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Insight HEART

SQUARE PHARMACEUTICALS LTD. BANGLADESH

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Of heart and kidney: a complicated love story

Introduction

The multiple connections that exist between the cardiovascular system and the kidney lead to a complex cardiovascular and renal medicine relationship. It is well established in the literature that chronic kidney disease (CKD) is an important and independent risk factor for cardiovascular disease (CVD). This article is an overview of the current knowledge in the joint cardiological and nephrological fields on the heart–kidney interrelation topic.

The cardio-renal link is a well-documented chain of events that can be initiated by either of the organs involved. The relatively recently proposed term of 'cardio-renal syndrome' (2008), although easily accepted in theory, encounters taxonomic difficulties as its definition is not globally approved yet.

The CKD concept

The concept of CKD was introduced by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) in 2002 and has been defined as: kidney damage (abnormalities in the blood or urine – albuminuria/proteinuria/haematuria – and abnormal imaging or pathology tests) for more than 3 months and/or estimated glomerular filtration rate (eGFR) $\leq$60ml/min/1.73m^2 for more than 3 months. Based on the level of kidney function (eGFR), CKD has five stages: stage 1 for eGFR $\geq$90; stage 2 for eGFR 60–89; stage 3 for 30–59; stage 4 for 15–29 and stage 5 for eGFR <15ml/min/1.73m^2 or 5D when the patient is dialysis dependent.

A workgroup established by KDIGO (Kidney Disease Improving Global Outcome – managed by National Kidney Foundation in USA) is currently revising the classification of KDOQI's 2002 CKD definition, analysing the necessity of including albuminuria level in the staging of CKD.

According to USRD (Unites States Renal Data) and European renal registries data, in both the USA and Europe the most frequent causes of CKD are diabetes and hypertension.

Although the prevalence of CKD in the general population is similar to diabetes prevalence, CKD is still a 'silent epidemic' ignored by most of the European governments' health plans (i.e. 2007 Italy's National Institute of Statistics Report did not include CKD among the chronic diseases), as the EUGLOREH programme revealed.

The prevalence of CKD in various populations

CKD is becoming an economic burden and a public health issue all over the world. A systematic review of the studies conducted in Europe, America, Asia, and Australia in 2008 showed that the median prevalence of CKD in the general population was 7.2% (for those over 30 years old) and varied from 23.4 to 35.8% for the elderly (more than 64 years old), with a slightly higher prevalence among women.

In the US CVD patient population, the prevalence of CKD varies from 50% to more than 60% (up to 9-times higher than in the general population), depending on the CV diagnosis (congestive heart failure or acute myocardial infarction in Medicare hospitalized patients).

Data on the prevalence of CKD in CVD patients in Europe is scarce, but seems to correspond with the US results. Our data from Romania show a prevalence of CKD stage 3–5 in the general population of 11.7%, based mainly on GFR <60 ml/min/1.73m^2, in a cohort of over 19,000 patients.

Personal data analysing more than 2000 high-risk patients (CVD, stroke, diabetes, peripheral artery disease) hospitalized in a county hospital in

western Romania showed a prevalence of CKD ranging between 34 and 46%, a significantly 2-fold higher risk of in-hospital mortality and a significantly higher prevalence of acute kidney injury in the CKD group.

The prevalence of CVD in the CKD population

Compared to non-CKD patients, where the prevalence of CVD ranges between 13.9% (men) and 9.3% (women), the prevalence of CVD among stage 1–5 non-dialysis (ND) CKD patients is 17.9% (men) and 20.4% (women) and rises up to 40% in patients starting dialysis, and at this stage up to 85% of the patients having impaired left ventricular function or structure (echocardiographic criteria).

Cardiovascular mortality follows the same trend, from 40% in the US general population to more than 50% in ND-CKD patients and 15-times higher in end-stage renal disease (ESRD) patients than the general population.

