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ORIGINAL ARTICLE

Comparison of computed tomography coronary angiography (CTCA) alone vs. CTCA with selective FFR_{CT} in patients presenting with stable chest pain: a FORECAST trial substudy

Mohamed Kira [1,2], Lavinia Gabara [1,2], Mohamed Abouelasaad[1], Hussein Bashar [1,2], Ahmed Elserwey [1,2], Zoe Nicholas [1], Campbell Rogers [3], Sam Wilding [4], Pamela S. Douglas[5], Mark Hlatky [6], and Nick Curzen [1,2,*]

[1]Coronary & Structural Heart Research Group, University Hospital Southampton NHS FT, Tremona Road, Southampton SO16 6YD, UK
[2]Faculty of Medicine, University of Southampton, Southampton, UK
[3]HeartFlow, Inc., Mountain View, CA, USA
[4]Clinical Trials Unit, University of Southampton, Southampton, UK
[5]Division of Cardiology, Department of Medicine, Duke University Medical Centre, Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC, USA
[6]Department of Health Policy and Department of Medicine (Cardiovascular Medicine), Stanford University School of Medicine, Stanford, CA, USA

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Abstract

Aims

The original FORECAST trial was designed to compare a strategy of computed tomography coronary angiography (CTCA) and selective FFR_{CT} to standard care in patients attending Rapid Access Chest Pain clinics in UK centres. This is a prespecified analysis of the FORECAST trial to compare outcomes between the patients in the experimental arm (CTCA + selective FFR_{CT}) and patients in the reference arm who underwent CTCA alone as their initial test of choice.

Methods and results

The FORECAST trial recruited 1400 patients randomized between two strategies: (i) initial test of choice at the discretion of the healthcare provider (standard care arm) or (ii) CTCA ± FFR_{CT}. Prior to randomization, clinicians stated their preference for choice of the first test if the patient were to be randomized to standard care. A total of 459 patients (66%) in the standard care pathway were selected for CTCA as the first test of choice. Similarly, 453 (65%) of the patients who were subsequently randomized into the experimental arm were selected for CTCA as initial test prior to that randomization. This comparison is an intention-to-test (ITT) analysis comparing the post-randomization outcomes of the population of patients who were selected for CTCA as the test of first choice prior to randomization (labelled as the CTCA stratum). The following comparisons were made: (i) primary trial outcomes at 9 months including (a) total cardiac costs, (b) use of other tests, (c) clinical events, and (d) time to final management plan; (ii) a comparison between the CTCA stratum groups and the remainder of the standard care arm (i.e. patients randomized to standard care who were selected for an initial test other than CTCA). Of the CTCA stratum patients, there was no significant difference between randomized groups in the median total cardiac costs at 9 months [£594 (IQR 570–1127) in the experimental arm vs. £594 (574–966) in the usual care arm

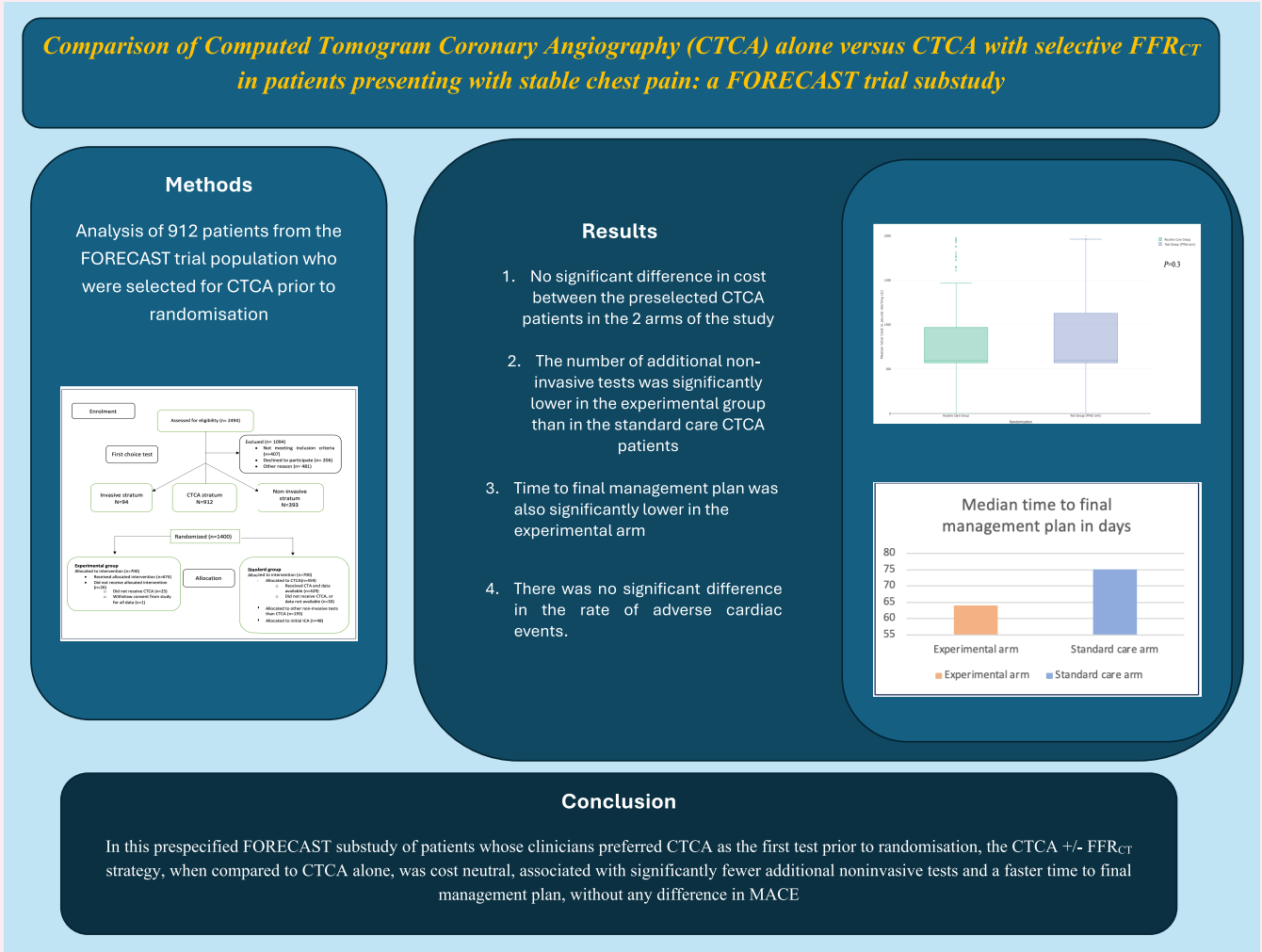
* Corresponding author. E-mail: nick.curzen@uhs.nhs.uk

