

**Impact of intravascular ultrasound on chronic total occlusion percutaneous
revascularization**

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Abstract

Aim: We sought to investigate the impact of IVUS use on chronic total occlusion (CTO) PCI using data from a contemporary registry of consecutive patients and applying a propensity score matching analysis.

Methods and results: We evaluated 514 successful CTO-PCIs, median age: 67 years (IQR: 58-73), 83.5% males. IVUS-guided PCI was performed in 184 (35.8%) of cases. After using 1:1 propensity matching score analysis, two groups of 182 patients each (IVUS-guided vs. angiography-guided CTO-PCI group) were produced to form the study population.

In the IVUS-guided group the median maximum stent diameter was larger and the median total stented segment was longer compared to the angiography-guided group [(3.5 mm, IQR: 3.0-4.0 vs. 3.2 mm, IQR: 3.0-3.5, $p < 0.001$) and (60.0 mm, IQR: 38.0-91.3 vs. 38.0 mm, IQR: 32.0-70.5, $p < 0.001$), respectively]. In the IVUS-guided group, retrograde recanalization was more frequently encountered compared to the angiography-guided PCI group (30.2% vs. 20.9%, $p=0.04$). Procedural time was significantly longer in the IVUS-guided group, without any difference in fluoroscopy time, radiation dose and contrast volume. Multivariate linear regression analysis showed that IVUS use was the strongest independent factor associated with larger maximum diameter stents ($p<0.001$) and a strong independent predictor for total stented segment length during CTO-PCI ($p<0.001$).

Up to 8 years follow-up, there was no difference in the incidence of the composite endpoint of all-cause death, cardiac death, myocardial infarction and target vessel revascularization between the IVUS-guided PCI and the angiography-guided PCI groups (hazard ratio: 13.7% vs. 15.9%, respectively, log-rank: $p = 0.67$, median follow-up time: 49.0 months, IQR: 33.0-67.0).

Conclusions: Use of IVUS in CTO-PCI was associated with larger stent diameter and longer stented segments. Despite more frequent use of IVUS in retrograde CTO-PCI, there was no

difference in long-term adverse events between IVUS and angiography CTO-PCI groups; nevertheless, the study was not powered to assess clinical outcomes.

Introduction

Over the last years, the procedural success rates of percutaneous coronary interventions (PCI) for chronic total occlusions (CTO) have substantially been improved by the refinement of the applied techniques and technologies (1, 2). Nevertheless, the distinct and complex morphological features that accompany CTO lesions, such as high plaque burden, heavy calcification, increased length and negative vessel remodelling, are associated with increased risk of restenosis and re-occlusion (3-5). In this setting, intravascular ultrasound (IVUS) represents a useful adjunctive tool able to accurately assess lesion length, identify the appropriate landing zone and guide optimisation after stent deployment (6). Features like stent under-expansion and geographical miss have been considered powerful modifiable factors associated with future stent failure (7-10). IVUS can guide stent diameter and length selection aiming to adequate lesion and inflow/outflow disease coverage and optimal stent expansion. In this study, we sought to investigate the impact of IVUS utilisation during CTO-PCI in various procedural metrics such as stent size and length, procedural and fluoroscopy time, radiation dose, contrast volume, as well as the association of IVUS-guided CTO-PCI with in-hospital complications and long-term outcomes after successful CTO recanalization.

Methods

Study population and database

This was an observational study based on the prospective collection of clinical, angiographic and procedural data of consecutive patients undergoing successful CTO-PCI in a tertiary cardiac centre since the onset of a dedicated CTO programme (Essex Cardiothoracic Centre, Basildon, United Kingdom). From June 2012 until November 2018, 660 CTO-PCIs were performed, and 514 successful procedures were included in the current study. As part of the

programme and for auditing purposes all data were prospectively recorded in a dedicated CTO database. For parameters not specific for CTOs, the database uses data collected as part of the BCIS (British Cardiovascular Intervention Society) National PCI Audit dataset collected under the auspices of the National Institute for Cardiovascular Outcomes Research and is compliant with UK data protection legislation. These data include patient's demographic, cardiovascular risk factors, comorbidities and procedural data like arterial access, attempted vessel(s), use of adjunctive tools (e.g., intracoronary imaging, rotablation etc), balloons and stents used, periprocedural and in-hospital complications. According to the definitions of the BCIS dataset, stent size in cases of post-dilatation reflects the size of the largest device (stent or post-dilatation balloon) used (11). Patients' survival information was obtained by linkage of patients' National Health Service numbers to the Office of National Statistics, which records live status and the date and cause of death for all deceased patients. Finally, myocardial infarction and target vessel revascularization were assessed using hospital records.

CTO PCI procedure

In all patients, the indication of revascularization was symptoms of stable angina and in the absence of typical symptoms evidence of inducible ischaemia on non-invasive functional tests according to the current recommendations (12). CTOs were defined as coronary lesions with Thrombolysis In Myocardial Infarction (TIMI) grade 0 flow of at least three months in duration(3). The J-CTO and EuroCTO (CASTLE) scores were used to evaluate procedural complexity (13). All patients signed an informed consent prior to the procedure.

