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Short Report

Prevalence of cardiovascular risk factors in a nationally representative adult population with inflammatory bowel disease without atherosclerotic cardiovascular disease



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ABSTRACT

Background and aims: Chronic inflammation is associated with premature atherosclerotic cardiovascular disease (ASCVD). We studied the prevalence of cardiovascular risk factors (CRFs) amongst individuals with IBD who have not developed ASCVD.

Methods: Our study population was derived from the 2015 – 2016 National Health Interview Survey. Those with ASCVD (defined as myocardial infarction, angina or stroke) were excluded. The prevalence of CRFs among individuals with IBD was compared with those without IBD. The odds CRFs among adults with IBD was assessed using logistic regression models.

Results: In our study population of 60,155 individuals, 786 (1.3%) had IBD. IBD was associated with increased odds hypertension (odds ratio [OR] 1.71, 95% confidence interval [CI] 1.39–2.09), diabetes (OR 1.68, 95% CI 1.22–2.32), hypercholesterolemia (OR 1.62, 95% CI 1.32–2.99) and insufficient physical activity (OR 1.38, 95% CI 1.16–1.66).

Conclusion: IBD is associated with higher prevalence of CRFs. Early screening and risk mitigation strategies are warranted.

1. Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory condition of the gastrointestinal tract comprising Crohn's disease (CD), ulcerative colitis (UC) and indeterminate colitis. IBD is believed to be triggered by a dysregulated local mucosal immune response to commensal intraluminal microbes in genetically predisposed individuals [1,2]. CD and UC differ in the extent and type of intestinal inflammatory response,

however, both are characterized by the presence of systemic inflammation and often, extra-intestinal clinical manifestations [1].

Inflammation plays a key role in atherogenesis as well as plaque destabilization [3]. There is compelling evidence demonstrating that conditions characterized by chronic inflammation such as rheumatoid arthritis, systemic lupus erythematosus and psoriasis are associated with accelerated atherosclerosis and higher risk of premature atherosclerotic cardiovascular disease (ASCVD) [4,5]. In this context, recent studies

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; CD, crohn's disease; CDC, centers for disease control and prevention; CI, confidence interval; CRF, cardiovascular risk factors; IBD, inflammatory bowel disease; NHIS, National Health Interview Survey; OR, odds ratio; UC, ulcerative colitis.

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have also portrayed an increased risk of ASCVD in patients with IBD [6,7].

There is, however, a paucity of data in terms of the burden of cardiovascular risk factors (CRF) among IBD patients who have not yet developed clinical ASCVD. This knowledge can shed light on the intermediate mechanisms that result in an increased risk of ASCVD in IBD, identifying opportunities for enhanced early preventive efforts. Accordingly, in this study we sought to describe the prevalence of CRFs among patients with IBD from a nationally representative US sample who had not developed clinical ASCVD.

2. Methods

We used data from the 2015–2016 National Health Interview Survey (NHIS), a cross-sectional household interview survey conducted annually by the National centre for Health Statistics under the auspices of the Centres for Disease Control and Prevention (CDC). Our study utilized publicly available de-identified data and therefore was exempt from IRB approval. The survey collects information on the health of the civilian non-institutionalised population using a multi-stage, complex design in order to produce nationwide estimates [8]. We included all adults ≥ 18 years of age without established ASCVD. This was self-reported and included coronary artery disease (“Yes” to any of the following 3 questions: “Have you ever been told by a doctor or other health professional that you had ... coronary heart disease?”, “... angina, also called angina pectoris?”, “... a heart attack (also called myocardial infarction)?”) and stroke (“Yes” to the following question: “Have you ever been told by a doctor or other health professional that you had a stroke?”). Presence of IBD was self-reported and ascertained as an affirmative response to: “Have you ever been told by a doctor or other health professional that you had Crohn’s disease or ulcerative colitis?” CRFs were also self-reported and included hypertension, diabetes, hypercholesterolemia, smoking, obesity (BMI ≥30 kg/m²; calculated by self-reported height and weight), and insufficient physical activity. Insufficient physical activity was defined as not participating in >=150 min per week of moderate-intensity aerobic physical activity, >=75 min per week of vigorous-intensity aerobic physical activity, or a total combination of ≥150 min per week of moderate/vigorous-intensity aerobic physical activity. Further, for the present analyses we created a CRF profile, with 3 mutually-exclusive categories based on the presence of individual CRFs: 0–1 (“optimal”), 2–3 (“average”), and ≥ 4 (“poor”) [9,10].

