THE IMPACT OF THE COVID-19 PANDEMIC ON RECOVERY FROM CARDIAC SURGERY: 1 YEAR OUTCOMES

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ABSTRACT AND KEYWORDS

AIMS

The outbreak of COVID-19 was potentially stressful for everyone, and possibly heightened in those having surgery. We sought to explore the impact of the pandemic on recovery from cardiac surgery.

METHODS AND RESULTS

A prospective observational study of 196 patients who were ≥18years old undergoing cardiac surgery between 23rd March and 4th July 2020 (UK lockdown) was conducted. Those too unwell or unable to give consent/complete the questionnaires were excluded. Participants completed (on paper or electronically) the impact of event (IES-R) (distress related to COVID-19), depression (CES-D) and EQ-5D-5L (quality of life, HRQoL) questionnaires at baseline, one week after hospital discharge, and six weeks, six months and 1-year post-surgery.

Questionnaire completion was >75.0% at all timepoints, except at one week (67.3%). Most participants were male (147 (75.0%)), white British (156 (79.6%)) with an average age 63.4years. No patients had COVID-19. IES-R sand CES-D were above average at baseline (indicating higher levels of anxiety and depression) decreasing over time. HRQoL pre-surgery was high, reducing at one week but increasing to almost pre-operative levels at six weeks, and exceeding pre-operative levels at six months and 1-year. IES-R and CES-D scores were consistently higher in women and younger patients with women also having poorer HRQoL up to 1-year after surgery.

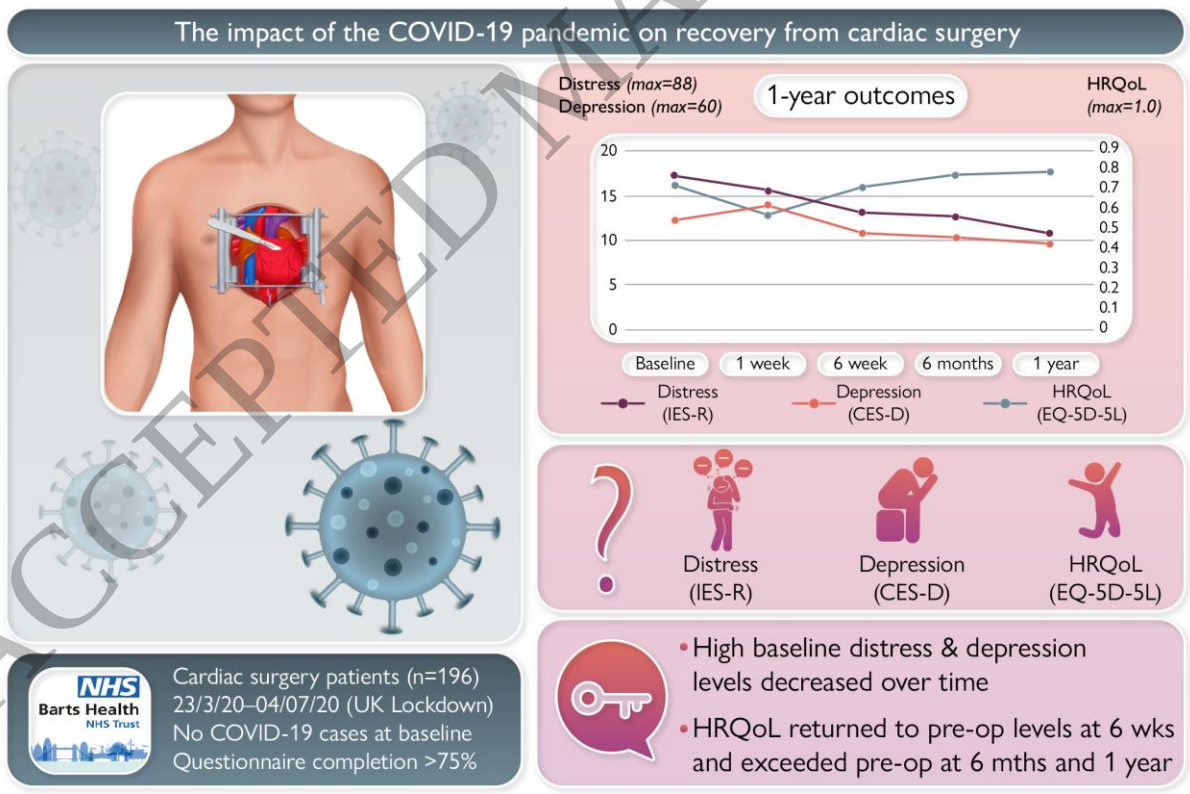
CONCLUSION

High levels of distress were observed in patients undergoing cardiac surgery during the COVID-19 pandemic with women and younger participants particularly affected. Psychological support pre- and post-operatively in further crises or traumatic times, should be considered to aid recovery.

REGISTRATION

Clinicaltrials.gov ID:NCT04366167

KEYWORDS: COVID-19; cardiac surgery procedures; quality of life; depression; distress



Graphical Abstract

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INTRODUCTION

The World Health Organisation declared the outbreak of SARS-CoV-2 (COVID-19) a public health Emergency of international concern on January 30th 2020. By the end of March 2020 there had been almost 34,000 deaths worldwide, with patients experiencing underlying cardiovascular disease having a particularly poor prognosis [(1)]. The impact on those undergoing surgery for cardiovascular disease was unknown, although reports from the H1N1 pandemic indicated that an 'unexpected and dramatically extraordinary hospital course' [(2)] or a complicated post-operative course [(3)] could be expected. Early surgical studies from COVID-19, albeit small samples (n<35), concluded that surgery in those with COVID-19 had a high risk of death [(4), (5)] and that surgery might accelerate disease progression in those incubating COVID-19 [(4)].

At the beginning of the COVID-19 pandemic there was much uncertainty, and very little was known about COVID-19. The UK government ordered the stopping all essential contact and travel on 16th March 2020 and entered a full 'stay at home' lockdown on 23rd March 2020. While the need to suspend UK elective surgery was recognised [(6)], urgent and emergency cases continued to require proper management while protecting resources for the response to COVID-19 [(7)]. Inevitably, cardiothoracic surgical services were severely affected. There was a >50% reduction in dedicated cardiac theatres and ICU beds [(8)], and in some countries services were restructured to form regional cardiac surgery hubs [(9), (10)]. The UK experienced a 52% reduction in cardiac surgical activity [(11)], while worldwide it is estimated that 81.7% of cardiac surgeries were cancelled during the first three months of the pandemic [(12)]. Furthermore, swabbing protocols to detect COVID-19 pre-procedure were introduced, visitors were not permitted during any in-hospital visit, and pre-surgical triage and post-surgical follow-up were done virtually [(10)].

The impact of this unprecedented situation on recovery for those receiving cardiac surgery during the pandemic was not known. Evidence prior to the pandemic suggests there is a considerable psychological burden of undergoing major cardiac surgery [13, 14]. For example, patients are at increased risk of depression [15] and anxiety [16] and those with depressive or anxiety symptoms tend to have poorer post-operative outcomes and health-related quality of life (HRQoL) [17, 16]. Therefore, it was anticipated that the COVID-19 outbreak would be additional stressful for people, especially in those with underlying chronic diseases who are at higher risk for COVID-19 (18) or in those having urgent or emergency cardiac surgery. Equally, symptoms of a traumatic event occur after one month but can also be delayed by several months (19), with older adults particularly at risk [20]. Thus, we sought to explore and describe the impact of the COVID-19 pandemic on recovery up to one-year from heart surgery.

METHODS

Study design and setting

The CardiacCovid study is a prospective single centre (UK) observational cohort study conducted between March 2020 (UK lockdown started for the COVID-19 pandemic) and August 2021 in one of the largest cardiovascular centres in Europe. Participants gave written informed consent to participate and were given questionnaires relating to the impact of the event (the pandemic), depression and health-related quality of life (HRQoL) to complete for baseline (pre-surgery), one week after hospital discharge and at six weeks, six months and 12 months after surgery.

