**Coronary perforation complicating percutaneous coronary intervention in patients with a history of coronary artery bypass surgery: an analysis of 309 perforation cases from the British Cardiovascular Intervention Society database**

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**Abstract**

**Background:** The evidence base for coronary perforation (CP) occurring during percutaneous coronary intervention in patients with a history of bypass surgery (PCI-CABG) is limited and the long-term effects unclear. Using a national PCI database, the incidence, predictors and outcomes of CP during PCI-CABG were defined. **Methods and Results:** Data was analysed on all PCI-CABG procedures performed in England and Wales between 2005 and 2013. Multivariate logistic regressions and propensity scores were used to identify predictors of CP and its association with outcomes. During the study period, 309 coronary perforations were recorded during 59,644 PCI-CABG procedures with the incidence rising from 0.32% in 2005 to 0.68% in 2013 (p<0.001 for trend). Independent associates of perforation in native vessels included age, chronic occlusive disease intervention, rotational atherectomy use, number of stents, hypertension and female gender. In graft PCI, predictors of perforation were history of stroke, NYHA class, and number of stents used. In-hospital clinical complications including Q-wave MI (2.9 vs. 0.2%, p<0.001), major bleeding (14.0 vs. 0.9%, p<0.001), blood transfusion (3.7 vs. 0.2%, p<0.001), and death (10.0 vs. 1.1%, p<0.001) were more frequent in patients with coronary perforation. A continued excess mortality occurred after perforation, with an odds ratio for 12-month mortality of 1.35 for perforation survivors compared to matched non-perforation survivors without a CP (p<0.0001). **Conclusions:** Coronary perforation is an infrequent event during PCI-CABG but is closely associated with adverse clinical outcomes**.** A legacy effect of perforation on 12-month mortality was observed.

**Keywords**

Coronary perforation, coronary artery bypass surgery, percutaneous coronary intervention, complications, national database, tamponade

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**INTRODUCTION**

Coronary perforation (CP) is a rare but serious complication of percutaneous coronary intervention (PCI) with a previously estimated incidence of ~0.4%.1 Although there are several published series of coronary perforation, the rarity of the complication has previously been limited to small numbers of cases derived from single centre experience.2-8 Most recently we have published a national analysis of temporal trends, predictors and outcomes of coronary perforations in the United Kingdom and reported that previous coronary artery bypass surgery (CABG) was an independent associate of coronary perforation during PCI.9 Given the association between coronary perforation and PCI in patients with a history of CABG surgery (PCI-CABG), a greater understanding of coronary perforation in this patient cohort is therefore warranted.

In patients with prior CABG surgery, it has been assumed that coronary perforations might be less likely to cause cardiac tamponade due to a potential protective role of pericardial adhesions and frequent removal of part of the pericardium. However, several small case series illustrate a range of complications associated with coronary perforation, and demonstrate that it is not always a benign event. Rapid blood extravasation has been reported to be associated with loculated collections that may be difficult to drain and compression a variety of cardiac structures.10 Other complications of a perforation in such patients include rupture of blood into lung tissue with haemoptysis, or into the pleural space with a massive haemothorax.11 Indeed, in one literature review the 30-day mortality was as high as 22%.12 Finally, previous publications have not stratified their analyses according to the site of perforation, and whether outcomes are different in cases where a perforation occurs in the native vessel or the bypass graft.

Therefore, the primary objective of the present study was to define the incidence and temporal trends of coronary perforation associated with PCI in patients with a history of by coronary bypass surgery (PCI-CABG) through analysis of a national PCI database, with stratification according to whether the site of perforation was a native vessel or a bypass graft. Secondary objectives were to describe factors independently predictive of coronary perforation in this cohort and to define the impact of this complication on short and long-term clinical outcomes.

**METHODS**

*Study design, setting and participants*

We retrospectively analysed prospectively gathered national data from all patients with history of CABG surgery who underwent percutaneous coronary intervention (PCI-CABG) in England and Wales between January 2005 and December 2013. During the study period, 64,117 were recorded as undergoing PCI with a prior CABG history. Patients with a missing field for coronary perforation in the database (n=4,473) were excluded from the analysis leaving a final study population of 59,644 patients. The study was approved by review board of the National Institute of Clinical Outcomes Research and by the Healthcare Quality Improvement Partnership (HQIP).

