Computed tomography cardiac angiography prior to invasive coronary angiography in patients with previous bypass surgery: the BYPASS-CTCA trial

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Abstract

Background

Patients with previous coronary artery bypass grafting (CABG) often require invasive coronary angiography (ICA). However, in these patients the procedure is technically more challenging and has a higher risk of complications. Observational studies suggest Computed Tomography Cardiac Angiography (CTCA) may facilitate ICA in this group, however this has not been tested in a randomized controlled trial.

Methods

This study was a single-centre open-label, randomized controlled trial, assessing the benefit of adjunctive CTCA in patients with previous CABG referred for ICA. Patients were randomized 1:1 to undergo CTCA prior to ICA, or ICA alone. The co-primary endpoints were procedural duration of the ICA (defined as the interval between local anaesthesia administration for obtaining vascular access and removal of the last catheter), patient satisfaction post-ICA using a validated questionnaire, and the incidence of contrast-induced nephropathy (CIN). Linear regression was used for procedural duration and patient satisfaction score, whilst CIN was analysed using logistic regression. We applied the Bonferroni correction with p<0·017 considered significant and 98.33% confidence intervals presented. Secondary endpoints included incidence of procedural complications and 1-year major adverse cardiac events.

Results

Over 3 years, 688 patients were randomized with a median follow-up of 1.0 years. The mean age was 69.8± 10.4 years, 108 (15.7%) were women, 402 (58.4%) were Caucasian and there was a high burden of comorbidity (85.3% hypertension,53.8% diabetes). The median time from CABG to angiography was 12.0 years and there were a median of 3 (IQR 2-3) grafts per participant. Procedure duration of the ICA was significantly shorter in the CTCA+ICA group (CTCA+ICA 18.6 ± 9.5 min vs ICA alone 39.5 ± 16.9 min, 98.33% CI -23.5 to -18.4, P<0.001), alongside improved mean ICA satisfaction scores (1=very good to 5=very poor) (-1.1 difference, 98.33% CI -1.2 to -0.9, P<0.001), and reduced incidence of contrast-induced nephropathy (3.4% vs 27.9%, OR 0.09, 98.33% CI 0.04-0.2, P<0.001). Procedural complications

(2.3% vs 10.8%, OR 0.2 95% CI 0.1 to 0.4, P<0.001) and 1-year major adverse cardiac events (16.0% vs 29.4%, OR 0.4, 95% CI 0.3-0.6, P<0.001) were also lower in the CTCA+ICA group.

Conclusions

In patients with prior CABG, CTCA prior to ICA leads to reductions in procedure time and contrast-induced nephropathy, with improved patient satisfaction. CTCA prior to ICA should be considered in this group of patients.

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Clinical Perspective

What Is New?

- This study showed for the first time in a randomized clinical trial that in patients with prior CABG undergoing invasive coronary angiography, adjunctive CTCA improves patient safety, optimises the angiographic procedure and increases patient satisfaction.

What Are The Clinical Implications?

- Upfront CTCA prior to invasive coronary angiography resulted in reduced procedure times, improved patient satisfaction and lower incidence of contrast induced nephropathy
- Lower incidence of procedural complication and clinical events out to 12 months were also seen
- This suggests that CTCA should be considered prior to invasive coronary angiography in patients with prior CABG.

INTRODUCTION

Coronary artery bypass graft surgery (CABG) is the commonest adult cardiac procedure in the developed world with around 250,000 patients undergoing the procedure per year in the United States (1). Despite advances in percutaneous coronary intervention (PCI), CABG has a major role in the management of patients with coronary artery disease, especially those with multi-vessel or left main stem disease (2). However, due to accelerated progression of native coronary artery disease post-CABG and the high failure rates of saphenous vein grafts, around one in five patients will require an invasive angiogram within three years of their CABG with up to 15% requiring further revascularization within five years (3, 4).

Invasive coronary angiography (ICA) in the post-CABG patient, whilst remaining the gold standard for coronary and graft evaluation, is more challenging than in patients without grafts. An increased number of vessels to engage, variable location of bypass graft ostia, and often incomplete information available regarding the number and type of grafts placed, leads to procedures lasting longer, high levels of contrast and radiation exposure, and an increased risk of complications (e.g. stroke and contrast-induced nephropathy) compared with patients without previous CABG (5-10). The benefits of procedural developments in ICA have also been questioned with the possibility of greater contrast use and procedure length with radial access, compared with femoral in the post CABG patient (11). Therefore, the development of techniques to facilitate safer and more efficient ICA are needed.

Computed tomography cardiac angiography (CTCA) is a useful clinical tool in the assessment of patients with previous CABG, providing a non-invasive evaluation of the number and location of bypass grafts, and being highly accurate at detecting graft stenoses, with sensitivity and specificity in excess of 95% (12, 13). Prior observational studies have demonstrated the potential benefit of CTCA prior to ICA in reducing procedural time, contrast administration and radiation exposure (14, 15). The BYPASS-CTCA study was designed to assess, in a randomized trial, whether CTCA prior to ICA led to improved procedural metrics, safety and patient satisfaction.

