial step in cascade screening is to obtain lipid levels and apply diagnostic criteria to all first-degree relatives. Each of these individuals who are found to have FH then become new cascade indices with additional first-degree relatives to assess for FH. The probability of FH is 50% in first-degree relatives, 25% in second-degree relatives, and 12.5% in third-degree relatives. Cascade screening may be life saving, especially in young patients, who might not otherwise undergo lipid level testing.

Cardiologists Leading the Way

Because elevated lipids levels are strongly associated with atherosclerosis and CV events, diagnosis of FH early in the course of the disease allows for earlier treatmen that may prevent CV events, such as MI, and prolongs survival. Guidance by the NLA states that screening and diagnosis of FH in both adults and children is the responsibility of all primary healthcare professionals and relevant specialists. Cardiologists are likely to see a greater proportion of individuals with FH as a result of treating patients who present with CV events, and are therefore in an ideal position to initiate screening and to diagnose FH. In addition to identifying individuals with FH within the cardiology practice, cardiologists may also play a leading role in CHD prevention by referring patients' relatives for cascade

screening by primary care practitioners or lipid specialists.

Treatment Goals and Lipid Specialist Consultation

Lifelong management of high lipid levels in patients with FH is essential, with most adult patients requiring high doses of high-potency statins **(atorvastatin, rosuvastatin, pitavastatin, simvastatin)**. The NLA Expert Panel Report on FH recommends an LDL-C goal of <160 mg/dL or an LDL-C level reduction of at least 50% in patients with FH and no other risks. Higher-risk patients with FH require intensified drug treatment and more aggressive treatment goals of LDL-C <100 mg/dL and non–HDL-C <130 mg/dL. The higher-risk patients include current smokers and those with clinically evident CHD or atherosclerotic CVD, diabetes, a family history of very early CHD (age <45 years in men and <55 years in women), 2 or more CHD risk factors, or Lp(a) levels ≥30 mg/dL as measured by isoform-insensitive assay. **Ezetimibe** or another drug used in combination with a high-dose statin will most likely be required for these high-risk individuals but should be weighed against the drawbacks of combining therapies (eg, adverse effects, decreased adherence, cost). Intensification of therapy may also be considered if lipid levels remain above recommended goals or for lower-risk patients with

Table 3. Management and Treatment Goals in Patients With FH

Goal: LDL-C reduction of at least 50% from baseline	
	Cardiologists not specializing in lipid management are encouraged to consult with or refer patients to a lipid specialist.
Adults	
	Lifestyle modifications
	Reduced fat intake with supplementation of plant stanol or sterol esters and soluble fiber.
	Referral to registered dietitian or other qualified nutritionist encouraged.
	Exercise and adjustment of caloric intake to ensure a healthy body weight.
	Limit alcohol consumption and, most important, avoid all tobacco products.
Drug treatment of FH	
	Initiate with moderate to high doses of high-potency statins titrated to achieve LDL reduction goal.
	If initial statin not tolerated, change to alternative statin or every-other-day statin dosing.
	If initial statin therapy is contraindicated or poorly tolerated, ezetimibe, a bile acid sequestrant (colesevelam), or niacin may be considered.
	Combination drug therapy is required in most patients who cannot use a statin.
	Combination drug therapy should be used in patients not at goal with maximally tolerated doses of statins.
	Consider concomitant risk factors for myopathy, concomitant medications, and presence of other disease conditions and lipid abnormalities when selecting additional drug combinations.
Other options	
	LDL apheresis may be an option for certain patients who cannot achieve goal with drug therapy.
	Rarely, ileal bypass or liver transplantion may be considered treatment options.
Women of childbearing age	
	Conduct prepregnancy counseling with instructions to stop statins, ezetimibe, and niacin at least 4 weeks prior to discontinuing contraception
	(or immediately in the case of unintended pregnancy) and not to use these medications during pregnancy or lactation.
	Other lipid-lowering medications (eg, colesevelam) may be considered under healthcare practitioner guidance.
	LDL apheresis should be considered for pregnant women with HoFH or significant atherosclerosis.
Children	
	Goal: 50% reduction in LDL level or LDL level <130 mg/dL
	Children with FH should be managed by a lipid specialist.
	After initiation of diet and physical activity, statins are preferred drug treatment.
	Treatment may be initiated at age 8 years or older, or at younger ages in special cases (eg, HoFH).

Abbreviations: FH, familial hypercholesterolemia; HoFH, homozygous familial hypercholesterolemia; LDL, low-density lipoprotein; LDL-C, low-density lipoprotein cholesterol.

FH who initially attain >50% reduction in LDL-C levels. Management goals provided by the NLA Expert Panel Report on FH are summarized in Table 3.

Special consideration should be given to patients with severe FH and/or HoFH, who will require initation of therapy early in life and ongoing monitoring, and in the majority of whom LDL apheresis may be required. Two treatment alternatives for HoFH have become available since the ACC survey and NLA Expert Panel recommendations were published in 2011. Lomitapide is a microsomal triglyceride transfer protein inhibitor approved by the US Food and Drug Administration (FDA) in December 2012. Lomitapide is indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce LDL-C, total cholesterol, apo B, and non–HDL-C levels in patients with HoFH.