*Setting, data source, and study size*

Data on PCI practice in the United Kingdom were obtained from the British Cardiovascular Intervention Society (BCIS) dataset that records this information prospectively and publishes this information in the public domain as part of the national transparency agenda.13 The data collection process is overseen by The National Institute of Cardiovascular Outcomes Research (NICOR) (http://www.ucl.ac.uk/nicor/) with high levels of case ascertainment. In 2013, 98.6% of all PCI procedures performed in the National Health Service hospitals in England and Wales (www.bcis.org.uk/) were recorded on the database. The BCIS-NICOR database contains 113 clinical, procedural and outcomes variables with approximately 80,000 new records added each year. The participants of the database are tracked by the Medical Research Information Services for subsequent mortality using the patients' NHS number (a unique identifier for any person registered within the NHS in England and Wales). Although the BCIS dataset is UK wide, only patients from England and Wales have mortality tracked by the Office of National Statistics, and so the current analysis is restricted to patients from these 2 countries.

*Study definitions*

We analysed all recorded PCI-CABG procedures that were undertaken in England and Wales between January 1st, 2005 and December 31st, 2013. Coronary perforation was defined as evidence of extravasation of dye or blood from the coronary artery during or following the interventional procedure. This was determined either by angiographic appearances consistent with dye outside of the vessel lumen or by echocardiographic evidence of a pericardial effusion. Patients were categorised according to whether they sustained a coronary perforation during PCI-CABG or not. Study definitions were used as in the BCIS-NICOR database. Specifically, pre-procedural renal failure is defined as any one of the following: creatinine >200µmol/l, renal transplant history, or dialysis. The outcomes examined were in-hospital mortality, 30-day mortality, 1-year mortality, 5-year mortality, in-hospital re-infarction, in-hospital emergency cardiac surgery, in-hospital cardiac tamponade, in-hospital stroke and in-hospital major bleeding (defined as gastrointestinal bleed, intra-cerebral bleed, retroperitoneal hematoma, blood or platelet transfusion, or an arterial access site complication requiring surgery). Complex CTO techniques were defined as dual arterial access, rotational/laser atherectomy, penetration catheter, micro-catheter, Crossboss/Stingray balloon, and intra-vascular ultrasound use.

*Data analyses*

We examined the baseline and procedural characteristics of participants by coronary perforation status and native vessel or graft PCI. We tested for associations between each categorical variable and coronary perforation using a Chi-squared test, and for continuous variables we used one-way analysis of variance. We then performed separate multivariate analyses of the predictors of perforation by vessel type using multivariate logistic regression to investigate the influence of variables that have the potential for being included in the linear component of a proportional hazard model. We selected a final model for each outcome by using forward stepwise variable selection and an inclusion criterion of p<0.1. Variables included in these analyses were age, gender, body mass index (BMI), Canadian Cardiovascular Society (CCS) angina class, New York Heart Association (NHYA) class, previous myocardial infarction (MI), history of hypertension, history of stroke, glycoprotein inhibitor (GPI) use, dual arterial access, use of rotational atherectomy, micro-catheter use, chronic total occlusion (CTO) presence, CTO attempted, right coronary intervention, and trainee operator. Final model selection was done as follows: we first imputed missing data on baseline covariate using multiple imputations with chained equation (missing data points are presented in Supplementary Table 1). To examine the associates of perforation and test if those associates show a trend over time (from 2006 to 2013), a Cochran-Armitage test for trend was used. Individual logistic regressions were done on the imputed data set for each of the MACE events according the perforation status of the patients to quantify the independent association between perforation and outcomes.

Finally, from the subset of patients who survived up to 30 days, we explored the association between perforation at procedure and mortality at 12-months a time to event analysis was performed using Kaplan-Meier curves, log-rank tests and Cox proportional hazard model to estimate the corresponding hazard ratio. To adjust for baseline imbalances, we performed a propensity score analysis in order to balance for important covariates that might bias estimates for causal inferences. The following variables that were associated with 12-month mortality in the 30-day survivors were used in the propensity score analysis: gender, age at procedure, NHYA status, BMI previous MI, previous CABG, diabetes, baseline disease severity, hypertension, smoking status, renal insufficiency, and Q wave on ECG. The propensity scores for each patient was derived using the inverse probability of treatment weight (IPTW). More precisely, one estimates the probability that a particular patient is assigned to one of the two groups as a function of that individual's covariates (the propensity score). Each individual observation was then given a weight equal to the inverse of this propensity score to create two pseudo-populations of exposed and unexposed patients who now represent what would have happened to the entire population under those two "treatment" conditions. The advantage of this method is that it is inclusive as it uses all patients in a study, therefore no loss of sample occurs as in other conditioning methods such as matching or stratification. We also normalized the weights by dividing them by the mean weight. Those weights were then used to derive weighted Kaplan-Meier curves and weight hazard ratios.

