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Motoric cognitive risk syndrome and cardiovascular diseases and risk factors in the Canadian population: Results from the baseline assessment of the Canadian longitudinal study on aging

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ABSTRACT

Background: Motoric Cognitive Risk Syndrome (MCR) is a pre-dementia syndrome. The aim of this study was to examine whether there is: 1) an association between MCR and cardiovascular diseases and risk factors (CVDRF) in the Canadian population, and 2) a specific MCR-related CVDRF profile (i.e., cardiovascular diseases (CVD) versus cardiovascular risk factors (CVRF) versus both) when comparing different age groups.
Methods: A total of 29,569 participants free of dementia were recruited in the Canadian Longitudinal Study on Aging. Participants were categorized into groups by their age and MCR status (with MCR versus without MCR). Overweight/obese, smoking, waist to hip circumference ratio (WHCR), systolic blood pressure and diastolic blood pressure levels were CVRF. Diabetes type I and II, hypertension, heart disease and attack, peripheral vascular disease, angina, stroke and rhythmic disease were CVD.
Results: A higher prevalence of CVRF in MCR was shown in the youngest age groups (i.e., 45–54 and 55–64) compared to the other age groups. MCR was positively associated with CVDRF, except in the oldest age group (i.e., ≥75). In this group, the only significant association with CVRF was with diastolic blood pressure, which was negatively associated with MCR. Diabetes and hypertension were not associated with MCR.
Conclusions: MCR is associated with CVDRF in both younger and older individuals. A stronger association was present for CVRF factors in younger adults and for CVD in older adults.

1. Introduction

Motoric Cognitive Risk Syndrome (MCR), which is defined by the association of slow gait speed and cognitive complaint, has been associated with cognitive impairment and decline (Verghese et al., 2012). Thus, MCR may be used to screen individuals at risk of dementia (Verghese et al., 2012). MCR is usable in various primary care settings and at the population level because its two components are easy to assess and are already a part of the routine physician visit for older patients (Drootin, 2011; Falk et al., 2018; Hildreth and Church, 2015; Moncada and Mire, 2017). Dementia is a major chronic morbidity without any curative treatment; however, the onset and progression can be delayed and slowed down by identifying individuals at risk and controlling for cognitive decline risk factors (Deschaintre et al., 2009; de La Torre, 2012; Jack, 2010; Sekhon et al., 2017). Better understanding the dementia-related risk factors associated with MCR may be helpful for improving dementia prevention.

The physiopathology of MCR is still a matter of debate (Verghese et al., 2012; Beauchet et al., 2016; Verghese et al., 2014a; Verghese et al., 2014b). MCR has been associated with the occurrence of both Alzheimer Disease (AD) and Vascular Dementia (VD) (Verghese et al., 2012; Beauchet et al., 2016; Verghese et al., 2014a; Verghese et al., 2014b). However, the strength of the association of MCR with incident dementia depends on its type, with a greater hazard ratio being

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reported with VD compared to AD (Beauchet et al., 2016). Recently, it has been demonstrated in a meta-analysis that MCR was significantly associated with cardiovascular diseases and risk factors (CVDRF) (Beauchet et al., 2018). This meta-analysis underscored that few studies have examined the association between MCR and CVDRF, and most of them recruited older adults referred to memory or geriatric centres, with a lack of focus on the general population (Beauchet et al., 2018). It should be noted, that the Canadian population was not considered in any of those studies or the meta-analysis (Beauchet et al., 2018). This is concerning as CVDRF are highly prevalent in the Canadian population, as the second leading cause of death in Canada, with a trend for increased prevalence (Public Health Agency of Canada, 2017; Statistics Canada, n.d.a). Moreover, the fact that there are major differences in lifestyle (i.e. diet, physical activity, etc.) and genetics (i.e. ethnic backgrounds, geographical variation, etc.) between the populations included in the meta-analysis and the Canadian population emphasizes the need for targeting the Canadian population (Beauchet et al., 2018). Furthermore, it has been shown that cardiovascular risk factors (CVRF) in middle life are important risk factors for dementia, suggesting that the profile of association of CVRF and cardiovascular diseases (CVD) with a pre-dementia stage like MCR may change with group age (Kivipelto et al., 2006; Whitmer et al., 2005).

