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Assessment of the radial artery access site and its use in invasive cardiac procedures

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This thesis is dedicated to my mother and father for

their unconditional love and support.

TABLE OF CONTENTS

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Finally, my utmost thanks and gratitude go to my wife, Amy and my children, Megan, Lucy and Finn. It would not have been possible to finish writing the thesis without their selfless love, support, encouragement and smiles. I hope I have made you proud.

ABSTRACT

Vascular access via the radial artery has recently been shown to reduce access site related vascular complications but is associated with a significant learning curve. Radial artery spasm, arterial puncture failure, vascular anomalies, failure to reach the ascending aorta and concern regarding higher radiation exposure with the transradial are some obstacles that impede widespread uptake of this technique.

This study was performed to assess some of these learning curve issues and to explore the use of transradial access in high-risk patient subgroups. Six interlinked projects were setup for this study and a total of 3125 patients evaluated.

Access site vascular complications remain unacceptably high in contemporary practice as discussed in **Chapter 2**. The transradial approach could minimise such complications.

Radial artery anomalies are relatively common and are a common cause of transradial procedure failure as detailed in **Chapter 3**. Forearm arterial diameter variations and the effect of sublingual GTN were discussed in **Chapter 4**. The radial artery is bigger than the ulnar artery and GTN increases their diameters by an average of 15-22%. The issues with radiation exposure were studied as detailed in **Chapter 5**. With strict control of various variables and optimal radiation protection, we demonstrated that there is no difference in radiation exposure between transradial and transfemoral diagnostic angiography when performed by an experienced operator.

The application of transradial technique in 2 high-risk patient subgroups was analysed as detailed in **Chapter 6.** Transradial rescue angioplasty for failed reperfusion and percutaneous right and left heart catheterisation via the arm approach without interruption to Warfarin therapy are found to be safe and effective.

These findings have important clinical implication and may help shorten the learning curve and optimise procedure technique including high-risk patient subgroups, thereby help to further drive the adoption of transradial approach.

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CHAPTER 1

INTRODUCTION

1.1 HISTORICAL PERSPECTIVE OF INVASIVE CARDIAC PROCEDURES

"There are three stages in the history of every medical discovery. When it is first announced, people say that it is not true. Then, a little later, when its truth has been borne in on them, so that it can no longer be denied, they say it is not important. After that, if its importance becomes sufficiently obvious, they say that anyhow it is not new." (1)

-Sir James Mackenzie, 1853-1925

Amongst the greatest achievements in cardiovascular medicine in the past century has been the introduction, development and refinement of the invasive diagnostic and therapeutic modalities of cardiac catheterisation and related catheter-based interventions. The development of coronary angiography and angioplasty have revolutionised the diagnosis and management of cardiovascular disease in almost every way. The history of these techniques that have evolved over the last century is an exciting, instructive testament to the scientific spirit and method. Cournand, Richards and Forssmann, the three pioneers in cardiac catheterisation were awarded the Nobel Prize for Medicine or Physiology in 1956 (2).

Cardiac catheterisation

The early years

The history of diagnostic and therapeutic catheterisation of hollow organ systems is ancient. The Egyptians are known to have performed bladder catheterisation in 3000 B.C. using bronze, silver and gold pipes (3). Around the time of Hippocrates (400 B.C.), air and water were pushed through hollow reeds or brass pipes into cadaver

aortas in an attempt to understand the function of the cardiac valves (4). Harvey catheterised the inferior vena cava of a cadaver in 1651 and proved that venous blood flowed toward the lungs not toward the periphery, contrary to prevailing opinion (4). The first intravenous injection into a living subject was performed in 1665 by Wren when he injected into a dog. Major became the first to deliver an injection into a human in 1667 (5). Lower, later used the first vascular catheter (silver pipes connected by a quill) to transfuse blood from the carotid artery of a sheep to the jugular vein of a human in the same year (5).

The earliest known case of cardiac catheterisations of a living animal was performed by Stephen Hales in 1711, by inserting brass pipes through the venous and arterial systems into the ventricles of a horse via the jugular vein and the carotid artery (6) [Figure 1]. Variations on the technique were performed over the subsequent century, with formal study of the cardiac physiology of a dog by Claude Bernard in 1847 (7). Fick published his formula for calculating cardiac output using oximetric measurements in 1870 (8), which was validated by Grehant and Quinquaud in 1886 using experimental right-heart and arterial catheterisation (9).

The discovery of x-rays by Roentgen on November 8, 1895 played a pivotal in the subsequent developments in invasive cardiology (10). This led to production of fluoroscopic images of a beating heart by Williams (10), and the first cadaver's brachial arteriogram by Haschek and Lindenthal, both in 1896 (11). Baumgarten in 1899 performed the first coronary arteriograms on animal cadaver hearts (12).

Figure 1. First documented cardiac catheterisation, right and left heart study performed by Hales (left) in 1711. (From the Bettmann Archieves.)
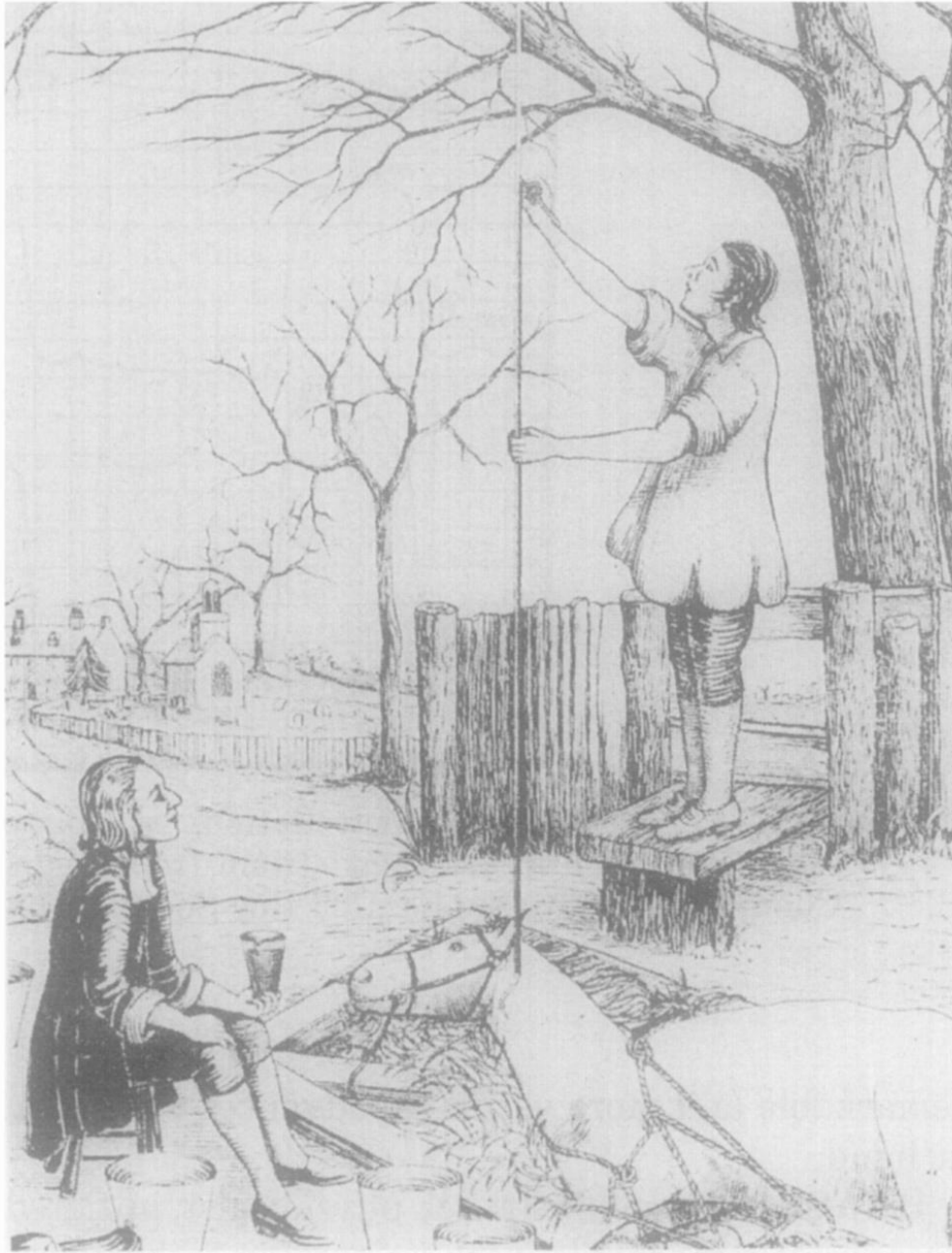
Cardiac catheterisation of humans

"The cardiac catheter was the key in the lock"

-Andre Cournand, 1895-1988

Right heart catheterisation

The first human heart catheterization was performed in July 1929 when Werner Forssman inserted a ureteric catheter into his own right atrium via a cut down of his left ante-cubital vein (13). He documented the position of the catheter in his right atrium with a chest roentgenogram (Figure 2).

Figure 2. First documented human catheterisation investigating central delivery of drugs for cardiac arrest as 25-year-old surgical resident, Forssmann passed urethral catheter via left basilica vein cutdown into right atrium and then took this roentgenogram. (From Forssmann W. Klin Wochenschr 1929;8:2085-7)
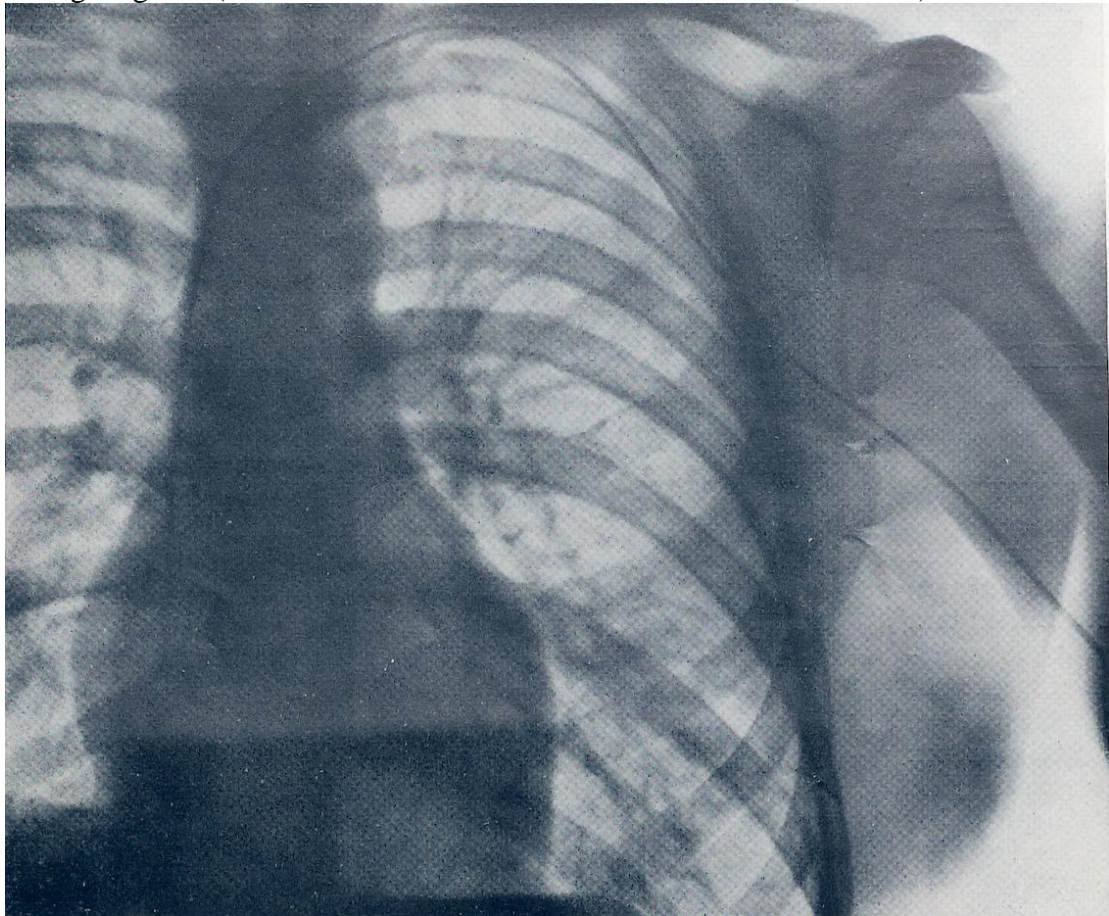
Although Forssmann's pioneering work was recognised as important from the start, he was nonetheless ridiculed and vilified as a "dangerous quack" by the medical community. He had been told by his superiors that "such methods are good for a circus, but not for a respected hospital" and that his "ideas were too crazy to give him a clinical position" (14). Finally discouraged by cardiac work, Forssmann turned to urology in 1931, served as a German army surgeon during World War II, and then as a country doctor after the war in a small town. Although he never engaged in cardiac research after 1931 or even held any cardiology faculty appointments, he was awarded a Nobel Prize in 1956, along with fellow catheterisation pioneers Cournand and Richards. Resisting the expectation of him to return to cardiology research, Forssmann concluded, "The subject has progressed too far in the interim, and when I considered it objectively I was certain I'd never catch up..... I decided it was more honest to content myself with the role of 'leading fossil'" (15). Forssmann died of a myocardial infarction in 1979 without ever having returned to work in cardiology (16).

Following Forssmann's daring self-catheterisation, catheters were placed in a similar manner into the right ventricle by other pioneers over the next few years, and measurements of pressure and cardiac output (using the Fick principle) were performed. Cournand and Richards first began their classic studies of right-heart physiology in 1936. They catheterised the right ventricle in 1942 and the pulmonary artery in 1944 (7), and published a series of papers on simultaneous right-heart pressure measurements and oximetry-based studies of cardiac output. Cournand and Richards shared the Noble Prize in Physiology or Medicine in 1956 with Forssmann

for their work in the discovery of cardiac catheterisation and haemodynamic measurements.

By the end of 1940s, right-heart catheterisation and its use in pressure recording, oximetry and angiography had become so advanced that the technique is little different today, except for the balloon-tipped catheters and advances in catheter materials.

Left heart catheterisation

Although early pioneers performed retrograde left-heart catheterisation in animals, the application of the technique to human followed numerous crude, daring and risky methods by advancing catheters into the left ventricle or left atrium by direct antegrade routes. The retrograde route was only applied much later.

Reboul and Racine performed the first percutaneous ventricular needle puncture of both ventricles in dogs for the injection of contrast in 1933 (17). Rousthoi performed experimental retrograde left-heart catheterisation in animals in the same year using needle puncture of the aorta for access, but never performed left ventriculography (18). Nuvoli duplicated the approach for the first time in a human in 1936, with fatal results (19). This direct aortic puncture technique later became the main method for aortic catheterisation although direct ventricular puncture technique persisted into the 1950s, especially for patients with aortic stenosis. Farinas performed the first retrograde aortography in 1941 via femoral artery cutdown access (20). Direct needle access of the aorta was gradually abandoned in favour of retrograde catheterisation utilising the brachial, radial (21), ulnar (22) or femoral arteries, first by cutdown and

later by percutaneous access. In 1953, Seldinger invented a technique for the percutaneous replacement of an access needle with catheters over the wires (23), which became widely applied for virtually all catheterisation techniques within the next decade, due to its simplicity and safety.

Selective coronary angiography

Nonselective opacification of the coronary arteries in patients undergoing ascending aortogram has been reported as early as in 1933 (18). Numerous ingenious yet cumbersome and ineffective methods for enhancing coronary opacification through the use of ascending aortic injections were devised. Such brute-force methods were however, clearly inadequate and hazardous.

Mason Sones initiated the next revolution in invasive cardiology when he performed the first selective coronary angiography in 1958, by accident (24). After performing a left ventriculogram in a patient with valvular disease, Sones pulled the catheter back for an aortogram. He did not, however, verify the catheter position before proceeding and was horrified to find the catheter accidentally intubated the right coronary ostium during cine-angiography. Before he could pull the catheter out, 40 ml of contrast was injected directly into the right coronary artery. The patient went into asystole and Sones managed to resuscitate him via coughing, which converted the rhythm to sinus bradycardia (25). Sones soon developed the new technique of selective coronary angiography with specially formed catheters, by using brachial artery cutdown access. Diagnostic-grade coronary angiograms were now possible, opening the way to accurate diagnosis of coronary artery disease, laying the groundwork for future revascularisation therapy.

Although Ricketts and Abrams introduced new preformed polyethylene coronary catheters and a percutaneous femoral artery approach in 1962 (26), Sones technique remained the standard until 1967 when Judkins (27) and Amplatz (28) separately reported a more practical and advanced group of preformed catheters for percutaneous use via femoral artery access. The arrival of Judkins and Amplatz catheters revolutionised and facilitated an explosive growth in percutaneous catheterisation via the femoral artery access, and fostered the critical transition from diagnostic catheterisation to therapeutic intervention by catheter methods.

Percutaneous coronary angioplasty

Figure 3. First percutaneous transluminal angioplasty, performed by Dotter in 1964 on left popliteal artery of an 82-year-old woman with gangrene who had refused amputation. Before (left), after (middle) and 2 years later (right). Patient's leg was salvaged. (From Dotter CT. Radiology 1980;135:561-4.)
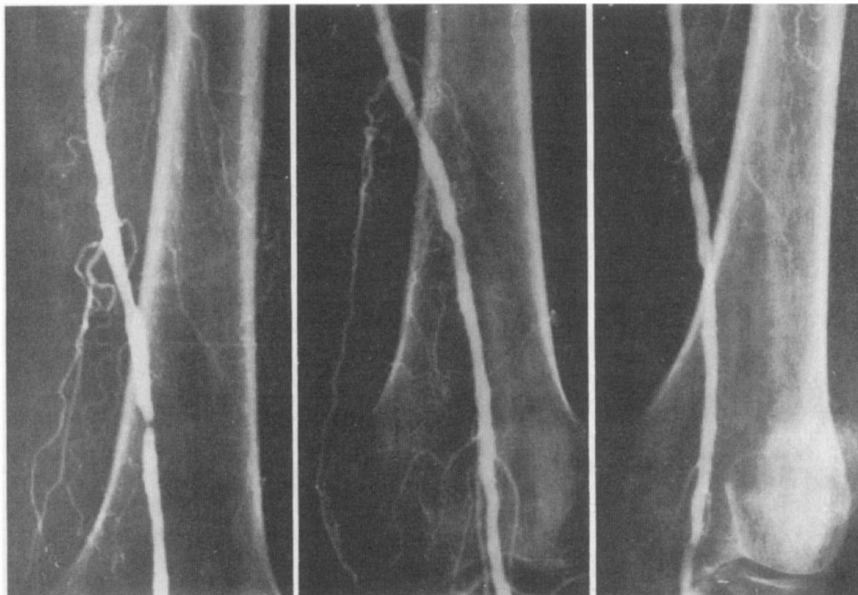
As is so frequently the case with important discoveries, the innovation of angioplasty was serendipitous. Such unexpected discovery, however, was immediately apparent to the operators. Opportunity thus favoured the prepared mind. In 1963, Dotter inadvertently recanalised an occluded right iliac artery by passing a percutaneous catheter retrogradely through the occlusion to perform an abdominal aortogram (29). The dawn of interventional era began. Dotter and Judkins went on to perform the first intentional transluminal angioplasty on an 82 year-old lady in 1964 (30), successfully curing her gangrenous left foot caused by popliteal artery stenosis (Figure 3).

Building on Dotter and Judkins' work and his own research involving balloon-tipped catheters, Andreas Gruentzig used his double-lumen balloon catheter with success in experimental and human peripheral angioplasty (31). By 1976, Gruentzig had miniaturised his double-lumen system for use in the coronary arteries (32). After successful animal studies followed by cadaver studies, he presented his experimental results at the American Heart Association in November 1976 which were met with scepticism and derision (33). Undeterred, Gruentzig went on to perform the first coronary angioplasty in an awake human in Zurich, on September 16, 1977 (34). The patient was a 37-year-old insurance salesperson (same age as Gruentzig at the time) with a focal proximal left anterior artery stenosis. The patient consented to angioplasty even after being informed that he would be the first person so treated. Gruentzig later published a report on his first five cases in a letter to the editor of Lancet in February 1978 (35). Of note, the insurance salesperson underwent surveillance cardiac catheterisation 1 month and 10 years after the initial procedure despite the lack of recurrent symptoms; there was no restenosis (Figure 4). Recognition of Gruentzig's triumph was immediate and widespread. Unlike in 1964

and 1976, the medical community was ready to embrace percutaneous revascularisation, and the era of percutaneous coronary intervention (PCI) began.

Figure 4. First percutaneous transluminal coronary angioplasty (PTCA) in a conscious patient. *Left*, right anterior oblique view of left anterior descending artery before PTCA on September 16, 1977. *Right*, same view of same patient's artery 10 years later on September 16, 1987 demonstrating persistent patency of dilated segment. (From Douglas JS et al. in Hurst JW. The heart. 7th ed. New York:McGraw-Hill, 1990)

Pre PTCA   10yr Post PTCA
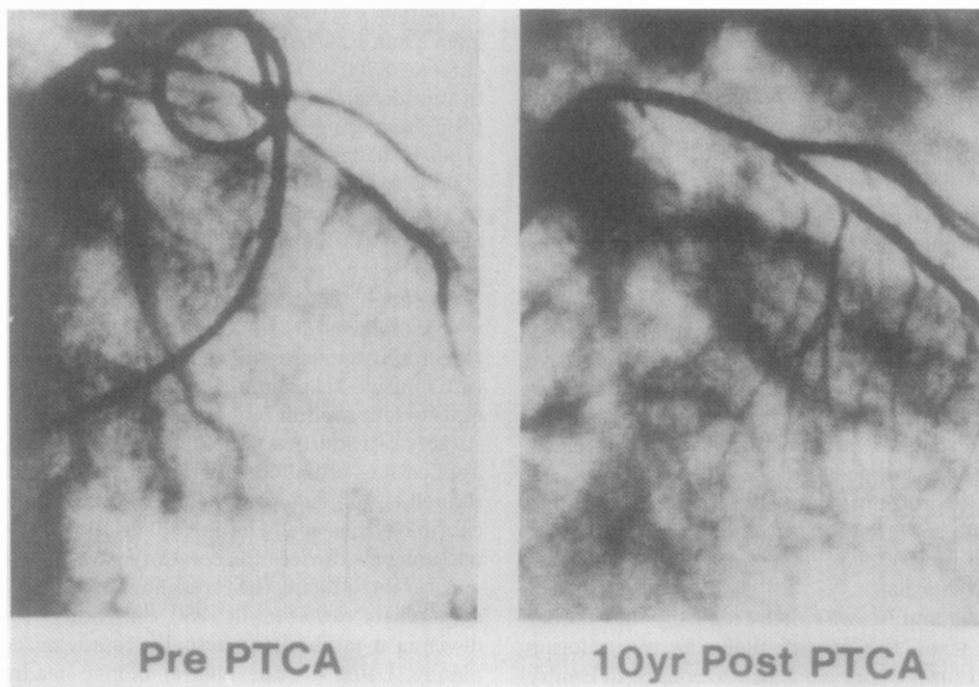
The unrelenting progress in interventional cardiology over the last thirty years has been breathtaking, with no sign of slowing down. From plain-old-balloon angioplasty to bare metal stenting and more recently to the drug eluting stent; from 9 French to 5 French equipment; from single vessel to multi-vessel angioplasty and from angioplasty in stable patient to primary angioplasty for acute myocardial infarction. Not to mention the ever evolving new adjunct devices and new pharmacological agents to aid improve the results and outcomes of percutaneous coronary angioplasty.

Transradial catheterisation

Transradial access appeared early in the development of cardiac catheterisation techniques with the first description of transradial central arterial catheterisation and attempts at coronary artery imaging using radial artery cutdown and 8 to 10 French catheters published by Radner in 1948 (21). Limitations of contemporary equipment resulted in the shift to larger vessels such as brachial and femoral arteries for most catheter based procedures. The radial artery has, however, been safely employed for many years for haemodynamic monitoring (36, 37). It is an attractive access site for cardiac procedures because of its favourable neurovascular anatomy. It has a superficial course of the wrist which facilitates percutaneous puncture, and overlies the forearm bones facilitating compression haemostasis. No major nerves or veins lie close to the radial artery, limiting the risk of neurological damage or arterio-venous fistula formation. The forearm and hand have a dual blood supply, with the ulnar artery limiting the risk of ischaemic complications if radial artery occlusion occurs as a consequence of the procedure. These advantages are offset by the relatively small calibre of the radial artery, which precluded its routine use for cardiac procedures when only large calibre catheterisation equipment was available between the late 1950's and mid 1980's.

In the late 1980's and early 1990's, advances in materials science and engineering technology facilitated the miniaturisation of catheterisation equipment, which was compatible with introduction into the relatively small calibre radial artery. These developments coincided with an explosive rise in the rate of femoral complications associated with the introduction of coronary stents and the use of multiple potent antiplatelet and anticoagulant agents. These two factors led cardiologists to evaluate

the use of the radial artery as an access site for diagnostic and therapeutic cardiac procedures.

In the pursuit of minimising procedure related vascular complications, Lucien Campeau started exploring the feasibility of radial access coronary angiography using 5 French catheters in October 1986. His first 30 patients were men with an apparent large radial artery, an easily palpable ulnar artery and a normal Allen's test. This was followed by 70 consecutive patients of both genders with a normal Allen's test, and reported the first series of diagnostic cardiac catheterisations performed via the radial artery in 1989 (38), reporting an overall success rate of 88%. Significant complications occurred in 2% (2 cases) comprising artery dissection and radial artery occlusion, both without symptoms of ischaemia of the hand.

The radial approach for diagnostic coronary angiography was soon adopted by Otaki in Osaka, Japan, who reported his case series of 40 patients, in whom the femoral approach was difficult or contraindicated (39). Procedure failure occurred in 1 patient (3%) and there were no major complications.

Kiemeneij and Laarmann reported the first transradial coronary interventional series in 1993 (40, 41), and are credited for popularising the transradial technique. Despite the observed reduction in peri-procedural bleeding and reported improvements in patient comfort, the transradial approach was only utilised by a few early adopters mainly in Asia and parts of Europe, and remained a niche technique for the next decade.

As experience with the transradial approach grew over the next decade, it was repeatedly demonstrated that the transradial approach has minimal severe vascular complications but with similar procedural success when compared to the transfemoral approach. A learning curve for developing proficiency in transradial procedures (42) as well as cost effectiveness (43-45) was noted in small observational studies. A series of randomised trials have compared radial and femoral access, with a recent meta-analysis confirming that the radial approach reduces access site complications and is therefore safer (46).

The first large scale transradial interventional programme in the UK was established at the University Hospital of North Staffordshire in 1998 (47). It also provided the unique opportunity of a transradial interventional fellowship programme at Onze Lieve Vrouwe Gasthuis, Amsterdam, under the guidance of Kiemeneij and Laarmann. Coupled with the development of transradial programmes in other centres in the UK, the radial approach has grown from under 1% to over 50% of all percutaneous coronary interventions (48).

1.2 OVERVIEW OF ACCESS SITE ISSUES

The arterial access site chosen for percutaneous cardiac procedures can have an important influence on procedural costs and procedural related morbidity and mortality. Access site complications can cause major disability and death. With the exponential rise in cardiac catheterisations and the use of multiple potent antiplatelet agents as standard practice during percutaneous coronary intervention, containing access site complications is an important clinical challenge. This section provides a brief overview of the access site issues related to the technically challenging brachial

cut-down approach, the preferred percutaneous Seldinger femoral approach and the transradial approach.

