European Journal of Heart Failure (2018) **20**, 989–997
doi:10.1002/ejhf.1163

RESEARCH ARTICLE

Cognitive performance in late adolescence and long-term risk of early heart failure in Swedish men

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Received 3 August 2017; revised 9 January 2018; accepted 22 January 2018; online publish-ahead-of-print 19 February 2018

Aims Heart failure (HF) incidence appears to increase among younger individuals, raising questions of how risk factors affect the younger population. We investigated the association of cognitive performance in late adolescence with long-term risk of early HF.

Methods and results We followed a cohort of Swedish men enrolled in mandatory military conscription in 1968–2005 ($n = 1\ 225\ 300$; mean age 18.3 years) until 2014 for HF hospitalization, using data from the Swedish National Inpatient Registry. Cognitive performance (IQ) was measured through a combination of tests, separately evaluating logical, verbal, visuospatial, and technical abilities. The results were standardized, weighted, and presented as stanines of IQ. The association between IQ and risk of HF was estimated using Cox proportional hazards models. In follow-up, there were 7633 cases of a first HF hospitalization (mean age at diagnosis 50.1 years). We found an inverse relationship between global IQ and risk of HF hospitalization. Using the highest IQ stanine as reference, the adjusted hazard ratio for the lowest IQ with risk of HF was 3.11 (95% confidence interval 2.60–3.71), corresponding to a hazard ratio of 1.32 (95% CI 1.28–1.35) per standard deviation decrease of IQ. This association proved persistent across predefined categories of HF with respect to pre-existing or concomitant co-morbidities; it was less apparent among obese conscripts (*P* for interaction =0.0004).

Conclusion In this study of young men, IQ was strongly associated with increased risk of early HF. The medical profession needs to be aware of this finding so as to not defer diagnosis.

Keywords Heart failure • Adolescence • Intelligence • Population

Introduction

Heart failure (HF) is rare in younger people, with an estimated prevalence of about one per 1000 people aged <55 years.[1] Marked mortality reductions have been reported among younger patients aged 18–54 years from 1987 to 2001.[2] However, the prognosis is still poor: approximately one in ten patients die within a year of the first hospitalization.[2,3] We have also found a continuous increase in HF incidence among younger people, which is the reverse of the decreasing trend observed in the older population,[2,4–6] although others have found no significant trends for HF hospitalization.[7]

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The reasons for the divergent trends in younger and older subsets of the population are unknown. The increasing prevalence of overweight and obesity in younger people may be important.[8] We have recently documented a marked, monotonic increase in the long-term risk of HF in adolescent men, beginning with body mass index (BMI) levels that are considered normal.[9] Cardiorespiratory fitness and muscular strength have also been independently associated with risk of HF in the present cohort.[10]

Other factors that have gained increasing interest during the last decade are childhood and adolescent intelligence. Prospective studies have identified a negative association between IQ measured in childhood or adolescence and both cardiovascular risk factors and coronary heart disease (CHD),[11–14] which is known to cause HF. Socioeconomic factors, such as educational attainment in adulthood,[15] adverse social circumstances, and lifestyle-related factors measured in early life,[16] have been suggested as potential mediators. Furthermore, early-life IQ may act as an indicator of general bodily system integrity—an ability to respond more efficiently to environmental challenges or insults.[17] In the present study, we used data from the Swedish Military Service Conscription Registry (containing information about cognitive performance in approximately 1.8 million young Swedish men) and the Swedish National Inpatient Registry (IPR) to examine the effect of cognitive performance in late adolescence on the future risk of hospitalization for early HF. To our knowledge, no investigations have been published on this subject.

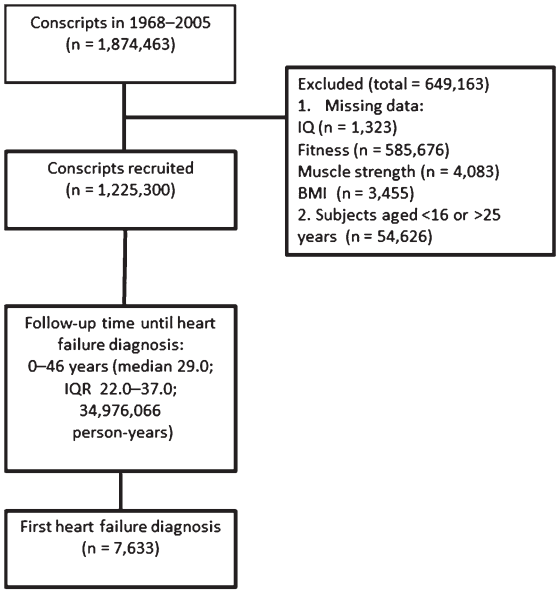

Figure 1 Flow chart of included and excluded conscripts, based on recommendations in Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).[18] The figure shows median years of observation (follow-up time), total person-years of observation (person-years), and numbers of incident heart failure. BMI, body mass index; IQR, interquartile range.