We have the opportunity with the Canadian Longitudinal Study on Aging (CLSA), which is a population-based prospective and observational study, to overcome the previously described limitations of our meta-analysis (Raina et al., 2009). Indeed, the CLSA has various strengths for examining the association of MCR with CVDRF, CVD and CVRF; such as a very large sample size (n = 51,352), recruitment of participants who are community dwellers in the general population and varying in age (45–85 years old) (Raina et al., 2009). Thus, the participants pool is not limited to the older population (Raina et al., 2009).

The aim of this study was to examine whether there is 1) an association between MCR and CVDRF in the Canadian population, and 2) a specific MCR-related CVDRF profile (CVD versus CVRF versus both) when comparing different age groups. We hypothesized that there was a positive association between MCR and CVDRF in the Canadian population and that this association may be influenced by age.

2. Methods

2.1. Population and study design

Participants selected in the present study are a Comprehensive Cohort of the CLSA baseline data. A total of 51,388 participants have been recruited in the CLSA. Among them, 21,241 completed a computer-assisted telephone interview (Tracking Cohort) and 30,097 completed both face-to-face, laptop computer-assisted in-home interviews and data collection site visits for additional computer-assisted interviews and clinical assessments (Comprehensive Cohort) (Raina et al., 2009). Thus, only participants in the Comprehensive Cohorts were potential participants for this study. The subset of CLSA participants, who had a baseline assessment including a physical examination with a completed 4-meter walking test and the absence of a dementia diagnosis were selected for this study (n = 29,569; 98.2%). Of participants not included in this study, 0.45% (n = 136) lacked walking speed, 1.25% (n = 375) had dementia or AD, and 0.06% (n = 17) did not meet either criteria.

2.2. Clinical assessment

The CLSA Comprehensive participants selected for this study had comprehensive, standardized physical examinations and questionnaire-based measures of demographics (e.g., age, sex), physiological, psychological, social functioning, lifestyle, behavior, and socio-demographic. Of these variables, only the following ones were recoded for this study: country of birth (Canada versus other); high education level (i.e., grade 9 or higher); total number of medications taken; independent place of living (i.e., not residing in an assisted living dwelling/institution); Indigenous identity (self-identifying as Aboriginal); living alone (i.e. single, separated, divorced or widowed); and low household income (i.e., CAD, < $50,000 annual). The variable country of birth was combined from various questions inquiring about the participants' country of birth (i.e. the US, Germany, India, etc.), it was categorized as those born in Canada versus any other country. The variable high education level was coded from the question “What is the highest grade of elementary or high school you have ever completed?”, where options were combined as lower than grade 9 or grade 9 and higher. The variable total number of medications taken was coded by considering all variables relating to the participant taking medications or undergoing other treatment, these were considered/tallied and included. The variable “Dwelling type” was recoded with “House (single detached, semi-detached, duplex or townhouse)”, “Apartment or condominium” and “Hotel, rooming or lodging house” being considered as not residing in an assisted living dwelling/institution. The variable “Aboriginal Identity” was included as is, with participants asked to self-identify as Indigenous. The variable “Marital/partner status” was recoded with “Single, never married or never lived with a partner”, “Widowed”, “Divorced” and “Separated” being merged into living alone. The variable “Total household income” was recoded with “Less than $20,000” and “$20,000 or more, but less than $50,000" tallied together after considering the Canadian household low-income cutoff for an average family of 4 (Statistics Canada, n.d.b).

2.3. Definition of motoric cognitive risk syndrome

Subjective cognitive complaint using the variable ‘trouble concentrating’ or the self-reported ‘memory problem’ variable combined with slow gait defines MCR. Participants who self-reported “sometimes”, “occasionally” or “always” for the variable “trouble concentrating” and/or “yes” for the variable “memory problem” were considered to have a subjective cognitive complaint. To determine the ‘trouble concentrating’ variable, participants were asked the following: “how often did you have trouble keeping your mind on what you were doing?”. Moreover, the variable ‘memory problem’ was determined by the question “has a doctor ever told you that you have a memory problem?”.