The study complies with the Declaration of Helsinki and received National Health Service (NHS) Health Research Authority Yorkshire and The Humber Sheffield Research Ethics Committee approval (reference 20/YH/0132, 15.04.2020). The study is registered with clinicaltrials.gov (NCT04366167) and is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Study population: Inclusion and exclusion criteria

Adult patients (≥18 years of age) undergoing cardiac surgery between March 23rd 2020 and July 4th 2020 (UK COVID-19 national lockdown, when elective surgery was mainly suspended) were eligible for inclusion. Potential participants were identified from in-patient and theatre lists by a member of the study team and were approached prior to surgery where possible, or prior to hospital discharge. As research ethics approval was received on 15th April 2020, patients who had surgery prior to this date, and who were not in-patients at study commencement, were also contacted retrospectively. If recruited to the study after surgery, retrospective completion of the baseline questionnaires reflecting on pre-surgery state was undertaken. Those unable or unwilling to give written informed consent and/or to complete the questionnaires were excluded.

Data collection and measurement

Clinical data

Demographic information, pre-operative risk factors (including EuroSCORE), medical history, pre-operative details and immediate post-operative outcome (for example, hospital length of stay, mortality) were obtained from the local National Institute for Cardiovascular Outcomes Research (NICOR) adult cardiac surgery database (https://www.nicor.org.uk/national-cardiac-audit-programme/datasets/). Other clinical data, for example COVID-19 status on admission (defined as a positive COVID-19 polymerase chain reaction (PCR) test prior to surgery) and depression history, were obtained from local electronic sources and the participant, recorded on a standardised proforma and entered onto a bespoke database to link with the other clinical data and questionnaire data. Whether participants had COVID-19 during follow-up, COVID-19 vaccinations or participated in cardiac rehabilitation was obtained via the telephone call at 1-year.

Questionnaires

Participants completed the following questionnaires for baseline (pre-surgery status collected either contemporaneously or retrospectively), one week after hospital discharge and at six weeks, six months and 1-year after surgery:

a) IES-R Impact of event scale: The Impact of Events Scale (IES) is a psychometrically robust questionnaire [(21)] and one of the most widely used measures of event-specific distress and measures distress experienced by serious life changes/events. The IES-R (revised version) [(22)] is a 22 item self-report scale where each item is reported on a five point Likert scale from 0 (not at all) to 4 (extremely) with respect to how distressing each item has been during the past week. Scale scores are formed for the three subscales, which reflect intrusion (for example, intrusive thoughts/feelings, nightmares; 8 items) avoidance (for example numbing of responses, avoidance of feelings; 8 items), and hyperarousal (for example anger, irritability, difficulty concentrating; 6 items). The total mean IES-R score is 12 [(22)] and a score of ≥33 has been suggested as the best cut-off for a probable diagnosis of post-traumatic stress disorder (PTSD) [(23)].

b) EQ-5D-5L (health-related quality of life): The EQ-5D-5L (24) is a standardised, simple generic measure of health-related quality of life, which exhibits excellent psychometric properties across a broad range of populations, conditions and setting [(25)] and is well received by patients [(26)]. It has been the National Institute for Health and Care Excellence (NICE) preferred adult HRQoL measure since 2008 and is the most widely used general HRQoL measure in UK and Europe [(27)]. It consists of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) each with five levels of health response reflecting escalating problems in each domain. These dimensions can be converted to a single index value, which reflects how good or bad a health state is according to the preferences of the general population of a country/region with a higher value indicating better HRQoL. Additionally, the EQ-5D-5L contains a visual analogue scale (VAS) ranging from 0-100 (0 being the worst possible health imaginable and 100 being the best possible health imaginable).

c) CES-D (Centre for Epidemiological Studies Depression Scale). The CES-D (28) is a well-known, freely available, widely used tool for depressive symptoms in a broad range of populations. It is psychometrically robust in cardiovascular patients [29] and has previously been used in cardiac surgery patients [30]. The CES-D is a 20-item self-report adult instrument designed to measure common symptoms (behavioural, cognitive and affective) of depression that have occurred over the past week, such as poor appetite, hopelessness, pessimism, and fatigue. All questions are answered on a scale of 0-3, with 0 indicating no symptom presence and with 3 representing symptoms "most or all of the time." CES-D scores range from 0 to 60 with higher scores indicating more severe depressive symptoms. A score of 16 or higher identifies subjects with potentially clinically meaningful depression.

Collectively, the questionnaires take approximately 20 minutes to complete. Both the CES-D and IES-R were available to use without permission or cost. Trust-level approval was already in place for electronic EQ-5D-5L use, and separate approval was sought and obtained from the EuroQoL Research Foundation for EQ-5D-5L paper use, noting its deviation from protocol use (some patients completed the baseline measure retrospectively). Questionnaires were completed using the Amplitude™ patient reported outcomes platform, or on paper (with return stamped self-addressed envelope provided), depending on participant preference. If paper copies were received, responses were entered onto the Amplitude™ system by a member of the research team. Efforts to minimise loss to follow-up included using up to three automated (email) reminders and at least one telephone call from a member of the research team at each time-point. Furthermore, a member of the research team was available to assist the participant in completing the questionnaires, if needed.

Patient and public involvement (PPI)

This study has had active PPI through concept, delivery, analysis, interpretation and dissemination. A specific PPI panel of 11 patient members was established, with two members representing patients on the interdisciplinary study steering group.

Statistical methods

Baseline characteristics and scores were summarised using means and standard deviations (SD) or medians and interquartile ranges (IQR) for continuous variables and counts and percentages for categorical variables. The characteristics were compared to those of patients undergoing surgery at the same centre in the corresponding time-period in 2019 (pre-pandemic). The baseline scores for IES-R, EQ-5D-5L and CES-D were compared descriptively for those where questionnaires were completed retrospectively following surgery versus those where questionnaires were completed prospectively prior to surgery.

Given the unknown impact, spread and duration of the COVID-19 pandemic at the time the study was designed, it was not possible to predict the number of patients likely to be enrolled in the study, nor the proportion who would be diagnosed with COVID-19. Therefore, a formal sample size calculation was not performed.

Separate mixed effects models for repeated measures (MMRM) were used to assess changes in IES-R, EQ-5D-5L, and CES-D scores over time by including the baseline measurements as an additional outcome and an indicator variable for follow-up visit only. This model accounts for the baseline values of each measure, while also incorporating all follow-up measurements, and enables the inclusion of participants with missing measurements. Unstructured variance-covariance matrices were used to allow for the anticipated correlations between repeated measurements over time. In order to assess the adjusted effects of age (years), sex (male or female), ethnicity (Asian, black or white), diabetes (yes or no), and surgery urgency (elective or emergency/urgent) on each of the outcome scores, MMRMs including an indicator variable for follow-up visit, each of the aforementioned covariates (with age modelled as a

linear effect), and interactions between each covariate and follow-up visit were used. Finally, the unadjusted effect of the EuroSCORE-II on each of the outcome scores was assessed using MMRMs containing an indicator variable for follow-up visit, a linear effect for the EuroSCORE-II, and their interaction. The impact of the EuroSCORE-II was assessed separately from other pre-specified covariates of interest because calculation of this risk score involves age, sex, diabetes and surgery urgency. For each of the models described effects at each follow-up visit were estimated and corresponding 95% confidence intervals and p-values calculated. The MMRMs used assume that any missing outcome data is missing at random (MAR). All analyses were conducted using Stata IC version 16.0 by authors EB, MD and TC.

