Revascularisation strategies in patients with significant left main coronary disease during the COVID-19 pandemic

Brief title: Left main revascularization during COVID-19

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Abstract

**Background:** There are limited data on the impact of the COVID-19 pandemic on left main (LM) coronary revascularisation activity, choice of revascularisation strategy and post-procedural outcomes.

**Methods:** All patients with LM disease (≥50% stenosis) undergoing coronary revascularisation in England between 01/01/2017 and 19/8/2020 were included (n=22,235), stratified by time-period (pre-COVID: 01/01/2017-29/2/2020; COVID: 1/3/2020-19/8/2020) and revascularisation strategy (percutaneous coronary intervention (PCI) vs. coronary artery bypass grafting (CABG). Logistic regression models were performed to examine odds ratio (OR) of 1) receipt of CABG (vs. PCI) and 2) in-hospital and 30-day postprocedural mortality, in the COVID-19 period (vs. pre-COVID).

**Results:** There was a decline of 1,354 LM revascularisation procedures between 1st March and 31st July 2020 compared with previous years’ (2017-2019) averages (~48.8%). An increased utilisation of PCI over CABG was observed in the COVID period (receipt of CABG vs. PCI: OR 0.46 [0.39, 0.53] compared with 2017), consistent across all age groups. No difference in adjusted in-hospital or 30-day mortality was observed between pre-COVID and COVID periods for both PCI (odds ratio (OR): 0.72 [0.51, 1.02] and 0.83 [0.62, 1.11], respectively) and CABG (OR 0.98 [0.45, 2.14] and 1.51 [0.77, 2.98], respectively) groups.

**Conclusion:** LM revascularisation activity has significantly declined during the COVID period, with a shift towards PCI as the preferred strategy. Postprocedural mortality within each revascularisation group was similar in the pre-COVID and COVID periods, reflecting maintenance in quality of outcomes during the pandemic. Future measures are required to safely restore LM revascularisation activity to pre-COVID levels.
**Introduction**

Significant left main (LM) coronary artery disease is a Class 1 indication for revascularisation, given its prognostic importance and the large myocardial territory it supplies. While there have been recent debates about the optimal revascularisation strategy for LM disease, both percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery are viewed as acceptable revascularisation strategies, based on patient comorbidities and overall anatomical complexity.

The coronavirus pandemic has led to a significant strain on healthcare services, with previous reports demonstrating a substantial reduction in cardiac procedural activity since the start of the pandemic. This is particularly relevant for procedures requiring admission to an intensive care unit (ICU) and prolonged hospitalisation (such as CABG surgery), at a time when such resources were prioritised for critically unwell patients with COVID-19.

Moreover, patients with cardiac conditions are at a higher risk of COVID-19 related mortality than the general population and, in the UK, were advised to shield meaning that significant numbers of elective cardiac procedures were cancelled.

Little is known about the impact these national policy level changes and healthcare service restructures may have had on the revascularisation of significant LM disease. Furthermore, it is unclear whether there has been in change in the choice of revascularisation strategy in patients with significant LM disease during the pandemic, and if such changes in strategy were associated with higher post-revascularisation mortality in this group of patients.

The UK is unique in that administrative and clinical data are systematically and routinely collected for all National Health Service (NHS) admissions, including for CABG surgery, percutaneous coronary intervention (PCI) procedures, and mortality. The present study sought to examine impact of the COVID-19 pandemic on LM procedural activity, choice of revascularisation strategy and associated postprocedural mortality for patients with

**Methods**

**Data Source, Study Design and Population**

Data for all adults (aged ≥18 years) with significant LM disease (≥50% stenosis) who underwent coronary revascularisation through PCI or CABG surgery between 1st January 2017 and 19th August 2020 in England were drawn from the British Cardiovascular Intervention Society (BCIS) national audit of PCI (NAPCI) and the British Society of Cardiothoracic surgery (SCTS) national adult cardiac surgery (NACSA) registries, both of which are managed by the National Institute for Cardiovascular Outcomes Research (NICOR), and commissioned by the Healthcare Quality Improvement Partnership (HQIP). (17-19) Each contain data on clinical and procedural characteristics, as well as in-hospital death for all procedures undertaken in England. Cases were deterministically linked with data of death as recorded in the Civil Registrations of Death dataset using each individual’s unique NHS identifier (final follow up 1st October 2020). (20)