We obtained national estimates for the proportion of individuals with and without IBD using survey-specific descriptive analyses. We used weighted univariate and multivariable logistic regression models to evaluate the association between IBD and CRFs. We also used a multinomial logistic regression analysis (using optimal cardiovascular risk factor as reference) to evaluate the association between IBD and cardiovascular risk factor profile. Additionally, we conducted subgroup analyses of the association between IBD and CRFs by age groups (non-elderly [<65 years] vs. elderly [≥ 65 years]) in order to assess the differential relationship, if any, between CRFs and IBD by age. We obtained variance estimations and person-level weights for the pooled cohort from the Integrated Public Use Microdata Series website (<http://www.ipums.org>) [11]. All analyses were performed using Stata version 16.1 (StataCorp, College Station, TX).

3. Results

Of 66,700 participants included in the 2015–2016 NHIS, 60,155 did not have clinical ASCVD and were used to define our study population. Of these, 786 (1.3%) had IBD and 59,299 (98.57%) did not have IBD, representing 2.6 million and 221.1 million adults, respectively, in the US. Elderly individuals (those aged ≥ 65 years) represented 21.9% of the study population with IBD, and 16% of those without IBD (Table 1).

In the overall study population, individuals with IBD had significantly higher prevalence of hypertension (39% vs 27%), diabetes (12%

Table 1
Demographic characteristics and prevalence of cardiovascular risk factors and risk factor profile by IBD status in individuals without ASCVD from the National Health Interview Survey 2015–2016.

| | Overall population | | Age <65 years | | Age ≥65 years | | p-values | p-values |
|-----------------------------------|--------------------|--------------------|----------------|--------------------|---------------|-------------------|----------|----------|
| | IBD [n(%)] | No IBD [n(%)] | IBD [n(%)] | No IBD [n(%)] | IBD [n(%)] | No IBD [n(%)] | | |
| Sample | 786 | 59,299 | 570 | 46,327 | 216 | 12,972 | | |
| Weighted sample | 2621,113 (1.2) | 221,128,345 (98.8) | 2047,846 (1.1) | 185,769,382 (98.9) | 573,259 (1.6) | 35,358,971 (98.4) | | |
| Age (years), mean (SD) | 53.1 (16.6) | 48.6 (18.1) | 45.6 (12.7) | 41.4 (13.3) | 72.8 (6.4) | 73.6 (6.5) | | |
| Sex, n (weighted%) | | | | | | | | |
| Male | 266 (38.6) | 26,374 (47.7) | 211 (41.1) | 21,287 (48.9) | 55 (29.6) | 5087 (41.6) | | 0.014 |
| Female | 520 (61.4) | 32,925 (52.3) | 359 (58.9) | 25,040 (51.1) | 161 (70.4) | 7885 (58.4) | | |
| Race/ethnicity | | | | | | | | |
| Non-Hispanic white | 618 (75.9) | 39,014 (65.1) | 437 (74.1) | 29,150 (62.6) | 181 (82.1) | 9864 (77.8) | | |
| Non-Hispanic Black | 56 (6.4) | 7323 (12.3) | 44 (6.3) | 5968 (13.0) | 12 (6.6) | 1355 (9.0) | | |
| Non-Hispanic Asian | 22 (3.8) | 3435 (6.2) | 16 (3.9) | 2860 (6.5) | 6 (3.6) | 575 (4.8) | | |
| Hispanic | 81 (13.9) | 8698 (16.4) | 65 (15.6) | 7638 (17.9) | 16 (7.6) | 1060 (8.3) | | |
| Risk factors | | | | | | | | |
| Hypertension | 320 (39.1) | 18,221 (27.3) | 173 (31.0) | 10,601 (21.5) | 147 (68.1) | 7620 (58.1) | | 0.024 |
| Diabetes | 90 (12.4) | 5077 (7.8) | 50 (9.6) | 2844 (5.8) | 40 (22.1) | 2233 (18.5) | | 0.34 |
| Hypercholesterolemia | 265 (33.5) | 15,212 (23.7) | 156 (27.4) | 9016 (19.0) | 109 (55.3) | 6196 (48.4) | | 0.14 |
| Smoking (current vs former/never) | 136 (15.7) | 9403 (15.0) | 123 (18.0) | 8293 (16.3) | 13 (7.2) | 1110 (8.1) | | 0.72 |
| Obesity | 257 (32.6) | 19,045 (31.8) | 181 (32.0) | 15,242 (32.3) | 76 (34.6) | 3803 (29.0) | | 0.16 |
| Insufficient physical activity | 416 (55.8) | 28,295 (47.7) | 277 (52.4) | 20,696 (45.6) | 139 (68.2) | 7599 (58.9) | | 0.04 |
| CRF profile | | | | | | | | |
| Optimal | 319 (43.7) | 30,177 (56.0) | 275 (51.5) | 26,293 (60.4) | 44 (16.7) | 3884 (32.0) | | <0.001 |
| Average | 338 (43.3) | 21,480 (35.9) | 217 (38.1) | 15,248 (33.0) | 121 (61.6) | 6232 (51.2) | | |
| Poor | 97 (12.9) | 5285 (8.2) | 54 (10.4) | 3217 (6.6) | 43 (21.7) | 2068 (16.8) | | |