Methods

Participants

We undertook a prospective cohort study using data retrieved from the Swedish Military Service Conscription Registry. From 1901 to 2005, all 18-year-old Swedish men were obliged to enlist for military service under Swedish law. Exemptions were granted only for severe chronic medical or mental conditions, functional disabilities documented by a medical certificate, and incarceration (2–3% each year). The original cohort for this study comprised all Swedish men born between 1950 and 1987 who enlisted for military service in 1968–2005 ($n = 1\ 874\ 463$) (*Figure 1*).[18] We excluded males who enlisted early or late (age < 16 or > 25 years; $n = 54\ 626$) or who had missing data on cardiorespiratory fitness ($n = 585\ 676$), muscular strength ($n = 4083$), BMI ($n = 3455$), or cognitive performance ($n = 1323$). Accordingly, 1 225 300 men were included. The ethics committee of the University of Gothenburg approved this study.

Data collection

During the period 1968–2005, all enlisted men underwent standardized physical and cognitive examinations at one of six conscription centres. During a 2-day examination, the conscripts were examined by a psychologist and a physician. Weight, height, and blood pressure were measured, and morbidities were documented. Cardiovascular fitness was measured using cycle ergometer testing; maximal work capacity expressed in Watts (Wmax) was divided by body weight and transformed into a 'standard nine' (stanine) score of 1–9. As part of the physical evaluation, isometric muscle strength was measured in terms of knee extension, elbow flexion, and hand grip; the results were weighted and transformed into the stanine score (1–9).[10] The procedures, including elements of validity and reliability, have been described in detail elsewhere[19] and are further described in the online supplementary *Methods*.

Cognitive performance tests

Four cognitive tests were used, covering the following areas: logical, verbal, visuospatial, and technical cognition. The tests were slightly amended in 1980. The logical test measured the ability to understand written instructions and apply them to a problem-solving task. Before 1980, the verbal test examined the ability of concept discrimination; after 1980, it examined the capability to select the correct synonym or antonym from a given set of words. Before 1980, the visuospatial test contained questions about puzzles in 2-D; after 1980, the test evaluated the capacity to identify the correct 3-D image from a series of 2-D drawings (metal folding). Finally, the technical intelligence test contained problem-solving tasks, requiring knowledge of basic mathematics and physics. The cognitive performance tests have previously been described in detail.[20] The test scores of the four cognitive domains were totalled and given equal weighting, thereby providing a global intelligence score as a measure of general cognitive performance. To determine the long-term stability of the data sets, we standardized the test results against data from previous years to obtain scores from 1 (low) to 9 (high; henceforth referred to as IQ category or stanine scores); we did the same with the results of the four subtests. Before 1996, raw data were not electronically recorded, and only stanine scores could be accessed for statistical analysis. Therefore, we used only stanine scores in the present study.

Parental education

We obtained information on parental education from the longitudinal integration database for Health Insurance and Labour Market Studies (LISA; 80% coverage). The LISA database at Statistics Sweden was initiated in 1990, and it includes all registered residents aged 16 years and older. The database integrates data from the labour market and educational and social sectors. The classification has seven categories: <9 years, pre-high school education of 9 years, high school education, university (<2 years), university (≥2 years), postgraduate education, and postgraduate research training. The highest level achieved of either parent was used.

Follow-up procedures

Sweden has a general health care system that provides low-cost universal care to all Swedish residents. There is mandatory reporting of discharge diagnoses for all inpatient care patients to the nationwide Hospital Discharge Register. Register coverage gradually increased from 1968 to 1986; it was complete by 1987. Since 2001, diagnoses for patients in hospital outpatient care have also been recorded. The unique Swedish personal identity number allowed for data linkage from the Swedish Military Service Conscription Registry to the IPR.

A large percentage of patients with HF had other primary aetiological diagnoses; thus, the first-ever HF diagnosis code in any position was accepted as HF. From 1968 to 1986 the International Classification of Diseases, eighth revision (ICD-8) was in use; from 1987 to 1996, ICD-9; and thereafter, ICD-10. HF was defined as follows: 427.00 and 427.10 (ICD-8); 428 (ICD-9); and I50 (ICD-10). Associated co-morbidities were included in the analysis until the first HF discharge diagnosis and are listed in the online supplementary *Methods*. Because of overlapping HF aetiologies, we assigned mutually exclusive causes of HF in the following hierarchical order: 1, congenital heart disease and valvulopathies; 2, ischaemic heart disease, diabetes, or hypertension; 3, cardiomyopathy; and 4, other causes.

