THISTLE QA

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Please read this bit first

The HPCSA and the Med Tech Society have confirmed that this clinical case study, plus your routine review of your EQA reports from Thistle QA, should be documented as a "Journal Club" activity. This means that you must record those attending for CEU purposes. Thistle will **not** issue a certificate to cover these activities, nor send out "correct" answers to the CEU questions at the end of this case study.

The Thistle QA CEU No is: **MT00025.**

Each attendee should claim **THREE** CEU points for completing this Quality Control Journal Club exercise, and retain a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

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Cardiac Biomarkers

Research is rapidly expanding in the field of cardiac biomarkers. This will allow our background knowledge about an individual's risk to expand, thus improving the actions taken to address this risk.

Biomarkers must fulfil specific requirements if they are to qualify for clinical use. In particular, the biomarker's value above already known risk estimates should have been consistently demonstrated in numerous prospective studies. However, to date, only a few cardiac biomarkers have fully satisfied these requirements and, consequently, have found widespread clinical utilization: these include blood cholesterol, glucose, CK and cardiac troponins (cTns). However, the evidence is accumulating in favour of a wider use of several novel biomarkers, such as C-reactive protein (CRP), B-type natriuretic peptides (BNP) and micro-albuminuria, in the future.

Unfortunately, the major obstacle in the clinical qualification of body fluid biomarkers (such as those in plasma, serum or urine) is related to the biological dynamic nature of these molecules, proteins or enzymes, which are subjected to both biological variability as well as analysis-related variability. Ever since the recognition of hypercholesterolemia as a global cardiac risk biomarker several decades ago, there is a myth that a particular biomarker can be used in all patient populations, from different ethnicity, co-morbidities and concomitant drug therapies, when the evidence for this is inconclusive.

C-reactive Protein

The acute-phase reactant CRP fulfils many of the characteristics of a clinically informative biomarker. The most important issues here are as follows:

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- The assay to measure CRP has been standardized in the context of the CRP utilization in cardiac risk assessment, enabling the detection of even subtle levels of protein (highly sensitive CRP [hsCRP].
- CRP predictive capacity was observed in various ethnic groups, given that most studies have been conducted in white caucasian populations

- The independent predictive value of hsCRP towards cardiac risk has been demonstrated in numerous prospective studies in diverse population groups: the general population, asymptomatic individuals, high-risk groups and in specific patient cohorts with different CVD phenotypes (coronary heart disease, atrial fibrillation, peripheral artery disease and ischemic stroke)

Without disregarding the clinical promises of this inflammatory biomarker, there are several reservations regarding its use in primary and secondary prevention settings. There are still ongoing debates about the stability of CRP in stored (frozen) samples of plasma or serum as well as about its biological intra-individual variability. Furthermore, there is a lack of consistency in the results of prospective studies evaluating the predictive value of hsCRP. Therefore, experts presently recommend that hsCRP may assist in cardiac risk estimation in intermediate-risk groups but m ore evidence is clearly required to prove the ability of CRP to change managerial strategies on an individual level.

B-type Natriuretic Peptides

In the setting of heart failure, there is compelling evidence in favour of the use of BNP to increase the diagnostic accuracy of the condition. There are several other potential settings where the utility of natriuretic peptides is expected to be beneficial. Numerous studies have reported on the short- and long-term prognostic significance of natriuretic peptides towards recurrent cardiac events and mortality. In the primary prevention setting, natriuretic peptides could identify asymptomatic individuals at increased cardiac risk. Several recently conducted population-based studies (in the general population, as well as in high-risk patient groups) have demonstrated the independent predictive value of N-terminal-pro-brain natriuretic peptide above that provided by classical risk factors. Although promising as a biomarker, across the cardiac risk continuum, natriuretic hormones are still in the early stages of widespread clinical use.
Microalbuminuria
Special interest has been allocated to the parameter of glomerular endothelial dysfunction, microalbuminuria. All diabetic subjects should undergo screening for microalbuminuria, in order to detect the earliest signs of diabetic nephropathy. There are substantial observational data regarding the association between urinary albumin excretion and increased CVD risk and mortality in people with diabetes and hypertension. Therefore, screening for microalbuminuria in hypertension is advised. Currently, there is debate over the evidence to justify broad use of microalbuminuria measurement for the purposes of guiding primary and secondary cardiac risk. However, low-grade microalbuminuria (< 30 mg/daily or > 5 μg/min overnight) has been reported to predict incident cardiac risk in the general population.

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Five-year View

The future of cardiovascular biomarkers is bright. It is hoped that in 5 years, many of the questions that cardiovascular medicine is now facing with regards to biomarker discovery and utilization will be answered. New specific indications for clinical use of CRP and natriuretic peptides will hopefully be established.

CPD Questions:

1. What specific requirements must a new cardiac biomarker satisfy before it can be routinely used?
2. hsCRP is a promising biomarker? True or false?
3. What are the limitations of using microalbuminuria as a risk biomarker?