In type 1 and 2 diabetic patients, any amount of albuminuria/proteinuria (which means that the patient is a CKD diabetic patient) is associated with an increase in cardiovascular risk and mortality. Peripheral artery disease (PAD) has a prevalence of 7% in stage 1–5 ND-CKD and 17– 48% in CKD-5D patients, respectively. Sudden cardiac death has a 5.5% rate annually and represents approx. 22% of all dialysed patient deaths.

Mortality and CV risk

The patient diagnosed with CKD stage 3 typically has a higher risk of dying of CVD than of starting renal replacement therapy, based on the observation that the prevalence of CKD stage 5 (ESRD) is approximately 30-times lower than the prevalence of CKD stage 3. The adjusted hazard ratio for death increases from 1.2 (for eGFR 45–59 ml/min/1.73m^2) to 5.9 (for eGFR <15ml/min/1.73m^2) and the adjusted hazard ratio for cardiovascular events has the same trend: 1.4 (for eGFR of 45–59ml/min/1.73m^2) to 3.4 (for eGFR <15ml/min/1.73m^2).

However, new studies on diabetes mellitus CKD patients reported more optimistic results regarding the mortality–ESRD competition: most of the old diabetic patients with severe renal insufficiency and high-level albuminuria reached ESRD during the 3 years of follow up.

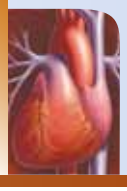
CKD, expressed mainly by reduced eGFR (<60ml/min/1.73m^2) and albuminuria/proteinuria (>30mg/24 h or albumin/creatinine ratio >30 mg/g or ≥1 on specific dipstick) is an independent cardiovascular risk factor and the diagnosis of CKD implies a 'very high cardiovascular risk patient'. The newly-released ESC/EAS Guidelines for the management of dyslipidaemias added CKD as a very high global cardiovascular risk criterion, along with known CVD, type 2 diabetes, type 1 diabetes with microalbuminuria, and very high levels of individual risk factors. This is a new approach to CV risk assessment; previous ESC/EAS guidelines on cardiovascular disease prevention in clinical practice and those on arterial hypertension mentioned the kidney only from the target organ damage perspective, although the KDOQI Clinical Practice Guidelines for Chronic Kidney Disease have recommended that 'all patients with chronic kidney disease should be considered in the "highest risk" group for cardiovascular disease, irrespective of levels of traditional CVD risk factor' since 2000. This emphasis of CKD in the later cardiology guidelines suggests that cardiologists became fully aware of the importance of a diseased kidney in the cardiovascular prognosis.

Markers of CKD – reduced eGFR and albuminuria/ proteinuria – have been evaluated in numerous studies that have revealed an association between these markers and progression to ESRD, mortality, and cardiovascular disease. The lower the eGFR, the higher the probability of progression to ESRD, death, or CVD, while albuminuria was found to be a factor which, directly proportional to its severity, aggravates the prognosis when combined with low eGFR, as well as a factor that, independently from low eGFR and other cardiovascular factors, increases CVD and all-cause mortality in high-risk population and in general population cohorts.

Low eGFR increases CV risk in patients with CV disease (heart failure, myocardial infarction, arterial hypertension) and also in the general population. A recently published meta-analysis on 7 million participants reported that a 30% lower eGFR increases by 20–30% the risk of major vascular events and all-cause mortality. Albuminuria per se, a marker of endothelial dysfunction, measured as albumin/creatinine ratio and considered abnormal when exceeding 30 mg/g (KDIGO), is associated with high CV risk in the general population (MONICA, HUNT studies), as well as in the at-risk population (HOPE, LIFE studies, Mogensen report).

Given the previously presented data, one can draw the conclusion that there is a vicious circle between the heart and the kidney, which involves a mutually aggravating interrelation. Moreover, many of the traditional risk factors are the same for CKD as for CVD, acting as promoters of endothelial dysfunction, which affects organ perfusion by atherosclerosis in larger vessels and 'vascular rarefaction' in microcirculation, and represents one of the common pathways to kidney and heart damage.

Traditional CV risk factors involved in CVD and progression of CKD are: age, male gender, genetic background, obesity, hypertension, dyslipidaemia, diabetes, increased fibrinogen and other coagulation factors, and smoking.



