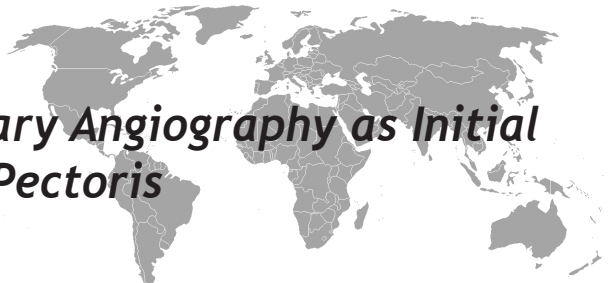

Computed Tomography Coronary Angiography as Initial Work-Up for Unstable Angina Pectoris

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ABSTRACT

Computed Tomography Coronary Angiography (CTCA) is a rapid, non-invasive diagnostic tool for coronary artery disease (CAD). Rapid Access Chest Pain Clinics (RACPC) were introduced in UK in 2000, in order to assess rapidly patients with chest pain. To evaluate the use of CTCA as initial work-up for unstable angina pectoris in a primary care-based RACPC. Eighty-eight (n=88) patients were examined by a consultant cardiologist and referred for CTCA if indicated. CTCA was performed with a 640 slices, 320-row CT scanner. Thirty-five (n=35) patients were discharged without further investigations; 50 (mean age 59.8 years; 24 male) were referred for CTCA and 3 were referred directly for an invasive angiography (IA). Following CTCA, 17 patients were discharged. Seventeen (n=17) patients with no history of CAD, but with positive CTCA findings and eleven (n=11) patients with known CAD but without new lesions on CTCA were discharged after optimisation of medical treatment. Five (n=5) of the 50 patients eventually underwent IA; 2 were referred for CABG; 3 continued with medical treatment. No major adverse cardiac events were recorded in a 6-months' follow up period. The cost for each patient who underwent CTCA was £1,087; 94% of patients rated their experience as good or excellent. The time interval from RACPC visit-to-definitive diagnosis was <3 weeks in 50% of patients, <6 weeks in 90%. Use of CTCA as initial investigation in Primary Care, is both clinically and cost-effective. CTCA should be considered in the initial diagnostic work-up of unstable angina pectoris patients, with or without prior history of CAD.

Key words: *Rapid access chest pain clinic, unstable angina pectoris, coronary ct angiography, primary health care*

Unstable Anjina Pektoris için Başlangıç Work-Up Olarak Bilgisayarlı Tomografi Koroner Anjiyografi

ÖZET

Bilgisayarlı tomografi koroner anjiyografi (BTKA) koroner arter hastalığı (KAH) için non invazif hızlı bir araştırma aracıdır. 2000 yılında Birleşik Krallıkta (UK) göğüs ağrısı olan hastalara hızlı bir şekilde yardımcı olmak için hızlı ulaşılan göğüs ağrısı klinikleri (RACPC) kurulmuştur. Çalışmanın amacı birinci basamak tabanlı RACPC de unstable anjina pektoris için başlangıç work-up olarak BTKA kullanımını araştırmaktı. Seksen sekiz (n=88) hasta bir konsultan kardiyolog tarafından muayene edildi ve eğer endikasyon varsa BTKA çekildi. BTKA bir 640 slices, 320 -row BT skaner ile uygulandı. Otuz beş (n=35) daha ileri araştırma yapılmadan taburcu edildi. 50 (ortalama yaş 59.8 yıl;24 erkek) hastaya BTKA çekildi ve 3 hasta doğrudan invazif anjiyografiye (IA) gönderildi. BTKA sonrası 17 hasta taburcu edildi. KAH öyküsü olmayan, fakat pozitif BTKA 'si olan 17 hasta ve bilinen KAH öyküsü olan fakat BTKA'sinde yeni lezyon saptanmayan 11 hasta medikal tedavisi düzenlenerek taburcu edildi. Elli hastanın 5'ine IA yapıldı, 2'si CABG'ya yönlendirildi, 3'ünde medikal tedavi ile devam edildi. 6 aylık takip periyodu sonrası herhangi bir majör yan etki kaydedilmedi. BTKA yapılan her hastanın maliyeti £1,087idi; hastaların %94'ü deneyimlerini iyi veya mükemmel olarak derecelendirdiler. RACPC başvurusu ile kesin tanı arasındaki zaman aralığı hastaların %50'sinde <3 hafta, %90'ında <6 hafta idi. Birinci basamakta başlangıç araştırma yöntemi olarak BTKA kullanımı hem maliyet hem de klinik olarak etkindi. BTKA hem KAH olan hem de olmayan unstable anjina pektoris hastalarında başlangıç teşhis work-up olarak değerlendirilmelidir.

