



CJC Open 2 (2020) 265-272

Original Article

COVID-19 Pandemic: Global Impact and Potential Implications for Cardiovascular Disease in Canada

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ABSTRACT

Background: The literature indicates that cardiovascular disease (CVD; including stroke), older age, and availability of health care resources affect COVID-19 case fatality rates (CFRs). The cumulative effect of COVID-19 CFRs in global CVD populations and the extrapolated effect on access to health care services in the CVD population in Canada are not fully known. In this study we explored the relationships of factors that might affect COVID-19 CFRs and

A growing number of publications indicate that underlying cardiovascular disease (CVD; including stroke), older age (65 years or older), and availability of health care resources can affect the risk of fatality from COVID-19.¹⁻⁷ Underlying CVD confers up to a 4 times greater COVID-19 mortality risk relative to those without CVD.^{4,8} Moreover, upwards of 20% of hospitalized COVID-19 patients develop cardiac injury with a mortality rate as high as 51%.^{4,9} Variation in health care resource availability and accessibility was linked to

Received for publication May 21, 2020. Accepted June 3, 2020.

Ethics Statement: The present article adheres to ethical guidelines.

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RÉSUMÉ

Contexte : La littérature indique que les maladies cardiovasculaires (MCV, incluant les accidents vasculaires cérébraux), l'âge avancé et la facilité d'accès aux ressources de soins de santé ont une incidence sur les taux de létalité (TL) des cas de COVID-19. L'effet cumulatif du TL de la COVID-19 dans l'ensemble de la population atteinte de MCV et l'impact anticipé sur l'accès aux services de santé dans la population atteinte de MCV au Canada ne sont pas entièrement connus. Cette

regional disparities in COVID-19 mortality rates⁷ and differences in the reporting of COVID-19 test rates might influence the interpretation of case fatality rates (CFRs).¹⁰ The cumulative effect of the proportion of the population with CVD, proportion of the population 65 years of age or older, and availability of essential health services on COVID-19 CFRs in global CVD populations is not known.

Further to the immediate effect that an increased risk of COVID-19 mortality will have on individuals with CVD, this

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https://doi.org/10.1016/j.cjco.2020.06.003

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estimated the potential indirect effects of COVID-19 on Canadian health care resources.

Methods: Country-level epidemiological data were analyzed to study the correlation, main effect, and interaction between COVID-19 CFRs and: (1) the proportion of the population with CVD; (2) the proportion of the population 65 years of age or older; and (3) the availability of essential health services as defined by the World Health Organization Universal Health Coverage index. For indirect implications on health care resources, estimates of the volume of postponed coronary artery bypass grafting, percutaneous coronary intervention, and valve surgeries in Ontario were calculated.

Results: Positive correlations were found between COVID-19 CFRs and: (1) the proportion of the population with CVD ($\rho = 0.40$; P = 0.001); (2) the proportion of the population 65 years of age or older ($\rho = 0.43$; P = 0.0005); and (3) Universal Health Coverage index ($\rho = 0.27$; P = 0.03). For every 1% increase in the proportion of the population 65 years of age or older or proportion of the population with CVD, the COVID-19 CFR was 9% and 19% higher, respectively. Approximately 1252 procedures would be postponed monthly in Ontario because of current public health measures.

Conclusions: Countries with more prevalent CVD reported higher COVID-19 CFRs. Strain on health care resources is likely in Canada.

pandemic might have long-lasting implications for health care resources supporting CVD populations. Additional strain on the health of CVD populations and health care resources is implicit, because of a combination of factors including postponement of nonurgent CVD medical appointments and procedures to create capacity for COVID-19 patients, adherence to appropriate public health measures, and rationing of personal protective equipment.^{11,12} The extrapolated effect on access to health care services in the CVD population in Canada has not been reported. This information may inform health care demand caused by disruption to the continuity of CVD care.