METHODS

TRIAL DESIGN AND OVERSIGHT

The trial design has been described previously (16). This study was a single-centre, randomized controlled trial performed at St Bartholomew's Hospital, the largest cardiac centre in the UK, that evaluated a strategy of CTCA prior to ICA in patients with prior CABG. The trial was approved by an independent ethics committee and supported by the Barts Cardiovascular Clinical Trials Unit (CVCTU). The trial was funded by the National Institute for Health and Care Research, Research for Patient Benefit Scheme, the funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

PATIENTS

Patients considered eligible were those aged 18 or over, with a history of previous CABG who had been referred for invasive coronary angiography and were able and willing to give written informed consent. Exclusion criteria were patients with cardiac arrest, cardiogenic shock, ST-elevation myocardial infarction, patients with chronic renal failure with an estimated glomerular filtration rate<20mls/min, pregnant women, patients unable to tolerate CTCA (contrast allergy, inability to tolerate beta-blockers), and those with a current life-threatening condition other than vascular disease that may prevent a subject from completing. Eligible patients were approached either at their pre-angiography assessment visit (for elective patients) or on the ward prior to invasive angiography (acute patients). They were enrolled after giving written informed consent.

RANDOMIZATION AND TREATMENT

Patients were randomly assigned in a 1:1 ratio to a strategy of CTCA prior to ICA, or ICA alone. Randomization was performed using an online electronic randomization system and was stratified by acute coronary syndrome (ACS) presentation. Block randomization was used with block size varied randomly, the allocation algorithm was written by the study statistician in Stata (Version 14) using the "*ralloc"* command

PROCEDURES

For patients allocated CTCA, all CTCAs were performed using a third-generation dual-source CT scanner (Somatom FORCE, Siemens, Germany). In elective ICA cases CTCA was planned to be performed at least 2 weeks before ICA, in patients presenting with ACS the CTCA and ICA were performed within 24-48 hours based on scanner availability and clinical pathways. All CTCA scans were reported by an independent accredited radiologist/cardiologist detailing the graft anatomy, ostial location and presence of disease. All coronary angiograms were performed either by, or under the supervision of, an interventional cardiologist. The choice of vascular access and whether to cannulate patent bypass grafts on CTCA were left to the discretion of the operator, however it was recommended not to image grafts found to be occluded on CTCA.

OUTCOMES

The primary outcome of the study was a co-primary endpoint consisting of ICA procedure duration (defined as the interval between local anaesthesia administration for obtaining vascular access and removal of the last catheter), patient satisfaction scores post-ICA (based on a validated questionnaire), and the incidence of CIN (≥0·3mg/dl or ≥26·5μmol/L increase in creatinine within 48hours or ≥1.5x within 1 week as defined by the Kidney Disease Improving Global Outcomes (KDIGO) criteria) (17, 18). Secondary endpoints included: radial access rates, contrast amount (ml) and radiation exposure administered during ICA, the number of catheters used during ICA, the number of grafts not identified during ICA, ICA-related complications (coronary or aortic dissection, procedural-related MI (SCAI definition), stroke, bleeding and vascular access complications), major adverse cardiac events (MACE) and major adverse kidney events (MAKE)(19). MACE was defined as all-cause mortality, cardiac mortality, myocardial infarction (not including procedural-related MI) and unscheduled revascularisation. MAKE was defined as all-cause mortality, new onset renal replacement therapy and persistent worsening renal dysfunction (>50% baseline creatinine)(20).

STATISTICAL ANALYSIS

The study was sized to ensure each of the three co-primary endpoints were sufficiently powered. The primary endpoint requiring the largest sample size was CIN; 510 patients provides 80% power (significance level 0.05) to demonstrate a CIN reduction of 60%,

assuming an estimated CIN incidence of 12% in the control arm. We applied the Bonferroni correction and used α=0·017 in the calculations. This gives a total sample size of 618 which was increased to 688 after accounting for dropouts.

The statistical analysis plan (available with the protocol) was finalized before any analysis by trial-group assignment. Primary analyses were presented with 98.3% confidence intervals, and p-values less than 0.017 were deemed to be statistically significant (to preserve an overall α=5% split over 3 co-primary endpoints using the Bonferroni method of adjustment). The main analysis of primary endpoints was conducted on an intention-to-treat (ITT) population consisting of all those randomized who had available data regardless of which procedures they underwent. The primary outcome of CIN was analysed using logistic regression, while linear regression was used for procedural duration and patient satisfaction score. For all primary endpoint analyses, estimates were made unadjusted, and adjusted for ACS and creatinine level at baseline. Pre-specified subgroup analyses were performed on primary outcomes by incorporating and testing interaction terms into the models. In addition, a sensitivity analysis will be conducted for the CIN endpoint excluding subjects who did not undergo an ICA. Analyses of secondary outcomes were not adjusted for multiplicity. For the analysis for secondary endpoints, differences between trial groups were estimated using Cox Proportional Hazards models for survival outcomes, Poisson regression for count outcomes, linear regression for continuous outcomes, and logistic regression for binary outcomes. Secondary endpoints are presented with 95% confidence intervals. For the MACE endpoint a Kaplan-Meier plot will be used to show cumulative incidence in the two treatment groups over 1-year follow up. All analyses were conducted with the use of Stata software, version 17·0 (StataCorp).

