Vascular Risk Factors, Risk Score, and COVID-19: Community-based Cohort Study

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Abstract

Studies of groups of COVID-19 patients suggest that those admitted to hospital with existing cardiovascular disease (CVD) experience a markedly increased risk of progression to intensive care and mortality (prognosis), it is unknown if established CVD risk factors are associated with the occurrence of the infection, particularly in community samples (aetiology). We used data on from the UK Biobank study, a prospective cohort study with linkage to hospitalisation for COVID-19. In an analytical sample of 356,914 study members (194,167 women) there were 700 hospitalisations (300 women) for COVID-19. After adjustment for confounding factors, unfavourable levels of a series of CVD risk factors – cigarette smoking (odds ratio; 95% confidence interval: , physical inactivity, obesity, diabetes, and blood lipids – were related to an elevated occurrence of COVID-19, the only exception being blood pressure. When we entered selected CVD risk factors into the Framingham model, an increased likelihood of COVID-19 was apparent in the higher CVD risk categories whereas intermediate scores were not associated with the infection. If replicated, these finding may have implications for clinical practice and the identification of at-risk groups to be targeted if or when an effective vaccine is developed.

Introduction

Evidence from prognostic studies of groups of COVID-19 patients suggest that those admitted to hospital with existing cardiovascular disease (CVD) experience a markedly increased risk of progression to intensive care and mortality.[1] While obesity also appears to be related to unfavourable outcomes in COVID-19 patients,[2] it is unknown if this and a series of other established CVD risk factors are associated with the occurrence of the infection, particularly in community samples. More widely, there is evidence from cardiovascular research to suggest that prognostic risk factors may reveal opposing relationships to that seen for aetiological factors. For instance, British people of South Asian ancestry have a higher incidence of coronary disease but lower mortality once diagnosed with coronary disease.[3] For the first time to our knowledge, we therefore examined if unfavourable levels of classic CVD risk factors, both individually and collectively within the Framingham model,[4] were implicated in the primary prevention of COVID-19 in a community-based prospective cohort study. Assessing the predictive value of the Framingham index for COVID-19 has potential clinical utility as this tool is widely used in general practice.

Methods

We used data from UK Biobank, a prospective cohort study, the sampling and procedures of which have been well described. Baseline data collection took place between 2006 and 2010 across centres in the UK giving rise to a sample of 502,655 people (448,919 from England) aged 40 to 69 years (response rate 5.5%).[5] Ethical approval was received from the North-West Multi-centre Research Ethics Committee.

Cigarette smoking, physician-diagnosed diabetes, highest educational attainment, ethnicity, and physical activity in the prior month were self-reported using standard enquiries. Body mass index

was based on direct measurements of height and weight. Blood pressure was measured in the seated position with the average of two readings used, and total cholesterol and high-density lipoprotein were assayed from a non-fasting blood sample. The Framingham risk score was computed using sex-specific multivariable functions comprising age, total and high-density lipoprotein cholesterol, systolic blood pressure, smoking, and diabetes status.[4] Provided by the Public Health England agency, data on COVID-19 covered the period 16th March until 26th April 2020. Nose and/or throat swabs were taken from hospitalised patients and detection of SARS-CoV-2 can be regarded as an indication of a severe manifestation of the disease.

Results

In an analytical sample of 356,914 study members (194,167 women) there were 700 hospitalisations (300 in women) for COVID-19. Unfavourable levels of all individual CVD risk factors were related to an elevated occurrence of COVID-19 in age- and sex-adjusted analyses (**Table 1**), the only exception being blood pressure. The magnitude of these effects was diminished somewhat after adjusting for a range of covariates but they remained statistically significant at conventional levels. When we entered selected CVD risk factors into the Framingham model, an increased likelihood of COVID-19 was apparent in the higher CVD risk categories whereas intermediate scores were not associated with the infection. Again, adjustment for covariates attenuated this relationship. With the Framingham index predicated upon predicting incident (new cases) vascular events in a population initially free of CVD, we recomputed effect estimates based on this sub-group (338,553 people, 634 COVID-19 events) and our results were essentially unchanged.

