Short Communication

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Predictors of 1- and 12-month mortality in bifurcation coronary intervention: a contemporary perspective

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Aim: Bifurcation-PCI is performed frequently, although without extensive evidence to back up a definitive solution for its complexity. We set out to identify factors associated with 1- and 12-month mortality after bifurcation-PCI between 2017 and 2021 in our tertiary centre in Wales, UK. **Results:** Of 732 bifurcation PCI cases (mean age 69; 25% female), 67% were in ACS, 42% were left main PCI and 25.3% involved two-stent strategy. 30-day and 12-month mortality were 1.9% and 8.2%, respectively. Age, diabetes, smoking and renal failure are associated with mortality after bifurcation-PCI, while the choice between provisional and 2-stent strategies did not impact mortality/TLR. **Conclusion:** Awareness of 'real-world' outcomes of bifurcation-PCI should be used for appropriate patient selection, technique planning and procedural consent.

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Coronary bifurcation lesions are stenoses involving the origin of significant side branches [1]. They develop as a consequence of biophysical factors such as turbulence at the carina of bifurcating vessels and subsequent shear stress, with an estimated prevalence of 15–20% in patients with coronary artery disease [2,3].

Coronary bifurcation disease is an independent risk factor for poor outcomes following percutaneous coronary intervention (PCI) [4,5]. This is thought to relate to technical complexity of bifurcation PCI that may lead to periprocedural complications which may contribute to both acute and late morbidity and mortality [4,6] as well as to suboptimal lesion preparation, stent coverage and expansion, with their potential deleterious consequences.

Despite the description of several bifurcation PCI techniques, using either one stent (provisional) or two-stent strategies, 'real-world' data on bifurcation PCI outcomes remain limited [4,7]. This may be due to underreporting of complications related to bifurcation PCI in observational registries [4].

The aim of this study was to examine 'real-world' periprocedural outcomes, target vessel revascularisation (TLR) rates and predictors of mortality in patients who underwent bifurcation PCI as part of routine clinical practice in an UK tertiary cardiac centre.

Patients & methods

Study participants

We present a retrospective analysis of the PCI registry between January 2017 and December 2021, from Swansea Bay University Health Board, a tertiary cardiac centre in the United Kingdom, serving a population of approx. 1 million. All bifurcation PCI cases were identified and included in this study by manual screening of all reports included on the database. The stent platforms used during the study period were 81 micron everolimus-eluting

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(nonerodible polymer) cobalt–chromium stents. The study design was approved by the local clinical governance board. A consort flow diagram of study design is shown in Supplementary Figure 1.

The local PCI registry conforms to the guidelines from the National Institute of Cardiovascular Outcomes Research (NICOR) and the British Cardiac Intervention society (BCIS) to inform patients and the public on PCI outcomes in UK National Health Service (NHS) centres [8]. UK interventional cardiologists are mandated to enter all the PCI procedures, including complications, onto these datasets as part of professional revalidation. In our centre the interventional data is collected using software provided by Change HC (www.changehealthcare.co.uk/enterprise-imaging/cardiology).

Design of the study

We documented the following clinical parameters in all patients undergoing bifurcation PCI: age, gender, smoking history (current or ex-smoker), preprocedural renal failure (defined as creatinine >200 μmol/l, renal transplant history, or dialysis as per the BCIS/NICOR definition), diabetes mellitus, previous PCI to any vessel, previous coronary artery bypass grafting (CABG), family history of coronary artery disease (CAD), Q wave on ECG, out of hospital cardiac arrest (OOHCA), New York Heart Association (NYHA) heart failure class, Canadian Cardiovascular Society (CCS) angina class, acute coronary syndrome (ACS) status and target vessel for PCI. We documented the following procedural variables: use of microcatheter, cutting balloon, rotational atherectomy, intravascular lithotripsy (IVL), drug-eluting balloons (DEB), intravascular imaging (intravascular ultrasound, IVUS or optical coherence tomography, OCT), arterial access site, use of pressure wire and procedural complications (side branch loss, dissection, shock induced by procedure, perforation, slow flow, direct current cardioversion [DCCV]) as well as survival status at one and 12 months after PCI. Our outcomes were one and 12 month-mortality and rate of TLR.

