‘Doctor, what should I do for my high blood cholesterol?’

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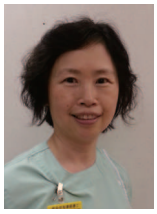

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Many private clinical laboratories in Hong Kong nowadays have an aggressive marketing strategy. People were approached through various means and offered ‘body check packages’ at a low price. People only need to go to the laboratory for blood taking and such ‘body checks’ usually include blood cholesterol measurement. Not much clinical counselling service is included in the package and if the blood cholesterol is ‘above limits’, people had to consult their own doctors for advice. Hence we might be faced with the question ‘Doctor, what should I do with my high cholesterol?’

The first part of the answer is ritualistic – life style changes such as the low cholesterol diet but most patients already had such knowledge either from the Internet or from their aunties. They wish to know more, especially whether medical (drug) treatment is necessary if it is still high despite life style changes.

When the author was a house officer, the teaching was that the upper limit of normal of cholesterol is 200 mg/dl (5.2 mmol/l) and if it is >240 mg/dl (6.2 mmol/l) despite life style changes, then drug treatment is needed. (At that time the SI units were not used in Hong Kong). The drug used at that time was cholestyramine which is a bile acid sequestrant and had quite a bit of unpleasant gastrointestinal side effects. Later other medications such as fibrates, statins and ezetimibe, which were better tolerated and more effective, were available.

Such approach was reasonable because the cholesterol of 6.2 mmol/l is usually regarded as high and hence would require treatment. Medicine has progressed over these 40 years and it is now it was too simplistic to base the decision on blood cholesterol alone. Many ‘guidelines’ on this topic have been published by professional bodies such as the American College of Cardiology (ACC), American Heart Association (AHA), the European Society of Cardiology/European Atherosclerosis Society (ESC/EAS), the Canadian Cardiovascular Society (CCS), the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines and the American Association of Clinical Endocrinologist (AACE). This is not surprising as cardiologists, endocrinologists, nephrologists and of course the family physicians all need to tackle the hypercholesterolaemia problem. The myriad of guidelines from different ‘stakeholders’ may be confusing at times and hence a detailed analysis of the case scenarios might be useful.

Case 1:

*A 64 year old male person was found to have **total cholesterol was 6.1 mmol/l** on medical check. His HDL cholesterol 1.84 mmol/l and the LDL cholesterol 3.5 mmol/l. He is a non-drinker and a non-smoker. He has history of hypertension but no diabetes mellitus. He was health conscious all along and had been avoiding high cholesterol foods. His blood pressure was 120/70 mm Hg while on medication.*

High blood cholesterol is a well-known risk factor for coronary heart disease CHD) and its mortality bears a linear relationship with the cholesterol level. It was later found that the high density lipoprotein (HDL) cholesterol has protective effect on the blood vessels while the low density lipoprotein (LDL) cholesterol is artherogenic. The Framingham study showed that apart from cholesterol, smoking habits, sex, age and hypertension were also important. It would therefore be too simple to base the

Figure 1

Figure 2

treatment plan on the total cholesterol factor alone. The Framingham group designed a chart to help the clinicians to make the holistic view of the situation. (Figure 1) The chart takes into account of whether the patient is a diabetic, the age, the sex, smoking, the systolic blood pressure and the ratio of the total cholesterol to HDL cholesterol.

Note that the tool used the **ratio of total cholesterol to HDL cholesterol ratio** and a ratio of >6 is a call for action. From the chart, the Framingham risk score can be determined and the details were described elsewhere. [1] Alternatively, the score can be calculated from an apps which can be downloaded for free [2]. The application has a greater predictive power because it takes into account of whether the patient is taking hypertensive medication and whether he/she had peripheral vascular diseases. (Figure 2)

The criticism of the Framingham Score is that it does not take into account of body mass index and activity level and other medical conditions of the patients. The study was predominately done on a white population in the United States. It was said the original equation over-estimated the risk of men in the UK by 5%. [3] The UK QRISK2 risk assessment models tried to address these problems and it took into accounts of other factors such as the presence of chronic kidney disease (CKD), deprivation and 'self-assigned ethnicity' etc but the Framingham risk score is still widely used.

From the Framingham score calculation, the above patient has a 10 year Global CVD Risk of 15.6%, which was moderately high. According to the ESC 2007 guideline, the target level is LDL cholesterol was <3 mmol/l and total cholesterol <5 mmol/l. For this reason, he was given a statin. Note that the ESC guideline utilizes the LDL level (the 'bad' cholesterol') instead of the total cholesterol/HDL cholesterol ratio as in the Framingham study.

Case 2:

Let us consider a hypothetical scenario if the above patient has diabetes mellitus as well.

