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Utilization of Functional Tests Prior to and Adherence to Guidelines on Coronary Angiography

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1. Introduction

Coronary angiography is one of the most commonly performed investigations in clinical cardiology and remains the "gold standard" in the anatomical diagnosis of coronary artery disease. It is often required to establish the diagnosis of coronary disease and to provide a map of a patient's coronary artery anatomy prior to percutaneous coronary intervention or coronary artery bypass surgery.

Despite its importance, invasive coronary angiography should not be performed in all patients suspected to have coronary artery disease. Functional tests, such as stress ECG, echo or nuclear perfusion imaging, are often recommended as initial tests for many of these patients. These functional tests are widely available and practised. In addition to their diagnostic value, functional tests provide independent and additional prognostic information (Marwick et al., 1997). Furthermore, functional tests are often required to guide management of patients with intermediate lesions on invasive coronary angiography. According to the Bayesian theorem, the impact of a screening test is most significant in patients with intermediate pre-test probability of disease. Furthermore, cost-effectiveness analyses often reveal that the use of screening tests in these patients is the most favourable approach. Despite the established roles of functional tests and their extensive incorporation in best practice guidelines, there is little data on the extent of their use and on how the results of such tests are utilised prior to referral to coronary angiography in patients with low to intermediate pre-test probabilities of coronary disease.

Guidelines have proliferated in cardiology in recent years. Major professional bodies like the American College of Cardiology, American Heart Association and the European Society of Cardiology have published guidelines on a wide range of cardiovascular disorders and cardiovascular investigations. These guidelines incorporate the latest evidence base and provide recommendations, which are intended to improve the quality of patient care and clinical outcomes whilst minimising costs. These recommendations are based on the most effective and evidence-based strategies. The American College of Cardiology and American Heart Association have published comprehensive guidelines on the use of coronary angiography (Scanlon et al., 1999). The guidelines were initially published in 1987 and were revised in May of 1999. These guidelines provide recommendations for coronary

angiography in clinical scenarios such as patients with known or suspected coronary artery disease, stable or unstable angina pectoris, acute coronary syndromes, recurrence of symptoms after revascularization, congestive heart failure or other conditions.

There has been considerable interest in evaluating compliance with guidelines in clinical practice. This is particularly pertinent as improved compliance with treatment guidelines is associated with better clinical outcomes in patients with acute coronary syndromes (Schiele et al., 2005). Despite the widespread dissemination of the guidelines on coronary angiography, the compliance rate with these guidelines in clinical practice and the relationship between compliance and results of angiography has not been prospectively evaluated.

As discussed in other chapters, computed tomography (CT) coronary angiography is now increasingly being used to evaluate patients with suspected coronary artery disease. The American College of Cardiology, together with other professional bodies, has published criteria for the appropriate use of CT coronary angiography (Hendel et al., 2006). CT coronary angiography will increasingly be incorporated into clinical practice as an important imaging modality for the evaluation of patients suspected to be suffering from coronary artery disease. An important consideration for clinicians and administrators will be the diagnostic value of imaging tests and their cost effectiveness in these patients. More data has recently become available regarding the incremental value of functional testing and other imaging modalities like CT coronary angiography in patients with suspected coronary artery disease. In particular, the incremental value of non-invasive testing in risk stratification and the prediction of adverse events in these patients will be of interest in guiding practice and, more importantly, health care policy.

2. Utilisation of functional tests prior to coronary angiography

As discussed earlier, despite their well-documented clinical usefulness, there is little information on the pattern of use of functional tests in patients prior to undergoing invasive coronary angiography. In particular, for patients who are subsequently found to have no significant coronary artery disease on coronary angiography, it will be interesting to examine how and why they ended up having invasive coronary angiography. It may be argued that, for these patients, a "failure" of the investigative algorithms led them to undergo an invasive test, which may not have been indicated and should not have been performed. These tests should have been avoided as they exposed the patient to needless risks and might have been unnecessary monetary, resource and manpower wastes. By examining where the process has "failed", one will hopefully be able to learn how to minimise future such "failures". The purpose of our study was to analyse the patterns of use and the results of functional tests in patients found to have normal coronary arteries on invasive coronary angiography.

2.1 The study - methods
Over a 7 and a half-year period, a total of 6,409 patients underwent 8,069 coronary procedures at our hospital. Our hospital is the only tertiary referral centre serving a population of about 800,000 people. Only patients referred for coronary angiography for evaluation of coronary artery disease were included in the analysis. Angiographic studies on patients referred for valvular or haemodynamic indications were excluded from the

analysis. Patients with documented coronary artery disease referred for coronary angioplasty or other percutaneous intervention were also excluded. Therefore, the study included 6,053 patients who underwent a total of 6,830 coronary angiographic procedures.

Of the 6,830 procedures, 4,610 were for male patients and 2,220 were for female patients. The mean age of the patients was 60.9 ± 11 years. Clinical information, including age and gender, referrer details, indications for angiography, type of the study and subsequent results, was prospectively collected and entered into a computerised database.

Coronary angiography was performed according to standard techniques via either the femoral, brachial or radial approaches. Patients with no angiographically detectable disease or irregularities in any of the epicardial coronary arteries were considered to have normal coronary arteries on angiography. Patients who had previously undergone coronary artery bypass surgery and who were found to have patent bypass grafts on angiography were not considered to have normal coronary arteries.

