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ORIGINAL STUDIES

The impact of coronary perforation in percutaneous interventions involving the left main stem coronary artery in the United Kingdom 2007–2014: Insights from the British Cardiovascular Intervention Society database

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Abstract

Background: Percutaneous coronary intervention (PCI) is increasingly utilized for treatment of coronary disease involving the unprotected left main stem (ULMS). However, no studies to date have examined the outcomes of such interventions when complicated by coronary perforation (CP).

Methods: Using the British Cardiovascular Intervention society (BCIS) database, data were analyzed on all ULMS-PCI procedures complicated by CP in England and Wales between 2007 and 2014. Multivariate logistic regressions were used to identify predictors of ULMS CP and to evaluate the association between this complication and outcomes.

Results: During 10,373 ULMS-PCI procedures, CP occurred more frequently than in non-ULMS-PCI (0.9 vs. 0.4%, $p < .001$) with a stable annual incidence. Covariates associated with CP included number of stents used, female gender, use of rotational atherectomy and chronic total occlusion (CTO) intervention. Adjusted odds of adverse outcomes for ULMS-PCI complicated by CP were higher for peri-procedural complications including cardiogenic shock, tamponade, side-branch loss, DC cardioversion, in-hospital major bleeding, transfusion requirement, and peri-procedural myocardial infarction. There were also significantly increased odds for in-hospital major adverse cardiac events (MACCE, OR 8.961, 95% CI [4.902–16.383]) and 30-day mortality (OR 5.301, 95% CI [2.741–10.251]).

Conclusions: CP is an infrequent event during ULMS-PCI and is predicted by female gender, rotational atherectomy, CTO interventions or number of stents used. CP was associated with significantly higher odds of mortality and morbidity, but at rates similar to previously published all-comer PCI complicated by CP.

KEYWORDS

complications, left main stem, outcomes, percutaneous coronary intervention, perforation

Hussain I. Hussain and Majd B. Protty contributed equally to this study.

1 | INTRODUCTION

Left main stem (LMS) coronary artery stenosis is associated with significant morbidity and mortality and has traditionally been treated by coronary artery bypass grafting (CABG).[1] Recently, however, there has been an increasing amount of evidence emerging in favor of utilizing percutaneous coronary intervention (PCI) in patients with unprotected LMS disease unprotected left main stem (ULMS-PCI).[2] This has been the result of advancements in the PCI field, which saw the rise of using drug-eluting stents, the precision of intravascular imaging and the utility of risk stratification tools to refine patient selection.[1]

Coronary perforation (CP) is a rare but serious complication of PCI which has been shown to have an incidence of ~0.4% of all procedures.[3] The rate of perforations complicating ULMS interventions has been reported to be in the region of 1.2% from single-center experience.[4] However, the literature surrounding ULMS perforation, its predictors and likely outcomes are very limited.

Studies examining predictors of perforation in all-comer PCI have suggested that increasing age, female gender, chronic total occlusion (CTO) intervention, number and length of stents used, and rotational atherectomy are associated with an increased rate with perforation.[3,5] Overall, perforation was observed to lead to higher rates of 30-day mortality.[3,5] Despite this, it is unclear whether these predictors and outcomes apply to ULMS-PCI complicated by perforation.

Therefore, the primary objective of this study was first to define the incidence, temporal trends, predictors, and outcomes of perforation associated with ULMS-PCI through analysis of the British Cardiovascular Society (BCIS) national PCI database.

2 | METHODS

2.1 | Study design, setting, and participants

We retrospectively analyzed national data from all patients undergoing ULMS-PCI in England and Wales between January 2007 and December 2014. During the study period, a total of 10,373 patients underwent ULMS-PCI. Patients were excluded if CP status was not recorded. The study was approved by review board of the National Institute of Clinical Outcomes Research and by the Healthcare Quality Improvement Partnership (HQIP).