Some of them (age, genetic background, hypertension, and diabetes) increase susceptibility to or directly initiate the kidney damage. High levels of proteinuria, high blood pressure, poor glycaemic control, and smoking are renal progression factors that worsen the cardiovascular outcome too. CKD-specific risk factors (anaemia, hypoalbuminaemia, acidosis, volume overload, natriuretic peptides, proteinuria, CKD-mineral and bone disorder, and other markers of endothelial damage) are subject to intense research.

Is CVD the same in the CKD population as in the general population?

This question was raised by KDIGO at a 2010 conference that gathered international experts in nephrology, cardiology, neurology, and other relevant clinical specialties, who analysed current data on CVD and CKD.

Coronary artery disease and myocardial infarction have a particular pattern in CKD, mainly by medial vessel calcification and diffuse involvement and carry a high risk of death inversely proportional to the renal function and it is rather dificult to detect with conventional methods, which require contrast media, due to the renal toxicity of this substances. Cardiac biomarkers (MB creatine kinase and cardiac troponines) might be elevated in the presence of renal failure alone.

Congestive heart failure, especially diastolic, is the most frequent cardiac disease in CKD patients. The main mechanism appears to be the myocardial remodelling by fibrosis, which leads to left ventricular stiffening and diastolic failure. Myocardial stunning during dialysis worsens the prognosis. The best diagnostic tool is echocardiography, while the natriuretic peptides (BNP and NT-proBNP) are less useful.

Atrial fibrillation is the most common arrhythmia in CKD patients (prevalence of 15–20% in CKD-5D) and has a high incidence of left atrium emboli causing ischaemic stroke, but the primary prevention of stroke with the use of warfarin anticoagulation has revealed an increased risk of bleeding in haemodialysed patients.

Apart from traditional risk factors, such as age, smoking, male sex, diabetes, and hypertension, PAD is associated with kidney-specific risk factors: dialysis duration, Kt/V (a measure of dialysis adequacy), low parathyroid hormone, low serum albumin, high phosphorus, inflammation, and malnutrition.

Using ankle–brachial index for PAD diagnosis is not very accurate because of the high percentage of calcified vessels; toe–brachial index and pulse volume recordings should be used instead.

Sudden cardiac death is not a straightforward diagnosis in dialysed patients because of the high mortality risk at any time. There is only little data on the underlying cause of sudden cardiac death, but the existing evidence in CKD-5D points towards stroke (Japan), hyperkalaemia, ventricular arrhythmias, and coronary artery disease, while in the general population, coronary artery disease is the leading cause.

Prevention and treatment of CVD in CKD patients

Prevention is the most desirable action for increasing the CKD patient's chance of survival, but an even more difficult task than in the general population. Evidence-based treatments and measures are poor, most of the trials excluding patients with kidney failure. Managing CKD patients should target lowering the CV risk factors and target organ damage reduction (cardiac, cerebrovascular, peripheral artery, and residual renal function).

Although they had not been analysed in randomized trials, lifestyle changes should be made, in terms of smoking cessation, exercise, weight loss, and low salt diet. A 2010 meta-analysis on diabetes-related CKD patients showed a 7/3 mmHg lower systolic/diastolic blood pressure when dietary salt intake was reduced by 8.5 g/day, a result similar with a single antihypertensive drug therapy, reinforcing the fact that the salt intake restriction of up to 5–6 g/day recommended for general population should be respected by diabetic CKD patients too.

Daily aspirin has a positive effect on cardiovascular risk, even in dialysed patients, but with a higher rate of bleeding events. When used for secondary prevention in CKD patients with coronary artery disease, doses of 75–160 mg/day should be preferred.

Hypertension is a matter of intense debate among nephrologists, the target blood pressure value being <130/80 mmHg or even less (<125/75 mmHg) in the presence of proteinuria/albuminuria. However, there is certain data suggesting that values lower then 130/80 mmHg in CKD patients might increase adverse effects, making randomized controlled trials on this particular matter essential.