Comparison of arterial access sites complications

Brachial artery access route

When a surgical cut down approach to the brachial artery is employed for cardiac procedures, operator skill and experience are important factors in limiting the rate of complications associated with this technically demanding approach. Skilled high volume operators can achieve low complication rates even in the setting of intensive antithrombotic therapy (49). For less skilled or infrequent operators, most series consistently reported a 5-10% incidence of major complications (50-54) (Figure 5). Major neurovascular complications resulting in acute arm ischaemia or median nerve palsy occur in around 5% of patients (Figure 6). An alternative method to this approach employs a percutaneous Seldinger technique to position a sheath in the brachial artery. This technique is technically much simpler than a surgical cut down, but is associated with a similar risk of important neurovascular complications (55). Because of these issues brachial access is now rarely employed.

Figure 5. Neurovascular complications after brachial artery cut-down procedures.
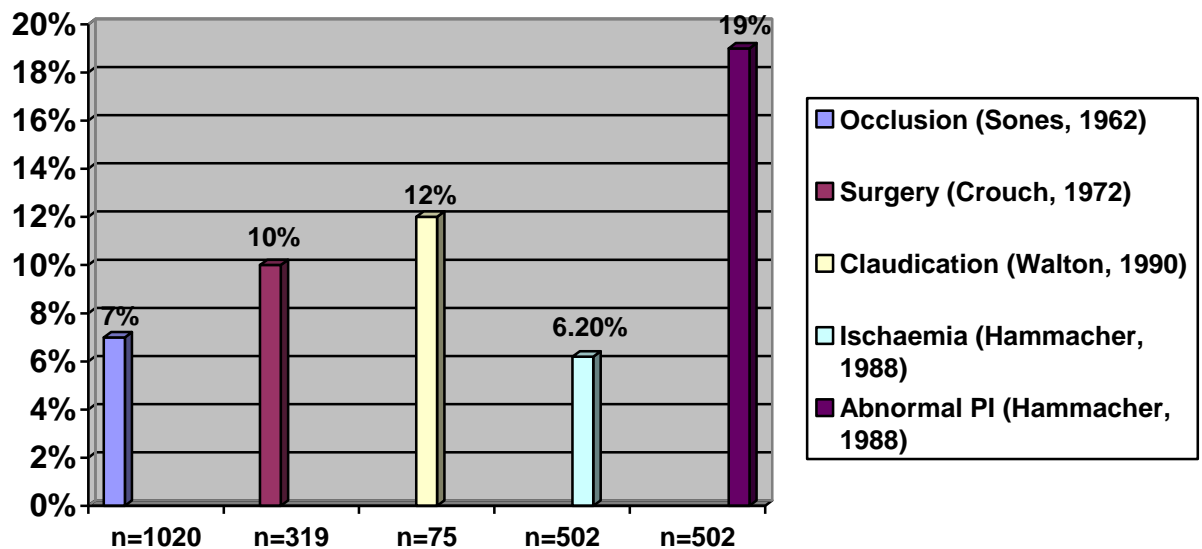
Figure 6. Median nerve palsy following coronary angiography via the brachial artery.

Femoral artery access route

Percutaneous femoral approach catheterisation revolutionised the practice of invasive cardiology following the introduction of the Seldinnger technique and remains the access of choice in many institutions (56). The femoral approach facilitates rapid and

simple access to the left side of the heart and usually facilitates good catheter support as well as access to large-diameter devices. Such advantages are partially offset by bleeding complications, often mandating prolonged bed rest and further treatment (including compression or thrombin injection for a pseudoaneurysm, blood transfusion or surgical intervention) (Figure 7 & 8). These can lead to further discomfort and a longer hospital stay, consuming additional institutional resources. In a minority of patients femoral vascular complications can be severe and lead to death. The incidence of significant neurovascular complications ranges from 1% following a simple diagnostic procedure to 17% when large bore catheters are employed in association with aggressive antithrombotic therapy in PCI (Figure 9) (57-61). One-third of patients who sustain an iatrogenic femoral nerve injury related to a cardiac procedure have a permanent neurological deficit (62). Concealed retroperitoneal bleeding, although uncommon, is an ominous complication that has a reported mortality rate of 15% (63).

Figure 7. Large femoral haematoma post femoral cardiac catheterisation.
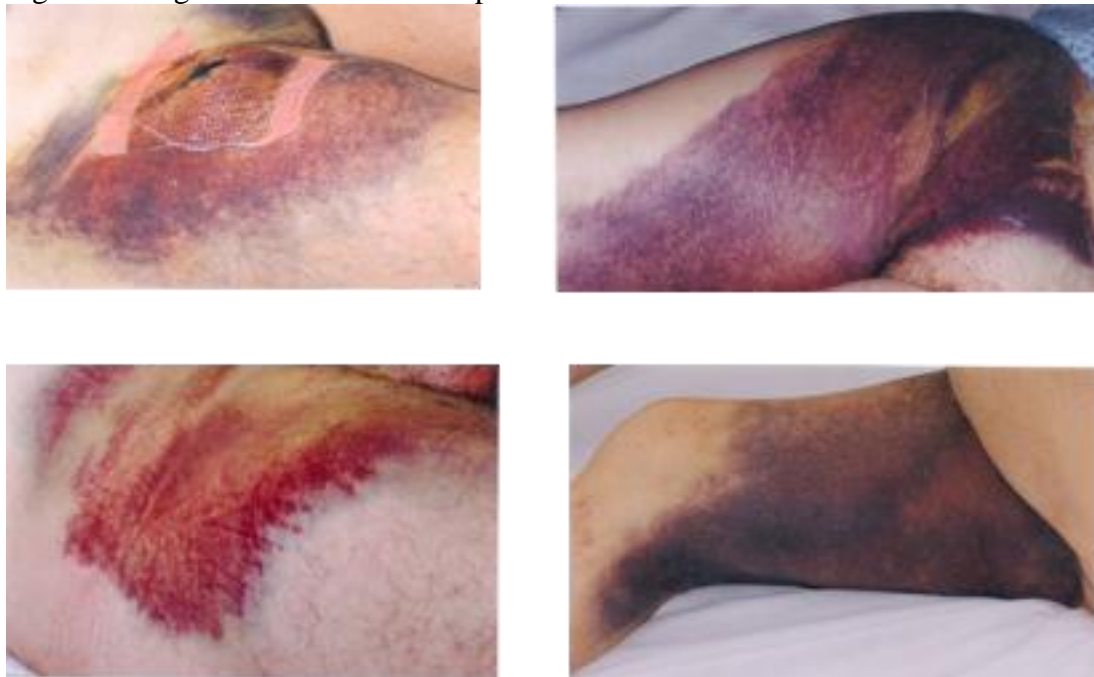
Figure 8. Pseudoaneurysm post femoral access cardiac catheterization.

Figure 9. Femoral access site complications in current practice.
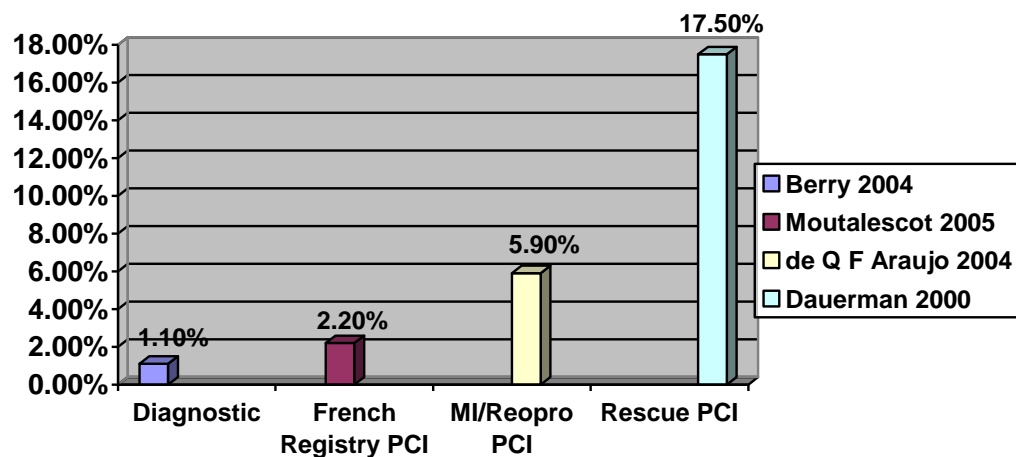
Indeed there may be a relationship between major bleeding after PCI and increased risk of long term mortality, as reported in subgroup analysis of many trials and registries (64-67). Kuchulakanti et al retrospectively analysed 10669 patients treated by PCI over a seven year period and reported an incidence of vascular complications post PCI of 10.3% (66). Their main finding was that patients with vascular complications post PCI had a significantly higher incidence of in-hospital complications including death, myocardial infarction and coronary artery bypass grafting compared to patients without vascular complications. They also had

significantly higher incidence of non-Q wave myocardial infarction and mortality at 1 year. Reduction of vascular access site complications is therefore a critical challenge in PCI procedures.

A meta-analysis of 10 observational studies involving 133,597 patients with acute coronary syndromes confirmed that major bleeding is a strong predictor of in-hospital and 30-day death and acute myocardial infarction (68). Bleeding was associated with 7-fold and 3-fold increase in 30-day death and myocardial infarction respectively. Rao et al also demonstrated that patients with acute coronary syndromes who developed anaemia during hospital admission and required transfusion had a more than 3-fold increase in the risk of death and myocardial infarction at 30-day (69).

The MORTAL study retrospectively examined the association between access site, transfusion, and outcomes in over 32,000 patients who underwent PCI in British Columbia, Canada from 1999 to 2005 (67). The main finding showed that vascular access site complications was significantly reduced with the use of the radial access site, which was associated with a 50% reduction in transfusion rate and a relative reduction in 30-day and 1-year mortality of 29% and 17%, respectively (P<0.001).

Although all these studies were observational, they nonetheless convey important messages for practicing interventional cardiologists suggesting that access site complications, major bleeding and transfusion are prognostic predictors of patient's outcome. Reduction of such complications is therefore a critical challenge.

Numerous vascular closure devices have been developed in recent years to obtain an efficient arteriotomy closure immediately at the end of the procedure. Evidence based data supporting the use of these vascular closure devices are disappointing and meta-analysis of 30 randomised trials (with a total sample size in excess of 40000 patients) concluded that vascular closure device is only marginally more effective than standard manual compression in the setting of diagnostic CA, and may increase the risk of haematoma and pseudoaneurysm in the setting of PCI (70, 71). In addition to these complications, access via a brachial or femoral access site is impossible in 5–10% of patients, due to anatomical variation, peripheral vascular disease or obesity, and the radial access site may allow such patients to be investigated and treated.

Radial artery access route

Multiple studies have compared the radial approach with femoral or brachial access. The best known study, the Access Trial (72) examined the relative merits of the percutaneous brachial, femoral and radial access sites in 900 patients undergoing elective PCI. It demonstrates that the radial approach is the safest, with no significant vascular complications occurring, compared to rates of 2% in the femoral group and 2.3% in the brachial group. There was no increase in total procedure duration or radiation exposure when transradial procedures were compared with percutaneous femoral procedures. A meta-analysis of 12 randomized control trials by Agostoni et al (which includes the Access Trial) further confirmed that the transradial approach is a highly safe technique with comparable procedural duration, radiation exposure and clinical results to that of the transfemoral approach (46). More importantly, vascular access site complications are virtually abolished (0.3%) by the transradial approach.

Given the demonstrated reduction in the risk of vascular complications, the radial artery is a particularly attractive option in the setting of anticoagulation, post thrombolysis or aggressive antiplatelet therapy. Hildick-Smith et al reported low rate of radial access complications in fully anticoagulated patients with INR > 2 who had transradial coronary angiography (73). In a comparison of vascular access site complications in patients undergoing PCI with adjunctive intravenous GP IIbIIIa inhibitor therapy, 7.4% of the transfemoral patients had a major vascular access site complication (despite the use of weight adjusted heparin, small calibre guiding catheters and femoral artery closure devices in the majority of these patients), compared to none of the similarly treated radial patients (74). In the setting of rescue PCI with adjunct GP IIbIIIa inhibitor, the reported rate of major femoral vascular complications ranges from 20-39% (75-78) and around 10% even if vascular closure devices are employed (79). Emerging data assessing the efficacy of transradial PCI in such setting have all reported near complete elimination of vascular complications and with comparable procedural success rate as the transfemoral approach (80).

Other related issues

Patient comfort and preference are also important considerations in the comparison of these access sites. Delayed mobilisation after transfemoral procedures is common, due to inguinal pain, while bed rest itself has been shown to have an adverse effect on outcome (81, 82). Patients undergoing elective transradial PCI can be mobilised immediately after the completion of these procedures with no adverse effects or risks, which allows PCI to be performed on a day case basis (83, 84). Coronary angiography via the radial artery as opposed to the femoral artery is associated with short-term improvements in quality of life, whilst at the same time reducing hospital costs (44,

85). The radial approach for intervention was preferred by 73% of patients in whom preceding diagnostic films were acquired by the femoral route (86). As a result of the shorter hospital stay and reduced complication rates associated with transradial procedures, hospital costs of coronary stent deployment can be reduced by 15% when compared with the femoral route (44).

Although the transradial technique fulfills the requirements for a safer access site for interventional procedures with the added advantages of cost savings and improved quality of life, the transfemoral approach remains the preferred technique for most cardiologists. This is to a large extent due to the significant learning curve associated with the transradial technique (which ranges from radial artery puncture failure, radial artery spasm to catheter manipulation difficulties especially in relation to upper limb arterial anatomical variations), even for experienced femoral operators, as well as concerns regarding higher radiation exposure to both the operators and the patients. There is also a general misconception that with improvement in technology and equipment used, femoral access site vascular complications have become infrequent.

1.3 AIM OF THE THESIS

The aim of this thesis is to evaluate upper limb arterial anatomy and function, procedural technique and clinical applications of the transradial access site in relation to invasive cardiac procedures.

HYPOTHESES TO BE TESTED

1. There is a reduction in vascular complications in transradial compared to transfemoral cardiac procedures.

2. Radial artery anatomical variation influences the outcome of transradial cardiac procedure and complications.

3. Radial artery diameter vary in relation to age, sex, height, hand dominance, smoking, the presence of certain disease subgroups (hypertension, chronic renal failure, diabetes mellitus and peripheral vascular disease) and Glyceryl Trinitrate.

4. There is no difference in radiation exposure in transradial and transfemoral coronary angiography when performed by experienced radial and femoral operators respectively.

5. Radial access can be applied to high risk patient subsets with minimal vascular complications.

PLANS

This research study is subdivided into six projects:-

Project 1 – Vascular complications study.

Project 2 – Radial artery anatomical variation study.

Project 3 – Study of radial artery diameter and the effect of GTN on radial artery.

Project 4 – Comparison of radiation exposure in transradial and transfemoral diagnostic coronary angiography

Project 5 – Transradial rescue percutaneous coronary intervention.

Project 6 – Percutaneous left and right heart catheterisation in fully anticoagulated patients using the arm approach.

The following chapters discuss the theoretical background to the methods used to evaluate the above objectives. There then follow sequential chapters detailing and discussing studies investigating vascular complications, radial artery anatomy and function, procedural technique and clinical applications of the transradial access site in relation to invasive cardiac procedures, followed by final chapter summarising the results and discussing implications and future directions.

Overall, such in-depth information may help shorten the learning curve and optimise transradial procedure technique with improve outcome, and thereby help drive the adoption of transradial approach. It should also help to extend the use of the radial access site into high-risk patient subgroups.

CHAPTER 2

ACCESS SITE COMPLICATIONS

2.1 INTRODUCTION

Femoral arterial puncture is the most common method of vascular access for coronary angiography (CA) and percutaneous coronary intervention (PCI). Peri-procedural bleeding complications as a result of PCI are common and occur in up to 5% of cases performed in patients presenting with acute coronary syndromes (ACS). A substantial proportion of the bleeding occurs at the vascular access site (87-91). Such complications are not insignificant as findings from observational studies indicate that major bleeding is associated with an increased risk of recurrent ischaemic events and death (92, 93). Indeed, a femoral haematoma requiring transfusion is an independent predictor of 1-year mortality (94).

Strategies to reduce bleeding include improved puncture technique, more individual tailored and monitored anticoagulant and antiplatelet treatments and alternative arterial access. Vascular access via the radial artery, a superficial and easily compressible artery, has been shown to reduce risk of access site bleeding and other vascular complications in meta-analysis of randomised trials (46, 95). Transradial access is, however, a technically more demanding technique and coupled with a natural resistance to change, this has made the use of this approach still a minority worldwide. Furthermore, there is also a general misconception that with improvement in technology and equipment used, femoral access site vascular complications have become less frequent although anecdotal experience suggests that many of these complications may be under-reported (58).

This primary aim of this study was to investigate the rate and extent of vascular complications between the transradial and transfemoral routes in patients undergoing

CA and PCI, in 'contemporary real world' practice. The secondary aim was to assess the impact on length of in-patient stay as a result of these complications and the efficacy between the Radi-Stop® and the TR Band™ transradial compression devices.

2.2 METHODS

Study Subjects

All patients undergoing elective, urgent or emergency cardiac catheterisations in the Cardiology Department of University of North Staffordshire were prospectively studied over a 3-month period from 8th January to 7th April 2007. One thousand and fourteen consecutive patients were recruited over this period. Patients were admitted to the cardiac catheter laboratory per indications and the procedures performed as per standard protocol. The choice of arterial access was selected as per operator skill and preference.

Data collection

A 2-side study sheet was attached to the patient's admission note (Attachment 1) and was prospectively completed by clinical staff members during a 3-month period. Patient demographics, procedure details, post procedural haemostasis care, any vascular complications and patient outcome were collected.

Access site haemostasis was assessed by trained nursing staff and any vascular complications recorded on the data sheet. These were later verified by research team. A haematoma was defined as any swelling around the arterial puncture site and was categorised as being >5cm or < 5cm. Bleeding events were classified according to the Global Utilisation of Streptokinase and Tissue Plasminogen Activator for Occluded

Coronary Arteries criteria (96). Severe bleeding is defined as a substantial haemodynamic compromise, moderate bleeding by the need of transfusion and minor bleeding as neither requiring transfusion nor resulting in haemodynamic instability.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics 19.0 (IBM Corp., Armonk, New York, USA). The distribution of continuous data was determined using the 1-sample Kolmogorov-Smirnov test. Categorical data were presented as absolute values and percentages whereas continuous data were presented as mean ± standard deviation. Student's t test and Mann-Whitney U test were used to compare continuous data as appropriate. Categorical data were compared using the Chi-Square test with the appropriate degree of freedom. A p value of less than 0.05 was considered to be statistically significant.

2.3 RESULTS

Patients and procedural characteristics

A total of 1014 patients were studied, comprising 405 patients from the transradial group and 609 patients from the transfemoral group, with a mean age of 62.3±10.9 and 62.5±11.0 respectively (Table 1). Just over 50% of the transradial group of patients had the procedures done electively compared to 63% of the transfemoral group. Fifty-five and sixty-one per cent of the transradial and the transfemoral groups underwent PCI respectively. Procedures were done using 5 French and 6 French systems apart from 6 patients (1%) from the femoral group where 7 French systems were used.

Table 1. Patient and procedural characteristics. -overall

	RA (n=405)	FA (n=609)	P value
Age	62.3±10.9	62.5±11.0	NS
Male (%)	73	64	NS
BMI	28.7±6.1	28.2±5.0	NS
Diabetes (%)	15%	11%	NS
Renal Impairment (%)	5%	7%	NS
Peripheral vascular disease (%)	4%	5%	NS
Drugs (%)			
Aspirin	81.0 %	85.1 %	NS
Clopidogrel	29.9 %	31.0%	NS
Unfractionated Heparin	100	55.0%	<0.0001
Glycoprotein IIbIIa inhibitor	21.0%	19.9%	NS
Thrombolytic agent	1.2%	1.0%	NS
Warfarin	5.2%	0%	<0.005
5F:6F:7F (%)	30:70:0	1:97:2	N/A
Angio (%)	39	45	NS
PCI (%)	28	25	NS
Adhoc PCI (%)	33	30	NS
Procedure duration (mins)	41.7±25.5	37.8±27.6	0.03
Elective:Urgent:Emergency (%)	53:39:8	63:31:6	N/A
Vascular complications, n(%)	36 (8.9)	98 (16.1)	0.002
Small haematoma, n(%)	24 (5.9)	61 (10.0)	0.029
Large haematoma, n(%)	5 (1.2)	24 (3.9)	0.014
Others minor complications	7 (1.7)	13 (2.1%)	0.161
Transfusion, n (%)	0	1	0.576
Vascular intervention	0	1	0.576
Total additional LOS[*] (days)	5 (1-3)	63 (1-9)	0.006
Average additional LOS[*] (days)	1.67	2.4	NS
Angioseal	0	39 (6.4%)	N/A
Angioseal related vascular complications	0	3 (7.7%)	N/A

* LOS = length of stay

Seven patients (4.5%) had an unsuccessful radial procedure as a result of failed puncture (2 patients), radial artery spasm (4 patients) and radial artery dissection (1 patient). These patients had their procedure completed using the femoral route. There was no access site cross over from the femoral group.

Procedure duration was statistically longer with the transradial procedures than the transfemoral procedures. However the time used to remove the femoral sheath and the time to ambulation was not taken into consideration, as this would significantly increase the overall transfemoral procedure duration.

Access site and vascular complications

Ninety-eight vascular complications (16.1%) were observed in all transfemoral procedure compared to 36 (8.9%) in the transradial group, p=0.002 (Table 2). Of these, 61 (10.0%) were small femoral haematoma and 24 (3.9%) large femoral haematoma. Although diagnostic angiography performed via the transfemoral approach did not appear to be associated with statistically significant small haematoma compared to transradial approach, the risk of large femoral haematoma remains unacceptably high (Table 3). Transfemoral PCI, especially if performed in the context of acute coronary syndrome or unstable patients was associated with significantly higher risk of vascular complications (Table 4). Use of vascular closure device was also associated with a relatively high rate of vascular complications.

No deaths occurred during the study period. There was one moderate femoral bleeding post PCI for unstable angina requiring 2 units of transfusion. One large femoral haematoma required thrombin injection as it did not respond to prolonged external compression. Overall, an additional 63 days were spent in the hospital as a result of femoral access site complications compared to 5 additional days for radial access site complications, p=0.006.

Table 2. Vascular complications and access site selection.

	RA (N=405)	FA (n=609)	P value
Small haematoma, n (%)	38 (5.9%)	61 (10.0%)	0.029
Large haematoma, n (%)	5 (1.2%)	24 (3.9%)	0.14
Other minor complications	7 (1.7%)	13 (2.1%)	0.161
Overall complications	36 (8.9%)	98 (16.1%)	0.002
Transfusion	0	1 (0.7%)	0.576
Vascular intervention	0	1 (0.7%)	0.576

Table 3. Characteristics of patients who underwent diagnostic angiography.

	RA (n=157)	FA (n=272)	P value
Age	63.2±11.2	61.7±11.3	NS
Male (%)	69	62	<0.05
BMI	29.1±6.4	28.4±5.1	NS
Diabetes (%)	17	10	NS
5F:6F:7F (%)			N/A
Elective:Urgent: (%)	78:22	87:13	N/A
Single: Multiple Puncture (%)	89:11	95:5	
Access site cross over (%)	7 (4.5%)	0	0.001
Vascular complications, n(%)	13 (8.2)	34 (12.5)	0.016
Small haematoma, n(%)	10 (6.4)	19 (7.0)	0.195
Large haematoma, n(%)	2 (1.3)	11 (4.1)	0.005
Others	1 (0.6)	4 (1.5%)	0.529
Procedure duration (mins)	42.6±24.6	37.2±29.3	0.03
Total additional LOS[*] (days)	1	25	<0.0001
Average additional LOS[*] (days)	1	2.2	NS
Angioseal	0	11 (4.1%)	N/A
Angioseal related vascular complications	0	1 (9.1%)	N/A

* LOS = length of stay

Table 4. Characteristics of patients that underwent PCI.

	RA (n=248)	FA (n=337)	P value
Age	61.8±10.7	63.1±10.8	NS
Male (%)	75	66	<0.05
BMI	28.5±5.8	28.1±4.9	NS
Diabetes (%)	15	11	NS
5F:6F:7F (%)	20:80:0	1:98:1	N/A
Elective:Urgent:Emergency (%)	53:39:8	63:31:6	N/A
Single:Multiple puncture	91:9	90:10	NS
Access site cross over	0	0	N/A
Vascular complications, n(%)	23 (9.3)	64 (19.0)	<0.0001
Small haematoma, n(%)	15 (6.1)	44 (13.1)	0.002
Large haematoma, n(%)	3 (1.2)	13 (3.9)	0.03
Others	5 (2.0)	7 (2.1%)	0.743
Procedure duration (mins)	41.1±26.1	38.3±26.1	0.035
Total additional LOS* (days)	4 (1-3)	38 (1-9)	<0.0001
Average additional LOS* (days)	2	2.6	NS
Angioseal	0	28 (8.3%)	N/A
Angioseal Vasc Comp	0	2 (7.1%)	N/A

* LOS = length of stay

Radial access and vascular complications

Just fewer than 40% of all procedures were done via the transradial approach during the study period. The compression devices used during the study period were Radi-Stop® (Figure 10) and the TR Band™ 9figure 11) and these were analysed separately to assess the efficacy of the devices (Table 5). The ratio of usage of Radi-Stop® to the TR Band™was 1.9:1. There were more male patients in the Radi-Stop® group than the TR Band™ group. The TR band appeared to be associated with a higher rate of minor vascular complications including small haematoma but there was no difference in the rate of large haematoma.

Table 5. Patient characteristics for Radi-Stop® Vs TR Band™

	RADI (n=266)	TR Band (n=139)	P value
Age	61.1±10.9	64.7±10.7	NS
Male (%)	84	52	0.005
BMI	29.3±6.1	27.5±5.8	NS
Diabetes (%)	16	14	NS
5F:6F (%)	24:76	42:58	N/A
Elective:Urgent:Emergency (%)	58:36:6	45:45:10	N/A
Vascular complications, n(%)	14 (5.3)	22 (15.8)	0.0001
Small haematoma , n (%)	11 (4.2)	13 (9.3)	0.003
Large haematoma, n (%)	2 (0.8)	3 (2.1)	0.079
Others, n (%)	3 (1.1)	4 (2.9)	NS
Angio (%)	38	42	NS
PCI (%)	62	58	NS
Procedure duration (mins)	43.4±26.1	41.3±24.1	NS
Total additional LOS* (days)	2	3	NS

* LOS = length of stay

Figure 10. Radi-Stop®

Figure 11. TR Band™

TR Band™

2.4 DISCUSSION

Numerous studies have previously demonstrated that access site bleeding complications are high for both transfemoral CA and PCI (97-101). In addition, patients who had a femoral procedure also experienced more groin pain, longer periods of bed rest and hospital stay. Other studies compared complication rates after

CA or PCI performed with either transfemoral or transradial access and concluded that radial access is safer with significantly lower risk of vascular complications (44, 47, 102).

Access site bleeding complications remain the commonest non-cardiac complication following a percutaneous cardiac procedure (103, 104). Our study confirms that access site vascular complications via the femoral artery remain unacceptably high at 16.1%. Although neither death nor severe bleeding occurred in this study period, such complications could lead to prolongation of hospital admissions.

Indeed, the observed additional 63 days spent in hospital as a result of vascular complications in our study are a financial burden to the healthcare system. The cost could rise even more considerably in the event of a fatal or severe bleeding episode, which have also been shown to be an independent predictor of mortality, reinfarction and stroke (69, 91, 92, 105). Our data indicate that a substantial amount of hospital expenditure through prolonged admission and related cost may arise because of these complications.