Mean walking speed was considered using the time taken to complete the 4 Meter Walking Test (seconds and milliseconds). The participants were instructed to stand behind the start line with their toes touching the start line, and to walk (once instructed) until past the finish line (Raina et al., 2009). The participants were also allowed to practice once (Raina et al., 2009). The stopwatch was started after the instructions were given and the research staff member said (Ready, Set) "Go" and the stopwatch was stopped once the participant had completely passed the finish line (Raina et al., 2009). Slow gait, was defined by walking speed one standard deviation (SD) below the average of the cohort for each individual sex and age group in accordance with the original criteria described by Verghese et al. (2012). The mean walking speed cut-offs for each sub-group were: 0.68 m/s (for 75+ males), 0.64 m/s (for 75+ females), 0.77 m/s (for 65–74-year-old males) 0.73 m/s (for 65–74-year-old females), 0.81 m/s (for 55–64-year-old males), 0.79 m/s (for 55–64-year-old females), 0.85 m/s (for 45–54-year-old males) and 0.84 m/s (for 45–54-year-old females).

2.4. Definition of cardiovascular diseases and risk factors

Overweight/obese, smoking, waist to hip circumference ratio (WHCR), systolic blood pressure, diastolic blood pressure, diabetes Type I and II, hypertension, heart disease and attack, peripheral vascular disease, angina, stroke and rhythmic disease were CVDRF measured in the CLSA. Overweight/obese was defined by body mass index (BMI) $\geq$ 25 kg/m^2. Smoking was measured as a current or former

smoker for the question “What is your smoking status?". When considering both systolic and diastolic blood pressure the average for all 6 readings was considered. Diabetes was defined by participants answering yes to the question, "Has a doctor ever told you that you have diabetes, borderline diabetes or that your blood sugar is high?”. Hypertension was defined by participants answering yes to the question, “Has a doctor ever told you that you have high blood pressure or hypertension?”. Heart disease and attacked was defined by participants answering yes to any of the following two questions: (A) “Has a doctor ever told you that you have heart disease (including congestive heart failure, or CHF)?” or (B) “Has a doctor ever told you that you have had a heart attack or myocardial infarction?”. Peripheral vascular disease was defined by participants answering yes to “Has a doctor ever told you that you have peripheral vascular disease or poor circulation in your limbs?”. Angina was defined by a yes to “Has a doctor ever told you that you have angina (or chest pain due to heart disease)?”. Stroke was defined by a yes to any of the following questions “Has a doctor ever told you that you have experienced a Stroke or CVA? (cerebrovascular accident)?” and/or “Has a doctor ever told you that you have experienced a ministroke or TIA (Transient Ischemic Attack)?” and/or “Has a doctor ever told you that you suffer from the effects of a stroke, CVA (cerebrovascular accident), mini-stroke or TIA (Transient Ischemic Attack)?”.

2.5. Ethics

The study was conducted in accordance with the ethical standards set forth in the Helsinki Declaration (1983). Participants in the CLSA provided written and informed consent for the CLSA. The Jewish General Hospital Ethics Committee (Montreal, Quebec, Canada) approved the study protocol. This research has been conducted using the CLSA Baseline Comprehensive dataset version 3.0 under Application Number 161002, and data access was approved by the CLSA Data and Sample Access Committee.

2.6. Statistics

Means and standard deviations (SD) or frequencies and percentages were used as appropriate to examine participants’ characteristics. Participants were separated by age groups (i.e., 45–54, 55–65, 65–74 and 75+) and MCR diagnosis (i.e., with versus without MCR). An unpaired *t*-test or Chi-square test were used as appropriate, for between-group comparisons. As numerous analyses were carried out, the P-values were calculated to be ≤ 0.0007 (number of comparison 76). Moreover, multiple logistic regressions were performed to examine the association of MCR (dependent variable) with CVDRF, CVD and CVRF (used as independent variables) in the entire population and the different age groups (i.e., 45–54; 55–64; 65–74; ≥ 75). The following clinical characteristics were adjusted by age (only in the total population category), sex, Indigenous identity, country of birth-Canada, independent place of living, living alone, low household income, high education level and the number of medications taken daily. P-values ≤ 0.05 were considered statistically significant for the multiple logistic regression. All statistics were performed using SPSS (version 23.0; SPSS, Inc., Chicago, IL).