The antihypertensive drugs used for blood pressure control that have also demonstrated cardiac and renal protection effect are the combination of renin–angiotensine system (RAS) suppressors with calcium-channel blockers (benazepril and amlodipine in ACCOMPLISH study).

A meta-analysis from 2008 on CKD patients revealed significant risk reduction of CV outcomes on CKD patients of all causes when treated with RAS blockade compared to placebo (0.84, 95% CI 0.78–0.91, p<0.0001) and 44% less

CV events in nondiabetic patients treated with RAS inhibition than with other antihypertensive medication, while CKD patients with proteinuria have the most benefit from RAS blockade treatment.

Lipid-lowering therapy with statins showed no cardiovascular benefit in dialysis patients in two major studies: 4D (Die Deutsche Diabetes-Dialyse) and AURORA (A study to evaluate the Use of Rosuvastatin in subjects On Regular haemodialysis: an Assessment of survival and cardiovascular events).

The SHARP (Study of Heart and Renal Protection) trial (simvastatin plus ezetimibe vs. placebo in ~9500 CKD patients, of which more than two-thirds were pre-dialysis patients) results were published: 17% reduction in major atherosclerotic events and 15% reduction on major vascular events but no positive effect on mortality in the treated group. The SHARP trial results are congruent with the previously mentioned trials that showed no cardiovascular benefit of starting statin therapy in patients already on dialysis and reinforce the idea that the cardiovascular disease changes its pattern while the CKD progresses (from atheroma to calcifications).

A meta-analysis on ~4500 CKD stage 3 patients showed a 23% reduction of cardiovascular risk when pravastatin was used. The 2011 ESC/EAC guidelines for dyslipidaemia acknowledge the cardio-protective role of lowering low-density lipoprotein cholesterol in CKD patients and recommends a target of (<70 mg/dl (<1.8 mmol/l) in moderate to severe CKD, achieved mainly by the use of statins.

Glycaemic control is requested in diabetic CKD patients, both for CV and renal protection. The recommended HbA1c target of <6.5% is being seriously questioned in a recent study performed on more than 23,000 diabetic CKD stage 3 and 4 patients where cardiovascular events, death, and progression to ESRD were higher with HbA1c >9% but mortality followed a U-shaped curve, increasing at HbA1c <6.5% and >8%.

CKD-mineral and bone disorder promotes vessel calcification, intimal (atherosclerosis), and medial (arteriosclerosis), which are associated with cardiac events and arterial stiffness. Reducing calcium burden by using non-calcium phosphate binders in the presence of vascular calcifications is a KDIGO recommendation.

Anaemia treatment with erythropoietin-stimulating agents should target a haemoglobin level between 11–12 g/dl. The unexpected results of Trial to Reduce Cardiovascular Events with Aranesp Therapy (TREAT) study, which analysed the risk of death, CV events, or renal events in diabetic CKD patients, showed no benefit in the darbepoetin arm compared to placebo. Following these results, the next KDIGO anaemia guidelines will, probably, include some changes in the recommendations on the use of erythropoietin-stimulating agents.

Treatment of acute myocardial infarction in CKD patients is almost similar to non-CKD patients, with the caveat that CKD population is not very well represented in the myocardial infarction trials. Serious perioperative complications after coronary artery bypass graft surgery occur up to 7-times more frequent in ND-CKD patients.

Clopidogrel was successfully used in CKD patients diagnosed with acute coronary syndrome, proving to be beneficial and safe even in patients with low kidney function.

Regarding congestive heart failure treatment, there is strong evidence as to the benefit of bisoprolol or carvedilol use in CKD. The use of beta-blockers in CKD patients with systolic heart failure was recently investigated in a meta-analysis and the results clearly stress a relative risk reduction of 28% in all-cause mortality and of 34% in cardiovascular mortality compared to placebo. Angiotensin-converting enzyme inhibitors and angiotensin-II receptor blockers, aldosterone antagonists, and direct renin inhibitors, although very useful and recommended when proteinuria is present, should be used under nephrological specialist supervision in CKD stages 4 and 5 patients.