2.2 | Setting, data source, and study size

Data on PCI practice in the United Kingdom were obtained from the BCIS data set that records this information prospectively and publishes this information in the public domain as part of the national transparency agenda.[6]

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. The BCIS-NICOR database contains 121 clinical, procedural and outcomes variables, and in 2014, 98.6% of all PCI procedures performed in the National Health Service (NHS) hospitals in England and Wales (www.bcis.org.uk/) were recorded on the database with approximately 100,000 new records currently added each year. The accuracy and quality of the BCIS data set has previously been ascertained.[7]

Entry of all PCI procedures by UK interventional operators is mandated as part of professional revalidation. The participants of the database are tracked by the Medical Research Information Services for subsequent mortality using the patients' National Health Service (NHS) number (a unique identifier for any person registered within the NHS in England and Wales). Although the BCIS data set is UK wide, the participants of the database are tracked by linkage with life status information held by the Office of National Statistics (ONS) using each patient's unique NHS number, and therefore only patients from England and Wales have mortality data available.

2.3 | Study definitions

We analyzed all recorded ULMS-PCI procedures that were undertaken in England and Wales between January 1, 2007 and December 31, 2014. CP was defined as in the BCIS guidance document as evidence of extravasation of dye or blood from any coronary artery during or following an interventional coronary procedure. Other study definitions were used as in the BCIS-NICOR database. Specifically, preprocedural renal failure is defined as any one of the following: creatinine >200 μmol/L, renal transplant history, or dialysis. Pre- or post-PCI disease severity was defined as a stenosis ≥50% in the case of the left main artery. Intravascular imaging was a combination of intravascular ultrasound and optical coherence tomography. An access site complication was defined as either a false aneurysm, hemorrhage (without hematoma), hemorrhage with delayed hospital-discharge, retroperitoneal hematoma, arterial dissection, or any access site complication requiring surgical repair. The clinical outcomes examined were in-hospital mortality, in-hospital MACCE (defined as a combination death, peri-procedural stroke, or peri-procedural myocardial infarction after PCI), in-hospital major bleeding (defined as either gastrointestinal bleed, intra-cerebral bleed, retroperitoneal hematoma, blood or platelet transfusion, access site hemorrhage, or an arterial access site complication requiring surgery), in-hospital reinfarction, in-hospital emergency cardiac surgery, tamponade, and 12-month mortality.

2.4 | Data analyses

The study flow is illustrated in Figure S1. Procedures with a protected LMS or missing LMS protection status were excluded as were procedures where the perforation status was blank. Statistical analysis was performed using the R coding environment (Open Source, version 3.5.1). Multiple imputations were carried out using the *mice* package to reduce the potential bias from missing data, assuming missing at random mechanisms. We used chained equations to impute the data for all variables with missing information and generated 10 data sets

to be used in the analyses. We examined the baseline and procedural characteristics of participants by CP status. We explored crude baseline comorbidities using a Chi-squared test for categorical variables and the Wilcoxon-Mann–Whitney test for continuous variables.

A multiple logistic regression model was developed to identify variables associated with CP. The potential predictor variables in the model included age, body mass index (BMI), sex, smoking, hypertension, previous stroke, peripheral vascular disease, renal disease, previous MI, EF < 30%, previous PCI, diabetes, number of vessels diseased at baseline, CTO attempted, number of stents used, STEMI, Q wave on ECG, GPIIBIIIA inhibitor use, clopidogrel, prasugrel, ticagrelor, bivalirudin, radial access, dual access, largest balloon/stent, longest balloon/stent, vessels/lesions attempted, in-stent restenosis attempted, thrombectomy, rotational atherectomy, imaging, operator status, penetration catheter, laser atherectomy, and micro-catheter use.

To examine the influence of perforation on ULMS-PCI outcomes, we built on and included the previously described baseline model to investigate the independent odds of shock, tamponade, cardioversion, dissection, side branch loss, slow flow phenomenon, gastrointestinal bleeding, transfusion, in-hospital major bleeding, peri-procedural myocardial infarction, arterial complication, acute kidney injury, in-hospital MACCE, in-hospital, 30 day, and 12 month death.