Statistical analyses

We used the R coding environment (Open Source). Multiple imputations were carried out using the *mice* package to reduce the potential bias from missing data (Supplementary Table 1), assuming missingness completely at random mechanisms. This is an open-source package that imputes missing values with plausible data values, drawn from a distribution specifically designed for each missing data point. We used chained equations to impute the data for all variables with missing information and generated five datasets to be used in the analyses. We examined co-variates associated with 30-day, 12-month mortality and TLR. We explored crude baseline comorbidities using a Chi-squared test for categorical variables and the Wilcoxon–Mann-Whitney test for continuous variables.

Results

Baseline characteristics of bifurcation PCI cases included in the study

The number of bifurcation PCI increased year-on-year during the study period from 27 in 2017 to 258 in 2021 (almost by a factor of 10; $p < 0.001$). The baseline clinical characteristics of the whole cohort and per year of study are presented in Table 1. The proportion of patients with CCS or NYHA class 3 or more symptoms decreased over the study period ($p < 0.01$). The proportion of patients with a history of MI varied significantly between the years, with the lowest rates in 2020 at 16.7% of all cases ($p < 0.001$).

Procedural characteristics of bifurcation PCI cases

Intracoronary imaging was used increasingly during the study period rising from 18.5% in 2017 to 48.1% of cases in 2021 (Table 2; $p < 0.001$). This was accompanied by an increase in the rate of left main PCI, the use of cutting balloons, intravascular lithotripsy and drug-eluting balloons (Table 2; $p < 0.01$). There was a significant decline in the use of two-stent bifurcation techniques in favour of a single stent provisional technique over the study period, accompanied by a decrease in femoral or dual arterial access (Table 2; $p < 0.01$).

Clinical outcomes of bifurcation PCI

The unadjusted outcomes of bifurcation PCI overall and per year are presented in Table 3. We found a 1.8% prevalence of coronary dissection, 0.7% shock induction, 0% coronary perforation, 0.5% slow flow, 0.1% DCCV and 1.0% side branch loss. ‘Real-world’ rates of TLR were 2.3% whereas mortality was recorded in 1.9% (30 days) and 8.2% (12 months) of cases. There were no significant changes in the rate of complications over the study period.

Table 1. Baseline characteristics of cases included in the study.

	2017	2018	2019	2020	2021	p-value	Overall
n (%)	27 (2)	104 (7)	133 (8)	210 (14)	258 (15)	**<0.001**	732 (10)
All PCI volume, n	1341	1407	1637	1551	1769		7705
Age, mean (SD)	65.78 (11.39)	69.47 (10.71)	68.45 (11.80)	69.58 (11.50)	69.30 (11.04)	0.501	69.12 (11.28)
BMI, mean (SD)	29.59 (5.24)	28.90 (5.73)	28.67 (6.09)	28.29 (5.12)	28.76 (5.20)	0.748	28.66 (5.43)
Female, n (%)	6 (22.2)	27 (26.0)	29 (21.8)	43 (20.5)	74 (28.7)	0.287	179 (24.5)
ACS, n (%)	24 (88.9)	64 (61.5)	93 (69.9)	140 (66.7)	171 (66.3)	0.097	492 (67.2)
CCS 3+, n (%)	23 (88.5)	73 (85.9)	75 (76.5)	168 (85.7)	162 (73.0)	**0.006**	501 (79.9)
NYHA 3+, n (%)	20 (76.9)	45 (55.6)	30 (31.9)	48 (24.4)	69 (32.1)	**<0.001**	212 (34.6)
Diabetes mellitus, n (%)	5 (18.5)	22 (21.2)	35 (26.3)	42 (20.1)	72 (28.0)	0.258	176 (24.1)
Severe LVSD, n (%)	1 (4.0)	13 (13.7)	11 (8.9)	19 (9.6)	30 (12.3)	0.498	74 (10.8)
Smoking history, n (%)	13 (54.2)	62 (66.7)	90 (77.6)	123 (69.5)	150 (68.2)	0.148	438 (69.5)
Renal disease, n (%)	1 (3.7)	5 (4.8)	4 (3.0)	6 (2.9)	9 (3.5)	0.926	25 (3.4)
Previous MI, n (%)	6 (22.2)	39 (37.9)	42 (31.6)	35 (16.7)	78 (30.2)	**<0.001**	200 (27.4)
Previous CABG, n (%)	2 (7.4)	10 (9.6)	17 (12.8)	10 (4.8)	18 (7.0)	0.092	57 (7.8)
Previous PCI, n (%)	5 (18.5)	31 (29.8)	43 (32.3)	70 (33.3)	103 (40.1)	0.091	252 (34.5)