Significant LM disease was defined on the basis of angiographic data available in both the NAPCI and NACSA datasets. We excluded patients with missing data on death (PCI: 633 cases; CABG: 61 cases) and excluded CABG patients who received PCI in the preceding 30 days (n=222) (flow diagram: **Supplementary Figure S1**). Patients were stratified according to revascularisation modality (CABG surgery and PCI) as well as the period during which the procedure was undertaken (pre-COVID: 1st January 2017-29th February 2020; COVID: 1st March 2020-19th August 2020). Procedural risk was assessed using the Logistic EuroSCORE and British Cardiovascular Intervention Society (BCIS) 30-day mortality score for CABG and PCI cases, respectively, using coefficients previously described for both scoring systems. (21,22)
**Outcomes**

The primary outcomes were 1) the receipt of CABG or PCI for significant LM disease and 2) in-hospital and 30-day mortality from the date of the procedure.

**Statistical Analysis**

We examined rates and patient and procedural characteristics of patients undergoing PCI and CABG, as well as in-hospital and 30-day mortality before and during the COVID pandemic (pre-COVID: 1st January 2017-29th February 2020; COVID: 1st March 2020-19th August 2020). Similar comparisons were performed for each calendar year. The number of PCI and CABG surgery procedures for each of the months January-July were compared between the 2017-2019 average and 2020 to estimate the percentage change (Δ) in procedural activity and, in turn, the projected deficit in cases in 2020 as a result of the pandemic. Data between 1st – 19th August 2020 was not used to calculate procedural activity as there may have been a lag between data submission by participating hospitals and availability in the NHS Digital database. Continuous variables were summarized using median and interquartile range (IQR) and compared using the Kruskal-Wallis test. Categorical variables were summarized as percentages and analysed using the Chi squared (X²) test. Multiple imputation with chained equations was performed for variables with missing data prior to model fitting, with a total of 10 imputations and model estimates combined using Rubin’s rules.(23) The frequency of missing data prior to imputation is provided in Supplementary Table S1. Multivariable logistic regression models were fitted to examine 1) the likelihood of receipt of CABG compared with PCI and 2) associated in-hospital and 30-day mortality in the COVID-19 period (with pre-COVID as reference), adjusting for the variables summarized in Appendix A. We report the association of COVID-19 period with the outcomes using odds ratios (OR) with corresponding 95% confidence intervals (CI). In order to estimate the adjusted probability of death in the CABG and PCI groups in both the pre-COVID and COVID time periods,
multivariable logistic regression models were performed with an interaction term between revascularisation strategy (PCI vs. CABG) and time period (pre-COVID vs. COVID), adjusting for the variables in Appendix A, followed by the margins command to generate adjusted probabilities of mortality in each group. Statistical analyses were performed using Stata 16 MP (College Station, TX).

**Ethical Approval**

The UK Secretary of State for Health and Social Care has issued a time limited Notice under Regulation 3 (4) of the NHS (Control of Patient Information Regulations) 2002 (COPI) to share confidential patient information. The study complies with the Declaration of Helsinki. This work was part of a work stream endorsed by the Scientific Advisory Group for Emergencies (SAGE), the body responsible for ensuring timely and coordinated scientific advice is made available to UK government decision makers. SAGE supports UK cross-government decisions in the Cabinet Office Briefing Room (COBR)) and by NHS England, which oversees commissioning decisions in the NHS, and NHS Improvement, which is responsible for overseeing quality of care in NHS hospitals.

**Results**

A total of 22,235 cases of revascularisation involving significant LM disease were recorded between 1st January 2017 and 19th August 2020, of which 62.9% (n=13,994) were PCI and 37.1% (n=8,241) were CABG.

