Mortality Due to CV Disease

The human heart is an amazing organ. If you live for 80 years with an average 80 heartbeats per minute, your heart will have contracted over 3.3 billion times. At an average output of 5L/min, it will have pumped over 210 million liters of blood. Assuming proper function, the main determinant to how hard the heart works is resistance to the outflow of blood. Our common measure of that resistance is called blood pressure.

On November 13, the American College of Cardiology and the American Heart Association released the 2017 Guideline for High Blood Pressure in Adults. Table 1 is an estimate of the percent of the US population that will be classified as hypertensive with the new guidelines compared to the prior guidelines.

<table>
<thead>
<tr>
<th>Age group, y</th>
<th>Overall percent</th>
<th>Overall, age-sex adjusted percent</th>
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<tbody>
<tr>
<td></td>
<td>SBP/DBP ≥130/80 mm Hg or Self-Reported Antihypertensive Medication (2017)</td>
<td>SBP/DBP ≥140/90 mm Hg or Self-Reported Antihypertensive Medication (2003)</td>
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<td>20-44</td>
<td>30%</td>
<td>19%</td>
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<tr>
<td>45-54</td>
<td>50%</td>
<td>44%</td>
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<tr>
<td>55-64</td>
<td>70%</td>
<td>63%</td>
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<tr>
<td>65-74</td>
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<td>75%</td>
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<td>75+</td>
<td>79%</td>
<td>85%</td>
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</table>

Overall, age-sex adjusted percent

<table>
<thead>
<tr>
<th>Overall percent</th>
<th>Men (n=4717)</th>
<th>Women (n=4906)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>46%</td>
<td>32%</td>
</tr>
<tr>
<td>Men</td>
<td>48%</td>
<td>43%</td>
</tr>
<tr>
<td>Women</td>
<td>31%</td>
<td>32%</td>
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</tbody>
</table>

On November 13, the American College of Cardiology and the American Heart Association released the 2017 Guideline for High Blood Pressure in Adults. Table 1 is an estimate of the percent of the US population that will be classified as hypertensive with the new guidelines compared to the prior guidelines.
CASE #1

Coronary Artery Fistula

By James Kadouch, MD
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A 34-year-old male applied for life insurance. He had no significant cardiac history or cardiovascular risk factors. Two years prior to the application he was evaluated for left sided chest pain associated with shortness of breath that occurred while seated at work. An exercise nuclear myocardial perfusion imaging (MPI) study which showed inducible ischemia in the anterolateral wall prompted a cardiac catheterization which showed small fistulas between the left main and left anterior descending arteries and the pulmonary artery. He also had an exercise stress echocardiogram which showed no evidence of inducible ischemia.

The case was reviewed by another interventional cardiologist who stated that these coronary artery fistulas were “too small to result in a symptomatic coronary steal syndrome.” Moreover, the atypical nature of symptoms which showed no relation to exertion and the lack of inducible ischemia on exercise stress echocardiogram made ischemia due to coronary steal unlikely. This led to a recommendation for no further intervention. Instead an investigation for non-cardiac causes of this applicant’s chest discomfort was begun.

What is a coronary artery fistula and what are the mortality implications?

Definition
A coronary artery fistula (CAF) is usually a congenital anomaly of a coronary artery such that it communicates either with a chamber of the heart (coronary-cameral fistula) or any segment of the systemic or pulmonary circulation (coronary arteriovenous fistula).

Fistulas are rarely acquired due to trauma, postcardiac surgery or angioplasty. And they occur very rarely because of coronary aneurysm rupture.

Etiology
In early fetal development, the primitive, loosely packed myocardium is nourished via sinusoids which communicate with the heart cavities. Persistence of these sinusoids may lead to coronary artery cameral fistulae. At approximately 32 days of gestation the myocardium becomes more compact and the sinusoids disappear to be replaced by a network of veins, arteries and capillaries that may have connections with other mediastinal vessels. Persistence of these connections leads to the formation of coronary artery fistulae.

Epidemiology

CAF are present in 0.002% of the general population and are visualized in nearly 0.25% of patients undergoing catheterization. They account for 0.2-0.4% of congenital cardiac anomalies. Approximately 50% of pediatric coronary vasculature anomalies are coronary artery fistulae. No race or sex predilection has been noted.