CTO-PCI was performed by using contemporary CTO-PCI principles and crossing strategies (4). Treatment strategy and recanalization techniques for each case were determined according to the operator's discretion. The techniques used for vessel recanalization were categorised

into antegrade wire escalation (AWE), antegrade dissection and re-entry (ADR) and retrograde approach (RA) as described in a previous study from the same registry(5). All PCIs were performed using second generation drug eluting stents. The use of IVUS was determined by operator's preference. IVUS was used for stent planning (i.e. vessel sizing, lesion length assessment and lesion preparation) +/- optimisation (i.e. post-dilatation). There was no prespecified protocol regarding stent sizing selection and stent optimization criteria. An illustration of IVUS-guided CTO-PCI is shown in **Figure 6**. Occasionally, IVUS was used as an adjunct tool to vessel wiring (i.e. proximal cap ambiguity delineation, re-entry), but this indication was rare and was not documented separately. One of the two commercially available IVUS catheter transducers was used, either the solid state 20-MHz Eagle Eye transducer (Volcano Therapeutics, Rancho Cordova, CA) or the mechanical 40-MHz Opticross transducer (Boston Scientific, Natick, Massachusetts). In-hospital complications included any of the following: death, acute kidney injury (AKI) requiring renal replacement therapy (RRT), stroke, major bleeding requiring blood transfusion, perforation and pericardial effusion requiring pericardiocentesis or surgical intervention (tamponade).

Statistical analysis

To reduce treatment selection bias and potential confounding factors and to adjust for significant differences in characteristics of patients and lesions or predilection factors favouring IVUS use, a non-parsimonious ranking propensity-score matching analysis with a nearest neighbor 1:1 matching algorithm with callipers of 0.2 SDs of the logit of the propensity score was performed. The observed groups of IVUS-guided PCI and angiography-guided PCI were matched based on the following characteristics that could bias IVUS use: CTO complexity scores including the J-CTO and EuroCTO (CASTLE) scores; age; chronic kidney

disease; previous PCI and target CTO vessel; and they were balanced for other baseline demographic data such as gender, hypertension, diabetes and hypercholesterolaemia. All quantitative variables were tested for normal distribution according to the Kolmogorov-Smirnov test. Continuous variables are reported as median [interquartile range (IQR)]. Categorical variables are expressed as frequency and proportion. Continuous variables were compared using the Mann-Whitney U test. Categorical data were compared using the Pearson chi-squared test. A multivariate linear regression analysis adjusted for potential confounders was performed to determine independent predictors of maximum stent diameter and total stent length. In addition, for evaluating the impact of the level of IVUS experience in CTO-PCI metrics, we analysed the association of IVUS use with CTO-PCI metrics after creating two groups of CTO-PCI cases based on IVUS level of experience including an early experience group (2012-2014) and a late experience group (2015-2018). Finally, Kaplan Meier analysis with log-rank test was performed to evaluate the impact of IVUS in long-term incident of the composite endpoint of all-cause death, cardiac death (CD), myocardial infarction (MI) and target vessel revascularization (TVR) as well as individual outcomes after successful recanalization of coronary CTOs. Statistical analysis was performed with SPSS, Version 24.0 (IBM Corp., Armonk, NY, USA) with R version 3.2.2 (The R foundation for Statistical Computing, Vienna, Austria) SPSS extension for propensity score analysis.

Results

During the study period, 514 successful CTO-PCI cases were identified and included in the analysis. Intravascular ultrasound-guided PCI was performed in 184/514 cases (35.8%). There was a significant rise in IVUS uptake from 10% in 2012 up to 44% in 2018 ($p < 0.001$) (**Figure 1**). After propensity score matching, 2 groups of 182 patients each were produced to form

the final study population. Clinical baseline characteristics of the two study groups are summarised in **table 1**. Both groups were well matched for most of the baseline characteristics including the prevalence of diabetes, hypertension, dyslipidaemia, chronic kidney disease, cerebrovascular and peripheral vascular disease, history of current smoking, history of previous PCI and CABG, left ventricular systolic function and age.

Procedural characteristics of the two study groups are summarized in **table 2**. There was no difference with regards to the IVUS use across the different strata of CTO complexity scores either J-CTO or EuroCTO (CASTLE) scores. However, in the IVUS-guided CTO-PCI group, retrograde approach was more frequently encountered as the successful PCI strategy compared to the angiography-guided PCI group (30.2% vs. 20.9%, $p=0.04$). There was almost two-fold more frequent use of rotablation in the IVUS-guided PCI; however, this difference did not reach statistical significance (3.8% vs. 1.6%, $p = 0.2$). The IVUS-guided PCI group was associated with larger maximum stent diameter compared to the angiography guided group: 3.5 mm, IQR: 3.0-4.0 vs. 3.25 mm, IQR: 3.0-3.5, $p < 0.001$. Furthermore, the IVUS-guided group had longer total stented segment: 60.0 mm, IQR: 38.0-91.3 vs. 38.0 mm, IQR: 32.0-70.5, $p < 0.001$. (**Figure 2**). Although, IVUS use was associated with longer overall procedural time compared to angiography-guided PCI group (138.0 min, IQR: 102.8-180.0 vs. 108.0 min, IQR: 108.0-160.0, $p < 0.001$), there was no statistically significant difference between the groups regarding fluoroscopy time, procedural radiation dose area product (DAP) and total contrast volume (**table 3, figure 3**). Furthermore, the impact of IVUS use on maximum stent diameter, total stent length and procedural time remained similar when the analysis was performed separately in the two groups of early and late IVUS experience. However, in the early IVUS experience group, IVUS-guided CTO-PCI was associated with significantly higher radiation DAP and contrast volume (**table 3**). In the IVUS-guided PCI group there was a significant

reduction of contrast volume between the time period of early IVUS experience (2012-2014) vs. late experience (2015-2018), [300.0 ml (IQR: 230.0-350.0) vs. 250.0 ml (IQR: 190.0-300.0), respectively, $p = 0.002$].

After adjusting for multiple confounding factors including age, chronic kidney disease, hypertension, diabetes, hyperlipidaemia, EuroCTO (CASTLE) score, J-CTO score, gender, BMI and previous CABG, the use of IVUS was the strongest independent factor associated with the deployment of larger maximum stent diameter during CTO-PCI (beta coefficient = 0.185, 95% CI: 0.086-0.282, $p < 0.001$) (**table 4**). Furthermore, IVUS use was a strong independent predictor associated with longer total stented segment (beta coefficient = 10.845, 95% CI: 5.491-16.199, $p < 0.001$). Additional independent predictors of longer total stented segment included the use of RA and ADR recanalization approach, and RCA-PCI (**table 5**).

