UPPER LIMB ISCHAEMIA: A TWELVE YEAR EXPERIENCE

by

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DECLARATION OF AUTHENTICITY

I, Dr Johannes Marthinus du Toit, hereby declare that the work on which this dissertation is based, is my own. I have fully and specifically acknowledged sources from which material has been adapted. Furthermore, the information contained within this document, was gathered and utilized specifically to fulfil the purposes and objectives of this study and has not been previously submitted to any other university for a higher degree.

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Date: 8 September 2014

ABSTRACT

Upper limb ischaemia – a twelve year experience

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Introduction: Upper limb ischaemia (ULI) is a relatively uncommon, but well recognized vascular entity. The sequalae of impaired function or amputation of an arm can be devastating to the individual with loss of independence and / or livelihood. There remains much to be learned that can only be established through good quality studies. This project was aimed at developing a comprehensive, but broad overview of ULI, specific to the population we serve.

Aims: The objective was to review the Vascular Surgery Unit's experience with ULI, with particular emphasis on *defining the pattern and distribution of disease* and pathological profile, *describing key demographic* and *clinical features* and reporting on *conventional clinical outcomes*. Areas of interest, with the potential for further research, were identified.

Methods: *Retrospective descriptive study*. All patients that underwent a surgical intervention for ULI between January 2000 and December 2011, were included in the audit. Approval from the Department of Surgery Research Committee and Human Research Ethics Committee was obtained prior to accessing data *(Appendix 1 & 2)*. A research folder was compiled for each patient. On completion of the data collection process, the findings were analyzed and compared to current literature on this topic.

Results: *Sixty-four patients* with ULI were managed surgically during the 12 year study period. A *male: female ratio of 0.60* (as opposed to 0.96 from 2011 Census figures), was reported. The thrombo-embolic subgroup of patients (n=30), were notably younger than expected (mean age of 55 years) compared to the UEAOD subgroup (n=12, mean age of 57 years). Approximately *48% were of mixed ethnicity*, correlating well with 2011 Census figures. Referrals were predominately received from Secondary Hospitals (84%) situated within the Cape Metropole. *55% Presented with acute ULI*, of which 40% were classified as Rutherford grade IIa and 17% diagnosed with established compartment syndrome. The majority of chronic ULI patients, presented with *signs of tissue necrosis (48%).* Other indications for intervention included upper extremity claudication symptoms (31%), rest pain (14%) as well as neuro-vascular symptoms (7%). A *disproportionately high prevalence of cigarette smoking (83%,* with an average of 31 pack years) was identified in the UEAOD subgroup. 27% Of patients were not receiving adequate pharmacological therapies aimed at addressing pre-existing risk factors, as proposed by the TASC II document. *Thrombo-embolism was the single largest aetiological factor identified (47%),* with the majority of occlusions (57%) occurring at the level of the brachial artery. A left-sided predominance with a ratio of 2:1, was noted. Approximately 47% of patients with UEAOD, were younger than 55 years. A clear proximal pattern of disease was observed (66% of lesions within the subclavian artery). Eighty-nine procedures were performed in 64 patients (78 open, 5 exclusively endovascular with a combined open / endovascular approach implemented in 6 patients). The *30-day mortality rate was 7.8%. Systemic complications* were observed in 13% with 23% sustaining some form of *procedural complication*. Twenty amputations were performed in 64 patients, of which 6 were major amputations. The *30-day amputation rate* after an attempt at revascularization, was 12.5%. Adherence to follow-up was poor (51% at 6 months), limiting interpretation of follow-up data.

Conclusion: Although few firm conclusions could be drawn, this review has expanded our overall perspective of ULI, specific to the population we serve. It is anticipated that the publication of our institutional data will create a clinical awareness and facilitate future research projects in this field. A collaborative research effort between South African vascular units will facilitate comparison of different institutional experiences and enable pooled data analysis, perhaps further defining the pattern of upper limb vascular disease by identifying distinct geographical confounders.