Overall incidence of radial vascular complications in our study was relatively high at 8.9%. This was driven by small haematoma and other minor vascular complications. The incidence of large haematoma complication was low at 1.2%. An additional 5 days was spent in hospital as a result of radial access site complications thereby giving a net 58 days saved compared to femoral access site related vascular complications.

An unexpected finding was that the TR Band was associated with a higher rate of small haematoma formation than the RadiStop. This was likely related to the fact that the TR band does not immobilise the wrist. It does, however, have the advantage of allowing for accurate gradual deflation of compression on the wrist. Both types of devices are designed to have unilateral compression of the radial artery, hence avoiding venous congestion of the forearm, reducing the potential risk of an upper arm deep vein thrombosis (106). There are newer dedicated radial compression devices that are now available in the market which may further improve the efficacy of radial access site haemostatic management.

In summary, transfemoral access site bleeding complications remain unacceptably high in contemporary practice. Transradial access can reduce such risk, especially access site related major bleeding complications, resulting in better patient outcome and much lower additional length of stay in hospital. The transradial access should therefore be the access site of choice.

Attachment 1

Assessment of Vascular Complications   UHNS 2007

A. Patient Details
Name:_____   Hospital No: _____   Age: _____

Sex: F ☐   M ☐   Ht: _____   Wt: _____   BMI: _____

Date of Admission: _____   Date of discharge: _____

Medications:
Aspirin   ☐   Unfractionated Heparin   ☐
Clopidogrel   ☐   GP IIb/IIIa inhibitor   ☐
LMWH   ☐   Thrombolytic agent   ☐
Warfarin/other anticoagulant   ☐   INR: _____

B. Procedure Details
Date of Procedure: _____   Operator: _____

Indications:
Diagnostic☐   Stable angina☐   ACS☐   TnT +ive ACS☐   STEMI☐
Failed reperfusion☐   Valvular disease☐   PFO/ASD☐   HF aetiology☐
Others: _____

Case: Elective   ☐   Urgent   ☐   Emergency ☐

Types of Procedure: LHC   ☐   PCI   ☐   LHC+RHC ☐
                              Ad hoc PCI ☐   Rescue PCI ☐   IABP   ☐
                              Others: _____

Routes of Procedure: RFA☐   LFA☐   RRA☐   LRA☐

Numbers of Puncture: Single ☐   Multiple ☐

Sheath: 5F☐   6F☐   7F☐

Use of intra-procedure anticoagulant:
Heparin: 2500U☐   5000U☐   7500U☐   10000U☐
GP IIb/IIIa inhibitor   ☐

C. Post Procedure Care

ACT: _____

Methods of Haemostasis:

Manual pressure	☐	Angioseal	☐	Fem Stop	☐
Radi-Stop	☐	TR Band	☐	Radial D-Stat	☐

Areas in which post procedure care is provided:

Recovery area in Lab	☐	Ward 76	☐
MAU	☐	Others	☐

D. Vascular Complications

Complication: Yes ☐   No ☐

If yes, types of complication:

Vagal episode	☐	Haematoma < 5cm	☐
Haematoma > 5cm	☐	Pseudoaneurysm	☐
AV fistula	☐	Retroperitoneal bleed	☐
Groin pain	☐	Wrist pain	☐
Minor bleeding	☐	Major bleeding	☐
Severe bleeding	☐	Limb ischaemia	☐

Others: _____

Onset of haematoma:

Catheter laboratory	☐	Before sheath removal	☐
During sheath removal	☐	After sheath removal	☐
Unknown	☐		

Intervention required for complications:

Out patient Observation	☐	In patient Observation	☐
Ultrasound Scan	☐	CT Scan	☐
Transfusion	☐	Radiologist intervention	☐
Surgical review	☐	Vascular surgery	☐

Additional length of stay:
Number of days: _____

CHAPTER 3

RADIAL ARTERY ANATOMICAL VARIATION AND ITS INFLUENCE

ON TRANSRADIAL CORONARY PROCEDURAL OUTCOME

3.1 INTRODUCTION

Since its initial description as a safe and feasible access route for cardiac catheterisation(38, 40) the radial artery has been increasingly used for percutaneous coronary procedures. The main advantage over the femoral artery is a reduced risk of vascular complications, particularly in the presence of multiple antiplatelet and antithrombotic agents (46, 72-74, 80, 107, 108). This is attributed to the favourable neurovascular anatomy of the radial artery where it runs superficially, separated from major nerves. Immediate ambulation and facilitation of day case intervention also favour the radial approach (44, 83-85). The transradial technique is, however, associated with a significant learning curve even for experienced femoral operators (42, 109-111). Anecdotal evidence suggests that once the learning curve is passed, most transradial procedure failures are due to anatomical variations but there are currently limited data on such information (112). We therefore undertook to establish the frequency of radial artery anomalies from radius to the radio-brachial anastomosis and their relation to procedure outcome in patients undergoing a first transradial coronary procedure.

3.2 METHODS

Study population

This was a multicentre prospective study involving four tertiary centres in the UK: - University Hospital of North Staffordshire [UHNS], Brighton and Sussex University Hospital [BSUH], Freeman Hospital and Newcastle University [FHNU] and Manchester Heart Centre [MHC]. A total of 1540 patients undergoing their first transradial coronary procedure were recruited from January 2006 to June 2007. Four hundred and fifty five patients were recruited from UHNS, six hundred and thirty four

patients from BSHU, three hundred and fifty five patients from FHNU and ninety six patients from MHC. Only patients undergoing diagnostic angiography and coronary intervention were studied. Procedures were performed or supervised by experienced high volume radial operators (personal experience of >1000 cases). Patients with a previous transradial procedure were excluded.

Radial artery cannulation

Radial artery puncture was performed with a dedicated radial cannulation needle and guidewire according to operator preference. A short hydrophilic sheath (11cm) was inserted and an arterial vasodilator (containing 200-400μg isosorbide dinitrate and 2.5-5.0mg of verapamil) given according to local protocols. Heparin (2,500–5,000 iu.) was given either as part of the vasodilator cocktail or in the aortic root.

Retrograde radial arteriography

Retrograde radial arteriography was performed following administration of the arterial vasodilator to define radial artery anatomy from mid-radius to radio-brachial anastomosis. A solution of 3mls of contrast mixed with 7mls of blood (to dilute the contrast and minimise any discomfort from contrast injection) was injected briskly through the side arm of the sheath with radiographic acquisition at the elbow in an anteroposterior projection. If a high-bifurcating radial origin was identified, a further arteriogram was obtained higher up the arm to identify the point of anastomosis to the brachial artery.

Transradial coronary procedures

Retrograde radial arteriography was performed prior to coronary intubation in all patients. In patients who had a failed transradial puncture, it was at the discretion of the operator to attempt the contralateral radial artery or use the transfemoral approach. The arterial sheath was removed immediately after completion of the transradial procedure and haemostasis achieved using a unilateral radial compression system (RADI-Stop®, RADI Medical Systems, Uppsala, Sweden or TR Band™, Terumo Medical Corporation, Tokyo, Japan).

Classifications and Definitions

Forearm arterial patterns with clinical relevance to transradial cardiac catheterisation were classified using a modification of McCormack's, Uglietta's and Rodriguez-Niedenfuhr's definitions [Table 6] (113-115).

Table 6. **Modified classifications of forearm arterial patterns**

1. Normal anatomy
2. High-bifurcating radial origin, rejoins at
   a. Lower third of humerus
   b. Middle third of humerus
   c. Upper third of humerus
   d. Axillary
3. Radial loop with recurrent radial artery
4. Extreme radial artery tortuousity
5. Others

The site of anomalous origin was determined with reference to the intercondylar line of the humerus, which is a fixed line representing the proximal border of the antecubital fossa. Bifurcation of the brachial artery proximal to this line is considered a variant pattern. A high-bifurcating origin was further sub-classified into lower third of humerus, middle third of humerus, upper third of humerus or axillary according to the site of anastomosis with the main vessel. High-bifurcating radial artery calibre was also categorised as <2.0mm, 2.0-2.5mm, 2.5-3.0mm and >3.0mm by visual comparison with the arterial sheath.

A radial artery loop was defined as the presence of a full 360º loop of the radial artery distal to the bifurcation of the brachial artery. Extreme radial tortuosity was defined as the presence of a bend of more than 90º in the contour of the vessel. Anatomical variations that did not fit into these specified categories were grouped together and categorised as "other" anomalies.

Procedural duration was defined as time interval elapsed from when the patient entered to when they left the catheterisation laboratory. Procedural success was defined as completion of the planned procedure via the initially selected radial access route. Minor vascular complications were defined as haematoma <5cm, vessel dissection without ensuing ischaemia, pseudoaneurysm and localised infection. Major vascular complications were defined as haematoma >5cm, any access site complications that required surgical or radiological intervention, >3gm/dl haemoglobin drop due to access site bleeding, bleeding requiring transfusion, limb ischaemia and/or compartment syndrome.

Data collection

Patient demographics, procedural data, and radial arteriography findings with specific details of any anomalies and local vascular complications were collected on a specifically written data management database (PATS Dendrite).

Statistical analysis

Statistical analysis was performed using SPSS 19.0 (IBM Corp., Armonk, New York, USA). Categorical data were presented as absolute values and percentages whereas continuous data were presented as mean ± standard deviation. The nature of distribution of the data was determined using 1-sample Kolmogorov-Smirnov test. Student's t test and Mann-Whitney U test were used to compare continuous data as appropriate. Categorical data were compared using the Chi-Square test with the appropriate degree of freedom. Both univariate and multivariate regression analysis were used to examine potential correlation between radial artery anomaly and variables such as sex, age, hypertension, diabetes and peripheral vascular disease. A p value of less than 0.05 was considered to be statistically significant.

3.3 RESULTS

Patients and procedural characteristics

A total of 1540 patients were studied with mean age 63.6±11.1 years and 70.6% male. Baseline patient and procedural data are summarised on Table 7. Diagnostic coronary angiography was performed in 32.8%. Most procedures were attempted via the right radial artery and over 50% of procedures were performed using 5F sheaths and catheters. Transradial procedural success was 96.8% with 2.9% of patients requiring

femoral access for procedure completion. Procedures were abandoned in 0.3% (5 cases).

Table 7. Baseline clinical and procedural characteristics

Clinical characteristics	No. of patients (n=1540)	%
Age in years (range)	63.6±11.1 (24-90)	
Male : Female	1088 : 452	70.6 : 29.4
Any of the following risk factors	1003	65.1
Hypertension	662	43.0
Diabetes	345	22.4
Peripheral vascular disease	135	8.8
Previous cardiac surgery	68	4.4
Types of procedure		
Diagnostic angiography	505	32.8
Ad hoc PCI	590	38.3
Elective PCI	445	28.9
Procedural characteristics		
Access attempted		
Right radial : Left radial	1432 : 108	93 : 7
RA puncture failure	7	0.5
Procedural success	1490	96.8%
Sheath gauge 5F : 6F : 7F	780 : 739 : 21	50.6 : 48.0 : 1.4
Procedure duration (min)		
Diagnostic angiography	30.3±15.21	NA
Ad hoc PCI	48.4±21.4	NA
Elective PCI	47.4±22.2	NA
Fluoroscopy time (min)		
Diagnostic angiography	6.0±5.3	NA
Ad hoc PCI	11.1±7.5	NA
Elective PCI	11.8±8.6	NA
Vascular complications		
Minor	13	0.9
Major	2	0.1

Data in number, mean±SD and percentage.
PCI: percutaneous coronary intervention

Radial artery anatomy and procedural outcome

There were 7 cases (0.5%) of radial puncture failure. Retrograde radial arteriography was obtained in 1533 patients. Anomalies were noted in 212 (13.8%) and these patients were significantly older (mean age 67.1 years versus 64, p<0.001) more

commonly female (36% versus 28%, p=0.02) with significantly higher procedure

failure rates (14.2% versus 0.9%, p<0.0001) [Figure 12]. Although procedure duration

and fluoroscopy time were longer in patients with anomalies, these were not

statistically significant.

Figure 12. Comparison of patient and procedural data in patients with normal radial anatomy and radial anomalies.
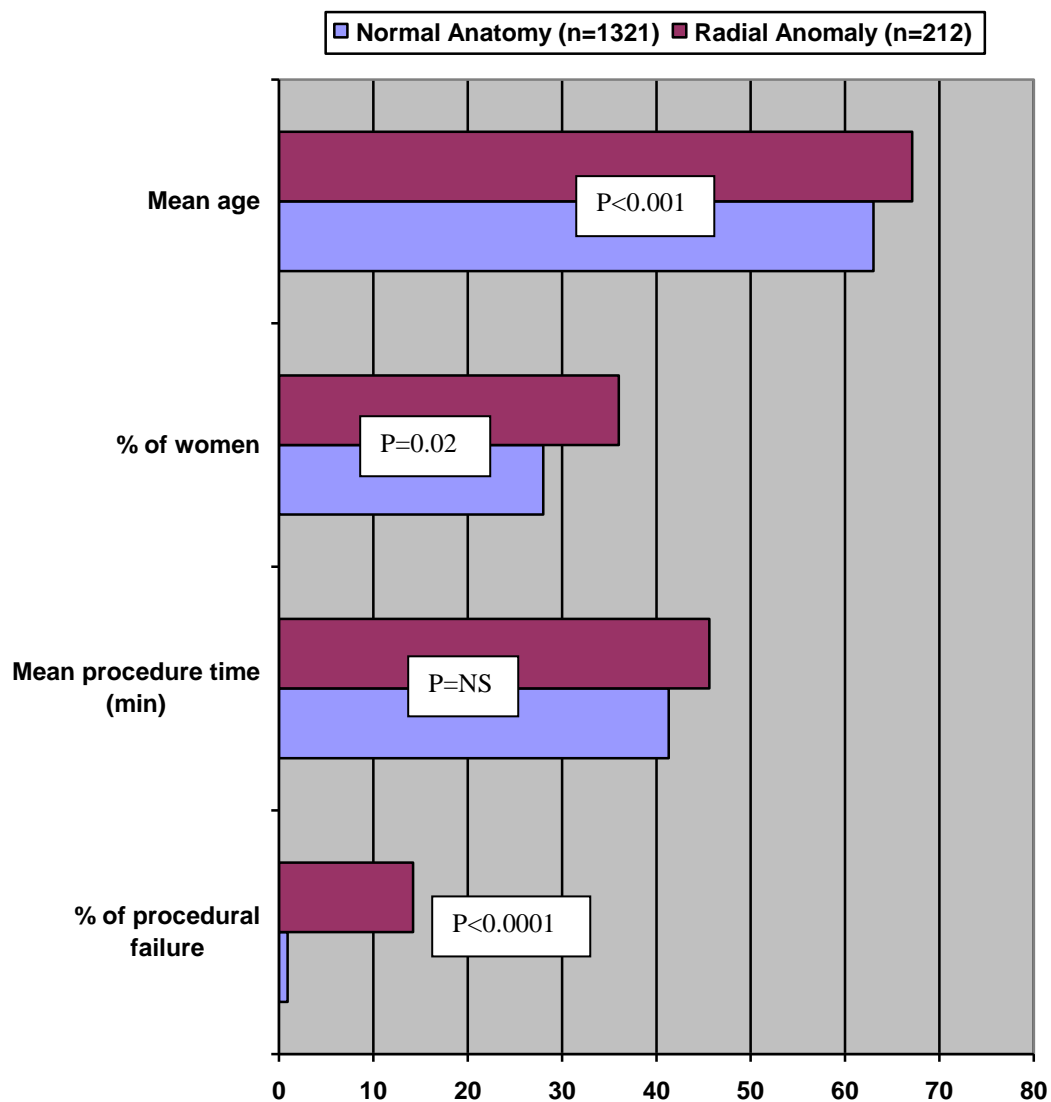
Normal radial artery anatomy

Normal radial artery anatomy (Figure 13) was present in 1321 patients (86.2%). Transradial failure rate was low in patients with normal radial anatomy, with 12 failures out of 1321 patients (0.9%). Procedure failures were due to profound radial artery spasm (5 patients, 0.4%), severe brachial artery stenosis (1 patient, <0.1%), tortuous subclavian artery (4 patients, 0.3%), radial artery dissection (1 patient, <0.1%) and dissection of axillary artery (1 patient, <0.1%).

Radial anomalies

A summary of anomaly types and associated failure rates is shown in Figure 14. Table 8 compares patient characteristics and procedural data for different radial anatomical patterns. Patients with radial artery loops were significantly older than patients with normal anatomy or high bifurcation while extreme radial tortuosity was seen in the oldest group. Age was the only independent predictor related to presence of radial artery anomaly.

High-bifurcating radial origin

This was the most frequent radial anomaly (Figure 15) observed in 108 patients with a frequency of 7.0%. The majority of these vessels rejoined the brachial artery at the level of mid or upper humerus and were of small calibre with over 85% being < 3mm in diameter (Figure 16). Importantly, although a high-bifurcating radial artery was not associated with a high incidence of transradial failure (5 of 108 patients; 4.6%), many of these anomalous vessels were of small calibre and frequently required use of 5F catheters with hydrophilic wires to complete the procedure without inducing spasm.

Figure 13. Normal radial artery anatomy

Radial artery

Brachial artery

Ulnar artery

Interrosseous and Median artery

Brachial artery

Radial artery

Ulnar artery

Interrosseous artery
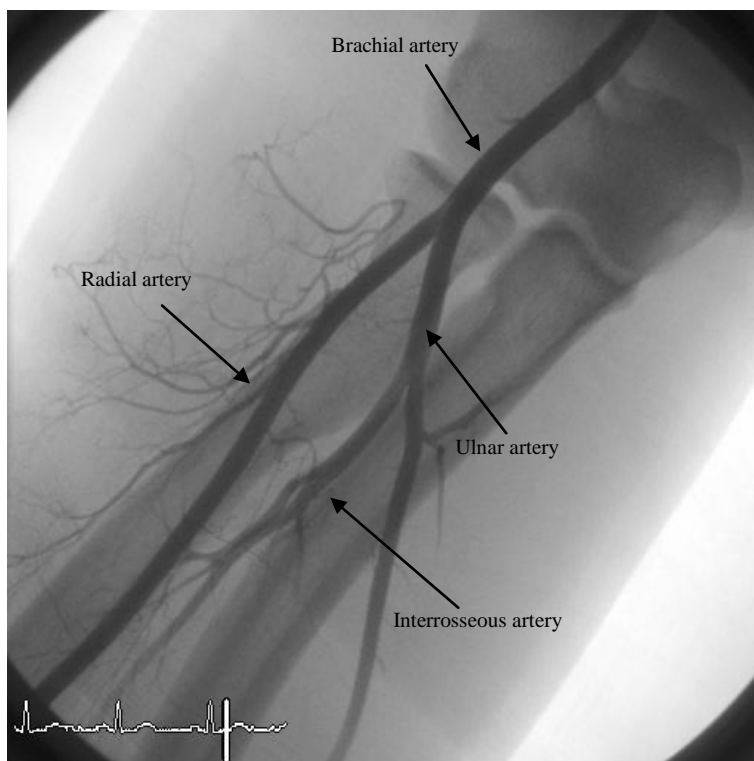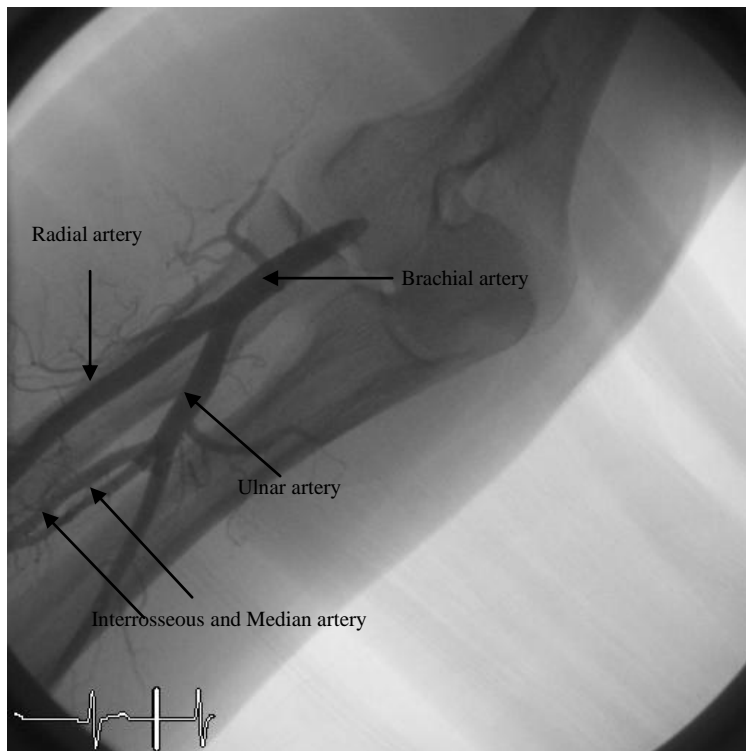
Figure 14. Types of radial anomaly and their rates of procedural failure**.**
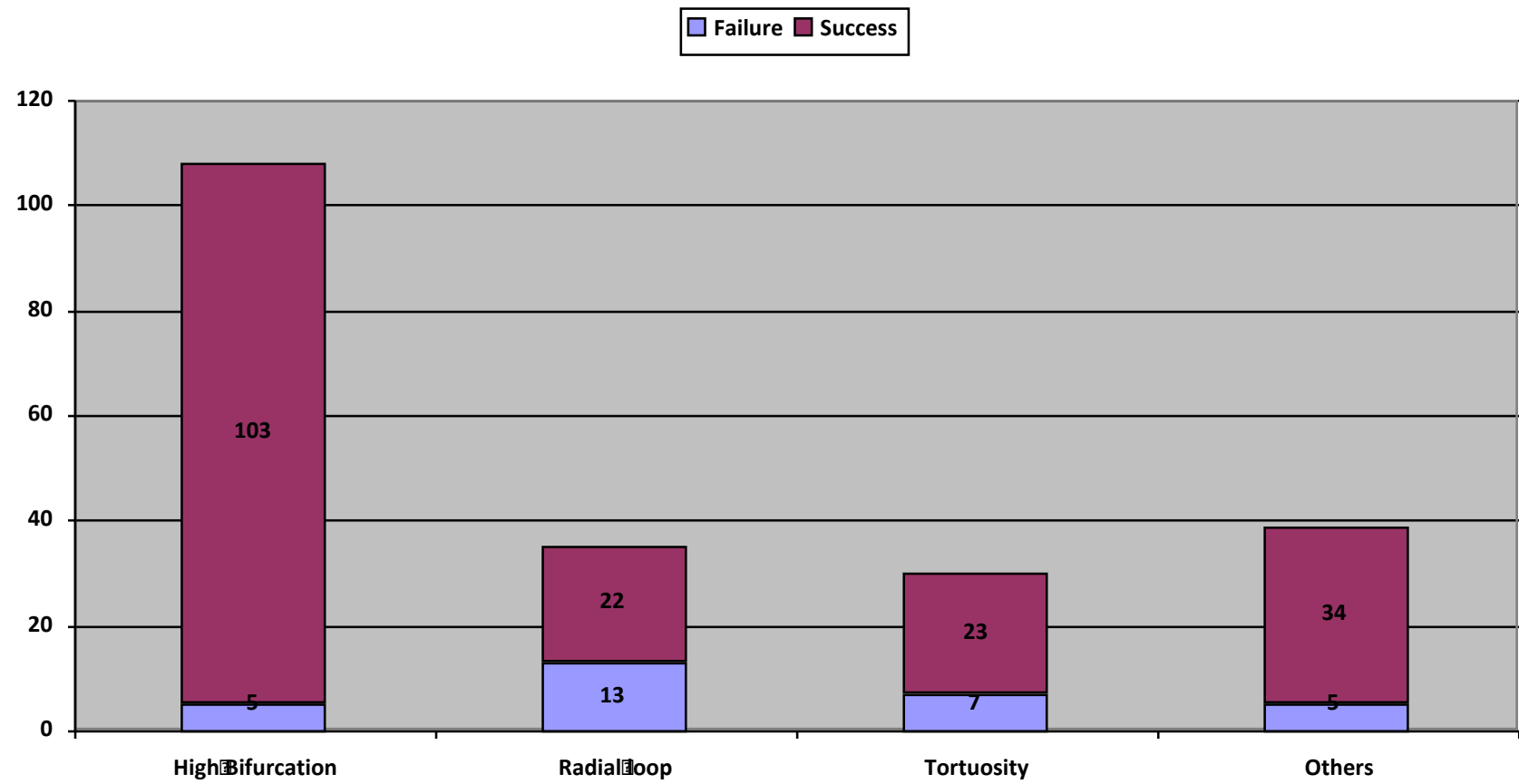
Table 8. Variations of patients and procedural data in relation to radial artery anatomy.

No. of patients (n=1533)	Normal Anatomy	High Bifurcations[*]	RA Loops[*]	Tortuous RA[*]	Other Anomalies[*]
No. of patients	1321	108	35	30	39
% of women	28	29^{α}	49^{β}	50^{β}	33^{α}
Age	63.0 ± 11.0	$65.5\pm10.8^{\alpha}$	$69.8\pm10.4^{\Omega}$	$72.2\pm7.7^{\Omega}$	$65.1\pm11.8^{\alpha}$
Procedure duration (min)	41.3 ± 21.5	$45.2\pm23.2^{\alpha}$	$49.4\pm17.1^{\alpha}$	$41.0\pm12.7^{\alpha}$	$42.1\pm19.2^{\alpha}$
Fluoroscopy time (min)	9.7 ± 8.0	$9.3\pm6.5^{\alpha}$	$10.0\pm6.6^{\alpha}$	$10.7\pm6.5^{\alpha}$	$9.6\pm7.1^{\alpha}$
% of failures[§]	0.9	4.6^{α}	37.1^{Ω}	23.3^{π}	$12.9\%^{\alpha}$

[*]p value comparing radial anomaly to normal anatomy provided when relevant.
$^{\alpha}$p=NS; $^{\beta}$p<0.05; $^{\Omega}$p<0.0001; $^{\pi}$p<0.005
[§]Percentage of failure to radial artery anatomical finding

Figure 15. High bifurcating radial artery that rejoins the brachial artery at the middle third of humerus
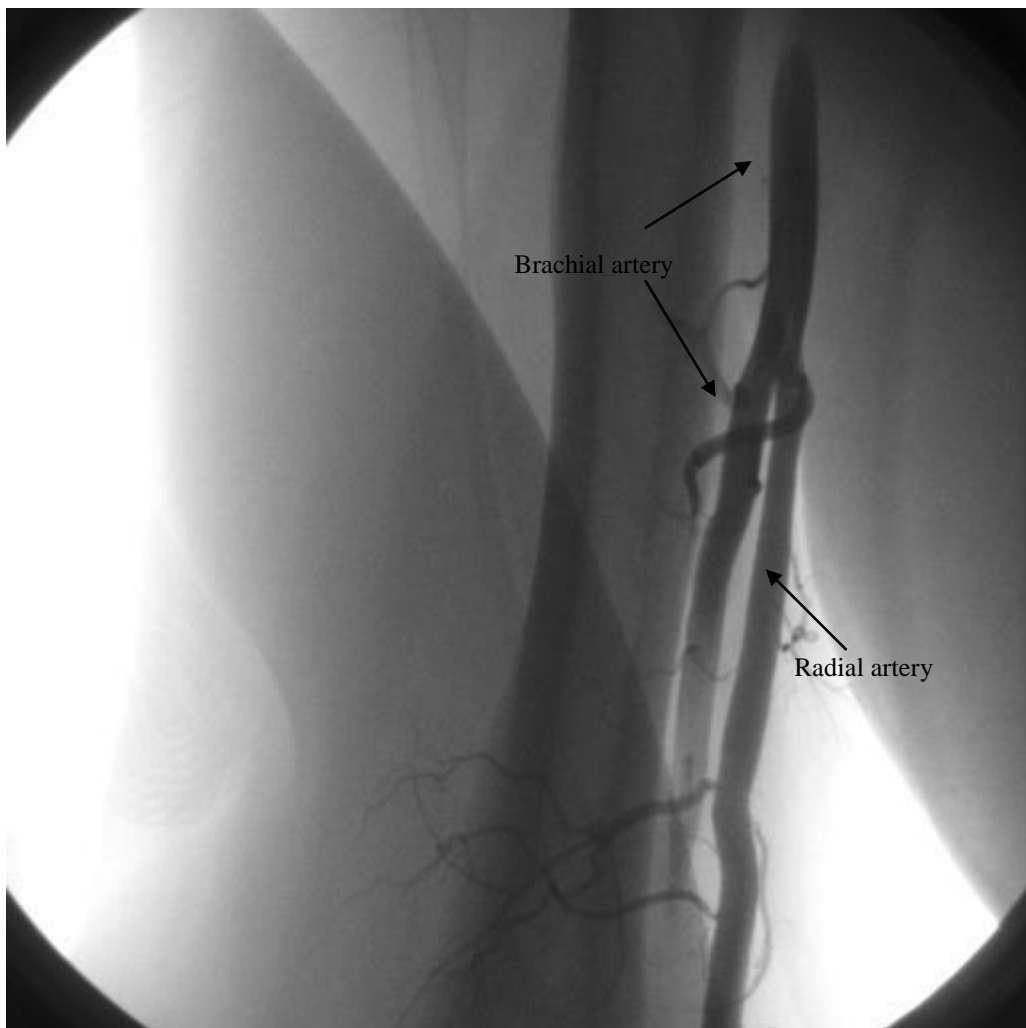
Figure 16. High-bifurcating radial artery – anastomosis sites and diameters.

