

# Impact of COVID-19 on Health-related Quality of Life in Patients With Cardiovascular Disease: A Multi-ethnic Asian Study

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## Research

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# Abstract

## Background

Little is known about the impact of the global coronavirus disease-2019 (COVID-19) pandemic on patients with cardiovascular disease (CVD), the biggest global killer and major risk factor for severe COVID-19 infections. We aim to explore the indirect consequences of COVID-19 on health-related quality of life (HRQoL) of patients with CVD.

## Methods

Eighty-one adult outpatients with CVD were assessed using the EQ-5D, a generic health status instrument with five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), before and during the pandemic. Changes in the EQ-5D dimensional responses were compared categorically as well as using the dimension-specific sum-score (range 1 to 3, with a higher score indicates worse health). The responses and sum-score were compared using the exact test of symmetry and the paired t-test, respectively.

## Results

These patients [mean age (SD) 59.8 (10.5); 92.6% males; 56% New York Heart Association (NYHA) functional class I] had coronary artery disease (69%), heart failure (28%), or arrhythmias (15%). None experienced change in NYHA class between assessments.

About 30% and 38% of patients reported problems with at least one of the EQ-5D dimensions pre- and during the pandemic, respectively. The highest increase in health problems was reported for anxiety/depression (12.5% pre-pandemic vs 23.5% during pandemic;  $p = 0.035$ ) with mean domain-specific score from 1.12 (SD 0.33) to 1.25 (SD 0.46) ( $p = 0.012$ ). There was no meaningful change in other dimensions as well as overall HRQoL.

## Conclusion

The COVID-19 pandemic is associated with a significant worsening of the mental health of patients with CVD.

## Introduction

Coronavirus disease 2019 (COVID-19) is a global pandemic with unprecedented medical, economic and social consequences. Much of the global scientific attention has been on the management of critically ill COVID-19 patients and public health efforts to reduce transmission, in order to prevent overwhelming healthcare system resources. These efforts have included a combination of changes in healthcare provision and delivery, as well as compulsory confinement and restriction on free movement.

COVID-19 is known to result in potentially severe cardiovascular complications [1, 2]; patients with pre-existing cardiovascular disease (CVD) suffer worse outcomes with COVID-19 infection [3]. Beyond these direct consequences, COVID-19 has reshaped the delivery of cardiovascular care – non-critical and elective procedures are postponed, and distancing imperatives have led to rapid scaling of telemedicine and cancellation of cardiac rehabilitation. The repeated public health messages that those with chronic conditions should practice social and physical distancing may adversely affect the health-seeking behavior of patients with CVD. All these may culminate in worse outcomes for patients with CVD, the biggest killer globally [4]. Indeed, data from affected countries show reductions in hospital admission for myocardial infarctions and strokes [5], but those who presented were sicker and had worse outcomes, suggesting delayed presentation [6, 7].

Pandemics are known to affect infected and non-infected persons in a myriad of ways. Studies evaluating the impact of COVID-19 on non-infected persons have focused largely on the psychological consequences [8, 9]; both small and large studies have been conducted in general population, healthcare workers, and those with pre-existing psychiatric diseases. Little is known about the impact of COVID-19 on physical and mental health of patients with CVD. We aimed to, using the EQ-5D, evaluate the impact of COVID-19 on health-related quality of life (HRQoL) in a multi-ethnic Asian cohort with CVD, hypothesizing that the physical capacity and mental health of these patients would be adversely affected by COVID-19.

## Methods

### Study design and setting

This was a longitudinal survey involving a multi-ethnic Asian cohort of adult outpatients with known CVD, from a tertiary center in Singapore.