3 | RESULTS

3.1 | Incidence of CP and baseline demographics during ULMS-PCI by perforation status

Crude numbers of ULMS-PCI increased significantly during the study period, as did ULMS-PCI activity of as a percentage of the total PCI (increasing from 2.0 to 4.1%, $p < .001$ for trend, Figure 1a/b). During the study period, a total of 10,373 patients underwent ULMS-PCI for any indication, of whom 96 (0.9%) experienced CP. The frequency of ULMS perforation was higher than in non-ULMS-PCI (0.9 vs. 0.4%, $p < .001$). The total number of ULMS-PCI increased from 583 in 2007 to 2,030 in 2014 with a stable rate of perforation (Figure 1c). The baseline characteristics of ULMS-PCI patients with and without CP are presented in Table 1. CP was associated with increasing patient age, female sex, hypertension, and number of diseased vessels at baseline ($p < .05$, unadjusted).

3.2 | Procedural variables during ULMS-PCI by perforation status

The procedural variables for patients with and without CP by vessel type are presented in Table S1. ULMS-PCI cases with perforation were associated with more vessels and lesions attempted, CTO intervention, thrombus aspiration, rotational atherectomy, micro-catheter use, and the use of more stents during the procedure ($p < .05$, unadjusted).

3.3 | Predictors of CP during ULMS-PCI in England and Wales 2007–2014

Using multivariate analyses, only a limited number of covariates were found to be associated with CP during ULMS-PCI. After adjusting for baseline comorbidities, the only patient-related factor significantly associated with an increased incidence of perforation was female gender (odds ratio [OR] 1.887, 95% confidence intervals [CIs] [1.134–3.141]).

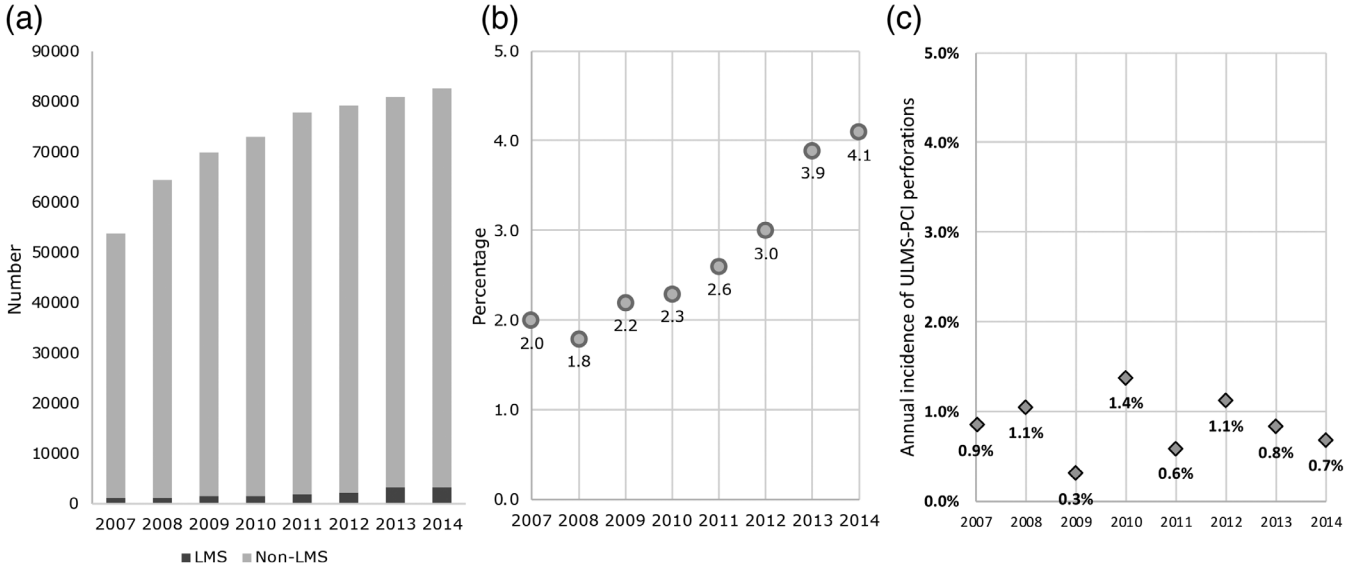

FIGURE 1 Trends in LMS-PCI performed in England and Wales 2007–2014. (a) Crude numbers of LMS (dark gray bars) and nonLMS-PCI (light gray bars); (b) percentage of total PCI performed represented by LMS-PCI ($p < .001$ for trend); (c) percentage of ULMS-PCI complicated by perforations relative to all ULMS-PCI ($p = .178$, not significant, for trend)