**Procedural activity**

Overall, there was a decline in procedural activity for LM revascularisation during the pandemic, with an estimated total deficit of 1,354 cases between 1st March and 31st July 2020 compared with previous years’ (2017-2019) averages (Δ -48.8%), with the greatest decline observed in July 2020 (Δ-60.6%). *(Supplementary Table S2)* This was evident in both PCI
and CABG groups, with a significant decline in the 7-day rolling average number of procedures beginning at the start of UK-wide lockdown (23rd March 2020). (Figure 1)

Choice of revascularisation strategy

Pre-COVID, PCI accounted for 61.9% of all left main revascularisation procedures, whereas during the COVID period, this has risen to 77.6%. (Table 1) Compared with 2017, the odds of receipt of CABG over PCI increased in 2018 and 2019 (OR 1.85 95% CI 1.70, 2.03 and 1.46 95% CI 1.33, 1.61, respectively) but were similar in the start of 2020 before the COVID pandemic (January-February 2020 OR: 1.13 95% CI 0.95, 1.34, p=0.176). However, there was a decline in odds of receipt of CABG (vs. PCI) in the COVID period compared with the pre-COVID period (OR 0.46 95% CI 0.39, 0.53). (Figure 2, Supplementary Table S3)

Patient and procedural characteristics

Overall, patients undergoing PCI were older, more frequently male, more likely to be admitted electively and to receive PCI for an ACS indication compared with those undergoing CABG. (Table 1) Patients undergoing PCI also had a higher prevalence of left ventricular (LV) impairment (moderate or severely impaired) compared with CABG. However, all these differences were similar in the pre-COVID and COVID time periods (Table 1), as well as in individual year subgroups of the pre-COVID period (Supplementary Table S4). Patients undergoing CABG had a higher prevalence of smoking history, diabetes (only in the pre-COVID group), previous history of myocardial infarction (MI) and cerebrovascular accidents (CVA, including transient ischaemic attack and stroke), hypertension and peripheral vascular disease (PVD) compared with those undergoing PCI. Furthermore, patients undergoing CABG were at a higher risk of all-cause post procedure mortality compared with PCI, as evidenced by the Logistic EuroSCORE and PCI risk score. This pattern of differences, however, was consistent in the pre-COVID and COVID periods.
In terms of procedural characteristics, patients in the PCI group were more likely to be in cardiogenic shock at presentation in the pre-COVID and COVID time periods, whereas the CABG group were more likely to require circulatory support in the form of intra-aortic balloon pump or inotropes at any point during the admission.

Compared with the pre-COVID time period, patients undergoing PCI in the COVID time period were more likely to undergo a procedure via radial access (81.2% vs. 74.5%), using intravascular ultrasound (52.6% vs. 42.4%) and with drug eluting stents (DES; 92.0 vs. 90.1%).

Patients undergoing CABG in the COVID period were less likely to undergo concomitant valve surgery (7.0% vs. 11.5%) and more likely to have an on-pump CABG (85.5% vs. 93.3%) than in the pre-COVID period.

**In-hospital and 30-day mortality**

Overall, the crude rate of 30-day mortality after LM revascularisation declined over the study period (2017: 6.7% to March-August 2020: 5.7%). However, after adjustment, there was no difference in the odds of mortality after LM revascularisation over different time points when compared with 2017. (Table 2, Figure 3)

The unadjusted rates of in-hospital and 30-day mortality were higher in PCI than CABG in the pre-COVID period (6.5% vs. 2.2% and 8.4% vs. 2.5%, respectively) (Table 3), a pattern that was consistent in individual years of the pre-COVID period (Supplementary Table S5). However, only 30-day mortality was higher in PCI than CABG in the COVID period (6.5% vs. 3.0%) with no difference in in-hospital mortality between PCI and CABG (4.4% vs. 2.1%, p=0.062). (Table 3)

After adjustment for baseline patient and procedural characteristics, 30-day mortality was higher for PCI than CABG in the pre-COVID period (6.6% [6.2%, 7.0%] vs. 4.9% [4.4% vs. 5.5%]), primarily driven by higher post-discharge mortality (1.5% [1.3%, 1.8%] vs. 0.5%
[0.3%, 0.7%]) whereas no difference in in-hospital or 30-day mortality was observed between PCI and CABG in the COVID period. (Table 3, Figure 4)

No difference in in-hospital or 30-day mortality was found between the pre-COVID and COVID periods for each of the PCI and CABG groups (Table 4).