RESULTS

Participants

During the study period 325 patients had surgery of whom 298 (91.7%) were screened for participation and 203 (68.1%) provided written informed consent (Figure 1). A further seven participants were excluded resulting in analysis being conducted on n=196 (Figure 1). Retrospective completion of baseline questionnaires occurred ~~(~~73.0%~~)~~ and overall questionnaire completion was >75.0% at all timepoints, except one week after surgery (67.3%) (Figure 1). The cohort characteristics are detailed in Table 1. Overall, the majority of patients were male (75.0%), of white background (79.6%) undergoing urgent or emergency surgery (59.7%) (as elective surgery was effectively postponed) with a median EuroSCORE of 1.6. No patients had COVID-19 at time of surgery. The characteristics of the cohort were similar to a comparative sample during non-COVID times (2019) at this centre (Table 1), although it is noted that 21 patients who died after surgery but before enrolment into this study were excluded who were likely to be of higher surgical risk (Figure 1). Particular differences in the study population included a smaller number of patients undergoing surgery (325 vs 581), a smaller proportion undergoing elective surgery (40.3% vs 57.8%) and having a longer length of hospital stay (9.0 days vs 7.0 days), but lower mortality (0.5% vs 2.8%). During the year of follow-up there were 7 (3.6%) deaths, 23 (11.7%) tested positive for COVID-19, 161 (82.1%) received COVID-19 vaccinations and 109 (55.6%) completed cardiac rehabilitation.

The impact of event, health-related quality of life and depression scores

Table 2, Figure 2 and Supplementary Table 1 show the results from each questionnaire at each time-point. No differences were observed in baseline scores comparing those who completed the questionnaires retrospectively or prospectively (data not shown).

The impact of the pandemic

The impact of the pandemic was high at baseline and decreased over the time following surgery. The observed mean IES-R score was higher than expected at baseline (17.4) remaining high at one week (15.6), six weeks (15.4) and six months (15.4) and decreasing to 10.8 at 1-year post surgery. There is a clear trend over one year in a decreasing impact with a reduction of 5.65 points (95% CI 2.92 to 8.39) from the MMRM model and closed to the expected levels (Table 2, Figure 2 and Supplementary Table 2). Overall, 34/196 (17.3%) scored >33 (suggestive of PTSD) at baseline reducing to 11/149 (7.5%) at 1-year. All subscale scores were higher at baseline and decreasing over time, although hyperarousal responses were lower at all time-points than intrusion or avoidance responses, where similar levels were observed.

Health-related quality of life

HRQoL was high pre-surgery (mean 0.73), reducing at one week (mean 0.58) and then increasing to almost pre-operative levels at six weeks (mean 0.72). The mean score at six months and 1-year exceeded pre-surgery levels (mean 0.78 and 0.80, respectively) with the increase from baseline at 1-year estimated to be 0.06 (95% CI 0.01 to 0.10). Over a third of participants still had issues in all categories except self-care at 1-year. In respect of the VAS scores (out of 100) there was a progressive improvement in the overall HRQoL after surgery at each time-point.

Depression

Mean CES-D score was 12.3 pre-surgery, which increased at one week (an estimated increase from baseline of 2.53 (95% CI 0.91 to 4.15)) and then decreasing over time such that at 1-year post-surgery there was a change decrease from baseline of 1.96 (95% CI 0.05 to 1.96). At baseline, 28.9% scored >16 (indicative of depression) with 22.2% continuing to score highly at 1-year after surgery.

The association of age, sex, ethnicity, diabetes, surgical risk and surgery urgency on outcome

The impact of the pandemic

Older participants were affected less by the pandemic at all timepoints (Table 3) although female sex was associated with higher IES-R scores, compared to men, with the point estimate consistently higher at all timepoints (Figure 3a). Similarly, greater pre-operative risk (higher EuroSCORE) was associated with lower IES-R score, but at baseline only Table 3). No evidence of associations with ethnicity, surgery urgency or diabetes status was observed, although the numbers in some categories were small (Supplementary Table 2).

Health-related quality of life

Although no association with age (Table 3), diabetes, surgery urgency or ethnicity was observed (Supplementary Table 2), female sex was associated with lower HRQoL at one week, six weeks and 1-year after surgery (with the direction of point estimate also indicating lower HRQoL at six months) (Figure 3b). Similarly, greater pre-operative risk (higher EuroSCORE) was associated with lower EQ-5D-5L score at six weeks (Table 3).

Depression

Female gender has higher observed CES-D scores, indicating higher levels of depression at all time-points with the largest difference seen at one week (4.29 (95% CI 0.40 to 8.18) (Figure 3c). Similarly, older age was associated with lower CES-D scores at baseline, six weeks and six months after surgery

with an observed difference also seen at one week. No association was observed with ethnicity, surgery urgency, diabetes or EuroSCORE (Table 3 and Supplementary Table 2).

DISCUSSION

We undertook a prospective observational cohort study at one of the largest cardiovascular centres in Europe, to explore and describe the impact of the COVID-19 pandemic on recovery up to one-year from heart surgery. Overall, we observed high levels of pandemic-related distress, and found that anxiety and depression were higher at baseline and at 1-week after surgery. These levels then declined over time, with stabilised levels at 6 weeks and 6 months and the lowest levels observed at 1-year. Similarly, HRQoL was high pre-surgery and had returned to pre-operative levels by 6 weeks after surgery and continued improve exceeding pre-operative levels at 6 months and 1-year, which is the expected trajectory in non-COVID times. Approximately 17.3% had scores suggestive of PTSD at baseline. This is between the wide range (7.6% to 53.8%) reported in general population studies during the same time-period [31), (32), (33)]. Similarly, post-surgery IES-R scores suggestive of PTSD at all other time-points were within reported ranges (4%-24%) in a variety of cardiovascular populations (not including cardiac surgery) in non-COVID times [(34)]. As stated previously, we found scores indicative of clinical depression mirrored the trajectory of pandemic-related distress. However, those scoring ≥16 at all post-operative time-points (excluding 1-week after surgery), were also within ranges observed in pre-pandemic times (pre-CABG depression: 19% to 37%; post-CABG depression: 15%-33%) [(35)], although evidence is limited.

The stabilisation of pandemic-related distress and depression scores at 6 weeks and 6 months, and the increase in anxiety/depression as measured on the EQ-5D-5L between these time-points could potentially reflect the unfolding COVID-19 situation in the UK. Lockdown 2 occurred between 2nd November 2020 and 2nd December 2020 while lockdown 3 commenced on 6th January 2021 with decreasing restrictions introduced from 8th March 2021. For many, the 6 week and 6 month time-points would have fallen within

lockdown 1 and lockdown 2. Furthermore, the first COVID-19 vaccination was administered in the UK on 8th December 2020 and by the end of the 1-year follow-up for the study over 68 million vaccinations had been given [36]. This may have had a positive influence on some 6 month responses and the 1-year responses, considering that 81.2% of our participants had their vaccination by the time they completed their 1-year questionnaires. Despite this, just under half of participants were denied the opportunity to access to cardiac rehabilitation which may be why high levels of pain and discomfort (83.8%) and impairment of undertaking usual activities (73.1%) were still observed at six weeks post-surgery.

We observed that age, pre-surgical risk and sex had an impact on outcome. Older participants, who are particularly at risk of traumatic events [20], and those with higher pre-operative surgical risk, actually reported less pandemic-associated distress compared with younger participants and those with lower risk, respectively. Similarly, increased age was associated with less depression, particularly at 6 weeks and 1 - year. A potential reason for these findings, voiced by some participants and our PPI group, was that in these circumstances participants' felt that the need for surgery outweighed the risks of the pandemic and they had 'less to lose'. Considering sex, women were disproportionately affected by the pandemic as they tend to work in economically vulnerable positions, undertake more unpaid care work and are at increased risk of abuse during isolation periods [37] - all which are likely to have had an impact on their psychological and physical health [38]. Although our results reflect pre-pandemic findings in that women, compared to men, are more likely to experience depression at time of cardiac surgery [39], suffer greater post-operative morbidity burden [40] and have worse quality of life [41], the women in our study also reported higher levels of pandemic-related distress up to 1-year after surgery. Since anxiety is associated with poorer recovery after cardiac surgery [42] this also could have contributed to the poorer HRQoL we observed.