Patients who were subsequently found to have normal coronary arteries on angiography were identified. The clinical records of these patients were then reviewed. Their clinical characteristics and presenting symptoms, including risk factors for coronary artery disease, were analysed. Chest pain as the main presenting symptom was characterized on retrospective chart review as typical, atypical or non-anginal/non-specific pain. Five risk factors were considered: diabetes mellitus, cigarette smoking, hypertension, hypercholesterolemia and family history of coronary artery disease. Patients' pre-test probabilities of coronary artery disease were estimated from age, gender and presenting symptoms (Diamond & Forrester, 1979).

The types and results of functional tests, if performed for these patients, were recorded and analysed. Results of functional tests including exercise ECG, exercise or pharmacologic stress echocardiogram or nuclear myocardial perfusion studies were sought. None of the patients had CT coronary angiography as it was not available at the time of the study. Functional tests were considered negative if no evidence of inducible ischaemia was detected on testing and if the level of the stress was considered adequate. Functional tests were considered inconclusive if there was equivocal evidence of inducible ischaemia or if there was no inducible ischaemia at inadequate levels of stress.

Information on the physicians who referred these patients (referrers) for coronary angiography was also recorded. Referrers were classified into cardiologists or other physicians according to the field of specialisation. In particular, for cardiologist referrers, those who performed coronary angiography were considered proceduralists whilst cardiologists who do not perform angiography were considered non-proceduralists.

2.2 Results
2.2.1 Patients
Seven hundred and fifty six patients undergoing 762 procedures were found to have normal epicardial coronary arteries on angiography. This means that 11.2% of the coronary angiograms performed were for patients with normal coronary arteries. The mean age of these patients was 54.9 ± 11.5 years with female patients comprising 54.9%. Clinical information was obtainable in all but 4 patients (99.5%). The mean number of coronary risk factors was 1.5 ± 1. The mean pre-test probability of coronary artery disease was 41.7 ± 30% (median 46.1%, inter-quartile range 14.1 - 58.9%). Three hundred and thirteen patients underwent coronary angiography as hospital inpatients while 445 patients underwent coronary angiography as a day-only procedure on an outpatient basis. There were no

significant differences in gender distribution, number of coronary risk factors and pre-test probability of coronary artery disease between patients who underwent coronary angiography as inpatients and those who underwent the procedure as day-only patients. However, patients who underwent coronary angiography as inpatients were significantly younger and more likely to have presented with non-anginal chest pain (Table 1).

Parameters	Inpatient procedure (n=313)	Day-only procedure (n=445)	p
Men/Women	149/164	199/246	0.43
Age (years)	53.6 ± 12.5	55.8 ± 10.8	0.01
Number of risk factors	1.48 ± 1.1	1.49 ± 1	0.73
Presenting symptom n (%)			<0.001
Typical angina	62 (19.8%)	99 (22.2%)	
Atypical angina	110 (35.1%)	172 (38.7%)	
Non anginal chest pain	85 (27.2%)	71 (15.9%)	
Dyspnea	23 (7.3%)	48 (10.8%)	
Others	26 (8.3%)	34 (7.6%)	
Asymptomatic	2 (0.6%)	16 (3.6%)	
Pre-test probability of coronary disease (%)	39.6 ± 30	43.2 ± 29.8	0.11

Table 1. Clinical characteristics of patients who were subsequently found to have angiographically normal coronary arteries divided according to whether they were hospital inpatients or not at the time of angiography. (Reproduced with permission from: Leung DY, Lo ST, Liew CT, Wong A, Hopkins AP, Juergens CJ. Utilization of functional tests prior to coronary angiography in patients with angiographically normal coronary arteries. International Journal of Cardiology 2005; 104(3):326 – 331. Elsevier Limited)

2.2.2 Utilization of functional tests

Only 483 of the 758 patients (63.7%) had undergone functional tests as part of the diagnostic workup prior to coronary angiography. Two hundred and fifty three patients (33.4%) underwent exercise electrocardiography, 140 underwent stress nuclear perfusion imaging (18.5%), 9 underwent stress echocardiography (1.2%) and 81 underwent more than one functional test (10.7%). There were no significant differences in gender distribution, age, number of coronary risk factors and pre-test probability of coronary disease between patients who had undergone functional tests and those who had not. However, inpatients were significantly less likely to have undergone functional tests prior to angiography compared to day-only patients (Table 2).

Multiple logistic regression analysis identified inpatient status as the only independent predictor of undergoing functional tests prior to coronary angiography in these patients (OR 5.9, 95% confidence interval 5.0 - 7.0, p <0.001).

Of the 483 patients who underwent functional tests prior to coronary angiography, inducible ischaemia was detectable in only 241 patients (49.6%). Therefore less than half of the performed tests were positive. Functional tests were reported negative for inducible

Parameters	Functional tests (n = 483)	No functional tests (n=275)	p
Men/Women	218/265	130/145	0.57
Age (years)	55.3 ± 10.7	54.2 ± 12.8	0.2
Number of coronary risk factors	1.5 ± 1.1	1.45 ± 1.1	0.52
Pre-test probability of coronary disease (%)	42.5 ± 29	40.2 ± 31	0.32
Inpatient/day-only patient (n)	126/357	187/88	<0.001

Table 2. Clinical characteristics of the patients when subdivided according to whether they had undergone functional testing prior to coronary angiography. (Reproduced with permission from: Leung DY, Lo ST, Liew CT, Wong A, Hopkins AP, Juergens CJ. Utilization of functional tests prior to coronary angiography in patients with angiographically normal coronary arteries. International Journal of Cardiology 2005; 104(3):326 – 331. Elsevier Limited)

ischaemia for 245 patients. Of these, 151 patients achieved adequate stress levels whilst in 91 cases the results were inconclusive. Of the 151 patients with negative functional tests, 114 (75.5%) underwent coronary angiography as outpatients and 37 as inpatients. Only 22 patients (14.5%) had history of previous admission to hospital with chest pain prior to angiography.