Singapore is a densely-populated, multi-ethnic city state in the Asia-Pacific; majority of its 5.7 million population are Chinese, followed by Malays and Indians. It was one of the first few countries to be affected by COVID-19 outside China. In response to the COVID-19 pandemic, Singapore raised its Disease Outbreak Response System Condition alert to “orange,” the second highest level, on 7th February [10]. A surge in cases from 6th March 2020 onwards necessitated a partial national lockdown, termed as the Circuit Breaker, to be implemented on 3rd April 2020 [11]. Hospitals temporarily halted non-critical services; other measures included school closures, mask advisory, safe distancing regulations, and closures of beaches and playgrounds. There was gradual easing of the restrictions from 2nd June 2020, termed Phase 1 Safe Re-opening, where businesses that operate in settings with lower risks of transmission, selected schools and childcare centers were allowed to operate [12]. This was followed by Phase 2 Re-opening from 18th June 2020, where almost all activities were allowed except for large-scale events and venues, as well as entertainment venues [13].

### Study population

Briefly, Asian patients with known CVD were eligible if they were at least 21 years of age and had completed a HRQoL questionnaire prior to the COVID-19 outbreak and provided consent for future research. Patients were excluded if they were illiterate.

## Assessments

Our study used EQ-5D questionnaires for HRQoL assessments. The EQ-5D is one of the most commonly used generic preference-based health status questionnaires [14]. Three-level EQ-5D (EQ-5D-3L) contains five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each with three response levels (no problems, some/moderate problems or severe/extreme problems). It also has a visual analog scale (EQ-VAS) measuring health on the scale of 0 to 100, with a higher score indicating better health. A five-response level version was later developed (EQ-5D-5L) to enhance its sensitivity and reduce ceiling effect [15]. Both the versions have been psychometrically validated in a large number of diseases and conditions, including cardiovascular health [16].

Our study used official English and Chinese versions of EQ-5D-3L and EQ-5D-5L questionnaires. The utility scores for EQ-5D-3L and EQ-5D-5L were derived from the Singapore value set for EQ-5D-3L and its crosswalk algorithm, respectively [17]. Utility scores range from - 0.769 to 1, with higher scores indicate better health. Dimension-specific sum score was calculated as the mean of each dimension-specific item responses. Dimension-specific score range from 1 to 3 for EQ-5D-3L and 1 to 5 for EQ-5D-5L, with a higher score indicating worse health.

The EQ-5D-3L and EQ-VAS were administered to all study participants. In addition, a subset of participants also administered the EQ-5D-5L. EQ-5D-3L and EQ-5D-5L were administered in random order to avoid sequence effect on the responses. The pre-pandemic questionnaires were self-administered by the participants during physical outpatient visits. However, due to restrictions in face-to-face visits during the pandemic, the follow-up assessments were conducted remotely, either via the phone or through the mail.

In addition to EQ-5D questionnaires, the study collected sociodemographic and clinical information on patient CVD diagnosis, comorbidities and New York Heart Association (NYHA) functional class. Clinical information was recorded from patients' medical records available at the hospital. NYHA functional class was assessed during both pre- and during pandemic visits.

## Sample size

We anticipated that pandemic might have a mild-to-moderate impact on patients' HRQoL. The sample size for the study was estimated to detect a change of one-third of standard deviation (SD) (0.33 standardized effect size) based on dimension-specific scores. A sample size of 75 participants was required to detect the desired change with 80% power at a 5% two-sided level of significance using the paired t-test. The sample size was not adjusted for multiplicity due to the exploratory nature of this study.

## Statistical analysis

The mean (SD) of pre- and during-pandemic, and change in dimension-specific scores were calculated for all EQ-5D dimensions. Two-sided paired t-tests were used to assess the statistical significance of the change in the scores. The changes in scores were also presented with the standardized effect size (SES) estimated as the mean paired difference of during and pre-pandemic assessments divided by the standard deviation of pre-pandemic assessment. SES was considered small (0.2), medium (0.5), and large (0.8) according to Cohen's recommendation [18].

Dimension-level item responsiveness was evaluated using a percentage of participants in each of the severity level at pre- and during-pandemic assessments. The distribution of participants between the two assessments was compared using the McNemar-Bowker exact test of symmetry.

EQ-VAS and utility scores for EQ-5D-3L and EQ-5D-5L were analyzed similarly to dimension-specific scores.

The analysis based on the EQ-5D-3L and EQ-5D-5L data were considered as the primary analysis and sensitivity analyses, respectively, as EQ-5D-5L was administered to only a subset of participants.