With regards to the impact of IVUS on CTO-PCI in-hospital complications rate, there was no difference between the angiography and IVUS-guided CTO-PCI groups regarding the incidence of in-hospital death, AKI requiring RRT, major bleeding requiring blood transfusion, stroke, perforation and tamponade (**table 6**). Finally, the overall incident of the composite endpoint of all-cause death, CD, MI and TVR up to 8 years of follow-up was similar in the IVUS-guided vs. angiography-guided PCI group (hazard ratio: 13.7% vs. 15.9%, respectively, log-rank: $p = 0.67$, median follow-up time: 49.0 months, IQR: 33.0-67.0). With regards to the individual endpoints IVUS-guided CTO-PCI compared to angiography-guided CTO-PCI was associated with numerically lower rates of all-cause death (hazard ratio: 4.9% vs. 8.2%, respectively, log-rank: $p = 0.52$), CD (hazard ratio: 1.1% vs. 3.8%, respectively, $p = 0.12$) and MI (hazard ratio: 1.6% vs. 2.7%, respectively, $p = 0.49$), however the difference did not reach statistical significance. Finally, there was no difference between the two groups regarding the incidence of TVR (hazard ratio: 9.9% vs. 9.3%, respectively, $p = 0.38$) (**figure 5**).

Discussion

In the present study, we evaluated the impact of IVUS use in a real-world cohort of patients undergoing CTO-PCI with contemporary recanalization techniques in the context of a dedicated CTO-PCI programme. In order to reduce selection bias, potential confounding factors and to adjust for significant differences in patients and lesions characteristics propensity-score matching analysis was applied. The main findings of our study are as follows: 1) IVUS use was increased significantly overtime along with operators' experience. 2) IVUS was associated with the deployment of larger stents and was the strongest independent predictor of final maximum stent diameter. 3) IVUS was associated with longer total stented segment and was a strong independent predictor of the total stented segment. 4) Although IVUS was associated with longer procedural time, there was no difference regarding important safety metrics including radiation dose, fluoroscopy time and contrast volume compared to angiography-guided group. 5) IVUS use was associated with more frequent retrograde CTO recanalization, but the overall in-hospital complications rate and long-term adverse events including all-cause death, cardiac death, MI and TVR were similar between IVUS and angiography-guided PCI groups.

Recent studies on all-comers patients and during PCI for complex lesions have demonstrated that IVUS use is associated with superior clinical outcomes including CD, MI, stent thrombosis and ischemia-driven target lesion revascularization compared to angiography guided PCI (15-18). The presumed mechanisms of such favourable results are appropriate stent planning and optimisation. However, even within complex lesions, CTOs represent a discrete subset with distinct and complex morphological features such as increased lesion length, high plaque burden, heavy calcification and negative distal vessel remodelling. In this context, intuitively

the benefit by IVUS-guided stent deployment is expected to be greater. Nevertheless, the number of dedicated studies assessing procedural and clinical outcomes of IVUS-guided CTO-PCI is limited.

A 2015 study ("IVUS-CTO") randomised 402 CTO patients to IVUS-guided versus angiography-guided PCI after successful wire crossing. At 1 year, rates of MACE were significantly lower in the IVUS-guided group (2.6 % versus 7.1 %; hazard ratio 0.35; 95 % CI [0.13–0.97]; p=0.035). In addition, patients in the IVUS-guided group were more likely to receive high-pressure post-dilatation after stenting and had larger final minimum lumen diameter compared with the angiography group (19). In the same year a smaller study ("AIR-CTO") randomised 230 patients to IVUS-guided versus angiography-guided CTO-PCI and assessed in-stent late lumen loss (LLL) at one-year. In-stent LLL in the IVUS-guided group was significantly lower (0.28 ± 0.48 mm vs. 0.46 ± 0.68 mm, p=0.025). In addition, specifically for the CTO-PCI cases with "in-true-lumen" stents, there was significantly lower rate of restenosis in the IVUS-guided group (3.9% vs. 13.7%, p=0.021). At 2 years follow up, the IVUS guided group had a lower rate of stent thrombosis, but no different MACE overall, although the study was not powered to assess clinical outcomes (20). An older study (recruitment period January 2007 to December 2009) using data from a multicentre CTO PCI registry (n=402) showed that IVUS use was associated with significantly reduced rates of stent thrombosis, numerically lower rate of MI and reduced rates of target lesion revascularization in patients with long CTO lesions > 30 mm, but similar rates of MACE overall (21).

Our analysis offers complementary data to these previous studies, providing a possible mechanistic explanation of the better clinical outcomes observed with IVUS use. The larger final stent size could translate to larger final lumen area and the longer stented segment could mean appropriate lesion coverage with avoidance of geographical miss. Both are well