The goal of the Heart and Stroke Foundation of Canada (HSFC) is to work with its partners to expedite knowledge translation and facilitate changes to clinical practice with the aim of improving outcomes for people with CVD. In this study, an analysis of country-level epidemiological data was conducted to explore how the factors of the proportion of the population with CVD, the proportion of the population 65 years of age or older, availability of essential health services as defined by the World Health Organization (WHO) Universal Health Coverage (UHC) index, and COVID-19 test rate interact to affect COVID-19 CFR. Countries with higher proportions of the population with CVD and higher proportions of the population 65 years of age or older may have higher COVID-19 CFRs, and this effect might be modulated by the availability of health care services and test rates. The potential indirect effects of the pandemic on the provision of CVD health care services was determined by estimating the volume of postponed coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), and valve surgeries in Canada's most populous province. Last, qualitative

étude a exploré les liens entre les facteurs pouvant influencer le TL des cas de COVID-19 et a estimé le potentiel impact indirect de la COVID-19 sur les ressources de soins de santé au Canada.

Méthodes : Les données épidémiologiques à l'échelle du pays ont été analysées pour étudier la corrélation, l'effet principal et l'interaction entre le TL de laCOVID-19 et : 1) la proportion de la population souffrant de MCV, 2) la proportion de la population \geq 65 ans, et 3) l'accessibilité des services de santé essentiels tels que définis par l'indice de couverture sanitaire universelle (CSU) de l'Organisation Mondiale de la Santé. Pour les implications indirectes concernant les ressources de santé, des estimations du volume d'opération de pontages coronariens, d'interventions coronariennes percutanées et de chirurgies valvulaires reportées en Ontario ont été calculées.

Résultats : Des corrélations positives ont été trouvées entre le TL de la COVID-19 et 1) la proportion de la population souffrant de MCV (ρ = 0,40, P = 0,001), 2) la proportion de la population \geq 65 ans (ρ = 0,43, P = 0,0005), et 3) l'indice CSU (ρ = 0,27, P = 0,03). Pour chaque augmentation de 1 % de la proportion de la population \geq 65 ans ou de la proportion de la population souffrant de MCV, le TL de la COVID-19 était respectivement supérieur de 9 % et 19 %. Environ 1 252 interventions seraient reportées chaque mois en Ontario en raison des mesures de santé publique actuelles.

Conclusions : Les pays où les MCV sont plus répandues ont signalé un TL de la COVID-19 plus élevé. Il est probable que les ressources de soins de santé soient soumises à de fortes contraintes au Canada.

observations of indirect effects of COVID-19 on CVD populations are briefly discussed.

Methods

Data sources for analysis

COVID-19 CFR. Data on COVID-19 CFR according to country were obtained from global epidemiological data from January 21 to April 30, 2020 extracted from WHO Situation Reports¹³ and from the Johns Hopkins University Center for Systems Science and Engineering.¹⁴ Only countries with at least 60 days since first confirmed cases of COVID-19 were included in this study. The CFR as defined by the WHO is the proportion of reported cases of a specific disease or condition that are fatal within a specified time.

COVID-19 test rate. Data on COVID-19 test rate were obtained for 46 countries from the Our World in Data COVID-19 testing data set.¹⁵ Test rates were categorized into 1 of 3 reporting definitions: individuals tested, tests performed, or unclear/unknown. For countries that provided test numbers for individuals tested and tests performed per 100,000, values from the number of individuals tested per 100,000 were used. Test rates for the remaining 15 countries were obtained from Worldometers.info,¹⁶ and were classified as unclear/unknown because of the lack of reporting definition.

Proportion of the population with CVD. Data on CVD cases in 2017 according to country were obtained from the Institute for Health Metrics and Evaluation Global Burden of

Disease (GBD) Study 2017.¹⁷ Data on country-specific population size were obtained from the World Bank¹⁸ and United Nations¹⁹ for the year 2017 to ensure time period consistency with the GBD CVD data.

Proportion of the population 65 years old or older. Data on country-specific population age distribution were obtained from the World Bank¹⁸ and United Nations¹⁹ for the year 2017 to ensure time period consistency with the global CVD and health services data.