## Results

A total of 85 patients with pre-pandemic HRQoL assessments were approached between 29th April 2020 to 19th June 2020 for this study, and 84 (99%) agreed to participate. Data from 3 (4%) participants were excluded from the final analysis, as the baseline HRQoL survey was performed more than 2 years ago. The final number of participants whose data were analyzed was 81.

The mean age of the participants was 60 years (SD 11), the majority were men (93%), and the ethnic distribution reflected that of the general population. The majority of the participants had coronary artery disease (69%), followed by chronic heart failure (28%). Along with their CVD, the participants also reported having other comorbidities such as hypertension (62%), dyslipidemia (61%), and diabetes mellitus (49%). There was little functional limitation at baseline with 94% reporting NYHA functional classes I or II. There was no change in NYHA functional status during the pre- and during-pandemic visits for any of the participants. The baseline characteristics of the patients are summarized in Table 1.

Table 1  
Patient characteristics at pre-pandemic visit

Characteristics	N = 81
Age (years), mean (SD)	59.8 (10.5)
Male, n (%)	75 (92.6)
Ethnicity, n (%)	
Chinese	62 (76.5)
Malay	12 (14.8)
Indian	6 (7.4)
Others	1 (1.2)
Education, n (%)	
Primary (6 years) or less	13 (16.1)
Secondary (up to 11 years)	35 (43.2)
Diploma, university or higher	33 (40.7)
Household earning < S\$4000, n (%)	42 (51.9)
Heart problems, n (%)	
Coronary artery disease	56 (69.1)
Heart failure	23 (28.4)
Arrhythmia	12 (14.8)
Other heart problems	6 (7.4)
Comorbidities, n (%)	
Hypertension	50 (61.7)
Hyperlipidaemia	49 (60.5)
Diabetes	40 (49.4)
Stroke	9 (11.1)
Other	40 (49.4)
NYHA functional classification, n (%)	
I	45 (55.6)

SD, standard deviation; NYHA, New York Heart Association; EQ-VAS, EQ – Visual Analogue Scale; EQ-5D-3L, 3-level EQ-5D.

Characteristics	N = 81
II	31 (38.3)
III	5 (6.2)
Health status using EQ-VAS, mean (SD)	78.6 (12.6)
EQ-5D-3L utility score, mean (SD)	0.898 (0.20)
SD, standard deviation; NYHA, New York Heart Association; EQ-VAS, EQ – Visual Analogue Scale; EQ-5D-3L, 3-level EQ-5D.	

Among 81 patients who participated in the study, all completed EQ-5D-3L at both visits. A subset of 66 patients completed EQ-5D-5L in addition to EQ-5D-3L at both visits. There were no notable differences in baseline characteristics between patients who completed both questionnaires versus who completed only EQ-5D-3L, except for NYHA status and CVD diagnoses (Supplementary Table 1).

Using EQ-5D-3L at pre-pandemic, 24 of 81 participants (29.6%) reported problems in at least one dimension; the most commonly affected dimension was pain/discomfort (23.5%) followed by anxiety/depression (12.4%). During the pandemic, 31 participants (38.3%) reported problems in at least one dimension with the severity of the problems in each dimension similar to or worse than pre-pandemic (Fig. 1). Among all the dimensions, the highest increase in problems was reported for anxiety/depression with mean domain-specific score increased by 0.12 (SES = 0.373;  $p = 0.012$ ) (Table 2). There was no meaningful change in EQ-VAS (mean change = -0.01; 95% CI -2.87 to 2.85) as well as EQ-5D-3L utility score (mean change = -0.015; 95% CI -0.063 to 0.034).