3. Results

Table 1 provides a comparison of participants’ characteristics according to their age groups (i.e., 45–54, 55–64, 65–74, $\geq$ 75) and MCR diagnosis. Country of birth, Canada, was the only variable not significant in any age group. Participants with MCR were older than those without MCR within the age groups 65–74 and $\geq$ 75. A higher prevalence of females in participants with MCR compared to those without MCR in the age groups 45–54 and 65–74 were noted, whereas, opposite results were shown in the other age groups. Diabetes and peripheral vascular disease were more prevalent in participants with MCR compared to those without MCR. Participants with MCR had a significantly higher prevalence of CVRF and CVD compared to those without MCR: overweight/obese category (age group 45–54); smoking (age groups 45–54 and 55–64); systolic blood pressure (age group 55–64); diastolic blood pressure (age group 55–64); hypertension (age groups 45–54 and 55–64); heart disease or attack (age group 55–64); angina (age groups 45–54, 55–64 and 65–74) and stroke (age groups 55–64 and 65–74). Comparatively, a lower prevalence of participants with MCR compared to those without MCR for diastolic blood pressure in age group 65–74, for heart disease or attack and for stroke in the age group ≥ 75 was reported. For the other participants’ characteristics, significant differences were observed (please see Table 1).

Table 2 shows the results of logistic regressions exploring the association of MCR with CVDRF. The only negative association that was found was for diastolic blood pressure in age groups 65–74 and ≥ 75 (OR $\leq$ 0.99 with P $\leq$ 0.015). Diastolic blood pressure was positively associated with MCR in the age group 45–54 (OR = 1.01 with P = 0.019). The overweight/obese category was positively associated with MCR in age groups 45–54, 55–64, 65–74 (OR $\geq$ 1.30 with P $\leq$ 0.034). Smoking was positively associated with MCR in the total population and in age groups 45–54 and 55–64 (OR $\geq$ 1.44 with P $\leq$ 0.001). WHCR was positively associated with MCR in the total population and in age groups 45–54, 55–64 and 65–74 (OR $\geq$ 14.45 with P $\leq$ 0.001). Systolic blood pressure was positively associated with MCR in the age group 45–54 (OR = 1.01 with P = 0.002). Diabetes was positively associated with MCR in the total population and in age groups 45–54, 55–64 and 65–74 (OR $\geq$ 1.46 with P $\leq$ 0.001). Hypertension was positively associated with MCR in the total population and in age groups 45–54 (OR $\geq$ 1.11 with P $\leq$ 0.038). Heart disease or attack was positively associated with MCR in the total population and in age groups 55–64, 65–74 and ≥ 75 (OR $\geq$ 1.29 with P $\leq$ 0.029). Peripheral vascular disease was positively associated with MCR in the total population as well as age groups 45–54, 55–64, 65–74 and ≥ 75 (OR $\geq$ 1.77 with P $\leq$ 0.003). Angina was positively associated with MCR in the total population and in age groups 45–54, 55–64, 65–74 and ≥ 75 (OR $\geq$ 1.38 with P $\leq$ 0.041). Stroke was positively associated with MCR in the total population and in age groups 55–64, 65–74 and ≥ 75 (OR $\geq$ 1.50 with P $\leq$ 0.045).

4. Discussion

Our study found a higher prevalence of CVD in individuals with MCR as compared to those without MCR for all age groups, whereas, the higher prevalence of CVRF in MCR was shown in the youngest age groups (i.e., 45–54 and 55–64). In addition, MCR was positively associated with CVDRF, except in the oldest age group (i.e., ≥ 75). In this group, the only significant association was with diastolic blood pressure, which was negatively associated with MCR. Diabetes and hypertension were not associated with MCR.

The first main finding of this study was an overall higher prevalence of CVD in individuals with MCR compared to individuals without MCR. This result is consistent with our recent meta-analysis (Beauchet et al., 2018). The novelty of this last study is that younger (i.e., age group 45–54 and 55–64) adults are included as compared to previous literature, which only focused on individuals ≥ 60. Our findings also showed that this higher prevalence was shown for CVRF but only in the youngest age groups (i.e., 45–54 and 55–65) and not in the oldest age groups (i.e., 65–74 and ≥ 75). This result may be explained by the rate of death of patients with CVD, which increases with age. Thus, the probability to die because of CVD before 75 is high. The absence of higher prevalence of high blood pressure in the oldest age group may be related to the use of anti-hypertensive drugs, whereas, in the youngest group this disease could be ignored because it is more frequent and controlled with age. These results are consistent with the fact that we demonstrated a positive association of MCR with CVDRF, except for

Table 1
Comparisons of participants' characteristics according to age groups (i.e., 45–64, 55–64, 65–74, ≥ 75) and Motoric Cognitive Risk syndrome in participants of the Canadian longitudinal study on aging (n = 29,569).

