International Journal of Cardiology 176 (2014) 687–695

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Alopecia and its association with coronary heart disease and cardiovascular risk factors: A meta-analysis

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ARTICLE INFO

Article history:
Received 8 May 2014
Accepted 24 July 2014
Available online 1 August 2014

Keywords:
Alopecia
Coronary heart disease
Dyslipidaemia
Hypertension
Insulin resistance
Meta-analysis

ABSTRACT

Background: Alopecia has been associated with an increased risk of coronary heart disease as well as the following risk factors for cardiovascular disease: hyperinsulinaemia, insulin resistance, metabolic syndrome, dyslipidaemia, and hypertension. We performed a meta-analysis to quantitatively determine the level of risk of coronary heart disease and risk factors in individuals with alopecia.

Methods: A systematic literature search was conducted using several databases. We calculated pooled odds ratios and 95% confidence intervals using a random effects model.

Results: In total, 31 studies comprising 29,254 participants with alopecia were eligible for the meta-analysis and showed that alopecia is associated with an increased risk of coronary heart disease (OR 1.22, 95% CI: 1.07–1.39), hyperinsulinaemia (OR 1.97, 95% CI: 1.20–3.21), insulin resistance (OR 4.88, 95% CI: 2.05–11.64), and metabolic syndrome (OR 4.49, 95% CI: 2.36–8.53). Individuals with alopecia were also shown to be more likely compared to those without alopecia to have higher serum cholesterol levels (OR 1.60, 95% CI: 1.17–2.21), higher serum triglyceride levels (OR 2.07, 95% CI: 1.32–3.25), higher systolic blood pressures (OR 1.73, 95% CI: 1.29–2.33), and higher diastolic blood pressures (OR 1.59, 95% CI: 1.16–2.18).

Conclusions: Alopecia is associated with an increased risk of coronary heart disease, and there appears to be a dose–response relationship with degree of baldness whereby the greater the severity of alopecia, the greater the risk of coronary heart disease. Alopecia is also associated with an increased risk of hypertension, hyperinsulinaemia, insulin resistance, metabolic syndrome, and having elevated serum total cholesterol and triglyceride levels.

1. Introduction

The association between alopecia and coronary heart disease was first reported over 60 years ago [1]. Over the last six decades, there have been a significant number of epidemiological studies which have examined this relationship. Although some studies have found no relationship [2–5], the majority have supported the notion that suffering from baldness is detrimental to cardiovascular health. Specifically, studies have shown that coronary heart disease is more likely to occur to individuals with alopecia compared to non-bald individuals [6,7], that insulin resistance and metabolic syndrome are more likely to be present in individuals with alopecia than non-bald individuals [8–10], and that individuals with alopecia have higher cholesterol levels and blood pressures than individuals without baldness [11–13].

With population ageing presently occurring at unprecedented rates globally, the potential relationship between signs of ageing and cardiovascular disease is of particular interest. For example, a recent Danish study reported that looking old for your age, whether that be due to baldness, earlobe crease or xanthelasmata, is a marker of poor cardiovascular health [14]. Both baldness and cardiovascular disease share the common risk factor of ageing and with the demographic shift towards ageing populations that is occurring in both developed and undeveloped countries, it is expected that chronic and age-related diseases such as ischaemic heart disease, already the leading cause of death in the world will contribute a higher proportion to the overall disease burden [15,16]. As life expectancies increase, signs of early ageing such as hair loss could indicate individuals with accelerated biological ageing processes, and hence who are more susceptible to pathophysiological processes that occur with advancing age, such as atherosclerosis, insulin resistance, hypertension, and high blood cholesterol. Given this, quantitative data by way of meta-analysis confirming an association with coronary heart disease and established cardiovascular risk factors would be an important finding as it would potentially establish alopecia as an independent risk factor for cardiovascular disease and provide evidence for the use of alopecia as a visible clinical marker to identify patients with an increased risk of cardiovascular disease.