Statistical analysis

We calculated incidence rates and corresponding 95% confidence intervals (CIs) using the Poisson regression model. We used the Cox proportional hazards regression model to estimate associations between adolescent IQ and potential confounders with the risk of future hospitalization for HF. The follow-up period began at the time of conscription. Subjects were followed until the first HF diagnosis, death from other causes, emigration, or the end of follow-up on 31 December 2014 (whichever occurred first). We included the following as covariates: age at conscription; year of conscription; co-morbidities at baseline (hypertension, type 1 diabetes, and congenital heart disease); BMI; systolic and diastolic blood pressure; body height; parental education (highest achieved); stanine scores for cardiovascular fitness; and muscle strength. We refrained from making any adjustments for co-morbidities that occurred during follow-up as they may have acted as mediators in the development of HF rather than confounders.

We used IQ stanines (1–9) as a continuous variable for analyses. Muscle strength and cardiovascular fitness were scored 1–9 and classified as low (1–3 points), medium (4–6 points), or high (7–9 points). The highest achieved parental education level was also trichotomized with the categories of mandatory education (1), high school (2), and university, postgraduate, or postgraduate research training (3). Age at conscription, BMI, body height, and systolic and diastolic blood pressure were continuous variables. We also performed group-specific analyses for BMI, parental education, and cardiorespiratory fitness to explore the validity of the results in, respectively, people with different body compositions, in various socioeconomic groups, and with different fitness levels.

We employed cubic restricted splines with knots placed at the 5th, 35th, 65th, and 95th percentiles for conscription year, BMI, and Wmax. The proportional hazards assumptions were demonstrated as tenable using plots based on weighted residuals. Owing to the large number of observations, the *P*-values were very small and are therefore not reported. We undertook statistical calculations using SAS, version 9.4 (SAS Institute, Cary, NC, USA).

Results

Table 1 shows the characteristics of the study population with respect to their IQ. The mean age at conscription was 18.3 years and mean age at first HF diagnosis was 50.1 years. We observed increasing body height for higher IQ levels with a decrease in the proportion of overweight and obesity. Cardiovascular fitness and highest-achieved parental education increased substantially with increasing IQ. No specific trend was evident for muscle strength. The prevalence of co-morbidities recorded at baseline is presented in the supplementary material online, *Table S1*.

Table 2 displays the incidence of HF in the different IQ categories and divided into mutually exclusive associated conditions. During the 34 976 066 person-years of follow-up (minimum 0 years; maximum 46 years; mean follow-up 29 years), 7633 first-time HF hospitalizations in any diagnostic position were documented. Of those, HF was the main diagnosis in 3542 cases. The number of HF cases associated with congenital or acquired valvular disease was 982 (12.8%). CHD, diabetes, or hypertension was associated with 4280 cases (59.2%), cardiomyopathy with 898 cases (11.8%), and other causes with 1473 cases (19.3%). The total incidence of HF was 21.8 cases/100 000 person-years. There was a pattern of decreasing incidence with increasing IQ for HF of any cause as well as for the separate aetiologies. For all HF cases, the incidence ranged from 12.58 cases/100 000 person-years in the highest IQ category to 52.29 cases/100 000 person-years in the lowest. The corresponding figures for HF associated with congenital or acquired valvular disease were 1.50–5.65; they were 7.69–32.16 for HF associated with CHD, diabetes, or hypertension; 1.89–5.65 for HF associated with cardiomyopathy, and 1.50–8.84 for HF of any other cause.

Table 3 details the hazard ratios (HRs) with 95% CIs for HF hospitalizations across the different levels of cognitive performance; IQ stanine 9 is the reference category. Adjustment for co-morbidities at baseline (hypertension, diabetes, and congenital heart disease) and documented alcohol or substance abuse had minimal effect compared with the least adjusted model. Further adjustments for body height, systolic and diastolic blood pressure, parental education, cardiorespiratory fitness, and muscle strength attenuated the observed associations moderately. In the fully adjusted model, the HR for IQ stanine 1 was 3.11 for HF of any cause. For each standard deviation decrease in IQ, the corresponding HR was 1.32 (95% CI 1.28–1.35).

Figure 2 presents the adjusted HRs across the BMI groups. Among obese subjects, the association with lower IQ was weaker

Table 1 Baseline characteristics and age at first heart failure discharge by IQ stanine among male conscripts