Radial artery loop

A radial artery loop was observed in 35 patients (2.3%). These mostly involved the proximal radial artery just below the brachial bifurcation. A recurrent radial artery (occasionally two) was noted to arise from the apex of the loop in all cases, which was of small calibre and invariably assumed a straight path into the upper arm. The presence of a radial loop was associated with a high procedural failure rate with 13 out of the 35 procedures (37.1%, $p<0.0001$) failing to complete. Seven of thirteen patients had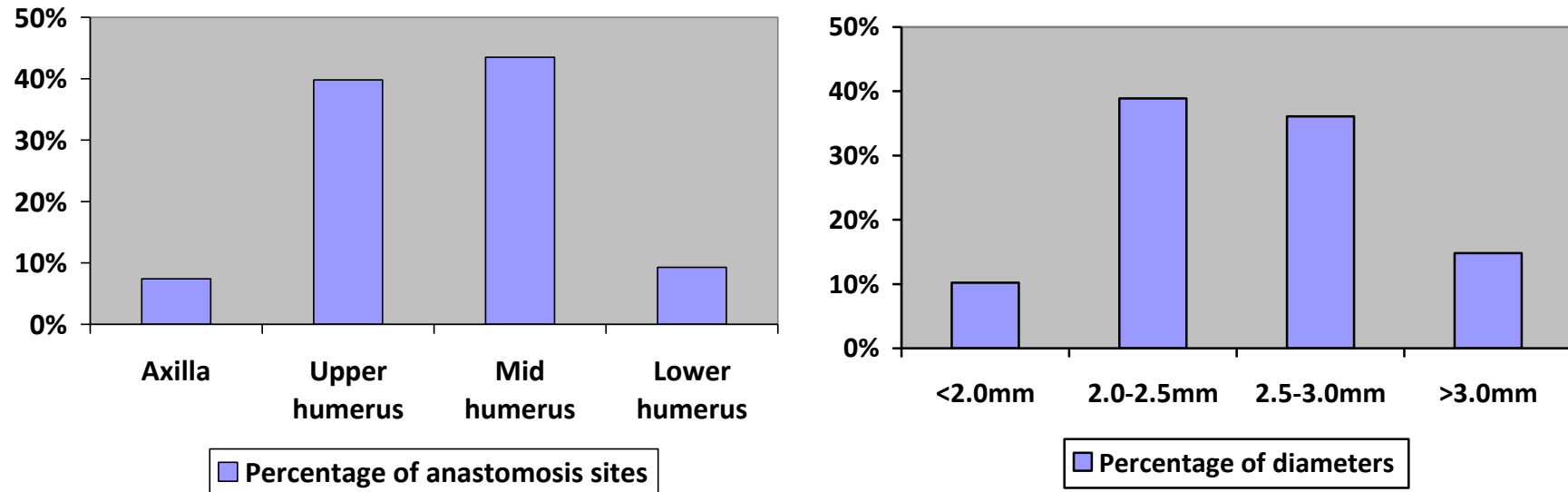 unfavourable radial loop anatomy with large diameter loops (Figure 17). These were considered to be insurmountable by the experienced radial operators and the procedure was abandoned from this access site. In the remaining 22 patients, the radial loops had a smaller diameter and were 'crossed' with a hydrophilic or an angioplasty wire. With the loop straightened, the procedure was successfully completed (Figure 18a-b).

Extreme radial artery tortuosity

Extreme radial artery tortuosity (Figure 19) was observed in 30 patients (2.0%). The presence of extreme radial tortuosity was also associated with a high procedural failure rate with 7 failures (23.3% $p<0.001$). These vessels were prone to severe radial artery spasm; this being the reason for procedure failure in all cases.

Other anomalies

Various other anomalies were present in 39 patients, giving a combined frequency of 2.5%. In 17 patients there was evidence of radial atherosclerosis (1.1%). Of clinical interest, in all such patients it was possible to cross with guide wires and catheters. However, in 5 patients (29.4%) there was procedural failure due to extreme

subclavian tortuosity including retro-oesophageal right subclavian artery (arteria lusoria). In the remaining 22 patients a range of minor anatomical variations (such as anomalous additional vessels and minor bifurcation variations) were present. These had no clinical significance since all cases were completed via the chosen radial access site.

Figure 17. Complex large radial artery loops. Note 2 remnant recurrent radial arteries assumed a straight path up the arm from the apex of the loop.
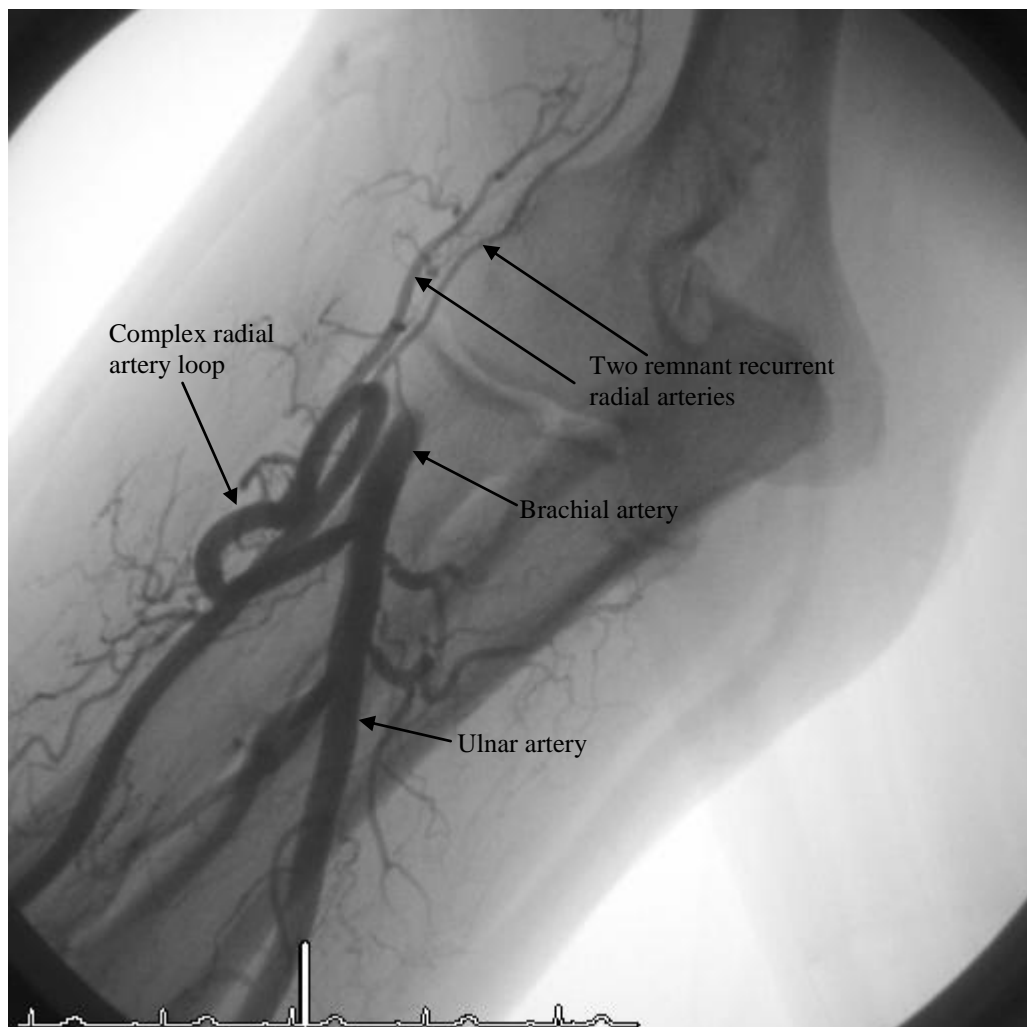
Figure 18a-b. Example of 'crossing' and straightening a radial artery loop. **Figure 18a:** 'Crossing' the loop with a hydrophilic 0.014" wire.

Figure 18b. Straightening of the loop with gentle anti-clockwise rotation of a 4 French multipurpose diagnostic catheter.

Figure 19. Extreme radial artery tortuosity. Note vessel calibre disparity around bend probably due to spasm.

Brachial artery

Ulnar artery

Tortuous radial artery
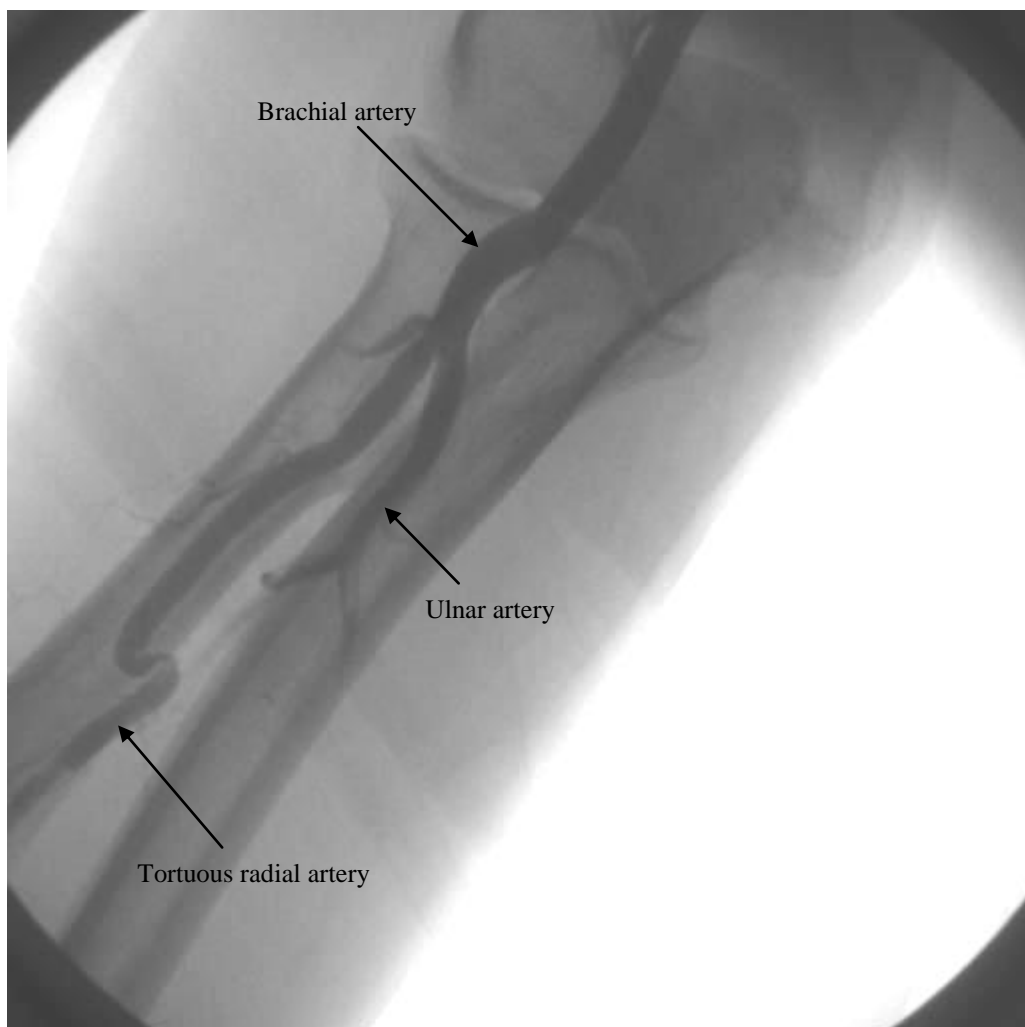
Vascular complications

No patients had bleeding requiring transfusion or surgical intervention. Access site vascular complications in 15 patients (1.0%) were treated conservatively. These were: small haematoma (8), large haematoma (2), radial artery dissection (2), immediate radial artery occlusion (2) and axillary artery dissection (1). Two patients with large haematoma were successfully treated with customised compression and arm elevation without evidence of compartment syndrome or hand ischaemia. The patient with

axillary artery dissection was also managed conservatively without ischaemic sequelae.

3.4 DISCUSSION

Transradial percutaneous coronary procedures have gained popularity because of reduced access site vascular complications and immediate patient mobilisation. Procedural success has been facilitated through technological enhancements and miniaturisation of equipment. Reported technical failure for transradial procedures is between 1-5% (72, 99, 116, 117) compatible with our overall figure of 3.2%. There are several reasons leading to failure: inability to puncture, artery spasm and anatomical variations. Whereas incidence of the former is documented (72, 99, 116, 117), information relating to radial artery anatomical variation is limited. Furthermore, there is a paucity of data on the presence of radial artery anomaly and its relation to procedure failure. Our data defines radial artery anomalies in patients undergoing a first transradial cardiac procedure. Furthermore we observed higher procedure failure rates in patients with radial artery anomaly, and of clinical interest, different anomalies were associated with different failure rates even for experienced operators. Comparisons of selected upper limb arterial anomaly studies are summarised on Table 9.

Autopsy studies of upper limb arterial anatomical variation reported a frequency of between 4 to 18.5% (113, 115, 118). Using 2-dimensional ultrasonography and colour doppler this figure was 9.6% (119) whilst arteriography studies reported between 7.4 to 22.8% (114, 120, 121). Not only were there wide variations in the occurrence of anomaly, there were also variations in the pattern of anomalies reported, partly due to

Table 9. A summary of selected upper limb arterial anomaly studies

Author	Types of Study	No. of Patients or Samples	Mean Age	Incidence of Anomaly						
				Overall (% & 95% CI)	High Radial Bifurcation	Radial Loop	Radial Tortuosity	Radial Hypoplasia	Stenosis/ Calcification	Other Anomalies
McCormack et al 1953	Autopsy	750	N/A	18.5 [15.9 - 21.5]	14.3	0	0	0	0	4.2
Rodriguez-Niedenfuhr et al 1959	Autopsy	384	N/A	14.3 [11.2 – 18.2]	13.8	0	0	0	0	1.0
Uglietta et al 1989	Arteriography	100	39	9 [4.6 – 16.4]	8	0	0	0	0	1
Yokoyama et al 2000	Ultrasonography	115	64.5	9.6 [5.3 – 16.5]	0	0.9	5.2	1.7	1.7	0
Yoo et al 2005	Arteriography	1191	60	7.4 [6 - 9]	2.4	0	4.2	0	0	0.9
Valsecchi et al 2006	Arteriography	2211	62.6	22.8 [21.1 -24.6]	8.3	0.8	3.8	7.7	1.7	0.5
Lo et al 2009	Arteriography	1026	64	15 [12.1 – 15.6]	7.8	2.1	2.4	0	1	1.8

differences in definitions. The frequency of anatomical variation was higher in autopsy studies as variation was defined according to the course of the artery in relation to muscle and nerve that would not be evident in arteriographic studies.

An interesting observation from the autopsy studies was an absence of radial artery tortuosity or hypoplasia. We postulate that radial artery tortuosity is only seen in the presence of a dynamic arterial circulation and therefore not observed at autopsy. The absence of hypoplasia in autopsy studies could be explained by arteriographic studies reporting existence of "normal" arteries with severe spasm (122). Radial artery hypoplasia was not reported in our study nor that by Yoo (120), and Louvard (112). It is also worth noting that radial artery loop was not a separate category but under the category of variation of anastomosis between brachial artery and radial or ulnar artery at elbow level. Furthermore, not all such anastomosis variations were full 360º loops as variations could be either in the form of a sling-like loop or rectilinear pattern (123). There is therefore no reported frequency of isolated full 360º radial loop from autopsy studies.

The most frequent radial artery anomaly observed is high radial bifurcation with a reported frequency range of 0% to 14.3%. The absence of high radial bifurcation was reported using ultrasonographic scanning suggesting that it is not reliable in identifying this type of anomaly (119). However, the small sample size and racial variation (115 exclusively Japanese patients) may have been contributory. Yoo et al reported a radial bifurcation incidence of 2.4% in 1191 Korean patients (120). The reported 7.0% in our study was comparable to the 8.3% reported by Valsecchi et al

(121) but lower than the 14% in autopsy studies (113, 115). Importantly, our study confirmed that this anomaly did not significantly impact on procedural success. In patients with high radial bifurcations with small calibre proximal artery, the use of 5 French equipment and/or a hydrophilic wire was required for procedure completion.

The presence of a radial artery loop is the commonest cause of procedure failure for experienced radial operators (112). The 2.3% frequency of a full 360º radial artery loop in our study is the highest reported. All loops were accompanied by a recurrent radial artery at the apex of the loop which invariably assumed a straight path into the upper arm. The presence of the remnant recurrent radial artery has potential to complicate the crossing and straightening manoeuvre, with a tendency for the wire to selectively 'follow' the path of the remnant artery thereby increasing risk of dissection or perforation especially if such anatomy has not been initially defined.

Although loops can often be crossed using either a hydrophilic or an angioplasty wire and then straightened with a 5F Judkin Right 4 configuration diagnostic catheter, these manoeuvres can induce spasm and pain, making subsequent catheter manipulation and advancement impossible. Our procedure failure rate of 37.1% in patients with a radial loop was high. However, more than half of these were patients with large diameter radial loop anatomy deemed impassable after radial arteriography, and procedures were completed via alternative access sites without attempting to cross the loops. The early definition of such anatomy at procedure outset informed the operator thereby avoiding potential complications.

Extreme radial artery tortuosity was also associated with significant procedure failure (23.3%). Our strict definition for extreme tortuosity differed from other studies with a consequent lower frequency of 2.0%, compared to 3.8%, 4.2% and 5.2% by Valsecchi et al, Yoo et al and Yokoyama et al respectively.

Other anomalies observed in our study included a low frequency of radial atherosclerosis. This may be an important marker for extensive extra cardiac vascular disease as many such patients were found to have tortuous subclavian vessels that could not be navigated, leading to procedural failure. Other minor variations in bifurcation anatomy had no influence on procedural outcome.

The acquisition of a radial arteriogram requires only a minimal contrast load, a small amount of additional radiation and trivial extra procedural time. This is offset by the provision of important information that aids the operator in planning an optimal procedure.

In summary, this study demonstrates that radial artery anomalies are relatively common and a cause of transradial procedure failure even for experienced radial operators. Retrograde radial arteriography helps to delineate underlying anomalies, identify patients with unfavourable anatomy thereby informing the operator to plan a strategy to overcome the anomaly or change access route with the potential to save time and avoid vascular complications. This can be performed with a minimum of contrast (3 mls) and should be considered part of a routine transradial procedure.

CHAPTER 4

RADIAL ARTERY DIAMETER AND ITS

RELATIONSHIP TO SUBLINGUAL GTN

4.1 INTRODUCTION

The radial artery is increasingly used as the preferred access route for diagnostic catheterisation and therapeutic percutaneous coronary intervention (PCI) since its introduction first by Campeau, followed by Kiemeneij and Laarman (38, 40). This is driven first by lower access site bleeding complications, improved post-procedural patient comfort, day case PCI and economic benefits (43-45, 72, 83, 84, 102, 107, 124-127), and more recently, by a reduction in mortality when radial access is employed for PCI (67). Procedural outcomes have been further evaluated in meta-analysis of randomised and observational trials confirming that radial access results in a reduction of major adverse events and death rate when compared to femoral access (46, 95, 128).

The transradial technique is, however, associated with a prolonged learning curve frequently related to difficulty in puncturing the radial artery and radial artery spasm, even for experienced femoral operators. Detailed knowledge of radial artery diameter and any manoeuvre to increase its diameter (for example with Sublingual Glyceryl Trinitrate [S/L GTN]) may help shorten part of the learning curve and optimise procedural technique, but such data in the western population is currently not available. This study aims to evaluate distal upper limb arterial diameters variation and their response to S/L GTN in both normal healthy population and in patients with pre-specified medical conditions.

4.2 METHODS

Study population

The study population consists of two groups of subjects: normal healthy individuals and patients with coronary artery disease, diabetes mellitus, hypertension, chronic renal impairment not on dialysis or peripheral artery disease. Healthy volunteers were recruited from staff at University Hospital of North Staffordshire (UHNS) and patients with pre-specified medical conditions from Cardiology in-patients. A total of 305 patients were recruited, of which 125 were healthy subjects. The study was approved by the Local Ethics Committee and a written informed consent was obtained from each patient. Patients who were unable to give consent or who were acutely unwell were excluded.

Ultrasound study of forearm arteries

Two-dimensional vascular images and colour doppler ultrasonic studies of both the right and left forearm arteries were performed by an experienced cardiologist using a SonoSite TITAN portable ultrasound system (SonoSite Inc. Bothell, WA, USA) with a 10MHz linear vascular transducer (Figure 20). The transducer was placed perpendicular to the arterial wall to acquire an optimal image of the vessel. Once in position, the site is marked so that the same region of the vessel is imaged during the study. The image was recorded in AVU format that and transferred to an external computer for analysis later.

The subjects lay supine in a stable temperature room with both arms naturally abducted and the wrist supported. The luminal inner diameters of both the right and left radial artery (RA) and ulnar artery (UA) were measured 1 to 4cm above the

respective styloid process at rest. These were then repeated after administering 800 µg

of S/L GTN to evaluate the effect of S/L GTN on the right RA and UA diameters. A

second dose of 800 µg of S/L GTN was administered after at least 30 minutes has

elapsed to assess the effect of GTN on the left RA and UA diameters. The mean inner

diameter was defined as an average value of several perpendicular readings.

Figure 20. SonoSite Titan ultrasound machine

Data Collection

In addition to bilateral arterial diameters, patient characteristics, wrist circumference, hand dominance, Allen's test and blood pressure (BP) pre and post GTN were all recorded. Wrist circumference was measured two centimetres above the radial styloid process.

Modified Allen's test

The modified Allen's test is performed by simultaneous compression of both the radial and ulnar arteries. The subject is then asked to make a fist and open his hand numerous times until the palm of the hand blanches. The compression on the UA is then realised. If there is an adequate collateral circulation, the normal colour of the palm returns within a few seconds. The Allen's test is defined as favourable if full blushing of the hand occurs with 10 seconds. The test is unfavourable if it takes more than 10 seconds for full blushing to occur. For subjects with an unfavourable Allen's test, it will be repeated after measurements of the upper limb arterial diameters post S/L GTN.

Reproducibility of measurements of forearm artery diameters

To assess reproducibility, the forearm diameters in 20 patients were measured twice on separate occasions a few weeks apart.

Statistics Analysis

Statistical analysis was performed using IBM SPSS Statistics 19.0 (IBM Corp., Armonk, New York, USA). Categorical data were presented as absolute values and percentages whereas continuous data were presented as mean ± standard deviation.

The nature of distribution of the data was determined using 1-sample Kolmogorov-Smirnov test. Student's t test and Mann-Whitney U test were used to compare continuous data as appropriate. Categorical data were compared using the Chi-Square test with the appropriate degree of freedom. Both univariate and multivariate regression analysis were used to examine potential correlation between radial artery diameter and variables such as sex, age, height, body mass index (BMI), hand dominance, hypertension, diabetes, chronic renal failure and peripheral vascular disease. A p value of less than 0.05 was considered to be statistically significant.

Intra-observer agreement was examined using intraclass correlation coefficient (ICC) and their 95% confidence intervals (CI).

4.3 RESULTS

Patients' characteristics

A total of 305 patients were studied. Baseline patient characteristics are summarised on Table 10. Figures 21a-h and 22a-h show the histograms and normal distribution curve diagrams of the diameters of both the left and right RA and UA in men and women. The incidence of unfavourable Allen's test was low, ranging from 0.6 to 5%. Interestingly, all unfavourable Allen's tests were augmented to become favourable by the use of S/L GTN.

Table 10. Baseline patient characteristics.