Abbreviations: CRF, cardiovascular risk factor profile; IBD, inflammatory bowel disease; SD, standard deviation.

Table 2
Odds of cardiovascular risk factors among adults with IBD without established ASCVD from the National Health Interview Survey 2015–2016.

| Variables (present vs absent) | Overall population | | | |
|-----------------------------------|--------------------|---------|------------------|---------|
| | Model 1 | | Model 2 | |
| | OR* (95% CI) | p value | aOR** (95% CI) | p value |
| Hypertension | 1.71 (1.39–2.09) | <0.001 | 1.62 (1.31–2.00) | <0.001 |
| Diabetes | 1.68 (1.22–2.32) | 0.001 | 1.52 (1.09–2.12) | 0.013 |
| Hypercholesterolemia | 1.62 (1.32–1.99) | <0.001 | 1.52 (1.23–1.88) | <0.001 |
| Smoking (present vs never/former) | 1.05 (0.82–1.34) | 0.70 | 1.09 (0.85–1.39) | 0.51 |
| Obesity | 1.04 (0.85–1.27) | 0.73 | 1.01 (0.82–1.24) | 0.92 |
| Insufficient physical activity | 1.38 (1.16–1.66) | <0.001 | 1.35 (1.13–1.63) | 0.001 |
| Risk factor profile† | | | | |
| Average CRF profile | 1.55 (1.24–1.92) | <0.001 | 1.50 (1.20–1.86) | <0.001 |
| Poor CRF profile | 2.03 (1.46–2.80) | <0.001 | 1.91 (1.36–2.69) | <0.001 |
| | <65 years | | | |
| Age <65 years | | | | |
| Variables (present vs absent) | Model 1 | | Model 2 | |
| | OR* (95% CI) | p value | aOR** (95% CI) | p value |
| Hypertension | 1.64 (1.27–2.12) | <0.001 | 1.62 (1.25–2.09) | <0.001 |
| Diabetes | 1.74 (1.14–2.64) | 0.010 | 1.65 (1.07–2.54) | 0.023 |
| Hypercholesterolemia | 1.61 (1.24–2.08) | <0.001 | 1.58 (1.22–2.05) | 0.001 |
| Smoking (present vs never/former) | 1.12 (0.86–1.46) | 0.38 | 1.11 (0.85–1.44) | 0.43 |
| Obesity | 0.99 (0.78–1.25) | 0.91 | 0.95 (0.75–1.21) | 0.70 |
| Insufficient physical activity | 1.31 (1.06–1.62) | 0.011 | 1.32 (1.07–1.63) | 0.009 |
| Risk factor profile† | | | | |
| Average CRF profile | 1.35 (1.06–1.73) | 0.016 | 1.36 (1.06–1.74) | 0.014 |
| Poor CRF profile | 1.86 (1.22–2.82) | 0.004 | 1.72 (1.12–2.64) | 0.014 |
| | ≥65 | | | |
| Age ≥65 years | | | | |
| Variables (present vs absent) | Model 1 | | Model 2 | |
| | OR* (95% CI) | p value | aOR** (95% CI) | p value |
| Hypertension | 1.54 (1.06–2.24) | 0.025 | 1.60 (1.09–2.33) | 0.015 |
| Diabetes | 1.26 (0.78–2.01) | 0.35 | 1.36 (0.85–2.19) | 0.20 |
| Hypercholesterolemia | 1.31 (0.91–1.90) | 0.14 | 1.36 (0.94–1.96) | 0.10 |
| Smoking (present vs former/never) | 0.88 (0.44–1.77) | 0.72 | 0.92 (0.46–1.86) | 0.82 |
| Obesity | 1.30 (0.90–1.86) | 0.16 | 1.23 (0.85–1.77) | 0.27 |
| Insufficient physical activity | 1.49 (1.02–2.19) | 0.039 | 1.49 (1.00–2.21) | 0.047 |
| Risk factor profile† | | | | |
| Average CRF profile | 2.31 (1.48–3.62) | <0.001 | 2.46 (1.56–3.88) | <0.001 |
| Poor CRF profile | 2.49 (1.45–4.26) | 0.001 | 2.60 (1.49–4.54) | 0.001 |