RESULTS

PATIENTS

Between November 6 2018 and August 23 2021, 688 patients were randomized: 344 in the CTCA+ICA group and 344 in the ICA-only group (Figure 1). In the CTCA group, 22 patients did not undergo ICA as a result of physician preference based on the CTCA result and 1 patient died prior to ICA. This meant there was a total of 321 patients in this group who underwent ICA (Figure 1). In the ICA alone group, 2 patients died post-randomization but prior to ICA resulting in 342 patients in this group undergoing ICA (Figure 1). Patients were followed up for a median of 1.0 years (377 days).

Baseline characteristics are shown in Table 1. In the CTCA+ICA group the median time from CTCA to ICA was 6.9 days (IQR 0.2-63.0 days). Shorter times were seen in the ACS group (median 0.3 days, IQR 0.1-13.7 days) compared with the elective group (median 26.9 days, IQR 3.1-91.8 days).

The overall median time from CABG to angiogram was 12.0 (IQR 5.7-19.2) years. In 24.0% of cases the graft details were unknown as the operation note was not available and there had been no subsequent angiogram, and 46.3% of patients had a prior coronary angiogram post CABG. The majority (92.8%) of patients had a left internal mammary artery (LIMA) graft, with arterial grafts comprising 34.2% of grafts overall and the remainder venous. The total number of grafts was similar between the two groups (2.9±0.9 in CTCA+ICA and 2.9±0.8 in ICA alone). In the CTCA+ICA group, 36.0% of grafts were patent or occluded on CTCA so were not invasively assessed, with 1 graft not found (0.3%). In the ICA alone group, 19.1% of all grafts were not imaged either due to being known to be occluded (prior angiography) or being unable to locate at the time of angiography (Table 2). Aortography, performed with a pigtail catheter and 40ml of contrast, was undertaken as part of invasive angiography in 1.2% of the CTCA+ICA group and 17.3% of the ICA-only group (P<0.001).

PRIMARY OUTCOMES

The mean ICA procedure duration was significantly reduced in patients in the CTCA+ICA group compared with patients undergoing ICA alone (CTCA+ICA 18.6 ± 9.5 min vs ICA alone 39.5 ±

16.9 min, P<0.001) (Figure 2A). This was an unadjusted difference of -20.9 min (98.3% CI -23.5 to -18.4) with no change seen after adjustment (-20.9, 95% CI -23.5 to -18.4, P<0.001). When comparing total procedure time (including PCI), procedure time remained significantly reduced in the CTCA+ICA arm with a mean difference of 10.8 min (CTCA+ICA: 70.4 $\pm$ 34.7 vs ICA: 81.2 $\pm$ 36.4, 95% CI -19.2 to -2.5, P=0.01). Finally, when combining the CTCA and ICA procedure durations, there remained a significant reduction in the CTCA+ICA group compared with ICA alone (22.1 $\pm$ 10.5 min vs 39.5 $\pm$ 16.9 min, P<0.001).

Patient angiography satisfaction questionnaires were completed for 662 (99.8%) of patients. Patient satisfaction scores (1=very good, 5=very poor) were significantly better in the CTCA+ICA group (1.5 $\pm$ 0.6) compared with the ICA alone group (2.5 $\pm$ 1.0) (Figure 3A) with a mean difference of -1.1 (98.33% CI -1.2 to -0.9, P<0.001). In the CTCA+ICA group, 96% of the patients rated their overall satisfaction as very good or good compared with only 46% of the ICA alone group (Figure 3B). This benefit was seen consistently across all elements of the questionnaire (Table S3) and across subgroups (Table S4). Across the study the mean satisfaction score was lower (i.e. more satisfied) amongst patients without a complication compared to those with (1.98 vs 2.73, p<0.001). In the CTCA+ICA group patient satisfaction with the CTCA scan was high with 98% of patients rating their satisfaction as being very good or good (Table S5).

Post-angiography renal function tests were available for 615 patients and demonstrated an overall CIN incidence of 16.1%. Incidence of CIN was significantly reduced in the CTCA+ICA group compared with the ICA alone group (3.4% vs 27.9%, OR 0.09, 98.33% CI 0.04-0.2, P<0.001) (Figure 2B). Furthermore, if patients in the CTCA+ICA group who underwent CTCA only (n=21) are included the difference persists and was consistent across the subgroups (Table S6).

SECONDARY OUTCOMES

Regarding secondary outcomes (Table 2), the CTCA+ICA group had significantly higher radial access rates, lower number of catheters used during ICA, reduction in fluoroscopy time, and a reduction in contrast used during ICA, which persisted even when adding the contrast used

during CTCA (CTCA+ICA 148.9 ± 50.6mL vs 173.0 ± 68.0mls, P<0.001). PCI rates were comparable with 139 patients (43.3%) in the CTCA+ICA group and 141 patients (41.2%) in the ICA group proceeding to PCI (Table S7).