Primary stroke prevention in atrial fibrillation in dialysed patients with anticoagulation is not recommended due to the high risk of haemorrhagic events, but secondary prevention can be used. For CKD stage 1–4 patients, the Food and Drink Administration has approved dabigatran as a stroke prevention medication in atrial fibrillation.

Conclusions

Nephrologists should become more concerned with lowering the CV risk of CKD patients than with their patient's progression to ESRD, while cardiologists should be aware of the danger a diseased kidney poses to the patient's cardiovascular system, and hence they should actively search for CKD presence in view of a more accurate risk grading of CV patients. Treating a CVD and CKD patient is a challenge especially when the kidney function is low (CKD stage 4–5/5D), since evidence-based measures are frequently missing, making the cardiology–nephrology cooperation mandatory.

Ref.: Of heart and kidney: a complicated love story. Dan Gaita, Adelina Mihaescu and Adalbert Schiller. European Journal of Preventive Cardiology,2014, Vol. 21(7) 840–846.

A Practical Approach to Investigation of Syncope

Syncope is caused by cerebral hypoperfusion. Most fainting is simply vasovagal syncope; the challenge lies in identifying the few patients who have potentially life-threatening causes. Patients usually present with simply the history, and no pathognomonic physical or diagnostic data. Even identifying a risk factor or substrate for syncope does not mean that it is the cause, because vasovagal syncope remains the most common cause. A safe and efficient approach is first to stratify patients to identify those who might be at risk of sudden death, then identify the cause and try to prevent recurrences. A systematic approach helps to avoid pitfalls in risk stratification and diagnosis.

Syncope is a transient loss of consciousness of rapid onset, short duration, and spontaneous recovery, associated with at least 1 of: (1) features indicative of specific forms of syncope (like vasovagal syncope); and/or (2) the absence of features suggesting another cause of loss of consciousness (like epileptic convulsions or hypoglycemia).

Patients with syncope constitute 1%-2% of emergency department visits; approximately 30%-50% are admitted. Although the overwhelmingly most common cause of syncope is vasovagal syncope, among patients presenting to the emergency department, vasovagal syncope comprises only approximately 50% of cases. Orthostatic hypotension and cardiac syncope each comprise approximately 7%. Approximately 30%-50% of patients with syncope leave the emergency department without a diagnosis. Although syncope raises concerns about serious risks, the reality is surprisingly good. The 30-day mortality is estimated at 0.7%, and the composite adverse 30-day outcome at 4.5%. Definitions of adverse outcome vary from a return visit to the emergency department to a procedure such as pacemaker insertion. The main problem is how to find the few at risk among the great majority who will do well, often in the absence of visible clues.

One key emerging insight is the distinction between risk stratification and diagnosis. Front-line workers often cannot establish a definitive cause of syncope, but can nevertheless sort patients into high or low-risk groups (Fig.1). High-risk patients are those that might have a fatal cause of syncope, and low-risk groups are those without a potentially fatal cause. For example, patients with syncope and structural heart disease might only have vasovagal syncope, but are a priori high-risk patients because they might have ventricular tachyarrhythmias.

There is good evidence for specific risk markers. They include (Fig. 2) syncope while supine or with marked exertion, without a prodrome, with structural heart disease or heart failure, with a family history of early sudden death, or with an electrocardiogram (ECG) indicative of tachyarrhythmic, bradyarrhythmic, cardiomyopathic, or ischemic heart disease. Baseline hypotension is also important. None of these is highly specific, but each raises a cautionary flag.

The absence of all of these factors identifies a low-risk patient. Younger than the age of 50 years, almost all patients have benign causes of syncope, other than the rare patient with a genetic cardiomyopathy or arrhythmia. In patients older than the age of 50 years the differential diagnosis is much wider.

History

The history of an unconscious spell provides a wealth of information. It is most useful for distinguishing vasovagal syncope and orthostatic hypotension from arrhythmic causes. Structure the history to glean insight from 3 distinct phases: (1) the context before symptoms; (2) prodromal symptoms; and (3) how the patient felt afterward. Try to get a bystander history.

