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Temporal trends in in-hospital outcomes following unprotected left-main PCI: an analysis of 14,522 cases from British Cardiovascular Intervention Society database 2009-2017

Tim Kinnaird^{aj} MD, Sean Gallagher^a MD, Vasim Farooq^a PhD, Majd Protti^a, PhD, Liam Back^a, MD, Paeder Devlin^a, MD, Richard Anderson^a MD, Andrew Sharp^a MD, Peter Ludman^d MD, Samuel Copt^f PhD, , Mamas A Mamas^{ij}, DPhil, and Nick Curzen^k, PhD.^aDepartment of Cardiology, University Hospital of Wales, Cardiff, UK; ^bDepartment of Cardiology, Bristol Heart Institute; , ^cBarts Heart Centre, London and University College London Hospitals; ^dInstitute of Cardiovascular Sciences, Birmingham University, UK; ^eDepartment of Cardiology, The James Cook University Hospital, Middlesbrough, UK; ^fDivision of Statistics, Biosensors SA, Morges, Switzerland; ^gDepartment of Cardiology, Golden Jubilee Hospital, Glasgow, UK; ^hDepartment of Cardiology, John Radcliffe Hospital, Oxford, UK; ⁱDepartment of Cardiology, Royal Stoke Hospital, UHNM, Stoke-on-Trent, UK; ^jKeele Cardiovascular Research Group, Institute of Applied Clinical Sciences, University of Keele, Stoke-on-Trent, UK, ^kDept of Cardiology, University Hospital NHS Trust, Southampton, UK;.

Corresponding Author:

Professor Tim Kinnaird
Consultant Interventional Cardiologist
Department of Cardiology,
University Hospital of Wales,
Cardiff, UK

Email: tim.kinnaird2@wales.nhs.uk

Phone: +44 2920 743938

Fax: +44 2920 744473

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Abstract

Background: Percutaneous coronary intervention is increasingly used as a treatment option for unprotected left main stem artery (uLMS-PCI) disease. However, whether patient outcomes have improved over time is uncertain. **Methods:** Using the United Kingdom national PCI database, we studied all patients undergoing uLMS-PCI between 2009 and 2017. We excluded patients who presented with ST-segment elevation, cardiogenic shock, and with an emergency indication for PCI. **Results:** Between 2009 and 2017, in the study-indicated population, 14,522 uLMS-PCI procedures were performed. Significant temporal changes in baseline demographics were observed with increasing patient age and comorbid burden. Procedural complexity increased over time, with the number of vessels treated, bifurcation PCI, number of stents used, and use of intravascular imaging and rotational atherectomy all increasing significantly through the study period. After adjustment for baseline differences, there were significant temporal reductions in the occurrence of peri-procedural MI ($p < 0.001$ for trend), in-hospital MACCE ($p < 0.001$ for trend), and acute procedural complications ($p < 0.001$ for trend). In multivariate analysis examining the associates of in-hospital MACCE, whilst age per year (odds ratio (OR) 1.02 (95% confidence intervals 1.01-1.03)), female sex (OR 1.47 (1.19-1.82)), and comorbidity were associated with higher rates of in-hospital MACCE, by contrast use of intravascular imaging (OR 0.56 (0.45-0.70)), and year of PCI (OR 0.63 (0.46-0.87)) were associated with lower rates of in-hospital MACCE. **Conclusions:** Despite trends for increased patient and procedural complexity, in-hospital patient outcomes have improved after uLMS-PCI over time.

Condensed abstract

Using the United Kingdom national PCI database, we studied all patients undergoing uLMS-PCI between 2009 and 2017. After adjustment for baseline differences, there were significant temporal reductions in the occurrence of peri-procedural MI ($p < 0.001$ for trend), in-hospital MACCE ($p < 0.001$ for trend), and acute procedural complication ($p < 0.001$ for trend). In multivariate analysis examining the associates of in-hospital MACCE, whilst age per year, female sex, and several comorbidities were associated with higher rates of in-hospital MACCE, by contrast use of intravascular imaging (OR 0.56 (0.45-0.70)), and year of PCI (OR 0.63 (0.46-0.87)) were associated with lower rates of in-hospital MACCE.

List of abbreviations

ACS – acute coronary syndrome

BCIS - British Cardiovascular Intervention Society

CABG – coronary artery bypass surgery

CVA – cerebrovascular disease

DES – drug-eluting stent

IVUS - intravascular ultrasound

LAD – left anterior descending

LMS - left main stem

LV – left ventricle

MACCE - major adverse cardiac or cerebrovascular events

MI – myocardial infarction

NYHA – New York Heart Association

PVD – peripheral vascular disease

PCI - percutaneous coronary intervention

uLMS-PCI – unprotected left main stem percutaneous intervention

Introduction

Percutaneous coronary intervention (PCI) is increasingly considered as a revascularisation strategy in certain anatomical and patient subsets of unprotected left main stem (uLMS) disease.