Patients were further divided into 3 subgroups according to their pre-test probability of coronary disease: low risk (pre-test probability <20%), intermediate risk (pre-test probability 20% to <80%) and high risk (pre-test probability ≥ 80%). There were no significant differences in the utilisation and the results of functional tests across the clinical risk subgroups for day-only patients (Figure 1, p = 0.2) or for inpatients (Figure 2, p = 0.76). However, a higher proportion of day-only patients underwent functional tests prior to angiography irrespective of pre-test probability of disease compared to inpatients.
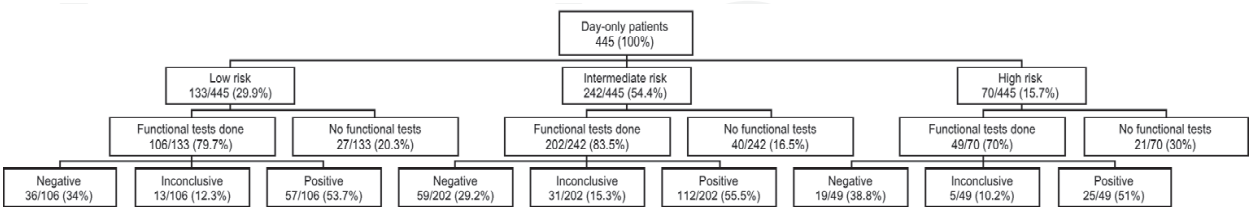

Fig. 1. Use and results of functional tests in patients undergoing coronary angiography as a day-only procedure. (Reproduced with permission from: Leung DY, Lo ST, Liew CT, Wong A, Hopkins AP, Juergens CJ. Utilization of functional tests prior to coronary angiography in patients with angiographically normal coronary arteries. International Journal of Cardiology 2005; 104(3):326 – 331. Elsevier Limited)

A total of 33 physicians referred these patients to our institution for coronary angiography. Twenty (60.6%) were cardiologists and 13 (39.4%) were other physicians. Patients referred by cardiologists were significantly more likely to have undergone functional tests compared
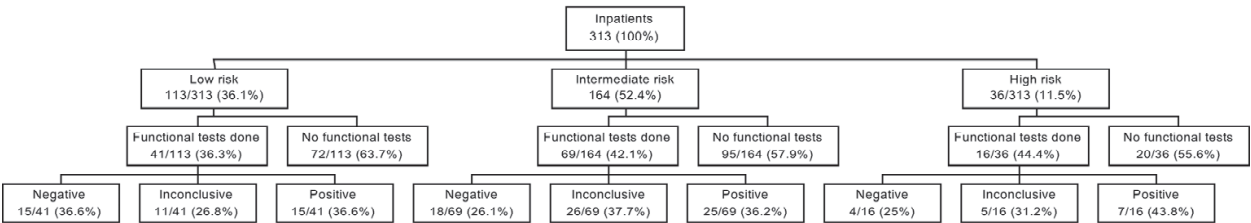
Fig. 2. Use and results of functional tests in patients undergoing coronary angiography as inpatients. (Reproduced with permission from: Leung DY, Lo ST, Liew CT, Wong A, Hopkins AP, Juergens CJ. Utilization of functional tests prior to coronary angiography in patients with angiographically normal coronary arteries. International Journal of Cardiology 2005; 104(3):326 – 331. Elsevier Limited)

with those referred by other physicians (66% vs 50.8%, p = 0.001). Of the cardiologists, 9 were proceduralists and 11 were non-proceduralists. There was no significant difference between procedural cardiologists and non-procedural cardiologists in the use of functional tests in patients prior to coronary angiography (68% vs 64%, p = 0.28).

2.3 Discussion
This study examined the use and results of functional tests in a large consecutive series of patients who were subsequently found to have angiographically normal coronary arteries at our institution over the study period. The overall utilisation of functional tests in our patients was only modest and a significant proportion of patients either had no functional tests done prior to angiography or proceeded directly to coronary angiography despite negative functional tests. Referrer characteristics and patient status, rather than pre-test probability of coronary artery disease, appeared to have a greater impact on the use of functional tests prior to angiography.

Functional tests have established and pivotal roles in the investigation and management of patients with suspected or confirmed coronary artery disease. They have a high sensitivity and specificity in the non-invasive diagnosis of coronary artery disease in patients with suggestive symptoms. Information like blood pressure, exercise capacity and heart rate response to exercise are of further prognostic value. The addition of cardiac imaging during functional tests provides incremental prognostic information (Marwick et al., 1999). Therefore, functional tests not only allow diagnosis of coronary artery disease but also allow clinicians to risk-stratify patients. Higher risk patients should be referred onto coronary angiography whilst lower risk patients can safely be managed without expensive and invasive investigations. In the American College of Cardiology/American Heart Association guidelines for coronary angiography, functional tests play a central role (Scanlon et al., 1999).

It has been suggested that the diagnostic as well as the follow up costs were lower for those who had undergone functional tests prior to coronary angiography, irrespective of the pre-test probability of coronary disease, without significant differences in the medium term outcome (Shaw et al., 1999a). The cost differences between the two strategies may reflect a decreased need for coronary angiography in patients with normal perfusion scan results (Shaw et al., 1999b). Functional tests, therefore, have the potential to accrue cost savings by acting as a "gate-keeper" for coronary angiography by excluding those with normal results who have no significant coronary disease and excellent short to medium term outcome.