TABLE 1 Baseline participant characteristics by coronary perforation status in patients undergoing LMS-PCI in England and Wales 2007–2014

Variables	Not perforated (*n* = 10,277)	Perforated (*n* = 96)	*p* value
Age (years), ±*SD*	70.2 ± 11.9	73.8 ± 10.4	.004
Female, no. (%)	2,952 (28.8)	38 (39.6)	.027
Smoker, no. (%)	5,696 (61.2)	50 (56.8)	.466
BMI (kg/m^2), ±*SD*	28.2 ± 12.8	28 ± 4.6	.480
Hypertension, no. (%)	6,141 (62.8)	65 (73.9)	.043
Diabetes, no. (%)	2,418 (24)	23 (25.6)	.826
Previous MI, no. (%)	3,718 (37.6)	36 (39.6)	.783
Previous stroke, no. (%)	733 (7.5)	11 (12.5)	.118
Peripheral vascular disease, no. (%)	1,080 (11)	13 (14.8)	.340
Q wave on ECG, no. (%)	1,232 (12.8)	5 (5.5)	.054
Renal disease, no. (%)	619 (6.3)	6 (6.7)	1.000
Creatinine (±mol/L), ±*SD*	107.8 ± 75.4	99.4 ± 38.8	.859
Previous PCI, no. (%)	2,725 (27)	21 (23.1)	.471
LVEF <30%, no. (%)	813 (12.6)	8 (10.7)	.744
Cardiogenic shock, no. (%)	0.0 (0.0)	0.0 (0.0)	—
ST elevation presentation, no. (%)	1,010 (9.8)	6 (6.2)	.307
Clopidogrel	7,637 (89.2)	74 (85.1)	.288
Prasugrel	314 (3.7)	2 (2.3)	.686
Ticagrelor	615 (7.2)	10 (11.5)	.184
Warfarin, no. (%)	134 (1.4)	0.0 (0.0)	—
No. of vessels diseased at baseline, ±*SD*	2.0 ± 1.0	2.3 ± 1.0	.035
Number of procedures per year (%)			
2007	578 (99.1%)	5 (0.9%)	1.000
2008	656 (98.9%)	7 (1.1%)	.884
2009	948 (99.7%)	3 (0.3%)	.057
2010	994 (98.6%)	14 (1.4%)	.152
2011	1,326 (99.4%)	8 (0.6%)	.239
2012	1,578 (98.9%)	18 (1.1%)	.446
2013	1,667 (99.2%)	14 (0.8%)	.773
2014	2016 (99.3%)	14 (0.7%)	.270

Abbreviations: BMI, body mass index; LMS, left main stem; MI, myocardial infarction; PCI, percutaneous coronary infection; SD, standard deviation.

Procedural variables significantly associated with an adjusted increased risk of perforation were number of stents used (OR 1.390, 95% CI [1.166–1.656]), number of CTO attempted (OR 2.036, 95% CI [1.350–3.072]) and use of rotational atherectomy (OR 2.494, 95% CI [1.305–4.765]). The full model with all covariates can be seen in Table S2.

3.4 | Clinical outcomes of ULMS-PCI by perforation status

The unadjusted incidence of procedural complications associated with CP in ULMS-PCI is shown in Table S3. Complications crudely associated with CP were shock, tamponade, cardioversion, major side branch loss, more residual disease, transfusion, in-hospital major bleeding, peri-procedural MI, and in-hospital MACCE ($p < .05$). Unadjusted mortality rates at 30 days, at 12 months and in-hospital were higher in cases where perforation occurred.