Key words: *Hızlı ulaşım göğüs ağrısı kliniği, unstable anjina pektoris, koroner BT anjiyografi, primer sağlık bakımı*

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INTRODUCTION

Coronary artery disease (CAD) remains the commonest cause of morbidity and mortality in the developed countries (1). Until recently invasive coronary angiography (IA) has been the gold standard for accurate assessment of the presence, extent and severity of CAD. However, it is an invasive procedure and not without complications, especially in high risk and unstable patients (2).

Computed tomography coronary angiography (CTCA) is a rapid, non-invasive diagnostic tool, which has gained increasing acceptance as an alternative means of accurate and safe detection of coronary atherosclerotic plaques and CAD (3-8). With the advent of technology, the performance of this modality has further improved, providing near 100% sensitivity and >90% specificity as well as further reducing radiation dosage to approximately 10% that of IA (9-12). Moreover, a CTCA study can be completed within minutes and along with its non-invasive characters may enable optimal CAD detection with decreased health care costs and fewer complications (13).

During the last decade, the introduction of rapid access chest pain clinics (RACPC) has significantly contributed towards improvement in CAD mortality in the UK (14-16). These specialist services provide an accelerated assessment of out-patients with stable chest pain and clinical suspicion of CAD (17-18). Patients referred to RACP from general practitioners, consultant cardiologists and/or emergency departments (when patients present with typical symptoms but diagnostic tests do not suggest acute coronary syndrome). In 2008, Bexley Care Trust established a community-based RACPC, led by a consultant cardiologist, with main aim to expedite and improve the quality of local cardiology services. Since December 2009, any patient attending the RACPC and requiring further investigation was referred for a CTCA study with a 640-slice CT scanner. This is the first line investigation for these patients, rather than an exercise stress or nuclear stress perfusion test.

An audit was performed of the first 88 patients referred to this RACPC to assess: (i) clinical effectiveness (ii) patient satisfaction and (iii) cost-effectiveness of using the CTCA, as the first line investigation in the evaluation of patients with suspicion of CAD.

MATERIALS AND METHODS

Patients

The study group comprised 88 consecutive patients, with recent onset chest pain, who were referred by their general practitioners (GPs) to the Bexley Care Trust RACPC. All patients were assessed by a consultant cardiologist, underwent a resting ECG, and those with clinical suspicion of CAD were referred for a CTCA. The following information was extracted from the medical notes: presence or absence of hypertension, diabetes, hyperlipidaemia and family history of CAD (first degree relative suffering a cardiac event under the age of 55years). Also the pre-test probability for CAD was estimated using the National Institute for Health and Clinical Excellence (NICE) guidelines for "Chest pain of recent onset" (19). The criteria used were: type of chest discomfort, age and gender, in addition to the traditional risk factors for CAD. Participants were grouped into three categories based on the estimated pre-test probability for CAD: low (1% to 30% probability), intermediate (31% to 70%), or high (71% to 99%).

Scan protocol

Imaging was performed with a 640 slice, 320-row CT scanner with 0.5mm detector elements, 350ms of gantry rotation time and up to 16cm of coverage in the Z direction (Aquilion® ONE, Toshiba Medical Systems). Prior to the CTCA, patients were prescribed oral beta-blocker therapy by the referrer, unless contraindicated. If heart rate remained >68 b/m, additional intravenous metoprolol was administered if appropriate immediately prior to scanning. GTN spray was given sublingually if the systolic blood pressure was ≥110mmHg. Scanning settings of about 450mA (range 350-580MA) and 100-120kV were used, depending on body mass index. Images were acquired prospectively at 70-80% and 30-80% of the RR interval for patients with heart rates up to 68 bpm and above 68 bpm respectively. The radiation exposure for the whole-heart CTCA was quantified with a dose-length product conversion factor of 0.014mSv/mGy×cm.