**RESULTS**

*Incidence and baseline demographics during PCI-CABG by perforation status and vessel type*

Patients with a history of CABG had significantly greater comorbidity than patients without previous CABG (Table 1). The proportion of patients undergoing PCI with a history of CABG surgery increased progressively during the study period from 7.7% in 2005 to 10.2% in 2013 (Figure 1A, p<0.001 for trend). A total of 309 coronary perforations were recorded during 59,644 PCI-CABG procedures (overall incidence 0.52%). There was no significant difference in perforation incidence between native vessel PCI and graft PCI (0.51 vs. 0.49% respectively, p=0.787). Additionally, the annualised rate of coronary perforation rose progressively from 0.32% in 2005 to 0.68% in 2013 (Figure 1B, p=0.001 for trend). Baseline characteristics of patients with and without perforation categorised by native vessel or graft PCI are presented in Table 2. Although coronary perforation was significantly more likely in stable angina PCI to native vessels (69.5 vs.60.3%, p=0.008), it was less likely in graft PCI (30.1 vs. 42.5%, p=0.031). The annualised patient demographics associated with coronary perforation are displayed in Figure 2 and illustrates an increase in case complexity during the study period.

*Procedural variables during PCI-CABG by perforation status and vessel type*

The procedural variables for patients with and without coronary perforation by vessel type are presented in Table 3. Baseline disease complexity was associated with coronary perforation in native vessels with a non-trainee primary operator, dual arterial access, CTO intervention rotational atherectomy, and micro-catheter use all more frequently observed when perforation occurred. In graft intervention, only use of rotational atherectomy and number of stents were associated with an increased risk of perforation. Potent dual anti-platelet therapy and glycoprotein inhibitor use were not associated with an increased risk of coronary perforation. Perforation was significantly more likely to occur as complex PCI strategies (dual access, rotational or laser atherectomy and micro-catheters) were used individually (Figure 3 left and centre panels) or in combination with a significant trend between zero and three or more strategies (Figure 3 right panel).

*Predictors of coronary perforation during PCI-CABG*

Using multivariate analyses, covariates found to be associated with native vessel coronary perforation are presented by vessel in Table 4. The patient-related factors associated with an increased risk of perforation were age per year (odds ratio (OR) 95% confidence intervals 1.04 [1.02-1.06], p<0.001), hypertension history (OR 2.31 [1.40-3.80], p=0.001), and female gender (OR 1.63 [1.07-2.50], p=0.024). Several procedural factors were strongly associated with an increased risk of native vessel perforation including CTO intervention (OR 3.48 [2.30-5.27], p<0.001) and rotational atherectomy use (OR 2.25 [1.29-3.93], p=0.004). In contrast, graft perforation appeared to be more unpredictable with only history of stroke (OR 1.56 [1.17-2.10], p=0.003), NHYA class (OR 2.14 [1.18-3.92], p=0.014), and number of stents (OR 1.49 [1.01-1.36], p<0.001) associated with an increased risk (Table 4).

*Clinical outcomes by perforation status*

All immediate procedural complications including cardiogenic shock induction, heart block, coronary dissection and major side branch occlusion were more likely when a coronary perforation occurred (Table 5) and were similar between native vessel and graft PCI (Supplementary Table 2). Tamponade leading to haemodynamic compromise occurred in 10.0% of patients (9.8% for native vessel PCI and 12.5% for graft PCI, p=0.576) although emergency reparative cardiac surgery was undertaken rarely (1.5%). The occurrence of tamponade after a perforation appears unpredictable with only femoral artery access (OR 4.117, 95% CI 1.062-15.957, p=0.041) and consultant operator (OR 4.27, 95%CI 1.17-15.6, p=0.028) associated with a higher risk.