In recent years, the landscape of PCI has changed significantly, with major advances in interventional technologies and techniques. For example, the development of low-profile stent platforms specifically tailored for LMS disease, microcatheters, guide-extension catheters, specialist guidewires, and, in particular, enhanced use of intravascular imaging have all improved procedural success and optimisation. A previous analysis of the United Kingdom National PCI Database demonstrated a temporal increase in use of intravascular imaging, and that imaging use was strongly associated with improved 12-month survival.(3) Furthermore, several large randomised trials have informed interventional cardiologists as to optimal bifurcation strategies and side branch management.(4-6) Finally, as uLMS-PCI procedural volumes have increased over time, the effects of operator experience may also be associated with improved patient outcomes. For example, an analysis of the United Kingdom National PCI Database observed improved patient outcomes when operator annualised uLMS-PCI volume exceeded 17 cases per year. (7)

However, whether the technological and technical advances, combined with operator experience have improved patient outcomes after uLMS-PCI over time is not well defined. Such evidence would potentially enhance patient choice and consent, and also inform MDT discussion. Therefore, we used the United Kingdom National PCI Database to study temporal trends in in-hospital clinical outcomes following uLMS-PCI over a nine-year period.

Methods

Study design and participants

Participants with PCI to a protected LMS were excluded from the analysis, and thus we analysed data from all patients undergoing uLMS-PCI in the United Kingdom between January 1st 2009 and December 31st 2017. We also excluded patients who presented with ST-segment elevation, cardiogenic shock, and

with an emergency indication for PCI. Thus, only patients without an immediate clinical need for uLMS-PCI were included in the analysis.

Study setting and sources of data

Data on PCI practice were obtained from the United Kingdom National PCI Audit dataset which records over 120 clinical, procedural and outcomes variables for every PCI performed in the UK, and thus approximately 100,000 new records are currently recorded each year. Entry of all PCI procedures by UK interventional operators is mandated as part of their professional revalidation. The accuracy and quality of the BCIS dataset has previously been ascertained.(8-9)

Study definitions

Study definitions were used as in the BCIS National PCI Audit dataset.(10) Pre- or post-PCI disease severity was defined as vessels with a stenosis $\geq 70\%$ in the case of the LAD, circumflex or right coronary arteries, or $\geq 50\%$ in the case of the left main artery. Chronic kidney disease was defined as chronic dialysis, history of renal transplant or a creatinine $> 200 \mu\text{mol/l}$. The clinical outcomes of interest were in-hospital mortality, in-hospital MACCE (defined as a composite of death, peri-procedural CVA or peri-procedural MI), in-hospital bleeding (defined as either gastrointestinal bleeding, intra-cerebral bleeding, retroperitoneal haematoma, blood or platelet transfusion, access site haemorrhage, or an arterial access site complication requiring surgery), and an acute coronary procedural complication (defined as a composite of no/slow flow, coronary perforation, coronary dissection, shock induction, emergency CABG and major side-branch loss). Periprocedural MI was defined as a > 2 increase in the upper limit of normal of CK-MB or troponin assays with or without new pathological Q waves or new LBBB.

Data analyses

We examined the baseline characteristics of patients undergoing uLMS-PCI and tested for significance using Cochran Armitage test for trends. Independent predictors of in-hospital MACCE after uLMS-PCI were evaluated using a multivariate logistic regression model to generate odds ratios, 95% confidence intervals and corresponding p-values. To select predictors to enter into the final multivariate model we used forward stepwise variable selection on the data and an inclusion criterion of $p < 0.1$. To correct for missing values, we imputed missing data on baseline covariates using multiple imputations with chained equations to adjust for missing data (Supplementary Table 1). Covariates included in the model were age, gender, clinical syndrome, cardiac enzyme status, NYHA class, previous MI, hypertension, diabetes, ejection fraction $< 30\%$, peripheral vascular disease, previous stroke, history of renal disease, Q wave on ECG, previous PCI, baseline disease severity, chronic total occlusion PCI, bifurcation LMS-PCI, no. vessels treated, intracoronary imaging use, glycoprotein inhibitor use, rotational atherectomy use, mechanical LV support use ad-hoc PCI, access site and year of PCI.

Results

uLMS-PCI crude numbers and trend in the United Kingdom 2009-2017

Between 2009 and 2017 14,522 uLMS-PCI procedures were performed in the study indicated population,. During the study period, there was a steady increase in the total annual number of PCIs performed in the United Kingdom (Figure 1, left panel, light blue bars) with a similar increase in annual uLMS-PCI volumes (Figure 1, left panel, dark blue bars). uLMS-PCI represented an increasing percentage of each yearly total, rising from 1.8% of total PCI in 2009 and 3.4% in 2017 (Figure 2, right panel).

Patient and procedural characteristics undergoing uLMS-PCI in the United Kingdom 2009-2017

There were significant changes in the baseline characteristics of patients undergoing uLMS-PCI over time (Table 1). Significant changes were observed in patient age (70.7 ± 12.2 yrs in 2009 vs. 71.6 ± 11.9 yrs in 2017, $p = 0.002$ for trend), female sex (33.1% vs. 29.4%, $p = 0.006$), diabetes mellitus (22.0% vs. 29.4%, $p < 0.001$), concomitant valvular heart disease (2.9% vs. 7.1%, $p < 0.001$), previous PCI (25.2% vs. 32.2%,

p=0.003), ACS presentation (49.9% vs. 54.4%, p<0.001) and number of diseased vessels (1.86 ± 0.95 vs. 2.12 ± 1.00 , p<0.001).

There were also important changes in the complexity of the uLMS-PCI procedure over time (Table 2). The number of vessels treated (1.99 ± 0.79 in 2009 vs. 2.17 ± 0.79 in 2017, p<0.001), bifurcation PCI (23.0% v. 28.4%, p<0.001), number of stents used (2.06 ± 1.45 vs. 2.30 ± 1.40 , p<0.001) and use of intravascular imaging (40.4% vs. 58.6%, p<0.001), rotational atherectomy (8.1% vs. 14.4%, p<0.001), and microcatheters (0.1% vs. 8.0%, p<0.001) all increased significantly through the study period. Use of glycoprotein inhibitors (24.1% in 2009 vs. 6.3% in 2017, p<0.001, LV support (5.7% vs. 2.2%, p<0.001) and femoral access (64.2% vs. 24.1%, p<0.001) decreased significantly over time (Table 2).