Another ~~key~~ finding to note were the results 1 week after discharge. Although pandemic-related distress was reduced from baseline, a decrease in HRQoL particularly related to pain and increased depression

were observed. Poorer outcomes at 1 week were also reflected in the reduced response rate (see limitations) as many indicated they felt too unwell to respond to the questionnaires. Traditionally, although not evidence-based, patients receive a follow-up appointment approximately six weeks after surgery. Certainly, it has recently been found that patients suffer highest morbidity 1week post-surgery and that 44% of patients would like an earlier review, including perhaps a telephone call which could help reassure, alleviate anxiety or assist in detecting early signs of complications [43]. In addition to this, some patients will have experienced prolonged periods of isolation, both in hospital and on discharge home, due to the pandemic lockdown rules, which can impact on psychological and physical health [44]. Therefore, patients are likely to benefit from earlier review routinely, but particularly during challenging times.

It is also interesting to note that despite conducting this study at the beginning of the pandemic and during the first UK lockdown, no patients in our study had COVID-19 at the time of enrolment. This offers the advantage that COVID-19 does not confound the results at time of recruitment, although 23 (11.7%) subsequently reported having COVID-19 during the 1-year follow-up study period.

Overall, this study addresses the significant gaps in the current evidence in this area of cardiovascular care. It is a methodologically robust study using a prospective design and is one of the largest cardiac surgery studies exploring recovery during the COVID-19 pandemic. This study also greatly benefited from the input of a PPI group to ensure the study was feasible and inclusive to potential participants. This was particularly important due to the possibly stressful circumstances patients were being approached under, and in retaining them over the course of a challenging year which included additional COVID-19 waves and national lockdowns. Despite these strengths, this study has several limitations. Firstly, due to the organisational restrictions imposed in this early phase of the pandemic, the majority of patients (73%) were recruited after surgery and completed the baseline questionnaires retrospectively. While prospective completion is preferred, as retrospective application has been shown to lead to recall bias and lower

HRQoL scores in trauma [45] and intensive care [46] patients, the difference is not thought to be clinically relevant [46]. Despite this potential bias retrospective evaluation of health status is still considered more appropriate than applying population norms [47]. Equally, on analysis we did not observe any differences in baseline scores comparing those who completed the questionnaires retrospectively or prospectively. Thus, the impact of this pragmatic approach is likely to have little impact on the results. Secondly, although questionnaire response rates were good at all timepoints, a lower response rate was achieved at one week after discharge, despite using a hybrid method of delivery which is considered best practice [48]. Mainly, this related to the retrospective nature of recruitment for those who had surgery prior to ethics approval being obtained and missing this time-point. However, as stated previously, we also observed poorer outcomes at this time-point which likely contributed to the willingness and ability of participants to complete them. Thirdly, this is an observational study and is limited by factors associated with this design, mainly selection bias and confounders, but also the type of data collected. However, considerable effort was made to address these limitations. Selection bias was minimised by attempting to recruit all eligible consecutive patients and by our hybrid approach to questionnaire delivery to limit barriers and encourage questionnaire completion to reduce loss to follow-up. We also adjusted for known confounders but we did not have detailed data on all health and psychosocial circumstances in the follow-up period which may have influenced questionnaire responses. We are also limited by only having data relating to event-related distress, depression and HRQoL. This was a pragmatic decision based on the complexities of the situation, considering participant burden at a difficult time, and also study resources at a time when staff were being redeployed to respond to the acute pandemic phase. However, a questionnaire-only study potentially underrepresenting the actual impact and experiences of patients. Therefore, we are conducting a complementary qualitative study to further understand the lived experience and impact of having cardiac surgery during a global pandemic. Finally, we equally did not have the resources to include those who had their surgery cancelled or postponed during this period, due to the higher number of patients that were affected by this. At the end of the first wave it was predicted that if countries increased their normal

surgical capacity by 20% after the pandemic it would take a median of 45 weeks to undertake these missed operations [12]. The impact of the pandemic on these patients is likely to be considerable.

Globally, the COVID-19 pandemic is far from over [49]. In March 2022 a large proportion of the world had been infected with the omicron variant and new variants are expected, where some may be more severe than omicron [50]. Differing country-level policies for managing the pandemic as well as vaccine inequality, particularly in low-and middle-income countries poses a significant barrier to a global end to the pandemic [51]. Therefore, our study is likely to be informative internationally for future variants and pandemic waves not only for patients undergoing cardiac surgery, but potentially other complex surgeries as well as interventional cardiology procedures. Of course, pandemics are not the only current global challenge – any scenario impacting on 'normal' healthcare delivery, for example conflict, major incidents, and climate emergencies, may impact on pre-intervention distress and subsequent recovery. Our key messages are that high levels of distress were observed relating to
the COVID-19 pandemic in patients undergoing cardiac surgery with women and younger participants particularly affected. Equally, pre- and post-surgery psychological support, earlier (remote) follow-up approximately 1-week after hospital discharge and adapting the delivery of cardiac rehabilitation should be considered to aid recovery.

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Teofila Bueser is a National Institute for Health Research (NIHR) Senior Nurse and Midwife Research Leader. The views expressed in this article are those of the author and not necessarily those of the NIHR, or the Department of Health and Social Care.

DISCLOSURE

The authors declare that there is no conflict of interest

DATA AVAILABILITY STATEMENT

The data underlying this article cannot be shared publicly due to the ethical restrictions on data sharing for this study. The data will be shared on reasonable request to the corresponding author, if appropriate sponsor and/or ethics committee approval is given.

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FIGURE LEGENDS

Figure 1: Modified CONSORT diagram: Study flow of patients having cardiac surgery during the COVID-19 pandemic and recruitment into the CardiacCovid study

Figure 2: Mean (95%CI) for a) IES-R, b) EQ-5D-5L and c) CES-D questionnaires at baseline, one week, six weeks, six months and one year after surgery for participants undergoing cardiac surgery during the COVID-19 pandemic

Figure 3: Questionnaire results (mean (95%CI) by sex in participants undergoing cardiac surgery during the COVID-19 pandemic at baseline, one week, six weeks, six months and one year after surgery: a) IES-R, b) EQ-5D-5L, c) CES-D

TABLES

Table 1: Characteristics of study participants undergoing cardiac surgery during the COVID-19 pandemic (n=196) and a comparative pre-COVID population from 2019

Variable	n(%) or mean (SD) (unless otherwise stated) (n=196)	Pre-COVID data [23rd March-4th July 2019] n(%) or mean (SD) (unless otherwise stated) (n=581)
Demographics		
Age (years/median [IQR])	65.0 [57.0-72.0]	65.0 [56.0-73.0]
Sex (Female)	49 (25.0)	140 (24.1)
Ethnicity		
White	156 (79.6)	196 (33.7)
Asian	29 (14.8)	93 (16.0)
Black	11 (5.6)	26 (4.5)
Other	0 (0.0)	29 (5.0)
Not stated/not known	0 (0.0)	237 (40.8)
Medical history		
Previous MI (yes)	72 (36.7)	186 (32.6)

Previous cardiac surgery (yes)	7 (3.6)	25 (4.3)
Renal function/dialysis	1 (0.5)	7 (1.2)
History of pulmonary disease	17 (8.7)	44 (7.6)
History of neurological disease	12 (6.1)	38 (6.5)
History of neurological dysfunction	5 (2.6)	14 (2.4)
History of depression	27 (13.8)	Not routinely recorded
Symptoms		
NYHA class		
I/II	131 (66.8)	354 (60.9)
III/IV	65 (33.2)	227 (39.1)
CCSC classification		
0/I/II	119 (60.7)	382 (65.7)
IIII/IV	77 (39.3)	199 (34.3)
Cardiac risk factors		
Current smoker	22 (11.2)	71 (12.5)
Hypertension	146 (74.5)	439 (77.8)
Diabetes	50 (25.5)	170 (29.3)