Overall, coronary complications occurred in 14.2% of PCI-CABG procedures with a perforation and 3.6% without (p<0.001). In-hospital clinical complications including Q-wave MI (2.9 vs. 0.2%, p<0.001), major bleeding (14.0 vs. 0.9%, p<0.001), blood transfusion (3.7 vs. 0.2%, p<0.001), renal failure (1.1 vs. 0.1%, p<0.001) and death (10.0 vs. 1.1%, p<0.001) were more frequent in patients with coronary perforation.

Mortality at all time points was greater in those patients with coronary perforation (Table 5) and was similar between native vessel and graft PCI (Supplementary Table 2). The 30-day mortality in patients experiencing a coronary perforation during graft PCI was similar to that observed in patients experiencing a perforation during native vessel PCI (10.8 vs. 10.7%, p=0.926). Temporal changes in mortality are displayed in Figure 3 and demonstrate a significant reduction during the study period (p=0.005). Using multiple logistic regression analyses, the adjusted odds of clinical outcomes are presented in Table 6 and indicate a significant impact of coronary perforation during PCI-CABG on all short and long term outcomes.

An excess of 12-month mortality in 30-day survivors for patients with and without perforation was associated with increased age and baseline comorbidity (Supplemental Table 3). Figure 4 (panel A) illustrates the Kaplan Meier plots for mortality by perforation status to 12-months confirming the significant impact of a perforation on patient survival. Figure 4 (panel B) illustrates Kaplan Meier plots for mortality using a landmark analysis for perforation survivors from 30 days to 12-months compared with propensity matched non-perforation survivors. Using propensity scores for each patient derived from the inverse probability of treatment weight, a legacy effect (i.e. a continued impact of perforation on mortality) was evident with a hazards ratio for 12-month mortality of 1.35 compared to those matched patients without a coronary perforation (p<0.001).

**DISCUSSION**

This analysis revealed an overall incidence of coronary perforation in patients undergoing PCI with prior CABG surgery of 0.52%, a rate higher than observed in a more general PCI population.9 This likely reflects the complexity of the case mix with advanced patient age and high rates of CTO intervention in patients with a history of CABG. Second, the presence of perforation in such patients was associated with higher morbidity and mortality, irrespective of whether the perforation occurred in a native vessel or a bypass graft. Third, the annual incidence of perforation increased significantly during the study period with perforation being associated with increasing age, history of hypertension, and previous MI or stroke.

Procedure complexity (likely driven by coronary disease complexity) appeared to predict perforation in native vessels with rotational atherectomy use and CTO intervention significantly more likely to be present when a perforation occurred. In contrast, perforation in graft vessels appeared unpredictable and less closely associated with procedural complexity, a finding which is important in itself. The association between CVA and perforation in vein grafts is a novel finding and it is conceivable that a previous stroke is a predictor of more advanced vascular disease and calcification, and this might lead to a greater chance of perforation during PCI. However, these associations are a novel finding, and are thus hypothesis generating and worthy of further study,

These data dispel the myth that perforation in patients with previous CABG is a benign event because of the presence of pericardial adhesions and the absence of a closed pericardial sac. However, in the current study although tamponade was lower than reported in a previous generalized PCI population (16.1%), it still occurred in over 10% of the population without a significant difference between graft and native vessel PCI.9 There are several possible explanations for this observation. Firstly, although the pericardium is often not repaired after CABG, this is not a universal approach. Particularly in younger patients, the pericardium may be closed to facilitate easier future redo surgery if required.14 Also a closed pericardium has been reported to paradoxically reduce post-operative tamponade after CABG surgery by protecting the heart from extra-pericardial bleeding meaning that some surgeons choose to repair the pericardium.15,16 There are also several case reports of localized effusions compressing a variety of cardiac structures. Loculated collections of blood after coronary perforation have been reported to compress the atria, the right ventricle or the pulmonary artery with rapid haemodynamic collapse.10,17 In practice, although pericardiocentesis of a global effusion in a closed pericardial sac is far from straightforward, percutaneous drainage of a loculated effusion is extremely challenging and high risk. Therefore, the management of pericardial tamponade in post CABG surgery patient is difficult and associated with poor outcomes. Additionally, unrestrained major haemorrhage into other body cavities such as the pleural cavity can occur with catastrophic outcomes.11,18 Finally, the observation that tamponade was an unpredictable event is relevant and reiterates the importance of early and proactive management of patients who experience a perforation.