Clinical and procedural outcomes after uLMS- in the United Kingdom 2009-2017

The crude unadjusted outcomes after uLMS-PCI by procedure year are presented in Table 3 and Figure 2 and show an increase in the number of successful lesions and a decrease in procedural complications, including peri-procedural MI, over time.

The adjusted annual rate of clinical outcomes indexed to the first year of study (2009) are presented in Figure 3 and illustrate significant temporal reductions in the occurrence of peri-procedural MI (p<0.001 for trend), in-hospital MACCE (p<0.001 for trend), and acute procedural complication (p<0.001 for trend). The odds ratios for in-hospital major bleeding and in-hospital death did not change significantly over time.

In multivariate adjusted modelling examining the associates of in-hospital MACCE, age per year (odds ratio (OR) 1.02 (95% confidence intervals 1.01-1.03)), female sex (OR 1.47 (1.19-1.82)), peripheral vascular disease (OR 1.55 (1.17-2.04)), chronic kidney disease (OR 2.36 (1.73-3.24)), ejection fraction <30% (OR 1.45 (1.09-1.93)), intra-aortic balloon pump (OR 5.53 (4.12-7.41)), and Impella use (OR 4.80

(1.61-14.33)) were associated with higher rates of in-hospital MACCE (Figure 4). Use of intravascular imaging (OR 0.56 (0.45-0.70)), and year of PCI (OR 0.63 (0.46-0.87)) were associated with lower rates of in-hospital MACCE.

Discussion

The findings of the current study can be summarised as follows: 1) In patients undergoing uLMS-PCI there were significant temporal changes in baseline demographics with increasing patient age and comorbid burden observed over time; 2) uLMS-PCI procedural complexity increased over time, with the number of vessels treated, likelihood of bifurcation PCI, number of stents used, use of intravascular imaging and rotational atherectomy all increasing significantly through the study period; 3) the adjusted annual rate of clinical outcomes illustrated significant temporal reductions in the occurrence of peri-procedural MI, in-hospital MACCE, and acute procedural complication; 4) in multivariate analysis, use of intravascular imaging and year of PCI were associated with lower rates of in-hospital MACCE.

Although there are many studies comparing uLMS-PCI and CABG, there is limited data on the temporal changes in patient outcomes after uLMS-PCI. Clearly, such data are relevant as context to clinical decision-making about the optimal revascularisation strategy for patients in this group. Previously published series of outcomes after uLMS-PCI have clear limitations including that they examine other aspects of the interventional procedure such as access site or imaging, are non-contemporary, do not provide data on temporal trends in patient outcomes, or study only relatively short historical time-frames.(11-16) Two previous larger scale studies have findings consistent with the current study. The IRIS-MAIN registry was a non-randomized, multi-centre, observational study from 50 hospitals in Asia(17) including a total of 5,833 patients with significant LMS disease. Of these, 2,866 were treated with PCI, and 2,351 with CABG. As in the current study there was an increased risk of patient comorbidities and anatomic complexity over time, with the number and length of stents also significantly increasing. In the PCI group, the rate of MACCE substantially decreased over time whilst, in

the CABG group, none of the cumulative rates of any of the outcomes changed significantly over time. Of note, the IRIS-MAIN studied patients treated between 1995 and 2013 and thus are not representative of contemporary PCI practice. Similarly, in an analysis of 4,085 uLMS-PCI cases from the Swedish Coronary Angiography and Angioplasty Registry (2005 to 2017), the 3-year major adverse cardiovascular and cerebrovascular event fell from 45.6% to 23.9% over the study period (18)

There are several major strengths of the current study. Firstly, it is much larger than any other single study of uLMS-PCI, and, more importantly, than any other national database analysis. Secondly, the current series reports procedures from a more contemporary time frame in comparison to previous studies, which, for example, reported outcomes with a large proportion of first-generation DES or bare metal stents. Thirdly, the longitudinal nature of this study provides for the first time, a clear cut observed reduction of MACCE over time in contemporary practice. Additionally, this is the first study of uLMS-PCI to have sufficient statistical power to perform a robust sensitivity analysis of MACCE associates. Finally, as one of the aims of the study was to help inform practice regarding planned uLMS-PCI outcomes over time, we excluded patients with an emergency indication for PCI. Thus, the current study of the “CHIP-indicated” population is the first analysis of uLMS-PCI outcomes in such a population. The exclusion of patients with an emergency indication is important as the overall study population outcomes are likely to be heavily skewed by high event rates in the small subset of emergency patients.

In considering the mechanisms of the observed improved patient outcomes there may be several plausible explanations underpinning the improved in-hospital outcomes following uLMS-PCI over time. Previous studies have demonstrated that in the majority of cases, disease involving the left main artery extends into its distal bifurcation.(19-21) This pattern of disease presented a technical challenge and may be one explanation for the higher MACCE rates following uLMS-PCI compared to non-uLMS-PCI. However, technical issues, such as accessing the circumflex (especially when it is retroverted), have largely been overcome by the advent of technologies such as angled microcatheters and techniques

including dual lumen catheter wiring.(22) Therefore, in the vast majority of cases, the circumflex can be wired and treated appropriately and peri-procedural complications as a result of side-branch loss thereby avoided.