	Male (n=150)	Female (n=155)	P value
Age	60.1±16.7	57.3±16.9	0.145
Height (m)	1.77±0.08	1.65±0.06	<0.0005
Weight (kg)	83.6±13.7	72.4±17.1	<0.0005
BMI	26.7±4.5	26.7±5.9	0.024
R wrist circumference (cm)	18.8±1.5	17.0±1.6	<0.0001
L wrist circumference (cm)	18.4±1.7	16.8±1.6	<0.0001
Negative R Allen's test (%)	6 (4%)	7 (4.5%)	N/A
Negative L Allen's test (%)	4 (2.7%)	8 (5%)	N/A
Bilateral Negative Allen's test (%)	1 (0.7%)	1 (0.6%)	N/A
Smoker (%)	57 (32%)	46 (30%)	0.64
Hypertension (%)	38 (25%)	44 (28%)	0.75
Diabetes (%)	31 (20.7%)	29 (18.7%)	0.82
Coronary artery disease (%)	45 (30%)	42 (27%)	0.56
Peripheral vascular disease (%)	8 (5.3%)	10(6.5%)	0.87
Chronic renal failure (%)	10(6.7%)	10(6.5)	0.92

Figure 21a. Histogram of right radial artery diameter pre GTN in men

Figure 21b. Histogram of left radial artery diameter pre GTN in men

Figure 21c. Histogram of right ulnar artery diameter pre GTN in men

Figure 21d. Histogram of left ulnar artery diameter pre GTN in men

Figure 21e. Histogram of right radial artery diameter post GTN in men

Figure 21f. Histogram of left radial artery diameter post GTN in men

Figure 21g. Histogram of right ulna artery diameter post GTN in men
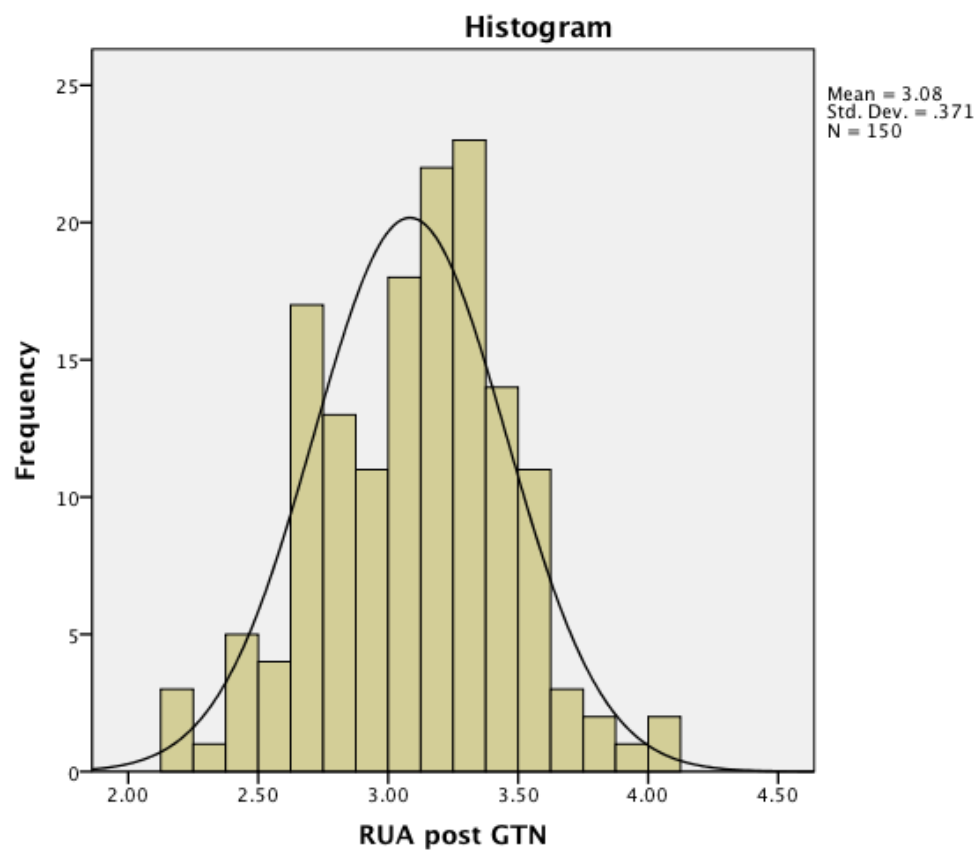
Figure 21h. Histogram of left ulna artery post GTN in men
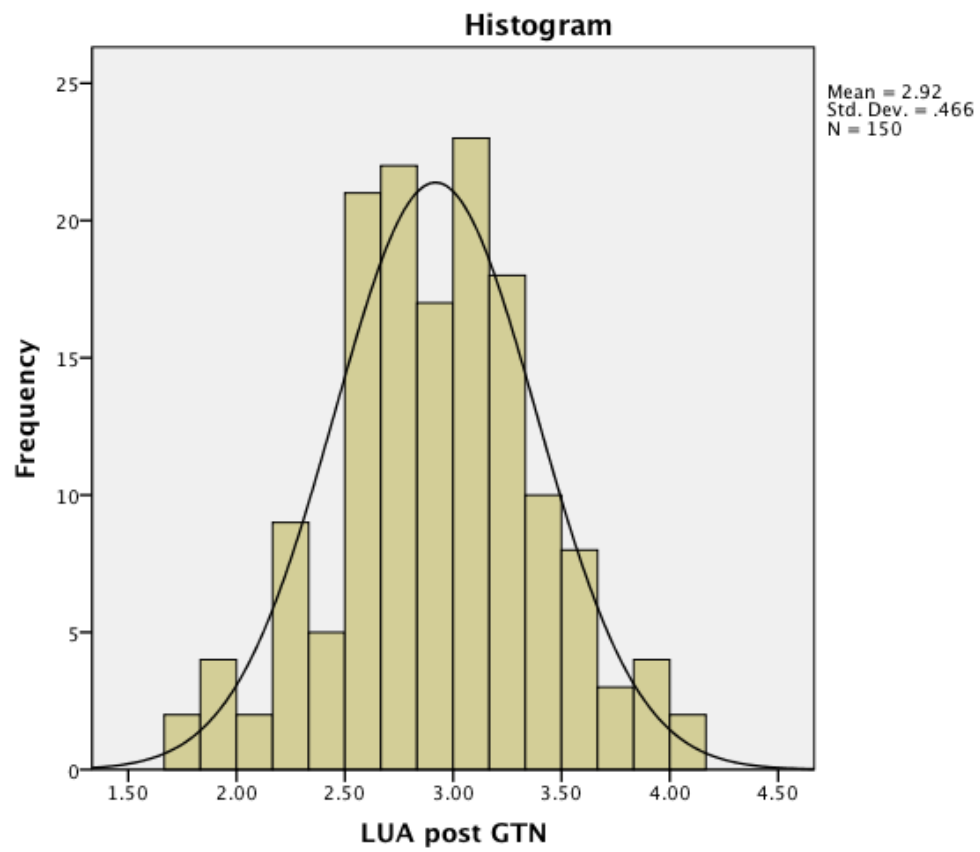
Figure 22a. Histogram of right radial artery diameter pre GTN in women
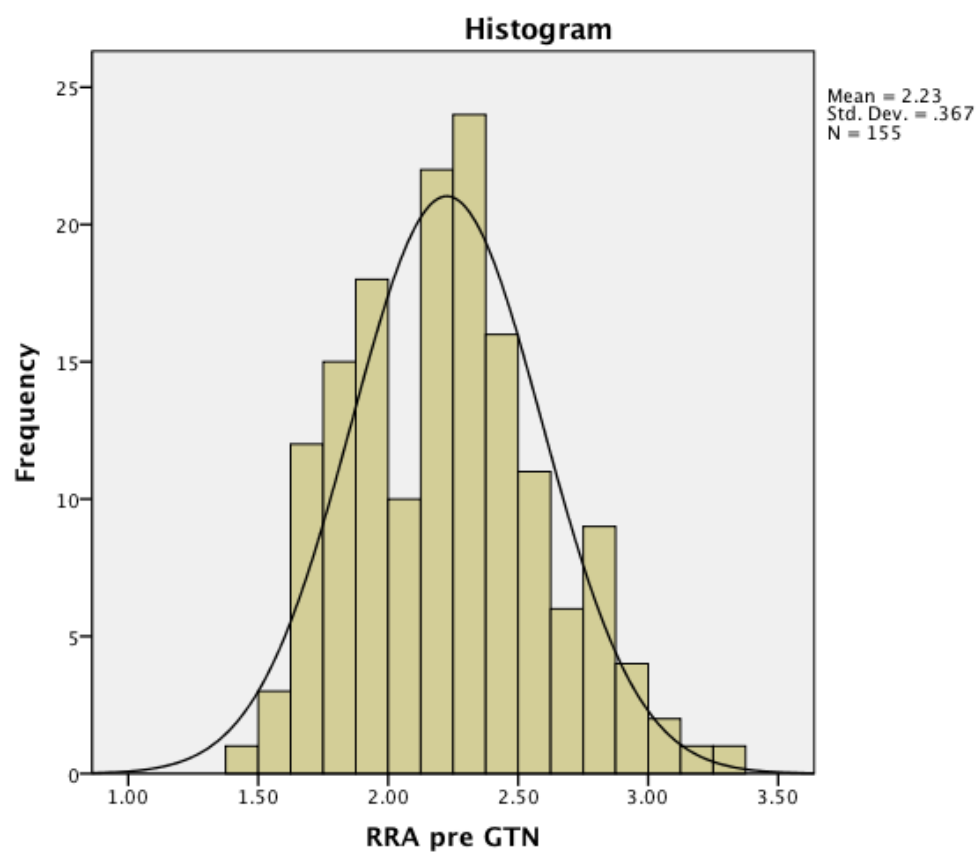
Figure 22b. Histogram of left radial artery diameter pre GTN in women
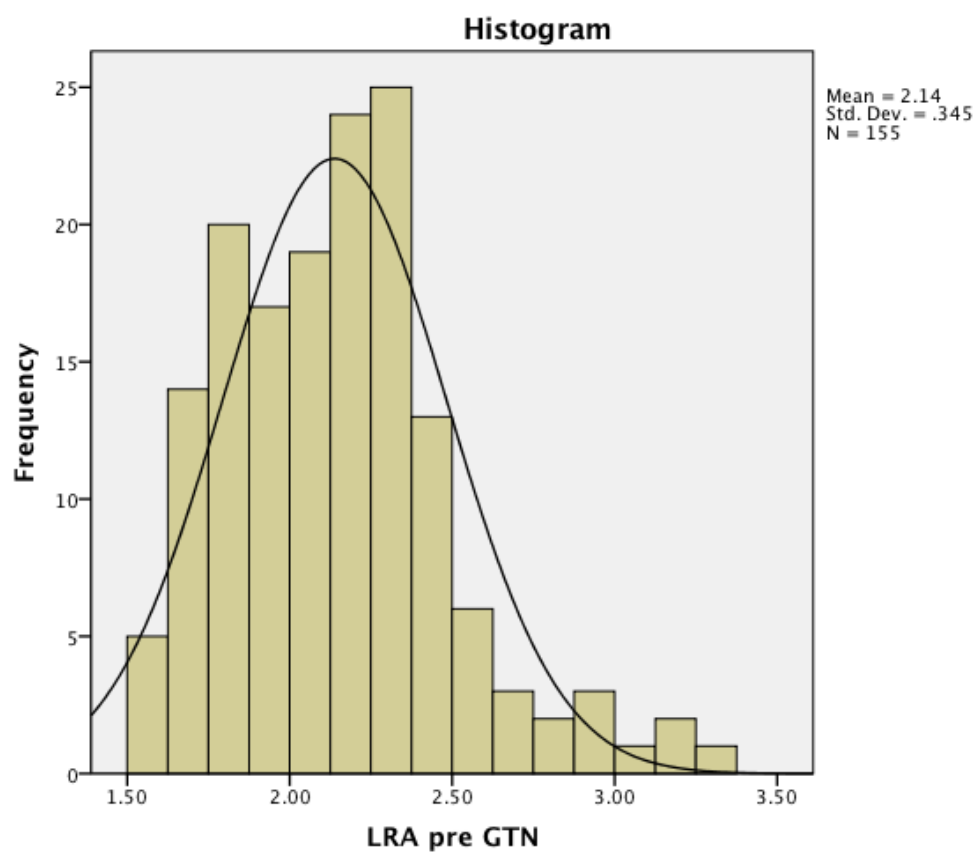
Figure 22c. Histogram of right ulna artery diameter pre GTN in women
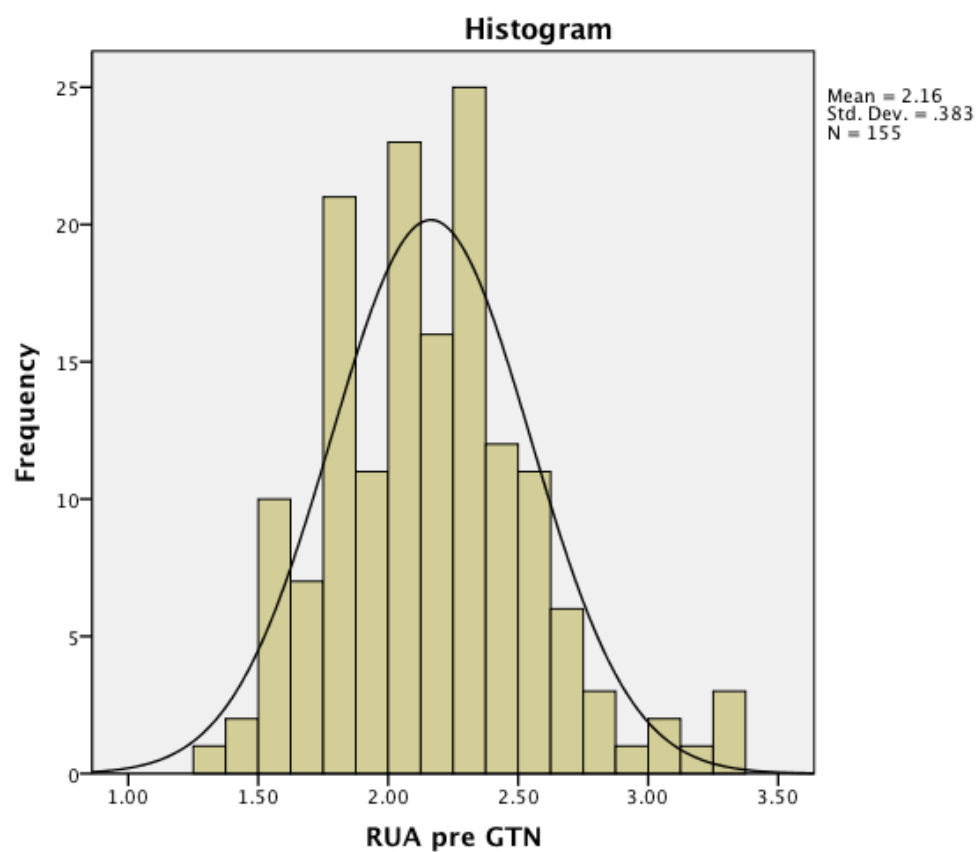
Figure 22d. Histogram of left ulna artery diameter pre GTN in women
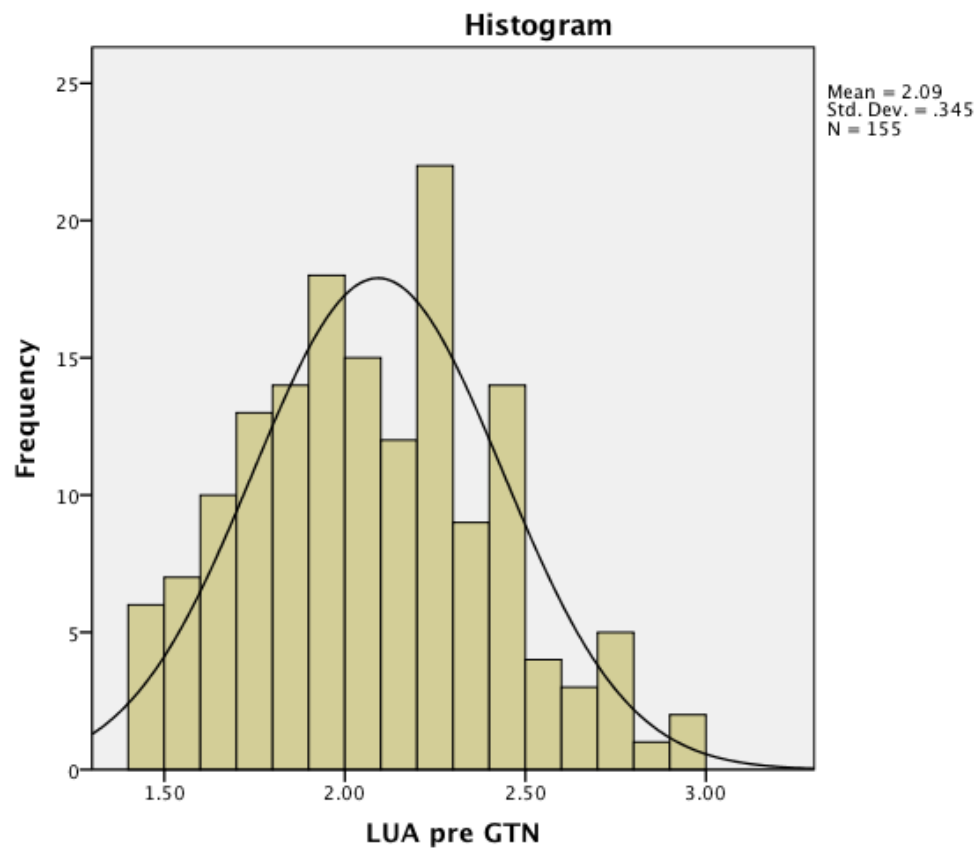
Figure 22e. Histogram of right radial artery diameter post GTN in women
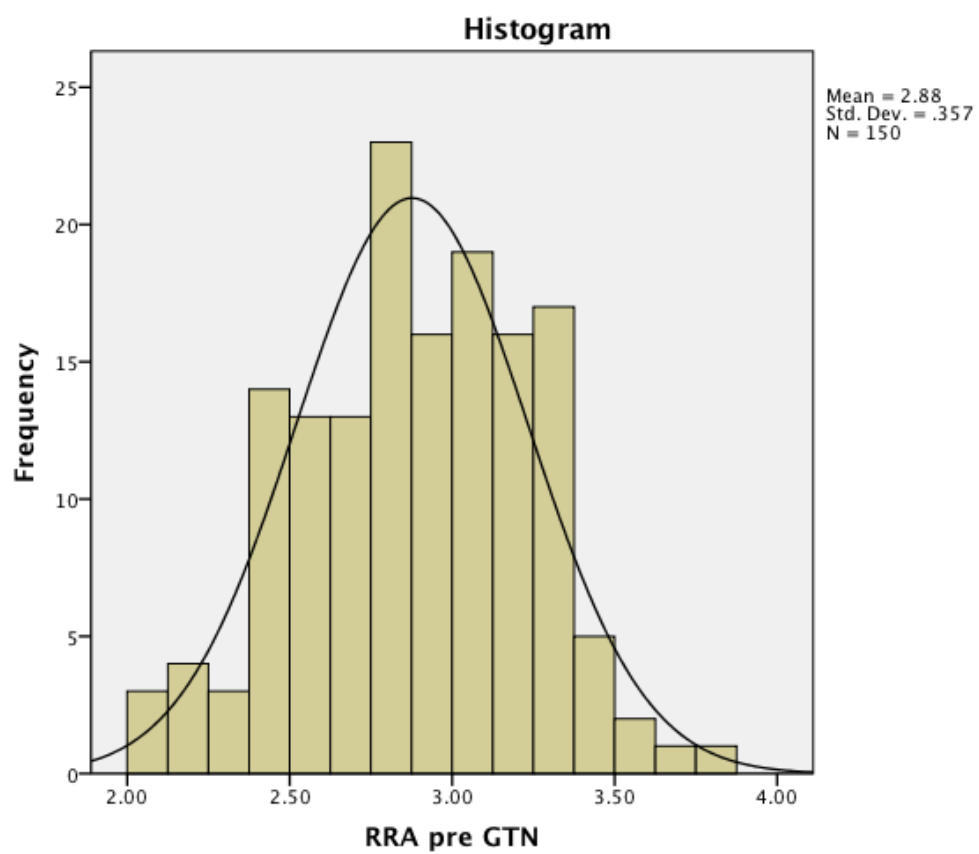
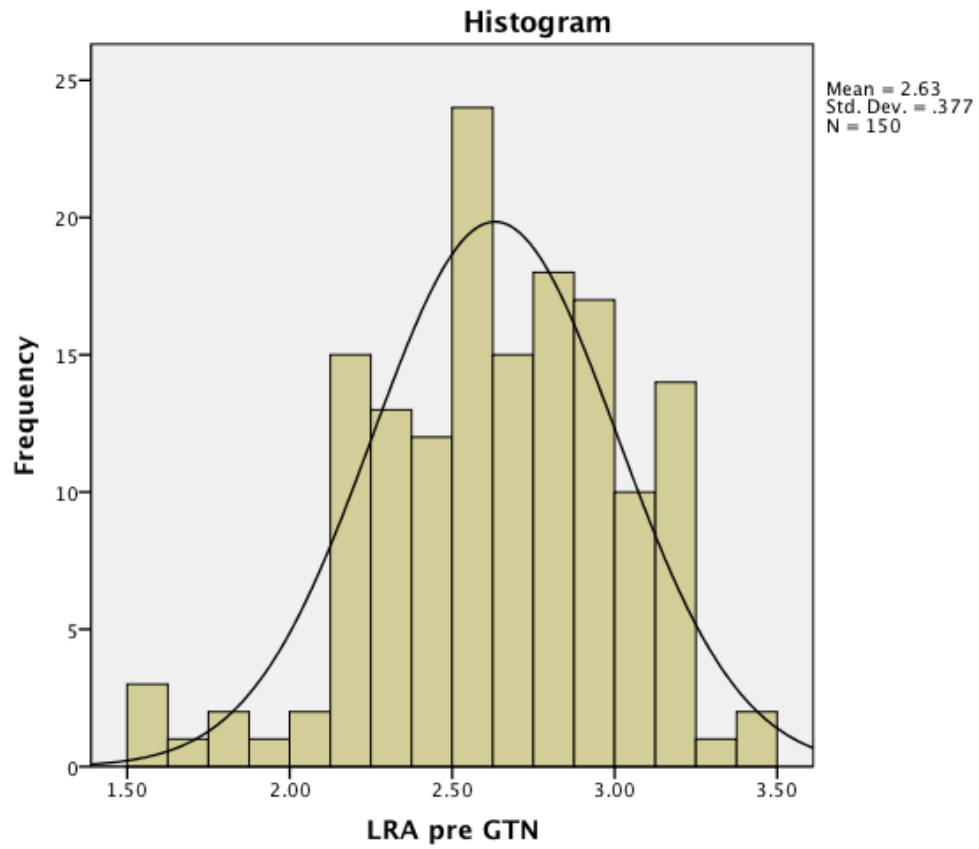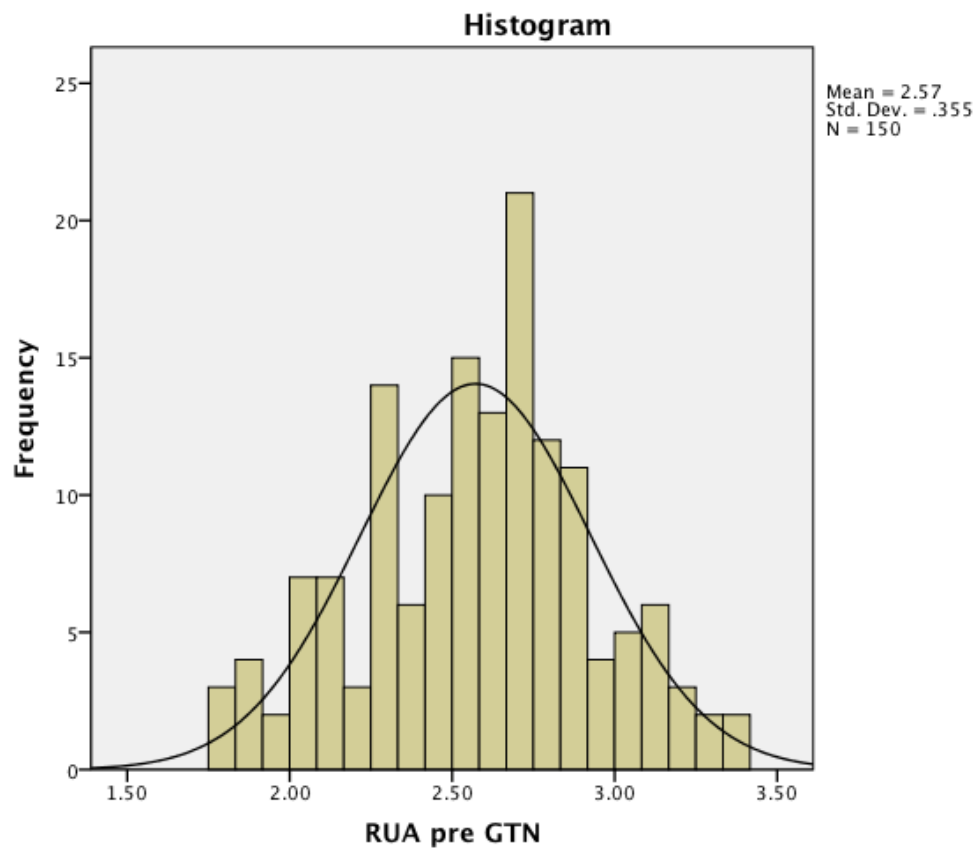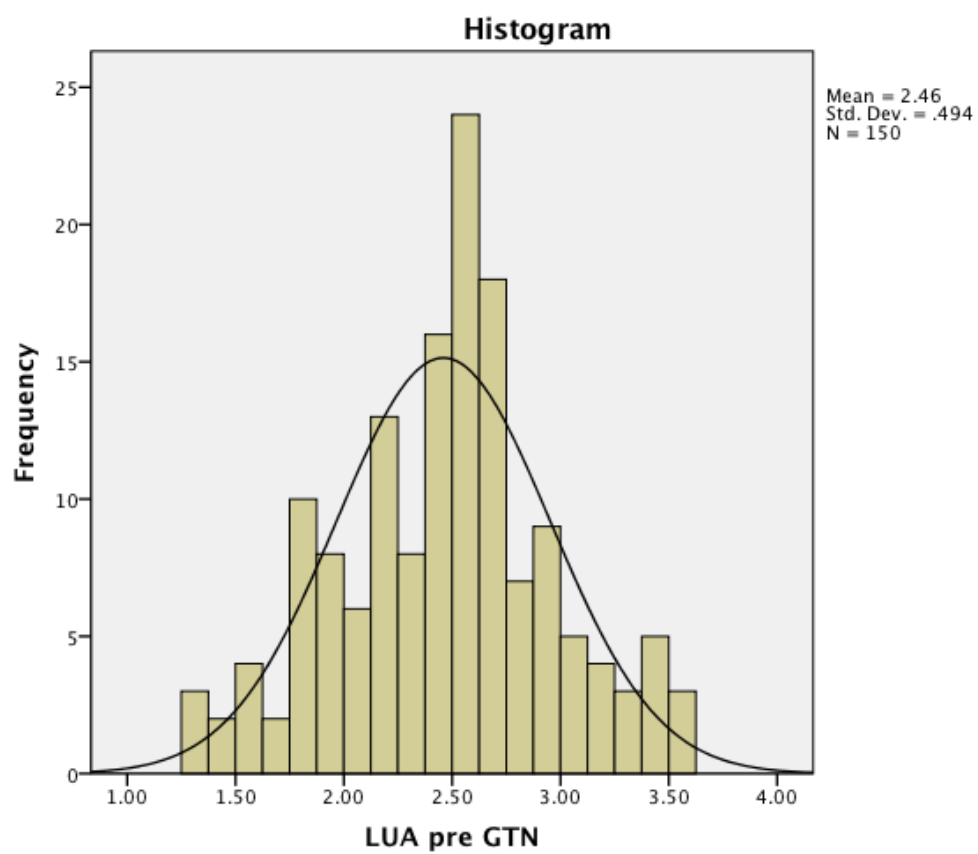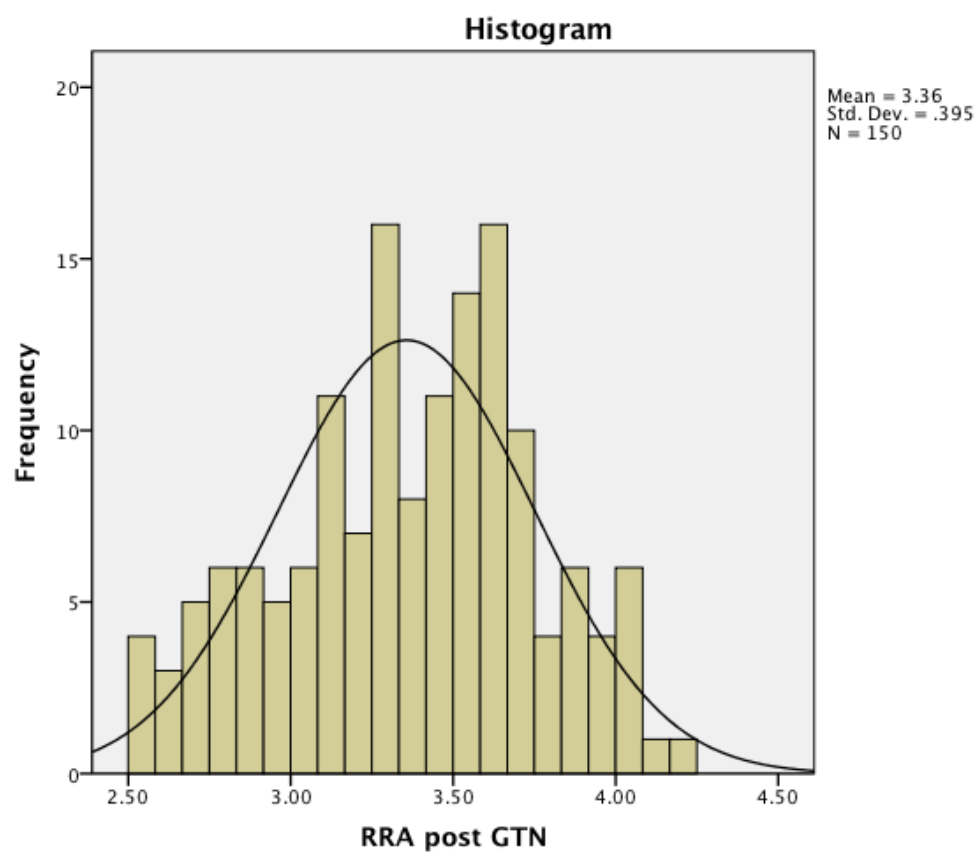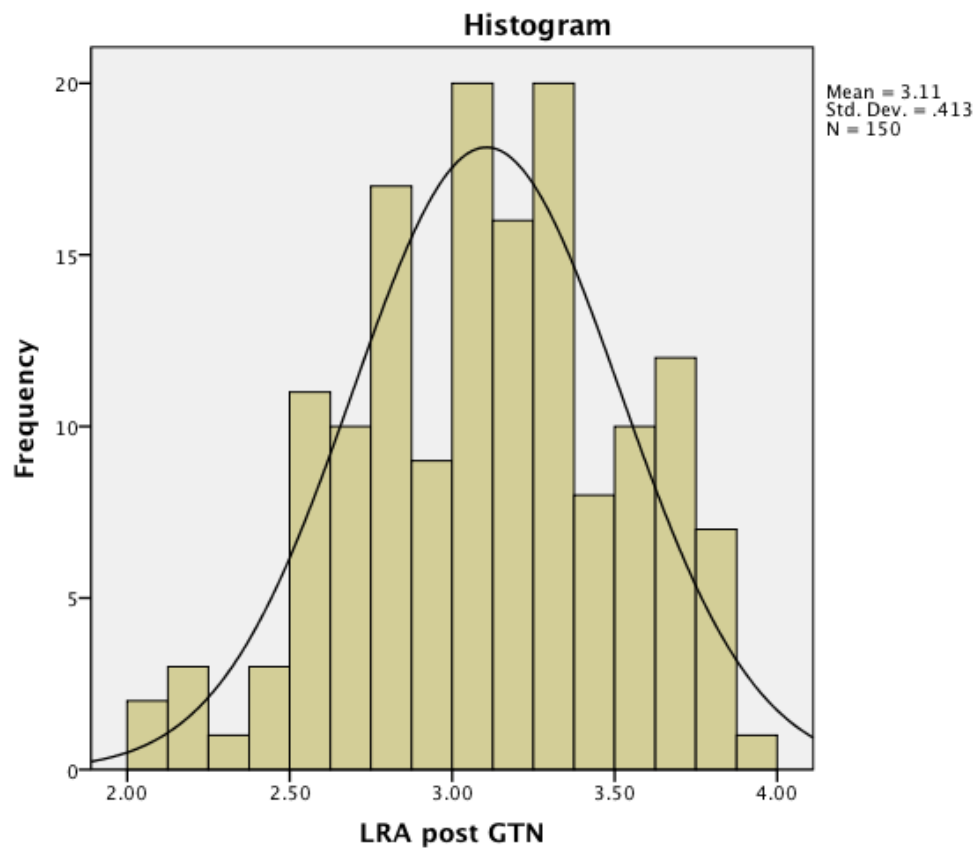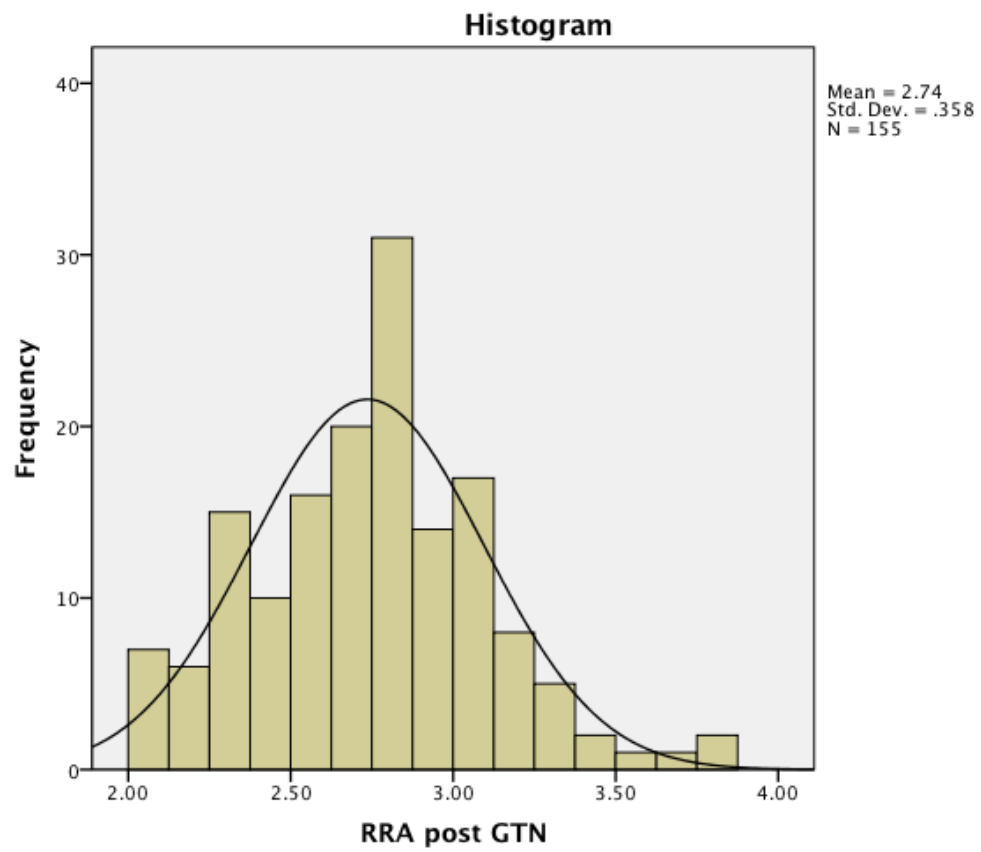**Figure 22f.** Histogram of left radial artery diameter post GTN in women
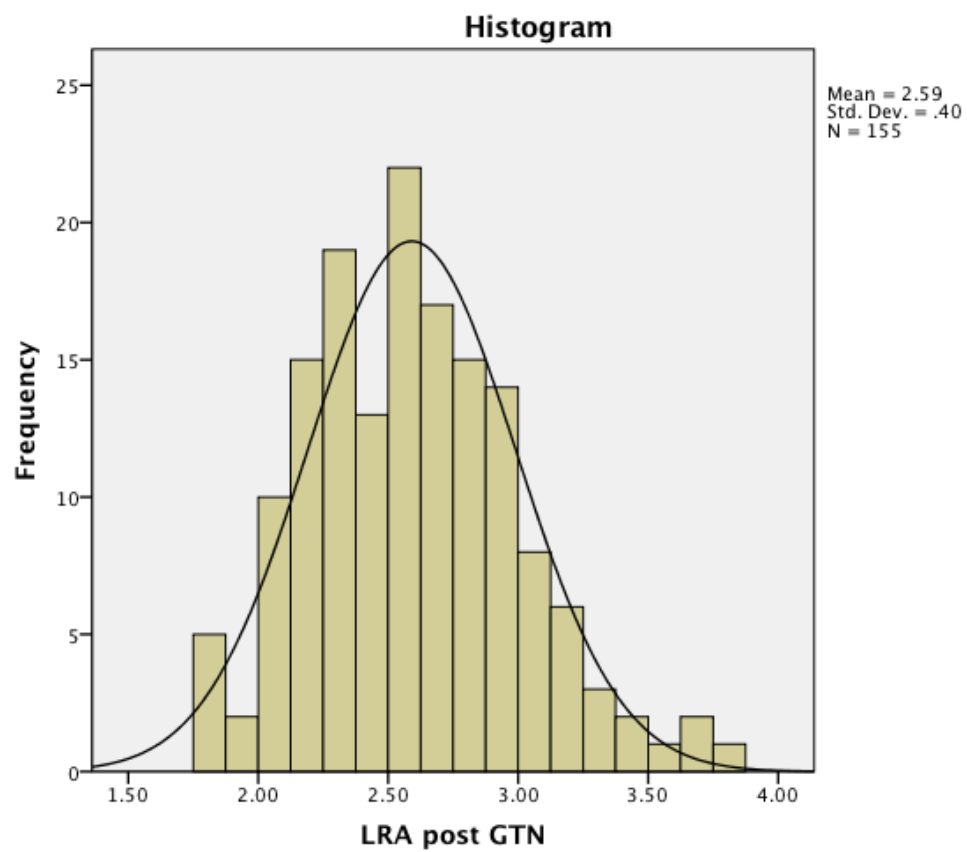
Figure 22g. Histogram of right ulna artery diameter post GTN in women
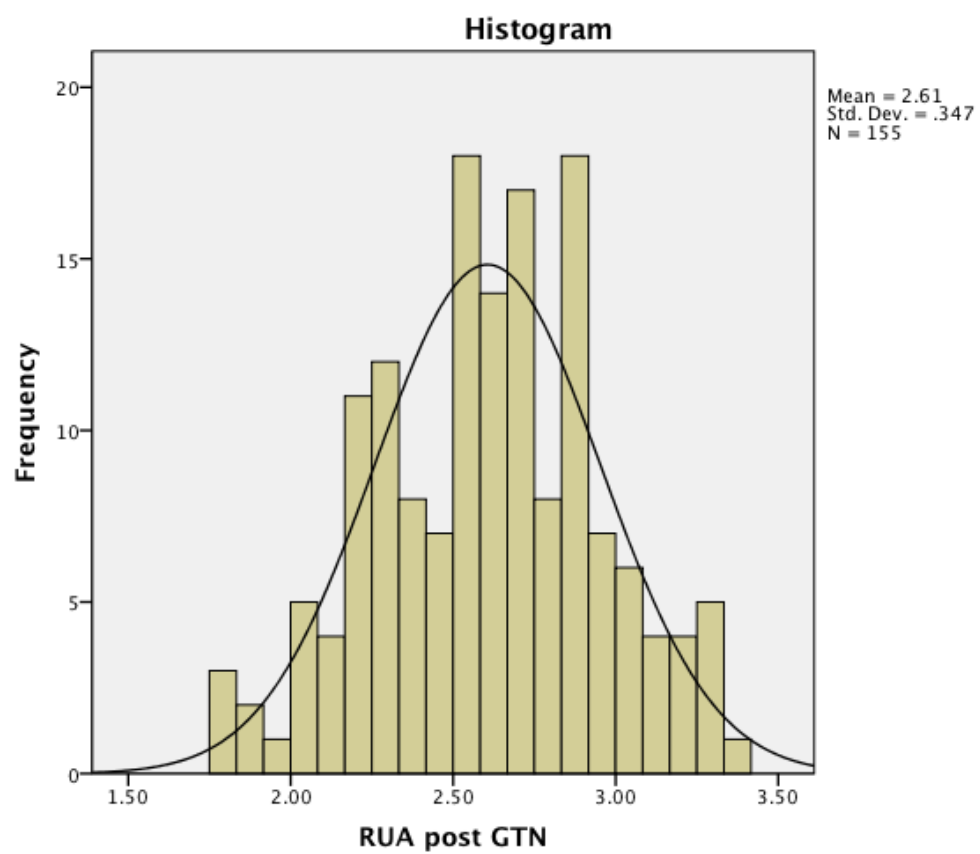
Figure 22h. Histogram of left ulna artery diameter post GTN in women
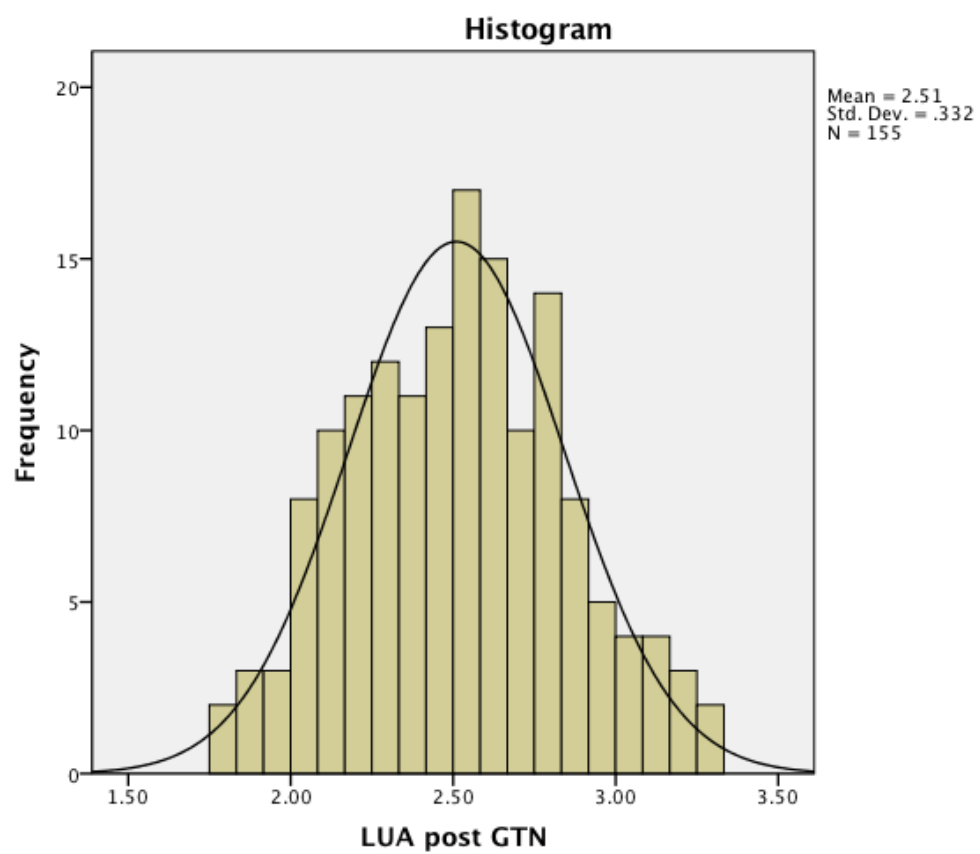
Diameters of forearm arteries and GTN