Diagnostic tips abound in the preceding activity. Patients fainting within the first 20 seconds of arising from lying or sitting almost always have orthostatic hypotension. The typical history involves fainting after the patient walked for a few feet to the kitchen or bathroom. Presyncope that reliably worsens with standing, yet with infrequent syncope, suggests classic orthostatic hypotension caused by use of drugs, dehydration, or autonomic neuropathy. A history dominated by exposure to pain, blood, or medical procedures, or quiet upright posture for more than a minute or two is almost diagnostic of vasovagal syncope. Syncope during strenuous exertion is a red flag for arrhythmias, although it can also be a subset of vasovagal syncope.

Prodromal symptoms of vasovagal syncope usually last less than 1-2 minutes, and can be absent. Progressive hypotension typically causes progressive weakness, presyncope, and visual blurring. Brief terminal warmth, probably due to abrupt paradoxical vasodilation, is common. Diaphoresis and pallor are due to compensatory reflexes, and nausea and vomiting are associated somatic vagal symptoms. Patients usually have only some of these symptoms; all are significant. Initial orthostatic hypotension and arrhythmic syncope have few or no prodromal symptoms.

Bystanders provide information that helps distinguish

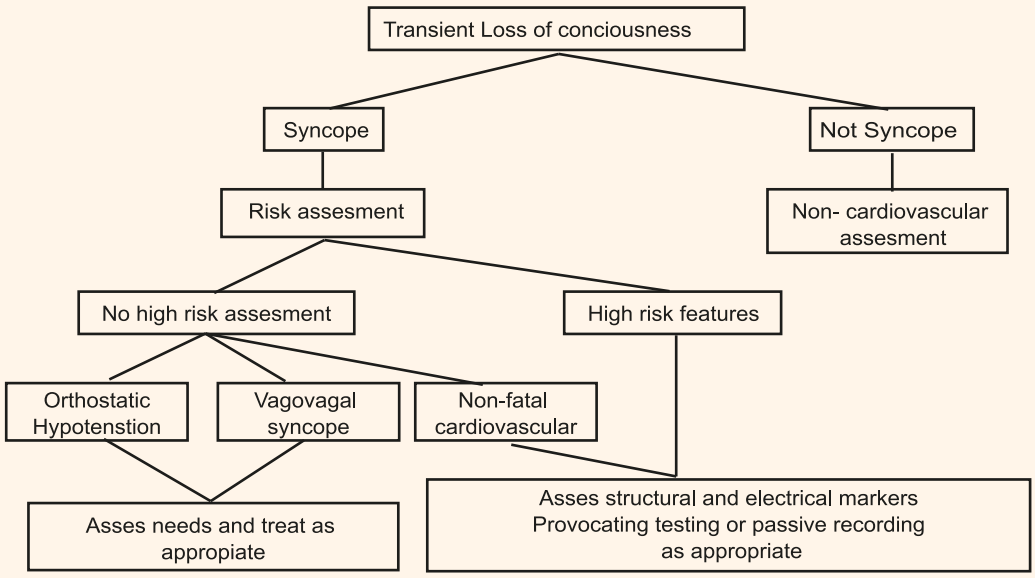


Figure 1. A risk-based approach to the syncopal patient. This approach focuses on first determining the safety of the patient, then determining a diagnosis. Most other algorithms first diagnose low-risk syncope, then risk stratify the rest.

A

High risk markers for syncope patients in emergency departements
Age > 60
1-2 spells
Precedding palpations
Syncope while supine or with marked exortion
Structural hearth disease or heart failure
Family history of early sudden death
Hypotension
Evidence of hemorrhage
Abnormal ECG

B

Point score for vasovagal syncope in health people < 60 years	Points
For cardiac syncope	
Bifasicular block, asystole, supraventricular techycardia, or diabetes	-5
Cyanosis noticed by bystander	-4
Age of first syncope >35 years	-3
Remembers something about spell	-2
For vasovagal syncope	
Presycope or syncope with prolonged sitting or standing	+1
Sweating or warm felling before a spell	+2
Presyncope or syncope with pain or medical procedure	+3
Vagovagal syncope if total > -3	