BMI (kg/m^2/median [IQR])	27.6 [24.7-30.5]	27.4 [24.6-31.1]
Examination and investigation		
LVEF: Good	138 (70.4)	438 (75.4)
Number of diseased vessels		
0	59 (30.1)	229 (39.4)
1	20 (10.2)	25 (4.3)
2	27 (13.8)	72 (12.4)
3	58 (29.6)	171 (29.4)
4+	32 (16.3)	84 (14.5)
Pre-operative risk assessment		
EuroSCORE (median [IQR])	1.6 [1.1-3.0]	1.7 [1.1-3.3]
Intra-operative details		
Operative priority		
Elective	79 (40.3)	336 (57.8)
Urgent	104 (53.1)	213 (36.7)
Emergency	13 (6.6)	31 (5.3)
Salvage	0 (0.0)	1 (0.2)
Operation type		

CABG	104 (53.1)	294 (50.6)
CABG + valve	24 (12.2)	42 (7.2)
Valve only	34 (17.3)	126 (21.7)
Major aortic	10 (5.1)	24 (4.1)
Other	24 (12.2)	95 (16.4)
Cardiopulmonary bypass used* (Yes)	183 (93.4)	545 (97.5)
Cardiopulmonary bypass time* (minutes/median[IQR])	93 [75-126]	98 [78-125]
Aortic cross clamp time* (minutes/median[IQR])	68 [54-95]	70 [51-90]
In-hospital outcome		
Return to theatre	3.0 (1.5)	33 (5.7)
Respiratory support (days/median[IQR])	1.0 [1.0-2.0]	1.0 [1.0-2.0]
Deep sternal wound infection	1 (0.5)	2 (0.3)
New neurological dysfunction	6 (3.1)	14 (2.4)
New haemofiltration/dialysis	11 (5.6)	31 (5.3)
ICU length of stay (days/median[IQR])	2.8 [2.0-4.1]	2.9 [2.0-4.6]
Post-operative length of stay	9.0 [7.0-14.0]	7.0 [5.0-10.0]

(days/median[IQR])		
In-hospital mortality	1 (0.5)	16 (2.8)

1 * ≥5 missing values

Table 2: The impact of event, health-related quality of life and depression scoring of participants undergoing cardiac surgery during the COVID-19 pandemic at baseline, one week, six weeks, six months and one year after surgery.

	Baseline N=196	**One week N=132**	**Six weeks N=159**	**Six Months N=159**	**One Year N=149**
IES-R					
IES-R, mean (SD): score range 0-88	17.4 (17.2)	15.6 (15.6)	13.3 (15.4)	12.6 (15.4)	10.8 (12.6)
IES-R, median (IQR)	11.5 (4.0-26.0)	10.5 (4.0-21.5)	7.0 (2.0-20.0)	7.0 (2.0-18.0)	5.0 (1.0-17.0)
IES-R Change from baseline, mean (95% CI)	-	0.43 (-2.98, 2.13)	-2.56 (-5.29, 0.16)	-4.34 (-7.08, -1.61)	-5.65 (-8.39, -2.92)
IES-R score>33 (PTSD), n (%)	34 (17.3)	17 (12.9)	19 (12.0)	14 (8.8)	11 (7.5)
Subscale: Avoid, mean (SD)	6.2 (6.8)	5.2 (5.9)	4.6 (6.0)	4.5 (5.8)	4.1 (5.4)
Subscale: Hyperarousal, mean (SD)	4.5 (5.1)	4.2 (4.4)	3.7 (4.5)	3.3 (4.5)	2.6 (3.5)
Subscale: Intrusion, mean (SD)	6.7 (6.8)	6.0 (6.2)	5.0 (6.0)	4.8 (6.0)	4.1 (4.9)
EQ-5D-5L					
EQ-5D-5L index, mean (SD): score range 0-1	0.73 (0.24)	0.58 (0.24)	0.72 (0.18)	0.78 (0.22)	0.80 (0.20)
EQ-5D-5L index, median (IQR)	0.75 (0.63-0.91)	0.63 (0.44-0.75)	0.76 (0.65-0.81)	0.83 (0.68, 1.0)	0.84 (0.72, 1.0)

EQ-5D-5L Change from baseline, mean (95% CI)	-	-0.16 (-0.21, -0.12)	-0.03 (-0.07, 0.01)	0.04 (-0.002, 0.08)	0.06 (0.01, 0.10)
Dimension: Mobility, n (%)*	75 (38.3%)	71 (53.8%)	55 (34.4%)	58 (36.3%)	55 (36.9%)
Dimension: Self-care, n (%)*	30 (15.3%)	71 (53.8%)	33 (20.6%)	32 (20.0%)	19 (12.8%)
Dimension: Usual activities, n (%)*	97 (49.5%)	117 (88.6%)	117 (73.1%)	61 (38.1%)	59 (39.6%)
Dimension: Pain / Discomfort, n (%)*	119 (60.7%)	121 (91.7%)	134 (83.8%)	93 (58.1%)	68 (45.6%)
Dimension: Anxiety / Depression, n (%)*	73 (37.2%)	59 (44.7%)	59 (36.9%)	68 (42.5%)	52 (34.9%)
EQ VAS, mean (SD): score range 0-100	61.8 (23.8)	62.0 (18.5)	72.6 (16.7)	76.6 (17.0)	78.7 (15.3)
CES-D					
CES-D, mean (SD): score range 0-60	12.3 (10.9)	13.9 (9.9)	10.8 (10.1)	10.4 (10.5)	9.6 (9.7)
CES-D, median (IQR)	10.0 (4.0, 17.5)	12.0 (6.0-20.0)	8.0 (3.0-16.0)	7.0 (3.0-15.0)	7.0 (2.0-13.0)
CES-D Change from baseline, mean (95% CI)	-	2.53 (0.91, 4.15)	-0.38 (-1.95, 1.19)	-1.26 (-3.09, 0.58)	-1.96 (-3.86, -0.05)
CES-D score ≥16 (depressed), n (%)	57 (28.9%)	46 (34.9%)	42 (26.3%)	36 (22.6%)	33 (22.2%)

Mean (SD) were calculated using the observed data. The change from baseline results are estimated from the mixed effects models for repeated measures.

Mean IES-R, EQ-5D-5L, and CES-D scores estimated using mixed effects models for repeated measures are presented in Supplementary Table 1.

Abbreviations: CES-D: Centre for Epidemiological Studies Depression Scale; EQ-5D-5L: EuroQoL Health Related Quality of Life instrument; EQ VAS: EuroQoL Visual Analogue Scale; IES-R: The Impact of Events Scale (Revised); PTSD: Post Traumatic Stress Disorder; SD: Standard deviation

*number (and proportion) experiencing any limitation.

Table 3: Association between outcome measures and age, sex and EuroSCORE in participants undergoing cardiac surgery during the COVID-19 pandemic at baseline, one week, six weeks, six months and one year after surgery.