Affordability and access to health services. The WHO UHC service coverage index²⁰ was used as a measure of availability of essential health services in each country.²¹ The UHC service coverage index is comprised of 16 tracer indicators, which cover 4 essential health services categories of reproductive, maternal, newborn, and child health; infectious diseases; noncommunicable diseases; and services capacity and access. Across countries, the median value associated with this index was 65 of 100, with a range of 22-86. The UHC index was evaluated as a continuous variable in this study.

Volume of selected CVD surgeries and procedures in Ontario. Canadian Classification of Health Intervention codes were used to capture the volume of selected CVD surgeries and procedures (CABG, PCI, and valve surgery) that occurred between April 1, 2018 to March 31, 2019 from the Canadian Institute for Health Information (CIHI) Discharge Abstract Database (Supplemental Tables S1 and S2). Valve surgery included excision or repair of the tricuspid, mitral, pulmonary, or aortic valves. Parts of this material are on the basis of data and information provided by CIHI. However, the analyses, conclusions, opinions, and statements expressed herein are those of the authors and not those of CIHI.

Statistical analyses

The relationships among key variables were assessed using Spearman rank correlations. These were calculated between COVID-19 CFR and: (1) proportion of the population with CVD; (2) proportion of the population 65 years of age or older; (3) UHC index; and (4) COVID-19 test rate. The Spearman rank correlation was chosen because it is nonparametric.

To further explore possible collinearity, a linear regression model was fitted with COVID-19 CFR as the outcome variable, and proportion of the population with CVD, proportion of the population 65 years of age or older, and UHC index as independent variables. All 3 independent variables were continuous.

Separate negative binomial regression models were used to explore the relationship between COVID-19 CFR and the following variables: (1) proportion of the population with CVD; (2) proportion of the population 65 years of age or older; and (3) UHC index. The interactions, including Proportion of the population with CVD \times UHC index and Proportion of the population 65 years or older \times UHC index were examined in each model, respectively. A Poisson regression model was considered first but because of overdispersion, this approach was not pursued.

Because COVID-19 testing practices influence the interpretation of CFR by varying the denominator of proven cases,

 Table 1. UHC indices of countries reporting COVID-19 test rate as the number of individuals tested per 100,000

Country	UHC index
Canada	89
Denmark	81
India	55
Italy	82
Japan	83
Luxembourg	83
Malaysia	73
Mexico	76
Nepal	48
Netherlands	86
Pakistan	45
Philippines	61
Qatar	68
Russia	75
Singapore	86
South Korea	86
Thailand	80
United Kingdom	87

Refer to Supplemental Table S3 for UHC index of all of the countries included in this study.

UHC, universal health coverage.

a second multiple regression model was applied to a subset of countries (18 of 65) for which COVID-19 test reporting practices were the same as Canada, namely test rate reported by the number of individuals tested per 100,000 as opposed to the number of tests performed per 100,000. As with the previous model, because of collinearity between proportion of the population with CVD and proportion of the population 65 years or older, 2 separate models were tested using negative binomial regression in this subcohort with COVID-19 CFR as the outcome variable: (1) COVID-19 test rate and proportion of the population with CVD; and (2) COVID-19 test rate and proportion of the population 65 years of age or older. All 3 independent variables were continuous. A stepwise selection method was used to determine best fit. UHC index was not included as an independent variable in these 2 models because the UHC index for 15 of the 18 countries was skewed to the upper range (ie, UHC index \geq 70; Table 1).

At the time of this study, the expected duration of imposed public health measures was unknown. Data on percentage decrease in CVD procedures were available from the CorHealth Cardiac Registry of Ontario on the volumes of: CABG, PCI, and valve surgery (CorHealth Ontario, unpublished data, 2020). The percentage decrease in activity was calculated by comparing the weeks of March 16 through May 3 in 2019 and 2020, and then applied to historical data from CIHI (fiscal year 2018-2019) to generate an estimate of monthly backlog specific to Ontario. Volumes of procedures reported in fiscal year 2018-2019 were similar to those reported in fiscal year 2017-2018, and thus the former and more recent fiscal year was used as the historical benchmark to estimate the backlog of procedures.