recognised and validated predictors of future stent failure (22). In our study, although IVUS-guided CTO-PCI was associated with numerically lower incident of all-cause death, CD and MI; there was no statistically significant difference in the overall incidence of the composite endpoint of adverse events or in the incidence of the individual endpoints, up to 8 years of follow-up. Like the previous studies, this can be explained by the sample size, which did not provide the statistical power to assess clinical outcomes. Another potential reason is the fact that additional comorbidities might contribute to all-cause mortality in the long-term basis. In addition, in the IVUS-guided PCI group the retrograde approach was more frequently used and rotablation use was numerically more frequent indicating an increased level of case complexity for this group. In this setting, IVUS use might have intuitively resulted in a substantial prognostic benefit in the more complex CTO PCI cases, with achievement of improved outcomes comparable to those in less complex cases. Furthermore, our study adds to the literature of IVUS use in CTO PCI, as it reports outcomes in a contemporary setting of complex CTO cases, current recanalization techniques and improved devices. Median J-CTO score was 2 and median total stent length was 48 mm, 15% of patients had previous CABG, 22% were diabetics and 44% had calcified lesions. In 40% of cases a dissection and re-entry technique (either antegrade or retrograde) was applied to achieve successful recanalization. In the IVUS-CTO study, dual access with contralateral injections was used only in around 50% of cases and AWE was the successful recanalization strategy in 91% of cases. In the AIR-CTO study, in 76% of cases 1st generation DES were used and antegrade approach was the successful strategy in 85% of cases. In contrast, in large contemporary CTO PCI cohorts, RA is the successful strategy in 1/3 of cases and ADR up to 20% in some registries (1,2). The modest complexity of CTO lesions in these previous studies might have obscured the actual impact of IVUS in the overall prognostic benefit post CTO-PCI.

The value of IVUS in CTO-PCI is not limited in the planning and optimisation of stent deployment. It can also aid wire crossing and successful recanalization by resolving proximal cap ambiguity, clarifying wire position during both antegrade and retrograde crossing attempts and facilitating wire re-entry from subintimal position or assisting the reverse controlled antegrade and retrograde tracking and dissection (reverse CART) technique (6). A recent multicentre registry (n=619) reported that intracoronary imaging (i.e. IVUS > 90%) was used in 35.7% of the cases for CTO crossing (23). Furthermore, the study showed that although intravascular imaging was used in more complex lesions, it was associated with similar rates of technical and procedural success compared to angio-guidance. The study reported longer procedural time when intravascular imaging was used, a finding observed in our study too. This is not a surprise as device set-up and measurements performance would inevitably add time to the procedure. However, our study showed that the important safety metrics of radiation dose and contrast volume were not different. This observation is in agreement with previous studies that evaluated the impact of IVUS use on radiation and contrast dose (24).

Finally, in our study, the interaction of IVUS use with the applied recanalization techniques was evaluated and we demonstrated that a RA was associated with a more frequent IVUS use during CTO-PCI. The extensive tissue damage and subintimal dissection during RA warrant a more thorough assessment of the vessel to allow proper stent sizing and full lesion coverage. This finding is also in keeping with the longer total stented segment in the IVUS-guided PCI group, which likely indicates better lesion coverage and avoidance of leaving uncovered vessel areas with large plaque burden and/or edge dissections.

Limitations

There are a number of limitations in our study. First of all, it is an observational, single-centre study. Such a study's design is prone to selection bias, but the all-comers unselected consecutive cases nature of our registry should eliminate this. Although propensity score matching has been applied uncorrected confounders cannot be excluded. Within the IVUS guided group, there was not a standardised protocol regarding the methodology used to determine stent sizing and optimization, however we provided a typical example of our study cohort on how to use IVUS to optimise stent implantation during CTO PCI. There was no independent core laboratory reporting of IVUS findings.

Conclusion

In conclusion, analysis of a dedicated CTO registry showed that IVUS use increased over time along with operators' experience. In the propensity matched population, IVUS use was associated with implantation of larger diameter stents and longer total stented segments. Although procedural time was prolonged, there was no difference in radiation and contrast dose compared to angiographically guided procedures. Finally, there was no difference between IVUS-guided and angiography-guided CTO-PCI regarding in-hospital complications and long-term clinical outcomes.

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Tables and Figures

Table 1. Baseline characteristics

Variable	Angiography guidance (N=182)	IVUS guidance (N=182)	p-value
Age, median (IQR)	66.0 (58.0-72.0)	66.5 (57-72.3)	
Men (%)	154 (84.6)	152(83.5)	0.8
Hypertension (%)	128 (70.3)	127 (69.8)	0.9
Diabetes mellitus (%)	40 (22.0)	41 (22.5)	0.9
Dyslipidaemia (%)	147 (80.8)	152 (83.5)	0.5
Peripheral vascular disease (%)	13 (7.1)	12 (6.6)	0.8
Cerebrovascular disease (%)	11 (6.0)	9 (4.9%)	0.6
Chronic kidney disease (%)	33 (18.1)	34 (18.7)	0.6
Family history (%)	96 (52.7)	77 (42.3)	0.05
Current smoker (%)	44 (24.2)	47 (25.8)	0.6
Previous PCI (%)	81 (44.5)	82 (45.1)	0.9
Previous myocardial infarction (%)	85 (46.7)	85(46.7)	1.0
Previous CABG (%)	28 (15.4)	25 (13.7)	0.7
LV function			0.8
Good (%)	127 (69.8)	133 (71.4)	
Moderate (%)	50 (27.5)	44 (24.2)	
Severe (%)	5 (2.7)	5 (2.7)	
CTO target vessel			0.6
LAD (%)	51(28.0)	46(25.3)	

LCx (%)	17(9.3)	13(7.1)	
RCA (%)	114(62.6)	123(67.6)	

IQR: Interquartile range; PCI: Percutaneous coronary Intervention; CTO: Chronic total occlusion; LAD: Left anterior descending artery; LCx: Left circumflex artery; RCA: Right coronary artery; LV function: Left ventricular function; CABG: Coronary artery bypass grafting

Table 2.