A recent meta-analysis [17] reported vertex baldness (but not frontal baldness) to be associated with an increased risk of coronary heart disease, however, it only included six studies in its analysis and did

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http://dx.doi.org/10.1016/j.ijcard.2014.07.079
0167-5273/

not consider the relationship between alopecia and cardiovascular risk factors. Therefore, the aim of this study is to conduct a comprehensive meta-analysis of existing studies to confirm the association of alopecia with coronary heart disease and various established cardiovascular risk factors, namely hyperinsulinaemia, insulin resistance, metabolic syndrome, dyslipidaemia, and hypertension.

2. Methods

2.1. Study protocol

This study was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [18].

2.2. Searching for relevant studies

A systematic search was performed through the following five electronic databases: MEDLINE (from 1950), EMBASE (from 1949), PubMed (from 1946), Current Contents Connect (from 1998), and Google Scholar (from 1992). These databases were searched using medical subject headings, text word and keyword searches (wherever possible) to identity relevant studies.

Our search strategy involved four searches, using combinations of the following key words: "alopecia", "baldness", "hypotrichosis", "pseudopelade", "coronary heart disease", "coronary occlusion", "heart disease", "myocardial infarction", "cardiovascular disease", "atherosclerosis", "dyslipidaemia", "hyperlipidaemia", "hypercholesterolaemia", "hypertension", "blood pressure", "insulin resistance", "diabetes", "hyperinsulinaemia", "metabolic syndrome", and "syndrome X". Additional manual searches were made using the reference lists from relevant studies to retrieve other papers relevant to our topic. No language restriction was placed on any of the literature search, however a search for unpublished literature was not performed and authors were not contacted for missing data.

2.3. Study eligibility

Studies which met the following inclusion criteria were included in the meta-analysis: [1] The risk point estimate was reported as an odds ratio, or the data was presented such that an odds ratio could be calculated; and [2] the 95% confidence interval was reported, or the data was presented such that a 95% confidence interval could be calculated. Studies that did not meet the above criteria were excluded.

2.4. Data extraction

Data was extracted via a standardized data extraction form, collecting information on the year of publication, country, continent, gender, study design, control group used, number of cases, number of controls, total sample size, adjusted variables, type of alopecia, severity of alopecia, risk estimate or data used to calculate the risk estimate, confidence interval or data used to calculate the confidence interval, and outcome (event of coronary heart disease, total cholesterol level, triglyceride level, HDL-cholesterol level, LDL-cholesterol level, systolic blood pressure, diastolic blood pressure, presence of metabolic syndrome, degree of insulin resistance, or serum insulin level). Coronary heart disease was defined as including any of the following: myocardial infarction, angina pectoris, ischaemic heart disease, and coronary revascularisation.

Where possible, we used adjusted odds ratios that were extracted in preference to non-adjusted ratios. Where more than one adjusted ratio was reported, the ratio with the highest number of adjusted variables was chosen. Where multiple risk estimates were available in the same study (for example, when studies reported on the risk estimates of different severities of alopecia) and an overall risk estimate was not reported, an average risk estimate was calculated. Where a risk estimate was not reported but data was reported in a 2×2 contingency table or as a mean and standard deviation, an odds ratio and 95% confidence interval were calculated.

2.5. Statistical analysis

Pooled odds ratios and 95% confidence intervals were calculated for the effect of alopecia on the risk of coronary heart disease and various established cardiovascular risk factors using a random effects model [19]. This was performed for: (1) the association of any degree of alopecia with coronary heart disease, hyperinsulinaemia, insulin resistance, metabolic syndrome, dyslipidaemia, and hypertension; and (2) the association of mild, moderate, and severe alopecia with coronary heart disease.