($P = 0.325$)]. The number of additional non-invasive tests was significantly lower in the experimental group than in the standard care CTCA patients [43 patients (8.9%) vs. 72 (16%), $P = 0.005$]. Time to final management plan was also significantly lower in the experimental arm [median 64 days (IQR 48–110) vs. 75 days (55–126), $P < 0.001$]. There was no significant difference in the rate of adverse cardiac events. Patients randomized to standard care who were not in the CTCA stratum had significantly higher median total cardiac costs when compared with either of the CTCA stratum groups, with median total cardiac costs of £908 (IQR 592–1161) vs. £594 (570–1123) vs. £594 (570–966), respectively ($P < 0.001$).

Conclusion

In this prespecified FORECAST substudy of patients whose clinicians preferred CTCA as the first test prior to randomization, the CTCA ± FFR_{CT} strategy, when compared with CTCA alone, was cost-neutral in the UK and associated with significantly fewer additional non-invasive tests. Time to final management plan was also significantly lower in the experimental arm [median 64 days (IQR 48–110) vs. 75 days (55–126) in the standard care CTCA arm ($P < 0.001$)].

Graphical Abstract



Keywords coronary artery disease • coronary computed tomography angiography • fractional flow reserve derived from computed tomography • major adverse cardiac events • healthcare cost

Introduction

The investigation of patients presenting with stable chest pain suspected to represent angina includes a menu of tests that assess coronary anatomy or physiology or both. The optimal approach remains contentious.[1] In the UK, the NICE 'CG95' guidelines[2] recommend computed tomography coronary angiography (CTCA) as the initial test in over 90% of such patients and thereby minimizes the early use of functional tests for myocardial ischaemia. Whilst PROMISE[3] suggested some advantage for CTCA over functional testing, CEMARC2[4] reported clinical equivalence between stress cardiovascular magnetic resonance vs. the NICE-recommended pathway. Both trials reported a lower rate of invasive coronary angiography (ICA) in the functional testing group.

The advent of FFR_{CT} has offered a test that provides data regarding both coronary atheroma and flow limitation. The evidence derived from PLATFORM,[5] ADVANCE,[6] FORECAST,[7] and PRECISE[8] has consistently demonstrated that a strategy employing CTCA with FFR_{CT} is associated with (i) a lower rate of ICA, (ii) lower proportion of ICA showing no significant coronary disease, (iii) no difference in clinical event rate, (iv) cost-saving or cost-neutralilty.

The FORECAST trial was designed to test a strategy of CTCA with selective FFR_{CT} compared with standard care testing in patients attending Rapid Access Chest Pain clinics in UK centres. There was no difference in resource utilization or quality of life or in clinical events between the strategies, although there was a significantly lower rate of ICA in the selective FFR_{CT} group. It is notable that CTCA was the investigation of choice in 65.5% in the standard care arm in FORECAST. This has led commentators to speculate as to the comparative performance of CTCA alone vs. CTCA with selective FFR_{CT} in these patients. A randomized comparison of this sort does not exist. In order to address this question in a hypothesis-generating fashion, we included in the FORECAST protocol a requirement that the frontline test to which the patient would have been allocated in a standard care environment by the assessing physician, i.e. in the absence of the trial, was recorded just prior to randomization. This generated a stratum of patients in both trial arms in whom the pre-randomization allocation was CTCA (CTCA stratum). It is this stratum that we have used for comparison, as part of a prespecified substudy, in order to achieve a degree of matching between the groups. Our aim was to compare patients in this CTCA stratum randomized to standard care with those randomized to CTCA with selective FFR_{CT} for the following parameters: (i) primary comparison at 9 months including (a) total cardiac costs, (b) use of other tests, (c) clinical events, and (d) time to final management plan; (ii) a comparison between the two CTCA stratum groups and the remainder of the standard care arm (i.e. patients randomized to standard care who were referred for an initial test other than CTCA).