Results

On April 30, 2020, 63 of 176 countries from the Johns Hopkins University data repository had confirmed cases of COVID-19 for at least 60 days (Supplemental Table S3). Spearman correlation analyses generated significant positive correlations of low/moderate magnitude between COVID-19

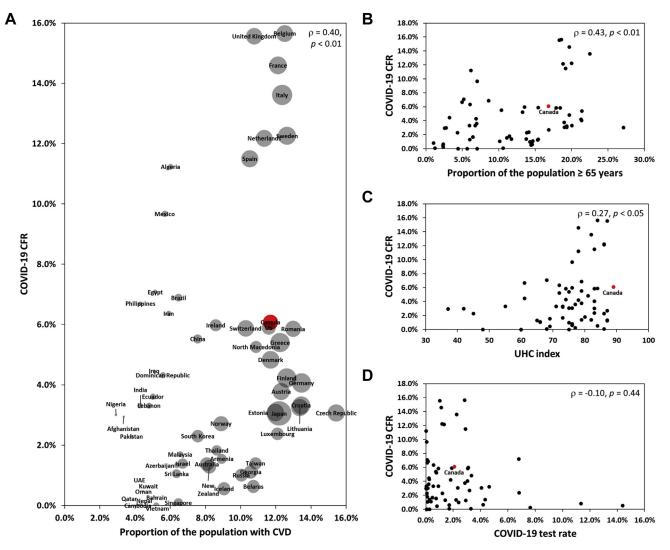


Figure 1. COVID-19 CFR, proportion of the population with CVD, 65 years of age or older, UHC index, and COVID-19 test rate. Scatter plots of (**A**) proportion of the population with CVD, including stroke and COVID-19 CFR, (**B**) proportion of the population 65 years old or older and COVID-19 CFR, (**C**) UHC service coverage index and COVID-19 CFR, and (**D**) COVID-19 test rate and COVID-19 CFR. In (**A**) the size of the bubbles corresponds to the proportion of the population 65 years of age or older. Data points representing Canada are highlighted in **red**. Spearman correlation coefficients are reported as ρ . Sample size of 63. CFR, case fatality rate; CVD, cardiovascular disease; UHC, universal health coverage; US, United States.

CFR and proportion of the population with CVD ($\rho = 0.40$; P = 0.001) and COVID-19 CFR and proportion of the population 65 years of age or older ($\rho = 0.43$; P = 0.0005). A significant positive correlation of low magnitude was found between COVID-19 CFR and UHC index ($\rho = 0.27$; P = 0.03; Fig. 1 and Table 2). Of note, the proportion of the population with CVD and the proportion of the population 65 years of age or older were highly correlated ($\rho = 0.93$; P = 0.0001).

The linear regression revealed a variance inflation factor of 7.5 and 7.9 for the variables proportion of the population with CVD and proportion of the population 65 years of age or older, respectively (Supplemental Table S4). This indicated high collinearity between these variables and identified the need to separate out these predictors to determine their unique relationships to COVID-19 CFR.

A total of 4 negative binomial regression models (1a, 1b, 2a, and 2b) were performed. Model 1a and 1b were used to examine

the effect of proportion of the population with CVD and UHC index on COVID-19 CFR (model 1a), as well as proportion of the population 65 years of age or older and UHC index on COVID-19 CFR (model 1b). The contributions of each predictor and their interactions in each model were assessed. In model 1a, neither proportion of the population with CVD nor UHC index emerged as significant predictors of COVID-19 CFR independently (Table 3). The interaction between UHC index and proportion of the population with CVD was marginally significant (interaction $\beta = 0.80$ [95% confidence interval (CI), 0.01 to 1.59]; P = 0.05; Table 3). In model 1b, the interaction between proportion of the population 65 years of age or older and UHC index on COVID-19 CFR was not significant (interaction $\beta = 0.32$ [95% CI, -0.11 to 0.76]; P = 0.15; Table 3).