Total effective dose (mSv) received during ICA was significantly reduced in the CTCA+ICA group (median 1.6, IQR 1.0-2.4mSv) compared with the ICA alone group (2.6, IQR 1.8-3.9mSv, p<0.001). However, the median total effective dose (using a conversion factor of 0.017) for the CTCA was 5.8mSv (IQR 3-9.9mSv), resulting in a combined radiation dose of 7.50 (IQR 4.5-11.6mSv) in the CTCA+ICA group which was significantly greater than the ICA alone group (2.6, IQR 1.8-3.9mSv, P<0.001).

In the CTCA+ICA group 99.7% of patients had complete diagnostic studies post-ICA (1 patient did not have a CTCA pre-procedure due to logistical reasons), compared with only 75.7% in the ICA alone group (P<0.001), where the remaining had bypass grafts that were not evaluated or quantified at the time of ICA.

Procedural complication incidence was lower in the CTCA+ICA group (2.3% vs 10.8%, OR 0.2 95% CI 0.1 to 0.4, P<0.001) (Table 3), driven by reduced vascular access complications and procedural MI. There was a significant reduction in incidence of 1-year MACE in the CTCA+ICA group compared with the ICA group (16.0% vs 29.4%, OR 0.4, 95% CI 0.3-0.6, P<0.001), driven by reduced rates of spontaneous MI (Table 3, Figure 4). There was a significant reduction in 1-year incidence of MAKE in the CTCA+ICA group compared with the ICA group (6.4% vs 10.2%, OR 0.6, 95% CI 0.3-0.97, P=0.04), driven by reduced frequency of persistent renal dysfunction (Table 3).

DISCUSSION

In this randomized controlled trial of patients with previous CABG undergoing ICA, CTCA prior to ICA resulted in reduced procedure times, increased patient satisfaction and lower incidence of CIN compared with ICA alone. Upfront CTCA was also superior for several secondary endpoints including reduced contrast dose, reduced ICA radiation exposure, and a lower number of angiography catheters used. Procedural complications were also reduced with upfront CTCA providing safer procedures with subsequent improved clinical outcomes (MACE) out to 1 year. This supports the routine use of adjunctive CTCA prior to ICA to facilitate safe and effective angiography and improve patient outcomes.

The study was designed to assess whether CTCA is a useful adjunct to planned ICA in patients with previous CABG. Previous observational studies have suggested upfront CTCA may reduce the exposure of patients to contrast, radiation and the clinical risks of invasive procedures (14, 15, 21). A recently presented randomized clinical trial (GREECE) has provided some preliminary data (22, 23). In GREECE, 153 patients with prior CABG and a clinical indication for coronary angiography were randomized to CTCA+ICA (n = 84) or ICA alone (n = 69). The study reported a primary endpoint of an *increased* total contrast volume in the CTCA+ICA arm compared with ICA alone (209 mL vs 165 mL, P=0.006), despite similar incidence of CIN (16% vs 13.8%, P=0.71). Total procedure time (28.5 vs 38.4min, P=0.02) and 30-day MACE (5% vs 16%; P= 0.02) were lower in the CTCA arm. These conflicting results likely highlight the underpowered nature of the trial but also uncertainty with the respect to the full utilisation of CTCA use in this group. Higher volumes of contrast use at ICA with prior CTCA are difficult to explain, however as the full results are as yet unpublished it is difficult to draw detailed comparisons to potentially explain the different results seen between GREECE and BYPASS-CTCA. The GREECE investigators did conclude, however, that a larger trial with newer CT scanners could lead to a different outcome, which was the case in our study (22).

The primary beneficial role of CTCA prior to ICA in patients with previous CABG is in providing information on the number and location of bypass grafts and, in particular, if they are patent or completely occluded. This potentially avoids “graft seeking” and facilitates selective engagement during ICA. As expected, this allowed for lower volumes of contrast use during ICA, which then expectedly leads to lower CIN incidence (24). The prognostic significance of

CIN has been hotly debated in recent years, but now there is emerging data that CIN post arterial contrast administration during angiography especially in patients with pre-existing renal dysfunction is prognostically important (25-27). The CIN incidence of 27.9% in the control (ICA-only) group was higher than estimated in our assumptions, although to our knowledge no study has specifically reported CIN incidence post ICA in CABG patients. The incidence of CIN in the ICA alone group did correspond to the average Mehran score of 11.0 however even allowing for the higher volume of contrast this was higher than in the CTCA group(24). We found that the effect was consistent when using the CIN criteria (≥25% or ≥0.5mg/dl increase in creatinine at 48hours) used in the Mehran model with incidence of 2.5% in the CTCA+ICA and 24% in the ICA alone group. Importantly the reduction in CIN remained in the ACS group despite the CTCA (and associated contrast load) often being performed on the same day (median 0.3). Whilst the increased incidence of CIN in the ICA alone group was associated with persistent renal dysfunction, there was no increase in the incidence of need for renal replacement therapy.