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TABLE OF CONTENTS

LIST OF TABLES AND FIGURES

Chapter 2: Literature review

Chapter 5: Results

ABBREVIATIONS

AULI	Acute upper limb ischaemia
CULI	Chronic upper limb ischaemia
PAD	Peripheral arterial disease
UEAOD	Upper extremity atherosclerotic occlusive disease
TED	Thrombo-embolic disease
CAD	Coronary artery disease
HPT	Hypertension
DM	Diabetes mellitus
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
CCA	Common carotid artery
BCA	Brachio-cephalic artery
SCA	Subclavian artery
RSA	Retro-oesophageal subclavian artery
ATOS	Arterial thoracic outlet syndrome
ASM	Anterior scalene muscle
PSD	Post-stenotic dilatation
TAO	Thromboangiitis obliterans
RP	Raynaud's phenomenon
RS	Raynaud's syndrome
RD	Raynaud's disease
HHS	Hypothenar hammer syndrome
PFO	Patent foramen ovale
ASD	Atrial septal defect
AF	Atrial fibrillation
MVP	Mitral valve prolapse
MR	Mitral regurgitation
IE	Infective endocarditis
CMO	Cardio-myopathy
MD-CTA	Multi-detector computed tomography arteriogram
MRA	Magnetic resonance arteriogram
ERNA	Equilibrium radionuclide angiography
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
PTA	Percutaneous transluminal angioplasty
ePTFE	Expanded polytetrafluoroethylene
ELISA	Enzyme-linked immunosorbent assay

CHAPTER ONE:

INTRODUCTION

Upper limb ischaemia is a relatively uncommon, but well recognized vascular entity caused by a wide range of aetiological factors. However, the sequalae of impaired function or amputation of an arm can be devastating to the individual with loss of independence and / or livelihood. There remains much to be learned that can only be established through good quality studies.

Due to the relative infrequency of this condition, few clinicians are familiar with the different aspects of diagnosis, investigation and treatment. The occupational ramifications and impact on quality of life in those affected can be substantial. A thorough understanding of this condition is essential if significant improvement in surgical outcome and limb functionality is to be made. These considerations were the inspiration behind the current study, with the purpose of improving colleagues' (as well as the author's) insight into the disease by *defining the pattern and distribution of disease and pathological profile, describing key demographic and clinical features and reporting on conventional clinical outcomes*.

The project was aimed at developing a comprehensive, but broad overview of upper limb ischaemia, specific to the population we serve. Areas of interest, with the potential for further research, were identified.

CHAPTER TWO:

LITERATURE REVIEW

1) GENERAL CONSIDERATIONS AND OVERVIEW

A computerized search of the National Library of Medicine and the National Institutes of Health MEDLINE database was undertaken using the Entrez PubMed (www.pubmed.gov) interface, followed by a secondary manual search of the article reference lists. The primary search strategy was developed to retrieve English language articles focusing on upper limb ischaemia published between 2000 and 2013; letters to the editor, editorials and other items of general commentary were excluded from the search. Studies reporting on upper limb ischaemia related to primary Raynaud's phenomenon and trauma were excluded, as they were beyond the scope of this review.

The above literature search resulted in a heterogeneous group of articles related to upper limb ischaemia. *No randomized trials or prospective studies were identified*. Clinical data were limited to case reviews derived from a range of sources, including district general hospitals, regional centres as well as specialist vascular units. Most of these publications reported on a single clinical (either acute or chronic) or aetiological (either traumatic or non-traumatic) aspect of upper limb ischaemia. Understandably, series that combine acute and chronic ischaemia are rare.[1,5-7] Often, by attempting to discuss two distinctly different disease processes concurrently, important individual characteristics may be obscured.

Popular research themes subsumed within the published surgical series, included comparisons of different management pathways (particularly operative versus non-operative management of acute upper limb ischaemia), clinical outcome of different interventional modalities (specifically percutaneous versus open surgical procedures) as well as reviews of specific aetiological entities. The applicable articles were reviewed, including relevant references from the perused material.

Due to the wide spectrum of underlying aetiologies and clinical presentations, it is of utmost importance that interesting findings from the literature are presented in a logical and structured manner. This may be accomplished by implementing a rigid clinical or aetiological framework. Instead, the relevant findings will be presented under the following headings, in order to accommodate for the complexities and heterogeneity associated with this condition.