*A 64 year old male person was found to have **total cholesterol was 6.1 mmol/l** on medical check. His HDL cholesterol 1.84 mmol/l and the LDL cholesterol 3.5 mmol/l. He is a non-drinker and a non-smoker. He has history of hypertension but he was a long-term diabetic. He was health conscious all along and had been avoiding high cholesterol foods. His blood pressure was 120/70 mm Hg while on medication.*

A diabetic pateint has high chance of developing CHD, the risk is as high as those who had history of CHD and hence diabetes mellitus is considered a CHD risk equivalent. Since the LDL cholesterol is atherogenic, the level should be kept below the 'normal' ideal level of 2.6-3.3 mmol/l. The target would be around 2.6 to 1.8 mmol/l, depending on the presence of other factor.

The above patient has a 10 year Framingham Global CVD Risk of 25.3%, which was high. According to the ESC 2007 guidelines, the target level is LDL cholesterol <2-2.5 mmol/l and total cholesterol <4-4.5mmol/l He was started on statin treatment. The plan was that if the target is not achieved, ezetimibe would be considered.

Case 3:

A 56 male diabetic patient was followed up in the renal clinic. His blood urea was 6.3 mmol/l, creatinine 84 umol/l, eGFR 87 ml/minute. His serum cholesterol 3.6 mmol/l, HDL cholesterol 0.9 mmol/l, LDL cholesterol 2 mmol/l. The urine microalbumin was elevated on two occasions and the HBA1C was 7.9%. He was not on statins. (Figure 3 and 4)

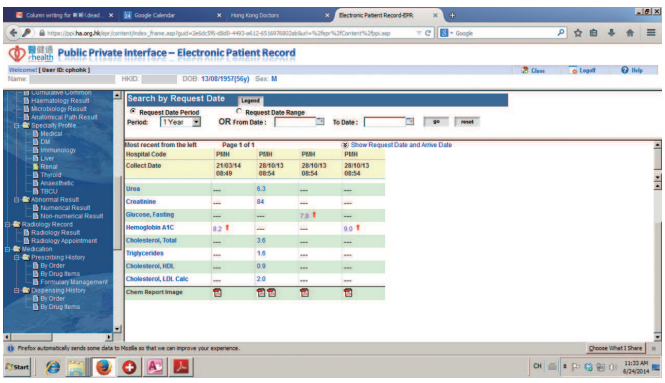

Figure 3

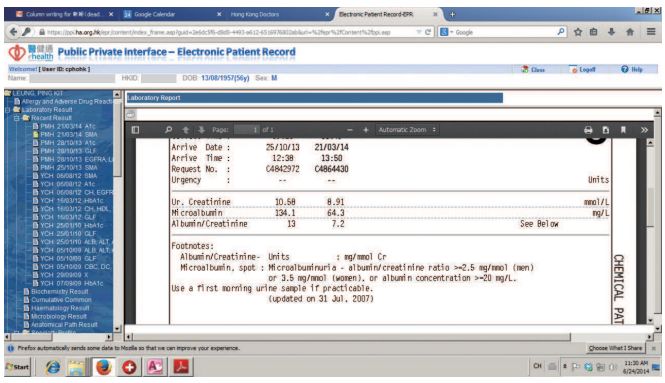

Figure 4

This patient has 'normal' renal function (eGFR 87 ml/minute) but he has CKD because he had microalbuminuria indicting that he has diabetic nephropathy. CKD patients have increased risk for CHD disease and like diabetics and CKD is also a CHD risk equivalent. As in diabetes mellitus, the level of LDL cholesterol would be reduced to a low level to protect the heart and brain blood vessels.

This patient has LDL cholesterol of 2 mmol/l which is the target for people at risk with CHD. It would be more ideal if it could be reduced to 1.8 mmol/l. In fact the KDIGO 2013 clinical guidelines recommended CKD patients with diabetes and age >=50 years be given a statin irrespective of the cholesterol level be given a statin. This was suggested to him but he declined.

Case 4:

A 63 year old female patient was followed up in the clinic for CKD. Her serum creatinine was 195 umol/l with the eGFR 24 ml/minute. The serum cholesterol was 5.9 mmol/l while on atorvastin 10 mg nocte. (Figure 5)

According to the KDIGO guidelines, for CKD patients > 50 years of age, a statin plus ezetimile are suggested. Even the normal level may be high for the high risk patient. For this patient, she was over the age of 50 and despite atorvastin, the serum cholesterol was still high. Ezetimile was added.