	All	IQ								
		1	2	3	4	5	6	7	8	9
	n = 1 225 300 (100%)	*n* = 32 462 (2.6%)	*n* = 74 897 (6.1%)	*n* = 124 070 (10.1%)	*n* = 185 657 (15.2%)	*n* = 270 402 (22.1%)	*n* = 217 514 (17.8%)	*n* = 164 496 (13.4%)	*n* = 100 569 (8.2%)	*n* = 55 233 (4.5%)
Age (years), mean (SD)	18.3 (0.7)	18.6 (1.1)	18.4 (0.8)	18.3 (0.7)	18.3 (0.7)	18.3 (0.6)	18.3 (0.6)	18.3 (0.6)	18.3 (0.6)	18.3 (0.6)
Age at HF diagnosis (years), mean (SD)	50.1 (7.9)	49.5 (7.7)	49.8 (7.5)	49.6 (7.8)	49.9 (8.0)	49.6 (7.8)	50.3 (8.1)	51.3 (7.8)	51.0 (7.8)	52.1 (7.3)
Height (m), mean (SD)	1.79 (0.07)	1.76 (0.07)	1.77 (0.07)	1.78 (0.07)	1.79 (0.06)	1.79 (0.06)	1.80 (0.06)	1.80 (0.06)	1.81 (0.06)	1.81 (0.06)
Weight (kg), mean (SD)	70.0 (10.2)	68.4 (11.9)	69.1 (11.3)	69.7 (10.9)	69.9 (10.5)	70.2 (10.2)	70.2 (9.8)	70.1 (9.5)	70.1 (9.3)	69.9 (9.1)
Body mass index (kg/m^2), mean (SD)	21.7 (2.8)	21.9 (3.4)	21.9 (3.2)	21.9 (3.0)	21.9 (2.9)	21.8 (2.8)	21.7 (2.6)	21.6 (2.5)	21.5 (2.5)	21.3 (2.4)
Systolic BP (mmHg), mean (SD)	128.2 (10.8)	127.8 (10.9)	128.0 (10.8)	127.9 (10.8)	128.1 (10.7)	128.2 (10.7)	128.3 (10.8)	128.5 (10.8)	128.4 (10.8)	128.2 (10.8)
Diastolic BP (mmHg), mean (SD)	67.3 (9.7)	68.0 (10.0)	67.4 (10.0)	67.2 (9.8)	67.3 (9.8)	67.0 (9.7)	67.4 (9.7)	67.4 (9.7)	67.4 (9.6)	67.4 (9.6)
Parental education (highest achieved), % (*n*)										
1–2	30.7 (362 783)	55.7 (16 617)	48.9 (34 709)	42.0 (49 778)	36.9 (65 938)	30.7 (80 444)	26.4 (55 550)	21.9 (34 978)	17.9 (17 461)	13.6 (7308)
3–5	53.9 (636 148)	41.8 (12 460)	47.7 (33 843)	52.9 (62 715)	55.5 (99 150)	57.3 (150 072)	56.1 (118 105)	54.0 (86 162)	50.6 (49 355)	45.3 (24 286)
6–7	15.4 (182 057)	2.5 (738)	3.3 (2357)	5.2 (6110)	7.5 (13 480)	12.0 (31 368)	17.6 (36 980)	24.1 (38 404)	31.4 (30 650)	41.0 (21 970)
Cardiorespiratory fitness, % (*n*)										
Low	3.9 (48 023)	11.4 (3703)	7.8 (5836)	5.8 (7176)	4.6 (8487)	3.6 (9619)	2.9 (6253)	2.4 (3924)	2.1 (2075)	1.7 (950)
Medium	53.8 (659 621)	68.0 (22 088)	65.0 (48 714)	62.3 (77 260)	58.3 (108 316)	55.2 (149 318)	49.9 (108 624)	46.9 (77 126)	44.3 (44 544)	42.8 (23 631)
High	42.2 (517 656)	20.6 (6671)	27.2 (20 347)	31.9 (39 634)	37.1 (68 854)	41.2 (111 465)	47.2 (102 637)	50.7 (83 446)	53.6 (53 950)	55.5 (30 652)
Muscle strength, % (*n*)										
Low	10.9 (133 326)	22.8 (7397)	15.2 (11 383)	12.4 (15 428)	11.0 (20 484)	9.6 (25 846)	9.7 (21 027)	9.6 (15 818)	10.0 (10 063)	10.6 (5880)
Medium	57.8 (708 363)	57.7 (18 719)	59.0 (44 220)	58.2 (72 163)	58.0 (107 589)	57.3 (155 031)	57.3 (124 690)	57.8 (95 067)	58.3 (58 633)	58.4 (32 251)
High	31.3 (383 611)	19.5 (6346)	25.8 (19 294)	29.4 (36 479)	31.0 (57 584)	33.1 (89 525)	33.0 (71 797)	32.6 (53 611)	31.7 (31 873)	31.0 (17 102)

HF, heart failure; SD, standard deviation.

