Biomarkers of Coronary Artery Disease Differ Between Asians and Caucasians in the General Population

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ABSTRACT

Coronary artery disease (CAD) markers have not been thoroughly investigated among Asians. The incidence of CAD, however, is rising rapidly in Asia. In this review, we systematically discuss publications that compare CAD biomarkers between Asians and Caucasians in the general population. A PubMed search yielded 5,570 hits, containing 59 articles describing 47 unique cohorts that directly compare Asians with Caucasians. Ten biomarkers were taken into account for this review: total cholesterol; triglycerides; high-density lipoprotein cholesterol; low-density lipoprotein cholesterol; C-reactive protein; glucose; insulin; glycated hemoglobin; fibrinogen; and plasminogen activator inhibitor-1. Triglycerides were 1.13-fold higher in South Asians than in Caucasians, and insulin levels were 1.33-fold higher. In Japanese and Chinese subjects, lower C-reactive protein levels were reported: 0.52 and 0.36-fold, respectively. Ethnicity-specific prognostic measures of CAD biomarkers were rarely reported. CAD biomarker levels differ between Asians and Caucasians and among Asian ethnic groups in population-based cohorts. The ethnicity-specific prognostic value of CAD biomarkers is yet to be determined.

Coronary artery disease (CAD) is the number 1 cause of death worldwide and will remain so for the next decades. In contrast to the declining numbers in the Western world [1], its incidence is expected to increase in other parts of the world, predominantly in Asia [2]. In our efforts to tackle this upcoming epidemic in Asia, primary prevention will have to play a central role, requiring reliable and robust predictive biomarkers.

To date, most CAD biomarker research has been conducted solely in Caucasian subjects. For example, the pivotal heart disease study, the Framingham Heart Study, consists almost exclusively of European descendants [3]. Based on little evidence, current risk markers such as C-reactive protein (CRP), low-density lipoprotein (LDL) cholesterol or high-density lipoprotein (HDL) cholesterol are generally accepted to be valid for other ethnic groups in addition to Caucasians, in whom the biomarkers were validated. In fact, little is known about the actual generalizability of these markers toward other ethnic groups. However, previous studies already indicated significant differences in the traditional risk factors and CAD prevalence between Asians and Caucasians, making it unlikely that current biomarkers can simply be generalized to other ethnicities [4—6]. Probably, different cutoff values and prognostic measures apply to the various populations and should be implemented accordingly.

The pressing need for ethnicity-specific cardiovascular disease (CVD) research has recently been underlined by the American Heart Association [7]. Work has been done by, for example, Tillin et al. [8] on recalibration of clinical risk scores as to serve other ethnic groups apart from Caucasians, but the value of CAD biomarkers in the Asian ethnic groups is largely unknown.

In an attempt to gather the available data on differences in CAD biomarkers between Asians and Caucasians at the general population level, we hereby provide a comprehensive overview on the current knowledge on biomarker levels and (when available) their predictive value for CAD in these populations.

Adaptation to a Western lifestyle, a phenomenon known as acculturation has a major effect on the cardiovascular risk of ethnic groups [9,10], indicating that there is an important environmental factor, on top of a possible true biological component, that explains interethnic differences. To reduce bias by environmental differences, the main results in this review are based on data from Asians in diaspora countries only (encompassing the majority of the available literature).

METHODS

Search criteria

This review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systemic Reviews and Meta-Analyses) guidelines [11]. We created a search syntax based on Asian and Caucasian ethnicity, biomarkers, and CAD, as well as their synonyms (Table 1). PubMed MEDLINE was systematically searched for publications meeting our inclusion criteria: adult population-based cohorts including at least 1 Asian ethnic group and

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TABLE 1. Search syntax as entered in PubMed on August 14, 2014