Discussion

Evidence from prognostic studies of hospitalised COVID-19 patients suggest that a series of

physical characteristics are linked to progression to intensive care and death,[1 2] and these relationships were also apparent in the present analyses for age, being male, existing diabetes, and overweight/obesity in relation to hospitalisation for the infection (**Table 1**). Further, a history of cardiovascular disease was related to an almost doubling of risk of COVID-19 (1.82; 1.60, 2.08). The replication of these relationships in the present dataset gives us confidence in our novel results for CVD risk indices.

Follow-up for COVID-19 events was up to 14 years after baseline examination and this can raise concerns about the stability of baseline data. After a median of 4.4 years, a representative subgroup of study participants were reassessed (N=19,772). For those risk factors featured in the Framingham algorithm that were captured at retesting, test-rest correlation coefficients were high for body mass index (0.93), systolic blood pressure (0.65), and cigarette smoking (0.84). This suggests that risk factors gathered at baseline have a high degree of stability. It is also the case that the UK Biobank study sample is based on the recruitment of 5.5% of the target population.[5] As has been demonstrated,[6] the data material is therefore inappropriate for estimation of risk factor or disease occurrence. These observations do not, however, seem to influence reproducibility of the association of established risk factors for non-communicable disease such as vascular disease.[6] We think the same reasoning can be applied to associations with communicable diseases.

In conclusion, in the present study, established CVD risk factors revealed associations with hospitalisation for COVID-19 at similar magnitude to those apparent for vascular outcomes. The Framingham Risk Score also offered some predictive utility and, if replicated, this finding may have implications for clinical practice and the identification of at-risk groups to be targeted if or when an effective vaccine is developed.

Conflict of interest: None declared.

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Table 1. Individual CVD Risk Factors and Framingham Risk Score in Relation to COVID-19 Hospitalisations (N=356,914)

	COVID-19 cases/Number at risk[a]	Age- & sex-adjusted RR (95% CI)	Adjusted[b] RR (95% CI)
Individual risk factors			
Age (per 5 year increase)	700/356,914	1.07 (1.02, 1.12)	1.05 (1.00, 1.11)
Male	400/162,747	1.59 (1.37, 1.84)	1.69 (1.45, 1.98)
Current Smoking	91/35,252	1.57 (1.24, 1.99)	1.46 (1.15, 1.86)
Physical inactivity	86/21,332	2.31 (1.84, 2.84)	1.58 (1.25, 2.00)
Obesity/Overweight	544/237,440	1.63 (1.36, 1.95)	1.45 (1.21, 1.74)
Diabetes	63/17,266	1.77 (1.36, 2.29)	1.31 (1.01, 1.74)
Systolic blood pressure (per SD increase)	700/356,914	1.03 (0.96, 1.12)	0.99 (0.92, 1.08)
Total Cholesterol (per SD increase)	700/356,914	0.82 (0.76, 0.89)	0.86 (0.80, 0.93)
High-Density Lipoprotein (per SD increase)	700/356,914	0.70 (0.64, 0.77)	0.77 (0.70, 0.85)
Framingham risk score (quintiles)		**Unadjusted RR (95% CI)**	**Adjusted[c] RR (95% CI)**
≤9	162/91,892	1.0 (ref)	1.0 (ref)
10-12	116/84,208	0.78 (0.62, 1.0)	0.71 (0.56, 0.90)
13-14	125/68,984	1.03 (0.82, 1.30)	0.91 (0.72, 1.15)
15-16	147/62,248	1.34 (1.07, 1.68)	1.15 (0.91, 1.45)
≥17 (highest risk)	150/49,582	1.72 (1.38, 2.15)	1.35 (1.05, 1.70)

[a]Sample sizes correspond to full analytical sample for analyses of continuous risk factors, and the category of interest in analyses of categorical risk factors. [b]Adjusted for age, sex, body mass index, physical activity, alcohol, education, and ethnicity. [c]Adjusted for body mass index, physical activity, alcohol, education, ethnicity. RR, relative risk. SD, standard deviation.