Methods

Population and comparison groups

This substudy was conducted on the FORECAST trial population (REC Reference 18/SC/0490, IRAS Project ID: 231037). The FORECAST trial (NCT03187639) has been described in detail previously.[7,9] In brief, the trial prospectively enrolled 1400 patients with stable chest pain who were randomized into two groups: (a) standard care, in which case they were referred for an initial test of choice [CTCA, ICA, stress electrocardiogram (ECG), stress magnetic resonance imaging (MRI), stress echo, nuclear perfusion scan] according to clinician discretion and local and/or national guidelines or (b) the experimental arm, consisting of CTCA followed by selective FFR_{CT} for those patients with at least one lesion of ≥40% in any coronary artery of a size suitable for revascularization.

The patients included in this substudy, which was prespecified in the trial statistical analysis plan, consist of those patients in whom CTCA was recommended as their initial test of choice 'prior to randomization' into either the standard care or CTCA with selective FFR_{CT} experimental arm. This represents a CTCA stratum of patients who then went on to be randomized to standard care or experimental arms of the trial, with these two groups from the CTCA stratum being the focus for the primary comparison of this study.

The secondary analysis in this paper compares the above-mentioned groups from the CTCA stratum with the remaining of the standard care arm (i.e. those not chosen for CTCA prior to randomization).

In this substudy, data are derived from the main trial baseline demographics, initial tests, subsequent tests, time to final management plan, total cardiac costs at 9 months, and major adverse cardiovascular events (MACE) at 9 months (defined as a composite of all-cause death, non-fatal myocardial infarction (MI), stroke, and cardiovascular hospitalization).

Statistical analysis

Statistical analysis was carried out using RStudio version 4.3.1, PBC (Boston, MA, USA). Continuous data are presented as mean (±standard deviation, SD) or median (+interquartile range, IQR), as appropriate, depending on data distribution. Categorical data are presented as frequency and percentage. Characteristics were compared using the Student's *t*-test or Wilcoxon rank sum test as appropriate for continuous variables and Pearson's χ^2 test or the Fisher's exact test for discrete variables. A two-sided *P*-value of 0.05 or less was considered to constitute statistical significance for all analyses.

Results

Between December 2017 and July 2019, 2494 patients with stable chest pain attending one of the 11 participating Rapid Access Chest Pain clinics were screened for study entry, from which 1400 patients were randomized to either the standard care or the experimental (CTCA ± FFR_{CT}) arms of the trial (*Figure 1A and B*). In the experimental group, 674 (96%) patients underwent CTCA, of whom 254 (38%) had their scans referred for FFR_{CT} analysis per protocol based upon the presence of at least one lesion of ≥40% in any epicardial coronary artery large enough to undergo stenting or bypass grafting. A total of 39 (15%) of these scans could not be analysed for FFR_{CT} due to technical/quality issues.

In the primary analysis of this substudy, patients who had CTCA specified as the test of first choice prior to randomization make up the CTCA stratum. This included 912 patients of the entire study population (65.5%) with 459 patients (65.5%) randomized to the standard care arm, and 453 patients (65%) to the experimental arm (CTCA ± FFR_{CT}). *Table 1* shows the demographics of patients in the CTCA stratum included in this study and indicates that the groups are well matched (see Supplementary data online, *Appendix Table S1* shows demographics of CTCA stratum patients included here, vs. invasive stratum and non-CTCA non-invasive stratum).

241 (34%) patients in the standard care arm were referred to an initial investigation other than CTCA following their assessment, of whom 193 (80%) patients had an initial non-invasive stress test (stress ECG, stress echocardiography, nuclear perfusion scan or stress cardiac MRI) and 48 (20%) patients were referred directly for ICA). These patients, along with the primary analysis patients comprised the population for the secondary analysis in this substudy.

Primary analysis: comparison in pre-randomization CTCA stratum population between standard care randomized arm and CTCA ± FFR_{CT} randomized arm

Cardiac-related resource utilization

There was no significant difference in the median total cardiac costs between the standard care or experimental groups of the CTCA stratum [£594 (IQR 570–996) vs. £594 (570–1127), $P = 0.325$] (*Table 2*), (*Figure 2*).