	Age 45–54		P-value*	Age 55–64		P-value*	Age 65–74		P-value*	Age ≥ 75		P-value*
	No-MCR (n = 6863)	MCR (n = 666)		No-MCR (n = 9036)	MCR (n = 663)		No-MCR (n = 6850)	MCR (n = 359)		No-MCR (n = 4752)	MCR (n = 380)	
Age, mean value ± SD	50.3 ± 2.7	50.4 ± 2.6	0.721	59.7 ± 2.8	59.9 ± 2.8	0.118	68.9 ± 2.8	69.5 ± 2.9	≤**0.001**	78.8 ± 2.9	79.8 ± 3.1	≤**0.001**
Female, n (%)	3492 (50.9)	403 (60.5)	≤**0.001**	4818 (53.3)	190 (28.7)	≤**0.001**	3368 (49.2)	252 (70.2)	≤**0.001**	2389 (50.3)	149 (39.2)	≤**0.001**
Indigenous, n (%)	371 (5.4)	58 (8.7)	≤**0.001**	334 (3.7)	32 (4.8)	0.028	195 (2.8)	16 (4.5)	0.182	84 (1.8)	6 (1.6)	0.001
Country of Birth Canada, n (%)	5802 (84.5)	545 (81.8)	0.064	7739 (85.6)	556 (83.9)	0.207	5339 (77.9)	287 (79.9)	0.377	3650 (76.8)	303 (79.7)	0.194
Independent place of living†, n (%)	6859 (99.9)	666 (100)	0.824	9018 (99.8)	660 (99.5)	0.176	6822 (99.6)	348 (96.9)	≤**0.001**	4663 (98.1)	362 (95.3)	0.001
Living alone‡, n (%)	1614 (23.5)	203 (30.5)	≤**0.001**	2520 (27.9)	234 (35.3)	≤**0.001**	2172 (31.7)	163 (45.4)	≤**0.001**	2094 (44.1)	182 (47.9)	0.340
Low household income‖	832 (12.1)	171 (25.7)	≤**0.001**	1890 (20.9)	225 (33.9)	≤**0.001**	2264 (33.1)	202 (56.3)	≤**0.001**	1914 (40.3)	190 (50.0)	0.002
High education level¶, n (%)	6840 (99.7)	661 (99.2)	0.147	8984 (99.4)	654 (98.6)	0.023	6701 (97.8)	340 (94.7)	≤**0.001**	4546 (95.7)	356 (93.7)	0.197
Number of medications daily taken	2.1 ± 1.8	2.8 ± 2.2	≤**0.001**	2.5 ± 2.0	3.3 ± 2.3	≤**0.001**	2.7 ± 2.0	3.7 ± 2.3	≤**0.001**	3.05 ± 2.0	3.6 ± 2.4	≤**0.001**
Cardiovascular risk factors												
Overweight/Obese§, n (%)	4453 (64.9)	490 (73.6)	≤**0.001**	6341 (70.2)	535 (80.7)	0.001	4993 (72.9)	281 (78.3)	0.021	3216 (67.7)	264 (69.5)	0.408
Smoking	782 (11.4)	129 (19.4)	≤**0.001**	929 (10.3)	112 (16.9)	≤**0.001**	459 (6.7)	34 (9.5)	0.043	169 (3.6)	20 (5.3)	0.089
Systolic Blood Pressure	116.0 ± 14.5	118.1 ± 15.4	0.001	120.8 ± 16.0	123.3 ± 17.2	≤**0.001**	125.7 ± 16.9	126.2 ± 17.8	0.575	128.5 ± 18.0	128.2 ± 18.9	0.717
Diastolic Blood Pressure	75.7 ± 9.9	76.5 ± 10.3	0.055	75.6 ± 9.7	77.5 ± 10.8	≤**0.001**	73.8 ± 9.5	71.2 ± 9.9	≤**0.001**	70.6 ± 9.8	69.3 ± 9.7	0.017
Cardiovascular Diseases												
Diabetes	682 (9.9)	126 (18.9)	≤**0.001**	1507 (16.7)	203 (30.6)	≤**0.001**	1434 (20.9)	122 (34.0)	≤**0.001**	1002 (21.1)	117 (30.8)	≤**0.001**
Hypertension	1299 (18.9)	181 (27.2)	≤**0.001**	3000 (33.2)	303 (45.7)	≤**0.001**	3105 (45.3)	190 (52.9)	0.005	2576 (54.2)	228 (60.0)	0.029
Heart Disease or Attack	244 (3.6)	26 (3.9)	0.644	771 (8.5)	113 (17.0)	≤**0.001**	1131 (16.5)	82 (22.8)	0.002	1209 (25.4)	129 (33.9)	≤**0.001**
Peripheral Vascular Disease	179 (2.6)	35 (5.3)	≤**0.001**	345 (3.8)	56 (8.4)	≤**0.001**	396 (5.8)	66 (18.4)	≤**0.001**	422 (8.9)	72 (18.9)	≤**0.001**
Angina	58 (0.8)	17 (2.6)	≤**0.001**	236 (2.6)	47 (7.1)	≤**0.001**	402 (5.9)	41 (11.4)	≤**0.001**	440 (9.3)	55 (14.5)	0.001
Stroke	81 (1.2)	17 (2.6)	0.003	225 (2.5)	43 (6.5)	≤**0.001**	337 (4.9)	34 (9.5)	≤**0.001**	481 (10.1)	68 (17.9)	≤**0.001**