Emerging data on optimal interventional strategies to address bifurcation disease may also contribute to improved outcomes after uLMS-PCI over time. As with other studies of non-LMS PCI - including the Nordic Bifurcation Study and the British Bifurcation Coronary Study - data on uLMS-PCI suggest that where possible, a provisional stepwise stent strategy is at least as good as a planned 2-stent strategy in patients with bifurcation LMS disease .(6, 23-26) Where a 2-stent approach is considered necessary, a greater understanding of optimal planned bifurcation strategies derived from several randomised comparisons of bifurcation techniques may also underpin some of the improved outcomes observed. In particular, the emergence of techniques such as the double kissing (DK)-crush technique in left main PCI may contribute to better outcomes, given their requirement for meticulous procedural technique. In a meta-analysis of 10 studies including 2364 patients, DK-crush was also associated with a lower risk of myocardial infarction (IRR, 0.19; 95% CI, 0.05-0.76; P=.02) when compared with standard crush, as well as lower risk of target-lesion revascularization when compared with culotte (IRR, 0.32; 95% CI, 0.12-0.83; P=.02) and crush (IRR, 0.07; 95% CI, 0.02-0.28; P<.001).(27) Additionally, the importance of proximal stent optimisation (POT) after uLMS-PCI has also been demonstrated in recent studies.(28)

Several previous studies have identified other possible mechanistic insights into improved patient outcomes after uLMS-PCI over time. (29-31) In particular, a previous analysis of the UK national PCI database confirmed the importance of intravascular ultrasound to guide uLMS-PCI, an observation likely due to enhanced lesion coverage, optimal stent expansion, and appropriate stent sizing and apposition.(3) Although IVUS usage increased significantly over the current study period, its use was included in the adjustment modelling and therefore the effects on patient outcomes minimised as far as possible. Similarly, radial arterial access has previously been shown to be associated with improved outcomes after uLMS-PCI.(12) However, although major changes in arterial access site choice was

observed over the study period, femoral access use was included in the adjustment modelling and therefore the effects of access site choice on patient outcomes should also be minimal.

The increase in operator volume and experience is likely to be a major factor in improving patient outcomes after uLMS-PCI. A previous study of the UK national PCI database demonstrated improved patient outcomes with higher operator uLMS-PCI volumes, a volume-outcome effect not seen with PCI in general.(7) After adjustment, the observed in-hospital survival (odds ratio 0.30, 95% confidence interval 0.14-0.56, $p<0.001$), in-hospital MACCE (OR 0.40, 0.24-0.66, $p<0.001$) and 12-month survival (OR 0.53, 0.36-0.79, $p<0.001$) were lower in highest quartile operators compared to lowest quartile operators, with individual operator volume closely correlated with 12-month survival (OR 0.999/case, $p<0.0001$). A similar association between higher uLMS-PCI operator volumes and improved patient outcomes was observed in a study of patients treated in a high-volume Chinese centre. (32)

In considering the limitations of the present study, although we attempted to correct for baseline differences over time, it remains possible that unmeasured confounders have biased the results. Additionally, the BCIS database does not capture details of anatomical data such as the location of disease with the LMS, complexity of lesions such as calcification or the presence, or type of distal LMS bifurcation disease. Therefore, we cannot provide detailed data on the relationship to the pattern of disease and outcomes over time. Similarly, whilst there are robust data regarding the type and number of stents used, there are no data provided on the exact technical approach used to treat the LMS disease. Therefore, the current analysis is describe any association between different bifurcation strategies on outcomes over time. Finally, due to technical issues with linkage of the national PCI database to post-discharge outcomes, we are unable to provide data on longer term MACCE rates over time.

Conclusions

Despite trends for increased patient and procedural complexity, in-hospital patient outcomes have improved after uLMS-PCI over time. These data help inform patient choice and consent, and MDT discussion.

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Figure Legends

Figure 1: Trends of uLMS-PCI in the United Kingdom 2009-2017. Left Panel: Change in total numbers of PCI in the study population (STEMI, emergency non-STEMI and cardiogenic shock excluded) in light blue bars and unprotected LMS-PCI (uLMS-PCI) in dark over time; Right Panel: Percentage of total-PCI represented by uLMS-PCI over time.

Figure 2: Acute procedural complications during uLMS-PCI in the United Kingdom 2009-2017. Panels indicate serial changes in coronary dissection ($p < 0.001$ for trend), shock induction by PCI (non-

significant trend), occurrence of slow flow ($p=0.02$ for trend), loss of a major side branch (non-significant trend), and all acute coronary complications combined including coronary perforation, ventilation required and DC cardioversion required ($p<0.001$ for trend).

Figure 3: Clinical outcomes following uLMS-PCI in the United Kingdom 2009-2017. Panels indicate annual odds ratios indexed to 2009 for clinical outcomes including peri-procedural MI ($p<0.001$ for trend), in-hospital death (non-significant trend), in-hospital MACCE ($p<0.001$ for trend), in-hospital major bleeding (non-significant trend), and acute coronary complications ($p<0.001$ for trend).

Figure 4: Associates of in-hospital MACCE. Multi-variate adjusted model for in-hospital outcomes following LMS-PCI in the United Kingdom 2009-2017 (significant factors highlighted in red, non-significant highlighted in black).