Procedural characteristics

Variable	Angiography guidance (n=182)	IVUS guidance (n=182)	p-value
Successful strategy			
AWE (%)	126 (69.2)	110 (60.4)	0.08
ADR (%)	18 (9.9)	17 (9.3)	0.9
RA (%)	38 (20.9)	55 (30.2)	0.04
J-CTO score			0.9
0 (%)	28 (15.4)	24 (13.2)	
1 (%)	51 (28.0)	49 (26.9)	
2 (%)	53 (29.1)	57 (31.3)	
≥3 (%)	50 (27.5)	52 (28.6)	
EuroCTO (CASTLE) score			0.4
0 (%)	24 (13.2)	16 (8.8)	
1 (%)	60 (33)	71 (39)	
2 (%)	57 (31.3)	59 (32.4)	
3 (%)	30 (16.5)	22 (12.1)	
≥4 (%)	11 (6.0)	14 (7.7)	
Bilateral injections (%)	164 (90.1)	171 (94.0)	0.2
Blunt cap (%)	67 (36.8)	82 (45.1)	0.1
Calcification (%)	79(43.4)	80(44.0)	0.9
CTO length > 20 mm (%)	105 (57.7)	105 (57.7)	1.0

Tortuosity - bent > 45° (%)	42 (23.1)	46 (25.3)	0.6
Max stent diameter (mm) (IQR)	3.25 (3.00-3.50)	3.50 (3.00-4.00)	<0.001
Max stent length (mm) (IQR)	38.0 (32.0-70.5)	60 (38.0-91.3)	<0.001
Number of stents (IQR)	3.0 (2.0-3.0)	2.4 (2.0-3.0)	0.9
Rotablation (%)	3 (1.6)	7 (3.8)	0.2
Procedural time (min) (IQR)	108.0 (78.0-160.0)	138.0 (102.8-235.5)	<0.001
Fluoroscopy time (min) (IQR)	33.9 (20.4-53.1)	36.7 (23.1-58.7)	0.2
Contrast volume (ml) (IQR)	250.0 (200.0-331.3)	250.0 (200.0-320.0)	0.9
Radiation DAP (mGy/cm²) (IQR)	17 112.5 (10121.0-27778.0)	18 506.6 (11106.8-26284.0)	0.5

IQR: Interquartile range; AWE: Antegrade wire escalation; ADR: Antegrade dissection re-entry; RA: Retrograde approach; J-CTO: Multicentre CTO registry in Japan score; CTO: Chronic total occlusion; DAP: Dose area product

Table 3.

CTO PCI metrics based on level of IVUS experience with two groups consisting of an early IVUS experience [(IVUS use in the study group at 30% of cases) (2012-2014)] and a late experience group [(IVUS use in the study group at 55% of cases) (2015-2018)].

Early IVUS experience (2012-2014)			
Variable	Angiography guidance (n=74)	IVUS guidance (n=43)	p-value
Max stent diameter (mm) (IQR)	3.00 (2.75-3.50)	3.50 (3.00-4.00)	0.001
Max stent length (mm) (IQR)	40.5 (28.0-70.0)	60.0 (40.0-92.0)	0.014
Procedural time (min) (IQR)	98.0 (73.5-139.3)	146.0 (106.0-186.0)	<0.001
Fluoroscopy time (min) (IQR)	29.9 (17.4-47.3)	41.4 (17.2-66.2)	0.1
Contrast volume (ml) (IQR)	240.0 (200.0-310.0)	300.0 (230.0-350.0)	0.012
Radiation DAP (mGy/cm ²) (IQR)	13 611.5 (6 742.3-21 105.5)	23 509.0 (11 062.0-33 624.0)	0.004
Late IVUS experience (2015-2018)			
Variable	Angiography guidance (n=108)	IVUS guidance (n=139)	p-value
Max stent diameter (mm) (IQR)	3.25 (3.00-3.50)	3.5 (3.00-4.00)	0.005
Max stent length (mm) (IQR)	38.0(32.3-75.3)	60.0 (38.0-91.00)	0.002
Procedural time (min) (IQR)	120.5 (83.0-175.8)	134.0 (100.0-178.0)	0.2
Fluoroscopy time (min) (IQR)	37.6 (20.8-57.4)	34.4 (24.0-55.3)	0.9
Contrast volume (ml) (IQR)	255.0 (200.0-340.0)	250.0 (190.0-300.0)	0.1
Radiation DAP (mGy/cm ²) (IQR)	18 655.5 (13 052.3-29 981.3)	17 840.0 (11 082.0-24 543.0)	0.1

IVUS: Intravascular ultrasound; CTO: Chronic total occlusion; PCI: Percutaneous coronary intervention; IQR: Interquartile range; DAP: Dose area product

Table 4.

Independent factors associated with maximum stent diameter. The use of IVUS was the strongest independent predictor of larger stent diameter during CTO PCI. The IVUS use was associated with an 18% larger maximum stent diameter during CTO PCI.

	Beta Coefficient	95% CI	P
IVUS	0.184	0.086-0.282	<i>< 0.001</i>
RCA PCI	0.172	0.055-0.290	<i>0.004</i>

IVUS: Intravascular ultrasound; RCA: Right coronary artery; PCI: Percutaneous coronary intervention

Table 5.

Independent factors associated with longer total stented segment during CTO PCI. Antegrade dissection and re-entry technique, IVUS use and RCA PCI were the strongest independent factors associated with longer total stented segment.

	Beta Coefficient	95% CI	P
IVUS	10.845	5.491-16.199	<i>< 0.001</i>
RCA PCI	20.635	14.218-27.737	<i>< 0.001</i>
ADR	17.848	7.959-27.737	<i><0.001</i>
RA	7.653	0.831-14.476	<i>0.028</i>
Dyslipidaemia	8.356	0.692-16.020	<i>0.033</i>

IVUS: Intravascular ultrasound; RCA: Right coronary artery; PCI: Percutaneous coronary intervention; ADR: Antegrade dissection and re-entry; RA: Retrograde approach

Table 6.

In-hospital complications in patients with IVUS and angiography guided PCI.