Table 2 Incidence of heart failure by IQ stanine

	All	IQ 1	2	3	4	5	6	7	8	9
HF as a main diagnosis										
n	3542	244	379	518	626	660	518	310	203	84
Cases per 100 000 person-years	10.12 (9.79–10.46)	25.03 (22.08–28.38)	16.91 (15.29–18.70)	14.39 (13.20–15.69)	11.72 (10.83–12.67)	8.65 (8.01–9.34)	8.37 (7.68–9.13)	6.66 (5.96–7.45)	7.17 (6.25–8.22)	5.47 (4.42–6.78)
HF in any diagnostic position										
n	7633	509	820	1024	1357	1436	1143	724	427	193
Cases per 100 000 person-years	21.82 (21.34–22.32)	52.29 (47.94–57.04)	36.63 (34.20–39.22)	28.47 (26.78–30.27)	25.42 (24.10–26.80)	18.83 (17.88–19.83)	18.48 (17.44–19.59)	15.57 (14.47–16.74)	15.08 (13.72–16.58)	12.58 (10.92–14.48)
HF with congenital or acquired valvular disease										
n	982	55	98	135	187	189	150	89	56	23
Cases per 100 000 person-years	2.81 (2.64–2.99)	5.65 (4.34–7.36)	4.38 (3.59–5.34)	3.75 (3.17–4.44)	3.50 (3.03–4.04)	2.48 (2.15–2.86)	2.43 (2.07–2.85)	1.91 (1.55–2.36)	1.98 (1.52–2.57)	1.50 (1.00–2.26)
HF with CHD, diabetes or hypertension										
n	4280	313	482	578	728	786	652	397	226	118
Cases per 100 000 person-years	12.24 (11.88–12.61)	32.16 (28.78–35.92)	21.53 (19.69–23.54)	16.07 (14.81–17.43)	13.63 (12.68–14.66)	10.31 (9.61–11.05)	10.54 (9.76–11.38)	8.54 (7.74–9.42)	7.98 (7.01–9.09)	7.69 (6.42–9.21)
HF with cardiomyopathy										
n	898	55	96	104	170	167	136	93	48	29
Cases per 100 000 person-years	2.57 (2.40–2.74)	5.65 (4.34–7.36)	4.29 (3.51–5.24)	2.89 (2.39–3.50)	3.18 (2.74–3.70)	2.19 (1.88–2.55)	2.20 (1.86–2.60)	2.00 (1.63–2.45)	1.70 (1.28–2.25)	1.89 (1.31–2.72)
HF, any other cause										
n	1473	86	144	207	272	294	205	145	97	23
Cases per 100 000 person-years	4.21 (4.00–4.43)	8.84 (7.15–10.91)	6.43 (5.46–7.57)	5.75 (5.02–6.59)	5.09 (4.52–5.74)	3.85 (3.44–4.32)	3.32 (2.89–3.80)	3.12 (2.65–3.67)	3.43 (2.81–4.18)	1.50 (1.00–2.26)

CHD, coronary heart disease; HF, heart failure.

Table 3 Adjusted hazard ratios for individual IQ stanines and per standard deviation decrease in IQ for heart failure categories