Heterogeneity, i.e. the proportion of variability across studies that was due to heterogeneity rather than sampling error, was assessed using Cochran's Q statistic and quantified using the I^2 statistic with results of 25%, 50% and 75% correlating with low, moderate and high levels of heterogeneity respectively [20]. Publication bias, i.e. the tendency on average to produce results that appear significant because negative or near neutral results are not published, was quantified using the Egger's regression model [21]. If publication bias was detected, the extent of bias was assessed using the "fail safe" method whereby the number of studies required to nullify our results was calculated. A fail safe (n) with a p-value less than 0.05 was considered to be significant. All analyses were performed using Comprehensive Meta-analysis (version 2.0), Englewood, NJ, USA (2005).

3. Results

3.1. Study characteristics

Using our pre-specified search strategy, 952 extracts were retrieved and 8 additional citations were obtained through reference lists. From 960 studies initially identified, 64 were considered potentially suitable (Fig. 1). After a full-text review, 31 studies met our inclusion criteria and were included in the final analysis. Selected characteristics of the included studies are presented in Tables 1 and 2. Of the 31 studies, 23 were case–control studies, four were cohort studies, and four were cross-sectional studies. Overall, these studies comprised data from a total of 50,956 participants, including 29,254 individuals with alopecia.

3.2. Coronary heart disease

There were eight studies comprising 46,278 participants included in the meta-analysis for coronary heart disease. We found an increased risk of coronary heart disease in individuals with alopecia, with a pooled odds ratio of 1.22 (95% CI: 1.07–1.39) (Fig. 2). There was a statistically significant heterogeneity ($I^2 = 74.21\%$, $p < 0.001$). The Egger's regression test for publication bias was not significant ($p = 0.28$).

A sub-group analysis by severity of alopecia was also performed, using 6 studies comprising 33,108 participants (Fig. 2). The risk of coronary heart disease was found to be greater in individuals with moderate alopecia (OR 1.27, 95% CI: 0.95–1.70) and severe alopecia (OR 1.27, 95% CI: 0.97–1.66), compared to mild alopecia (OR 1.05, 95% CI: 0.93–1.18). Although these findings were not statistically significant, the sub-group

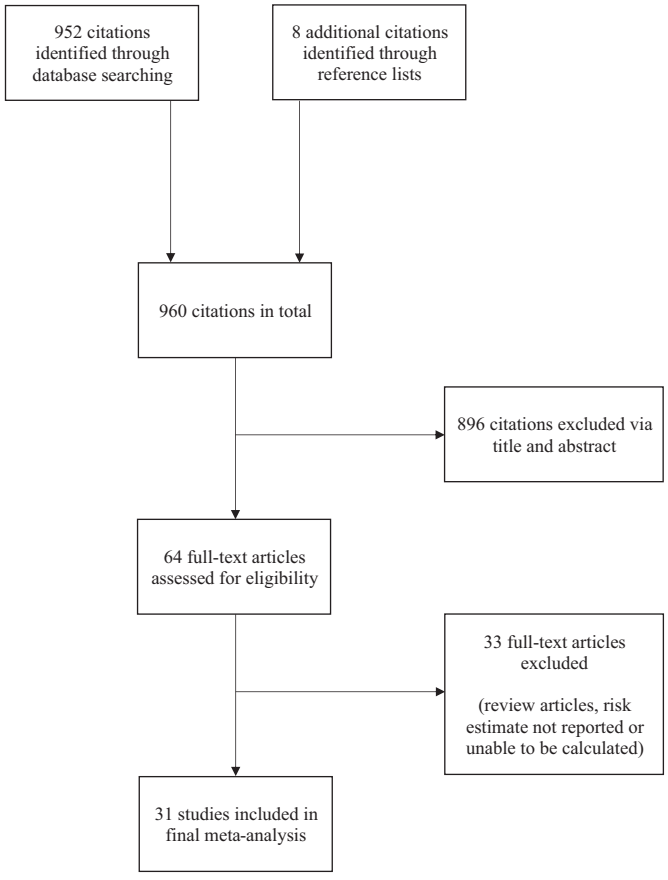

Fig. 1. Identification, inclusion and exclusion of studies.