Procedure times seen in the ICA-alone group in BYPASS-CTCA were comparable to the ICA-only group of the GREECE study (38.4min), and to other series in post-bypass patients (ranging from 21.9-60 min) (11, 22, 28, 29). The 18.6 min ICA time in the CTCA group is shorter than all of these afore-mentioned studies and suggests the utilisation of the information provided specifically by CTCA has led to this reduction, although it is important to highlight that overall patients in the CTCA did undergo two appointments, in itself a significant time commitment. This reduction in ICA procedure time was largely due to the need for fewer grafts being invasively imaged at the time of ICA since these grafts were identified as patent or occluded on the prior CTCA. This approach of targeted ICA, whilst reducing procedural duration, importantly demonstrated no safety signal, and in fact led to lower event frequency out to 1 year. With knowledge of exactly how many, if any, grafts needed to be engaged, those in the CTCA group had higher frequency of radial access and therefore unsurprisingly a lower frequency of vascular access complications (30). The reassurance of a patent LIMA on CTCA could mean increasing utilisation of the right radial route in this cohort avoiding the need for femoral access and avoiding invasive LIMA cannulation at the time of ICA, which correlates with the findings of L-RECORD, where left radial access was non-inferior to femoral access in CABG patients when the anatomy was known(31). Utilising CTCA and ICA in this synergistic

manner explains these low procedure times, complication frequency and reduced CIN incidence, which are arguably more consistent with metrics seen in non-CABG patients.

Despite the many positive procedural benefits of CTCA, which included a reduction in ICA effective radiation dose, overall there were significantly higher doses of radiation received by the patients who underwent upfront CTCA. No safety signal was seen in relation to this during the 1-year follow-up however this has to be acknowledged as a limitation of the combined (2 step) approach with any long-term consequences not known. It is however worth highlighting that radiation doses with newer CT scanners are likely to reduce and potentially the benefits at ICA may have been under-appreciated at our institution based on low frame rates and acquisition doses for invasive angiography and as a consequence, the higher combined metrics of CTCA and ICA may not be reflected at other centres.

The reduction in 1-year MACE seen in this study, driven by a reduction in myocardial infarction, is of interest although the trial was not powered for this endpoint, so this should be reviewed as hypothesis-generating only. Despite this, there is evidence of improvement in multiple variables and outcomes in the CTCA group that may affect MACE events during follow-up: higher rates of radial access, reduced procedural complications, higher rates of full diagnostic studies and therefore potentially complete revascularisation, reduced incidence of CIN and improved renal outcomes out to 1 year(25, 32). The synergistic benefits of these factors could potentially explain these findings, and importantly a similar signal was seen in the only other RCT assessing this question (GREECE) (22). Whether upfront CTCA reduces MACE should therefore be the focus of future research.

BYPASS-CTCA was a single-centre study, and as such the potential for application across other centres is uncertain. In particular, this approach will not be possible at centres where CTCA is not readily available to be performed and/or reported. The use of newer CT scanners may have contributed to the positive results demonstrated in BYPASS-CTCA compared to GREECE, and make the results less generalizable to centres with older scanners. The interpretation and application of information from CTCA also currently varies amongst clinicians. Even in this single centre, where many operators perform the studies, differing practice occurs, for example, whether to re-image grafts shown to be patent or completely occluded on CTCA.

The assumption that CTCA findings were accurate and grafts engagement at angiography was not mandated is a limitation of the study, although no safety concern was seen (MACE). Although planned, the cost-effectiveness evaluation of CTCA in this setting has not been completed so no conclusions around this can currently be made. Finally, by its nature, the trial was open-label which may have affected subjective endpoints (e.g patient satisfaction) although these subjective endpoints were assessed by individuals blinded to the patient allocation.

CONCLUSIONS

Invasive coronary angiography remains the gold standard for evaluation of both native coronary arteries and grafts, however in patients with previous CABG it is technically more challenging and associated with a higher risk of complications. This study has shown that the use of upfront CTCA prior to ICA leads to reduced procedure time, improved patient satisfaction and reduced contrast-induced nephropathy. CTCA prior to ICA, when logistically possible, should be considered in this group of patients.

Declaration of interests

FP receives institutional research support from Siemens Healthineers. All other authors have reported no conflicts of interest.