The diameters (in mm) of the right (R) and left (L) radial and ulnar arteries pre- and post-GTN are listed on Table 11. Men had significantly bigger RA and UA than women. The RA was bigger than the UA and the RRA bigger than the LRA in most men and women. GTN significantly increase the size of both the RA and UA. Mean % dilatation of the RRA, LRA, RUA and LUA in the men was 16.7±8.3, 18.3±6.8, 19.8±10.6 and 18.7±7.9 respectively, and was 22.9±7.9, 21.0±9.1, 20.8±11.7 and 20.1±9.6 respectively in women (Figure 23a&b). There were no difference in BP pre and post S/L GTN and none of the patients experienced any hypotensive symptoms.

Table 11. Diameters of radial artery, ulnar artery and blood pressure pre and post GTN

	Male (n=150)	**Female (n=155)**	**Mean diameter difference**	**P value**
Pre GTN				
RRA (mm)	2.88±0.36	2.23±0.37	0.65	<0.0001
LRA (mm)	2.63±0.38	2.14±0.35	0.49	<0.0001
RUA (mm)	2.57±0.36	2.16±0.38	0.41	<0.0001
LUA (mm)	2.46±0.49	2.09±0.35	0.37	<0.0001
Post GTN				
RRA (mm)	3.36±0.40	2.74±0.36	0.62	<0.0001
LRA (mm)	3.11±0.41	2.59±0.40	0.52	<0.0001
RUA (mm)	3.08±0.37	2.61±0.35	0.47	<0.0001
LUA (mm)	2.92±0.47	2.51±, 0.36	0.41	<0.0001
Blood Pressure (mmHg)				
Pre GTN	116/72±18/12	113/70±15/10	3/2	NS
Post GTN	110/68±16/9	106/65±12/9	4/3	NS

Figure 23a. Mean diameters (mm) and percentage change of radial and ulnar arteries pre and post S/L GTN in men.
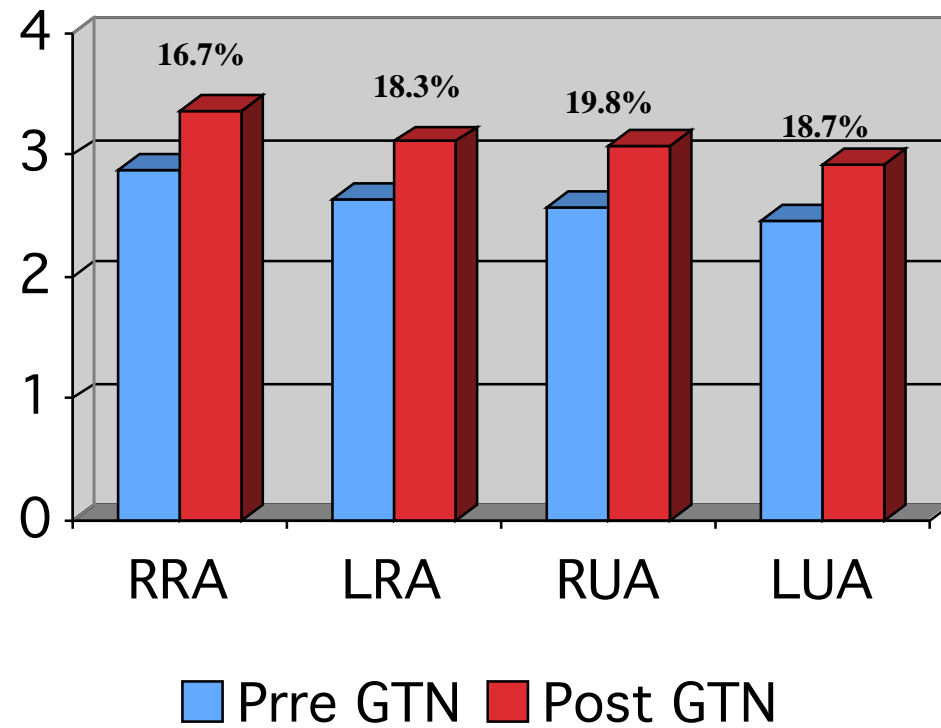
Figure 23b. . Mean diameters (mm) and percentage change of radial and ulnar arteries pre and post S/L GTN in women.
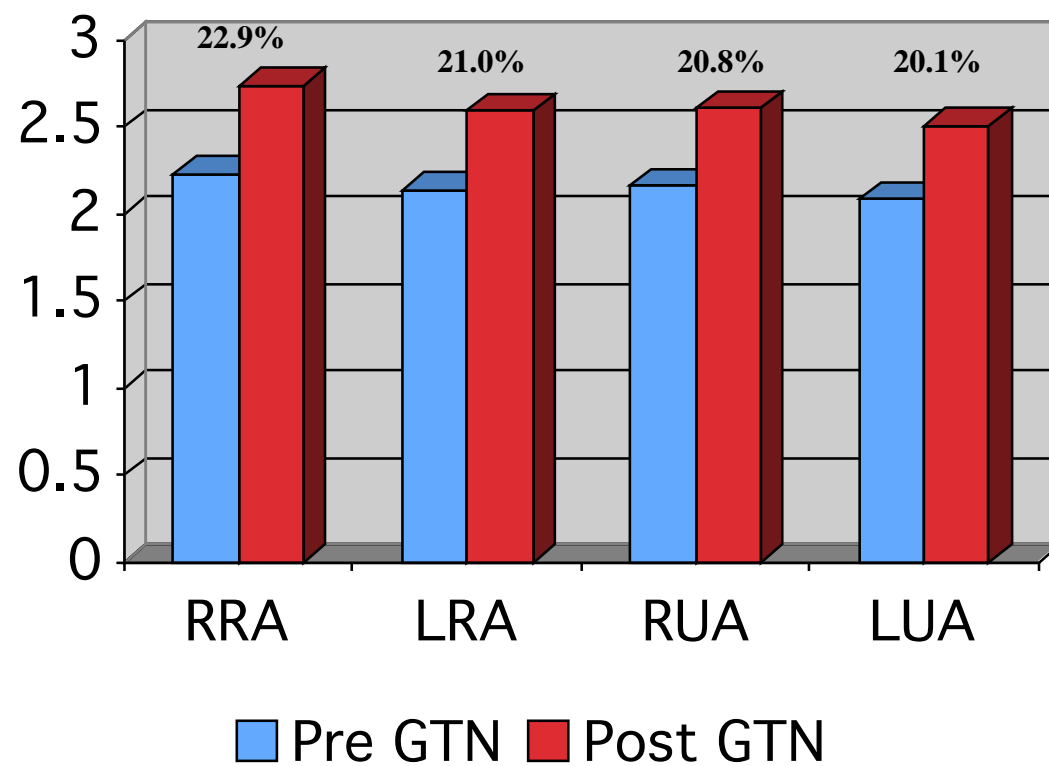
Radial artery diameters in relation to external diameters of arterial sheaths

Pre-GTN, only 47.1% and 21.9% of women had RRA bigger than 2.28mm (external diameter of a 5F sheath) and 2.52mm (external diameter of a 6F sheath), and 36.1% and 11.6% had a LRA bigger than a 5F and 6F sheath respectively (Figure 24b). Post-GTN, these increased to 91.6% and 78.9% of RRA bigger than a 5F and 6F sheath, and 79.4% and 61.9% for LRA respectively. In men, 95.3% and 84.0% had RRA bigger than a 5F and 6F sheath respectively, and 85.3% and 70.0% for LRA respectively. Post-GTN, these increased to 100% and 97.3% of RRA bigger than a 5F and 6F sheath, and 96.7% and 93.3% for LRA respectively (Figure 24a).

Intraclass correlation coefficients

ICC for intra-observer agreement was excellent ranging from 0.95 for left UA measurement (CI 0.91 to 0.97) to 0.97 for right RA measurement (CI 0.94 to 0.98).

Logistic Regression analysis

Both univariate and multivariate regressions were used to examine the potential correlation between radial artery diameter and variables such as sex, age, height, body mass index (BMI), hand dominance, coronary artery disease, hypertension, diabetes, chronic renal failure and peripheral vascular disease. Sex was the only independent predictor of RA size (odds ratio 2.01, CI 1.427-2.353, P<0.005).

Figure 24a. Percentage of men with RRA and LRA diameters >2.28mm and >2.52mm, respective external diameters of 5F and 6F arterial sheaths.
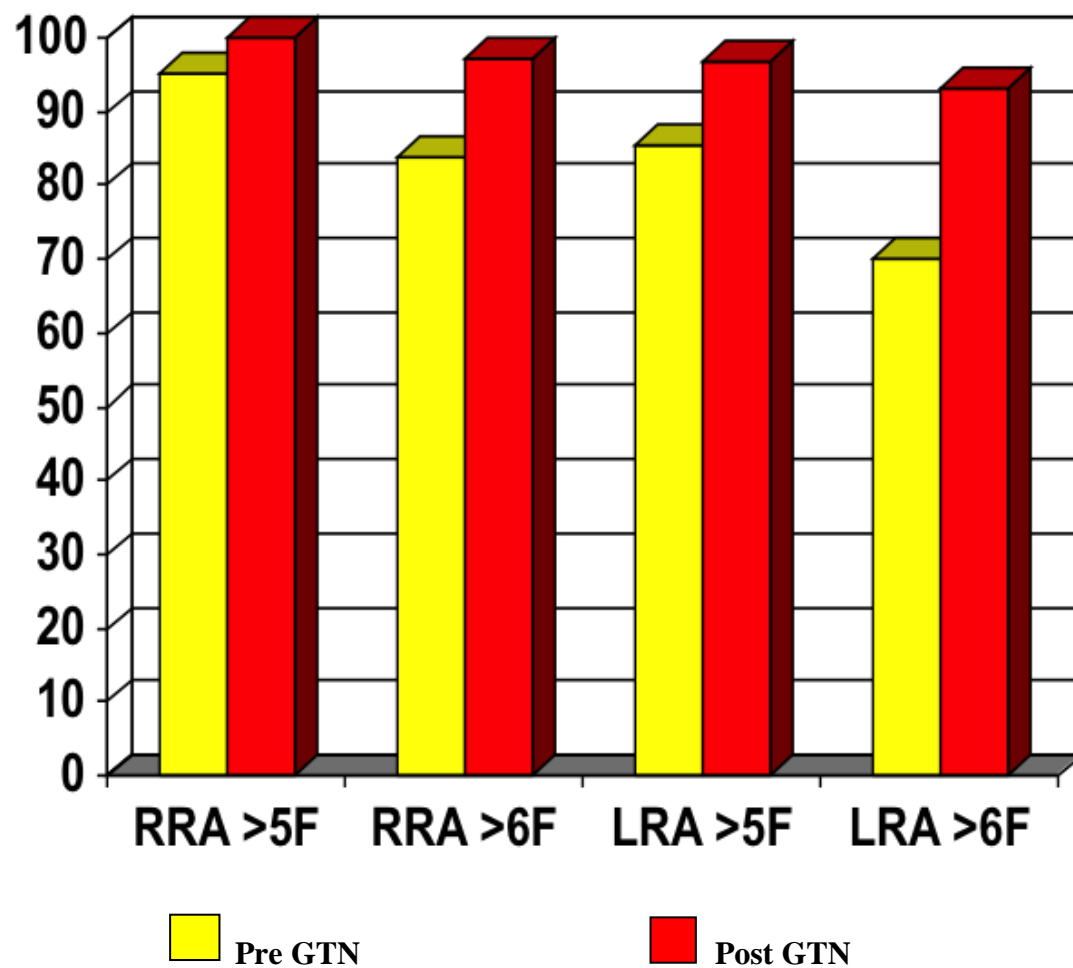
Figure 24b. Percentage of women with RRA and LRA diameters >2.28mm and >2.52mm, respective external diameters of 5F and 6F arterial sheaths.
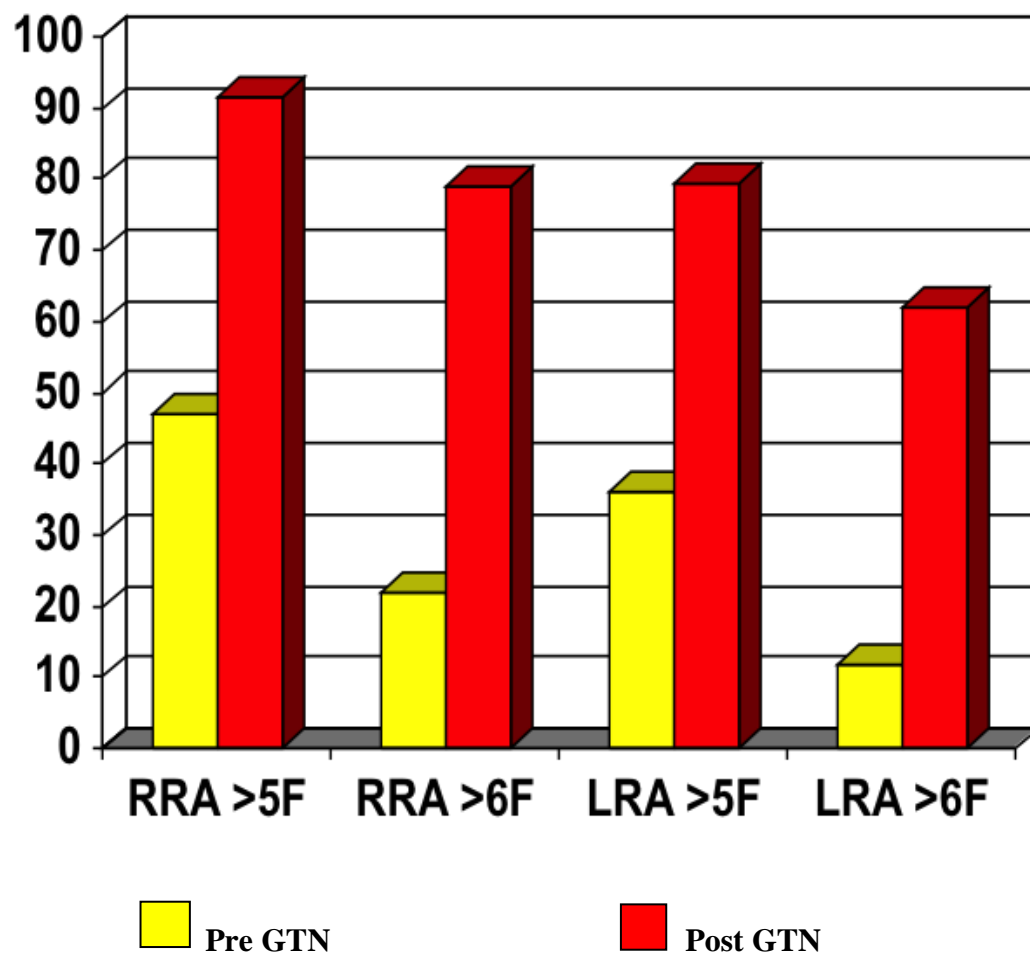
4.4 Discussion

The RA diameter plays an important role in the success of both arterial puncture and transradial cardiac procedures (120, 129, 130), especially during the learning curve. The mean RA diameter was shown to be 2.4±0.4mm in Japanese population (129), 2.6±0.4mm in Korean population (120) and 2.38±0.56mm in the Chinese population (131). Yan et al also measured the diameters of both left and right UA in the Chinese population, which were found to be of similar size to the RA (131). There are, however, limited data on the size of the forearm arterial system in the western population.