Bold values indicate statistical significance.
ACS: Acute coronary syndrome; CABG: Coronary artery bypass grafting; CCS: Canadian Cardiovascular Society; LVSD: Left ventricular systolic dysfunction; MI: Myocardial infarction; NYHA: New York Heart Association; PCI: Percutaneous coronary intervention; Renal disease: Chronic kidney disease 4+; SD: Standard deviation.

Table 2. Procedural characteristics of cases included in the study.

	2017	2018	2019	2020	2021	p-value	Overall
n	27	104	133	210	258		732
LMS-PCI, n (%)	8 (29.6)	42 (40.4)	68 (51.1)	97 (46.2)	91 (35.3)	**0.013**	306 (41.8)
Intracoronary imaging, n (%)	5 (18.5)	28 (26.9)	59 (44.4)	101 (48.1)	124 (48.1)	**<0.001**	317 (43.3)
Pressure wire, n (%)	3 (11.1)	4 (3.8)	13 (9.8)	18 (8.6)	33 (12.8)	0.122	71 (9.7)
Type of bifurcation, n (%)						**0.004**	
Culotte	9 (33.3)	16 (15.4)	14 (10.5)	16 (7.6)	26 (10.1)		81 (11.1)
DKC	1 (3.7)	3 (2.9)	4 (3.0)	14 (6.7)	10 (3.9)		32 (4.4)
Minicrush	3 (11.1)	8 (7.7)	10 (7.5)	3 (1.4)	5 (1.9)		29 (4.0)
Provisional	13 (48.1)	73 (70.2)	95 (71.4)	164 (78.1)	202 (78.3)		547 (74.7)
SKS	0 (0.0)	0 (0.0)	2 (1.5)	1 (0.5)	2 (0.8)		5 (0.7)
T stent	1 (3.7)	0 (0.0)	2 (1.5)	3 (1.4)	1 (0.4)		7 (1.0)
TAP	0 (0.0)	4 (3.8)	6 (4.5)	9 (4.3)	11 (4.3)		30 (4.1)
V stenting	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)		1 (0.1)
Two-stent bifurcation, n (%)	14 (51.9)	31 (29.8)	38 (28.6)	46 (21.9)	56 (21.7)	**0.005**	185 (25.3)
Femoral, n (%)	1 (3.7)	23 (22.1)	21 (15.8)	17 (8.1)	22 (8.5)	**<0.001**	84 (11.5)
Dual access, n (%)	1 (3.7)	10 (9.6)	13 (9.8)	6 (2.9)	12 (4.7)	**0.028**	42 (5.7)
Microcatheter, n (%)	1 (3.7)	8 (7.7)	15 (11.4)	11 (5.2)	24 (9.3)	0.245	59 (8.1)
Cutting balloon, n (%)	0 (0.0)	0 (0.0)	10 (7.5)	23 (11.0)	52 (20.2)	**<0.001**	85 (11.6)
Rota, n (%)	1 (3.7)	4 (3.8)	5 (3.8)	6 (2.9)	12 (4.7)	0.908	28 (3.8)
IVL, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.9)	16 (6.2)	**0.001**	20 (2.7)
DEB, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	5 (2.4)	38 (14.7)	**<0.001**	43 (5.9)

Bold values indicate statistical significance.
ACS: Acute coronary syndrome; DEB: Drug-eluting balloon; DKC: Double-kiss crush; IVL: Intravascular lithotripsy; LMS-PCI: Left main percutaneous coronary intervention; SKS: Simultaneous kissing stents; SD: Standard deviation; TAP: T and protrude.

Multivariate logistic modelling of 1- and 12-month mortality was used to adjust outcomes for baseline and procedural comorbidities. One-month mortality was associated with older age (OR: 1.11, 95% CI: 1.02–1.20) and diabetes (OR: 10.94, 95% CI: 2.41–49.68). Higher BMI was associated with lower odds of death at 30 days (OR: 0.81, 95% CI: 0.67–0.97), as shown in Figure 1. Co-variates associated with higher 12-month mortality are

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Table 3. Unadjusted outcomes of cases included in the study.