	Hazard ratio (95% CI)		
IQ stanine	**Model 1**	**Model 2**	**Model 3**
HF as main diagnosis (events/population)	3542/1 225 300	3542/1 225 300	3259/1 175 613
9 (reference)	1	1	1
8	1.31 (1.01–1.69)	1.31 (1.01–1.68)	1.29 (0.99–1.68)
7	1.23 (0.96–1.56)	1.22 (0.96–1.56)	1.15 (0.89–1.48)
6	1.56 (1.24–1.96)	1.56 (1.23–1.96)	1.42 (1.12–1.81)
5	1.74 (1.39–2.19)	1.74 (1.39–2.19)	1.56 (1.22–1.98)
4	2.21 (1.76–2.78)	2.21 (1.76–2.78)	1.95 (1.54–2.49)
3	2.74 (2.17–3.45)	2.73 (2.17–3.44)	2.28 (1.79–2.92)
2	3.15 (2.48–3.99)	3.14 (2.48–3.98)	2.42 (1.88–3.11)
1	4.45 (3.47–5.71)	4.44 (3.46–5.69)	3.32 (2.54–4.33)
Per SD decrease	1.44 (1.39–1.49)	1.44 (1.39–1.49)	1.34 (1.29–1.39)
HF in any diagnostic position (events/population)	7633/1 225 300	7633/1 225 300	7041/1 175 613
9 (reference)	1	1	1
8	1.20 (1.01–1.42)	1.20 (1.01–1.42)	1.16 (0.97–1.39)
7	1.25 (1.06–1.46)	1.24 (1.06–1.46)	1.17 (1.00–1.39)
6	1.50 (1.28–1.74)	1.49 (1.28–1.74)	1.38 (1.17–1.62)
5	1.66 (1.42–1.92)	1.65 (1.42–1.92)	1.48 (1.26–1.73)
4	2.09 (1.80–2.43)	2.09 (1.80–2.43)	1.84 (1.57–2.16)
3	2.36 (2.02–2.75)	2.36 (2.02–2.75)	1.99 (1.69–2.35)
2	2.97 (2.54–3.48)	2.97 (2.54–3.47)	2.38 (2.01–2.81)
1	4.08 (3.45–4.81)	4.06 (3.44–4.80)	3.11 (2.60–3.71)
Per SD decrease	1.40 (1.37–1.44)	1.40 (1.37–1.44)	1.32 (1.28–1.35)
HF hospitalization with congenital heart disease/valvulopathy (events/population)	982/1 225 300	982/1 225 300	919 /1 175 613
9 (reference)	1.00	1.00	1.00
8	1.31 (0.81–2.13)	1.31 (0.81–2.13)	1.17 (0.70–1.93)
7	1.27 (0.81–2.02)	1.27 (0.80–2.01)	1.20 (0.75–1.92)
6	1.63 (1.05–2.53)	1.62 (1.05–2.52)	1.48 (0.94–2.33)
5	1.80 (1.17–2.78)	1.80 (1.17–2.77)	1.61 (1.03–2.52)
4	2.38 (1.54–3.67)	2.38 (1.54–3.67)	2.16 (1.38–3.38)
3	2.57 (1.65–4.01)	2.58 (1.66–4.02)	2.25 (1.42–3.56)
2	2.95 (1.87–4.65)	2.94 (1.87–4.63)	2.62 (1.63–4.20)
1	3.73 (2.29–6.07)	3.70 (2.27–6.02)	3.19 (1.91–5.32)
Per SD decrease	1.38 (1.29–1.47)	1.38 (1.29–1.47)	1.35 (1.26–1.45)
HF hospitalization with CHD, diabetes, or hypertension (events/population)	4280/1 225 300	4280/1 225 300	3934/1 175 613
9 (reference)	1	1	1
8	1.04 (0.83–1.30)	1.04 (0.83–1.29)	1.01 (0.80–1.27)
7	1.12 (0.91–1.38)	1.12 (0.91–1.38)	1.03 (0.83–1.28)
6	1.41 (1.16–1.71)	1.40 (1.15–1.71)	1.26 (1.02–1.54)
5	1.52 (1.25–1.84)	1.51 (1.25–1.84)	1.31 (1.06–1.60)
4	1.86 (1.53–2.25)	1.85 (1.53–2.25)	1.54 (1.25–1.89)
3	2.21 (1.81–2.69)	2.20 (1.81–2.69)	1.72 (1.39–2.13)
2	2.89 (2.36–3.54)	2.89 (2.36–3.53)	2.11 (1.70–2.62)
1	4.11 (3.32–5.08)	4.08 (3.30–5.05)	2.83 (2.26–3.56)
Per SD decrease	1.43 (1.39–1.48)	1.43 (1.39–1.48)	1.31 (1.26–1.35)
HF hospitalization with cardiomyopathy (events/population)	898/1 225 300	898/1 225 300	842/1 175 613
9 (reference)	1	1	1
8	0.89 (0.56–1.42)	0.89 (0.56–1.42)	0.93 (0.58–1.51)
7	1.06 (0.70–1.60)	1.06 (0.70–1.60)	1.05 (0.68–1.63)
6	1.17 (0.78–1.74)	1.17 (0.78–1.74)	1.15 (0.75–1.75)
5	1.21 (0.81–1.79)	1.21 (0.81–1.79)	1.14 (0.75–1.74)
4	1.69 (1.14–2.51)	1.69 (1.14–2.51)	1.66 (1.09–2.52)
3	1.53 (1.02–2.32)	1.54 (1.02–2.32)	1.47 (0.95–2.29)
2	2.23 (1.47–3.37)	2.23 (1.47–3.38)	2.00 (1.28–3.12)
1	2.86 (1.82–4.49)	2.86 (1.82–4.49)	2.36 (1.45–3.86)
Per SD decrease	1.33 (1.24–1.42)	1.33 (1.24–1.42)	1.27 (1.18–1.37)
HF hospitalization, all other (events/population)	1473/1 225 300	1473/1 225 300	1346/1 175 613
9 (reference)	1	1	1
8	2.28 (1.45–3.59)	2.28 (1.45–3.60)	2.23 (1.39–3.59)
7	2.08 (1.34–3.24)	2.09 (1.34–3.24)	2.02 (1.28–3.21)
6	2.24 (1.45–3.44)	2.24 (1.46–3.45)	2.15 (1.37–3.38)
5	2.79 (1.82–4.26)	2.79 (1.82–4.27)	2.65 (1.69–4.14)
4	3.48 (2.28–5.33)	3.49 (2.28–5.34)	3.34 (2.13–5.24)
3	3.97 (2.58–6.10)	3.97 (2.58–6.11)	3.80 (2.41–6.00)
2	4.37 (2.81–6.78)	4.37 (2.81–6.79)	3.94 (2.47–6.29)
1	5.82 (3.67–9.23)	5.83 (3.68–9.25)	5.08 (3.11–8.32)
Per SD decrease	1.38 (1.31–1.46)	1.38 (1.31–1.46)	1.35 (1.27–1.43)

CHD, coronary heart disease; CI, confidence interval; HF, heart failure; SD, standard deviation.
Model 1: adjusted for age at conscription, year of conscription, conscription test centre, body mass index.
Model 2: additionally adjusted for co-morbidities at baseline (diabetes mellitus, hypertension, congenital heart disease, documented alcohol and substance abuse).
Model 3: additionally adjusted for body height, systolic and diastolic blood pressure, parental education, cardiorespiratory fitness, and muscle strength.