According to the Bayesian theorem, the post-test probability of coronary artery disease is dependent on the prevalence of the disease in the population being tested. Impact of screening tests is highest in patients with intermediate pre-test probability. Proceeding to coronary angiography without functional tests may be justifiable in patients with high pre-test probability of coronary artery disease. In patients with multiple coronary risk factors and typical angina, coronary angiography without functional tests may be more appropriate as the results of functional tests are less likely to obviate the need for angiography in these patients. Cost-effectiveness analyses by Patterson et al suggested that proceeding straight to coronary angiography in patients with high pre-test probability of disease (>80%) may be more cost-effective (Patterson et al., 1995). One would expect that the use of functional tests would be higher in patients with low to intermediate pre-test probability of coronary disease. However, the results of the present study showed that this is not the case; the use of functional tests in these patients was low (Figures 1 and 2). The use of functional tests was particularly low for hospital inpatients. Inpatients were less likely to have undergone functional tests prior to angiography compared with day-only patients across all three groups of pre-test probability of coronary disease. For intermediate risk patients, 83.5% of day-only patients compared with only 42.1% of inpatients had undergone functional tests prior to angiography. For low risk patients, 79.7% of day-only patients compared with only 36.3% of inpatients had undergone functional tests. This cannot be explained by any differences in risk factor profiles or pre-test probability of disease.

There could be a number of possible explanations for these findings. Hospital inpatients may be more likely to be perceived as unstable, which may have made the treating physicians reluctant to subject them to functional testing. Some of our regional referring hospitals do not have stress testing facilities and direct referral to our institution for coronary angiography might have been an easier solution. The delay in obtaining stress echocardiography or stress perfusion nuclear imaging contrasted with the overriding pressure to discharge patients from hospital may make such functional testing less attractive to treating physicians.

Functional tests are neither 100% sensitive nor 100% specific. In our study, a high proportion of patients with negative functional tests with adequate stress still proceeded to angiography. This may have resulted from the suspicion of a false negative functional test, frustration on the part of the physicians about the lack of a definitive diagnosis and the desire to answer the question "once and for all". However, despite the lack of 100% sensitivity, patients with normal stress echocardiograms or stress nuclear perfusion imaging had very low cardiac event rates on follow up, in the range of <0.5%/year (Metz et al., 2007). Functional tests may also be falsely positive. However, patient and test characteristics associated with false positive functional tests are well described. Exercise ECG is well known to be non-specific in young or middle aged women. The basal inferior wall changes on stress echocardiogram and diaphragmatic and breast attenuation artefacts on stress nuclear perfusion imaging are well-described sources of false positive findings. The recent advent of CT coronary angiography may help in ruling out coronary artery disease and its use in equivocal or un-interpretable functional tests is considered appropriate.

The increased use of coronary angiography, regardless of whether it is indicated or not, may have more than just an economic impact. In addition to the increased risks of procedural complications, increased diagnostic testing has been shown to result in an increased therapeutic intervention rate downstream (VerrilliWelch, 1996; Wennberg et al., 1996). While the concern of increased downstream therapeutic intervention is minimal in patients

with angiographically normal coronary arteries, the risks of procedural complications and the increased overall costs of investigations cannot justify indiscriminate use of angiography in patients with low to intermediate pre-test probability of disease.

There are considerable variations in the use of coronary angiography (Pilote et al., 1995), which was closely related to the availability of cardiac catheterization facilities (Every et al., 1993). With the use of angiography closely related to its availability, there have been concerns over the appropriateness of coronary angiography (Bernstein et al., 1999; Chassin et al., 1987b). A significant proportion of coronary angiography was found to be "inappropriate" (Gray et al., 1990), with "inappropriate" use of coronary angiography higher in high-use sites (Chassin et al., 1987a). In the study by Chassin et al (Chassin et al., 1987b), patients without angina or with atypical angina and who had not undergone exercise testing constituted the most common subgroup of inappropriate angiography. In a random audit of 320 patients referred for coronary angiography (Gray et al., 1990), only 53% of the patients had undergone functional tests prior to angiography. In a consecutive series of 3631 patients referred for coronary angiography, 5% were performed for inappropriate indications and another 33% for uncertain indications (Hemingway et al., 2001). Similarly, asymptomatic patients and patients with atypical angina or mild angina who had not undergone exercise testing comprised the majority of the inappropriate and uncertain indications. Furthermore, the appropriateness ratings for angiography predicted both the angiographic findings of coronary disease, subsequent rates of revascularisation and mortality rates after a mean follow-up time of 2.5 years (Hemingway et al., 2001).

There has been considerable interest in examining the difference in treatment (Borowsky et al., 1995), procedural use (Nash et al., 1997), and patient outcome between cardiologists and non-cardiologists in patients with coronary artery diseases. It has been reported that cardiologists were more likely than non-cardiologists to recommend "clinically necessary" coronary angiography (Borowsky et al., 1995). Some reports suggested that cardiologists were more likely to prescribe medical therapies of proven efficacy in the care of patients with myocardial infarction (Ayanian et al., 1994), while others suggested that myocardial infarct patients in the care of cardiologists had a lower risk-adjusted mortality rate (Nash et al., 1997). The results of our study suggested that cardiologists were more likely to have referred patients with suspected coronary artery disease for functional tests prior to angiography and procedural cardiologists were as likely as their non-procedural counterparts to utilise functional tests prior to referral for angiography.

Our study is only a single centre experience and may not reflect experience of other centres. We selected only patients with angiographically normal coronary arteries as these patients represent a lower clinical risk subgroup where functional tests should have been more widely used and clinically relevant. As a result of the selection, we did not include patients who had undergone functional tests but were not referred for angiography. Furthermore, our aim was to document the use of functional tests and not to judge whether referral of low to intermediate risk patients without functional tests was "appropriate" or not.