	2017	2018	2019	2020	2021	p-value	Overall
n	27	104	133	210	258		732
Dissection, n (%)	1 (3.7)	5 (4.8)	2 (1.5)	3 (1.4)	2 (0.8)	0.102	13 (1.8)
Shock induced, n (%)	0 (0.0)	3 (2.9)	0 (0.0)	1 (0.5)	1 (0.4)	0.061	5 (0.7)
Coronary perforation, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1.000	732 (100.0)
Slow flow, n (%)	0 (0.0)	1 (1.0)	2 (1.5)	0 (0.0)	1 (0.4)	0.407	4 (0.5)
DCCV, n (%)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.196	1 (0.1)
Sidebranch loss, n (%)	0 (0.0)	2 (1.9)	1 (0.8)	1 (0.5)	3 (1.2)	0.741	7 (1.0)
Arterial complications, n (%)	0 (0.0)	2 (1.9)	1 (0.8)	1 (0.5)	1 (0.4)	0.555	5 (0.7)
TLR, n (%)	0 (0.0)	2 (1.9)	2 (1.5)	7 (3.3)	6 (2.3)	0.726	17 (2.3)
Death within 30 days, n (%)	0 (0.0)	3 (2.9)	4 (3.0)	3 (1.4)	4 (1.6)	0.673	14 (1.9)
Death within 12 months, n (%)	1 (3.7)	9 (8.7)	13 (9.8)	18 (8.6)	19 (7.4)	0.832	60 (8.2)

DCCV: Direct current cardioversion; TLR: Target lesion revascularisation.