	Baseline		One week		Six weeks		Six Months		One Year	
	Mean Difference (95% CI)	**p-value**	**Mean Difference (95% CI)**	**p-value**	**Mean Difference (95% CI)**	**p-value**	**Mean Difference (95% CI)**	**p-value**	**Mean Difference (95% CI)**	**p-value**
IES-R										
Sex[1]										
Male	0		0		0		0		0	
Female	5.35 (-0.27, 10.96)	0.06	1.80 (-4.22, 7.82)	0.56	5.95 (0.12, 11.78)	0.05	4.43 (-1.04, 9.91)	0.11	4.09 (-0.90, 9.07)	0.11
Age (yrs)[2]	-0.23 (-0.46, 0.005)	0.06	-0.24 (-0.49, -0.003)	0.05	-0.23 (-0.46, -0.007)	0.04	-0.35 (-0.56, -0.14)	0.001	-0.20 (-0.39, -0.01)	0.04
EuroSCORE[3]	-0.51 (-0.96, -0.06)	0.03	-0.18 (-0.77, 0.41)	0.56	0.26 (-0.28, 0.80)	0.35	0.008 (-0.40, 0.42)	0.97	0.06 (-0.29, 0.41)	0.75
EQ-5D-5L										
Sex[1]										
Male	0		0		0		0		0	
Female	-0.07 (-0.15, 0.01)	0.09	-0.14 (-0.23, -0.05)	0.003	-0.07 (-0.13, 0.004)	0.06	-0.04 (-0.12, 0.05)	0.39	-0.11 (-0.19, 0.03)	0.01
Age (yrs)[2]	0.0008	0.6	-0.001	0.54	0.001	0.46	0.001	0.53	0.0002	0.92

	(-0.003, 0.004)		(-0.005, 0.003)		(-0.002, 0.004)		(-0.002, 0.004)		(-0.003, 0.003)	