Abbreviations: aOR, adjusted Odds Ratios; CI, confidence interval; cardiovascular risk factor profile.

* Unadjusted model /.

** Model adjusted for age, sex and race/ethnicity.

† Reference: Optimal CRF profile.

vs 8%), hypercholesterolemia (34% vs 24%) and insufficient physical activity (56% vs. 48%) compared with those without IBD (Table 1). In analyses stratified by age, there was a heterogenous distribution of risk factors across age groups. Amongst non-elderly participants, those with IBD had significantly higher prevalence of all of these risk factors except for obesity and smoking when compared with those without IBD. Among elderly participants, except for insufficient physical activity and hypertension, the prevalence of risk factors did not vary significantly between individuals with and without IBD.

In the overall adult population, compared to those without IBD, individuals with IBD had higher odds of hypertension (odds ratio [OR] 1.71, 95% confidence interval [CI] 1.39–2.09), diabetes (OR 1.68, 95% CI 1.22–2.32), hypercholesterolemia (OR 1.62, 95% CI 1.32–2.99) and insufficient physical activity (OR 1.38, 95% CI 1.16–1.66) (Table 2). In addition, using optimal CRF profile as reference, individuals with IBD had higher odds of average (OR 1.55, 95% CI 1.24–1.92) and poor CRF profile (OR 2.03, 95% CI 1.46–2.80) respectively, compared to individuals without IBD. These associations remained constant in magnitude and direction after adjusting for age, sex and race/ethnicity. In sub-group

analyses, the same patterns were seen in the non-elderly population, while among elderly individuals, those with IBD only had higher odds of reporting hypertension and insufficient physical activity compared to individuals without IBD.

4. Discussion

Our study from a nationally representative US population without established ASCVD showed a higher prevalence of CRFs among individuals with IBD when compared to those without it. This included a higher burden of diabetes, hypercholesterolemia, hypertension, and insufficient physical activity. Sub-group analyses by age showed that these associations were particularly strong in non-elderly persons, while some of the differences in CRF burden were attenuated among elderly participants.