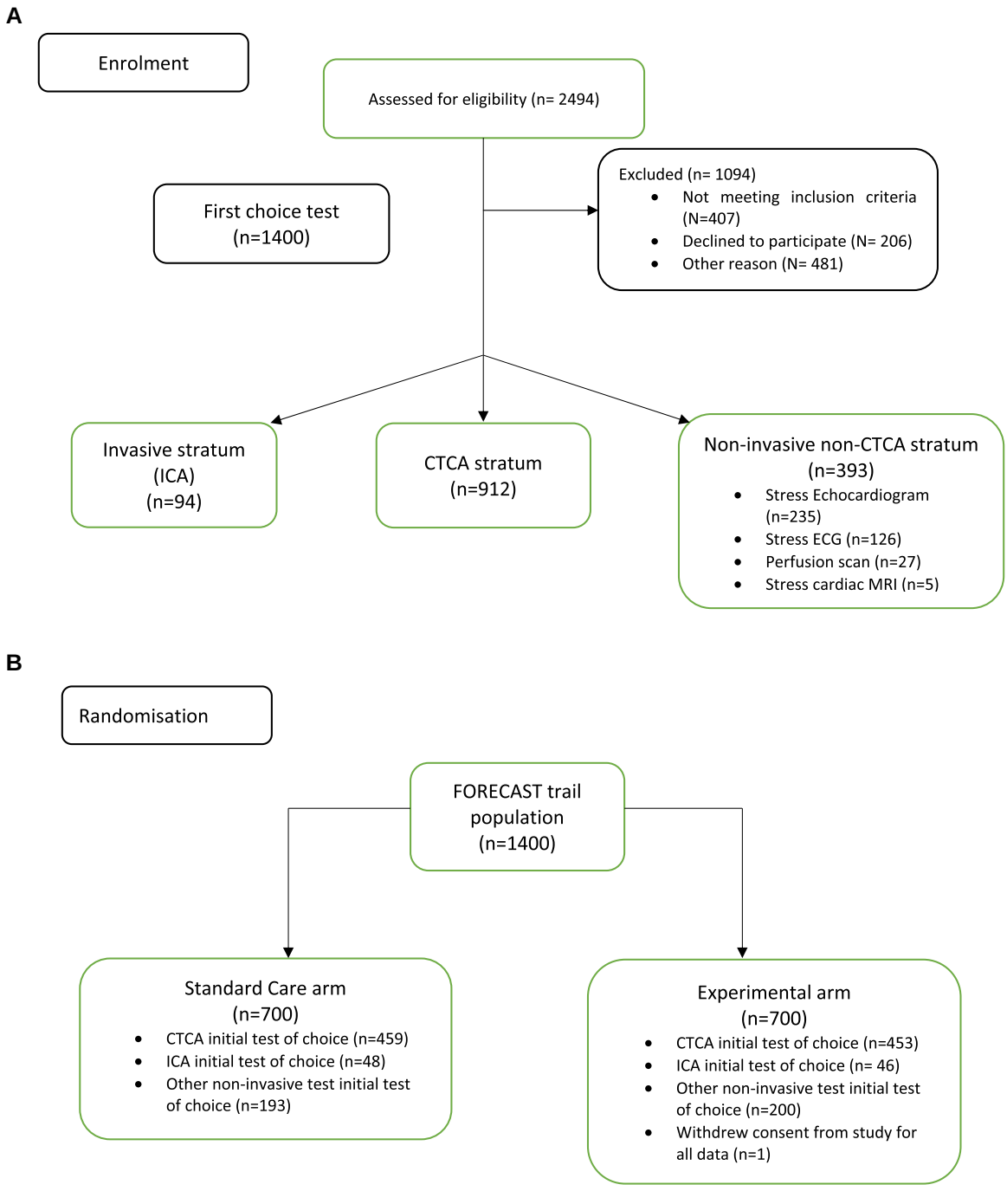


Figure 1 (A) Diagram demonstrating first choice test for patients included in FORECAST trial which is allocated into either of invasive stratum, CTCA stratum, or non-invasive non-CTCA stratum (ICA, invasive coronary angiogram; CTCA, computed tomography coronary angiography). (B) Diagram representing the first initial test selection for the entire FORECAST population, randomized to either standard care arm or experimental arm (CTCA ± FFRCT).

Further investigations

In the CTCA stratum, there was a significantly lower rate of further non-invasive tests in in the experimental randomized arm compared with the standard care randomized arm, with 43 patients (8.9%) in the experimental arm requiring further non-invasive investigations (stress echo, stress ECG, stress MRI, and nuclear perfusion scan) vs. 72 (15.7%) in the standard care arm ($P = 0.005$).

There was no difference in the rate of ICA between the groups (17% vs. 19%, $P = 0.551$). A breakdown of the comparative number of alternative tests is shown in *Table 3*.

Table 1 Demographics of patients in the CTCA stratum who were randomized to either experimental arm (CTCA ± FFRCT) or standard care

	Standard care CTCA arm, $N = 459$	Experimental arm (CTCA ± FFR_{CT}), $N = 453$	*P*-value
Age	58 (50–67)[a]	59 (51–67)[a]	0.542[b]
Gender			0.695[c]
Male	230 (50.1%)	221 (48.9%)	
Female	229 (49.9%)	232 (51.1%)	
Body mass index	28.6 (25.3–32.9)[c]	28.7 (25.3–33.6)[c]	0.695[b]
Ethnicity			0.119[c]
White	413 (90.0%)	400 (88.0%)	
Asian or Asian British	26 (5.7%)	39 (8.6%)	
Black of Black British	8 (1.7%)	8 (1.8%)	
Chinese or other	9 (2.0%)	3 (0.7%)	
Mixed	3 (0.7%)	1 (0.2%)	
Prefer not to answer	0 (0.0%)	2 (0.4%)	
Family history of CAD	281 (61.2%)	279 (61.6%)	0.150[c]
History of angina	157 (34.2%)	135 (29.8%)	0.154[c]
History of MI	0 (0.0%)	4 (0.9%)	0.060[d]
Diabetes mellitus	53 (11.5%)	60 (13.2%)	0.436[c]
Hypertension	149 (32.5%)	160 (35.3%)	0.362[c]
Hyperlipidaemia	120 (26.1%)	140 (30.9%)	0.111[c]
Renal impairment	7 (1.5%)	10 (2.2%)	0.474[d]

[a]Median (IQR).
[b]Wilcoxon rank sum test.
[c]Pearson's χ^2 test.
[d]Fisher's exact test.

Table 2 Total costs in the CTCA stratum, comparing the randomized arms in pound sterling (£) presented as mean, SD, median, and IQR

	Standard care CTCA arm, $N = 459$	Experimental arm (CTCA ± FFR_{CT}), $N = 453$	*P*-value
Mean	1272	1527	0.057[a]
SD	1777	2220	
Median	594	594	0.325[b]
IQR	570–966	570–1127	

[a]Welch two-sample *t*-test.
[b]Wilcoxon rank sum test.