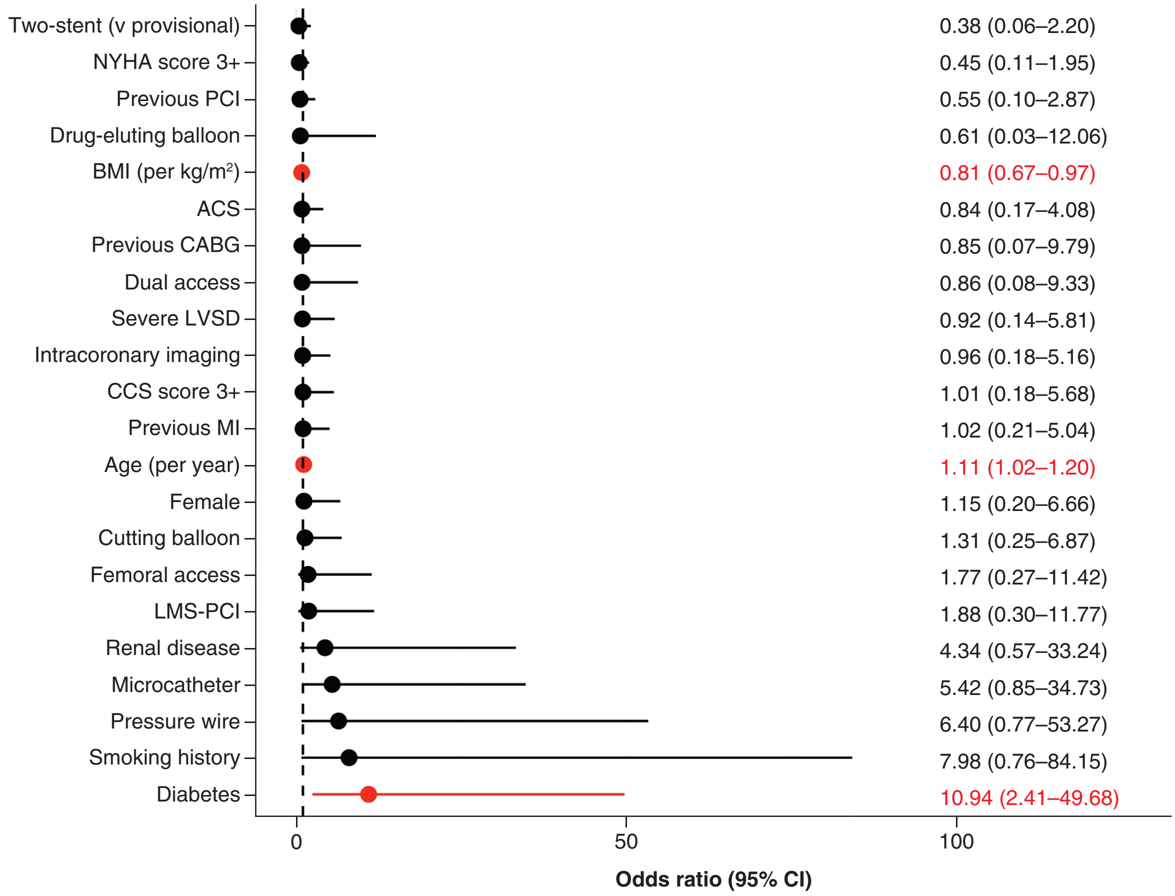

Figure 1. Multivariate-adjusted model for 30-day mortality in bifurcation PCI cases 2017–2021.
ACS: Acute coronary syndrome; CABG: Coronary artery bypass grafting; CCS: Canadian Cardiovascular Society; LMS-PCI: Left main percutaneous coronary intervention; LVSD: Left ventricular systolic dysfunction; MI: Myocardial infarction; NYHA: New York Heart Association; PCI: Percutaneous coronary intervention.

presented in Figure 2, demonstrating associations with older age (OR: 1.08, 95% CI: 1.04–1.12), diabetes (OR: 2.36, 95% CI: 1.22–4.57), smoking history (OR: 3.14, 95% CI: 1.32–7.46) and pre-existing renal disease (OR: 6.59, 95% CI: 2.26–19.20).