- Incidence and demographics
- Risk factors
- Aetio-pathology
- Anatomical basis of disease
- Clinical presentation and related management pathways
- Outcome

2) INCIDENCE AND DEMOGRAPHICS

Patients managed non-surgically are often excluded from these series. This prevailing limitation adds to the difficulty in determining the true incidence of upper limb ischaemia as well as establishing an accurate ratio of acute to chronic presentations. Most authors

agree that ischaemic conditions of the lower extremity are much more common than those of the upper extremity.[1-3] Upper limb revascularization procedures comprise approximately 4% of all vascular procedures performed and constitute around 15-18% of all interventions performed for critical limb ischaemia.[4,5]

There seem to be *unique demographic differences between upper and lower extremity bypass populations*.[8-10] Hughes et al[9] reviewed their single centre experience and noted that patients presenting for upper extremity revascularization do so at a relatively early age (average age 57 years) with a slight female preponderance of 55%, a fairly consistent finding throughout the literature.[2,5] In contrast, a contemporary cohort of lower extremity bypass patients from the same institution, had a mean age of 67 years with a primarily male preponderance of 62%.

The bypass population is not the only subgroup of patients reflecting subtle epidemiological differences between upper and lower limb cohorts. When considering acute limb ischaemia (defined as a sudden decrease in limb perfusion posing a potential threat to limb viability, presenting within 2 weeks of an acute event)[11], it is clear that this condition affect the lower limbs much more commonly (reported incidence of 1.3 cases per 100 000 per year),[4] than the upper limbs. Acute *upper* limb ischaemia (AULI) occurs in a slightly different patient population than acute *lower* limb ischemia,[12] partially explained by an unequal distribution of atherosclerotic occlusive disease, mostly affecting the lower limbs. AULI is also found in a more heterogeneous group of patients, presenting as a clinical manifestation of conditions such as inflammatory vasculitides, iatrogenic

disorders (drug related, arterial catheterization and radiation fibrosis), arterial thoracic outlet syndrome and atherosclerotic occlusive disease.

Embolic disease affect the upper limbs more frequently.[13] *Emboli are the most frequent cause of upper limb ischaemia.* Of all arterial embolizations, between 10 and 20% involve the upper limbs. However, a number of recent studies have estimated the frequency of peripheral arterial embolic occlusions, to be on the decrease.[14,15] Multiple factors are at play, continuously influencing the incidence of embolic phenomena. Even though the frequency of systemic emboli due to ischaemic heart disease is on the increase, the absolute number of embolic events is believed to have declined, mostly due to a decrease in the number of rheumatic heart disease patients as well as widespread use of long-term anticoagulation in the management of rheumatic heart disease and atrial fibrillation.[16-18]

As previously stated, series that combine both acute and chronic upper limb ischaemia are rare.[1,5,18,19] The largest of these included 172 patients undergoing revascularization procedures for upper limb ischaemia over a 20 year period.[1] The age of presentation depended heavily on the underlying aetiology at hand. The mean age of presentation of patients with thrombo-embolic disease was appreciably older (72.4 years) than those presenting with upper extremity atherosclerotic occlusive disease (62.5 years). This may partly explain the higher incidence of severe comorbid disease observed in patients presenting with thrombo-embolism, as opposed to atherosclerotic occlusive disease.

3) PREDISPOSING CONDITIONS

When considering the prevalence and contribution of predisposing conditions, it is important to interpret them in terms of the underlying aetio-pathology at hand. For instance, the presence of atrial fibrillation is a strong predisposing factor for cardio-embolic events, but not the development of atherosclerotic occlusive disease. This section will focus on traditional risk factors for atherosclerotic occlusive disease and their applicability to UEAOD.

3.1) Risk factors for atherosclerosis and the development of upper extremity atherosclerotic occlusive disease (UEAOD)

The best quality evidence regarding this topic takes the form of multiple consensus documents (including the TASC II document, American Heart Association and American College of Cardiology guidelines). However, it is important to note that most data pertaining to risk factors for non-coronary atherosclerotic arterial disease, have been extrapolated from studies primarily focusing on coronary artery disease (CAD), such as the Framingham Heart Study, Atherosclerosis Risk in Communities Study (ARIC),[19] Honolulu Heart Study,[20] and the Strong Heart Study.[21] With rare exception, the evidence from these studies suggests that *risk factors for non-coronary atherosclerotic arterial disease are generally similar and independent of the end organ affected*.

Despite the superfluous reports on the effects of atherosclerotic risk factors in lower extremity arterial disease, none such studies specific to UEAOD could be identified. The prospect of generating good quality population based data in future (specific to the UEAOD cohort), are unlikely, particularly in light of a recent (2008) document produced

by the American Heart Association.[22] In an attempt to clarify nomenclature pertaining to non-coronary atherosclerotic arterial disease, they suggested that the term PAD should incorporate both lower and upper extremity atherosclerotic arterial disease.