Previous studies have suggested that patients with IBD have a higher risk of ASCVD [6,7,12,13]. However, there is conflicting and scarce data regarding prevalence of CRFs in IBD. Some studies have shown higher [14], while others have shown lower [15] prevalence of CRFs in IBD

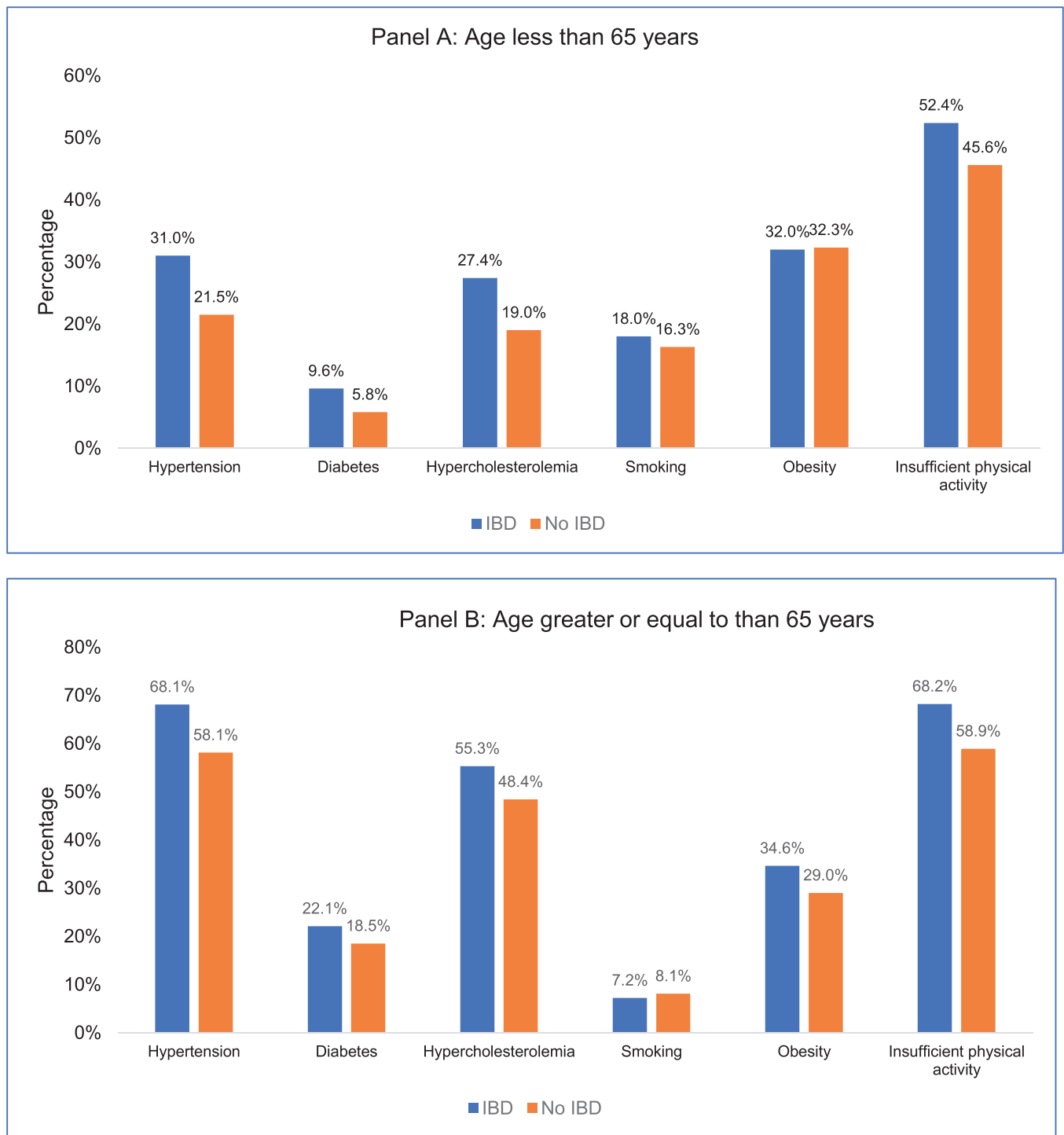


Fig. 1. Prevalence of cardiovascular risk factors by IBD status in individuals without ASCVD from the National Health Interview Survey (2015- 2016). Abbreviations: IBD, inflammatory bowel disease; ASCVD, atherosclerotic cardiovascular disease. Legend: Panel A- Age less than 65 years; Panel B- Age greater than or equal to 65 years.