Although some previous studies reported CAFs originate from the right coronary artery (RCA) in approximately 50% of cases, some authors mentioned that most CAFs originate from the left anterior descending artery (LAD). There are, however, certain predilections. More than 90% of fistulae open into right heart chambers or their connecting vessels. True AV fistulae to the veins themselves (coronary sinus or its major branches or the venae cava) are uncommon. Thus, about 40% connect to the right ventricle, 25% to right atrium, 15%-20% to the pulmonary artery, 7% to the coronary sinus and only 1% to the superior vena cava. Fistulas to the LV are very rare, representing about 3% of CAF.

Diagnosis

Coronary artery fistula can present in patients at any age but may be suspected in early childhood when a murmur is detected in an asymptomatic child or when symptoms of congestive heart failure are present. Older children with murmurs may present with symptoms of coronary insufficiency.
When CAF are small myocardial blood flow is not compromised, and the patient is usually asymptomatic. These small CAF are often discovered incidentally upon coronary angiography.

Various symptoms and signs may occur based on the type of fistula, shunt volume, site of shunt and presence of other cardiac conditions. When CAF are moderate to large, a continuous murmur may be heard on examination. In addition, there may be coronary artery steal, with resultant ischemia of the segment of myocardium distal to the fistula. This can cause chest pain, fatigue, palpitations or dyspnea. Increased blood flow causes the coronary artery proximal to the fistula to enlarge in a compensatory fashion.

With increasing age, symptoms are more likely to appear, and the incidence of complication rises. Heart failure is the most common complication in the setting of large CAF.

Fistula-related complications are present in 11% of patients younger than 20 years and in 35% of patients older than 20 years. Fistulae can be associated with the following complications:

- Myocardial ischemia
- Mitral valve papillary muscle rupture from chronic ischemia
- Ischemic cardiomyopathy
- Congestive heart failure from volume overload
- Bacterial endocarditis
- Sudden cardiac death
- Secondary aortic valve disease
- Secondary mitral valve disease
- Premature atherosclerosis

The chest radiograph and electrocardiogram are normal if the shunt through the fistula is small but may show evidence of chamber enlargement or ischemia with a larger shunt and coronary artery steal.

Significantly enlarged coronary arteries can be detected by two-dimensional echocardiography. The diagnosis of a coronary artery fistula can often be made with transthoracic two-dimensional and color Doppler echocardiography in children.

In adults, however, two-dimensional transesophageal echocardiography may be more sensitive for detection of the entrance and termination site of the shunt, which is characterized by a continuous turbulent systolic and diastolic flow pattern.
Coronary fistulae have also been detected noninvasively using 64-slice multidetector computed tomography. Multidetector row computed tomography (MDCT) cardiac imaging has provided excellent distal coronary artery and side branch imaging. Imaging of an entire 3-dimensional volume and the heart can be acquired within 20 seconds, with better temporal and spatial resolution than Magnetic Resonance. Several authors now advocate consideration of MDCT in imaging of coronary anomalies.

The size and anatomical features of the fistula can be reliably established during coronary angiography or with retrograde thoracic and aortic root aortography.

Natural history

In the small fistulas, the myocardial blood supply is not compromised enough to cause symptoms, and spontaneous closure usually occurs. However, some small fistulae can dilate over time.

Large fistulae progressively enlarge over time, and complications – such as congestive heart failure, myocardial infarction, arrhythmias, infectious endocarditis, aneurysm formation, rupture and death – are more likely to arise in older patients. Spontaneous closure has been rarely reported in the setting of large fistulae.

Treatment

The management of CAF in asymptomatic children is unclear and is dependent on the presence of symptoms, the clinical significance, the hemodynamic shunt dimension and the morphological appearance and characteristics of the fistula visualized with different imaging techniques.

Medical treatment for symptomatic relief is often used until investigations and operative repair can be performed. Most authors recommend CAFs be closed when there is a significant shunt flow (QP/QS=1.5:1) and/or when the patient is symptomatic. In a multicenter review, appreciably more problems related to operative risks and postoperative complications occurred after age 20 years.