In model 2 test rate was added as an independent variable and included only countries that reported the number of

Variable	1. COVID-19 CFR	2. COVID-19 test rate	3. UHC index	4. Proportion of the population 65 years old or older	5. Proportion of the population with CVD
1. COVID-19 CFR	-				
2. COVID-19 test rate	$-0.10 \ (P = 0.44)$	_			
3. UHC index	$0.27 \ (P = 0.03)$	$0.53 \ (P < 0.0001)$	-		
4. Proportion of the pop 65 years old or older	$0.43 \ (P = 0.0005)$	$0.37 \ (P = 0.003)$	0.58 (<i>P</i> < 0.0001)	-	
5. Proportion of the pop with CVD	$0.40 \ (P = 0.001)$	$0.43 \ (P = 0.0005)$	$0.52 \ (P < 0.0001)$	$0.93 \ (P < 0.0001)$	-

Coefficients are reported as ρ. UHC service coverage index for Taiwan was unavailable so the UHC service coverage index for China was used. Sample size of 63. CFR, case fatality rate; CVD, cardiovascular disease including stroke; pop, population; UHC, universal health coverage.

individuals tested per 100,000. There were 18 countries included in this analysis. Two separate models (models 2a and 2b) were used to explore the effect of proportion of the population with CVD and test rate (model 2a), and proportion of the population 65 years of age or older and test rate (model 2b) on COVID-19 CFR. In model 2a, test rate ($\beta = -0.39$ [95% CI, -0.70 to -0.08]; P = 0.01; Table 3) and proportion of the population with CVD ($\beta = 17.77$ [95% CI, 5.29 to 30.26]; P = 0.005; Table 3) were significant contributors to COVID-19 CFR. In model 2b, test rate ($\beta = -0.36$ [95% CI, -0.66 to -0.06]; P = 0.02; Table 3) and the proportion of the population 65 years of age or older ($\beta = 8.8$ [95% CI, 2.55 to 15.12]; P = 0.006; Table 3) were significant contributors to COVID-19 CFR.

The potential effect on health care resources in Ontario was estimated. In fiscal year 2018-2019, of more than 100,000 hospitalizations for CVD, 8485 CABG procedures, 20,077 PCI procedures, and 7212 valve surgeries were completed on patients with CVD in the province of Ontario. The percentage decrease in CABG, PCI, and valve surgery at cardiac centres in Ontario, calculated by comparing the weeks of March 16 through May 3 in 2019 and 2020, was 42% for CABG, 37% for PCI, and 45% for valve surgery. By applying the percentage decrease to historical CIHI data from fiscal year 2018-2019, approximately 297 CABG, 703 PCI, and 252 valve surgeries, for a total of 1252 procedures, would be postponed per month because of current COVID-19 public health measures (Table 4).

Discussion

To date, most publications on COVID-19 have been limited to cohorts from China, Italy, and the United States. Incorporating data from 63 countries, the findings from this study suggest that the cumulative effect and interaction of the proportion of the population with CVD, the proportion of the population 65 years of age or older, and availability of health care services on COVID-19 CFR is complex. Regression modelling showed a nuanced pattern of relationships between these variables. Surprisingly, the proportion of the population with CVD was only related to higher COVID-19 CFR in countries with a higher UHC index, such as Canada. Although further studies are necessary to fully understand this unexpected finding, one possible explanation is that more available essential health care services in these countries might lead to more individuals surviving and living with CVD relative to countries with less health care availability. Indeed, three-quarters of global CVD deaths take place in low- and middle-income countries,²² but CVD accounts for a higher