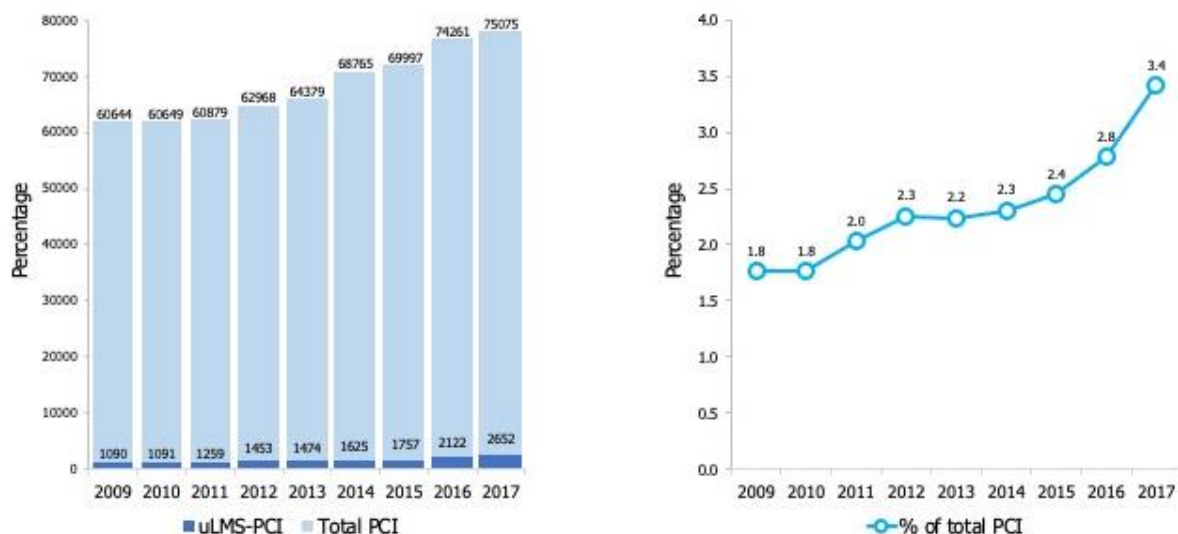


Figure 1: Trends of uLMS-PCI in the United Kingdom 2009-2017. Left Panel: Change in total numbers of PCI in the CHIP-eligible population (STEMI, emergency non-STEMI and cardiogenic shock excluded) in light blue bars and unprotected LMS-PCI (uLMS-PCI) in dark over time; Right Panel: Percentage of total-PCI represented by uLMS-PCI over time.

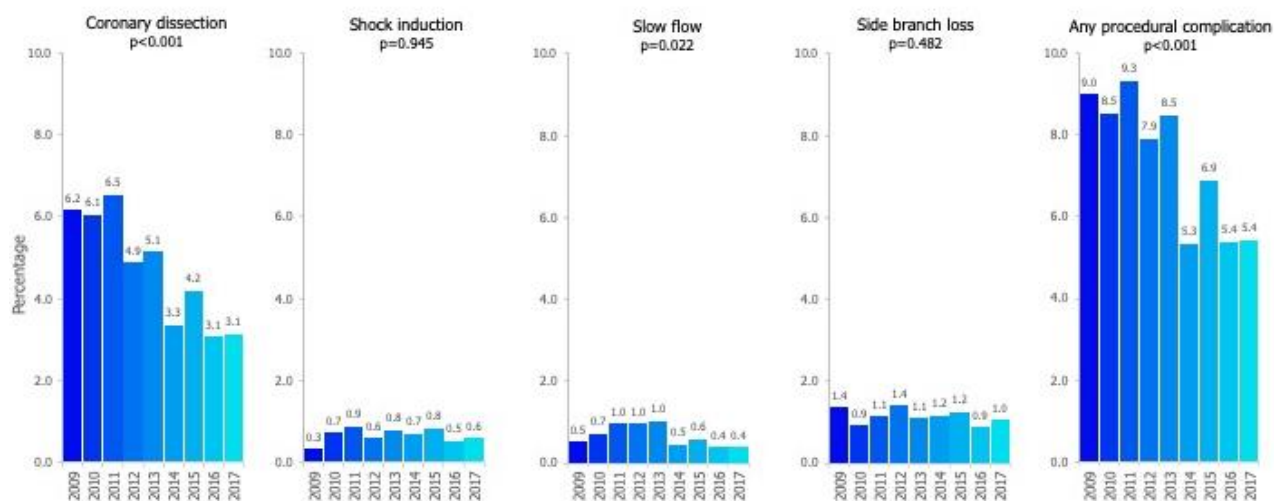


Figure 2: Acute procedural complications during uLMS-PCI in the United Kingdom 2009-2017. Panels indicate serial changes in coronary dissection ($p<0.001$ for trend), shock induction by PCI (non-significant trend), occurrence of slow flow ($p=0.02$ for trend), loss of a major side branch (non-significant trend), and all acute coronary complications combined including coronary perforation, ventilation required and DC cardioversion required ($p<0.001$ for trend).