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Figures and Tables

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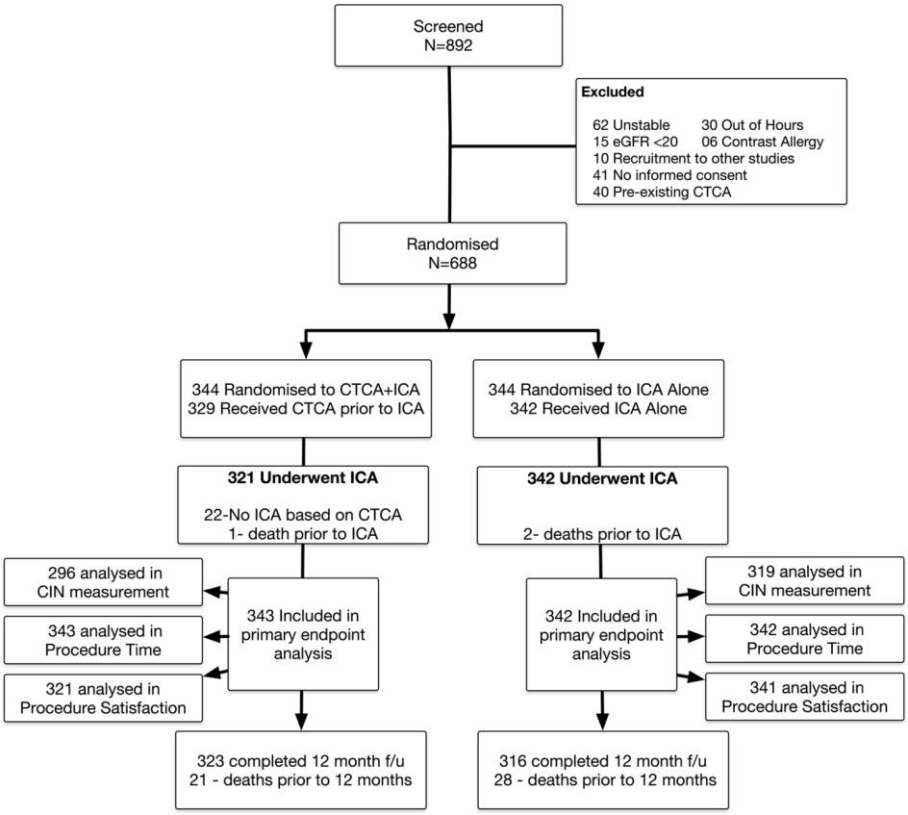

Figure 1. Study Consort Diagram. eGFR: Estimated glomerular filtration rate; CTCA: Computed Tomography Cardiac Angiography; ICA: Invasive Coronary Angiography; CIN: Contrast-Induced Nephropathy

Age (years), mean (SD)	69.0 (10.9)	70.6 (9.8)	69.8 (10.4)
Sex, n (%)			
Male	293 (85.2%)	287 (83.4%)	580 (84.3%)
Ethnicity, n (%)			
Asian	116 (33.7%)	144 (41.9%)	260 (37.8%)
Black	9 (2.6%)	15 (4.4%)	24 (3.5%)
White	218 (63.4%)	184 (53.5%)	402 (58.4%)
Mixed/unknown	1 (0.3%)	1 (0.3%)	2 (03%)
BMI (kg/m^2), mean (SD)	28.6 (5.0)	28.6 (4.5)	28.62 (4.8%)
Diabetes, n (%)	169 (49.1%)	201 (58.4%)	370 (53.8%)
Hypertension, n (%)	293 (85.2%)	294 (85.5%)	587 (85.3%)
Hypercholesterolemia, n (%)	262 (76.2%)	279 (81.1%)	541 (78.6%)
Family history, n (%)	39 (11.3%)	53 (15.4%)	92 (13.4%)
Prior PCI, n (%)	163 (47.4%)	169 (49.1%)	332 (48.3%)
Prior MI, n (%)	231 (67.2%)	236 (68.6%)	467 (67.9%)
Chronic Kidney Disease*, n (%)	142 (41.2%)	134 (38.9%)	276 (40.1%)
Atrial Fibrillation, n (%)	25 (7.3%)	25 (7.3%)	50 (7.3%)
Stroke, n (%)	22 (6.4%)	27 (7.9%)	49 (7.1%)
Smoking status, n (%)			
Non-smoker	138 (40.1%)	161 (46.8%)	299 (43.5%)
Ex-smoker	179 (52.0%)	154 (44.8%)	333 (48.4%)
Current smoker	27 (7.9%)	29 (8.4%)	56 (8.1%)
Presentation, n (%)			
Unstable angina	25 (7.2%)	27 (7.9%)	52 (7.6%)
NSTEMI	128 (37.2%)	127 (36.9%)	255 (37.1%)
Stable angina	191 (55.5%)	188 (54.7%)	379 (55.1%)
Other	0 (0%)	2 (0.6%)	2 (0.3%)
LVEF (%), mean (SD)	50.5 (11.6)	49.4 (11.8)	49.4 (11.8)
Creatinine (umol/L), mean (SD)	101.94 (34.6)	99.9 (30.2)	100.92 (32.5)
eGFR (mL/min/1.73m^2), mean (SD)	65.79 (18.5)	66.3 (17.7)	66.05 (18.3)
Systolic BP (mmHg), mean (SD)	128.04 (16.8)	130.0 (17.1)	129.02 (17.0)
Diastolic BP (mmHg), mean (SD)	70.98 (9.2)	70.5 (9.4)	70.74 (9.3)

Table 1. Baseline Characteristics. MI: Myocardial Infarction, PCI: Percutaneous Coronary Intervention, eGFR: estimated glomerular filtration rate; * Chronic Kidney Disease defined as baseline eGFR<60ml/min/1.73m^2),