Complications	Overall (n=364)	Angiography guidance (n=182)	IVUS guidance (n=182)	p-value
Death (%)	0 (0)	0 (0)	0 (0)	1.0
AKI requiring RRT (%)	1 (0.3)	1 (0.5)	0 (0)	0.3
Stroke (%)	0 (0)	0 (0)	0 (0)	1.0
Perforation (%)	16 (4.4)	8 (4.4)	8 (4.4)	1.0
Tamponade (%)	9 (2.5)	4 (2.2)	5 (2.7)	0.7
Major bleeding requiring blood transfusion (%)	7 (1.9)	5 (2.7)	2 (1.1)	0.3

AKI: Acute kidney injury; RRT: Renal replacement therapy

Figure 1.

IVUS guided CTO PCI yearly prevalence. The use of IVUS guided CTO PCI depicts a significant increase from 10% in 2012 to 44% in 2018 ($p < 0.001$).

IVUS: Intravascular ultrasound; CTO: Chronic total occlusion; PCI: Percutaneous coronary intervention;

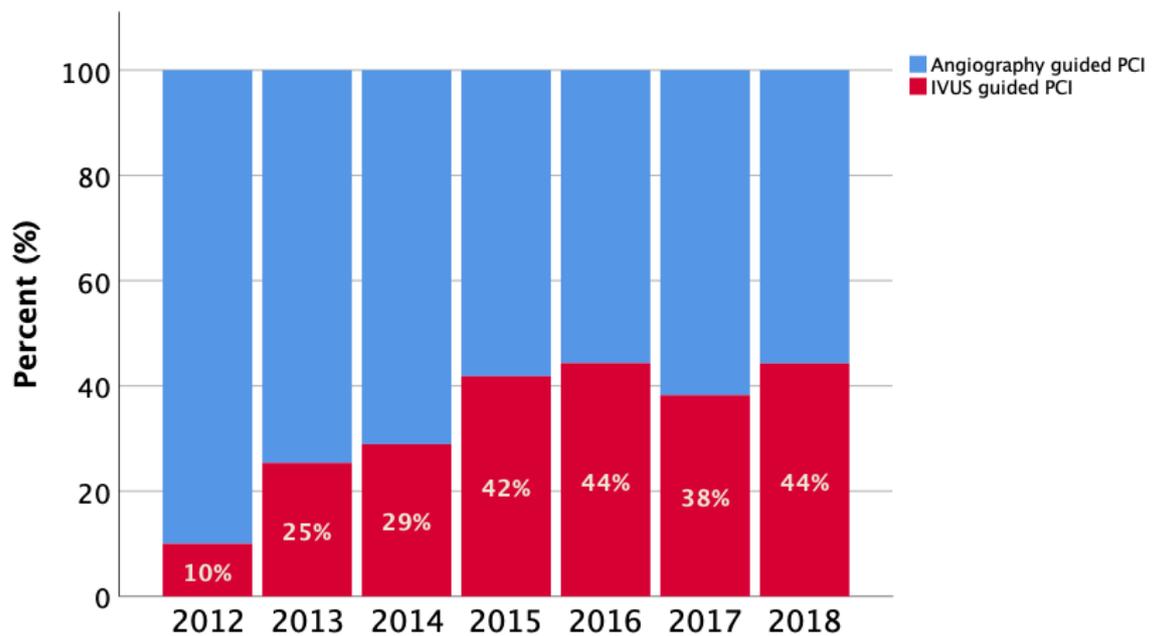


Figure 2.

Maximum stent diameter in patients undergoing angiography and IVUS guided CTO PCI. The IVUS guided CTO group had significantly larger maximum stent diameter. Boxplots represent IQR and horizontal black lines, within the boxplots, median values.

IVUS: Intravascular ultrasound; CTO: Chronic total occlusion; PCI: Percutaneous coronary intervention; IQR: Interquartile range