Recently published surgical series on UEAOD (*Table 1*), have reported the following prevalence of traditional atherosclerotic risk factors.

Table 1: Studies evaluating prevalence of risk factors in UEAOD

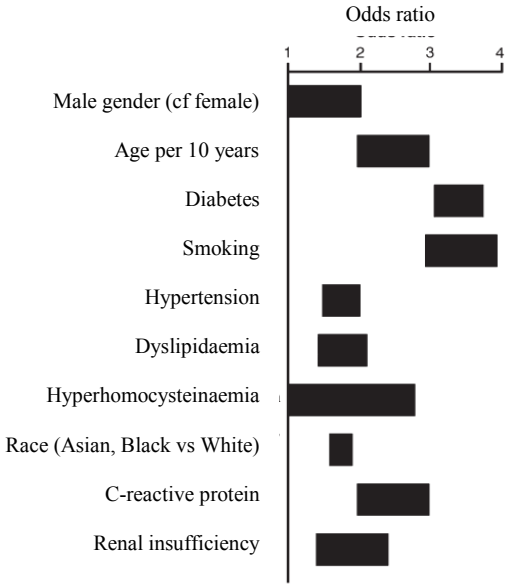
Study	**n**	**Smoking(%)**	HPT**(%)**	**DM (%)**
Hughes et al, 2013 [9]	55	35	Not reported	29
Spinelli et al, 2009 [23]	23	43	26	48
Hughes et al, 2007 [9]	20	Not reported	45	40

Hughes et al[9] noted a *statistically significant difference in the prevalence of diabetes mellitus in upper extremity bypass patients* (40%) compared to the lower extremity bypass population (83%). Differences in the prevalence of hypertension, coronary artery disease, congestive cardiac failure and tobacco use were not statistically significant.[9,23]

The criteria used to support a risk factor for UEAOD (as opposed to a strong association), require a prospective, controlled study showing that modifying the factor alters the development or course of the disease. Until such studies are produced, the best evidence on the impact of traditional risk factors on the development and progression of UEAOD, takes the form of extrapolated data from non-coronary atherosclerotic arterial disease

studies. The rest of this section will attempt to shortly review these traditional risk factors, including proposed therapeutic targets in the presence of disease.

Figure 1: Approximate odds ratio range for atherosclerotic risk factors as depicted by the TASC II document [24]



3.1.1) Tobacco products

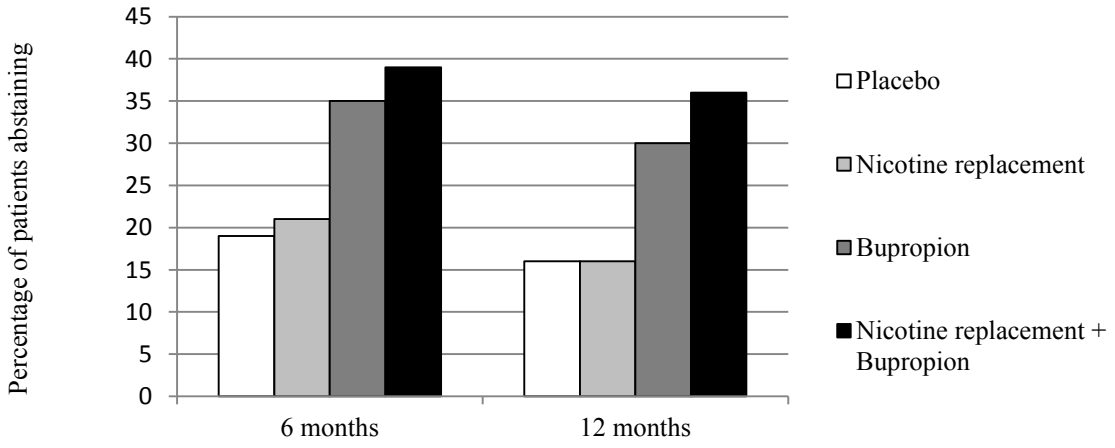
The relationship between smoking and PAD has been recognized since 1911, when Erb reported that intermittent lower limb claudication was three times more common among smokers than non-smokers.[24] Tobacco use is particularly prevalent in patients with UEAOD and seems to have a stronger causative association than the aforementioned risk factors. It has been suggested that the association between smoking and PAD may be stronger than that of smoking and coronary artery disease (CAD). The number of pack years is associated with disease severity, an increased risk of amputation, peripheral graft occlusion and mortality. Given these associations, smoking cessation has been the

cornerstone of PAD management. However, due to low smoking cessation rates achieved with medical therapy, modification of this risk factor may be particularly challenging.

