

**Computed Tomography Coronary Angiography (CTCA) prior to Chronic Total Occlusion (CTO)
Percutaneous Coronary Intervention (PCI) - a feasibility study**

TRIAL SUMMARY

Trial Title	Computed Tomography Coronary Angiography (CTCA) prior to Chronic Total Occlusion (CTO) Percutaneous Coronary Intervention (PCI) - a feasibility study
Summary of Trial design	Randomised, prospective, single centre feasibility study of CTCA prior to CTO PCI
Site and Chief Investigator	Sandwell and West Birmingham NHS Trust, Birmingham, United Kingdom Vinoda Sharma
Participant population	Patients undergoing CTO PCI
Planned sample size	20
Number of sites	1
Intervention duration	Prior to index CTO PCI procedure
Follow up duration	6 months
Planned trial duration	1 year
Primary objective	To determine if CTCA prior to CTO PCI results in improved procedural success rate?
Secondary objectives	i) To determine if CTCA prior to CTO PCI results in improved angina as determined by Seattle Angina Questionnaire (SAQ)? ii) To determine if CTCA prior to CTO PCI reduces the need for a second procedure due to improved procedural success rate? iii) Are there procedural differences between the intervention arm (CTCA) and usual care
Intervention	Randomised to CTCA versus no CTCA prior to CTO PCI

ABBREVIATIONS:

CABG: Coronary Artery Bypass Graft

CAD: Coronary Artery Disease

CTCA: Computed Tomography Coronary Angiogram

CTO: Chronic Total Occlusion

J-CTO: Japanese Chronic Total Occlusion

PCI: Percutaneous Coronary Intervention

QALYS: Quality Adjusted Life Years

QoL: Quality of Life

SAQ: Seattle Angina Questionnaire

Trial Protocol Synopsis

Item	Description
<p>Title</p>	<p>Computed Tomography Coronary Angiography (CTCA) prior to Chronic Total Occlusion (CTO) Percutaneous Coronary Intervention (PCI)</p>
<p>Introduction</p>	
<p>Description of research question</p>	<p><i>Null Hypothesis:</i> CTCA performed prior to CTO PCI will not improve procedural success</p> <p><i>Existing knowledge:</i> A chronic total occlusion (CTO) is present in 15-20% of patients with angina who are referred for coronary angiography. Due to the complexity of occlusive coronary artery disease (CAD), including a high prevalence of calcium and tortuosity within long segments of disease, CTO PCI is associated with higher procedural complication rates (11). Inability to detect the intraluminal path in the CTO artery, combined with calcification and tortuosity can result in unsuccessful guidewire crossing and procedural failure. Successful CTO PCI has been shown to improve Quality of Life (QoL) at 12 months(4). These patients are more likely to be angina free at 12 months (5, 6) as assessed by the Seattle Angina Questionnaire (SAQ) (7, 8). CTO PCI in symptomatic patients is cost effective and results in greater quality-adjusted-life-years (QALYS)(9, 10).</p> <p>CTO percutaneous coronary intervention (PCI) procedure success rates increased from 68% to 79% between 2000 and 2011, and are as high as 90% when performed by high-volume CTO operators (2, 3). Complexity of the CTO is determined by several factors and several CTO complexity scores, derived from (invasive) angiographic lesion and clinical characteristics, have been shown to correlate with procedural success and complication rates (JCTO(12), PROGRESS(13), RECHARGE(14), Euro-CASTLE(15)). The most commonly utilised score is the J-CTO (Multicenter Chronic Total Occlusion Registry of Japan)(12) which assigns a score of 1 each to the angiographic CTO proximal cap (tapered or blunt), calcification, tortuosity (>45°), lesion length (≥20mm) and previous failure, with a maximum score =5. Scores ≥2 are considered CTOs that are difficult to perform and require advanced techniques for successful revascularisation.</p> <p>In a proportion of these patients, the first procedure either fails completely or partially succeeds in forming a tract within the occluded artery but this is inadequate for stent delivery and the patient requires a second procedure, occasionally a third for complete success and</p>