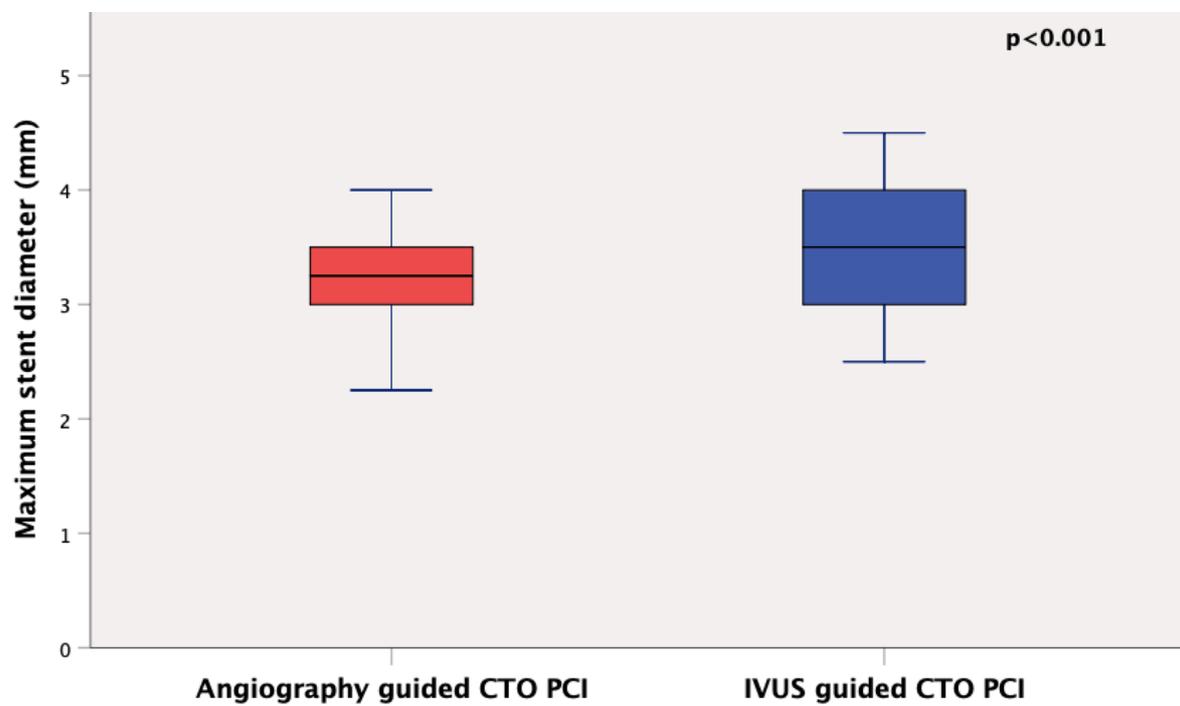


Figure 3.

Maximum total stented segment in patients undergoing angiography and IVUS guided CTO PCI. The IVUS guided CTO group had significantly larger total stented segment. Boxplots represent IQR and horizontal black lines, within the boxplots, median values.

IVUS: Intravascular ultrasound; CTO: Chronic total occlusion; PCI: Percutaneous coronary intervention; IQR: Interquartile range

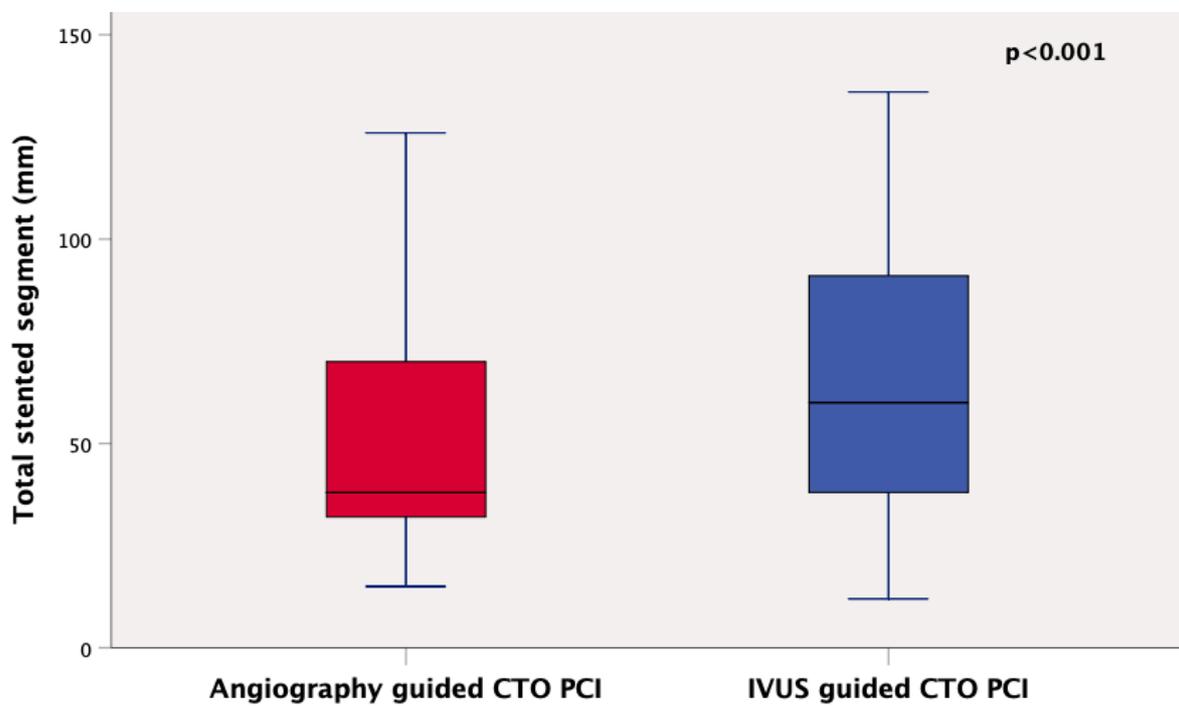


Figure 4.

Various procedural parameters in patients undergoing angiography and IVUS guided CTO PCI including total procedural time, fluoroscopy time, radiation DAP and contrast volume. The IVUS guided CTO group had significantly longer procedural time, whilst there was no difference regarding the other procedural parameters. Boxplots represent IQR and horizontal black lines, within the boxplots, median values.

IVUS: Intravascular ultrasound; CTO: Chronic total occlusion; PCI: Percutaneous coronary intervention; IQR: Interquartile range; DAP: Dose area product