Mipomersen, an antisense oligonucleotide inhibitor targeting mRNA for apo B-100, was approved in January 2013. Mipomersen is FDA approved as an adjunct to lipid-lowering medications and diet to reduce LDL-C, apo B, total cholesterol, and non–HDL-C levels in patients with HoFH. Cardiologists not specializing in lipid management of patients with FH should strongly consider consulting with or referring to, and potentially patient monitoring by, a lipid specialist. It is recommended that any patients requiring intensified treatment for lipid levels, those who are at high risk, or those who are intolerant of initial statin therapy should be referred to a lipid specialist to evaluate the necessity of using alternative treatment regimens. The NLA guidelines also highly recommend that children with FH be managed by a lipid specialist.

Summary

A 2011 survey of selected ACC members suggests that knowledge about FH among cardiologists may be limited, and that the prevalence and heritability of the disease, as well as the risk of premature CHD associated with FH, may be commonly underestimated. Furthermore, a possible diagnosis of FH may be overlooked due to focus on an acute CV event and to the rapid discharge of the patient from the hospital after CV events. However, cardiologists are in fact ideally poised to make a difference in successfully identifying FH, not only in patients who are index cases (who often present to the emergency department with acute CV events), but also in patients' relatives.

The disease process begins early in life, often long before clinical signs of disease are evident. Early diagnosis is therefore critical to reducing the risk of CVD in affected individuals. Given the greater risk of CHD and CV events associated with FH, cardiologists may see a greater proportion of patients with FH than would many other specialists. Cardiologists are therefore well positioned to diagnose FH and to ensure that cascade screening is applied. Diagnosing FH in the relatives of affected patients may allow for earlier treatment of this severe disease and may prevent unnecessary coronary events in those individuals.

The ACC survey demonstrated that knowledge about FH appears to be limited, although there is an overwhelming desire to know more about the disease. With increased awareness of the true prevalence of FH among patients and their relatives, a thorough understanding of the CHD risks, and a clear diagnostic picture to apply in the clinic, cardiologists will become crucial in the care of the patient with FH.

Key points to understand and communicate regarding FH include the following:

1. HeFH occurs in 1 out of every 300 to 500 individuals, whereas HoFH is thought to occur more in the range of 1 out of every 1 million individuals.

2. Management of LDL-C levels is the cornerstone of treatment of FH. Intensified drug treatment is required in higher-risk patients with FH, defined as those with clinically evident CHD or other atherosclerotic CVD, diabetes, a family history of very early CHD (age <45 years in men and <55 years in women), 2 or more CVD risk factors, including current smoking, or Lp(a) levels ≥30 mg/dL using an isoform insensitive assay. In these patients, the goal is to achieve LDL-C levels <100 mg/dL and non–HDL-C levels <130 mg/dL.

3. Special consideration should be given to the management of patients with severe and/or HoFH.

4. Early detection, aggressive treatment, and consultation with or referral to lipid specialists when appropriate are necessary to prevent premature CHD and its comorbidities and associated mortality.

Cardiologists who encourage cascade screening and initiate proper lipid-lowering treatment can be instrumental in preventing atherosclerosis and CV events in individuals who might not otherwise receive a diagnosis of or treatment for FH. In certain high-risk or treatment-refractory patients, cardiologists may need to comanage FH with a lipid specialist to ensure that therapeutic interventions are optimized. FH is a serious disease that requires early intervention, lifelong treatment, and regular follow-up. Cardiologists can make a substantial positive impact on the clinical pathways of patients with FH.

Ref: Familial Hypercholesterolemia: An Under-recognized but Significant Concern in Cardiology Practice. JoAnne M. Foody.
Clin. Cardiol. 37, 2, 119–125 (2014)

Treating Cardiac Disease in Pregnancy

Pregnancy is a Challenge to the Cardiovascular System

Pregnancy implies multiple physiological changes (e.g., circulating volumes, vascular resistance and heart rate, among others).

Adaptive mechanisms to pregnancy may become maladaptive in a compromised circulation.

Management of the risk of bleeding, thrombosis and teratogenicity of different drugs may be a challenge.

Pregnancy Should Be Proactively Discussed With All Women With Known Heart Disease Who are of Child-Bearing Age

Prepregnancy counseling is important in order to empower women to make informed choices and to attempt to optimize both maternal and fetal outcomes.

There are several risk score systems that can be used to estimate the risk of an adverse outcome (e.g., Cardiac Disease in Pregnancy and ZAHARA study score, among others).

Women who are not known to have pre-existing heart disease but who develop a cardiac condition during pregnancy have a worse outcome.

Women Over the Age of 40 Years are at Higher Risk of Developing Ischemic Coronary Events During Pregnancy

ß-blockers and aspirin are the treatments of choice for cardiac ischemia symptoms during pregnancy.