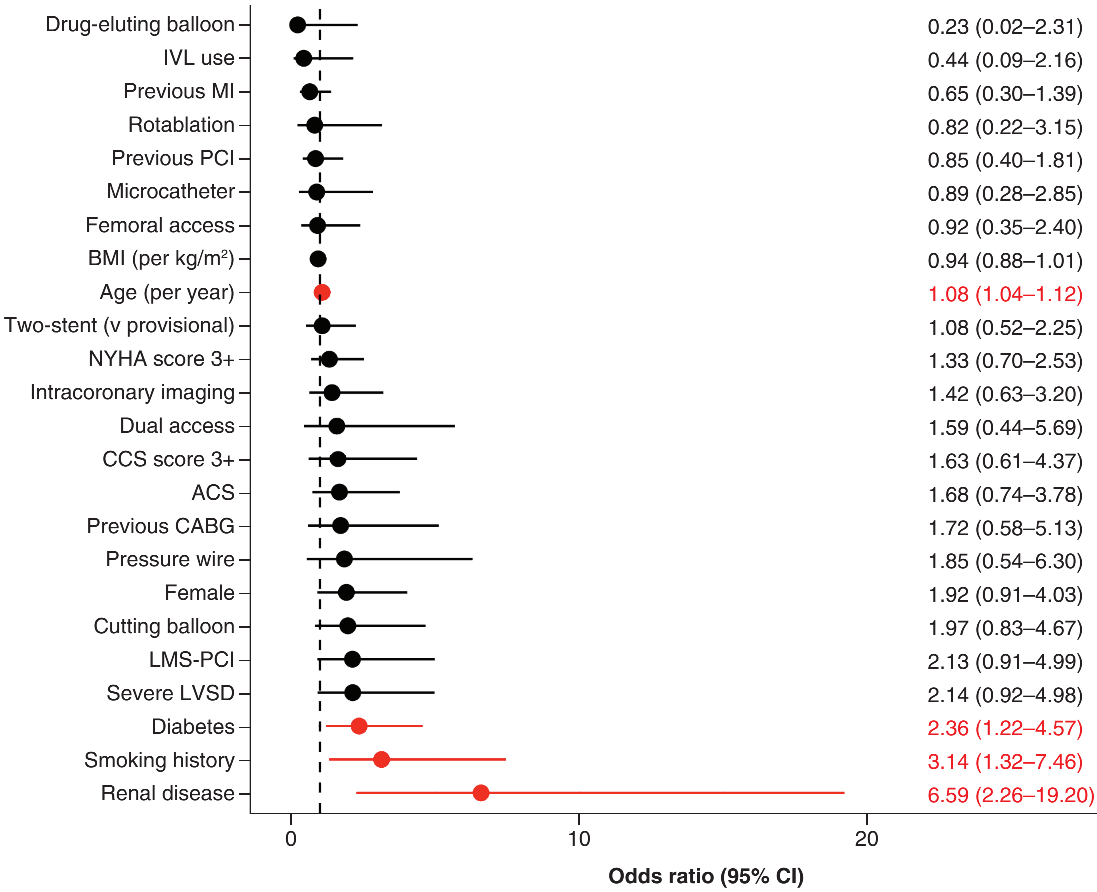

Figure 2. Multivariate-adjusted model for 12-month mortality in bifurcation PCI cases 2017–2021.
ACS: Acute coronary syndrome; CABG: Coronary artery bypass grafting; CCS: Canadian Cardiovascular Society; IVL: Intravascular lithotripsy; LMS-PCI: Left main percutaneous coronary intervention; LVSD: Left ventricular systolic dysfunction; MI: Myocardial infarction; NYHA: New York Heart Association; PCI: Percutaneous coronary intervention.

Subgroup analysis of provisional versus two-stent bifurcation PCI techniques demonstrated no difference in unadjusted mortality or TLR (Supplementary Table 2). Multivariate logistic modelling of TLR demonstrated no significant association between any of the co-variates with TLR (Supplementary Figure 2). None of the adjusted models demonstrated associations of two-stent (versus provisional) techniques with mortality (Figures 1 & 2) or TLR (Supplementary Figure 2).

Discussion

In this study, we investigated mortality, periprocedural complications and TLR in patients who had bifurcation PCI in a tertiary cardiac centre in the UK. Using this 'real-world' data on bifurcation PCI, we identified risk factors (such as diabetes and age) associated with mortality at 30 days and 12 months in this complex patient group, and found no differences in outcomes between two-stent and provisional strategies both before and after adjustment for co-variates. Our data informs the on-going debate and controversy regarding the use of provisional stenting [9,10].

We found that this patient group had a mortality of 1.9% and 8.2% at 30-day and 12-month, respectively. The 30-day mortality rates are similar to those of all-comer PCI, which have previously been reported to be around 1.5% [11]. The 12-month mortality rate in our study is 8.2%, which is broadly within the previously reported range of 4–8% in smaller 'real-world' studies [8,12]. We speculate this may be due to the large proportion of LMS PCI procedures (41.8% of our cohort, Table 2) which carry a higher mortality particularly in this comorbid population, as we reported previously [13]. Reassuringly, the rates of TLR reported in this study are similar to contemporary rates published by other registries and meta-analyses, around 1–5% [12,14,15].

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There were no differences in mortality between two-stent and provisional strategies in the unadjusted dataset (Supplementary Table 2) and this variable was not predictive of mortality following adjustment (Figures 1 & 2). This is in line with evidence from a large meta-analysis that demonstrates no difference in mortality between bifurcation techniques [16]. The rates of TLR were also similar between two-stent and provisional strategies, despite previously published studies suggesting that two-stent strategies were associated with higher TLR than provisional strategy [14,15]. It is worth noting that the choice of strategy in the cases included in this study was up to operator discretion/heart team decision, and not randomized. Therefore, the similar TLR rates between two-stent and provisional suggest good 'real-world' outcomes driven by sound clinical decision making, which may be more important that the technical element of bifurcation PCI alone [17].

Diabetes and older age were significantly associated with 30 day mortality (Figure 1), and alongside smoking history and pre-existing renal disease were significant risk factors for 12 month mortality in bifurcation PCI (Figure 2). Diabetes mellitus is a strong predictor of stent failure through in-stent restenosis, by altering inflammation signals and impairing healing mechanisms that follow stent implantation [18]. Both older age and pre-existing renal disease have been shown to predict major adverse cardiac events in all-comer PCI [19]. Smoking history, alongside age and renal disease have all been shown to be predictors of worsening coronary calcifications, likely through altering vascular smooth muscle remodelling, which adds to the complexity and the risk of bifurcation PCI [20–22]. Therefore, it is not surprising that these factors appear to predict mortality following bifurcation PCI (Figure 2). Interestingly, BMI was associated with a protective effect (reduced mortality) at 30 days (Figure 1). This is in line with the previously described paradox of higher BMI and lower mortality post-PCI [23].