Image analysis

The images were viewed on a Vitrea workstation by both an experienced cardiac radiographer and a consultant radiologist. In cases of significant discrepancy in opinions, a 2nd consultant radiologist reviewed the images. The coronary artery calcification (CAC) was assessed using dedicated software and quantified according to the

***Table 1**. Patient characteristics and coronary artery disease risk factors (n: 50)*

Age (years), mean (range)	*59.8 (32-81)*
Male gender, n (%)	*24 (48)*
BMI, mean (range)	*28 (23- 40)*
Obese (BMI >30kg/m^2) n(%)	*16 (32)*
Hypercholesterolemia, n(%)	*26 (52)*
Diabetes mellitus, n(%)	*6 (12)*
Family history of CAD (%)	*28 (56)*
Smoking, n(%)	*15 (30)*
Hypertension, n(%)	*27 (54)*
Pre-test probability	
Low	*21(42)*
Intermediate	*14(28)*
High	*15(30)*

scoring algorithm by Agaston et al. (20) CAC score was not estimated in patients with previous interventional therapy. Assessment of each of the major coronary arteries, left main stem (LMS), left anterior descending (LAD), circumflex (LCx) or right coronary artery (RCA) was made and any plaque deposition graded as normal (none), minimal (1-25% stenosis), mild (26-50% stenosis), moderate (51-70%) or severe (>70%) stenosis in LAD, LCx, RCA; except for LMS where a >50% stenosis was graded as severe (21).

Coronary plaques were further classified as non-calcified, calcified or mixed. Non-calcified plaque was defined as any discernible structure that could be assigned to the coronary artery wall and had CT attenuation below the contrast-enhanced coronary lumen but above the surrounding connective tissue or epicardial fat. Calcified plaque was defined as any structure with a CT attenuation of >130 Hounsfield Units (HU) that could be visually distinguished from the contrast-enhanced coronary lumen (22).

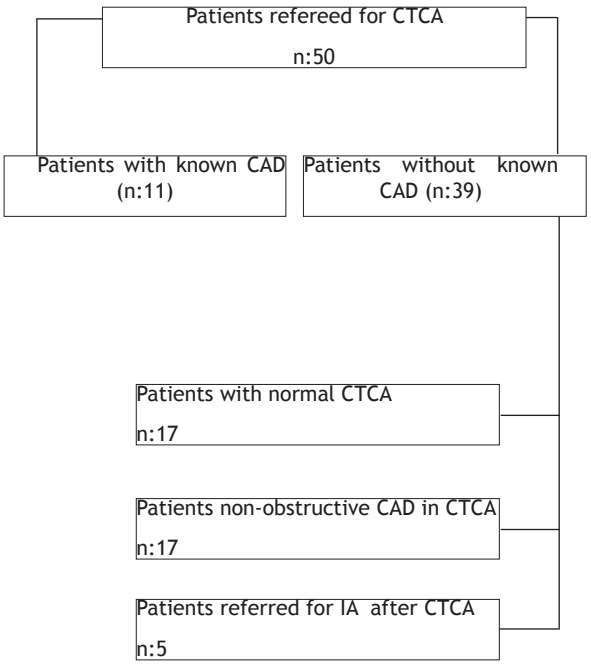

***Figure 1**. The outcome of the patients referred for CTCA.*

Patients' acceptance

Patients' acceptance and satisfaction for the CTCA was evaluated by means of a questionnaire with grades from 1=poor, 2=below average, 3=average, 4=good and 5=excellent for the following parameters: How helpful were the information provided about the test?, How comfortable have you felt during the test?, Have you been satisfied with the quality of service provided by the staff during your visit for a CT coronary angiogram?

***Table 2**. Prevalence (%) of varying degrees of atherosclerosis detected by CTCA in the coronary arteries of 43 patients (patients with previous intervention therapy were not included) .The maximum stenosis in each vessel was recorded. In one case the visualisation of the right coronary artery was not diagnostic and is not included.*

Coronary artery	*Normal 0% n (%)*	*Minimal 1-25% n (%)*	*Mild 26-50% n (%)*	*Moderate 51-70% n (%)*	*Severe >70% n (%)*
LMS	*37(86)*	*4(9.3)*	*0*	*2(4.6)*	*0*
LAD	*19 (44.1)*	*3 (6.9)*	*15(34.9)*	*4(9.3)*	*2(4.6)*
LCx	*28 (65.1)*	*6 (13.9)*	*6 (13.9)*	*2 (4.6)*	*1(2.3)*
RCA	*25 (58.1)*	*7 (16.2)*	*6 (13.9)*	*4 (9.3)*	*1(2.3)*
Grafts	*0*	*0*	*4 (100)*	*0*	*0*

Table 3. Patients' satisfaction of CTCA, (graded from 1:poor to 5:excellent)