C

Predicting recurrence of vasovagal syncope	
Faints in proir year	Likehood or recurrence in next year
0	7%
1	25%
2 or 3	40%
4 or 6	50%
> 6	70%

Figure 2. Predicting the future of syncope patients. (A) High-risk markers for syncope patients in the emergency department; (B) diagnostic point score for vasovagal syncope vs cardiac syncope in patients without structural heart disease; (C) likelihood of vasovagal syncope recurrence depends on syncope frequency in the previous year.

among epileptic seizures, various causes of syncope, and pseudosyncope. There might be a history of convulsions, almost always due to myoclonus, which comes in a dazzling array of presentations. Stiff quivering is the most common but more coarse movements are not infrequent. Incontinence is not a useful finding. Pallor usually denotes vasovagal syncope, and cyanosis is more common with arrhythmic syncope. A useful set of signs for pseudosyncope is slumping carefully to the floor, a benign indifference, and consistent lack of trauma, closed eyes, and lack of change in skin colour or diaphoresis.

After vasovagal syncope, the patient is usually dazed for a brief while, and often exhausted. Sleeping to recover is not rare. The patient might feel wretched, tremulous, and nauseated. These symptoms are rare with other causes of syncope. Three scoring systems distinguish syncope from epileptic seizures, vasovagal syncope from other causes in patients with normal hearts, and vasovagal syncope from ventricular tachycardia in patients with structural heart disease. They are approximately 90%-93% accurate; 1 system is shown in Figure 2.

Physical Examination

No physical findings are completely diagnostic of syncope or its causes. Search carefully for signs of substrates like those of severe aortic stenosis, hypertrophic cardiomyopathy, dilated left ventricle, carotid sinus supersenistivity, and orthostatic hypotension.

Only a minority of patients require further investigation There is no standard investigation pathway, investigations depend on clinical suspicion and whether the results will affect outcome.

The purposes of investigation are to: (1) exclude a structural substrate like left ventricular dysfunction; (2) capture risk factor data like ejection fraction or bundle branch block; (3) capture data during clinical syncope; and (4) induce syncope and relate it to clinical events.

Diagnostic Tests

Most tests are positive in only 1%-4% of patients, but the use of tests like brain computed tomography scans remains widespread. Goal-directed investigation leads to better and ore efficient decision-making. Remember: target the investigation to the patient.

A 12-lead ECG has low diagnostic yield but is effective because it is inexpensive. It should be examined for evidence of conduction disease, repolarization abnormalities, QT prolongation or abbreviation, ischemic heart disease, and ventricular hypertrophy. Pay particular attention to the right precordial leads for signs of Brugada, arrhythmogenic right ventricular cardiomyopathy, and long QT syndrome, and to the inferolateral leads for early repolarization syndrome and long QT.

ECG monitoring is recommended if an arrhythmic cause is highly suspected after initial evaluation. It is also useful to exclude an arrhythmic cause if sinus rhythm is documented during symptoms. ECG monitoring can be achieved using several means. The yield of extended monitoring is often disappointingly low because of the sporadic nature of syncope and low recurrence rates. In-patient telemetry should be reserved for patients with underlying structural heart disease who have a high risk of arrhythmic events. Even in high-risk populations, the yield of 72-hour telemetry is a low 16%.

Another means is 24- to 48-hour Holter monitoring. One month of monitoring has a diagnostic yield of 12% for arrhythmic syncope and 12% for sinus rhythm during syncope. One-month event recorders have better diagnostic utility than 48-hour Holter monitors. Implantable loop recorders have the highest diagnostic yield, with a battery life up to 3 years. There is reasonably good evidence that implantable loop recorders should be used in older patients early after the initial encounter, if reasonable diagnostic uncertainty persists. They increase the diagnostic yield, decrease time to first diagnosis, and are cost-neutral or cost-effective. On the whole, they establish a diagnosis in 30%-40% of patients over 2-3 years. At least half the time they simply detect sinus rhythm during syncope.