Severe LV systolic dysfunction (LVSD) was not predictive of poor survival. This is despite evidence to the contrary in recent literature from the BCIS UK-wide data where severe LVSD led to worse in-hospital and longer term outcomes [19,24]. This equivocal finding may be due to the small proportion of patients in this study with severe LVSD (10.8%; Table 1) which may reduce the power of the study to detect differences with this co-variate. Similarly, ACS presentations were not associated with worse outcomes which suggests that an *ad-hoc* strategy for bifurcation PCI in ACS patients does not infer worse outcomes [25].

In line with published literature, the prevalence of bifurcation PCI in this dataset was 10% of all coronary procedures (Supplementary Figure 1) [2,3]. Over the course of the study period, we noted an increase in the use of intracoronary imaging and adjunctive strategies such as cutting balloons, IVL and DEB devices. Recent evidence has demonstrated a role for intracoronary imaging in complex bifurcation lesions such as LMS-PCI, leading to improved 30-day and 12-month mortality [26]. While we did not find statistically significant association between survival and intracoronary imaging in all comer bifurcation PCI, the study was not powered to detect that and this is a question that needs answering in larger studies/registries of bifurcation interventions. Of interest is the increasing use of DEB devices, which may at times influence the operator to favour a provisional strategy with a DEB kissing inflation in lieu of implanting a side branch stent [27], although this is not supported by robust data at the current time. This, alongside the improvements in provisional stenting backed up by evidence for proximal optimisation techniques [28], may in part explain the much larger increase in the proportion of provisional cases (48.1% increasing to 78.3%) during the study period compared with two-stent strategies (Table 2). This of course is in the context of overall higher number of bifurcation PCI over the study period (Table 2) and is in line with the European Bifurcation Club consensus guidelines to pursue provisional strategy as first line where possible [29], a strategy somewhat at variance with that advocated by the group behind the DK-CRUSH family of RCTs [30,31].

Limitations of the study

Firstly, the database does not record SYNTAX score, troponin levels or Medina classification and therefore we are unable to provide any further insights about the impact of these variables on outcomes of bifurcation PCI. Secondly, the location and cause of complications (Table 3) is not distinguished by our database. Thirdly, the database does not distinguish between upfront two-stent bifurcation procedures and those which were planned provisional but required conversion to two stents. Finally, despite aiming to correct for baseline differences, the observational and retrospective nature of our study may still have unmeasured confounders such as frailty, technical difficulties or operator expertise/volume which may impact on outcomes of bifurcation PCI [32]. Consequently, conclusions need to be interpreted in the context of the nature of the study design.

Conclusion

In a 'real-world' cohort of patients undergoing bifurcation PCI, co-variates directly associated with 30-day mortality were age, diabetes mellitus while BMI was inversely associated with mortality. Mortality at 12-month was associated with age, diabetes mellitus, smoking history and renal disease. There was no difference in TLR or mortality between provisional and two-stent bifurcation techniques both before and after adjustment for co-variates. Awareness of the 'real-world' outcomes of bifurcation PCI in this patient group should be used for appropriate patient selection, technique planning and procedural consent.

Summary points

- Bifurcation PCI is a complex procedure which is performed in the presence of coronary disease in a significant side branch of the stented main vessel.
- However, real-life data on hard outcomes of bifurcation PCI remain limited.
- In databases from a UK tertiary centre, bifurcation PCI volumes increased since 2017 to 2021.
- Covariates associated with higher 12-month mortality include age, diabetes mellitus, renal disease and smoking status.
- Overall mortality from bifurcation PCI in this 'real-world' cohort was at 1.9% (30 days) and 8.2% (12 months).
- The rate of TLR at 12 months was 2.3%.
- There was no significant difference in mortality or TLR between provisional and two-stent bifurcation PCI cases both before and after adjustment for co-variates.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/suppl/10.2217/fca-2023-0058

Author contributions

MB Protty, A Choudhury and A Hailan led on conceptualization and developed methodology. T Valenzuela, A Sharaf, J Shome and S Hasan carried out data curation. MB Protty, T Valenzuela, A Sharaf, J Shome and S Hasan carried out initial data analysis. All authors contributed to original drafting as well as review and editing of manuscript. A Choudhury and A Hailan provided overall supervision.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The study design was approved by the local clinical governance board as a quality governance project.

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