	1	2	3	4	5
Information provided	*0*	*0*	*3 (6)*	*14 (28)*	*33 (66)*
Comfortingly	*0*	*0*	*3 (6)*	*12 (24)*	*35 (70)*
Overall experience	*0*	*0*	*3 (6)*	*12 (24)*	*35 (70)*

RESULTS

Thirty-five (n=35) of the 88 patients were discharged after initial clinical assessment without further investigation. Three were referred directly for IA and the remaining 50 patients were referred for CTCA. The demographics and risk factors for CAD of these patients are shown in Table 1. Of them, eleven had a known history of CAD; four were under medical treatment and the other seven had already undergone previous interventional therapy (two coronary artery bypass graft surgery-CABG, three percutaneous transluminal coronary angioplasty -PTCA and two had undergone both CABG and PTCA). No significant side effects were reported during the tests.

Quality of CTCA Images

A total of 200 native arteries were visualized; in 175 (87.5%) the quality of CT images was good and allowed accurate estimation of the degree of coronary obstruction. In 17 (8.5%) arteries, the images were regarded of moderate quality but sufficient to allow estimation of the degree of coronary stenosis. In 8 arteries (4%), the quality was regarded as poor and vessel calibre was unable to be assessed due to breathing artefacts (3 arteries) or severe calcification (5 arteries). The quality of images in 11 grafts (4 LIMA and 7 vein grafts) was good.

CTCA findings

Of the 43 patients with no previous interventional therapy, 17 (39.5%) had no stenosis, 4 (9.3%) minimal, 12 (27.9%) mild, 6(13.9%) moderate and 4 (9.3%) had severe stenosis. The results of the CTCA per artery are presented in Table 2. The two patients with previous CABG had patent grafts and the two patients with previous CABG and stent had patent grafts and stents. Of the three patients with previous PTCA; one had a patent stent (LAD); one had patent a stent (RCA) but a new soft plaque causing no significant obstructive stenosis in the same stent artery and the last one had stent stenosis (LAD) with retrograde filling but further investigation was not performed as the supplied myocardium area was not viable (from echocardiography one year before RACPC visit).

Relation between CTCA findings, CAC scores and plaque composition

Nineteen patients had a CAC score of 0, 15 had 1-400 and 9 had >400. Of the 19 patients with CAC score 0; two had mild stenosis due to soft plaque both of them in LAD. Of the 15 patients with CAC score 1-400, four had minimal coronary stenosis, 8 mild stenosis and 3 had severe stenosis. Of the 9 patients with CAC score >400, two had mild coronary stenosis, 6 moderate stenosis and 1 had severe stenosis. A total number of 72 plaques were recorded; 13 non-calcified, 44 calcified and 15 mixed. It's worth to mention that from the 13 non-calcified plaques, 2 causes minimal stenosis, 3 mild stenosis, 5 moderate stenosis and 3 severe stenosis. From the patients with CAC score 0; two had soft plaque in proximal LAD, causing mild stenosis.

Relation between pre-test probability of CAD with CTCA findings

Among the 21 patients with low pre-test probability, 14 patients had normal CTCA and the remaining 7 patients had no significant obstructive atherosclerotic disease. Fourteen patients had an intermediate pre-test probability of which 3 had normal CTCA. Nine patients from this group had evidence of no significant obstructive atherosclerotic disease and only 2 patients had obstructive CAD. Finally, among the 15 patients with a high pre-test probability; all patients had atherosclerotic disease but in 13 it was no significant obstructive while in 2 patients obstruction was significant.

Duration of investigation

The time from the initial attendance at the RACPC to the final visit (discharge or referral for further investigation) was: Under 3 weeks in 25 (50%) of the patients, Under 4 weeks in 35 (70%) of the patients, Under 6 weeks in 45 (90%) of them.

Five patients had one additional follow-up visit for optimization of their medication, before they were discharged.

Cost effectiveness

The average cost was £1,087 per patient (£86 for the cardiology consultation, £15 for the ECG, £900 for the CTCA).