Table 2  
Comparison of EQ-5D-3L dimension scores at pre- and during-pandemic visits

<b>Dimension</b>	<b>Pre-pandemic</b>	<b>During pandemic</b>	<b>P-value</b>
<b>Mobility</b>			
Mean score (SD)	1.099 (0.30)	1.099 (0.30)	
Mean change (95% CI)	0.000 (-0.078, 0.078)		> 0.999
Standardized effect size	0.000		
<b>Self-care</b>			
Mean score (SD)	1.025 (0.16)	1.012 (0.11)	
Mean change (95% CI)	-0.012 (-0.055, 0.030)		0.567
Standardized effect size	0.075		
<b>Usual activities</b>			
Mean score (SD)	1.111 (0.32)	1.086 (0.28)	
Mean change (95% CI)	-0.025 (-0.110, 0.061)		0.567
Standardized effect size	0.078		
<b>Pain/discomfort</b>			
Mean score (SD)	1.235 (0.43)	1.222 (0.45)	
Mean change score (95% CI)	-0.012 (-0.126, 0.101)		0.829
Standardized effect size	0.028		
<b>Anxiety/depression</b>			
Mean score (SD)	1.123 (0.33)	1.247 (0.46)	
Mean change (95% CI)	0.123 (0.028, 0.218)		0.012
Standardized effect size	0.373		
Dimension score was compared between two visits using the paired t-test.			
EQ-5D-3L, 3-level EQ-5D; SD, standard deviation; CI, confidence interval.			
Response levels were compared between two visits using the McNemar-Bowker exact test of symmetry.			
EQ-5D-3L, 3-level EQ-5D.			

A higher proportion of patients reported problems using the EQ-5D-5L compared to the EQ-5D-3L both at pre-pandemic and during pandemic visits. A total 32 of 66 participants (48.5%) reported problems in at



least one dimension at pre-pandemic with the majority reported problems in pain/discomfort (39.4%), followed by anxiety/depression (25.8%). During the pandemic, 37 participants (56.1%) reported problems in at least one dimension with the severity of the problems in each dimension similar to or worse than pre-pandemic. Similar to EQ-5D-3L data, the highest increase in problems was reported for anxiety/depression with mean domain-specific score increased by 0.26 (SES = 0.516;  $p = 0.007$ ) (Supplementary Table 2). There was no meaningful change in the EQ-5D-5L utility score (mean change = -0.036; 95% CI -0.084 to 0.012).

## Discussion

Our study involving patients with chronic CVD reported worse HRQoL in several aspects of health during the COVID-19 outbreak, despite stability in their CVD. Specifically, there was increased anxiety and depression on serial EQ-5D-3L assessments. Results were more pronounced using EQ-5D-5L. The increase in anxiety and depression during the outbreak was clinically (small-to-moderate effect size) as well as statistically significant. To our knowledge, this is one of the first studies evaluating the impact of COVID-19 pandemic on the HRQoL of non-infected persons with CVDs.

Infectious diseases outbreaks are known to have health, social and economic implications, for infected and non-infected persons alike. Prior studies have shown the adverse psychological impact of COVID-19 and its containment measures in COVID-19 patients, frontline workers, patients with pre-existing psychiatric diseases and the general population [8, 9]. Our findings are consistent with prior literature, and further extended those reports by providing the perspectives of those with CVD.

The increase in anxiety and depression amongst our study participants, is unsurprising and may be explained by the following: 1) The swathe of information, from official organizations to social media platforms, re-iterating the increased risks of COVID-19 with CVDs, 2) Postponements of non-critical CVD follow-up appointments, and the emphasis on social and physical distancing may have altered their perception of healthcare accessibility, 3) Separation from family and friends during the Circuit Breaker, leading to social isolation, 4) Mask-wearing requirement in public areas, resulting in dyspnea for some people, and 5) Economic concerns, given the closures of businesses. Lingering memories of the devastating impact of the Severe Acute Respiratory Syndrome (SARS) outbreak in 2003, with 238 cases and 33 deaths in Singapore, may have also contributed to anxiety and depression [19]. An understanding of the relative contribution of these factors would have been helpful in shaping future policies and interventions; unfortunately, such data were not collected in this brief study.

The magnitude of change in HRQoL was small. In particular, there was little change in the physical dimensions of HRQoL, which partly reflected the stability of the participants' underlying CVDs between the surveys done at baseline and during the COVID-19 outbreak. The subgroups bearing the brunt of the pandemic and its containment measures are usually the elderly [20], females [21–23], less educated [23, 24], and those from the low socioeconomic status [25, 26]. Our study participants of mostly older, middle-class males may not have been the vulnerable group. Furthermore, support from the government in

response to the pandemic – rapid ramping up of resources and capabilities in terms of COVID-19 testing and provision of care, assurance that non-COVID care would not be compromised, shift towards telemedicine, and massive stimulus packages to cushion the economic impact, might have somewhat mitigated the impact of the pandemic.