(P for interaction =0.0004); however, the analyses produced wide CIs attributable to the small size of the obese group. Parental education and cardiorespiratory fitness showed no significant interactions for the effect of IQ on the development of HF.

Discussion

The present study shows that low cognitive performance in early adulthood is associated with increased risk of early incident HF and that the risk is greatest for people with the lowest IQ. The results were similar regardless of concomitant associated conditions. To our knowledge, this is the first study to identify such a relationship.

Our results are in line with those of several studies that investigated the relationship between early-life IQ and cardiovascular disease.[11–13] In a recent meta-analysis using pooled data from four longitudinal cohort studies, Dobson *et al.*[14] found a 16% (relative risk 1.16; 95% CI 1.07–1.26; $P < 0.001$) increased risk of future cardiovascular disease (defined as hospitalization for cardiovascular disease, CHD, or stroke) per standard deviation decrease in childhood IQ. In the present study, the HR per standard deviation decrease in IQ was 1.32 (95% CI 1.28–1.35) for HF in any diagnostic position, in the fully adjusted model. The strong associations that we found could be explained by HF being secondary to CHD; however, our findings were equally strong with HF associated with other conditions. Cardiomyopathies are a heterogeneous group of diseases with multifactorial origins, limiting conclusions drawn from this observation. The association may be explained by increased burden of behavioural risk factors as well as genetic factors associated with cognitive function. Future studies should investigate the association while considering various subtypes of cardiomyopathy. The increased risk between low IQ and of HF associated with congenital heart disease may tentatively be a result of reverse causality, as a congenital condition may cause cognitive impairment or limit participation in educational activities. However, men with known serious medical conditions, such as congenital heart disease, were exempted from conscription. Also, given that congenital heart disease is comparatively rare, any effect on cognitive function would be very limited in size.

There is evidence indicating that the association between early-life IQ and future risk of CHD may be explained by socioeconomic factors, such as educational attainment in adulthood,[15] or adverse social circumstances and lifestyle-related factors measured in early life.[16,21] In the present study, adjustments for other factors, including childhood socioeconomic factors, accounted only for a small part of the association between intelligence and risk of HF. In the statistical model, we included parental education and body height at conscription as markers of socioeconomic position and social circumstances in childhood. However, those two markers may not completely capture the social circumstances in childhood. Adversity in childhood has been suggested to affect health in later life via complex interplay between harsh family environments, including neglectful or harsh parenting and chaotic home life, childhood socioeconomic factors, as well as genetic and epigenetic factors. Each may independently predispose to maladaptation across multiple biological systems causing allostatic load and leading to increased cardiovascular risk.[22] There is emerging evidence regarding genetic factors as an important cause for the association.[23] Whether the association is caused by pleiotropic effects, consistent with the system integrity hypothesis, or constitutes evidence of a causal pathway between genetic predisposition and disease is unknown. It may also be speculated that higher IQ offers a conduit to healthy behaviour and environments through the ability of achieving a higher education. Thus, the observed association may be mediated by socioeconomic factors not considered in this study.

Group-specific models with respect to BMI status (*Figure 2*) revealed a lack of association between IQ and HF in obese subjects; there were weaker associations between IQ and HF in overweight and underweight participants compared with those with normal BMI. The small size of the obese group resulted in low analytical precision; that point needs to be considered when interpreting our results. Interaction analyses confirmed a significant effect of the interaction term on the outcome ($P = 0.0004$).

Cardiovascular disease typically presents in higher ages, though the clustering of risk factors may occur in early life and continue into adulthood.[24] A possible pathway by which early-life intelligence may affect future morbidity is an unhealthy lifestyle. It has been suggested that low intelligence leads to trouble understanding and applying information about favourable and adverse health behaviour as well as treatment regimens.[25] Behavioural risk factors such as physical inactivity, unhealthy dietary habits and smoking, may elicit this effect, increasing the risk of obesity, insulin resistance and hypertension, all known causes of HF. Furthermore, insufficient control of developed risk factors, including lacking adherence to medical treatments and lifestyle interventions, may accelerate this process. In the present cohort, cognitive function was found to be associated with cardiorespiratory fitness[26]—a factor previously associated with HF risk[10]—as well as adherence to statin treatment 1 and 2 years after the first myocardial infarction.[27] A study linking the Scottish Mental Survey 1932 and the Midspan studies identified no difference in IQ scores between ever smokers and never smokers; however, the relative rate of smoking cessation was significantly higher in subjects with higher IQ scores.[28]

Another study reported that inadequate health literacy in patients with diabetes or hypertension was significantly associated with less knowledge about their condition and self-management skills.[29] Furthermore, there is evidence that cognitive function is associated with health literacy, which is a predictor of HF knowledge, self-care, and mortality among HF patients.[30]

In the present study, we found a distinct trend of decreasing risk of HF and declining incidence of almost all co-morbidities with increasing IQ. However, in the higher IQ categories, the trend was less discernible. It is possible that at some point, knowledge about healthy behaviour and disease management becomes sufficient; that phenomenon may contribute to the above pattern.