Case 5:

A CKD patent progressed to ESRD after years of follow up. His serum creatinine was 1200 umol/l and the serum cholesterol was 5.1 mmol/l despite atorvastin and ezetimile. He was put on chronic haemodialysis. (Figure 6)

CKD patient with ESRD has high cardiovascular risk. According to three large randomized trials, no conclusive benefit of statin therapy was shown in this subset of patients. The KDIGO guidelines stated that 'in adults with dialysis-dependent CKD, we suggest that the statins or stain/ezetimibe combination **not** to be started'. Probably the blood vessels were so damaged that any benefit of the statins would be small. For ESRD patients, there is no need for statins despite the high cholesterol. Since he had been on the lipid treatment all along, the guideline recommends the treatment to be continued.

Summary

The treatment of hypercholesterolaemia is complicated as shown by the multitude of clinical guidelines from different academic bodies. It moved from total cholesterol in the early days to the cholesterol components (the LDL cholesterol or the total cholesterol/HDL ratio). It seems that now the emphasis has shifted from laboratory results to overall clinical status of the patients.

Lipid abnormalities are significant causes of CHD but they are only one of the risk factors in vascular damage, other factors like smoking and blood pressure would also needed to be taken into account. The treatment plan should be based on the patient's risk status in addition to the lipid levels and a more holistic assessment such as the Framingham Risk Score or QRISK2 score would be appropriate. Diabetes mellitus and CKD are important risk considerations.

Reference

(1) Dr Ho Chung Ping, Ms Wong Sui Lan, Doctor, do I need to take long term blood pressure medications? HKMA CME Bulletin June
(2) Qx calculate http://www.qxmd.com/apps/calculate-by-qxmd, last accessed 29 June, 2014
(3) Welcome to QRISK 2 2014 calculator http://www.qrisk.org/. last accessed 29 June, 2014
(4) Marcello Tonelli, Lipid management in Chronic Kidney Disease: Synopsis of the Kidney Disease: Improving Global outcomes 2013 Clinical Practice Guideline, Annals of Internal medicine, downloaded from http://annals.org/ on 12/12/2013

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Sex/Age : F/63 Date of Birth : 01 Jan 1951
Clinic No : 9778
Form No: ID Doc: A927228(6)

Report No: **1402743920** Collected: **02 May 2014 18:00** Received: **02 May 2014 18:53** Printed: **28 Jun 2014**

Specimen: Blood (unless otherwise indicated)

	Result 結果	Unit 1 單位 1	Adult Range 成人參考值	Result 結果	Unit 2 單位 2	Adult Range 成人參考值
Biochemistry						
Sodium 鈉§	136	mmol/L	134 - 145	136	mEq/L	134 - 145
Potassium 鉀§	4.6	mmol/L	3.4 - 5.4	4.6	mEq/L	3.4 - 5.4
Bicarbonate 二氧化碳單	18 ↓	mmol/L	21 - 32	18.0 ↓	mEq/L	21.0 - 32.0
Urea 尿素§	19.6 ↑	mmol/L	3.4 - 8.9	118 ↑	mg/dL	20 - 53
^Creatinine 肌酐§	195 ↑	umol/L	53 - 88	2.20 ↑	mg/dL	0.60 - 0.99
Albumin 白蛋白§	40	g/L	36 - 48	4.0	g/dL	3.6 - 4.8
Total Cholesterol 總膽固醇§	5.9 ↑	mmol/L	< 5.2	228 ↑	mg/dL	< 201

ATP III Ref. 總固醇參考值 (Reference revised on 20/7/2011)

LDL-C		Total Cholesterol		LDL-C		Total Cholesterol	
<2.6	Optimal	<5.2	Desirable	<100	Optimal	<200	Desirable
2.6-3.3	Near optimal	5.2-6.1	Borderline high	100-129	Near optimal	200-239	Borderline high
3.4-4.1	Borderline high	>6.2	High	130-159	Borderline high	>240	High
4.2-4.9	High			160-189	High		
>5.0	Very High			>190	Very High		

Figure 5

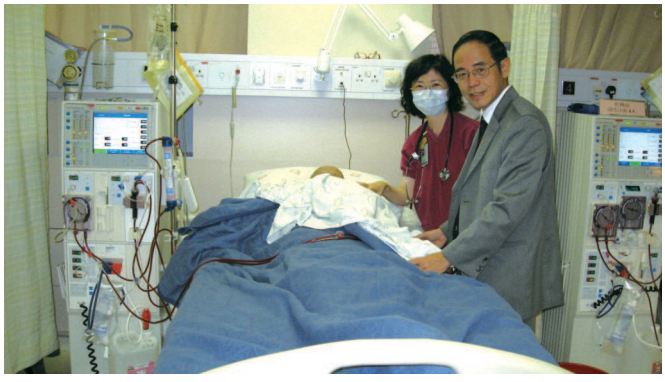

Figure 6