	<p>reconstruction of the fully occluded artery.</p> <p>Angiographically, the CTO artery usually shows a short proximal portion of dye filled artery prior to the occlusion. In most patients there are some collaterals from the contralateral coronary artery which try to fill part of the occluded CTO artery. However the actual body of the CTO is not visible angiographically.</p> <p>Computed Tomography Coronary Angiography (CTCA) can delineate the coronary anatomy in 3-dimensions, determining atherosclerotic plaque and occlusion location, severity and morphology. This makes it an attractive modality to assess the coronary CTO. Development of a CTCA based complexity score for stratifying CTOs by difficulty resulted in the CT-RECTOR score (Computed Tomography Registry of Chronic Total Occlusion Revascularization, table 1)(16). Variables included in this score are multiple occlusions, blunt stump, severe calcification, bending, duration of CTO ≥ 12 months and previously failed PCI (all scored 1). The CT-RECTOR score correlates with the J-CTO score and has a better area under ROC curve (ROC AUC 0.83 for CT-RECTOR score and 0.71 for J-CTO, $p < 0.001$) and predicts CTO PCI success (16)</p> <p>The role of routine CTCA pre-CTO PCI is as yet undefined as current practice involves the use of CTCA in patients who have had an unsuccessful CTO PCI attempt or previous coronary artery bypass grafting (CABG).</p> <p><i>Need for a feasibility study:</i></p> <p>Current practice at our centre involves the use of CTCA in patients who have had an unsuccessful CTO PCI attempt or previous coronary artery bypass grafting (CABG) but the role of routine CTCA pre-CTO PCI is as yet undefined.</p> <p>The small additional investment of a CTCA could help plan/improve a complex procedure and may reduce the need for additional procedures and readmissions.</p> <p>The mean acute treatment cost of a CTO PCI is approximately (combined day-case –ordinary elective spell) £6933 (9, 17) whereas the approximate cost of a CTCA is £360 (as per local billing). Elective readmission for a failed CTO PCI procedure would entail an additional financial (to the provider) and emotional cost (to the patient).</p> <p>The cost of an additional CTO PCI procedure aside, readmission and bed charges themselves can reach £1000/day (readmission =£255/day)(17)and bed</p>
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	<p>cost=£600/day). Including the cost of a second CTO PCI procedure (combined day-case –ordinary elective spell) £6933 (9, 17), the overall cost can total to £10,000. In contrast, the cost of a CTCA is £360 (as per local billing). Financial costs are one part of the issue, but a second CTO PCI procedure can also heighten patient anxiety and discomfort which are well known in patients prior to any PCI.</p> <p>A feasibility study will help establish the role of a CTCA prior to CTO PCI to positively influence strategy and/or outcomes.</p>
Objectives	<p><i>Primary:</i></p> <p>i) Does performing a CTCA prior to CTO PCI improve the success of the CTO procedure?</p> <p><i>Secondary:</i></p> <p>i) To determine if CTCA prior to CTO PCI results in improved angina as determined using the Seattle Angina Questionnaire (SAQ) by SAQ.</p> <p>ii) To determine if CTCA prior to CTO PCI reduces the need for a second procedure (due to improved procedural success rate).</p> <p>iii) To assess if there are procedural differences between the intervention arm (CTCA) and usual care arm</p>
Comparators	CTCA versus no CTCA prior to CTO PCI
Trial design	Randomised (1:1), prospective, single centre study
Methods (see figure 1)	
Study setting	Sandwell and West Birmingham NHS Trust, Birmingham, United Kingdom
Eligibility Criteria	<p><i>Inclusion Criteria:</i></p> <p>Patients meeting all the below criteria will be included</p> <ul style="list-style-type: none"> • ≥18 years • CTO with J-CTO score≥2 • Appropriate indication for CTO PCI • Adequate CTCA images for analysis <p><i>Exclusion criteria:</i></p> <p>Patients meeting any of the following criteria will be excluded</p> <ul style="list-style-type: none"> • <18 years of age • CTO with J-CTO score<2 • Inadequate/degraded CTCA images • Pregnant/lactating women • Patients with severe contrast allergy • Patients unable to provide written informed consent