All clinical end-points were significantly more likely to occur in patients experiencing a coronary perforation. There was a 10-fold increase in in-hospital mortality and a 7-fold increase in 30-day mortality. For both end-points, the magnitude of the effect of a perforation was greater than observed in a previous cohort of all patients (with or without CABG history) with a perforation.9 This may reflect the high frequency of comorbidity observed in patients with a history of CABG which includes advanced age, and high rates diabetes, vascular and renal disease. However, despite increases in patient and procedural complexity, it is encouraging to observe that mortality declined steadily during the study period. The avoidance of surgical repair is clearly highly desirable, and the utilisation of covered stents, as well as a wider appreciation of techniques such as “ping-pong” guides, embolisation coils, distal fat or thrombus embolisation to treat wire tip perforations, have facilitated improved acute management of perforations and improved survival.19-25 However despite this, the incidence of major adverse events in patients with coronary perforation was high and these data are a reminder that whilst coronary perforation during PCI is a relatively rare event, its occurrence is associated with poor outcomes.

A continued excess mortality occurred in patients with a perforation after 30-days in patients matched with patients without a perforation. There are several plausible reasons that might explain this observation. Firstly, the number of successful lesions was significantly less in cases complicated by perforation. Residual disease burden has been closely correlated with adverse outcomes after PCI and thus one explanation for the excess mortality after perforation may be the presence of on-going ischaemia due to untreated coronary stenosis.26,27 Other mechanistic possibilities for the observed effect include side branch loss with peri-procedural MI,28 access site complications,29 major bleeding,30-31 and transfusion,32 all of which were significantly more common with perforation and individually each are associated with excess 12-month mortality. Finally, covered stent use may also be associated with poor 12-month outcomes. Small series have reported high rates of stent thrombosis, restenosis and mortality with their use.33

**LIMITATIONS**  
The BCIS database does not differentiate between coronary perforations resulting from guide-wire and perforations due to balloon or stent inflation. Additionally, the database does not record the Ellis classification of coronary perforation. Therefore, a sub-stratification by perforation severity was not possible. In addition, the BCIS database does not record use of other treatment strategies such covered stents, pericardial drains or embolisation techniques. Although operator level data is now available in the CCAD database, it has only been available for the most recent 2 years. Therefore, it was not included in the analysis. However, it seems unlikely that there is a centre specific effect that is independent of other procedural characteristics. Finally, whilst we have attempted to adjust for differences in baseline covariates/clinical characteristics, there remains the possibility of residual confounding which might in part contribute to the findings of the study.

**CONCLUSIONS**

Coronary perforation is an infrequent event during PCI in patients with prior CABG but has a significant impact on morbidity and mortality. A legacy effect of perforation on 12-month mortality was observed.

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**CONFLICTS OF INTEREST**

There are no conflicts of interest for any authors relevant to this work.

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**FIGURE LEGENDS**

Figure 1: A) Annualised percentage of patients undergoing PCI in England and Wales with a history of coronary artery bypass surgery (CABG), p<0.001 for trend; B) Annualised rates of coronary perforation rates in patients with a history of CABG, p=0.001 for trend.

Figure 2: Baseline and procedural characteristics associated with perforation in patients undergoing PCI with a prior CABG plotted over time (2005 to 2013); p<0.001 for all trends.

Figure 3: Left and centre panels - incidence of coronary perforation indexed for complex strategy (dual vs. single arterial access, use or not of rotational atherectomy, use or not of laser atherectomy and use or not of a micro-catheter), p value for comparison within each strategy; Right panel – incidence of coronary perforation with number of complex PCI strategies used (dual access, micro-catheter, laser or rotational atherectomy, penetration catheter, IVUS or CrossBoss), p value for trend.

Figure 4: Annualised mortality for patients with coronary perforation during PCI in patients with a history of CABG 2005-2013 (p=0.005 for trend).

Figure 5: A) Unadjusted Kaplan Meier plots for mortality by perforation status to 12-months; B) IPTW adjusted Kaplan Meier plots for mortality by perforation status for perforation survivors from 30 days to 12-months compared to non-perforation survivors from 30-days to 12-months.