In conclusion, use of functional tests prior to coronary angiography was only modest and was particularly low for hospital inpatients in our large consecutive series of patients with angiographically normal coronary arteries. A significant proportion of patients proceeded to coronary angiography despite negative functional tests. Referrer characteristics and hospital inpatient status, rather than pre-test probability of coronary artery disease, appeared to have greater impact on utilization of functional tests.

3. Adherence to guidelines on coronary angiography

The American College of Cardiology and The American Heart Association initially published their guidelines on the use of invasive coronary angiography in 1987. An update was issued in 1999 (Scanlon et al., 1999). The guidelines examined the indications for coronary angiography in a wide range of commonly encountered clinical situations. These included patients with known or suspected coronary artery disease with minimal or stable symptoms, patients with unstable coronary symptoms, patients after myocardial infarction, patients after revascularisation, patients with heart failure or with haemodynamic instability, patients undergoing non cardiac surgery and patients with valvular or congenital heart disease. These guidelines incorporate the latest available evidence and provide guidance to clinicians to the best evidence based practice. Despite the wide dissemination of these guidelines, there is little information on how they are incorporated into daily clinical practice and how closely they are adhered to. It would be interesting to find out how compliant clinicians are with these guidelines and how compliance is translated into the clinical results. Furthermore, it will be helpful to identify areas where compliance is low so that further efforts may be spent on these problem areas to improve compliance.

3.1 The study - methods

A total of 802 consecutive patients referred to our cardiac catheterisation laboratory for coronary angiography were prospectively enrolled and evaluated over a 5-month period in 2002. Clinical history including coronary risk factors, presenting symptoms, electrocardiograms and laboratory test results were recorded prospectively. Chest pain as a presenting symptom was assessed and classified as typical angina, atypical angina or non-anginal chest pain. Five coronary risk factors were considered: diabetes mellitus, cigarette smoking, hypertension, hypercholesterolemia and family history of coronary artery disease. Electrocardiographic changes were considered ischaemic if there was horizontal ST segment depression or elevation of ≥ 1 mm or if there was symmetrical T wave inversion of ≥ 3 mm in ≥ 2 contiguous leads.

The physicians who referred these patients were classified as cardiologists or general physicians according to their primary field of specialisation. Cardiologists were further sub-classified into non-invasive or invasive cardiologists according to whether they performed coronary angiography. The type and results of functional tests, if performed, were recorded and information on left ventricular function, if available, was also collected. Functional tests were considered positive it there was evidence of inducible ischaemia on testing (ST segment deviation of ≥ 1mm on exercise electrocardiography, inducible new segmental wall dysfunction on stress echocardiography or reversible perfusion defects on nuclear perfusion imaging). They were considered negative if there was no evidence of inducible ischaemia on testing and if the level of the stress was considered adequate for exercise stress (peak heart rate $\geq 85\%$ age predicted maximum). Functional tests were considered inconclusive if there was equivocal evidence of inducible ischaemia or if there was no inducible ischaemia at inadequate levels of stress for exercise stress.

Patients with no irregularities detected in any of the epicardial coronary artery on angiography were considered to have normal coronary arteries on angiography. Patients with less than 50% diameter stenosis in any of the epicardial coronary arteries or its major branches were considered to have minor coronary artery disease. Angiograms on patients

who had previously undergone coronary artery bypass surgery and were found to have all bypass grafts patent (<50% diameter stenosis) and no ungrafted but stenotic native vessels on angiography were not considered to have significant flow limiting stenosis. Complications of coronary angiography, if any, were also recorded.

Compliance with guidelines on coronary angiography was assessed for these 802 patients by 2 independent assessors, blinded to the results of angiography, according to the American College of Cardiology/American Heart Association guidelines on coronary angiography (Scanlon et al., 1999). Referrals were considered compliant with guidelines if they fulfilled either the Class I or Class II indications. Referrals were considered non-compliant (outside guidelines) if they fulfilled Class III indications or none of the Class I or II indications. Disagreements between the 2 assessors were reconciled with arbitration by an independent third assessor. Intra-observer agreement was assessed with the same assessor evaluating compliance on the same 802 patients, 12 months after the initial assessment. Both assessments were done with the assessor blinded to the results of the initial assessment and coronary angiography.

3.2 Results
3.2.1 Patients characteristics

We evaluated a total of 802 patients (Table 3). The indications for coronary angiography were; assessment of chest pain with known or suspected coronary artery disease in 491 patients (61.1%), non ST segment elevation myocardial infarction in 127 patients (15.8%), ST segment elevation myocardial infarction in 72 patients (9%), congestive heart failure or dyspnoea in 70 patients (8.7%), valvular heart disease in 20 patients (2.5%), prior to non cardiac surgery in 11 patients (1.5%), arrhythmias in 5 patients and miscellaneous in 6 patients (0.8%). Two hundred and thirty six patients (29.4%) had had coronary angiography previously.

One hundred and nineteen patients (14.8%) were referred by general physicians (internists), 341 (42.5%) by non-invasive cardiologists and 342 (42.6%) by invasive cardiologists. Cardiac Troponin T levels were measured in 354 patients and a significantly higher proportion of patients referred by general physicians had raised cardiac Troponin T levels compared to those referred by cardiologists (56 of the 69 patients versus 141 of 285 patients, $p<0.001$)

3.2.2 Investigations prior to angiography

All patients had 12-lead electrocardiography before coronary angiography as part of the initial diagnostic work-up. Twelve-lead electrocardiography was normal in 261 patients (32.5%), showed non-specific changes in 174 patients (21.7%), was un-interpretable in 30 patients (3.7%) and showed ischemic changes in 337 patients (42%).