Time to final management plan

Time to a final management plan (i.e. time from initial assessment at the chest pain clinic to reaching a final management plan) was significantly lower in the experimental arm compared with the standard care group from the CTCA stratum [median of 64 days (IQR 48–110) vs. 75 days (55–126), $P < 0.001$] (*Table 4*).

Clinical events

There is no statistically significant difference between the two CTCA stratum groups in terms of MI, cerebrovascular accident (CVA), all-cause mortality and/or cardiac hospitalization (*Table 5*).

Secondary analysis: comparison between the two CTCA stratum groups and the standard care patients whose pre-randomization test choice was not CTCA.

First choice test

Out of the 193 patients of the standard arm whose initial test of choice was a non-invasive test other than CTCA (non-CTCA), 106 (55%) patients were referred for stress echocardiogram, 73 (38%) stress ECG, 13 (6.8%) nuclear perfusion scan, and 1 (0.5%) stress cardiac MRI. Altogether, 48 patients in this group were referred for ICA.

Cardiac-related resource utilization

The non-CTCA stratum subgroup of the standard care arm had significantly higher median total cardiac costs when compared with either of the CTCA stratum groups (i.e. the randomized experimental arm or the standard care arms), with median total cardiac costs of £908 (IQR 592–1161) vs. £594 (570–1123) vs. £594 (570–966), respectively ($P < 0.001$) (*Table 6*), (*Figure 3*).

Clinical events

There was no statistically significant difference in the rate of major adverse cardiac outcomes between the three subgroups including MI, CVA, cardiac hospitalizations, and/ or cardiac death (*Table 7*).

Discussion

This prespecified substudy of the FORECAST trial was focused on the important group of patients who were chosen, prior to randomization, to undergo CTCA as the initial test to evaluate their chest pain. We were able to compare the outcomes within this stratum of patients according to their subsequent randomized allocation to have their CTCA followed either by standard care testing or by selective FFR_{CT}. The main findings are as follows: (a) the CTCA + selective FFR_{CT} strategy is cost-neutral compared with CTCA alone; (b) compared with CTCA alone, the rate of non-invasive testing was significantly lower in the CTCA + selective FFR_{CT} group; and (c) the time to final management plan was significantly lower in the experimental arm than the CTCA group of the standard care arm. Finally, patients not allocated to CTCA as the test of first choice incurred significantly greater costs than those with CTCA as their first test.

The NICE 'CG95' guidelines recommend CTCA as the default first test in over 90% of patients presenting with stable new-onset chest pain. This theoretically largely eliminates the need for functional tests for ischaemia in such patients. Given the body of evidence that detecting coronary atheroma in this population is associated with prognostic benefit, probably via more optimal application of disease-modifying medical therapy, as seen in SCOT-HEART,[10] the logic behind this recommendation is clear. Furthermore, trials such as COURAGE[11] and ISCHEMIA[12] have consistently indicated that, in stable patients with angina without significant left main disease, there is no additional prognostic benefit for revascularization over and above optimum medical therapy (OMT). However, in front line clinical practice, such considerations are not so clear-cut.

Firstly, it is often the case that we require a definitive diagnosis regarding the patient's symptoms, and specifically whether they represent angina (i.e. myocardial ischaemia) or not. The presence of even significant coronary artery disease (CAD) in isolation does not correlate closely in many cases with whether the chest pain symptoms are due to