Intervention	<p>Experimental group: CTCA prior to CTO PCI Conventional group: CTO PCI</p> <p>Patients will be randomised to CTCA or no CTCA prior to CTO PCI (figure 1)</p>
Outcomes	<p>Outcomes</p> <p><i>Primary endpoint</i></p> <ol style="list-style-type: none"> i. CTO PCI success rate in CTCA arm versus no CTCA arm <p><i>Secondary endpoints</i></p> <ol style="list-style-type: none"> i. Angina by the SAQ summary score at 6 months ii. Compare the number of patients who required a second CTO PCI procedure in the CTCA arm versus no CTCA arm iii. Procedural differences between the intervention CTCA arm versus no CTCA arm including: <ol style="list-style-type: none"> a) Health Economics: <ul style="list-style-type: none"> • Cost saved per patient due to improved success and reduction in readmission or further procedure b) CTO PCI efficiency: <ul style="list-style-type: none"> • Wire crossing time • Procedure time c) CTO PCI safety outcomes: <ul style="list-style-type: none"> • Procedural complications (Ellis perforation, tamponade, acute kidney injury/contrast induced nephropathy, access site bleeding, donor vessel injury) • Radiation: CTCA dose, CTO PCI dose, and combined CTCA and CTO PCI dose • Contrast: CTCA volume, CTO PCI volume, and combined CTCA and CTO PCI volume d) Change in CTO PCI strategy hierarchy as a result of the CTCA review
Participant/project timeline	Please see figure 2
Sample size	This is a feasibility study- to ensure completion within a year, we have estimated 20 patients, randomised 1:1 to each arm (10 patients per arm) as a sample size in a moderate size hospital which performs approximately 100 CTO PCIs annually
Intervention assignment	Block randomisation with sealed envelope technique
Data collection, management and analysis	<ul style="list-style-type: none"> • eCRF and online database to collect demographic, procedural and SAQ information

	<ul style="list-style-type: none"> • SAQ summary score at 6 months post PCI • Blood samples pre and post PCI • Comparison of demographics, procedural details, procedural success and complications, bloods, SAQ, and financial cost between the CTCA and non-CTCA groups • Categorical variables will be presented as percentage and compared with the chi square or Fisher's test • Continuous variables will be presented as median (range) and compared with student's t-test or Mann Whitney test. • In addition, modelling will be performed by binary logistic regression analysis to predictors of CTO PCI success.
Monitoring	CTO PCI procedural adverse events will be reported as usual on the national database and this data will be collected in the eCRF.
Ethics	Ethical approval for this prospective study will be obtained All patients will be consented prior to inclusion in this study
Blood	Routine blood tests will be performed immediately before the CTO PCI and after the procedure prior to discharge as standard of care