Left ventricular function was assessed as part of the diagnostic work up before coronary angiography with echocardiography in 232 (28.9%) patients and with radionuclide ventriculography in another 123 patients (15.3%). Left ventricular function was assessed in a further 37 patients (3.6%) from previous contrast ventriculography. Left ventricular function was not assessed prior to coronary angiography in 410 patients (51.1%). Inpatients were significantly less likely to have their left ventricular function evaluated prior to coronary angiography compared with day-only patients (36.9% vs 62.9%, $p<0.001$). Of the 392 patients who had left ventricular function assessment, 149 (38%) had an ejection fraction of < 50% and 243 patients had normal function (ejection fraction ≥ 50%).

Age	62 ± 11 years
Male / Female (n)	522 / 280
Average number of coronary risk factors	2.7 ± 1.3
Medications, n (%)	
Aspirin	642 (80%)
Beta blockers	542 (67.6%)
Calcium antagonists	177 (22.1%)
Nitrates	289 (36%)
Angiotensin converting enzyme inhibitors	375 (46.8%)
Statins	547 (68.2%)
Clopidogrel	111 (13.8%)
Unfractionated heparin or enoxaparin	220 (27.5%)
Angiotension receptor blockers	103 (12.8%)
Inpatient / day only procedure (n)	433 / 369
Previous coronary artery bypass surgery, n(%)	89 (11.1%)
Previous percutaneous coronary intervention, n(%)	88 (11%)
History of myocardial infarction, n(%)	141 (17.6%)
Acute coronary syndrome during index hospital admission (for inpatients), n(%)	199 (24.8%)
Renal impairment, n(%)	71 (8.9%)

Table 3. The baseline clinical characteristics of the 802 patients. (Reproduced with permission from: Leung DY, Hallani H, Lo ST, Hopkins AP, Juergens CP. How compliant are we with guidelines for coronary angiography in clinical practice? Internal Medicine Journal 2007, Oct;37(10):699-704. John Wiley and Sons)

Serum cardiac Troponin T levels were measured in 347 of the 433 inpatients (80.1%) and were elevated to ≥ 0.03 ng/ml in one or more blood samples in 194 patients (44.8%). Cardiac Troponin T levels were measured in only 7 of the 369 day-only patients and were elevated in 3 patients (0.8%).

3.2.3 Functional test results

Functional tests were performed in 262 of the 369 (71%) day-only patients and in only 75 of the 433 inpatients (17.3%, p<0.001). Even after the 197 patients with raised cardiac Troponin T levels were excluded from analysis, inpatients were still significantly less likely to have

had functional tests prior to coronary angiography compared with day-only patients (28.5% vs 71.6%, p<0.001). Patients with history of percutaneous coronary intervention, coronary artery bypass surgery or documented myocardial infarction were significantly less likely to have functional tests prior to coronary angiography (79/224, 35.3%) than patients with no such history (258/578, 44.6%, p=0.016). Only 288 of the 491 patients (58.6%) referred for assessment of chest pain not associated with either non-ST elevation or ST elevation myocardial infarction had functional tests prior to angiography. One hundred and nine patients (13.6%) underwent exercise electrocardiography, 41 patients (5.1%) underwent exercise echocardiography, 57 (7.1%) underwent exercise nuclear perfusion scan and 130 patients (16.2%) underwent vasodilator stress nuclear perfusion scan. Table 4 shows the results of functional tests in these 337 patients.

	Positive functional test (n)	Negative functional test (n)	Total (n)
Adequate stress level (For exercise stress, n)*	81 (74)	23 (20)	104 (94)
Inadequate stress level* (For exercise stress, n)	65 (58)	38 (33)	103 (91)
Vasodilator stress (n)	108 (83)	22 (20)	130 (103)
Total (n)	254 (215)	83 (73)	337 (288)

Table 4. Results for functional tests in the 337 patients (The numbers in parentheses are the number of patients with assessment of chest pain as indications for coronary angiography in each category). (Reproduced with permission from: Leung DY, Hallani H, Lo ST, Hopkins AP, Juergens CP. How compliant are we with guidelines for coronary angiography in clinical practice? Internal Medicine Journal 2007, Oct;37(10):699-704. John Wiley and Sons)

3.2.4 Coronary angiography results

The coronary arteries were angiographically normal in 152 patients (19%) and showed only minor disease in another 111 patients (13.8%). One hundred and sixty six patients (20.7%) had single vessel disease, 145 (18.1%) had double vessel disease and 228 (28.4%) had triple vessel disease. Of the 89 patients who had previous coronary artery bypass surgery, 40 patients (45%) had no significant graft disease. The overall rate of angiography showing either normal or minor diseases was 37.7%. The overall complication rate of coronary angiography was low. There were 51 cases of access site haematoma (6.4%), one case for each of pseudo-aneurysm, arterio-venous fistula, neurologic deficit, significant arrhythmia and contrast allergy. No deaths as a result of the angiography were recorded.

3.2.5 Compliance with guidelines

Referrals for coronary angiography were considered outside the guidelines for coronary angiography in 34.3% and 36.2% as evaluated by the 2 independent assessors. The concordance rate between the 2 independent assessors was 88.2% (kappa 0.74, p<0.001). The concordance rate between the 2 independent evaluations by the same assessor was 97.5% (kappa 0.945, p<0.001).

Coronary angiography showed normal coronary arteries or only minor coronary disease in a significantly higher proportion of patients when the referrals were outside published guidelines compared with referrals within the guidelines (181 of the 264 referrals, 68.4% versus 121 of the 538 referrals, 22.6%, p<0.001).