Transcatheter embolization techniques using coils, bags or other devices can be performed on an outpatient basis at the time of diagnostic studies or later and may obviate the need for cardiac surgical intervention. Some fistulae are unsuitable for the transcatheter approach and are addressed surgically. A typical procedure includes a coronary artery bypass, opening the chamber into which the fistula drains, identifying the fistula and closing the abnormal communication with a patch or suture.
Prognosis

The main complications of CAFs are bacterial endocarditis, congestive heart failure, arrhythmia, pericardial effusion and premature atherosclerosis complicated by myocardial infarction or even sudden cardiac death. Myocardial infarction is seen rarely in cases of coronary to pulmonary artery fistulas. In a recent study, the prevalence of myocardial infarction was found to be 5%.

Results of both transcatheter and surgical approaches result in a good prognosis. Approximately 4% of patients may require additional surgery for recurrence.

Life expectancy is usually considered normal. However, the risk of degenerative atherosclerotic disease may be higher if ectasia and dilatation of the coronary artery persist or progress.

Returning to the case

It is unclear if the symptoms of this young male are related to a coronary steal syndrome because of the conflicting results of the nuclear myocardial perfusion study and the stress echocardiogram performed two years prior. Even if this fistula has been assessed as small, it involves two major coronary arteries, left main and LAD. It appears prudent to postpone and offer to reconsider with a more current evaluation of coronary artery disease including a transthoracic echocardiogram.

REFERENCES


Altay S et al BMJ Case Reports 2012; doi:10.1136/bcr-2012-006998.

Koenig PR et al. Congenital and pediatric coronary artery abnormalities, 2017 UpToDate
What are the mortality considerations for someone with a diagnosis of erythema multiforme?

Erythema multiforme (EM) is a dermatological eruption which has been associated with a hypersensitivity reaction.

EM most commonly occurs in adults 20-40 years of age; however, it can occur in patients of any age. There are numerous conditions associated with this disease. Infections are believed to be the etiological agent in up to 90% of cases with herpes simplex virus (HSV) being the most common. Other infectious agents associated with EM include mycoplasma pneumoniae, adenovirus, cytomegalovirus and multiple fungal infections. Drugs and vaccines have also been associated with the condition. Non-steroidal anti-inflammatory drugs, sulfonamides, antibiotics and vaccines for hepatitis B and diphtheria-tetanus have all been implicated.

With HSV associated erythema multiforme the pathogenesis is felt to be a delayed-type hypersensitivity reaction. HSV-viral DNA fragments are transported by peripheral blood mononuclear cells to distant skin sites. CD4+ Helper T cells become involved and initiate an inflammatory response. This inflammatory response then appears as an erythematous rash.

The rash is frequently sharply demarcated and slightly raised from the surface of the skin. Its periphery is pink or red and the central portion develops a darker red, sometimes purpuric color (Figure 1). This appearance of the rash is referred to as a target lesion with 1 or 2 concentric zones surrounding this central darker area. However, the appearance of the rash frequently varies on the same patient, thus the term “multiforme”. The rash is typically distributed in a symmetrical fashion, frequently involving the extensor surfaces of the distal extremities but can be on the face, neck and/or trunk.

Oral mucous membrane lesions are common with EM, impacting patients in ~70% of the cases. Lesions may involve the lip, the buccal or labial mucosa or tongue.

When associated with herpes simplex the EM lesions typically appear two to 17 days after a herpes simplex outbreak, develop over a three-day period and resolve in approximately two weeks.

CASE #2

**Erythema Multiforme**

A 34-year-old female is applying for $1 million of life insurance. Records reveal she was recently evaluated for a skin eruption mostly involving the distal extremities but which also involved the oral mucosa. There were minimal prodromal symptoms of mild fever and malaise present. There also was a history of an outbreak of herpes simplex approximately eight days prior to the onset of this skin eruption. She had been on no medications for the last several months.