and some a null association [16] between IBD and overall prevalence of CRFs. One potential explanation for these disparate findings is that the above-mentioned studies involved study populations of varying age ranges and with disparate racial/ethnic distributions. It is also possible that methodological differences in terms of study sample selection and inclusion criteria may have accounted for some of these differences.

Our study findings are unique and notable for several reasons. Firstly, ours is a nationally representative US-based population study of individ-

uals who have not yet developed ASCVD. The higher burden of CRFs in this population, represents an ideal actionable target for primary prevention of ASCVD. Secondly, we found that the association of IBD with CRFs was stronger amongst non-elderly compared to elderly participants. This finding could be explained by the fact that majority of IBD patients are diagnosed at relatively young age, and younger age is associated with very aggressive disease, signifying increased inflammatory burden [17,18]. Another reason is that as disease severity decreases

with age and individuals without IBD develop cardiovascular risk factors, the relative contribution of inflammation may be reduced. Therefore, patients with IBD may benefit from early screening and aggressive risk factor management. Longitudinal cohort studies and interventional research efforts are needed to determine the prognostic value of different risk factors and whether control of modifiable risk factors leads to improved outcomes. Thirdly, the positive association between IBD and individual CRFs as well as average/poor CRF profiles suggests that there may be clustering of cardiometabolic risk factors in IBD. Further studies are needed to unravel the complex interplay between the chronic inflammatory state induced by IBD, the adverse effects from specific therapies for patients with IBD (e.g., corticosteroids), and CRFs.

Some limitations are worth noting. Firstly, data on ASCVD, IBD and CRFs were obtained by self-report and are therefore susceptible to recall bias. However, previous data have shown that the prevalence of self-reported measures in NHIS is similar to that reported by the American Heart Association and the CDC [19,20]. Secondly, it cannot be ruled out that IBD participants may have higher "prevalence" of CRFs as a consequence of more frequent health-care encounters and screening opportunities compared to controls. Nonetheless, regardless of comparisons with non-IBD participants, the observed high prevalence of certain risk factors in patients with IBD is relevant on its own. Third, due to the small number of elderly participants with certain risk factors, our study may have been under-powered to detect statistically significant differences in burden of individual cardiovascular risk factors amongst those with and without IBD aged ≥ 65 years. Nevertheless, in the analyses of the associations between IBD and adverse CRF profiles, the associations were strong and statistically significant also among elderly participants, suggesting that 1) there is actually an association between IBD and adverse cardiovascular health also in this group and 2) the lack of statistically significant associations for most individual risk factors may have been due to insufficient statistical power. Finally, due to the cross-sectional nature of our study, we cannot infer causal associations between IBD and CRFs.

5. Conclusion

Individuals with IBD who have not developed clinical ASCVD have a higher prevalence of metabolic CRFs and insufficient physical activity than individuals without IBD. This is particularly true among non-elderly IBD patients. Early, aggressive screening and intensive modification of CRFs in young adult IBD patients may improve cardiovascular outcomes in these patients.

Author contributions

Conception or design of the work: TA, IA, MCA, KN
 Data collection: IA, JVE
 Data analysis and interpretation: IA
 Drafting the article: TA, IA
 Critical revision of the article: AKD, KG, BA, RB, SSV, MJB, JVE, MCA, KN, EQ, NM
 Final approval of the revised article: TA, IA, AKD, KG, BA, RB, SSV, MJB, JVE, MCA, KN, EQ, NM.

Fig. 1

Declaration of Competing Interest

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