Multivariate logistic modeling was used to adjust outcomes for baseline comorbidities (Table 2). This showed that perforation complicating ULMS-PCI inferred significantly higher odds of in-hospital major adverse cardiac events (MACCE, OR 8.961, 95% CI [4.902–16.383]), 30-day mortality (OR 5.301, 95% CI [2.741–10.251]), and 12-month mortality (OR 2.412, 95% CI [1.325–4.390]). There were also higher odds of peri-procedural complications, such as shock, tamponade, DCCV, side-branch loss, in-hospital major bleed, transfusion requirement, and peri-procedural MI ($p < .05$).

TABLE 2 Outcomes by coronary perforation status in patients undergoing LMS-PCI in England and Wales 2007–2014

Variable	Odds ratio	Lower CI	Upper CI	*p* value
Shock induced by procedure	14.884	6.540	33.873	<.001
DCCV	4.427	1.136	17.247	.032
Dissection	1.092	0.487	2.448	.830
Side-branch loss	13.172	5.846	29.677	<.001
Slow flow	1.781	0.387	8.202	.459
Arterial complication	1.211	0.247	5.944	.813
Transfusion	8.648	2.852	26.227	<.001
GI bleed	7.992	0.921	69.365	.059
In-hospital major bleed	30.019	15.158	59.450	<.001
Peri-procedural MI	9.019	3.380	19.025	<.001
Acute kidney injury	2.190	0.266	18.029	.466
In-hospital death	8.633	4.097	18.192	<.001
In-hospital MACCE	8.961	4.902	16.383	<.001
30-day mortality	5.301	2.741	10.251	<.001
12-month mortality	2.412	1.325	4.390	.004

Abbreviations: CI, confidence interval; LMS, left main stem; MACCE: major adverse cardiac and cerebrovascular events; MI, myocardial infarction; PCI, percutaneous coronary infection.

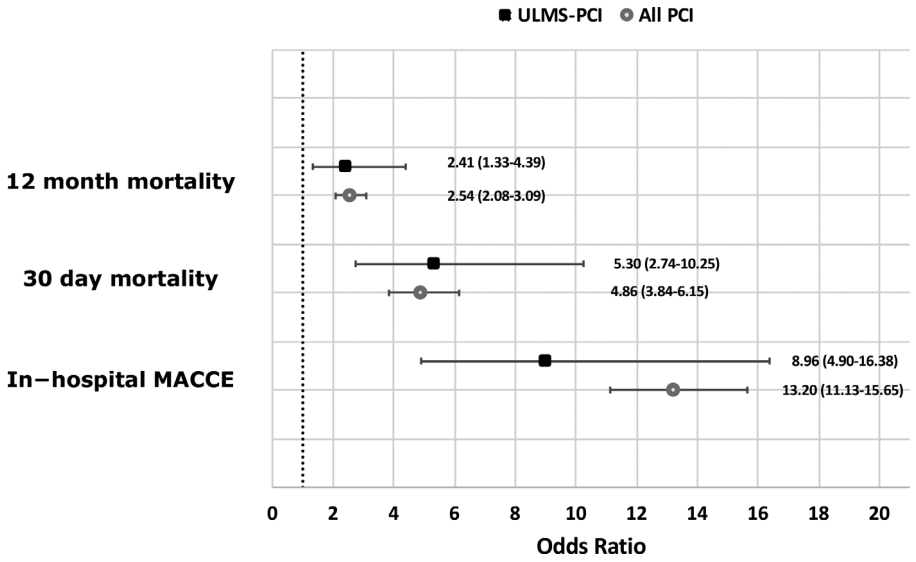

FIGURE 2 Outcomes of coronary perforation in patients undergoing unprotected LMS-PCI and all PCI.[3] Odds ratio with 95% confidence intervals demonstrating that outcomes of perforation in ULMS-PCI are no worse than all-comer PCI

4 | DISCUSSION

This is the first and largest study to date to describe the predictors and outcomes of perforation complicating ULMS-PCI using a large national PCI registry. We found the incidence of perforation complicating ULMS-PCI to be 0.9% which was stable over the study period (Figure 1b/c). After adjusting for baseline and procedural variables, independent predictors of perforation complicating ULMS-PCI were female gender, number of stents used, rotational atherectomy, and number of CTO attempted. Perforation in this context was independently associated with peri-procedural complications as well as morbidity and mortality at 30 days and 12 months.