Pregnant women with troponin-positive chest pain should undergo invasive assessment with coronary angiography, with close liaison between the cardiologist and obstetrician.

Drug-eluting stents can be used, but within a few months of delivery, bare-metal stent should be considered.

If primary percutaneous coronary intervention is not possible, thrombolysis can be used.

All Women With Known or Suspected Familial Aortopathies Must Receive a Specialist Review Prior to Pregnancy

In women who are at high risk of aortic dissection, pregnancy might deemed to be contraindicated.

Aortic root replacement might be indicated before pregnancy (i.e., Marfan syndrome with an ascending aorta diameter of >42 mm).

Dissection should be ruled out at the same time as acute ischemia or thromboembolism in all women with severe chest pain, hemoptysis or syncope during pregnancy.

Cardiomyopathy is One of the Most Common Causes of Morbidity During Pregnancy

Different types of cardiomyopathy might have different implications during pregnancy.

During pregnancy, standard treatment includes diuretics, ß-blockers and, occasionally, hydralazine and nitrates. Angiotensin-converting enzyme inhibitors should only be started after delivery.

Early data suggest that bromocriptine may significantly improve maternal outcomes in patients with peripartum cardiomyopathy.

Most Arrhythmias in Pregnancy are Benign Ectopies or Short-Runs of Atrial Arrhythmias

Most arrhythmia can be managed conservatively during pregnancy; however, antiarrhythmic drugs may be needed.

In an acute setting, most of the available therapeutic options can be used. Adenosine and ß-blockers can be use safely during pregnancy.

If cardioversion is required, the fetal heartbeat should be documented, ideally both before and after the cardioversion.

Patients With Pulmonary Artery Hypertension Should Be Advised Against Pregnancy

Patients with pulmonary arterial hypertension are quoted to have pregnancy-related mortalities rates of approximately 20–50%.

Ref. Women's Health. 2013;10(1):79-90.

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Cardiology News

Calcium/CVD Risk Debate Gets New Fodder From Analysis

Calcium supplementation with and without vitamin D does not increase the risk of coronary heart disease or all-cause mortality in elderly women, a new meta-analysis has shown. Presented by Dr Joshua Lewis at the World Congress on Osteoporosis, Osteoarthritis, and Musculoskeletal Disease, the Australian researchers observed no relationship between calcium supplementation with and without vitamin D and coronary heart disease risk in 18 clinical reports with data from more than 63500 elderly women.The findings contradict a 2010 meta-analysis in BMJ that reported calcium supplementation (without coadministered vitamin D) was associated with a significantly increased risk of MI in 8151 men and women. In that meta-analysis, calcium supplementation was associated with a relative 31% increased risk of MI. A similar meta-analysis that included trials with vitamin-D coadministration found similar results.

April 5, 2014; Seville, Spain. Abstract OC34.

NSAIDs Linked to Higher Atrial Fibrillation Risk

Taking nonsteroidal anti-inflammatory (NSAID) drugs appears to be associated with an increased risk for atrial fibrillation (AF), even after adjustment for ventricular end-diastolic dimension, known to be increased with NSAID use, a new study confirms. Patients using NSAIDs for 2 to 4 weeks had a 76% higher risk of developing AF compared with those who hadn't taken these pain medications, researchers found. The results suggest that the increased risk occurs shortly after starting treatment and may resolve over time. The underlying mechanism connecting NSAID use with AF isn't clear.The results suggest that the increased risk occurs shortly after starting a prescription for NSAIDs.

BMJ Open. Published online April 8, 2014

CVD Burden Declining Among Rich Countries

The global burden of cardiovascular disease (CVD) is highest in Eastern Europe and Central Asia and continues to affect large populations in South Asia, North Africa, and the Middle East, where it often afflicts young, working-age adults, according to a new report. In higher-income countries, including the UK, New Zealand, Ireland, Israel, and Norway, among a host of others, the number of disability-adjusted life-years (DALYs) lost to CVD is declining. The new data are part of the global cardiovascular disease atlas, published April 4, 2014 in Global Heart, launched by the World Heart Federation.

Circulation, Apr, 2013.

'Bendopnea': A New Symptom to Help Spot Sicker HF Patients?

Cardiologists in Texas have identified a new symptom to look for in patients with advanced heart failure—"bendopnea," which they define as "shortness of breath when bending forward." Nearly a third of patients with advanced heart failure who were referred to their cardiac catheterization lab had bendopnea. The study showed that patients with heart failure who have bendopnea have hemodynamic profile C—meaning that they have higher [left ventricular] filling pressure and lower cardiac index.

JACC Heart Fail 2014; 2:24–31.

Editorial Note

Dear Doctor,

We are happy to present the 33rd issue of "Insight Heart". It is a small endeavor to provde you compiled & updated information on cardiovascular diseases and its management. This issue is focused on ***"Familial Hypercholesterolemia"***. We will appreciate your thoughtful comments.

Thanks and regards.