There were no significant differences in complications of coronary angiography between the group where referrals were within guidelines (6.7%) and the group where referrals were outside guidelines (7.2%, p = 0.79).

Table 5 shows the compliance rate for each of the indications of coronary angiography. The compliance rates were high with indications of non-ST elevation and ST elevation myocardial infarction, valvular heart disease and arrhythmias. However, the compliance rates were lower with indications of assessment of dyspnoea or heart failure and prior to non-cardiac surgery and were particularly low with assessment of chest pain (n = 491, mean age 61.3 ± 11 years, 300 men). Two hundred and ninety five of these 491 patients (60%) were day-only patients. Only 288 of these 491 (58.7%) had functional tests and only 254 (51.7%) had assessment of left ventricular function prior to coronary angiography.

Indication	Non-compliant with guidelines n(%)	Compliant with guidelines n(%)	Total (n)
Assessment of Chest pain	230 (46.8%)	261 (53.2%)	491
Non-ST elevation myocardial infarction	1 (0.8%)	126 (99.2%)	127
ST elevation myocardial infarction	3 (4.2%)	69 (95.8%)	72
Dyspnea/heart failure	18 (25.7%)	52 (74.3%)	70
Valvular disease	4 (20%)	16 (80%)	20
Prior to non cardiac surgery	3 (27.3%)	8 (72.7%)	11
Arrhythmia	1 (20%)	4 (80%)	5
Others	4 (66.7%)	2 (33.3%)	6
Total	264 (32.9%)	538 (67.1%)	802

Table 5. The compliance rates for coronary angiography to the American College of Cardiology/American Heart Association guidelines according to the indications for angiography. (Reproduced with permission from: Leung DY, Hallani H, Lo ST, Hopkins AP, Juergens CP. How compliant are we with guidelines for coronary angiography in clinical practice? Internal Medicine Journal 2007, Oct;37(10):699-704. John Wiley and Sons)

Concentrating on referrals from cardiologists (n=683), referrals from non-invasive cardiologists were significantly more likely to be outside published guidelines compared

with referrals from invasive cardiologists (141 of the 341 referrals, 41.3% versus 103 of the 342 referrals, 30.1%, p = 0.002). Multivariate logistic regression analysis identified younger age (OR 1.04 for every year younger, 95% CI 1.029 – 1.048, p<0.001), female gender (OR 2.67, 95% CI 2.24 – 3.19, p<0.001), day-only procedure (OR 2.27, 95% CI 1.91 – 2.69, p<0.001) and non-invasive cardiologist referrer (OR 1.41, 95% CI 1.19 – 1.67, p = 0.046) to be independent predictors of non-compliance with published guidelines.

When patients with raised cardiac Troponin T (n = 197) were excluded from the multivariate analysis, day-only procedure was no longer a significant independent predictor of non-compliance. Younger age (OR 1.04 for every year younger, 95% CI 1.03 – 1.05, p<0.001), female gender (OR 2.24, 95% CI 1.87 – 2.69, p<0.001) and non-invasive cardiologist referrer (OR 1.47, 95% CI 1.29 – 1.67, p = 0.004) remained independent predictors of non-compliance with guidelines.

3.3 Discussion

In our large consecutive series of patients referred for coronary angiography, we found that more than a third of the referrals were outside the American College of Cardiology/American Heart Association guidelines for coronary angiography. The inter-observer and intra-observer agreement in assessing compliance were high. The rate of coronary angiography showing either normal coronary arteries or only minor diseases was significantly higher when the referrals were outside guidelines. The compliance rate was particularly low with indications of assessment of chest pain. Younger age, female gender, day-only procedure and non-invasive cardiologist referrals were independent predictors of non-compliance with the guidelines.

Practice guidelines have proliferated in clinical medicine in the past 2 decades in all major fields. The compilation and publication of these practice guidelines represent efforts by professional bodies to incorporate an ever-expanding evidence based medicine into best clinical practice. A systemic review suggested significant improvement of care after introduction of clinical guidelines although the size of the improvement varied considerably (GrimshawRussell, 1993). The dissemination and implementation of these guidelines have emerged as major challenges. Furthermore, awareness of these guidelines does not necessarily equate to compliance. Therefore, the full potential for these guidelines to improve health care delivery and clinical outcomes has yet to be completely realized.

A number of studies have found significant gaps between clinical practice and guidelines in a number of areas (Brand et al., 1995; Leape et al., 2003; Vikman et al., 2003). In a study of antithrombotic therapy in atrial fibrillation, a report found that only 47% of the eligible patients received warfarin according to published guidelines and 4 patients had a stroke during a 12-month follow-up period (Nair et al., 2005). These 4 patients were not on warfarin despite recommendations by the guidelines. In a random audit of Medicare data in 5 US states showed that 30% of percutaneous coronary angioplasties was rated as Class III indications according to the 1988 American College of Cardiology/American Heart Association guidelines whereas 24% were class III by use of the 1993 guidelines (Leape et al., 2003). Similar gaps were found between clinical practice and the European Society of Cardiology guidelines for the management of non-ST elevation myocardial infarction (Vikman et al., 2003) and only about 50% of patients post myocardial infarction received beta blockers as recommended by the guidelines (Brand et al., 1995).