Outcome

After the results of the CTCA (figure 1), 17 patients with normal CTCA were reassured and discharged. In 17 patients without a previous known history of CAD, and in whom CTCA show no significant obstructive CAD, there was optimisation of medical treatment and discharge. Similar for the 11 patients with a known history of CAD all were discharged, since the CTCA hadn't demonstrated new obstructive lesions. Eventually, 5 patients underwent IA based on CTCA results (4 patients) or clinical judgment (1 patient). Two were referred for CABG, while the remaining 3 were managed conservatively. In the patients who finally underwent CABG, CTCA had underestimated the degree of stenosis in RCA when compared with the IA findings (moderate stenosis according with CTCA, severe stenosis according with IA). In the 3 patients on medical treatment, there was agreement between CTCA and IA findings while the pressure wire studies revealed them as non-obstructive atherosclerotic plaques. Six-month follow-up was available in the 45 patients, who were discharged without further investigations. In this period, two patients visited Accident and Emergency Department with chest pain, one with normal arteries and one with mild coronary stenosis. In both cases, the pain was considered to be non-cardiac origin and the patients weren't admitted.

Patient acceptance

There was a high level of patient satisfaction. The results (Table 3) showed high overall satisfaction of average 4.6 out of 5 (min=3, max=5).

DISCUSSION

Chest pain is a common complaint among the general population. Although it is frequently of non-cardiac aetiology, it remains a considerable source of concern and anxiety (23,24). However, a substantial proportion of patients in the high-risk group for CAD, either waits too long before seeking professional advice and/or face significant waiting times they do so. RACPCs were introduced in UK in 2000 and to date there is a network of over 160 RACPCs across England (16-18, 25). Assessment in a RACPC, includes a detailed medical history and examination, ECG, blood tests and where indicated (in accordance with established protocols, available resources and local expertise) a non-invasive and functional studies i.e. exercise treadmill test (ETT), stress echocardiography, MR imaging for stress induced wall motion abnormalities or nuclear perfusion scanning, in an effort to detect evidence of myocardial ischemia. To the best of our knowledge, this is the first study, assessing the use of a 640-slice, 320-row CT scanner as first-line investigation of patients with stable chest pain.

An important feature of CTCA is its ability to confirm the presence of atherosclerotic disease, provide information about the arterial wall and the lumen; validate accurately soft and intermediate plaques (4-6, 26). It is well known, that the risk of plaque rupture depends mostly on the plaque type (composition) rather than plaque size (volume); most ruptures occur in plaques containing a soft, lipid-rich core, which is covered by a thin and inflamed cap of fibrous tissue (27-29). Patients with proven non -obstructive coronary atherosclerosis require lifestyle modification together with lifelong medical treatment.

In this retrospective study, we included patients with known history of CAD, as well as those with previous medical, interventional or surgical therapies. Furthermore, for the first time a RACPC was based in the community, as part of the Primary Care Trust. Given that CTCA has a very high negative predictive value for CAD, CTCA in selective patients with unstable angina pectoris might be an alternative to a functional test for excluding significant coronary stenosis. In our cohort, only the group with objective CTCA findings of significant CAD were eventually referred for further invasive investigation. The high degree of CTCA patient acceptance is also noteworthy, as it is a non-invasive, pain-free and rapid test.

Although, CTCA provides us with important structural information, it lacks the ability to detect the presence of myocardial ischaemia, while it does share some of the disadvantages of a conventional angiography study, including ionized radiation exposure and the risk of contrast nephropathy. Patients with CTCA evidence of significant stenosis should undergo further functional imaging (nuclear stress test, stress echocardiography, MRI perfusion test) to exclude significant ischemia. NICE guidelines suggest that patients with low likehood of

CAD should undergo CT calcium scoring, and CTCA if calcium score is 1-400.19 However this pathway we will misdiagnose around 10% of patients with CAC score 0 and atherosclerosis due to non-calcified plaque (30-32). Finally, the European society of cardiology guidelines (2006) recommend the CTCA in patients with a low pretest probability, with a non-conclusive exercise ECG or stress imaging test (level of evidence C) (33). The use of functional imaging studies as first investigation could be a useful strategy for patients with unstable angina pectoris and low or intermediate CAD probability, as they could be used to select those patients who will benefit from CTCA or a conventional angiogram.

In conclusion, CTCA when used as first line evaluation for patients with unstable angina pectoris can reduce both cost and length of investigations while the test appears to have a high acceptance rate among the patients. The main limitation of the study is the lack of control group, and the small number of participants. We recognise that our evaluation might suffer from some of the problems/sources of bias inherent in a retrospective study/audit i.e. missing data from medical records review. In addition, the rather heterogeneous cohort should be considered as a possible limiting factor. Furthermore, the aforementioned strategy is not helpful for patients with real angina, without coronary obstruction. A prospective, randomized study that will enroll a more extensive and homogeny population group could lead in an effective algorithm for management of stable coronary artery disease.

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