EuroSCORE[3]	0.006 (-0.0007, 0.01)	0.08	-0.006 (-0.02, 0.004)	0.23	-0.01 (-0.02, -0.004)	0.002	-0.001 (-0.007, 0.005)	0.64	-0.0005 (-0.006, 0.005)	0.86
CES-D										
Sex[1]										
Male	0	0.08	0	0.03	0	0.09	0	0.13	0	0.14
Female	3.12 (-0.37, 6.62)		4.29 (0.40, 8.18)		3.30 (-0.48, 7.07)		3.04 (-0.84, 6.93)		2.92 (-0.96, 6.81)	
Age (yrs)[2]	-0.20 (-0.34, -0.05)	0.01	-0.12 (-0.28, 0.04)	0.14	-0.21 (-0.36, -0.07)	0.004	-0.21 (-0.36, -0.06)	0.01	-0.13 (-0.27, 0.02)	0.09
EuroSCORE[3]	-0.29 (-0.58, -0.01)	0.04	0.16 (-0.23, 0.54)	0.42	0.19 (-0.17, 0.56)	0.30	0.02 (-0.27, 0.30)	0.90	0.13 (-0.14, 0.40)	0.34

N=196. [1] Estimates are adjusted for age, ethnicity, surgery urgency and diabetes, [2] Estimates are adjusted for sex, ethnicity, surgery urgency and diabetes, [3] Estimates are unadjusted.

FIGURES

Figure 1: Modified CONSORT diagram: Study flow of patients having cardiac surgery during the COVID-19 pandemic and recruitment into the CardiacCovid study

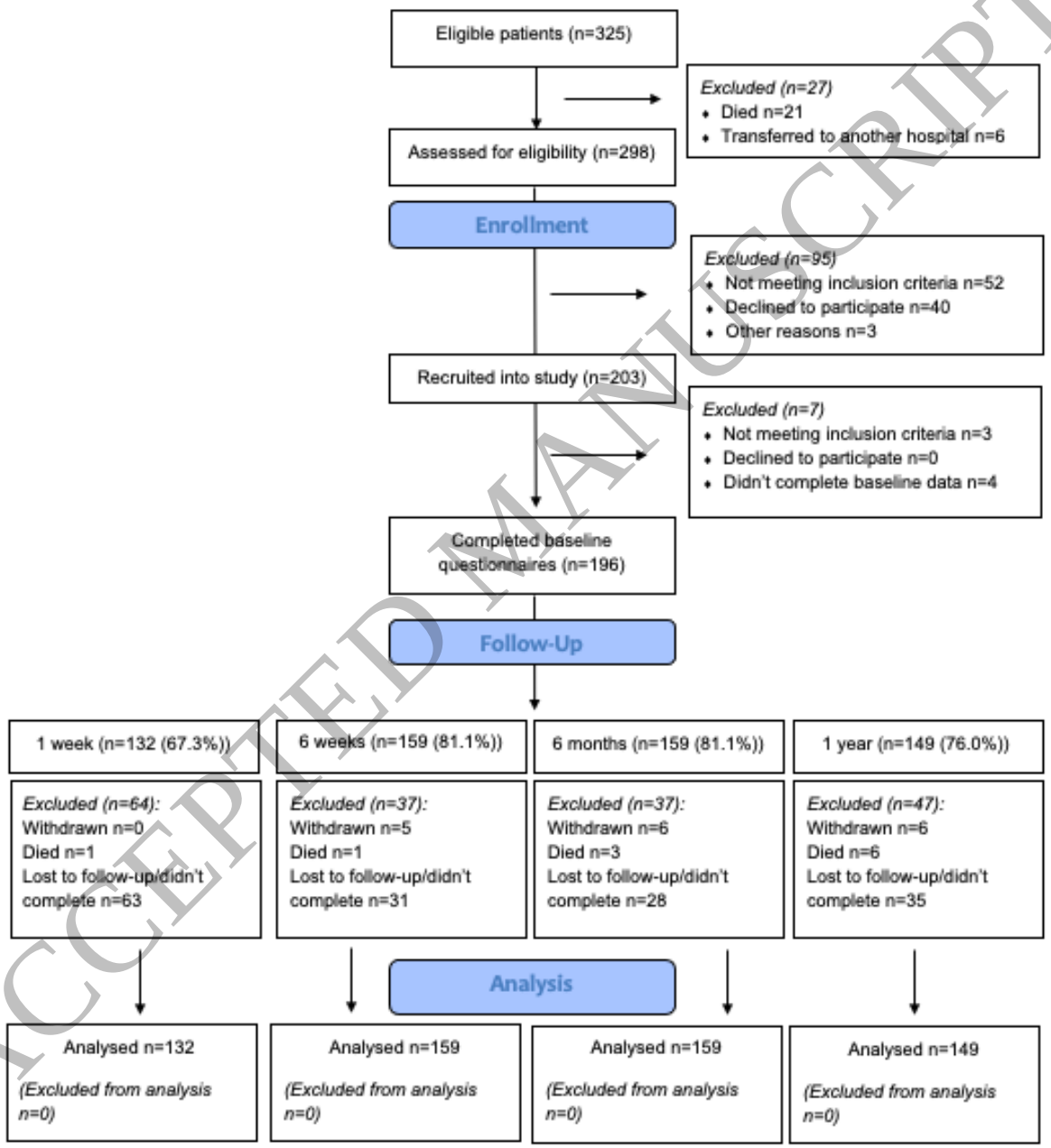
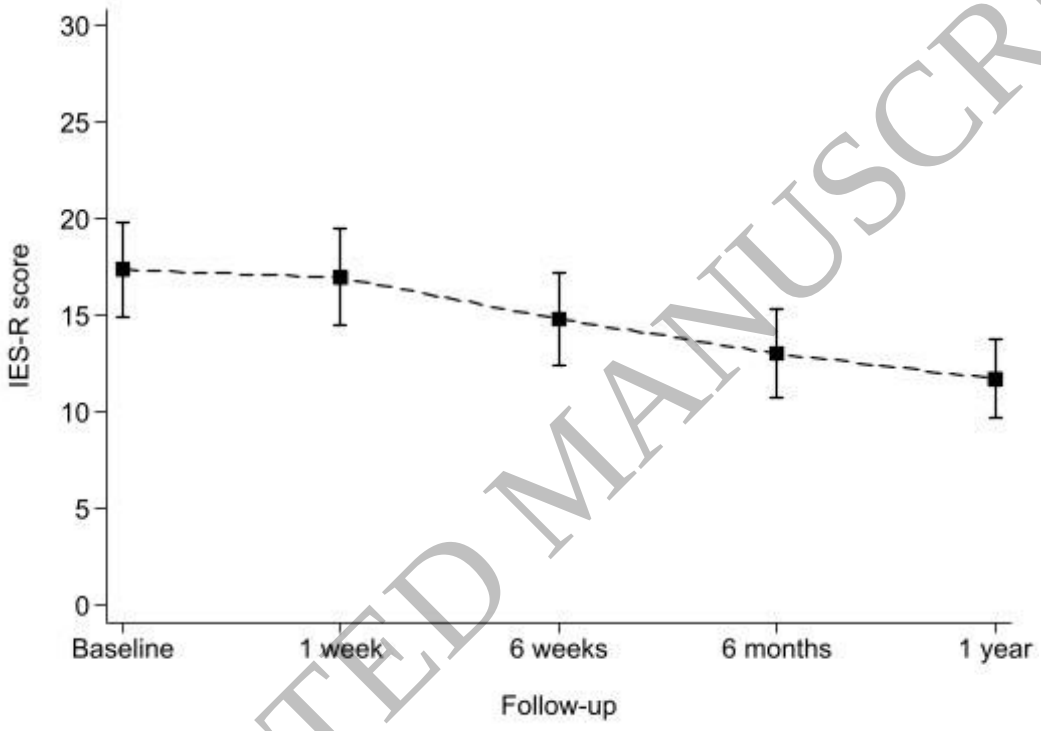
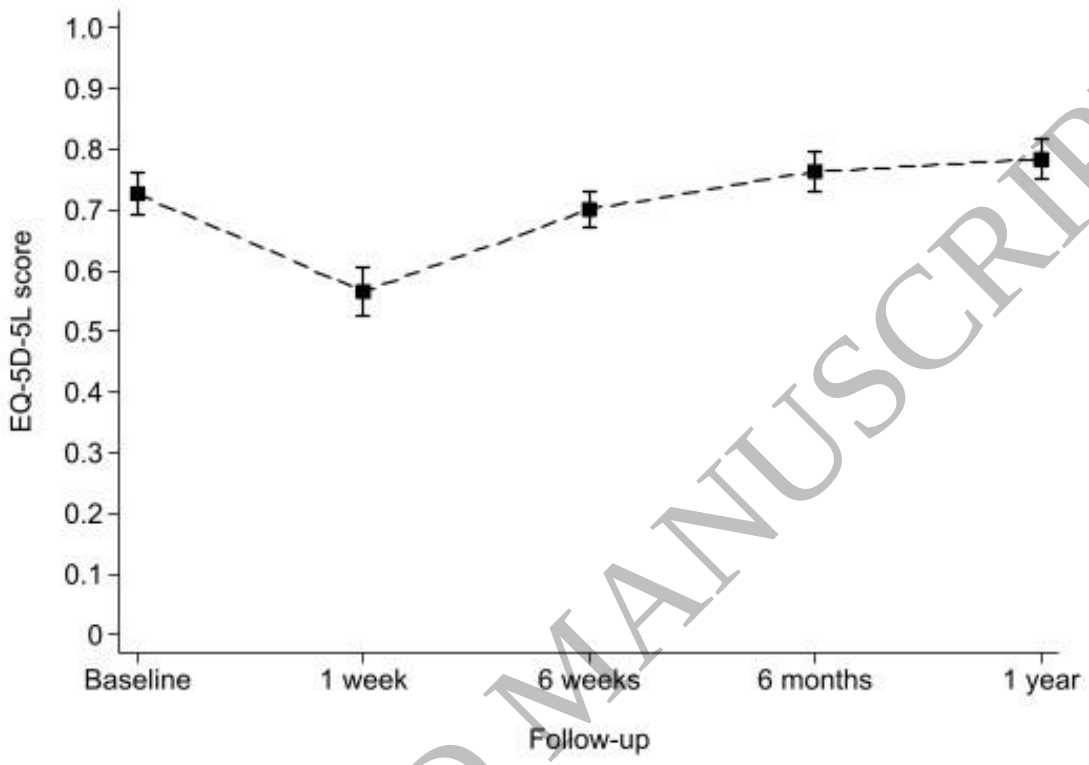