Radial access	247 (76.9%)	194 (56.7%)	<0.001
Number of Bypass grafts			
1	23 (7.1%)	23 (6.7%)	0.34
2	82 (25.5%)	75 (21.9%)	
3	143 (44.4%)	177 (51.8%)	
4	65 (20.2%)	62 (18.1%)	
5	9 (2.8%)	5 (1.5%)	
Mean number	2.9 ± 0.9	2.9 ± 0.8	
Procedure Time, mins	18.6 (9.5)	39.5 (16.9)	<0.001
Fluoroscopy Time, mins	8.1 (5.1)	14.9 (7.5)	<0.001
Radiation			
Air kerma, mGy	121.0 [85.0-188.0]	184.0 [124.8-301.0]	<0.001
DAP, uGym2	770.0 [510.5-1136.0]	1177.0 [827.0-1760.0]	<0.001
Effective Dose, mSV	1.6 [1.0-2.4]	2.6 [1.8-3.9]	<0.001
Contrast, mls	77.4 (49.1)	173.0 (68.0)	<0.001
Number of catheters during ICA	3 [2-4]	4 [3-5]	<0.001
Mehran Score	7.2 (4.2)	11.0 (5.5)	<0.001

Table 2. Invasive Coronary Angiography Procedural Data. Data as median [Q1–Q3] or mean value (±SD) or a number (percentage). DAP: dose area product; CTCA: Computed Tomography Cardiac Angiography; ICA: Invasive Coronary Angiography;

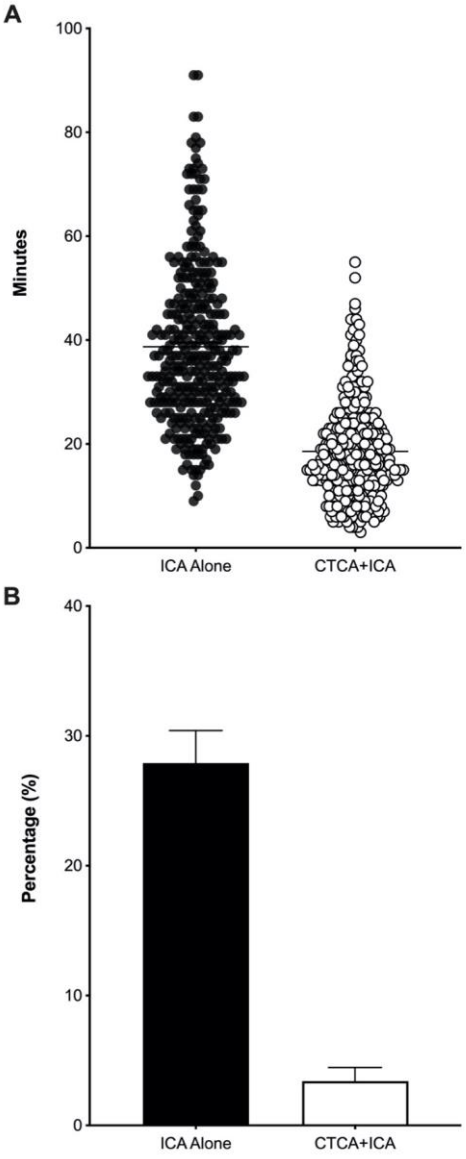

Figure 2. Procedural duration and Incidence of Contrast Induced Nephropathy. Figure 2A shows the violin plot of the procedural duration of the ICA for the 2 groups. Mean and SD are shown behind the scatter plots. Figure 2B shows the CIN incidence in both of the treatment

groups. CTCA: Computed Tomography Cardiac Angiography; ICA: Invasive Coronary Angiography; CIN: Contrast-Induced Nephropathy

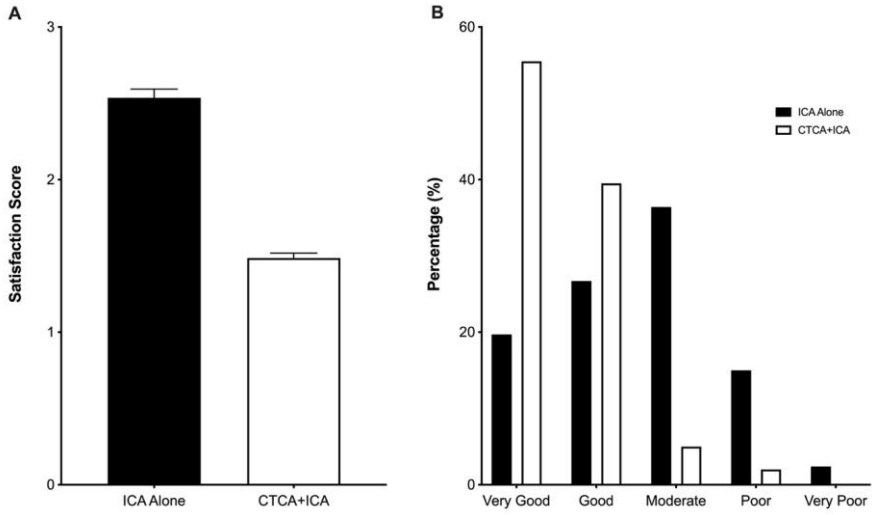

Figure 3. Patient Satisfaction Scores Figure 3A shows the mean overall patient satisfaction score of the ICA for both of the treatment groups. Figure 3B shows the breakdown of overall patient satisfaction for the two groups. CTCA: Computed Tomography Cardiac Angiography; ICA: Invasive Coronary Angiography; CIN: Contrast Induced Nephropathy