Tilt table testing is the most common provocative test. The goal is to trigger clinically reminiscent presyncope or syncope associated with hypotension and at times bradycardia. They are occasionally useful in distinguishing epilepsy from convulsive syncope, or clarifying pseudosyncope or postural orthostatic tachycardia syndrome. They have imperfect accuracy, imperfect reproducibility, numerous variables affecting outcome, and do not predict outcome or response to treatment.

Finally, they are not needed very much of the time. A good history provides more useful and more accurate information in more patients. Echocardiography is essential in patients suspected to have underlying structural heart disease. Further imaging using computed tomography, myocardial perfusion, cardiac catheterization, or magnetic resonance imaging is of limited value unless right ventricular or infiltrative cardiomyopathy or myocarditis is suspected. Exercise testing should be considered in patients with exercise-induced syncope or syncope after exertion. Electrophysiologic studies are rarely indicated, primarily when targeted by earlier specific findings. They occasionally are helpful in patients with syncope and bifascicular block, or with only moderately depressed left ventricular systolic function.

Ref.: A Practical Approach to Investigation of Syncope. Tarek Hatoum, MD, and Robert Sheldon, MD, PhD. Canadian Journal of Cardiology 30 (2014) 671-674.

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Cardiology News

Stress Angina Edges Ischemia as a Solo Risk Predictor in CLARIFY Registry

The CV-event risk was significantly elevated among patients with symptoms but no ischemia at stress testing compared with those who had neither symptoms nor objective ischemia in a large, prospective observational study of patients with stable CAD. But the risk wasn't elevated or reduced in patients with silent ischemia at stress testing. Moreover, in the study, most CV events occurred in patients without either angina or myocardial ischemia. It suggests that clinicians should implement rigorous secondary prevention in all patients with CAD, even those who are asymptomatic and test negative for ischemia.

August 11, 2014, JAMA Internal Medicine.

Digoxin in Early AF Ups Mortality Risk

In a large cohort of elderly veterans newly diagnosed with atrial fibrillation [AF], those who received initial treatment with digoxin had a >20% increased risk of dying within about three years compared with their peers. The risk increase was independent of age, sex, heart failure, kidney function, or concomitant use of beta-blockers, amiodarone, or warfarin.This study, based on more than 122 000 patients who participated in The Retrospective Evaluation and Assessment of Therapies in AF (TREAT-AF), virtually all of whom were men.

J Am Coll Cardiol 2014; 64:660–668

FFR- and IVUS-Guided PCI Do Not Reduce Mortality Long-Term

The use of fractional flow reserve (FFR) or intravascular ultrasound (IVUS) during PCI is not associated with improved long-term mortality rates when compared with standard angiography-guided PCI, according to a new observational study. The results are based on an analysis of 41 688 patients with stable angina and non-ST-segment-elevation MI (NSTEMI) included in the Pan-London (United Kingdom) PCI Registry. Compared with conventional PCI, there was no statistically significant difference in mortality among those treated with FFR- and IVUS-guided PCI after a median of 3.3 years.

JAMA Intern Med 2014; 174:1360-1366. Abstract

BP Control: Not Too Low, Not Too High Is Best

In a large, diverse population of patients being treated for hypertension, those who attained blood-pressure (BP) levels above or below an optimal range were more likely to die or develop end-stage renal disease (ESRD) during a three- to five-year follow-up. A BP of 137/71 mm Hg was associated with the lowest risk of death or ESRD (need for dialysis or a kidney transplant) during follow-up. However, for diabetic patients, the BP with lowest risk was 131/69 mm Hg, and for patients aged 70 and older, it was 140/70 mm Hg. Therefore, attaining very low BP levels or having poorly controlled, elevated BP levels both appear to be harmful in patients receiving treatment for hypertension.

August 12, 2014, Journal of the American College of Cardiology.

Editorial Note

Dear Doctor,

We are happy to present the 34th issue of "Insight Heart". It is a small endeavor to provide you compiled & updated information on cardiovascular diseases and its management. This issue is focused on ***"Hearth- Kidney relation on CVS"*** and ***"Synocpe"***. We will appreciate your thoughtful comments.

Thanks and regards.