Coronary artery disease		1. (atherosclero*[Title/Abstract] OR coronar*[Title/Abstract] OR cardiovascular[Title/Abstract] OR cardiac[Title/Abstract] OR myocardi*[Title/Abstract])
Biomarker	*AND*	2. (biomarker[Title/Abstract] OR biomarkers[Title/Abstract] OR marker[Title/Abstract] OR markers[Title/Abstract] OR level[Title/Abstract] OR levels[Title/Abstract] OR concentration[Title/Abstract] OR concentrations[Title/Abstract] OR enzyme[Title/Abstract] OR enzymes[Title/Abstract] OR peptide[Title/Abstract] OR peptides[Title/Abstract] OR protein[Title/Abstract] OR proteins[Title/Abstract] OR metabolite[Title/Abstract] OR metabolites[Title/Abstract] OR diagnos*[Title/Abstract] OR prognos*[Title/Abstract] OR lipid[Title/Abstract] OR lipids[Title/Abstract] OR risk factor*[Title/Abstract]) OR predict*[Title/Abstract])
Ethnicity	*AND*	3. ((asia*[Title/Abstract] OR chin*[Title/Abstract] OR indi*[Title/Abstract] OR Pakistan*[Title/Abstract] OR Banglades*[Title/Abstract] OR Japan*[Title/Abstract]) AND (Caucasian*[Title/Abstract] OR white*[Title/Abstract] OR europe*[Title/Abstract]))
Search result		1: 1,061,901 hits 2: 8,251,453 hits 3: 109,637 hits 1 AND 2 AND 3: 5,570 hits

a Caucasian ethnic group. Also, at least 1 blood-derived biomarker had to be measured in a context of CAD. Titles and abstracts were screened (by C.G.) and publications providing levels of CAD biomarkers in Asians and Caucasians were selected for this review.

Only studies that directly compared Asian individuals with Caucasian individuals were selected to ensure comparability of the measured biomarker levels within the study. Articles that solely report the presence or absence rather than the actual level of a particular risk factor or biomarker were excluded. Furthermore, studies that did not determine ethnicity on an individual basis and studies concerning children, CAD patients, or case-control studies were excluded, as they do not reflect the general population.

The Asian ethnic groups could be further divided into South Asians (i.e., Asians originating from India, Pakistan, Bangladesh, or Sri Lanka), Chinese, and Japanese.

EXTRACTION OF REPORTED MEASURES

From all included articles we extracted the cohort characteristics, the biomarker levels, and (when available) the prognostic measures of a biomarker per ethnic group. When 1 specific cohort was described in more than 1 article—as is frequently the case for large cohorts—the most extensive dataset on a particular biomarker was used, in other words, the publication with the largest number of subjects or (when dataset size was the same) the most recent publication.

To create a measure of comparison, relative differences between Asians and Caucasians are calculated within the studies, with the biomarker levels for Caucasians set at 1. For example, when the glucose level in Caucasians is 8 and in South Asians it is 12, the relative difference will be 12/8 = 1.5.

The average relative risks across the publications selected in this review are calculated by dividing the sum of the number of Asian and Caucasian individuals within the cohort × the relative risk in that particular cohort by the total number of individuals compared across the different cohorts. Hereby, the relative differences are weighted for cohort size.

Also, we calculated biomarker means per ethnic group, per comparison. Mean levels for Caucasians were thus calculated 3 times, as they are derived from different cohorts, comparing with different Asian ethnic groups.

RESULTS

Search

The search syntax was entered in the PubMed database on August 14, 2014 (Table 1). This search retrieved 5,570 hits. These 5,570 publications were screened by title and abstract, which initially yielded 111 publications. After considering the 111 full-text articles, 64 articles were excluded for the following reasons: only patients with established CAD were included (n = 14); actual biomarker levels were not provided (n = 16); there was no specific context of CAD (n = 16); the cohort was discussed more extensively in another article (n = 12); the article concerned only children (n = 5); individual ethnicity was not reported (n = 1). The search process (Fig. 1) resulted in 47 titles that provided biomarker levels in community population Asians and Caucasians in the context of CAD. Reference checking did not retrieve any additional articles.

Reported biomarkers

In the 47 articles retrieved from the search, 52 distinct biomarkers were reported. Of these, 31 biomarkers were reported only once, 7 were reported twice, 4 were reported 3 times, and 10 biomarkers were reported more than 5 times.

Only biomarkers that were reported 5 or more times were taken into account for this review. These were as follow: triglycerides (TG) from 27 cohorts; HDL cholesterol