	Table 3.	Negative binomial	regression models	with outcome	variable COVID-19 CFR
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	β coefficient	SE	95% CIs	χ^2	Р
Model 1a: $log(COVID-19 \text{ deaths}) = offset + p$	roportion of the populatio	n with CVD and U	HC Index		
UHC index	-0.03	0.03	-0.08 to 0.02	1.67	0.20
Proportion of the population with CVD	-54.35	31.30	-115.7 to 6.7	3.02	0.08
UHC index* (proportion of the	0.80	0.40	0.01 to 1.59	3.98	0.05
population with CVD)					
Model 1b: $log(COVID-19 \text{ deaths}) = offset + p$	roportion of the populatio	on 65 years old or ol	der + UHC index		
UHC Index	-0.01	0.02	-0.05 to 0.02	0.51	0.48
Proportion of the population 65 years	-20.90	17.70	-55.58 to 13.79	1.39	0.24
old or older					
UHC Index* (Proportion of the	0.32	0.22	-0.01 to 0.76	2.13	0.15
population 65 years old or older)					
Model 2a: $log(COVID-19 \text{ deaths}) = offset + tetters = offset + tet$	est rate + proportion of th	e population with C	CVD		
COVID-19 test rate	-0.39	0.16	-0.69 to -0.08	6.15	0.01
Proportion of the population with CVD	17.8	6.4	5.29 to 30.26	7.79	0.005
Model 2b: $\log(COVID-19 \text{ deaths}) = \text{offset} + te$	est rate + proportion of th	ne population 65 yea	ars old or older		
COVID-19 test rate	-0.36	0.15	-0.66 to -0.06	5.57	0.02
Proportion of the population 65 years	8.8	3.2	2.55 to 15.12	7.60	0.006
old or older					

Parameter estimates are reported as β coefficients; offset = log(COVID-19 cases). Sample size is 63 for model 1a and 1b; sample size is 18 for model 2a and 2b. CFR, case fatality rate; CI, confidence interval; CVD, cardiovascular disease including stroke; SE, standard error; UHC, universal health coverage. * UHC service coverage index for Taiwan was unavailable so the UHC service coverage index for China was used.

Procedure	2018-2019 volume	Number of procedures per month	Estimated reduction between the weeks of March 16 and May 3, 2020	Forecasted backlog of procedures per month
CABG	8485	707	42%	297
PCI	20,077	1673	37%	703
Valve surgery	7212	601	45%	252

Table 4. 2018-2019 Volumes of CABG, PCI, and valve surgery and expected reductions in activity in Ontario

Valve surgery includes repair or excision of tricuspid, pulmonary, mitral, and aortic valves, and does not include transcatheter aortic valve implantation. CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.

percent of disability-adjusted life-years in high-income than in low-income countries.²³ This in turn may lead to more individuals living with complex CVD characterized by multimorbidity and greater risk of poorer outcomes from COVID-19. Overall, these results suggest that public health measures and COVID-19 management specific to CVD populations in Canada are likely necessary because of the relatively high proportion of the population with CVD.

When evaluating the relationship for countries such as Canada that report COVID-19 test rate as the number of people tested per 100,000, COVID-19 test rate alone negatively affected COVID-19 CFR. That is, countries that conducted more COVID-19 tests had a lower COVID-19 CFR. For every 1% increase in COVID-19 test rate, one would expect the COVID-19 CFR to be 4% lower. This may be driven by causative and correlative factors. Countries that have higher test rates for COVID-19 are likely capturing a greater number of milder and asymptomatic cases, increasing the size of the denominator used to calculate the CFR and thereby reducing the CFR. These countries might have more available health care resources to treat people infected with SARS-CoV-2. However, when evaluating the interactions between test rate and the proportion of the population with CVD or the proportion of the population 65 years of age or older, no interactions were found. This means, independent of test rate, higher COVID-19 CFRs were observed in countries whose populations had higher proportions of CVD and individuals 65 years of age or older. For every 1% increase in the proportion of the population 65 years of age or older, or proportion of the population with CVD, one would expect the COVID-19 CFR to be 9% and 19% higher, respectively. Although the nature of the positive effect of CVD on COVID-19 CFR cannot yet be fully characterized at this early stage of the pandemic, postulated mechanisms include predisposition to cardiac injury, inflammation, hypoxia, and hypercoagulability.9