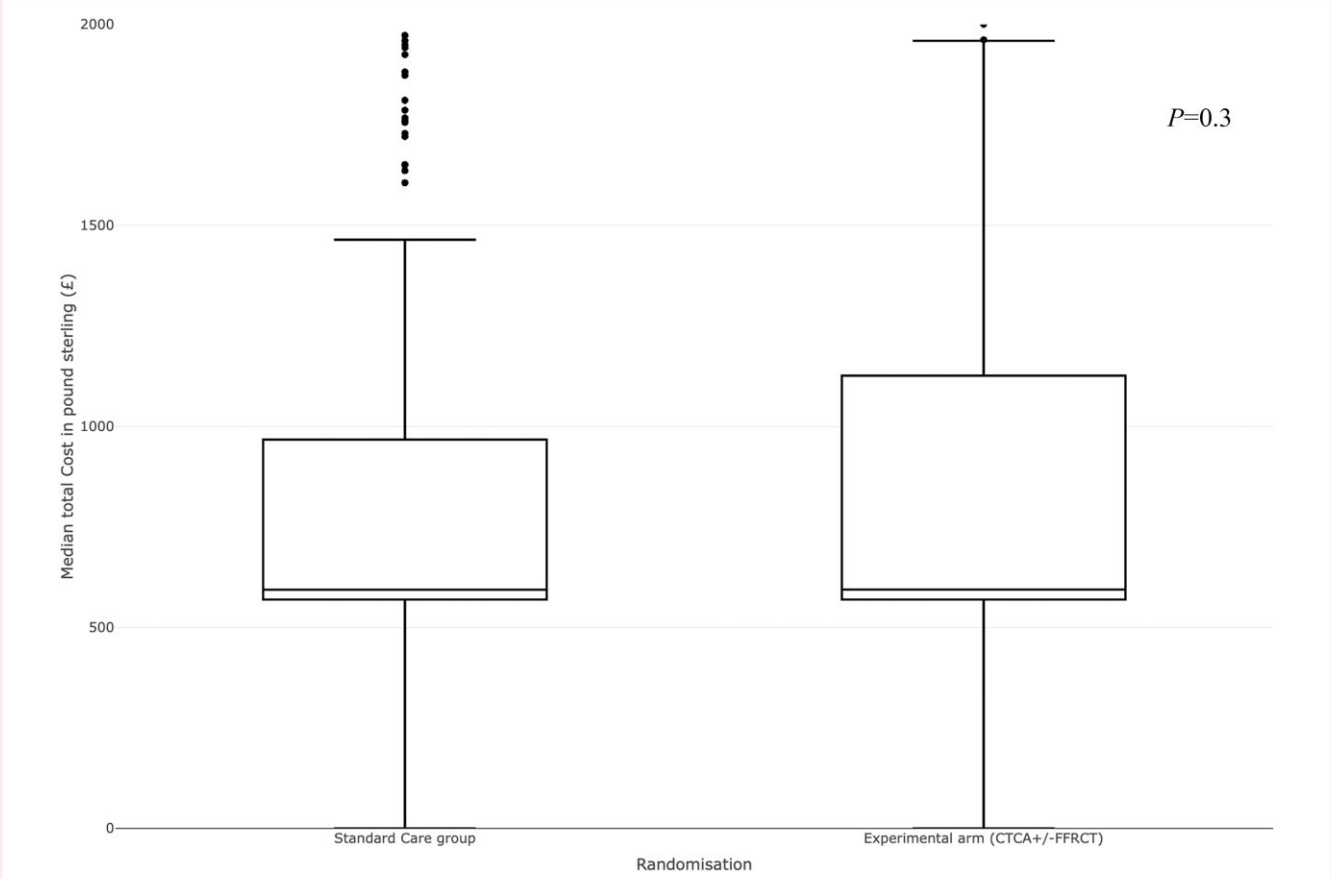


Figure 2 Total cardiac costs at 9 months in the CTCA stratum by randomization group represented as median (IQR). Distribution at 9-month costs in pound sterling (£) by randomized assignment. The top line of each box is the 75th percentile, the bottom line is the 25th percentile, and the line inside the box is the median (50th percentile).

Table 3 Further investigations required for the CTCA stratum by randomized group

	Standard care CTCA arm, $N = 459$	Experimental arm (CTCA ± FFR_{CT}), $N = 453$	*P*-value
Total number of patients who required additional non-invasive testing	72 (15.7%)	43 (8.9%)	**0.005**[a]
Stress echo	19 (4.1%)	9 (2.0%)	0.083[b]
Perfusion scan	19 (4.1%)	4 (0.9%)	**0.002**[b]
Stress MRI	11 (2.4%)	9 (2.0%)	0.826[b]
Stress ECG	28 (6.1%)	26 (5.3%)	0.818[a]
ICA	86 (18.7%)	78 (17.2%)	0.551[a]

The bold values represent statistically significant values ($P \leq 0.05$).
[a]Pearson's χ^2 test.
[b]Fisher's exact test.

Table 4 Time period required between randomization and reaching a final management plan in days represented as median (IQR) and mean (SD) in the CTCA stratum by randomized group

	Standard care CTCA arm, $N = 459$	Experimental arm (CTCA ± FFR_{CT}), $N = 453$	*P*-value
Median	75[a]	64[a]	**<0.001**[a]
IQR	55–126	48–110	
Mean	99[b]	88[b]	0.016[b]
SD	67	66	
No management plan finalized	18	20	

The bold values represent statistically significant values ($P \leq 0.05$).
[a]Wilcoxon rank sum test.
[b]Two-sample *t*-test.

myocardial ischaemia or not. Hence, a functional test may also be required, even if the patient is committed to disease-modifying therapy. Secondly, in those patients whose symptoms do demand revascularization, the availability of data about flow limitation and downstream myocardial ischaemia can play an important role in the targeting of appropriate vessels and lesions, especially for those patients committed to percutaneous coronary intervention (PCI).[13] Thirdly, an

assessment of the presence and extent of myocardial ischaemia is associated with better clinical outcome, although the relative predictive association of ischaemic burden compared with atheroma burden with adverse events is contentious.[14,15] Finally, the correlation between anatomical lesion severity and flow limitation causing downstream ischaemia is poor except in the case of very mild and very severe lesions. Given these factors, the availability of both atheroma extent and severity and vessel-specific flow limitation, as offered by FFR_{CT}, has several theoretical advantages.

Clinical studies, including PLATFORM,[5] ADVANCE,[6] FORECAST[7] and PRECISE[8] have consistently demonstrated that a selective FFR_{CT} strategy has the following benefits: (a) reduced rate of ICA; (b) reduced rate of ICA yielding no stenosis of ≥50%; (c) no increase in clinical event rate, despite fewer ICA; (d) similar rate of revascularization; (e) cost-neutrality or saving. In the main FORECAST trial, the overall strategy of selective FFR_{CT} in the study overall showed cost-neutrality and significantly fewer ICA.

In the current substudy, which was prespecified and included in the statistical analysis plan of FORECAST, we have performed a comparison between patients who are matched by being in the pre-randomization stratum of allocation to CTCA alone and who then went on to be randomized to either the standard care arm or the experimental arm of CTCA and selective FFR_{CT}. The need for this analysis was further stimulated by the commentary in response to the main FORECAST results that questioned (i) whether the high proportion of patients in the usual care arm who had CTCA might have diluted any benefit of the CTCA ± FFR_{CT} strategy in the test arm and (ii) whether FFR_{CT} would have any additional advantage over CTCA alone in this population, given that there has never been a randomized comparison of this nature.