Multiple randomized controlled trials have supported the use of an antidepressant, bupropion, in establishing improved smoking cessation rates. Jorenby et al (*Figure 2*) have shown that bupropion, when combined with nicotine replacement therapy, is more effective than either therapy alone.[25] This should be combined with non-pharmacological strategies, including physician advice at every patient visit and behavioural modification therapy, in order to achieve the best cessation rates.

Recently, substance abuse has been implicated in the processes of accelerated and precocious atherosclerosis as well as Thromboangiitis obliterans. Some of the finer pathological implications of tobacco use and other substances will be discussed in the section on aetio-pathology.

Figure 2: Comparative abstinence rates for bupropion, nicotine replacement therapy or both versus placebo (as reported by Jorenby et al)[25]



3.1.2) Diabetes mellitus

Many studies have shown an association between diabetes mellitus and the development of PAD. In patients with diabetes, for every 1% increase in haemoglobin A1c, there is a corresponding 26% increased risk of developing PAD.[26] Over the last decade, mounting evidence has suggested that insulin resistance plays a key role in the clustering of cardio-metabolic risk factors (also referred to as Metabolic syndrome or Syndrome X) which include hyperglycaemia, dyslipidaemia, hypertension, deep venous thrombosis and obesity.

3.1.3) Dyslipidaemia

In the Framingham study, a fasting total cholesterol > 7 mmol/L was associated with a doubling in the incidence of intermittent lower limb claudication. However, the ratio of total to high-density lipoprotein (HDL) cholesterol was the best predictor of risk for PAD. Although some studies have shown total cholesterol to be a powerful independent risk factor for PAD, others have failed to confirm this association.

Good quality evidence supporting the use of statins to lower LDL cholesterol in PAD patients, were obtained from the Heart Protection Study. [27] Over 20 500 subjects at high risk for cardiovascular events (including 6748 patients with PAD), were enrolled. Patients were randomized to simvastatin 40 mg, antioxidant vitamins, a combination of treatments or placebo, with a 5-year follow up period. Simvastatin 40 mg was associated with a 12% reduction in total mortality, 17% reduction in vascular mortality, 24% reduction in CAD events, 27% reduction in cerebrovascular events and a 16% reduction in non-coronary revascularizations. Similar results were obtained in the PAD subgroup, whether they had

evidence of coronary artery disease at baseline or not. Importantly, there was no threshold cholesterol value below which statin therapy was not associated with benefit. A limitation of this study was that the evidence in PAD was derived from a subgroup analysis of symptomatic PAD patients.

A more recent meta-analysis of 14 randomized trials pertaining to statin therapy, concluded that a 1 mmol/L reduction in the level of LDL cholesterol, was associated with a 20% decrease in the risk of major cardiovascular events.[28] This benefit was also not dependent on the initial lipid levels.

3.1.4) Hypertension

Hypertension is associated with all forms of cardiovascular disease, including a two- to three- fold increased risk of developing PAD. However, the relative risk for developing PAD is less than for diabetes or smoking. Current hypertension guidelines support the aggressive treatment of blood pressure in patients with atherosclerotic occlusive disease, targeting a blood pressure of 140/90 mmHg. In the subgroup of patients with diabetes or renal insufficiency, a blood pressure of 130/80 mmHg should be targeted.[29,31]

3.1.5) Hyperhomocysteinemia

The prevalence of hyperhomocysteinaemia in the PAD population, is significantly higher than in the general population (prevalence of 1%). It is reported that hyperhomocysteinaemia is detected in about 30% of young patients (aged 55 or below) with PAD. The suggestion that this condition may be an independent risk factor for atherosclerosis, has now been substantiated by several studies. As with cigarette smoking,

it may be a stronger risk factor for PAD than for CAD. While B-vitamin and / or folate supplementation can lower homocysteine levels, this does not reduce the incidence of cardiovascular events. Two studies investigating this supplementation regime in patients with CAD, demonstrated no benefit and even a suggestion of harm.[31,32]