To the best of our knowledge, our study is the only study that examines all the forearm arterial diameters and the effect of S/L GTN in western population using doppler ultrasound scan. It shows that the RA is bigger than the UA, in contrast to conventional human anatomy teaching (132). One plausible explanation is that the proximal UA is bigger than proximal RA before it bifurcates to give off the Interrosseou artery, and the distal UA becomes smaller than the RA at around the wrist. A study of forearm arterial anatomy in 24 cadevars by Riekkinen shows that the mean diameter of the RRA was 28% larger than the RUA, and the LRA 26% larger than the LUA (133). Haerle et al, on the other hand, demonstrates that the RA and UA are of similar size at the wrist level between the Germans and the Americans (134).

We found that men have bigger RA and UA than women, and the RRA is bigger than the LRA in most men and women. More importantly, less than 50% and 22% of women have a RRA that is bigger than the external diameter of a 5 French and a 6 French sheath respectively. This is considerably lower for the LRA. Such proportion

in the Asian population would be even lower as the mean diameters of their RRA is significantly lower than that of our study. This increases to more than 90% and 80% respectively with sublingual GTN. The use of GTN also has the added benefit of reducing arterial spasm (in part due to vasodilatation), thus should make arterial cannulation and catheter manoeuvre easier. It also has the theoretical benefit of reducing the risk of RA occlusion, which is influenced by the ratio of the RA diameter and the external diameter of the sheath (135).

An interesting observation with S/L GTN was its effect on blood circulation to the hand. All the patients whom were found to have an unfavourable Allen's test at the start of the study had their Allen's test repeated after administration of S/L GTN. The test invariably became favourable, indicating a dynamic circulation that is recruitable.

In summary, the RA is significantly smaller in women than men, with the majority of RA in women smaller than the external diameter of a 5F sheath prior to GTN. The RA is normally bigger than the UA and the RRA bigger than the LRA in most men and women. Sublingual GTN increases the size of the RA significantly and should make puncturing the RA easier, thereby shortening part of the learning curve associated with the transradial technique. Use of RRA with administration of GTN prior to all transradial cardiac procedures is the best policy.

CHAPTER 5

RADIATION EXPOSURE AND

ACCESS SITE SELECTION

5.1 INTRODUCTION

Radiation exposure during cardiac procedures is an essential consideration in relation to patient and operator safety as no dose of radiation may be considered safe or harmless (136, 137). The transradial access is increasingly utilised to perform percutaneous diagnostic and therapeutic coronary procedures in simple and complex patient groups as a result of lower access site bleeding complications, improved post-procedural patient comfort, and economic benefits (47, 83, 84, 111, 138-140). In addition, recent observational trials demonstrate a reduction in mortality when radial access is employed for percutaneous coronary intervention (PCI) (67, 141). Procedural outcomes have been further evaluated in meta-analysis of randomised and observational trials confirming that radial access results in a reduction of major adverse events and death rate when compared to femoral access (95, 128). This data has lead to the recommendation that radial access is now the gold standard for cardiac procedures (142).

An important potential limitation of transradial access is an apparent increase in radiation exposure to both patient and operator when compared to transfemoral access (102, 139, 143-146). This is a significant issue, since cardiac procedures result in considerable radiation exposure for patients and operators (147-155), and a significant radial dependent increase would be detrimental. However, the existing published data has major methodological flaws (156, 157). The majority of the pre-existing studies were poorly controlled and the observed differences in radiation exposure could be accounted for by variation in operator experience, angiographic view selection, procedure complexity, and the radiation protection protocol used (158, 159). We therefore sought to measure radiation exposure to patients and operators according to

access site, whilst controlling for other variables that are known to influence radiation exposure.

5.2 METHODS

Study design

In this study we sought to eliminate the effect of non-access site related influences on patient and operator radiation exposure. To minimise the effect of variation in procedural complexity, we studied only patients with symptoms of limiting chest pain undergoing first time diagnostic angiography (CA) at the University Hospital of North Staffordshire (UHNS). In order to investigate the effect of variations in operator expertise, we compared the performance of expert and intermediate operators for both access sites.

An operator was defined as an expert if they had performed >2000 cases using their chosen access site, and used this default route for >90% of cases. An operator was defined as having intermediate experience if they had performed 500-1000 cases transfemorally and transradially and used each access site with equal frequency.

The primary aim of this study was to evaluate operator and patient radiation exposure during diagnostic CA according to the access site and operator experience. The secondary aims were to evaluate access site specific components of procedural duration, fluoroscopy time (FT) and time to ambulation.

Study population

One hundred patients undergoing first time diagnostic coronary angiography at UHNS were recruited into the study. The experienced transradial (JN) and transfemoral (MG) operators each performed 25 consecutive studies using their default approach while the intermediate operator (TSL) performed 25 consecutive transradial studies followed by 25 consecutive transfemoral studies.

Procedures

Patients walked into the catheterisation laboratory and were positioned supine on the catheterisation table. The puncture area was cleaned with antiseptic and standard sterile drapes positioned. Following instillation of local anaesthetic a vascular sheath was positioned in the selected artery via a standard Seldinger technique. For transradial cases a transparent adhesive dressing was applied to limit sheath movement during catheter exchanges and a vasodilator/anticoagulant cocktail was administered. Image aquisition was performed on a digital single-plane cineangiography unit with an undertable X-ray tube (Integris, Phillips Medical Systems, Eindhoven, Netherlands) using a film speed of 12.5 frames/second. Left ventriculography was performed in all cases, using a film speed of 25 frames/second. All procedures were performed using 5 French catheters that were 100cm in length. For the transfemoral approach standard Judkins and angled pigtail catheters were utilised. For the transradial approach a hybrid catheter (Tiger II catheter, Terumo Corporation, Tokyo, Japan) was used for coronary angiography with an angled pigtail for left ventriculography.

A standardised sequence of views of the coronary arteries and left ventricle was performed for each procedure. Five standard views were performed for the left coronary system: left anterior oblique (LAO) 45º, LAO 45º cranial 30º, right anterior oblique (RAO) 45º cranial 30º, RAO 45º, and postero-anterior (PA) caudal 30º. Three standard views were performed for the right coronary system using LAO 45º, PA cranial 30º and RAO 45º. Left ventriculography was performed in RAO 45º alone.

After acquiring the images, radial sheaths were removed immediately and a compression device was applied to obtain haemostasis (TR band, Terumo Corporation, Tokyo, Japan). The radial patients then mobilised immediately and walked from the table to the recovery area. The transradial patients were then encouraged to mobilise immediately within the recovery area. Following image acquisition the femoral patients were moved to a trolley which was transferred to the recovery area. The femoral sheath was removed and haemostasis secured by manual pressure, followed by four hours bed rest prior to mobilisation.

Radiation protection

An optimised radiation protection protocol was employed by all operators. This included a standard 2-piece lead apron and a thyroid shield worn by each operator. Under-table leaded flaps attached to the table and a transparent leaded glass suspended from the ceiling (both 0.5mm lead equivalent) were utilised by each operator in all procedures. For the transradial procedures, the patient's right arm was fully adducted, after the radial sheath was inserted. Conventional measures such as maximising the operator's distance from the radiation source and minimising the field of view were applied in all cases.

Measurements and data collection

Operator effective dose (ED, as μSv) was assessed using an electronic personal dosimeter (EPD) incorporating a silicon diode (Figure 25) worn by each operator outside the protective lead apron just under the left clavicle. The EPD is highly sensitive and has the ability to register radiation doses as low as 0.1 μSv. Patient radiation exposure was assessed using the diamentor on the X-ray tube and expressed as dose area product (DAP as $Gy.cm^2$). Fluoroscopy time (FT) was defined as the total screening time of the procedure. Procedural duration was defined as the time elapsed (in minutes) from local anaesthetic infiltration to removal of the last catheter upon completion of the procedure. Time to ambulation was defined as the time elapsed (in minutes) from sheath removal to patient ambulation.

Statistical analysis

The distribution of continuous data was determined using the 1-sample Kolmogorov-Smirnov test. Normally distributed data (presented as mean ± 1 standard deviation [SD]), and non-parametric data (as median and inter-quartile range [IQR]) were compared using the Student's t test and Mann-Whitney U test respectively. Categorical data were presented as absolute values and percentages and compared using the Chi-Square test. Both univariate and multivariate regression analyses were used to examine potential correlation between continuous variables. A p value of <0.05 was considered to be statistically significant.

Figure 25. Electronic personal dosimeter

5.3 RESULTS

Patient characteristics

100 consecutive patients undergoing elective coronary angiography comprised the study population. Baseline patient characteristics are detailed in Table 12. The patients investigated by the radial expert operator were significantly older than those investigated by the femoral operator, but all other patient characteristics were similar.

Radiation exposure and procedural data per access route and operator experience

Primary endpoint: Radiation exposure

For procedures performed by the intermediate operator, there were no significant differences in radiation exposure to either the operator or patients according to access site (Table 13b). Similarly, there were no statistically significant differences in radiation exposure according to access site for the procedures performed by the expert operators (Table 13a). Operator and patient radiation doses were, however, significantly increased when comparing the intermediate operator to the expert operators for both radial and femoral access sites (table 13e & 13f).

Secondary endpoint: Procedural duration, fluoroscopy time and time to ambulation per access route and operator skill level

Procedural duration was prolonged in both transradial groups as compared to the respective transfemoral group (Table 14). The intermediate operator recorded larger procedure durations than the expert operators for both access sites. There was, however, no difference in FT according to access site at either experience level. The

time to ambulation was significantly longer among patients undergoing transfemoral

procedure (Table 13a-13b).

Table 12. Patient characteristics

	Radial expert operator (n=25)	Femoral expert operator (n=25)	P value	Radial intermediate operator (n=25)	Femoral intermediate operator (n=25)	p value
Male (%)	68	64	NS	72	68	NS
Age (years)	69.8±7.4	61.4±11.2	0.003	67.4±8.3	66.1±7.7	NS
Weight (kg)	81.6±13.7	87.5±17.4	NS	75.5±9.2	76.5±7.7	NS
Height (m)	1.68±0.09	1.68±0.11	NS	1.7±0.07	1.69±0.08	NS
BMI	28.7±3.2	30.9±5.8	NS	26.1±2.6	26.8±2.4	NS
Hypertension (%)	56	48	NS	60	52	NS
Diabetes (%)	24	20	NS	20	20	NS
CAD	32	28	NS	24	28	NS

BMI: body mass index
CAD: coronary artery disease

Table 13: Comparison of radiation and procedural data per skill level.
ED: effective dose; DAP: dose area product; FT: fluoroscopy time

Table 13a. Radial expert Vs femoral expert

	Radial expert (n=25)	Femoral expert (n=25)	P value
Operator ED (μSv)	6.4±4.7	6.1±5.6	0.85
Patient DAP (Gy.cm^2)	21.7±6.5	22.4±8	0.74
Procedure duration (min)	10.4±2.7	7.3±2.3	<0.001
FT (min)	1.9±0.9	1.7±1.5	0.69
Time to ambulation (min)	7.2±2.9	257.2±31.5	<0.0001

Table 13b. Radial intermediate Vs femoral intermediate

	Radial intermediate (n=25)	Femoral intermediate (n=25)	P value
Operator ED (μSv)	8.8±4.3	8.5±6.5	0.86
Patient DAP (Gy.cm^2)	25.4±4.8	25.2±8.3	0.90
Procedure duration (min)	13.6±2.7	11.3±3.2	0.12
FT (min)	2.4±0.9	2.2±1.2	0.39
Time to ambulation (min)	8.0±2.7	255.3±40.1	<0.0001

Table 13c. Radial expert Vs femoral Intermediate

	Radial expert (n=25)	Femoral intermediate (n=25)	P value
Operator ED (μSv)	6.4±4.7	8.5±6.5	0.14
Patient DAP (Gy.cm^2)	21.7±6.5	25.2±8.3	0.68
Procedure duration (min)	10.4±2.7	11.3±3.2	0.093
FT (min)	1.9±0.9	2.2±1.2	0.235
Time to ambulation (min)	7.2±2.9	255.3±40.1	<0.0001

Table 13d. Radial intermediate Vs Femoral expert

	Radial intermediate (n=25)	Femoral expert (n=25)	P value
Operator ED (μSv)	8.8±4.3	6.1±5.6	0.002
Patient DAP (Gy.cm^2)	25.4±4.8	22.4±8	0.41
Procedure duration (min)	13.6±2.7	7.3±2.3	0.001
FT (min)	2.4±0.9	1.7±1.5	0.001
Time to ambulation (min)	8.0±2.7	257.2±31.5	<0.0001

Table 13e. Radial Expert Vs Radial intermediate

	Radial expert (n=25)	Radial intermediate (n=25)	P value
Operator ED (μSv)	6.4±4.7	8.8±4.3	0.36
Patient DAP (Gy.cm^2)	21.7±6.5	25.4±4.8	0.12
Procedure duration (min)	10.4±2.7	13.6±2.7	0.001
FT (min)	1.9±0.9	2.4±0.9	0.014
Time to ambulation (min)	7.2±2.9	8.0±2.7	<0.0001

Table 13f. Femoral expert Vs femoral intermediate

	Femoral expert (n=25)	Femoral intermediate (n=25)	P value
Operator ED (μSv)	6.1±5.6	8.5±6.5	0.29
Patient DAP (Gy.cm^2)	22.4±8	25.2±8.3	0.138
Procedure duration (min)	7.3±2.3	11.3±3.2	0.001
FT (min)	1.7±1.5	2.2±1.2	0.003
Time to ambulation (min)	257.2±31.5	255.3±40.1	0.91

119

Table 14. Comparison of radiation and procedural data per skill level.

	Radial expert (n=25)	Femoral expert (n=25)	Radial intermediate (n=25)	Femoral intermediate (n=25)
Operator ED (µSv)	6.4±4.7	6.1±5.6*	8.8±4.3*	8.5±6.5
Patient DAP (Gy.cm^2)	21.7±6.5	22.4±8	25.4±4.8	25.2±8.3
Procedure duration (min)	10.4±2.7$^{\#}$	7.3±2.3	13.6±2.7$^{\#}$	11.3±3.2$^{\#}$
FT (min)	1.9±0.9$^{\#\#}$	1.7±1.5	2.4±0.9$^{\#\#}$	2.2±1.2$^{\#\#}$
Time to ambulation (min)	7.2±2.9$^{\#\#\#}$	257.2±31.5	8.0±2.7$^{\#\#\#}$	255.3±40.1

ED: effective dose; DAP: dose area product; FT: fluoroscopy time

*   radial intermediate significantly greater than femoral expert only (p=0.002)
\#   all significantly longer than femoral expert (p<0.001)
\#\#   all significantly longer than femoral expert (p<0.01)
\#\#\#   radial procedures significantly shorter than femoral procedures (p<0.0001)

Table 15. Studies comparing radiation exposure in transfemoral and transradial cardiac catheterisation.

Reference	Femoral Artery				Radial Artery			
	N	DAP (Gy.cm^2)	FT (min)	Operator Rad Exp (µSv)	N	DAP (Gy.cm^2)	FT (min)	Operator Rad Exp (µSv)
Mann(143), 1996 - PCI	126			8.8	138			13.5
Larrazet(160), 2003 - ad hoc PCI	184	138	12		218	175	17	
Sandborg(144), 2004 - CA	40	38±22	4.6±4		36	51±25	7.5±4	
- CA + PCI	42	47±34	12.5±9		24	75±47	18.4±9	
- All	82	43±29	8.6±8		60	61±37	11.9±9	
Geijer(161), 2004 - PCI	114	69.8	16.4		55	70.5	18.1	
Lange(145), 2006 - CA	103	13.1±8.5	1.7±1.4	32±39	92	15.1±8.4	2.8±2.1	64±55
- PCI	48	51±29.4	10.4±6.8	110±115	54	46.3±28.7	11.4±8.4	166±188
Brasselet (146), 2008 - CA	181	(µSv) 37.5	2.3	13.0	239	(µSv) 59.0	4.5	29.0
- ad hoc PCI		103	7.0	41.0		125.5	10.0	69.5

DAP = dose area product; FT = fluoroscopy time; RAD Exp = radiation exposure, CA – coronary angiography, PCI – percutaneous coronary intervention.

5.4 DISCUSSION

There are limited published data directly comparing radiation exposure associated with transradial and transfemoral approaches [Table 15] (102, 139, 143-146, 160). There is a trend to increased fluoroscopy time and higher radiation exposure in association with the use of radial access. However, all but one of these are small, non-randomised observational studies, and with limited control of the patient, operator and equipment variables which could affect radiation exposure independent of vascular access site.

This study is the first to attempt to isolate and investigate the role of access site selection in radiation exposure during cardiac procedures whilst tightly controlling for other potential confounding variables. Our data indicates that when other variables are controlled for, transradial access is not associated with an increase in fluoroscopy time or radiation exposure to operators or patients. We have shown a small (2 to 3 minute) increase in on table procedure duration for transradial cases. Following this patients mobilise immediately and are self-caring. As reported in previous studies patients investigated by transfemoral access require considerably more aftercare and mobilisation is delayed for several hours. For both access sites, the intermediate operator recorded a 25-30% increase in operator radiation exposure, and a 10-15% increase in patient radiation exposure when compared to the expert operator, reflecting a learning curve effect for both access sites.

The design of our study was dictated by the need to isolate the potential independent effect of access site selection on radiation exposure. We also aimed to investigate the effect of variation in operator expertise by comparing results for expert and

intermediate level operators. In a study of this nature, a randomised design is usually preferable. This would require operators equally skilled in performing procedures from both access sites. In our institution the expert operators use their default access site almost exclusively, and so have limited expertise in the alternative site. This is a common pattern in contemporary practice. Randomising cases for an operator who is a high volume operator in one access site, but only an occasional user of the other access site, could generate erroneous results due to the effect of differing levels of expertise. We therefore chose to study and compare consecutive cases performed by our expert operators to minimise the potential confounding effect of this variable.

We also set out to investigate results for intermediate level operators in both access sites. To do this we needed to compare an operator trained to an intermediate level in both transradial and transfemoral procedures. Our interventional fellow (TSL) had been trained in the use of both access sites from early in his catheterisation training and regularly used both access sites in routine practice, therefore providing an ideal subject for this section of the study. By comparing his results with those of the expert operators we were able to identify and quantify expertise related effects for both access sites. The patient characteristics of our study groups were well balanced, with the only significant difference relating to a small increase in mean age in the radial expert group. The potential confounding effects of height, weight and BMI are therefore minimised, and the small difference in age in one group is unlikely to generate major patient related differences in radiation exposure.

The transradial learning curve has previously been studied in detail (42, 110). Louvard *et al* reported procedural failure of 10% in the first 50 cases, improving to 3-

4% after 500 cases and stabilises at less than 1% after performing more than 1000 cases (42). Based on Louvard's data, we selected expert operators whose procedural experience would limit the effects of the learning curve and an intermediate operator who had completed the most difficult early part of his learning curve. This is in contrast to the majority of published studies where the radial operators typically have only performed 50-200 transradial cases and are compared with highly experienced transfemoral operators (162, 163). In these studies, learning curve effects may have had a major influence on results leading to misleading high values for transradial related radiation exposure when relatively inexperienced transradial operators were compared to expert transfemoral operators.

A unique feature of our study was the strict control of other variables including angiographic view selection and procedural complexity, which influence radiation exposure to the patient and the operator (136, 144, 164-170). It is therefore, an accurate, like-for-like comparison of variation in radiation exposure during diagnostic coronary angiography performed via both access sites utilising current best practice. Radiation data (for both transradial and transfemoral routes) from our study compare favourably to the data published by Brasselet *et al* (146) and Lange *et al* (145), both of whom reported considerably higher fluoroscopy times, patient and operator radiation exposure values. For example, the operator radiation exposure doses reported by Brasselet *et al* (146) were approximately 2- and 4-fold higher than those of our trainee and experienced radial operators respectively. Similarly, the doses reported by Lange *et al* (145) were 6- and 10-fold higher. This inter-study variation in radiation exposure may be explained by differences in patient-related factors (e.g. body mass index, procedural complexity), and procedure-related factors (e.g. operator

expertise, operator fatigue, equipment performance, acquisition duration, and training and supervision in radiation-reducing techniques), which were uncontrolled for. In addition, our study reports results derived from contemporary transradial practice. The data on transradial access in previous studies was generated at a point in time when transradial equipment and technique was at an earlier stage of development. In contemporary practice, many procedural refinements have improved outcomes and simplified the procedure (138). Contemporary operators are now well informed about issues such as forearm anatomical variations (171) and radial specific catheters (such as the Tiger catheter) have been designed to facilitate rapid simple coronary cannulation (172). Therefore contemporary transradial operators would be expected to have improved performance compared with historical controls.

To date, the study by Lange *et al (145)* is the only randomised study comparing operator and patient radiation exposure utilising experienced radial and femoral operators. Although they reported significantly higher radiation exposure to the transradial operator, there was no difference in the patients' radiation exposure for either route. As operator radiation exposure is largely a result of back-scatter radiation, such discrepancy in radiation exposure could be attributed to a difference in application of radiation shielding devices. Close scrutiny of the methods in this study reveals that the transfemoral operator had additional radiation shielding (7" protective shield flap attached onto the table) that was not used by the transradial operator. Consequently, it was not surprising that their transradial operator received a significantly higher radiation exposure. This is in keeping with Mann *et al* who demonstrated a significant reduction in radiation exposure for a transradial operator over a transfemoral operator could be achieved with the use of additional shielding

(143). More recently, the transparent lead glass screen has also been shown to reduce operator eye dose by 19-fold (173), although correct positioning of the lead glass screen is of crucial importance. Thus the suboptimal radiation protection protocol employed by the transradial operator in the Lange study greatly diminishes the reliability of the results.

Our study demonstrated that transradial procedure duration is minimally prolonged compared to transfemoral cases. This is a reflection of the need for additional procedural manoeuvres in transradial cases compared to transfemoral procedures. These include administration of intra-arterial vasodilators and heparin following sheath insertion, application of adhesive dressings to secure the arterial sheath, and reposition of the arm to facilitate optimal radiation protection. The differences in procedure duration and FT between the intermediate and expert operators also served to show that a learning curve still exist for both the transradial and transfemoral approach. It should be emphasised that our procedure duration did not include the time elapsed from sheath removal to haemostasis. If such duration were included, the total procedure duration for both procedures would have been similar.

We also demonstrated that the time to patient ambulation is markedly reduced for transradial procedures. After an elective transradial procedure patients normally mobilise and ambulate immediately to encourage overall well-being and normality. This results in improved patient comfort, a lower work-load for nursing staff (174), and a faster turnover of patients undergoing procedures. These factors will yield potential advantages in institutional efficiency and economy. Furthermore, these same factors, when allied with the established reductions in access site-related bleeds,

support a case for day-case coronary intervention in suitable individuals, which will enhance the economic gains.

Limitations

This was a non-randomised study, but the study design was specifically tailored to the requirements of our objective. Femoral closure devices were not used. Although these reduce time to ambulation in transfemoral cases, there is a device related increase in cost and they do not have a proven effect on complications rates (175). The numbers studied were relatively small, and our findings require confirmation in a larger data set. We have not studied operators with limited expertise (less than 500 cases) but our data and pre-existing literature suggests that learning curve effects would lead to higher values for FT and radiation exposure for these operators and for both access sites. Our study was confined to diagnostic coronary angiography only. We have previously performed observational studies on single and multi vessel PCI in our institution, and demonstrated no increase in FT or radiation exposure in radial cases (176) suggesting that the results of the present study can be extrapolated to interventional cases.

In summary, transradial diagnostic coronary angiography is not associated with higher radiation exposure to the operator or the patient compared to the transfemoral route when performed by operators of similar experience employing contemporary technique and meticulous radiation protection measures. The time required to patient ambulation is markedly reduced following a transradial procedure. Procedures performed by operators with lower levels of experience generate higher radiation exposure regardless of which access site is employed. Careful attention to radiation

monitoring and protection is required when trainees perform even relatively simple

procedures such as coronary angiography.

CHAPTER 6

APPLICATION OF RADIAL ARTERY ACCESS

IN TWO HIGH RISK PATIENT SUBGROUPS

6.1 INTRODUCTION

As the radial approach for cardiac catheterisation has been shown to be safe and effective with minimal vascular access site complications compared to the femoral approach (46, 95), such technique is therefore intuitively suited for patients with high bleeding risk. There are currently limited data on the use of transradial approach in high risk patient subgroups especially if these patients are unstable. Transfemoral approach remains the preferred route in such patients despite being associated and responsible for at least two thirds of the bleeding complications that occur in patients with acute coronary syndrome managed by invasive strategy (88, 177, 178). This is mostly a result of the common belief that the transradial approach requires a specific skill set which further increases the procedure complexity of such patients thereby adversely affecting their outcome.

This chapter comprises of two studies that aim to evaluate the safety and feasibility of utilising the radial access site in the following two high risk patient subgroups: -

(1). Patients undergoing rescue angioplasty after failed thrombolytic treatment for acute ST segment elevation myocardial infarction, and

(2). Patients undergoing left and right heart catheterisation without termination of their warfarin therapy.

6.2 STUDY 1: TRANSRADIAL RESCUE ANGIOPLASTY

6.2.1 Introduction

Intravenous thrombolysis remains the treatment of choice in most countries for patients presenting with an acute ST segment elevation myocardial infarction. The

incidence of failure to reperfuse is reported to be between 30% and 50% and is associated with an adverse prognosis (179). For these patients with reperfusion failure, rescue percutaneous coronary intervention (PCI) can be used, but major access site bleeding is a risk with the femoral approach. Although percutaneous coronary intervention (PCI) via the radial artery route has been established as a safe access site in stable patients with low rates of neurovascular complications, little data is available on transradial rescue angioplasty. We assessed the procedural and clinical outcomes of patients treated with transradial rescue angioplasty for failed thrombolysis at two institutions performed by two radial operators between April 1999 and March 2005.