Our current findings suggest that there may indeed be some clinical advantage to the selective FFR_{CT} strategy in terms of (i) reduced non-invasive testing burden and (ii) reaching a final management plan faster, this being achieved in a cost-neutral manner. These benefits are seen without any difference in clinical events. These data indicate that there would be merit in a head-to-head randomized comparison of these two strategies. It is certainly likely that confirmation of these findings would yield a strategy considered preferable to patients given that it would offer fewer tests and a quicker final plan.

There are several important limitations to this study. Firstly, the groups are matched only according to their pre-randomization stratum. Discussion regarding techniques such as propensity matching were considered to be inappropriate in this population and unnecessary given trial design. As shown in *Table 1*, the groups are, in fact, well matched. Secondly, we cannot know why clinicians preferred CTCA over other initial tests. Another potential consideration of the trial is that the costs in this study were based on UK National Health Service cost tariffs, and may not be generalizable to other countries with different cost structures in their health delivery systems, though the trial investigators have conducted a comparative analysis comparing costs in the FORECAST trial based on US healthcare cost weights with results showing that initial evaluation using CTCA ± FFR_{CT} had similar US costs as standard care pathways.[16] Thirdly, in the experimental group, 15% of patients could not have the intended FFRCT analysis as a consequence of variety of technical issues relating to quality of the CTCA scan. This rate of failure has gradually declined in front line practice since this trial recruited in association with improvements in scanner quality as well as an awareness of the importance of acquisition standards including routine nitrates and attaining lower target heart rates.

In conclusion, this prespecified substudy indicates that the strategy of CTCA with selective FFR_{CT} is associated with the need for fewer non-invasive tests and a faster time to a final management plan than a strategy of CTCA alone, despite equivalent total cardiac costs and clinical outcomes. These findings indicate that a formal randomized comparison between CTCA alone and selective FFR_{CT} is now warranted in these patients.

Table 5 Incidence of adverse cardiac events in the CTCA stratum by randomized group

	Standard care CTCA arm, *N* = 459	Experimental arm (CTCA ± FFR_{CT}), *N* = 453	*P*-value[a]
Any cardiac event[b]	44 (9.6%)	44 (9.7%)	0.948[c]
Any MI	1 (0.2%)	6 (1.3%)	0.068[a]
Death	0 (0.0%)	2 (0.4%)	0.246[a]
CVA	0 (0.0%)	0 (0%)	N/A
Hospital admission for cardiac cause	44 (9.6%)	42 (9.3%)	0.871[c]
Any revascularization	56 (12.2%)	59 (13.0%)	0.708[c]
PCI[d]	44 (9.3%)	43 (9.2%)	0.962[c]
CABG[b]	11 (2.6%)	15 (4.0%)	0.422[c]

[a]Fisher's exact test.
[b]MI, myocardial infarction; CVA, cerebrovascular accident; CABG, coronary artery bypass grafting.
[c]Pearson's χ^2 test.
[d]PCI, percutaneous coronary intervention.

Table 6 Comparison in total cardiac costs between the two CTCA stratum groups and patients randomized to standard care, whose pre-randomization test of choice was not CTCA (non-invasive and ICA), in pound sterling (£) represented in mean (SD) and median (IQR)

	ICA-first standard care, *N* = 48	Non-CTCA first non-invasive standard care, *N* = 193	Standard care CTCA arm, *N* = 459	Experimental arm (CTCA ± FFR_{CT}), *N* = 453	*P*-value
Mean	3958	1392	1272	1527	**<0.001**[a]
SD	3313	1812	1777	2220	
Median	1988	908	594	594	**<0.001**[a]
IQR	1697–4708	592–1161	570–966	570–1127	

The bold values represent statistically significant values ($P \leq 0.05$).
[a]Kruskal–Wallis rank sum test.