Discussion

The present study is the first to examine the choice of revascularisation strategy in patients with significant LM disease as well as postprocedural mortality, in a contemporary and unselected nationwide cohort during the COVID-19 pandemic. Several important findings can be concluded from our study. First, we find that the overall revascularisation volume for LM disease has significantly declined during the COVID period, with a deficit of more than 1,300 cases (~49% decline) between March and July 2020 compared with previous years’ averages for these months. While no other study has looked at this specific cohort, our findings are commensurate with the overall decline in activity observed during the pandemic for all cardiac procedures. (9,11,14,24,25) Second, we observe significant differences in the choice of revascularisation between the pre-COVID and COVID periods, with a shift towards greater PCI utilisation in the COVID period. This finding was consistent across different age groups. Although differences in patient characteristics were evident between PCI and CABG groups, these were largely similar in the pre-COVID and COVID periods. Finally, we show that 30-day mortality after LM revascularisation remained unchanged over the years. Importantly, we find that adjusted in-hospital and 30-day mortality within each revascularisation group (PCI and CABG) was similar in the pre-COVID and COVID periods. We also show that only 30-day mortality was higher with PCI compared with CABG in the pre-COVID period, but no difference in in-hospital or 30-day mortality between PCI and CABG were observed in the COVID period.
Significant LM coronary disease of prognostic importance due to the large myocardial territory it supplies and is considered a Class 1 indication for revascularisation. (1,6) Historically, CABG has been the first choice for LM revascularisation, with PCI recommended as an alternative in patients at a high risk of CABG-related mortality. However, in the last decade several large-scale studies have suggested non-inferiority of PCI as an alternative modality in patients with low or intermediate anatomical complexity, a recommendation that has recently been adopted in international guidelines. (2-8) However, is unclear whether the choice of LM revascularisation has changed since the start of the COVID-19 pandemic, which has overwhelmed healthcare systems and led to a decline in cardiac procedural activity. (9) CABG procedures in particular were logistically challenging, due to the need for ICU admission and prolonged hospitalisation compared with PCI.

This is the first study to look at the trend of revascularisation choice in patients with significant LM disease in a contemporary procedural cohort. We observe a rise in the uptake of CABG as the LM revascularisation strategy of choice (vs PCI) between 2017 to 2019, but no difference in odds of receipt of CABG vs. PCI was observed in the first two months of 2020. From March 2020, coinciding with the start of the COVID-19 pandemic, there was a significant shift towards PCI, with patients 54% less likely to receive CABG compared with the pre-COVID period, despite adjustment for differences in patient and procedural characteristics. This pattern that was consistent across all age groups. These findings are likely due to the strain on health services during the pandemic, with the prioritisation of ICU resources for critically unwell COVID-19 patients, meaning that many CABG cases were cancelled or deferred. Patients with prognosis-modifying lesions such as significant LM stenosis were more likely to undergo PCI instead of delayed CABG or no intervention at all. Delays in the safe reintroduction of cardiac surgery services due to insufficient COVID-19 testing capacity, lack of bed availability and the resurgence in COVID-19 case numbers, were likely to play a role.
in decision-making regarding revascularisation strategy, with a shift towards LM PCI, which is associated with shorter length of stay and even a same day discharge (26), to avoid further growth in CABG waiting lists. This is certainly in keeping with European Society of Cardiology guidance during the COVID-19, which recommended Heart Team discussions on hybrid revascularisation (PCI and CABG) or full PCI for patients whose interventions cannot be postponed. (27) As evidenced by our analysis, procedural activity has not recovered even after the lift of lockdown restrictions in early July 2020. While the observed change in choice of revascularisation strategy may have been prudent during the height of the pandemic, operational changes are required to restore procedural activity to pre-COVID levels, when decisions on the ideal revascularisation strategy were primarily based on patient-related and anatomical factors rather than availability of resources.