In addition to the large number of deaths, the COVID-19 pandemic may put a strain on CVD health care resources and the health of the CVD population. Emergency public health measures, staff redeployment, and shifts in health care resources are resulting in the postponement of nonurgent procedures: preliminary estimates from this study, which only accounted for CABG, PCI, and valve surgery, already indicate a potential backlog of > 1200 procedures each month in Ontario alone. Because Ontario represents only 38% of Canada by population, the COVID-19 pandemic will have a notable effect on health care resources nationally. As provinces restart elective surgeries and procedures while health care resources continue to support treatment of existing and new patients with

COVID-19, as well as urgent CVD care, careful consideration of health care system planning is warranted to manage the imbalance between health care capacity and demand created as the direct and indirect consequences of the COVID-19 pandemic. Proactive planning of reinstitution of CVD care resources will be crucial to address this backlog. Further challenges to CVD management might include complications in patients who have delayed medical care because of COVID-19 fears. Anecdotal data suggest delayed presentation of CVD emergencies by patients because of fear to seek medical attention during the pandemic. A significant increase in the time from symptom onset to first medical contact has been reported in STelevation myocardial infarction patients.^{24,25} These delays can further worsen their conditions, leading to the need for more complex care and greater risk with interventions. Moreover, delays to the rapid triage of CVD patients are possible.¹¹

Study limitations

It is important to note that the results of all correlation analyses and regression modelling are on the basis of countrylevel data and the relationships reported between variables should not be generalized to the individual patient level. There were several limitations to this study. First, male sex has been reported to be a risk factor for COVID-19 mortality.²⁶ However, country-specific sex-disaggregated data for COVID-19 CFRs were unavailable at the time of this study and including sex as an independent variable in the analyses was not possible. Second, there was significant variation in how countries report COVID-19 test rate, which limited our ability to evaluate the full effect of this variable. Moreover, CFR is an indicator of disease fatality that does not consider differences in case ascertainment, and specificity and sensitivity of tests, which confounds the interpretation of CFR-based data. Third, although the WHO has provided guidance for standardized reporting of COVID-19-related deaths, countries might deviate from these guidelines and reporting variance was possible. Fourth, although this study provides insights into the potential implications of COVID-19, the small sample size of the country-level epidemiological data set at this early stage of the pandemic limits the estimation precision of the regression coefficients. Last, there were variations in how procedures were captured in the CIHI and CorHealth Cardiac Registry databases.

Conclusions

Our findings provide insight into the direct and indirect implications of COVID-19 on CVD populations and health care resources. Among countries with more available health care resources, a higher proportion of the population with CVD was related to higher COVID-19 CFR. Public health measures and COVID-19 management specific to CVD populations in Canada are thereby essential because of the relatively high proportion of the population with CVD. The pandemic has disrupted the provision of health care services for patients with CVD in Canada. This information may be of benefit to health care planners to guide reactive and proactive measures in the management of the COVID-19 pandemic in Canada, the planning for health system recovery, and triaging burgeoning wait lists.

Acknowledgements

The authors thank CorHealth Ontario, Brittany Gould, Joon Lee, Lavanya Uruthiramoorthy, and Norine Foley for their assistance.

Funding Sources

The authors have no funding sources to declare.

Disclosures

R.H.S. receives support from an HSFC Clinician-Scientist Award. T.S.F. is supported by an HSFC National New Investigator Award, a Michael Smith Foundation for Health Research Health-Professional Investigator Award, and a Vancouver Coastal Health Research Institute Clinician-Scientist award, and receives in-kind study medication from Bayer Canada. A.K. receives support from the Sauder Family and HSFC Chair in Cardiology and the Paul Brunes Chair in Heart Rhythm Disorders (Vancouver, British Columbia). The other authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2020.06.003.