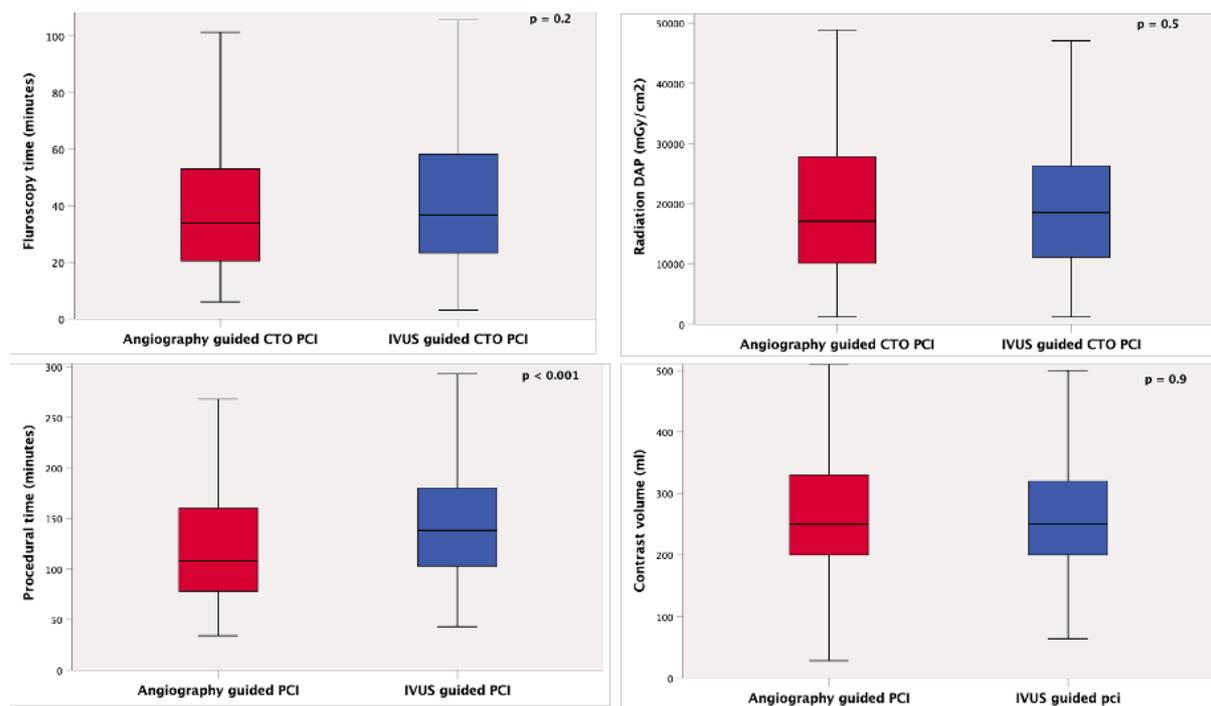


Figure 5.

All-cause death, cardiac death, MI, TVR and MACE defined as the composite endpoint of all-cause death, cardiac death, MI and TVR during long-term follow-up, up to 8 years in patients with angiography vs. IVUS-guided CTO PCI.

MI: Myocardial infarction; TVR: Target vessel revascularization; MACE: Major adverse cardiac events; IVUS: Intravascular ultrasound; CTO: Chronic total occlusion; PCI: Percutaneous coronary intervention.

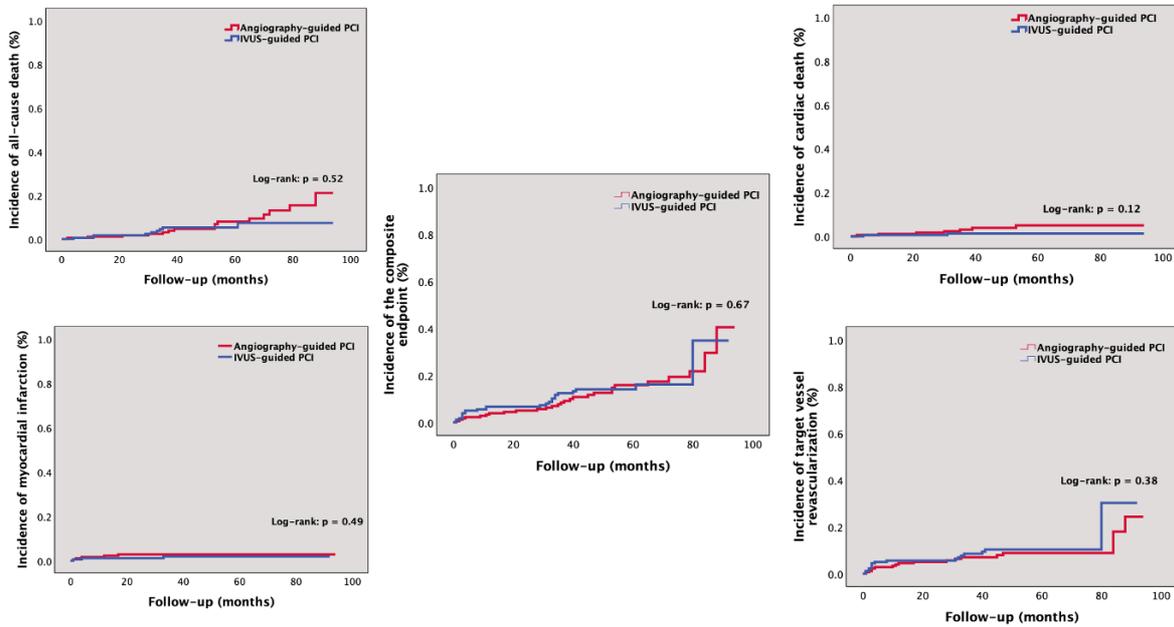


Figure 6.

IVUS guided CTO PCI; A. Initial angiography with contralateral injections to define CTO lesion characteristics; B. Successful antegrade wire crossing; C. Final angiographic result after IVUS guided DES implantation; D. Distal landing zone with reference cross sectional area and diameter estimated at 3 mm; E. CTO segment cross-sectional area and reference diameter estimated at 4.5 mm; F: Proximal landing zone with reference cross sectional area and diameter estimated at 4.5 mm. The overall lesion length requiring stent coverage from distal landing zone was estimated at 65 mm and therefore two overlapping DES 3.0 x 38 mm and 4.0 x 38 mm were successfully implanted and post-dilated with 3.5 and 4.5 mm non-compliant balloons based on media to media reference diameters as per IVUS measurements; G: Distal stent cross-sectional area with excellent absolute ($> 5.5 \text{ mm}^2$) and relative expansion ($>100\%$); E: Proximal stent cross-sectional area with excellent relative expansion ($>100\%$).

IVUS: Intravascular ultrasound; CTO: Chronic total occlusion; PCI: Percutaneous coronary intervention; DES: Drug eluting stents