MCR: Motoric Cognitive Risk. Comparison based on unpaired *t*-test or Chi-square test, as appropriate; †: Defined as not residing in an assisted living dwelling/institution; ‡: Defined as single, separated, divorced or widowed; ‖: Defined as CAD $ < 50,000; ¶: High education level- is defined as grade 9 or higher; §: Overweight defined as body mass index ≥ 25;P-value significant ≤ 0.0007 because of multiple comparisons (n = 76) indicated in bold.

Table 2
Multiple logistic regressions presenting the association of Motoric Cognitive Risk syndrome (dependent variable) with Cardiovascular Diseases and Risk Factors in all population and the different age groups (i.e., 45–54; 55–64; 65–74; ≥75) in different models (n = 29,569).

	OR [95%CI] P-Value				
	Total Population[2]	Age-groups			
	(n = 29,569)	45–54 (n = 7529)	55–64 (n = 9699)	65–74 (n = 7209)	≥75 (n = 5132)
Cardiovascular risk factors					
Overweight/Obese*	1.30	1.54	1.46	1.33	1.00
	[1.17;1.45]	[1.28;1.85]	[1.19;1.79]	[1.02;1.73]	[0.79;1.26]
	≤0.001	**≤0.001**	**≤0.001**	**0.034**	0.998
Smoking	1.55	1.75	1.44	1.31	1.42
	[1.36;1.78]	[1.42;2.17]	[1.16;1.80]	[0.90;1.92]	[0.88;2.30]
	≤0.001	**≤0.001**	**0.001**	0.158	0.155
Waist to Hip Circumference Ratio	14.45	12.58	47.74	59.70	2.39
	[7.42;28.14]	[3.69;42.88]	[14.76;154.47]	[11.77;302.78]	[0.48;11.81]
	≤0.001	**≤0.001**	**≤0.001**	**≤0.001**	0.286
Systolic Blood Pressure	1.00	1.01	1.00	1.00	1.00
	[1.00;1.01]	[1.00;1.01]	[1.00;1.01]	[0.99;1.01]	[0.99;1.01]
	0.185	**0.002**	0.271	0.965	0.899
Diastolic Blood Pressure	1.00	1.01	1.00	0.98	0.99
	[0.99;1.00]	[1.00;1.02]	[1.00;1.01]	[0.97;0.99]	[0.98;1.00]
	0.213	**0.019**	0.476	**≤0.001**	**0.015**
Cardiovascular Diseases					
Diabetes	1.46	1.53	1.53	1.63	1.26
	[1.30;1.63]	[1.21;1.93]	[1.25;1.87]	[1.27;2.10]	[0.99;1.62]
	≤0.001	**≤0.001**	**≤0.001**	**≤0.001**	0.064
Hypertension	1.11	1.24	1.19	1.04	1.05
	[1.01;1.23]	[1.02;1.51]	[0.99;1.42]	[0.82;1.30]	[0.83;1.32]
	0.038	**0.035**	0.060	0.765	0.695
Heart Disease or Attack	1.38	0.99	1.58	1.52	1.29
	[1.22;1.57]	[0.65;1.51]	[1.26;1.98]	[1.16;1.99]	[1.03;1.62]
	≤0.001	0.949	**≤0.001**	**0.002**	**0.029**
Peripheral Vascular Disease	2.23	1.77	1.89	3.00	2.18
	[1.91;2.59]	[1.21;2.59]	[1.39;2.57]	[2.23;4.04]	[1.65;2.89]
	≤0.001	**0.003**	**≤0.001**	**≤0.001**	**≤0.001**
Angina	1.70	2.31	1.87	1.97	1.38
	[1.42;2.04]	[1.31;4.08]	[1.33;2.63]	[1.38;2.82]	[1.01;1.88]
	≤0.001	**0.004**	**≤0.001**	**≤0.001**	**0.041**
Stroke	1.52	1.25	1.65	1.50	1.50
	[1.27;1.83]	[0.72;2.19]	[1.15;2.37]	[1.01;2.22]	[1.11;2.02]
	≤0.001	0.429	**0.007**	**0.045**	**0.009**