Finally, while HF has been associated with cognitive decline and dementia in the literature,[31] previous studies have not considered early-life cognitive function when assessing this relationship. Our results indicate that cognitive function in adolescence may be an important confounder of this relationship, as adolescent IQ is known to be associated with increased risk of cognitive impairment

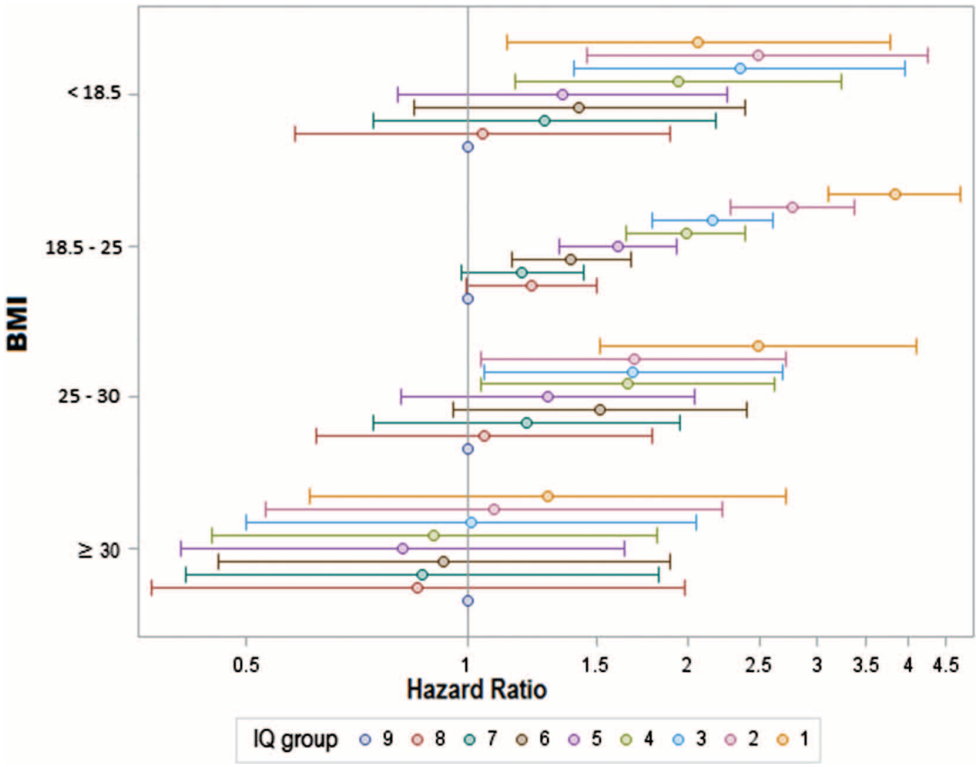

Figure 2 Hazard ratios for heart failure by IQ stanine with respect to body mass index (BMI) group.

and dementia.[32] Future studies of cognitive impairment in HF should take this into consideration.

Strengths and limitations

The strengths of this study include the large sample size and number of incident HF cases. However, some limitations should be considered. The diagnoses were recorded in the IPR for administrative purposes; not all were formally validated. Even so, hospital-recorded diagnoses of HF in Sweden have been shown to have high validity.[33] Additionally, the study population comprised only young men from a single country; future studies need to explore whether our results also apply to women, older men, and other ethnicities. Importantly, the mean age of 50 years among recorded cases is lower than in most HF populations. Accordingly, the results may not be generalizable to the majority of patients with HF. Lack of information regarding lifestyle and other socioeconomic factors at baseline and during follow-up, such as smoking and alcohol consumption, are potential sources of residual confounding.

Conclusions

Low cognitive performance in late adolescence was strongly associated with an increased risk of early incident HF. Additionally, low intelligence appeared to have a stronger impact in normal-weight individuals. If causal, these findings contribute to the body of evidence supporting the importance of cognitive function in early life for cardiovascular health throughout life. This knowledge could contribute to more efficient risk-factor management in the younger population.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Methods. Supplementary methods.

Table S1. Co-morbidities at baseline and registrations in the patient registry prior to and including index hospitalization.

Funding

This work was supported by grants from the following: the Swedish state under the agreement concerning research and education of doctors (grant number ALFGBG-427301); the Swedish Society for Physicians, the Health & Medical Care Committee of the Regional Executive Board, Region Västra Götaland, Sweden, and the Swedish Heart and Lung Foundation (grant number 2015-0438); the Swedish Research Council (grant numbers 2013-5187, 2013-4236); and the Swedish Council for Health, Working Life and Welfare (FORTE) (grant numbers 2007-2280, 2013-0325).

Conflict of interest: none declared.

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