6.2.2 Methods

Patient selection

A transradial program for PCI including rescue angioplasty has been instituted at the University Hospital of North Staffordshire since September 1998 (47) and at the Brighton and Sussex University Hospital since December 2001. Patients presenting with myocardial infarction within 12 hours of the onset of chest pain and evidence of failed reperfusion have usually been treated with rescue angioplasty, via the radial approach if under the care of JN/DHS (Dr James Nolan and Dr David Hildick-Smith). The technique employed has previously been described in detail (180). One hundred and five consecutive patients' data collected prospectively from the two centres were analysed retrospectively.

Patients received 5000-10,000 units of intravenous heparin at the start of the procedure. Clopidogrel and Aspirin were given in all patients who had a stent

procedure. Used of abxicimab (Reopro) was left to operator assessment of risk of bleeding and presence of heavy thrombus load. The femoral route was reserved for intra-aortic balloon pump (IABP), temporary pacing wire (TPW) or Swan-Ganz (SG) catheter insertion.

Patient and procedural data were prospectively collected and during a follow up period of 11±8 months. Acute myocardial infarction was diagnosed on the basis of typical chest pain lasting more than 30 minutes and associated with new electrographic changes (1mm elevation in 2 contiguous limb leads or 2mm elevation in 2 contiguous precordial leads). Failure to reperfuse was diagnosed based on previously described ECG criteria of failure of the ST segment elevation to fall by more than 50% in the lead with maximum elevation at 90 minutes following thrombolytic treatment (181). The chest pain to thrombolysis time and the thrombolysis to PCI time were recorded in all patients. Procedural duration was defined as the time elapsed from entering the catheterization laboratory to leaving the laboratory.

6.2.3 Results

Patients' characteristics and clinical outcomes are shown in Table 16. The patients were relatively young, predominantly male and had sizeable infarct with peak creatine kinase of 2823±1734 (706-6890) IU. Ten patients (9.5%) were in cardiogenic shock requiring IABP support. The mean time from chest pain to thrombolysis was 155±134 (10-685) minutes and mean time from thrombolysis to arrival in the catheterization laboratory was 221±139 (110-680) minutes. Forty nine patients (47.6%) received Streptokinase and 53 patients (52.4%) received Alteplase, Reteplase or Tenecteplase.

Radial artery cannulation failed in only 1 patient who had the procedure completed via the right brachial artery (femoral access precluded due to peripheral vascular disease). At initial coronary angiogram, 91 patients (86.7%) had absent or reduced flow in the infarct-related artery. Sixty two patients (59%) had single vessel disease and 8 patients (7.6%) had significant left main stem disease (LMS). Procedural success (TIMI 3 flow and < 30% residual stenosis) was achieved in 93 patients (88.6%). Eight patients (7.6%) had no-reflow phenomenon although one of them had a repeat procedure the next day and was successful with the use of Angiojet device.

Stents were deployed in 99 patients (94.3%) with a mean stent of 1.4±0.7. Abciximab was used in 37 patients (35.2%). The mean procedural duration was 60±22 (23-133) minutes and mean screening time was 11.7±7.2 (3-32) minutes. Overall mortality was 7.7% (8 patients). Of these, five patients died in hospital, all related to cardiogenic shock. Three patients died during post-discharge follow up. Two of the late deaths were non-cardiac, the other was a sudden death in a patient who had presented in cardiogenic shock. Of the two non cardiac deaths, one died 3 months after discharge from aggressive metastatic small cell carcinoma of the lung, the other died from acute subarachnoid haemorrhage diagnosed on post mortem. Other MACE rates (10.5%) were accounted for by target vessel reinfarction or reintervention and CABG. Unusually, there were no follow up target vessel reinfarction or reintervention.

Table 16. Patients characteristics and clinical outcomes for rescue PCI

Baseline charecteristics	No.	%
Male	90	85.7
Female	15	14.3
Age in years: mean±SD and range	60.7±11	37-85
History of angina/MI	36	34.3
History of peripheral vascular disease	8	7.6
Pain to lysis time (mean±SD minutes)	155±134	
Lysis to PTCA time (mean±SD minutes)	221±139	
AMI location		
Anterior	49	47.0
Inferior	56	53.0
Peak CK (mean±SD)	3105±1536	
Cardiogenic shock	10	9.5
Stents	99	94.3
GP2a3b use	37	35.2
IABP	14	13.3
Procedural success	93	88.6
Length of stay (days) (Mean±SD)	7±2	

Bleeding complications

There were no radial access vascular complications. Significant gastrointestinal bleeding requiring transfusion occurred in three patients (2.9%). There were four (3.8%) non-radial vascular access site haematoma. One was a haematoma in the patient who required brachial access and the others were femoral haematoma post IABP insertion, none of which required transfusion.

6.2.4 Discussion

Although thrombolytic therapy has long been shown to reduce mortality in patients with acute ST segment elevation myocardial infarction (182, 183), 90-minute TIMI 3 flow is only achieved in 50% of patients with a standard single fibrinolytic agent (184, 185). Adjunctive use of Abciximab with Reteplase may increase this to 70%. Primary percutaneous coronary intervention (PCI) on the other hand, restores TIMI 3 flow in 85% to 95% of patients (186, 187) but is not widely available in most

countries. The Primary Angioplasty in Myocardial Infarction (PAMI-1) trial showed that primary PCI is beneficial for high risk patients (188, 189). Patients with failure to reperfuse have also been shown to have a much worse prognosis (190). TIMI 0/1 flow combined has a 30-day mortality of 8.8 % compared to 3.7% with TIMI 3 flow (191).

An overview of the available data from early randomised trials and registries suggests that rescue PCI reduces the rate of adverse cardiac events after failed thrombolysis particularly in patients with a large infarction (75, 192). The most recently published randomised trials of rescue PCI (MERLIN and REACT) also show some beneficial effects on cardiac events (76, 77). This benefit is partially offset by a high rate of vascular complications when femoral access is employed. The reported rate of major femoral vascular complications ranges from 4-36%, with most studies reporting rates of around 10% (75-77).

Co-administration of Abciximab increases the femoral complication rate further. These major femoral complications often required transfusion or vascular intervention which increases the patients duration of hospitalization, costs and mortality. This high rate of femoral complications is therefore a major drawback of transfemoral rescue PCI, and offsets much of the beneficial effect on reduction of adverse cardiac events. We have previously reported that transradial access is highly effective in reducing vascular complications in stable elective patients (47). We have also studied transradial access in anticoagulated patients, reporting a similar low rate of vascular complications in patients with an INR > 2 (73). In this study of transradial rescue PCI patients we encountered no radial access site complications despite one third of the patients receiving additional Glycoprotein IIbIIIa inhibitor therapy. Although

important vascular complications such as compartment syndrome complicating a large forearm haematoma can occur as a result of radial access, these are very rare and did not occur in this small series despite the intensive antithrombotic regime employed. These results extend our previous investigations into this high risk subgroup, and indicate that transradial access is a safe and effective means of preventing vascular access complications in rescue PCI patients.

The data from this study is compatible with the only other published small study of transradial rescue PCI. Kassam et al (80) reported similar outcomes in their 45 transradial rescue PCI patients, with a 95% rate of successful radial cannulation and a 0% radial access site complication rate despite 100% usage of Glycoprotein IIbIIIa inhibitors. They also reported no increase in procedural duration, radiation exposure or equipment use for radial procedures when compared to a transfemoral group.

6.3 STUDY 2: PERCUTANEOUS LEFT AND RIGHT HEART CATHETERISATION IN FULLY ANTICOAGULATED PATIENTS

6.3.1 Introduction

Left and right heart catheterization remains the "gold standard" for accurate diagnosis in many cardiac conditions. For most patients it can be safely performed via a percutaneous femoral artery and vein approach (femoral approach) as a day case procedure with minimal risk. In some patients significant access site complications such as large haematoma, pseudoaneurysm or arterio-venous fistula formation occur, particularly when procedures are performed in anticoagulated patients (193). These risks can be reduced by temporary discontinuation of anticoagulants, and the European Society of Cardiology currently recommends that

the International Normalised Ratio (INR) should be <1.8 prior to femoral artery puncture(194).

For patients receiving oral anticoagulants, reducing the INR significantly increases the risks of local or systemic procedure related thromboembolic events (195). Thromboembolic risk is particularly high in patients with concomitant poor left ventricular function, atrial fibrillation, diabetes, or prosthetic heart valves (194, 195). In an effort to reduce this risk many patients are admitted to hospital prior to their procedure to allow careful monitoring of the INR while oral anticoagulation is withheld, with conversion to heparin (subcutaneous injection or intravenous infusion) to cover the period of thromboembolic risk. The experience of heparin used during pregnancy in women with prosthetic valves suggests that it is less effective than oral anticoagulation in the prevention of thromboembolism (194).

In keeping with this, even with careful monitoring and diligent conversion to heparin, thrombo-embolic complications, fulminant valve thrombosis and death have been reported with this regime (196). Left and right heart catheterization from the femoral approach in patients who require oral anticoagulants is thus not a simple day case procedure, and is associated with a considerable risk of bleeding, thromboembolism, increased hospital stay and costs.

Left heart catheterization from the radial artery was initially developed as a solution to the bleeding complications encountered with the anticoagulation regimes utilized in early coronary stent programs (72). This technique reduces the risk of serious bleeding complications, minimizes hospital stay and has been widely applied to

diagnostic and interventional procedures (47, 72). The first human right heart catheterization was reported by Forssman, who used a surgical cut down to canulate his own antecubital fossa vein in 1929 (197). Subsequent to this, percutaneous puncture of antecubital fossa veins to permit right heart catheterization has been well described. This obviates the need for surgical exploration and minimizes the risk of central venous cannulation (198-200).

The first reported right and left heart catheterisation from the arm in modern time was performed by accident when attempting a transradial left heart catheterisation (201). Such an approach has been shown to be technically feasible and has many of the same benefits that transradial arterial catheterisation offers (201). Anticoagulated patients are thought to be good potential candidates in view of the low incidence of access site vascular complications with this technique, but there are currently no data with this approach on this high risk patient subgroup. Our study aims to examine the safety and feasibility of performing left and right heart catheterization from the arm without interruption of oral anticoagulation therapy.

6.3.2 Methods

Study subjects

A catheterization programme utilizing transradial access for diagnostic and interventional cardiac procedures was instituted at the University Hospital of North Staffordshire in September 1998 and at the Brighton and Sussex University Hospital in December 2001. Patients on oral anticoagulant therapy who required elective right and left heart catheterization had the procedures performed via an arm approach unless contraindicated. Contraindications for an arm approach, both absolute and

relative, include unfavourable Allen's test, no palpable antecubital fossa veins, flexure deformity at the elbow, patients on haemodialysis and INR greater than 5.0. Data on consecutive non-anticoagulated patients who underwent a conventional percutaneous femoral approach during this time period were collected for comparison. The procedures were performed or supervised by consultants experienced in both transradial and transfemoral procedures (JN, DHS). All procedures were performed without sedation, under local anaesthetic and as day cases.

Vascular puncture and catheterisation technique

The anticoagulated patients were admitted to the cardiac catheter laboratory and prepared as for a standard right radial artery cardiac catheterisation (202, 203). The wrist and the antecubital fossa were cleaned with disinfectant (Chlorhexidine). Standard femoral drapes were employed with the additional puncture access point positioned over the antecubital fossa. A tourniquet was applied to the upper arm (away from the disinfected area), an antecubital fossa vein identified by palpation, and percutaneous puncture performed. A Seldinger technique was employed to insert a 6F sheath into the vein before the tourniquet was removed. The radial artery was then punctured and a 5F or 6F sheath inserted (Figure 26). Cannulation of the right heart was performed using a 6F Multipurpose A1 (MPA1) end hole catheter over a 0.035J shaped guide wire. Measurements of right sided pressures and oxygen saturations were obtained. Left heart catheterization, coronary angiography, and pressure measurements were performed via the radial artery as previously described (202, 203). In the non-anticoagulated patients 6F sheaths were positioned in the femoral artery and vein using a standard Seldinger technique. Pressure, oxygen saturation and angiographic data were obtained using MPA1, Judkins and pigtail catheters.

Figure 26. Right radial arterial sheath and right antecubital fossa vein sheath after insertion.

Haemostasis technique and postprocedural management

In the anticoagulated patients both the arterial and venous sheaths were removed at the conclusion of the procedure before leaving the catheter laboratory. A RadiStop (Radi Medical Systems, Uppsala, Sweden), a customized unilateral compression device designed specifically for transradial procedures, was employed for 4 hours to achieve arterial haemostasis. A pressure bandage was used for 2-4 hours to achieve venous haemostasis. The patients were allowed to mobilise immediately after leaving the catheter laboratory and were discharged after four hours observation. In the non-anticoagulated patients, the femoral sheaths were removed at the conclusion of the procedure in the recovery area. Haemostasis was achieved by direct manual

pressure to both puncture sites. A four hour period of bed rest was employed to minimize the risk of early re-bleeding. Patients were then mobilized and discharged after a further two hours. Procedure duration was defined as the time elapsed from patient entry to exit from the catheter laboratory. Fluoroscopy time, total patient radiation exposure from the in room diamentor reading and any procedure related complications were recorded for each patient.

6.3.3 RESULTS

A total of 59 patients were recruited, comprising 28 anticoagulated patients and 31 non-anticoagulated patients. Baseline patient characteristics in the two groups are outlined in Table 17. There were no significant differences in baseline characteristics between the two groups, apart from an INR of 2.5 ± 0.5 on the day of the procedure in the anticoagulated patients. The principal indication for left and right heart catheterization related to evaluation of valvular heart disease (48 patients, 81% of the study group) with a small proportion (19%) performed for evaluation of atrial septal defects (7 patients) or unexplained left ventricular dysfunction (4 patients). The commonest reason for chronic oral anticoagulation was the presence of atrial fibrillation (25 patients) with the remaining three patients receiving therapy for severe heart failure or mural thrombus.

Table 17. Baseline patient characteristics for left and right heart catheterisation

Characteristics	Percutaneous Arm approach (n=28)	Percutaneous Femoral approach (n=31)	P value
Age in years	60±12	63±14	NS
M:F ratio	13 : 15	16 : 15	
Weight (kg)	79.3±16	83.5±18	NS
Height (cm)	168±15	170±16	NS
BMI	27.2±7.5	29.4±6.5	NS
INR	2.5±0.5	1.1±0.1	P<0.005
Indications for procedure			
Mitral valve disease	17 (61%)	20 (65%)	NS
Aortic valve disease	6 (21%)	5 (16%)	NS
Heart failure	2 (7%)	2 (6%)	NS
Septal defect	3 (11%)	4 (13%)	NS

(mean±SD or number of patients and percentage of group)

Procedural data in the two patient groups is detailed in Table 18. There were no contraindications to a percutaneous arm approach in the anticoagulated patients. Left heart catheterization was successful achieved using percutaneous puncture of the radial artery in all anticoagulated patients. No significant problems with radial spasm were encountered. In 27 out of the 28 patients (96%) percutaneous puncture of an antecubital fossa vein (medial or lateral antecubital fossa vein) and right heart catheterization was successful. In one case direct cut down to identify and cannulate a suitable vein was employed as it proved impossible to successfully cannulate an antecubital fossa vein. Where difficulty in advancing the venous catheter was

encountered, a hydrophilic wire (Terumo Medical Corporation, Somerset, NJ) was successfully employed to gain access to the subclavian vein in all subjects, regardless of the initial venous puncture position. Full haemodynamic, oxygen saturation and angiographic data were obtained and there were no procedure related adverse cardiac events. All patients were able to mobilize immediately following the procedure, and were discharged as planned at 4 hours after satisfactory haemostasis. No thromboembolic or bleeding complications occurred in any of the cohort and no late complications were reported at six week follow up.

In all of the non-anticoagulated patients, conventional percutaneous femoral artery and vein access was obtained and the procedures were successfully completed with no complications. Procedure duration was significantly shorter in this group of patients. Fluoroscopy time and radiation exposure values were similar in both groups.

Table 18. Procedural data (mean±SD or number of patients and percentage of group)

	Percutaneous Arm approach (n=28)	Percutaneous Femoral approach (n=31)	P value
Access success (%)	27 (96%)	31 (100%)	
Procedural duration (min)	48±15	32±9	P<0.05
Fluoroscopy time (min)	10.5±6	8±4.5	NS
Radiation exposure (cGy.m2)	33.9±19	31±17	NS

6.3.4 Discussion

Although this study was performed in a relatively small group of patients, our experience of left and right heart catheterisation using percutaneous puncture of the radial artery and an antecubital fossa vein suggests that the technique is technically feasible, and facilitates safe investigation in fully anticoagulated patients. Since hospital admission is not required, costs (compared to those incurred by admission for adjustment of anticoagulation to facilitate a femoral procedure) can be constrained. More importantly, this technique minimises the thromboembolic risks associated with stopping oral anticoagulation. Since haemostasis at the arterial and venous access sites is easily achieved by direct pressure, the risk of access site bleeding complications is also minimised.

Although vascular punctures in anticoagulated patients have potential risks (uncontrolled haemorrhage, haematoma formation and compartment syndrome in particular) we did not encounter any haemostatic difficulties in this study. We have previously reported no significant access site bleeding in anticoagulated patients (most with an INR of 2-3) undergoing coronary angiography via the radial artery without interruption of oral anticoagulation (73). We have also studied transradial rescue angioplasty in patients who failed to reperfuse following thrombolytic therapy for acute ST segment elevation myocardial infarction, and reported no radial access site bleeding complications (108). The current study expands this data set, confirming that a combined percutaneous approach to the radial artery and antecubital fossa vein is safe even in a population of fully anticoagulated patients. Since we utilised separate arterial and venous access sites, the risk of arterio-venous fistula formation was also minimised.

A cut down to the brachial artery may sometimes be the only option in patients with severe peripheral vascular disease and bilateral unfavourable Allen's test undergoing cardiac catheterisation procedures. Although it has been shown that skilled operators can achieve excellent results with a low rate of access site complications even in anticoagulated patients (49), for inexperienced operators this technique is associated with unacceptably high access site complications (52). As an alternative, some femoral operators employ a percutaneous Seldinger approach to the brachial artery (204). The risk of access site complications associated with this technique is also unacceptably high for occasional operators (55), with anticoagulated patients being particularly susceptible to median nerve compression associated with haematoma formation (72, 205). Therefore in anticoagulated patients, the percutaneous approach to the brachial artery should be avoided, and a surgical approach reserved for skilled high volume operators.

Gilchrist et al reported on 41 left and right heart catheter studies utilising a combined percutaneous radial and forearm vein technique (201). The main procedural difference in this study was the preferential use of a distal puncture site located close to the wrist. In Gilchrist's series, forearm venous cannulation was not possible in 30% of patients. Our failure rate for percutaneous venous cannulation was only 4%. This improved success rate may reflect the use of a less technically demanding proximal venous puncture site, suggesting that the antecubital fossa may be preferable for these combined procedures. It would be unethical to utilise our technique if it resulted in increased complications, radiation exposure or patient discomfort. Our study shows no increase in complication rates. There was no significant increase in radiation exposure

with our technique, as evidenced by the similar fluoroscopy and radiation exposure measurements. Procedure duration was increased compared to a conventional percutaneous transfemoral approach. This was predominantly related to the time required for identification and puncture of a suitable forearm vein. With increasing experience, it is likely that the procedural duration will come down to a level comparable to that of a transfemoral approach. It should be noted that the procedural duration recorded did not include the longer period of bed rest and observation required in the transfemoral patients. Since the patients studied by a percutaneous arm approach are mobilized immediately, using this technique will lead to an overall reduction in the duration of hospital admission required for the procedure, minimizing resource requirements. Early mobilization will also improve patient comfort, improving procedure tolerability.

Vascular closure devices can be employed as an alternative to our strategy, with small studies demonstrating good results for left heart catheterization in anticoagulated patients (206). For left and right studies, the use of vascular closure devices does not solve the issue of achieving satisfactory haemostasis after femoral venous puncture in anticoagulated patients, when compression can be difficult or painful. In addition, vascular closure devices may fail or be contraindicated in a substantial proportion of patients, and may increase the risk of serious vascular complications (207, 208).

Although our data suggests that this technical refinement minimizes the problems associated with performing left and right heart catheterization in fully anticoagulated patients, the procedural risks associated with every invasive cardiac procedure are not abolished. If advances in non-invasive assessment techniques such as 3-dimensional

echocardiography, cardiac magnetic resonance and multi-slice computed tomography continue at their current pace, the need for assessment by catheterization may be greatly reduced, decreasing our reliance on invasive technology.

6.4 CONCLUSION

Whilst both these studies are small observational studies and not withstanding their limitations, they nevertheless highlight important points and issues in these 2 high risk patient subgroups.

In summary, our rescue PCI study confirms that, for experienced operators, a transradial approach substantially reduces the major access site complications associated with rescue PCI, allowing reperfusion with minimal vascular risk. Our data also suggest that utilizing a transradial approach does not compromise procedural outcomes in infarct PCI. Experienced operators could therefore employ radial access in a primary PCI program.

Our study on the use of a percutaneous arm technique for right and left heart catheterization suggests that in patients treated with oral anticoagulants, the combination of left heart catheterization via the radial artery and right heart catheterization via an antecubital fossa vein is a useful technique to reduce bleeding and thromboembolic risk without interruption to their anticoagulation therapy. In addition, this technique also allows early patient mobilisation day case discharge and substantial cost saving.

CHAPTER 7

CONCLUSIONS

7.1 SUMMARY OF RESULTS

Chapter 2 studies the incidence of vascular complications in the modern era in relation to femoral and radial access site. A total of 1014 patients are studied. The radial access site is associated with a lower incidence of vascular complications than the femoral access site. If a vascular complication does occur with the use of radial access site, it is often limited and can be treatment conservatively without causing any delay to patient discharge.

Chapter 3 studies the incidence of radial artery anatomical variation and its influence on procedural outcome in 1540 patients undergoing a transradial cardiac procedure. Anomalous radial artery anatomy is common (with an incidence of 15%) although in the majority of cases does not affect the outcome of a transradial procedure. The commonest type of anomaly is a high bifurcating radial origin which is often accompanied by a radial artery of a smaller calibre necessitating the use of 5F catheters. The presence of a radial loop is associated with frequent procedure failure.

Retrograde radial arteriography helps to delineate underlying anomalies and identify patients with unfavourable anatomy thereby informing the operator to plan a strategy to overcome the anomaly or change access route with the potential to save time and avoid vascular complications. This can be performed with a minimum of contrast (3 mls) and should be considered part of a routine transradial procedure

Chapter 4 studies the diameter and response to sublingual GTN of the right and left radial and ulnar arteries. The radial artery is bigger than the ulnar artery and the right

radial artery than the left radial artery in most men and women. GTN significantly increases the size of both the radial and the ulnar arteries. An important finding in this study is that majority of women have a radial artery smaller than the external diameter of a 5F sheath prior to administration of GTN.

Chapter 5 studies variation in radiation exposure to patients and operators during diagnostic transradial and transfemoral coronary angiography, utilising a standardised approach and radiation protection protocol. This study demonstrates that transradial procedures performed by experienced operators employing meticulous radiation protection are not associated with an increase in radiation exposure to the patients or the operators.

Chapter 6 studies the application of radial artery access in two high risk patient subgroups – patients undergoing transradial rescue PCI following failed thrombolytic treatment, and patients undergoing left and right heart catheterisation via the radial artery and an ante-cubital fossa vein without stopping their anticoagulant therapy.

In the rescue PCI group, the study demonstrates that transradial rescue PCI performed by experienced operators is safe and technically feasible, and offers a much reduced access site bleeding complications despite use of potent thrombolytic and multiple antiplatelet agents.

In the left and right catheterisation group, the study also demonstrates that left and right heart catheterisation can be safely performed via the radial artery and an

antecubital vein in most fully anticoagulated patients with a low bleeding and thromboembolic risk as well as allow early patient mobilization, day case discharge and substantial cost saving.

7.2 CONCLUSIONS

Although the radial artery access site is renowned for its much reduced vascular complications and has the added benefits of early mobilisation, better patient comfort post procedure, cost saving and facilitation of day case PCI, the femoral artery remains the preferred access site of choice for most cardiologists. This is to a large extent due to the significant learning curve associated with the transradial technique, even for experienced femoral operators, as well as concerns regarding higher radiation exposure to both the operators and the patients. There is also a general misconception that with improvement in technology and equipment used, femoral access site vascular complications have become infrequent.

This thesis provides comprehensive information on issues relating to the use of radial access site and explores its application in invasive cardiac procedures. Despite advances in equipment and improvement in pharmacological agents used, vascular access site complications remain a major problem in contemporary practice. We are also much more aware of the potential adverse implication associated with significant vascular complications, first from observations studies and registries, and more recently from meta-analysis and randomised studies. There is therefore a united drive to reduce bleeding complications amongst the cardiologists as well as commercial partners.

Information on radial artery anomalies, variation of radial and ulnar arteries diameters as well as the effect of GTN would help to shorten the transradial learning curve and optimise procedure technique. Sublingual GTN should make arterial puncturing easier as well as reduce the incidence of spasm which is the first hurdle to overcome during the learning curve. Retrograde radial arteriography should be undertaken routinely especially during the learning curve as it helps to identify patients with unfavourable anatomy. The operator could then formalise a strategy to overcome the anomaly or change access route to save time and avoid unnecessary vascular complications.

Our study on radiation exposure and access site selection should help refute some of the 'issues' on radiation exposure. More importantly, this study should also hightlight the importance of optimal radiation protection for both the operators as well as the patients. There have already been publications of large randomised trials comparing transradial and transfemoral approach and their data on radiation exposure is keenly awaited.

The radial artery is intuitively suited for high-risk patient subgroups. Since our assessment on its application in these groups of patients, we now routinely use the radial artery for all comer PCI including primary PCI.

7.3 CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

It is increasingly obvious that transradial approach should become the default approach for all (interventional) cardiologists. Although the transradial technique requires a specific skill set and is associated with a significant learning curve, information gathered for this thesis would help shorten part of the learning curve as well as optimise procedural technique. The majority if not all the trainee cardiologists will be proficiently trained in transradial approach in this country. Although there are still wide country-to-country variations, the drive to adopt the transradial approach has certainly gathered an unstoppable momentum.

Several large observational studies and randomised controlled trials of radial versus femoral access had also reported their findings over the last few years. Of note is the publication of the radial versus femoral access for coronary intervention in patients with acute coronary syndrome (RIVAL) trial (209). This was the largest randomised, multicentre trial involving 7021 patients in 32 countries. Although there was no difference in the primary outcome (a composite of death, MI, stroke or non-CABG related major bleeding) between the two groups, there was a 63% reduction in the risk of large vascular access complications with the transradial group. There was, however, a 61% relative risk reduction in the risk of death among ST elevation myocardial infarction (STEMI) patients treated via the radial route. A sub-group analysis also reported a 51% reduction in the risk of the primary outcome among PCI centres that performed the highest volume of radial procedures.

A recent meta-analysis of 9 randomised controlled trials that compared the outcomes of transradial versus transfemoral route in patients with STEMI PCI also

demonstrated a significant reduction in mortality, major adverse cardiac events and major access site complications in the transradial group (210). The findings of the meta-analysis therefore support the preferential use of radial access for STEMI PCI.

The transradial approach has also now spread to peripheral, renal and carotid interventions. The era for (coronary) intervention for the next 10 years will no doubt belong to the transradial world. Time will tell!

CHAPTER 8

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