The rash was described as having “target” lesions. An urgent evaluation was recommended as there was some concern by the provider initially evaluating the rash that this might be early Stevens-Johnson Syndrome (SJS). An ER visit occurred followed by a dermatological consultation. A clinical diagnosis of erythema multiforme was made. Topical corticosteroids were prescribed. Complete resolution of the symptoms occurred quickly and this was well documented during a follow up evaluation three weeks later.
EM is frequently an isolated event; however, it can be recurrent and at times can be persistent with lesions lasting several weeks or even months.

The diagnosis is most commonly made clinically by history and exam, but skin biopsies are occasionally necessary and can help exclude other conditions. Bullous pemphigoid and cutaneous small vessel vasculitis may present with a similar rash and require a biopsy and direct immunofluorescence studies for definitive diagnosis.

Stevens-Johnson Syndrome (SJS) has historically been confused with EM as well and, at one time, many believed these two diseases might be a variation of the same condition. However, currently these two dermatological eruptions are felt to be distinct. SJS is more commonly drug induced, and the rash is more macular compared to the papular nature of EM. SJS is typically a much more severe condition than EM.

Given the typical self-limited history of EM, treatment is generally symptomatic and limited to pain and pruritus interventions. However, for more severe cases, systemic glucocorticoid therapy may be required. Antiviral agents are frequently used when EM becomes recurrent.

Mortality is not typically adversely impacted with EM. However, it is important when confronted with a rash like this that the other causes of similar appearing rashes that have been associated with adverse mortality results (e.g., SJS, toxic epidermal necrosis, pemphigoid or paraneoplastic pemphigus) are eliminated from the differential diagnosis.
The overall mortality rate for Stevens-Johnson syndrome and toxic epidermal necrosis ranges from 5% to 19% in the US based upon a recent study. Bullous pemphigoid mortality is felt to range from 11%-48% based upon a variety of international studies. Rarely, EM can be associated with malignancy or confused with paraneoplastic pemphigus.

Returning to the case

In this particular case, the clinical diagnosis of erythema multiforme was made. No definitive biopsy was done but the history of a preceding HSV infection, the presence of the characteristic rash and the complete resolution of the symptoms is reassuring. It appears there is minimal to no excess mortality risk.

REFERENCES


Here is the latest EKG Puzzler to solve.

A 54-year-old male applied for life insurance with no symptoms or illnesses declared. What is the major abnormality in this EKG?

To find the answer, visit the Housecalls page at www.scorgloballifeamericas.com. Click on December 2017 Puzzler to confirm your findings.
Reinsurance is a knowledge industry, combining technical expertise and experience with developments in science. In addition to the many tools we use to conduct our activities — models, databases, pricing tools, reserving tools and so on — we also need personal judgments, human expertise, convictions, feelings even, to correctly underwrite. This is what we call the art of underwriting.

Expertise is an accumulation of learnings and experiences. Webinars are one way that SCOR shares expertise. During 2017, our medical team produced four webinars:

- **Mitral Aortic Valvular Diseases** (May 2017)
  Dr. James Kadouch
- **Somewhere over the Growth Chart: Juvenile Obesity** (July 2017)
  Dr. Regina Rosace
- **Lynch Syndrome** (October 2017)
  Dr. Bill Rooney
- **Obesity & Opioid Addiction** (December 2017)
  Dr. Richard Braun

Recordings of these webinars are available on our website, on the SCORcast page of our Knowledge Center (scorgloballifeamericas.com/en-us/knowledgecenter). If you would like to attend future webinars, please email your name, title, company name and email address to PGranzin@scor.com.

In addition to presenting quarterly webinars, our medical team in the Americas frequently presents at industry meetings, contributes to industry publications and provides specialized training to clients.

During 2017, the medical team presented during the Association of Home Office Underwriters annual meeting, the Canadian Institute of Underwriters, the annual meeting of the ACLI and several other regional underwriting meetings as well as numerous presentations for individual client companies and our SCOR underwriters.

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**The Art & Science of Risk**

Science is at the heart of SCOR’s DNA. SCOR researchers, medical directors and other experts share scientific developments and research results in SCOR inFORM, a newsletter which has covered a range of medical topics during the past 18 months. These and other publications are available on the SCOR website, in the Resource Library (scor.com/en/media).