OR: Odd Ratio; CI: Confidence Interval; All models are adjusted on participant's clinical characteristics; *: Overweight defined as body mass index ≥ 25; P-value significant (i.e., ≤0.05) in bold.

CVRF in the oldest age group and for diastolic pressure.

The lack of association between MCR and CVRF in ≥75 age group is opposite to the findings in the last meta-analysis (Beauchet et al., 2018). This contradictory finding may be due to some specific characteristics of the Canadian population, such as ethnicity, lifestyle and environment. In addition, the absence of significant association with diabetes and hypertension may be due to the fact that these two CVDs do not assess the consequences of CVDRF on a specific organ, as compared to the other CVDs used in our study.

The findings of our study revealed a negative association of MCR with high diastolic pressure in the older age group (i.e., 64–74 and ≥75). This association with diastolic blood pressure may be explained by the fact that it has been especially related to the occurrence of brain vascular diseases (Public Health Agency of Canada, 2009; Arvanitakis et al., 2018). However, the negative association with MCR is difficult to understand because in the majority of cases a high diastolic blood pressure has been related to adverse effects (Arvanitakis et al., 2018). It should be noted that lower blood pressure levels in the older population may be paradoxically associated with adverse effects like increased rate of death (Chobanian et al., 2003). In addition, some studies conducted in older adults (i.e., ≥75) demonstrated that low systolic and diastolic blood pressure have been associated with incident dementia (Chobanian et al., 2003; van Hateren et al., 2010).

This study has various strengths. First, there is a large number of community-dwelling population-based participants in Canada. Second, the participants are aged from 45 to 85 at the time of recruitment and not limited to older adults. Third, as the participants were not recruited from memory clinics, they were older population-based community-dwelling adults. However, some limitations need to be considered. This study is a secondary analysis of the existing study, whose study and data collection protocol were not created with the specific research questions of this study. Thus, the characterization of the outcomes may be non-optimal, as was explained above, because various variables from the CLSA were recoded and combined for this study. Moreover, it must be considered that one of the variables used to identify participants with subjective cognitive impairment was from the CESD-10 depression scale. Thus, depression or depressive symptomatology may be a confounder in our study. Slow gait speed and cognitive complaint are unspecific symptoms that can be found in individuals with depression or depressive symptomatology. That may cause overlap with MCR and thus influence the value of MCR risk for neurocognitive disorders. Furthermore, this study was a cross-sectional study and no causal inferences can be made. Lastly, the authors tried to be exhaustive in the CVDRF variable considered, but other potential confounders may have been missed.

5. Conclusion

MCR is associated with CVDRF in the Canadian population. Specifically, a stronger association was reported for CVRF factors in younger adults and CVD in older adults. These results suggest that CVDRF are involves in the physiopathology of MCR and emphasizes its complexity, which required more research.

Author's contribution

Study design HS and OB. Study conduct: HS and OB. Data collection: CLSA team. Data interpretation: HS and OB. Drafting manuscript: HS and OB. Revising manuscript content: GA. Approving final version of manuscript HS, OB and GA. HS takes responsibility for the integrity of the data analysis.

Declaration of Competing Interest

The authors declare no conflict of interest. The opinions expressed in this manuscript are the authors' own and do not reflect the views of the Canadian Longitudinal Study on Aging.

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