We observe a significant reduction in overall LM procedural activity, including PCI and CABG procedures, with a deficit of 1,300 cases between March and July 2020. However, 30-day mortality after LM revascularisation remains unchanged throughout the study period, even in the COVID period compared with pre-COVID, for both PCI and CABG procedures. While patient characteristics were largely similar in the pre-COVID and COVID periods, it is possible that unmeasured factors such as biological frailty and overall comorbidity burden may have been less prevalent among patients in the COVID period, reflecting a higher case selectivity by cardiologists and surgeons. Further, the increased use of IVUS for PCI cases in the COVID period may partially account for the lower mortality during that period, as shown in previous studies. (28) The increased use of IVUS may reflect the higher risk profile of patients being intervened on, who may have otherwise undergone CABG if it weren’t for the service pressures as a result of the COVID-19 pandemic but may also reflect that the decline in PCI volumes observed in the UK during the COVID pandemic resulting in less time pressures in the catheterisation laboratory that may facilitate the use of intravascular imaging.
Overall, these findings demonstrate a maintenance in quality of services during the pandemic despite operational changes and disruption of cardiology services. However, an important consideration should be given to patients who would have otherwise undergone LM revascularisation but were not prioritised due to the burden on health systems during the pandemic, or because of their shielding due to high risk of COVID-related death. There is limited data on the optimal timing of revascularisation in those with significant LM disease, with the available evidence being more than 30 years old. Nevertheless, given the significant myocardium that the LM portends, delays in LM revascularisation that have undoubtedly occurred due to COVID are likely to have increased the mortality rate significantly, particularly given that there is a deficit of more than 1,300 LM cases (>50% decline) between March and July 2020 compared with previous years’ averages.

**Strengths and Limitations**

First, while the British Cardiovascular Intervention Society NAPCI and British Cardiothoracic Society NACSA datasets capture many patient and procedural characteristics, these do not include measures of comorbidity such as Charlson or Elixhauser scores as well as frailty, which are important predictors of procedural mortality. It is possible that patients undergoing PCI were turned down for CABG following heart team discussions, owing to their significant frailty or comorbid burden, however, information on such discussions was not available, although this is the case in most national databases. Second, information regarding the overall procedural complexity, as measured by the SYNTAX score, was not available. Furthermore, significant proximal/ostial stenoses of the left anterior descending and left circumflex arteries, which are considered LM equivalents with equal prognostic significance to LM disease stenosis, are not captured in the NACSA database, meaning that they were not included in our analysis. Third, we were unable to follow up mortality for longer than 30 days post procedures so as to allow capture of all procedures up until 19th August 2020.
It is possible that longer-term follow up will demonstrate more pronounced differences in mortality between revascularisation strategies.

Conclusions

In our national analysis of a contemporary procedural cohort, we demonstrate that LM revascularisation has significantly declined during the COVID period, with a total deficit of more than 1300 cases compared to previous years’ averages and a shift towards PCI as the preferred revascularisation strategy. Adjusted in-hospital and 30-day mortality within each revascularisation group was similar in the pre-COVID and COVID periods, reflecting a maintenance in quality of outcomes following LM revascularisation despite the significant pressure on healthcare facilities during the pandemic. However, further measures are required to safely restore LM revascularisation activity, including PCI and CABG, to pre-COVID levels and deal with growing waiting lists to prevent long-term cardiovascular morbidity and mortality.

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Disclosure statement

The authors report no conflicts of interest, financial disclosures or relationship with the industry.

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Figures captions and legends:

**Figure 1.** Moving average of procedural activity for PCI and CABG procedures over the study period

**Legend:** UK-wide lockdown was introduced on 23rd March 2020; restrictions were lifted on 4th July 2020. CABG: coronary artery bypass graft surgery; PCI: percutaneous coronary intervention

**Figure 2.** Adjusted odds of receipt of CABG (reference is PCI) at different time points over the study period*

**Legend:** *Reference is year 2017; $P_{	ext{trend}} <0.001$

**Figure 3.** Adjusted odds of 30-day mortality after left main disease revascularization over the study period*

**Legend:** *Reference is year 2017

**Figure 4.** Adjusted mortality in PCI and CABG groups in the pre-COVID and COVID periods
Legend: CABG: coronary artery bypass graft surgery; PCI: percutaneous coronary intervention

Supplementary Figure 1. Flow diagram