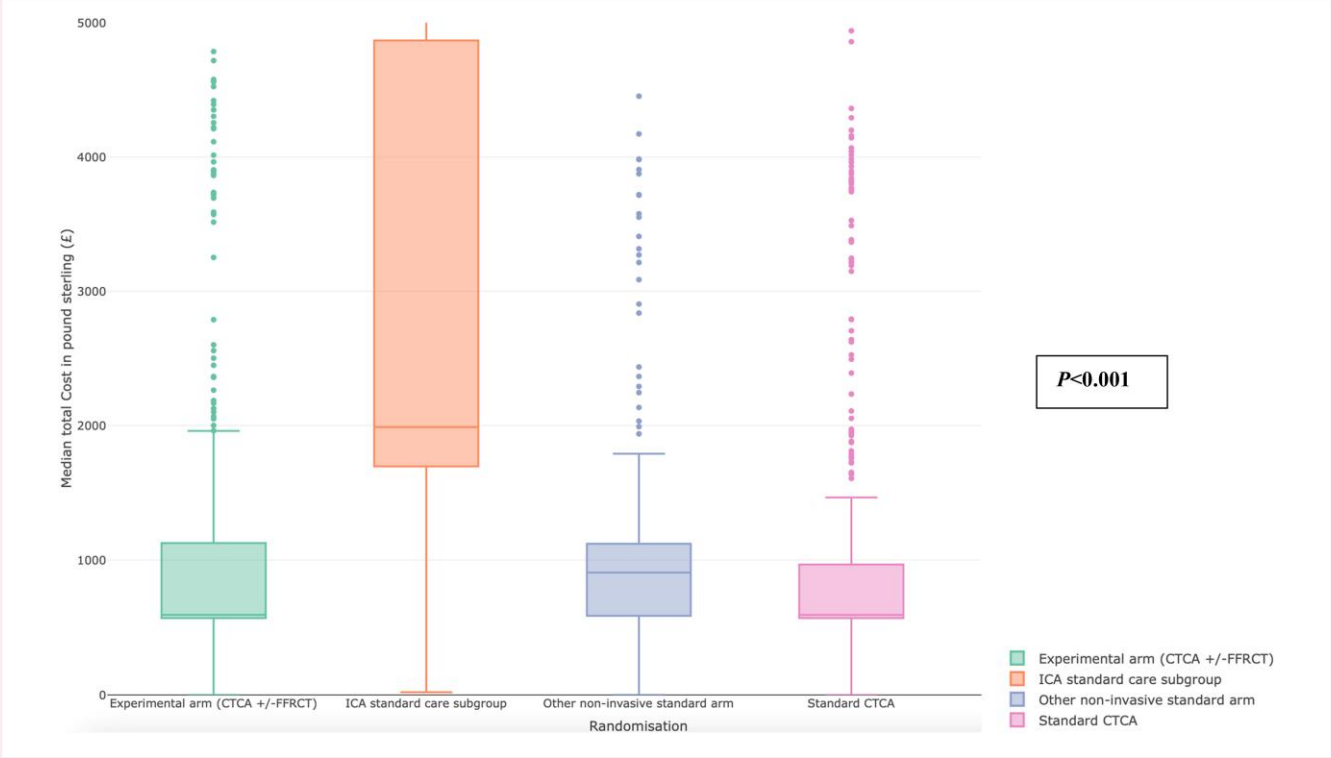


Figure 3 Total cardiovascular costs at 9 months in the four-patient subgroups from left to right; CTCA stratum experimental arm (CTCA ± FFR_{CT}); non-CTCA stratum standard care invasive subgroup; non-CTCA stratum standard care non-invasive subgroup, CTCA stratum standard care group. Represented as median (IQR). Distribution of 9-month costs in UK pounds by randomized assignment. The top line of each box is the 75th percentile, the bottom line is the 25th percentile, and the line inside the box is the median (50th percentile).

Table 7 Incidence of adverse cardiac events between the two CTCA stratum groups and patients randomized to standard care, whose pre-randomization test of choice was not CTCA (non-invasive and ICA)

	ICA-first standard care, *N* = 48	Non-CTCA first non-invasive standard care, *N* = 193	Standard care CTCA arm, *N* = 429	Experimental arm (CTCA ± FFR_{CT}), *N* = 436	*P*-value
Any cardiac event (death, cardiac hospitalization, MI, or CVA)	15 (31%)	15 (7.8%)	44 (9.6%)	44 (9.7%)	<0.001[a]
Any MI	1 (2.6%)	1 (0.5%)	1 (0.2%)	6 (0.7%)	0.2[a]
Death	0 (0%)	0 (0%)	0 (0%)	2 (0.2%)	0.4[a]
CVA	0 (0%)	1(0.5%)	0 (0%)	0 (0%)	0.2[a]
Hospital admission for cardiac cause	15 (31%)	15 (7.8%)	44 (9.6%)	42 (9.3%)	<0.001[a]
Any revascularization	19 (40%)	22 (11%)	56 (12%)	59(13%)	<0.001[a]
CABG	10 (21%)	6 (3.1%)	12 (2.6%)	16 (3.5%)	<0.001[a]
Time to final management plan	49 (33–96)	40 (20–77)	75 (55–126)	64 (48–110)	<0.001[a]

The bold values represent statistically significant values ($P \leq 0.05$).
[a]Kruskal–Wallis rank sum test.

Supplementary data

Supplementary data are available at *European Heart Journal - Imaging Methods and Practice* online.

Conflict of interest: Although this sub-analysis has received no funding from any organization, the original FORECAST trial was funded by an unrestricted research grant from HeartFlow. The company had no role in writing the protocol, prosecution of the study or its analysis, or drafting of the manuscript. N.C. reports unrestricted research grants from HeartFlow, Boston Scientific, Beckmann Coulter; consultancy/speaker fees from Abbott, HeartFlow, Boston Scientific, Phillips; travel sponsorship from Haemonetics, Abbott, Medtronic, Biosensors, and Edwards. C.B. reports grants from HeartFlow, Abbott, AstraZeneca, Boehringer

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Data availability

The data underlying this article were analysed using data originally collected for the FORECAST trial (NCT03187639) with permission from Southampton Clinical Trials Unit MP 131, Southampton General Hospital, UK. Data will be shared on request to the corresponding author with permission of Southampton Clinical Trials Unit.

Lead author biography

Mohamed Kira is a Cardiology Research Fellow at the University of Southampton and a Cardiology Trainee in the Wessex Deanery. He received an MBBCh (honours) from the Faculty of Medicine, Cairo University, and a PG Cert in Health and Biomedical Education from St George's University of London. He is currently pursuing a Doctorate in Medicine (DM) at the University of Southampton, with research interests in CAD and clinical outcomes.

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