There are several strengths of our study. First, all the HRQoL assessments were completed by participants themselves rather than proxies. Second, all participants had baseline assessments prior to the outbreak, thus acting as their own controls. Third, the impact of the pandemic on HRQoL was evaluated by two validated HRQoL measures (EQ-5D-3L and EQ-5D-5L) and both gave consistent results, leaving less room for random noise in the results. Fourth, the follow-up HRQoL assessment was carried out during the partial national lockdown which enabled us to adequately capture the impact of outbreak and containment measures on HRQoL.

Our study has a few limitations. First, the administration of HRQoL assessments was different pre-pandemic and during pandemic for some participants. All pre-pandemic HRQoL assessments were self-administered; majority of the follow-up assessments were administered by the interviewer over the phone. The follow-up assessments were conducted when physical outpatient visits were restricted. Although our preference was for self-administered assessments via email or post, some participants preferred interviewer-administered assessments over the phone. Therefore, we would not rule out some impact of this administration on their responses. Nevertheless, previous research has shown that interviewer-administration is likely to overestimate HRQoL, rather than underestimate [27]. That is, some participants could have under-reported their health problems. Therefore, our estimates of the impact of the pandemic on HRQoL should be considered as conservative estimates. Second, our study performed several hypotheses, including evaluating the pandemic impact on each dimension of EQ-5D separately, without multiplicity correction. There could be chances of inflated type-I error (false positive), and results should be considered as exploratory. Finally, our study was conducted in Asian patients with CVD. The findings may not be generalizable to other ethnicities or patient populations. We encourage further research in other countries and other disease groups to understand the impact of the pandemic.

The findings of adverse psychological impact on patients with CVD have important implications. It is plausible that the impact would be greater if our findings are extrapolated to more vulnerable populations – elderly, females, less educated, lower socioeconomic classes and poorly controlled CVD. Psychological ramifications can be long-lasting even after the pandemic has ended, and should not be ignored. At time of writing, there is no authoritative organizations that plans and coordinates psychological interventions in Singapore during the COVID-19 outbreak. In the meantime, cardiologists can do their part by proactively screening for psychological issues in patients who come for consultations, be it in-person or via telemedicine. Where necessary, psychosocial interventions can be implemented in collaboration with psychiatrists and psychologists.

## Conclusion

The COVID-19 pandemic and its containment measures is associated with a significant decline in the psychological health components of the HRQoL of patients with pre-existing CVD. Our data suggest a need for improved screening of psychological issues and timely implementation of psychosocial interventions in these patients during the pandemic.

## Declarations

### Ethics approval and consent to participate

This study was approved by the Institutional Review Board and conducted according to the World Medical Association Declaration of Helsinki. Verbal consent for participation was obtained over the phone, prior to follow-up survey.

### Consent for publication

Not applicable.

### Availability of data and material

The dataset used and analyzed during the current study are available from the corresponding author on reasonable request.

### Competing interests

None directly related to this work. SLL is supported by National University Health System Clinician Scientist Program; she has received research grants from National University Health System, National Kidney Foundation of Singapore and Singapore Heart Foundation. MG is a member of EuroQol Group. KLW, EL, FN and MC report no conflicts of interest.

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### Authors' contributions

KLW, SLL and MG conceived and designed the study. KLW, EL, FN and MC acquired the data. SLL and MG analyzed and interpreted the data. KLW and SLL drafted the manuscript; EL, FN, MC and MG critically revised the manuscript. All authors had full access to all of the data in this study and take complete responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved of the final version of the draft.

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## Figures



Response levels were compared between two visits using the McNemar-Bowker exact test of symmetry.

EQ-5D-3L, 3-level EQ-5D.

## Figure 1

Comparison of EQ-5D-3L responses at pre- and during pandemic visits

## Supplementary Files

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