	CTCA + ICA N=343	ICA N=342	Difference (95% CI)*	P value	Difference (95% CI)*	P value
Procedural Complications						
Total	8 (2.3%)	37 (10.8%)	0.2 (0.1 to 0.4)	<0.001	0.2 (0.1 to 0.4)	<0.001
Coronary or aortic dissection	1 (0.3%)	2 (0.6%)	0.5 (0.04 to 5.5)	0.57	0.5 (0.04 to 5.5)	0.56
Peri-procedural MI	2 (0.6%)	22 (6.4%)	0.1 (0.02 to 0.4)	0.001	0.1 (0.02 to 0.4)	0.001
Stroke	3 (0.9%)	1 (0.3%)	3.0 (0.3 to 29.1)	0.34	3.0 (0.3 to 29.0)	0.34
Vascular access	2 (0.6%)	15 (4.4%)	0.1 (0.03 to 0.6)	0.007	0.1 (0.03 to 0.6)	0.007
1 Year MACE	**N=344**	**N=344**				
MACE	55 (16.0%)	101 (29.4%)	0.5 (0.3 to 0.7)	<0.001	0.4 (0.3 to 0.6)	<0.001
All-cause mortality	21 (6.1%)	28 (8.1%)	0.7 (0.4 to 1.3)	0.30	0.7 (0.4 to 1.2)	0.19
Cardiovascular mortality	6 (1.7%)	13 (3.8%)	0.45 (0.2 to 1.2)	0.11	0.4 (0.2 to 1.1)	0.08
Non-fatal MI	32 (9.3%)	64 (18.6%)	0.5 (0.3 to 0.7)	<0.001	0.4 (0.3 to 0.7)	<0.001
Unscheduled revascularisation	20 (5.8%)	32 (9.3%)	0.6 (0.3 to 1.1)	0.09	0.6 (0.3 to 1.1)	0.09
1 year MAKE	**N=344**	**N=344**				
MAKE	22 (6.4%)	35 (10.2%)	0.6 (0.4 to 1.1)	0.08	0.5 (0.30 to 1.0)	0.04
All-cause mortality	21 (6.1%)	28 (8.1%)	0.7 (0.4 to 1.3)	0.30	0.7 (0.4 to 1.2)	0.19
New onset renal replacement	1 (0.3%)	1 (0.3%)	1.0 (0.1 to 16.1)	>0.99	0.9 (0.04 to 21.4)	0.96
Persistent renal dysfunction	0 (0%)	9 (2.6%)	-	0.004	-	-

Table 3. Outcomes. Procedural and 1-year Major Adverse Cardiac Events (MACE) and Major Adverse Kidney Events (MAKE) are listed. MI; Myocardial Infarction. Adjusted differences are corrected for baseline creatine and ACS presentation. *Difference indicates odds ratio for procedural complications and hazard ratios for cox proportional models

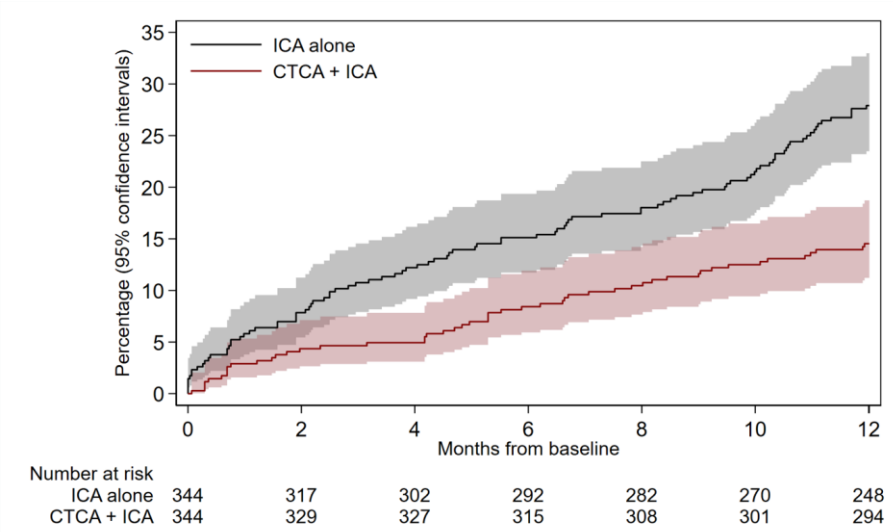

Figure 4. Major Adverse Cardiac Events (MACE) at 12 months. The cumulative incidence (% of population) of MACE during the 12 month follow-up period was estimated by the Kaplan–Meier method; differences were tested using the log-rank test.