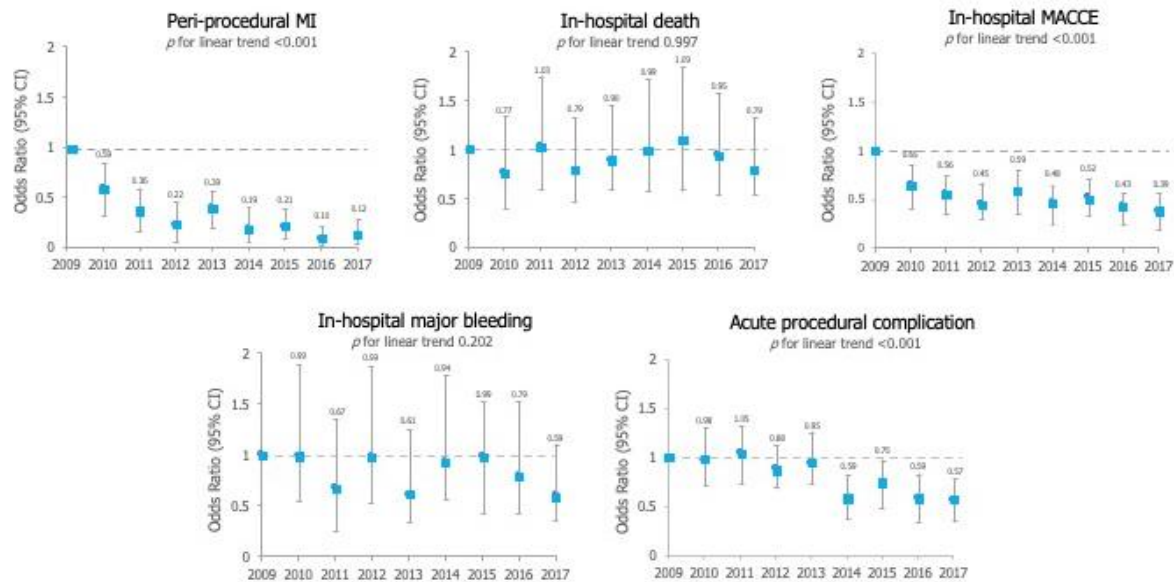


Figure 3: Clinical outcomes following uLMS-PCI in the United Kingdom 2009-2017. Panels indicate annual odds ratios indexed to 2009 for clinical outcomes including peri-procedural MI ($p < 0.001$ for trend), in-hospital death (non-significant trend), in-hospital MACCE ($p < 0.001$ for trend), in-hospital major bleeding (non-significant trend), and acute coronary complications ($p < 0.001$ for trend).

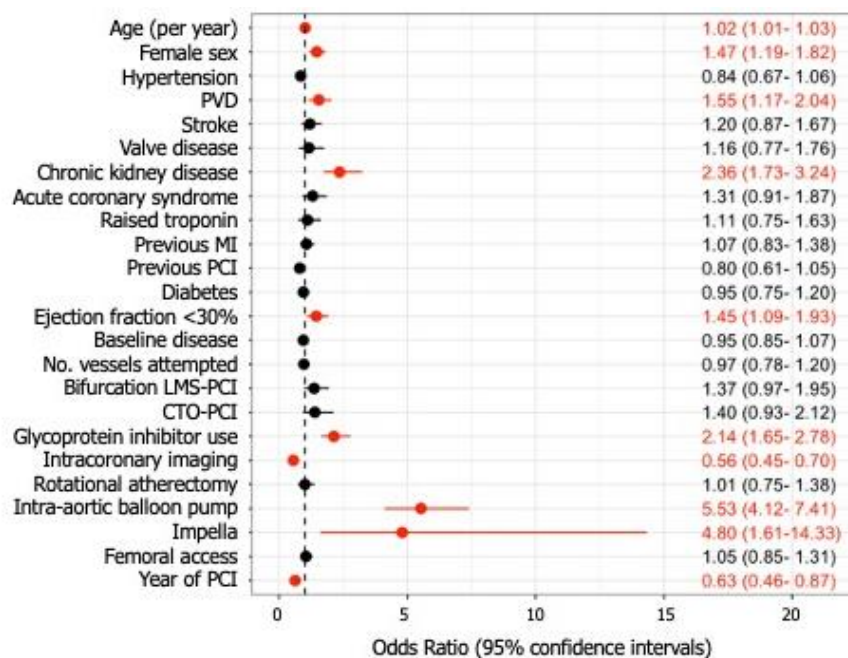


Figure 4: Associates of in-hospital MACCE. Multi-variate adjusted model for in-hospital outcomes following LMS-PCI in the United Kingdom 2009-2017 (significant factors highlighted in red, non-significant highlighted in black).

Table 1: Baseline characteristics of patients undergoing uLMS-PCI by procedure year in the United Kingdom 2009-2017