Figure 2: Mean (95%CI) for a) IES-R, b) EQ-5D-5L and c) CES-D questionnaires at baseline, one week, six weeks, six months and one year after surgery for participants undergoing cardiac surgery during the COVID-19 pandemic

a) IES-R



b) EQ-5D-5L



c) CES-D

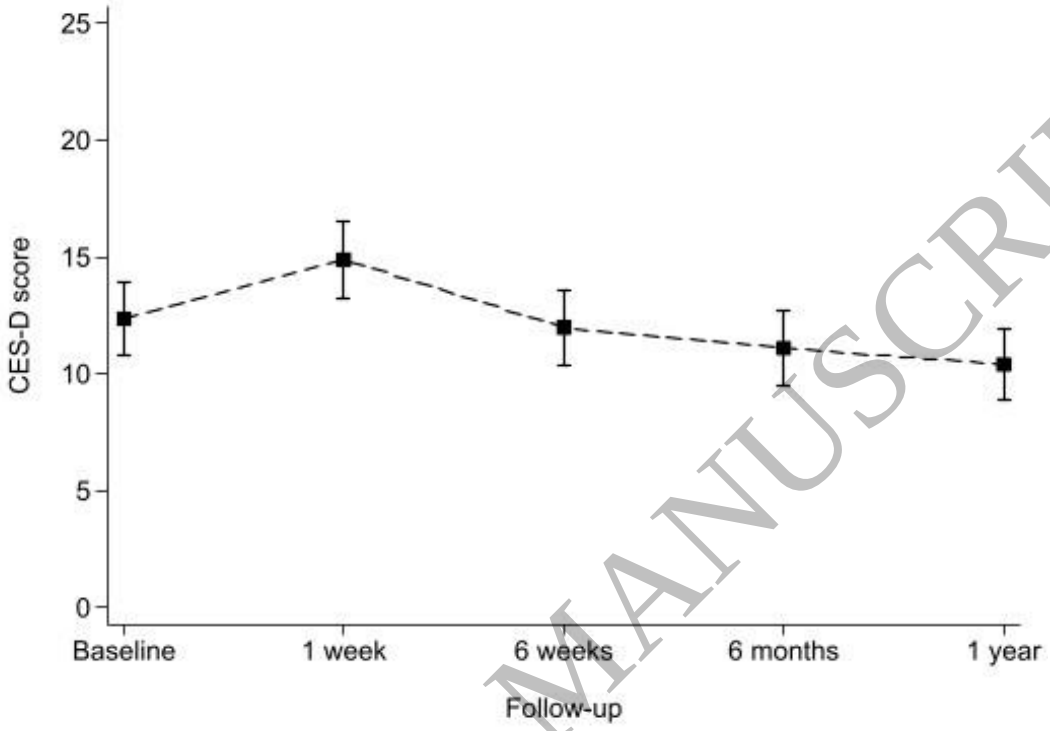
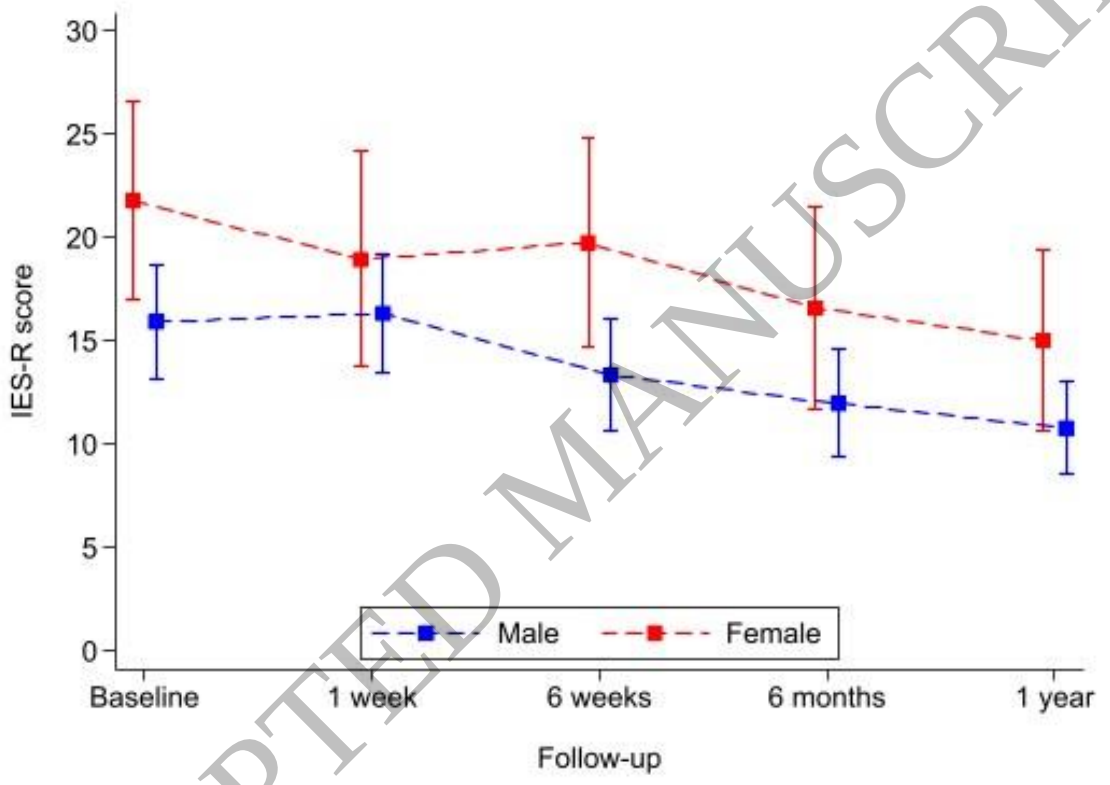
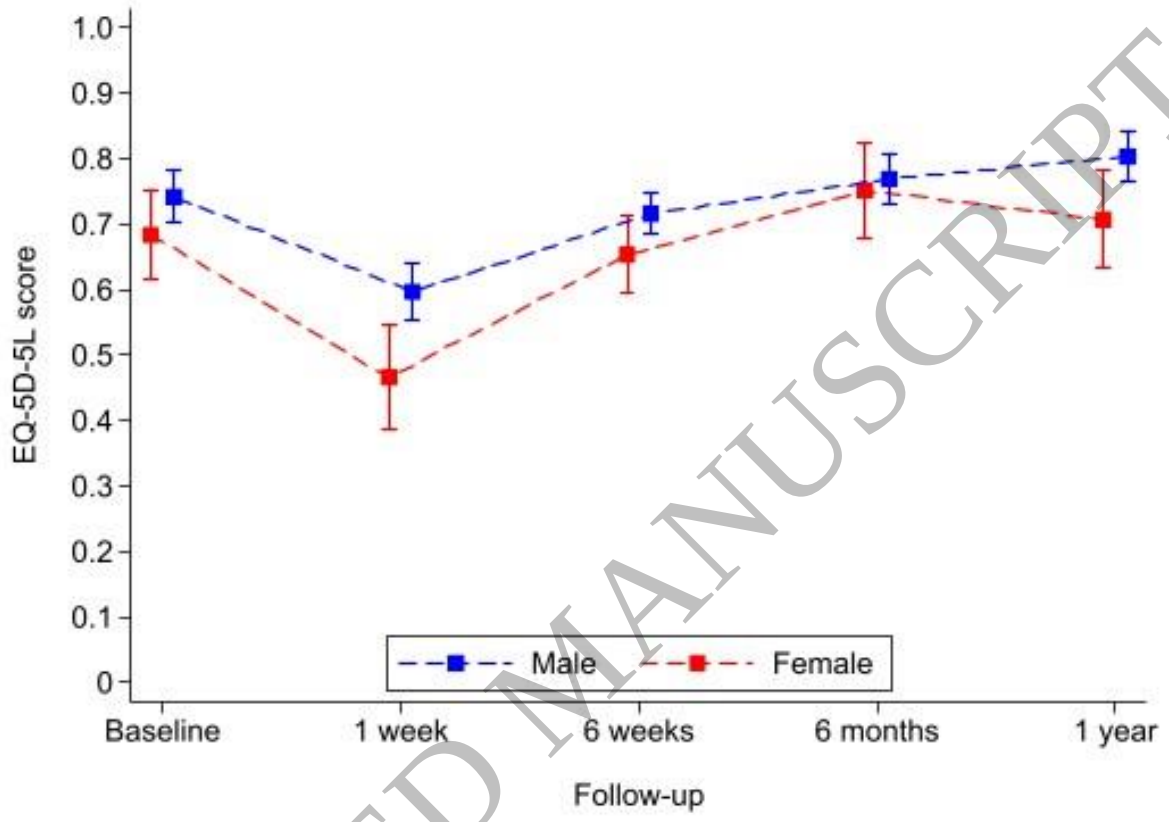


Figure 3: Questionnaire results (mean (95%CI) by sex in participants undergoing cardiac surgery during the COVID-19 pandemic at baseline, one week, six weeks, six months and one year after surgery: a) IES-R, b) EQ-5D-5L, c) CES-D

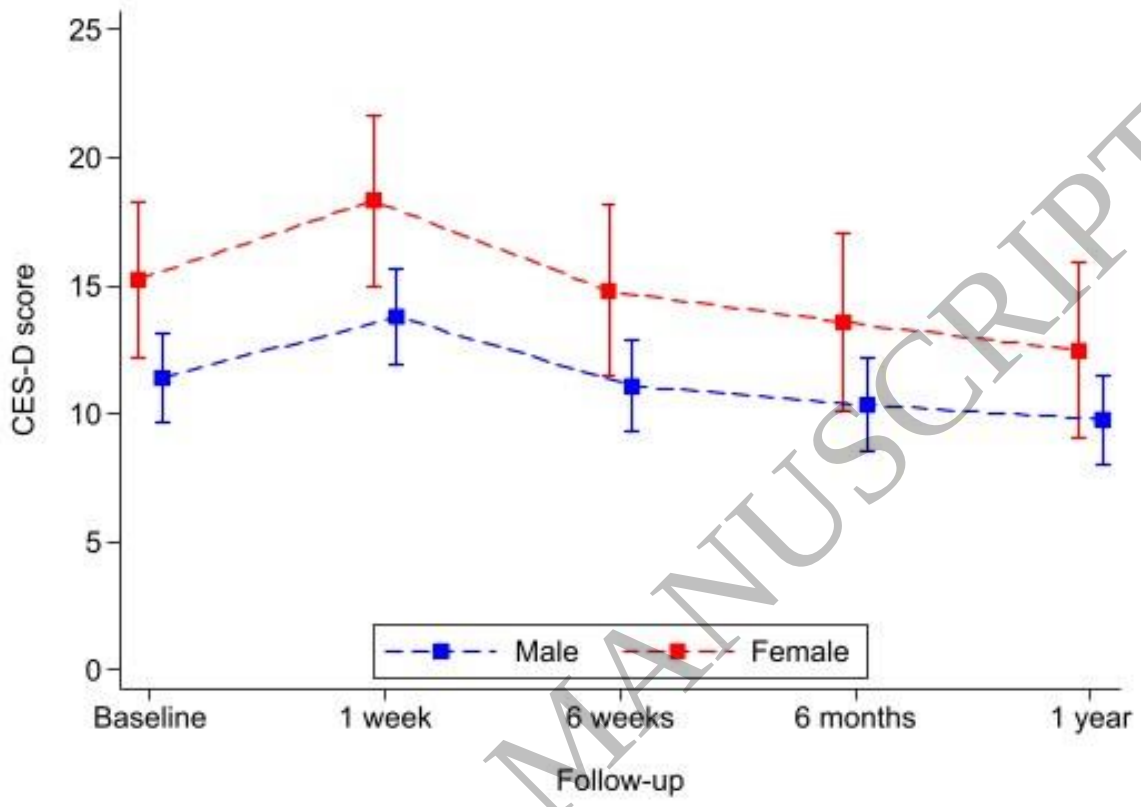
a) IES-R results by sex



b) EQ-5D-5L score by sex



c) CES-D score and sex



SUPPLEMENTARY FILES

Submitted as separate document