Adherence to guidelines has been suggested to lead to an improved clinical outcome. A clear relationship was found between extent of guideline implementation and one-year mortality in patients with acute myocardial infarction (Schiele et al., 2005). Compliance remained an independent predictor of survival even after adjustment for clinical risk. Similarly, compliance with the guidelines significantly improved prognosis in acute coronary syndrome regardless of risk score (Gulati et al., 2004) and resulted in an improved outcome in high risk patients with non ST elevation myocardial infarction (Vikman et al., 2004). In evaluating the impact of compliance with guidelines for coronary angiography, patient outcome such as survival may not be appropriate. Nevertheless, we were able to demonstrate that the rate of coronary angiography showing either normal coronary arteries or only minor diseases was significantly lower when the referrals were within the guidelines. Rates of normal coronary angiography may be a reasonable surrogate for measuring the impact of compliance as a high negative rate has significant implications due to inappropriate costs, superfluous resource utilisation and unnecessary risks for the patient.

Little is known about the barriers to compliance with guidelines by physicians. Potential barriers may include awareness, familiarity, disagreement with the guidelines, resistance to change, and absence of disincentives or penalties for not adhering to recommendations on the part of the physicians (Cabana et al., 1999). In addition to physician factors, our study also identified clinical parameters and scenarios that were predictive of non-compliance with the guidelines. Younger age and female gender were found to be predictors. One may postulate that physicians may be more aggressive in recommending coronary angiography outside guidelines in younger patients as they do not want to "miss" significant coronary disease in such patients. The compulsion for a "definitive" diagnosis and fear of litigation in an increasing medico-legal environment may also have contributed. Day-only procedure as a predictor of non-compliance may be explained by the fact that patients with acute coronary syndrome with raised cardiac Troponin T levels almost always underwent angiography as inpatients. This is supported by the fact that day-only procedure was not an independent predictor when patients with elevated Troponin levels were excluded from the multivariate analysis. In our study, non-invasive cardiologists were more likely to refer outside the guidelines for coronary angiography. This may be because non-invasive cardiologists are potentially less familiar with the guidelines. Furthermore, in the present study, clinical scenarios of assessment of chest pain in patients with suspected or known coronary artery disease appeared to be areas where the non-compliance rate was particularly high. These may be areas in which physicians have the most difficulties adhering to the recommendations of the guidelines.

Only a small proportion of patients, especially for inpatients, had functional tests prior to coronary angiography. Functional tests, which play an important role in the risk stratification of patients with suspected or confirmed coronary artery disease as depicted in the published guidelines, were performed in a relatively small proportion of the patients in our study. Our previous study on a different patient population also found a low rate of utilisation of functional tests. Referrer characteristics and inpatient status, rather than pre-test probability of coronary disease, appeared to have the greatest impact on utilisation of functional tests (Leung et al., 2005). Non-utilisation of functional tests

prior to coronary angiography was a common reason for "inappropriate" referral for coronary angiography, as established by previous studies (Chassin et al., 1987b; Gray et al., 1990).

Our study represents the experiences of a single tertiary referral hospital, and hence may not be representative of other centres around the world. However, we feel that our study population was representative as our institution is the only cardiac catheterisation laboratory in a public hospital tertiary referral centre serving a population of about 800,000. The aim of the present study was to evaluate compliance with the American College of Cardiology and American Heart Association guidelines for coronary angiography and not to judge whether the referrals were appropriate. Referral outside guidelines may be entirely appropriate depending on the patient's specific clinical situation. These guidelines for coronary angiography were published in 1999. As the evidence base has been evolving and improving, these guidelines may not reflect contemporary practice. Although the rate of angiography showing either normal coronary arteries or minor disease was significantly higher when the referrals were outside published guidelines, which can have significant cost-effective implications, our results do not allow us to perform cost-effectiveness analysis.

4. Conclusions

Coronary angiography is one of the most commonly performed cardiac procedures. It continues to play an important role in the management of cardiac patients and is indispensible in patients considered for coronary revascularisation. It is an invasive procedure not without significant risks and, together with its inherent costs, should not be carried out or repeated without sufficient justification. Functional tests, including stress ECG, stress echo, nuclear perfusion imaging and magnetic resonance imaging are all accepted functional tests that provide important diagnostic and prognostic information and should form part of the body of investigations in patients suspected to be suffering from coronary artery disease. More recently, CT coronary angiography is being used as a "ruling out" test and is considered an appropriate indication in certain subsets of patients with chest pain. Improvement in the use of these functional tests may lead to better risk stratification so that low risk patients may be spared the risks and costs of invasive coronary angiography and higher risk patients can have their angiography expedited. We identified that the use of functional tests, especially in low to intermediate risk patients, was suboptimal and have identified certain problematic areas where their use was very low. The ACC and AHA have published guidelines on coronary angiography. Although the guidelines were published in 1999, it is still a useful document applicable to clinical practice today. There is ample evidence to suggest, in multiple areas of cardiology, that adherence to guidelines was associated with improved patient outcomes. In our study, we found that the adherence to the guidelines on coronary angiography was only modest in certain indications and non-adherence led to a higher rate of normal coronary angiography. Attention should be paid to these problem areas to identify the underlying reasons for non-compliance so that efforts can be made by both individual physicians and professional bodies to improve the rate of compliance so that the full potential of these guidelines can be realised.

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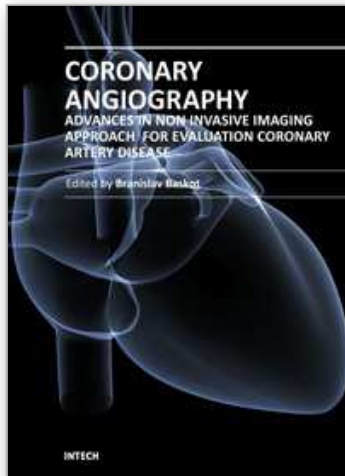
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