Variable	2009 (n=1089)	2010 (n=1091)	2011 (n=1259)	2012 (n=1453)	2013 (n=1474)	2014 (n=1625)	2015 (n=1757)	2016 (n=2122)	2017 (n=2652)	p-value
Age (years), \pm SD	70.7 \pm 12.2	71.3 \pm 12.1	71.3 \pm 11.5	72.3 \pm 11.6	71.8 \pm 11.6	71.6 \pm 12.0	71.6 \pm 11.8	71.7 \pm 11.6	71.6 \pm 11.9	0.002
Female sex, no. (%)	361 (33.1)	350 (32.1)	373 (29.7)	459 (31.6)	428 (29.1)	451 (27.8)	502 (28.6)	622 (29.3)	780 (29.4)	0.006
Body Mass Index, \pm SD	27.6 \pm 5.7	28.0 \pm 5.6	28.5 \pm 5.6	28.0 \pm 5.6	27.9 \pm 5.6	28.0 \pm 5.5	28.0 \pm 5.5	28.0 \pm 5.3	28.1 \pm 5.7	0.685
Hypertension, no. (%)	701 (64.7)	722 (66.5)	818 (65.6)	1,007 (70.0)	963 (66.8)	1,088 (67.8)	1,107 (66.2)	1,412 (67.1)	1,724 (67.3)	0.389
Diabetes mellitus, no. (%)	237 (22.0)	224 (21.0)	293 (23.8)	330 (23.4)	376 (25.9)	446 (27.7)	451 (26.0)	583 (27.9)	737 (28.4)	<0.001
Previous MI, no. (%)	339 (35.5)	368 (37.2)	461 (39.1)	515 (37.8)	531 (36.8)	592 (37.2)	618 (35.9)	707 (34.0)	901 (34.7)	0.008
Previous CVA/PVD, no. (%)	179 (16.5)	176 (16.2)	240 (19.2)	258 (17.9)	233 (16.2)	242 (15.1)	254 (15.2)	290 (13.8)	418 (16.3)	0.134
Chronic kidney disease, no. (%)	63 (5.9)	78 (7.3)	68 (5.5)	108 (7.9)	94 (6.6)	108 (6.8)	126 (7.3)	104 (5.0)	131 (5.1)	0.019
Valvular heart disease, no. (%)	32 (2.9)	42 (3.9)	44 (3.5)	60 (4.2)	67 (4.6)	69 (4.3)	84 (5.0)	130 (6.2)	181 (7.1)	<0.001
Previous CABG, no. (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	-
Previous PCI, no. (%)	274 (25.2)	288 (26.6)	355 (28.4)	369 (25.6)	460 (31.2)	505 (31.3)	572 (32.9)	693 (32.9)	842 (32.2)	0.003
ACS presentation, no. (%)	544 (49.9)	604 (55.3)	681 (54.1)	773 (53.2)	792 (53.7)	897 (55.2)	1,001 (57.0)	1,147 (54.1)	1,444 (54.5)	<0.001
Shock pre-procedure, no. (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	-
Ejection fraction (%), \pm SD	48.0 (11.6)	47.7 (11.8)	47.3 (12.2)	46.6 (12.5)	46.5 (12.8)	47.2 (12.1)	47.2 (12.4)	46.8 (12.7)	47.8 (11.9)	0.271

Ejection fraction <30%, no. (%)	70 (9.6)	70 (9.9)	97 (11.1)	129 (13.2)	139 (13.2)	111 (10.2)	133 (11.8)	166 (12.1)	18.3 (10.8)	0.530
No. of diseased vessels \pm SD	1.86 \pm 0.95	1.99 \pm 0.97	1.99 \pm 1.00	2.07 \pm 0.98	2.05 \pm 0.98	2.06 \pm 0.97	2.08 \pm 0.98	2.05 \pm 0.96	2.12 \pm 1.00	<0.001

Table 2: Procedural variables of patients undergoing uLMS-PCI by procedure year in the United Kingdom 2009-2017

Variable	2009 (n=1090)	2010 (n=1091)	2011 (n=1259)	2012 (n=1453)	2013 (n=1474)	2014 (n=1625)	2015 (n=1757)	2016 (n=2122)	2017 (n=2652)	p-value trend
No. of vessels attempted, \pm SD	1.99 \pm 0.79	2.02 \pm 0.80	2.04 \pm 0.80	2.08 \pm 0.81	2.11 \pm 0.79	2.08 \pm 0.78	2.13 \pm 0.79	2.11 \pm 0.79	2.17 \pm 0.79	<0.001
LMS/LAD/Cx target vessels, no. (%)	251 (23.0)	252 (23.1)	292 (23.2)	359 (24.7)	403 (27.3)	412 (25.3)	480 (27.3)	564 (26.6)	754 (28.4)	<0.001
CTO attempted, no. (%)	60 (6.0)	55 (5.3)	63 (5.3)	69 (5.0)	88 (6.2)	79 (5.0)	102 (6.0)	93 (4.6)	141 (5.6)	0.715
Restenosis, no. (%)	101 (9.9)	68 (6.3)	88 (7.2)	90 (6.3)	117 (8.2)	115 (7.3)	108 (6.3)	161 (7.9)	218 (8.7)	0.253
No. of stents used, \pm SD	2.06 \pm 1.45	2.11 \pm 1.39	2.15 \pm 1.42	2.20 \pm 1.44	2.21 \pm 1.52	2.16 \pm 1.42	2.20 \pm 1.38	2.18 \pm 1.39	2.30 \pm 1.40	<0.001
GPI used, no. (%)	239 (24.1)	225 (21.9)	204 (17.5)	209 (15.0)	163 (11.8)	152 (9.9)	138 (8.2)	125 (6.3)	152 (6.3)	<0.001
Intravascular imaging used, no. (%)	417 (40.4)	467 (44.6)	573 (47.6)	654 (46.5)	698 (49.5)	786 (48.3)	920 (52.8)	1,088 (54.7)	1,403 (58.6)	<0.001
Pressure wire, no. (%)	119 (11.6)	97 (9.3)	113 (9.4)	142 (10.0)	155 (11.0)	156 (9.8)	157 (9.0)	219 (11.0)	274 (11.5)	0.276
Rotational atherectomy, no. (%)	81 (8.1)	75 (7.3)	115 (9.8)	151 (11.0)	170 (12.1)	203 (12.8)	184 (10.8)	261 (12.7)	310 (14.4)	<0.001
Laser, no. (%)	2 (0.2)	7 (0.7)	7 (0.6)	5 (0.3)	10 (0.7)	7 (0.4)	4 (0.2)	6 (0.3)	4 (0.2)	0.823
Cutting balloon, no. (%)	58 (5.8)	62 (6.1)	67 (5.7)	75 (5.5)	107 (7.7)	105 (6.6)	112 (6.6)	173 (8.4)	180 (8.3)	<0.001
Microcatheter, no. (%)	1 (0.1)	6 (0.6)	19 (1.6)	36 (2.6)	51 (3.7)	63 (4.0)	109 (6.4)	133 (6.5)	173 (8.0)	<0.001
LV support, no. (%)	58 (5.7)	50 (4.8)	57 (4.7)	66 (4.7)	54 (3.8)	49 (3.1)	53 (3.1)	36 (1.8)	56 (2.2)	<0.001
Femoral access, no. (%)	691 (64.2)	623 (58.1)	699 (56.4)	667 (46.3)	654 (44.9)	625 (38.8)	560 (32.2)	559 (26.8)	629 (24.1)	<.0001