**Heart Valve Diseases**

Although the prevalence of heart valve diseases is low in the general population — around 2.5% — it is much higher in patients aged 75 years and older, reaching 10%–15%. The most common valve diseases are mitral regurgitation (mitral insufficiency) and aortic stenosis, which affect three patients of four. Then comes aortic regurgitation (aortic insufficiency), followed at some distance by mitral stenosis.

Improvements in healthcare during the past 30 years have contributed to a change in the distribution of causes of valvular heart disease. Thus, rheumatic valve disease, which once was predominant in young subjects, has gradually become less common. On the other hand, with the increase in life expectancy, degenerative causes have become more frequent. Moreover, it remains likely that the number of cases will continue to grow as the population ages.
Cancer Project
The increasing cancer incidence, the high prevalence of patients cured from cancer or living long-term – with or without recurrences – and the progress made in diagnosis and therapy have led to an increasing number of patients diagnosed with ‘early’ or low-stage cancers, often having better prognosis, more likely to have curative treatment, and giving rise to more so-called ‘long term survivors’.

Underwriters will then increasingly be reviewing patients with prior history of cancer. To properly balance the task of developing novel insurance products with the changes in cancer-related prognosis, algorithms and related simplified prognostic factor calculators have been developed, allowing accurate identification of categories of patients at risk for earlier relapses. This approach has also shown that a prior history of cancer does not preclude insurability at an affordable rate.

HIV Infection, Aging, Inflammation & Comorbidities
Since the introduction of the first antiretroviral therapies (ART) around the end of the 2000s, it has become clear that benefits of these treatments were considerably greater than their side effects, especially when introduced early. However, in spite of major progress made in treating HIV, these drugs cannot eradicate the infection and must be taken for life.

While ARTs are very effective at preventing AIDS, a lethal complication of HIV infection, a different complication of HIV infection has been discovered. Long considered, incorrectly, as a side effect of treatment, this long-term systemic inflammation results from chronic infection. This infection of the immune system induces a chronic, general inflammation that leads to accelerated aging of the immune system. It also leads to cardiovascular, bone and neurological complications and contributes to the emergence of cancers, independently of the immune deficiency.

Complications of chronic inflammation are all the more serious the later the treatments are initiated. However, fresh hopes are emerging with the most recent epidemiological data suggesting that early introduction of ARTs, continued without interruption, could eventually limit the incidence and severity of comorbidities associated with the chronic inflammation caused by HIV.

Breast Cancer in Women
Breast cancer in women is a real public health issue. All doctors, whatever their specialty, are confronted to some extent with patients with this type of tumor. It is the second most common type of cancer in the world. Breast cancer is responsible for more than 520,000 deaths each year, and is the fifth most frequent cause of death in the world.

Breast cancer represents 25% of cancers diagnosed worldwide and 31.5% of all malignant tumors identified in France. The figures sometimes translate an extremely heterogeneous reality of tumor pathology, in particular wide geographical and ethnic disparities. Recent epidemiological data as well as new diagnostic and therapeutic techniques, have led to the risk connected with cancer in general and breast cancer in particular being reevaluated.

For a copy of these or other inFORM newsletters, email your name, title, company name and email address to PGranzin@scor.com.
In one study of the US population 25% of cardiovascular events were attributed to hypertension. Other studies have indicated that a 20 mm Hg rise in systolic blood pressure and a 10 mm Hg rise in diastolic BP are each associated with a doubling of the risk of death from heart disease, stroke and other vascular diseases.

And a study from Scotland indicated that 37% of the improvement in heart disease deaths prevented or postponed between 2000 and 2010 was due to lowering of systolic BP. Hopefully, the overall effect of these new guidelines will be a future improvement in the incidence and mortality rates due to cardiovascular disease.

Speaking of the heart, in this issue of *Housecalls* Dr. Kadouch discusses a case of coronary artery fistula. Dr. Rooney presents a skin disorder that appears serious but is usually self-limited. And Dr. Rosace has an EKG Puzzler for your consideration.

This is our final issue for 2017, and all of the staff at SCOR wish you and yours a safe and happy holiday.