Figure 1: Patient flow pathway

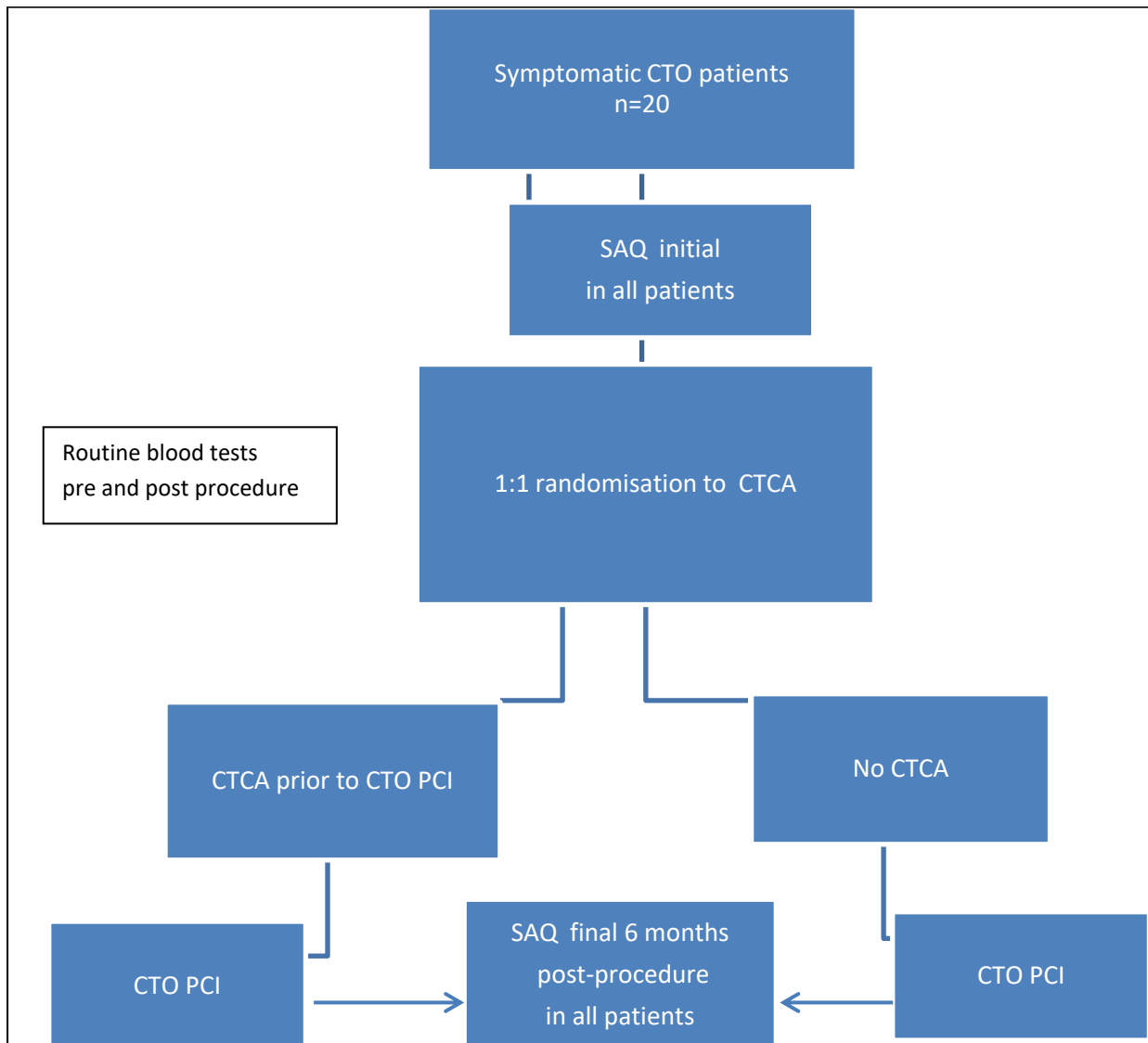
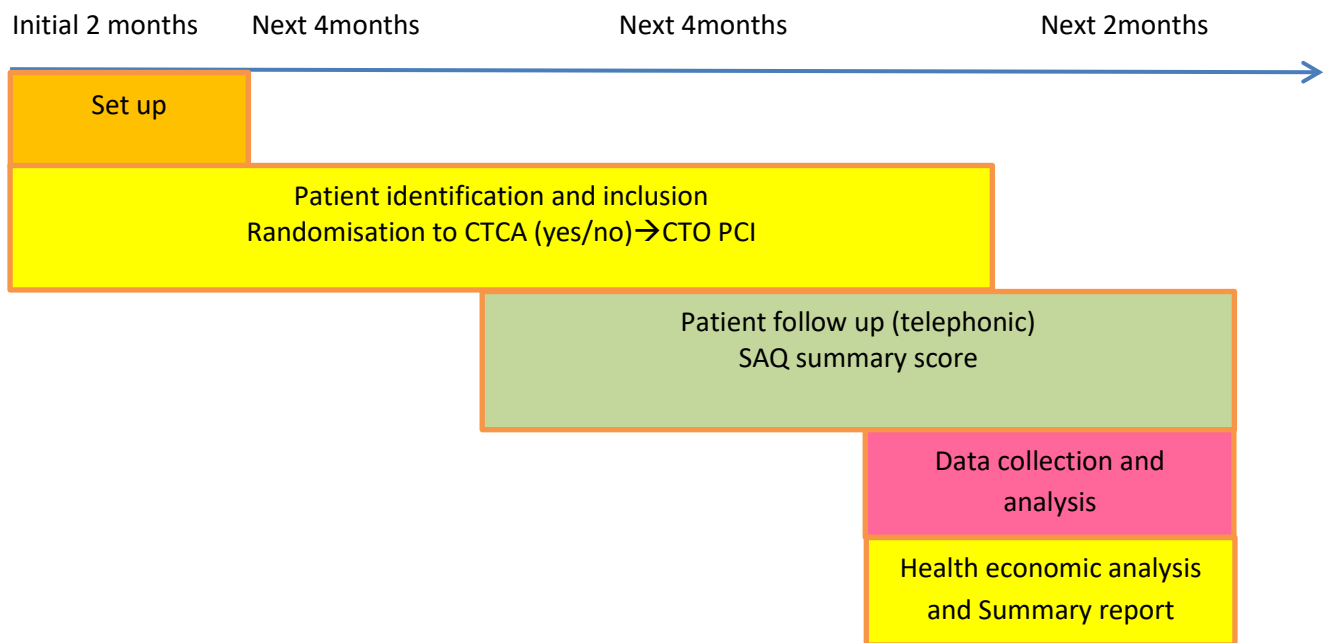


Figure 2: Participant/project Timeline



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17. Improvement N. 2019/20 National Tariff Payment System. 2019.

Appendix

Costing (approximate):

Grade of staff/Test required	Role	Cost per patient	Work Time Equivalent	Period of time	Total Cost all patients
CTCA per patient	-	£360/-	-	-	£7200
Blood tests per patient	-	£30 per set x2 lots=£60		-	£1200
Clinical fellow/registrar	Patient consent, review of blood tests, telephone follow up	-			£16,300
Total					£24,700