Dual access, no. (%)	78 (7.2)	61 (5.7)	85 (6.9)	115 (8.0)	67 (7.5)	102 (6.3)	137 (7.9)	151 (7.2)	226 (8.7)	0.0216
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Table 3: Crude unadjusted outcomes after uLMS-PCI by procedure year in the United Kingdom 2009-2017

Variable	2009 (n=1090)	2010 (n=1091)	2011 (n=1259)	2012 (n=1453)	2013 (n=1474)	2014 (n=1625)	2015 (n=1757)	2016 (n=2122)	2017 (n=2652)	p-value trend
Acute procedural outcomes										
No. successful lesions, \pm SD	2.03 \pm 1.16	1.94 \pm 1.04	1.98 \pm 1.06	2.00 \pm 1.04	2.03 \pm 1.09	2.00 \pm 1.06	2.07 \pm 1.09	2.02 \pm 1.04	2.13 \pm 1.10	<0.001
Major side branch loss, no. (%)	13 (1.4)	9 (0.9)	13 (1.1)	19 (1.4)	15 (1.1)	18 (1.1)	21 (1.2)	18 (0.9)	27 (1.0)	0.469
Coronary dissection, no. (%)	59 (6.2)	59 (6.1)	75 (6.5)	66 (4.9)	71 (5.1)	52 (3.3)	71 (4.2)	63 (3.1)	81 (3.1)	<0.001
Coronary perforation, no. (%)	5 (0.5)	14 (1.4)	9 (0.8)	15 (1.1)	12 (0.9)	8 (0.5)	14 (0.8)	20 (1.0)	18 (0.7)	0.469
Slow flow, no. (%)	5 (0.5)	7 (0.7)	11 (1.0)	13 (1.0)	14 (1.0)	7 (0.5)	10 (0.6)	8 (0.4)	10 (0.4)	0.022
Shock induction, no. (%)	3 (0.3)	7 (0.7)	10 (0.9)	8 (0.6)	11 (0.8)	11 (0.7)	14 (0.8)	11 (0.5)	15 (0.6)	0.948
Any complication, no. (%)	86 (9.0)	83 (8.5)	107 (9.3)	107 (7.9)	117 (8.5)	83 (5.3)	117 (6.9)	111 (5.3)	144 (5.4)	<0.001
Clinical Outcomes										
Peri-procedural MI, no. (%)	34 (3.1)	23 (2.1)	15 (1.2)	10 (0.6)	18 (1.2)	9 (0.6)	11 (0.6)	6 (0.3)	9 (0.3)	<0.001
Peri-procedural CVA, no. (%)	1 (0.1)	1 (0.1)	1 (0.1)	2 (0.1)	1 (0.1)	0 (0)	0 (0)	5 (0.2)	5 (0.2)	0.220
Transfusion, no. (%)	8 (0.7)	8 (0.7)	7 (0.6)	9 (0.6)	8 (0.5)	10 (0.6)	12 (0.7)	11 (0.5)	5 (0.2)	0.036
Access site complication, no. (%)	21 (2.1)	22 (2.1)	23 (1.9)	29 (2.0)	27 (1.9)	30 (1.9)	51 (3.0)	49 (2.4)	25 (1.0)	0.2631
Emergency PCI/CABG, no. (%)	2 (0.2)	7 (0.6)	8 (0.6)	8 (0.6)	4 (0.3)	3 (0.2)	10 (0.6)	5 (0.2)	7 (0.3)	0.539
Acute kidney injury, no. (%)	5 (0.5)	7 (0.6)	5 (0.4)	8 (0.6)	4 (0.3)	3 (0.2)	5 (0.3)	2 (0.1)	2 (0.1)	<0.001
In-patient mortality, no. (%)	22 (2.0)	20 (1.8)	28 (2.2)	28 (1.9)	29 (2.0)	34 (2.1)	40 (2.2)	40 (1.9)	43 (1.7)	0.510

In-patient MACCE, no. (%)	55 (5.0)	33 (3.0)	38 (3.0)	38 (2.6)	47 (3.2)	43 (2.6)	49 (2.8)	48 (2.3)	56 (2.1)	<0.001
In-patient major bleed, no. (%)	17 (2.0)	18 (1.6)	14 (1.1)	25 (1.7)	15 (1.0)	24 (1.5)	27 (1.5)	25 (1.1)	25 (0.9)	0.095