Compared to reports on perforation complicating all-comer PCI, the rates of perforation in ULMS-PCI were higher (0.9% vs. the reported 0.4%).[3] This likely reflects the complex/high risk nature of patients requiring this procedure and is consistent with other studies of patients with complex coronary anatomy, such as those undergoing PCI with CTO disease where higher rates of perforation were observed (1.4%).[8] Indeed, we found that CTO is a complicating factor and a predictor of perforation in ULMS-PCI, consistent with previous studies.[8] Despite the increase in the overall number of ULMS-PCI over the study period, there was no significant change in the rate of perforation. The observational nature of the study makes it difficult to determine the reasons for this, but we suspect that improvement in

toolkit safety profile over the study period may have offset any noticeable increase in the incidence of perforation.

In-hospital MACCE and mortality (30 days and 12 months) were significantly more likely in ULMS-PCI complicated by perforation, inferring a fivefold increased odds of death at 30 days (Table 2). These data are a stark reminder that although perforation during ULMS-PCI is a relatively rare event, when it does occur, there is an important association with poor outcome. However, compared to previously published studies on all-comer PCI complicated by perforation,[3] the odds ratios of in-hospital MACCE and mortality are comparable (Figure 2). This suggests that although the rates of perforation in ULMS-PCI are just over twice that in all-comer PCI, the outcomes are no worse and therefore should not detract from carrying out ULMS PCI when indicated.

The limited number of predictors associated with perforation shown in Table S2 makes it difficult to anticipate its occurrence. Indeed, in our study, with the exception of rotational atherectomy, the occurrence of perforation does not seem to be significantly associated with procedural variables (e.g., use of microcatheters, choice of access, or antiplatelet agent). The association we observed with the number of stents used may reflect the perforation treatment strategy deployed by the operator. Consequently, operators need to recognize this limitation of prediction and be prepared to tackle such complication arising by having the necessary tools, algorithms, and expertise on board in order to reduce the rate of the adverse outcomes described above (Table 2).

The complications that we have reported to be significantly associated with perforation in ULMS-PCI are likely related to the occurrence of perforation (shock, tamponade, in-hospital major bleed) and/or as a consequence of its treatment (shock, side-branch loss, peri-procedural MI, DCCV, transfusion) and are consistent with previous reports.[9,10] Indeed, the relatively recent advances in the treatment of CP with covered stents are likely responsible for the higher rates we have observed with major side branch loss and peri-procedural shock seen in our study, both of which shown to be strongly predictive of mortality.[9,11]

This analysis has several strengths. The BCIS data set includes >98% of all PCI procedures performed in the United Kingdom, which, therefore, reflects a national, real-world experience that includes high-risk patients encountered in daily interventional practice (who are often excluded from randomized controlled trials). Such large national registry data with unselected enrolment are important for evaluation of low-frequency complications, such as CP, particularly given that such low event rates would mean that single-center registries or randomized controlled trials would be grossly underpowered.

4.1 | Limitations

The BCIS database does not differentiate between CPs resulting from guide-wire and those perforations due to balloon or stent inflation or indeed the anatomical location of such perforations. Second, the database does not record guidewire data and therefore data on stiffness or coating and the incidence of CP cannot be provided. Third, the database does not record the Ellis classification of CP so that a substratification by perforation severity was not possible in this series. Moreover, the BCIS database does not record the use of other treatment strategies such covered stents, pericardial drains, or embolization techniques and therefore data on outcomes with respect to different therapies is not available. Furthermore, the follow-up period is limited to 2014 as more recent data with reliable linkage to outcomes are not available to the authors. Finally, because of the observational nature of this study, any conclusions may be influenced by unmeasured confounders, such as frailty or anatomical considerations.

5 | CONCLUSIONS

CP is an infrequent event during ULMS-PCI with very few predictors and a steady incidence over the study period of 7 years. It is associated with significantly adverse peri-procedural outcomes as well as increased morbidity and mortality. However, the likelihood of occurrence of these outcomes is similar to previous studies that examined perforation in all-comer PCI and therefore should not be a basis for avoiding indicated ULMS-PCI.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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