3.1.6) Chronic renal insufficiency

A strong association of renal insufficiency with PAD has been reported, with some recent evidence suggesting it may be causal. The HERS study (Heart and Estrogen / Progestin Replacement Study) reported an independent association of renal insufficiency with future PAD development in postmenopausal women.[33]

4) AETIO-PATHOLOGY

Multiple approaches to the classification of upper limb ischaemic conditions have been described. None are more clinically relevant than categorizing patients into acute or chronic ischaemia, according to the duration of their symptoms. This approach assists the clinician in deliberating the most appropriate management pathway, while honing in on the most common underlying aetiologies. Although essential in the clinical setting, this classification does not lend itself to an in depth discussion of different aetiological factors. A more appropriate classification system for discussion purposes is illustrated below (*Table 2*). Causes of ULI are divided into two broad categories, namely Upper Extremity Occlusive Disease (UEOD) and Thrombo-Embolic Disease (TED). The limited nature of this dissertation does not allow for in depth discussion of each and every aetio-pathological factor. Therefore, the most common and interesting aetio-pathologies in each category, will be discussed in more detail.

Table 2: A proposed aetio-pathological classification of upper limb ischaemia

UEOD	TED
Atherosclerosis (UEAOD) **Thromboangiitis obliterans** **Vasculitides** Small vessels: Connective tissue disorders Systemic sclerosis (Scleroderma) Mixed connective tissue disease Systemic Lupus Erythematosus Polymyositis / Dermatomyositis Sjögren's syndrome Rheumatoid arthritis Large vessels: Giant cell arteritis Takayasu's disease Radiation arteritis **Secondary vasospastic disorders** Drug-induced Iatrogenic Recreational Occupational Ammunition workers Cold exposure **Fibromuscular dysplasia**	**Cardiac source** Non-valvular: Atrial fibrillation Ischaemic cardiomyopathy Myocardial infarction Ventricular aneurysm Atrial myxoma Paradoxical emboli via PFO Valvular: Rheumatic heart disease Bacterial endocarditis Sequelae of cardiac valve replacement **Extra-cardiac source** Aortic: Ascending aortic aneurysm Non-specific / atypical Complicated atheromatous plaque Pseudo-aneurysm Post-traumatic / iatrogenic Aortic dissection Congenital anomaly Aberrant right subclavian artery Kommerrell's diverticulum Peripheral: Subclavian aneurysm Atherosclerotic / atypical Pseudo-aneurysm Post-traumatic / iatrogenic Entrapment syndromes Arterial thoracic outlet syndrome Quadrilateral space syndrome Brachial artery entrapment Arterio-venous fistula / graft Occupational Hypothenar Hammer Syndrome

4.1) Upper extremity occlusive disease (UEOD)

4.1.1) Upper extremity atherosclerotic occlusive disease (UEAOD)

Most series identify embolic disease, trauma and Thromboangiitis obliterans as the most common causes of upper limb ischaemia, followed by UEAOD.[1,9,10] However, Spinelli et al[23] identified atherosclerosis as the most common aetiology (74%) in their upper extremity bypass population. This disproportionately high number might be explained by the unusually high number of patients with dialysis-dependant renal failure (39%) in their study group.

Atherosclerosis may have a variable effect on different arterial segments, both with regards to the morphological pattern of disease (ostial, mono- or multi-segmental) as well as the degree to which the segment is affected. Despite this variability, it should still be regarded as a diffuse disease process affecting multiple vascular beds. Unfortunately, no substantial reports (outside of case reports), could be identified to elucidate and help differentiate the morphological pattern in UEAOD from other anatomical segments prone to the development of atherosclerotic arterial disease.

Atherosclerosis of the upper extremity may manifest in a number of ways. Atheroma formation may progress to occlusion or stenosis of the affected segment. These lesions develop slowly. Often, several decades will pass before a critical narrowing is evident and arterial flow is impaired. This slow progression, as well as the rather robust collateralization response, are possible reasons why upper extremity arterial disease is frequently asymptomatic.

Atheromatous plaque may ulcerate or rupture, resulting in embolization with distal small vessel occlusion, eventually propagating to form extensive arterial occlusion. Thrombosis occurs less commonly. An initial small mural thrombus may evolve to form a major, near-occlusive or occlusive thrombus. Ultimately, lesions progress to form organized, fibrotic thrombus.

UEAOD predominantly affect the proximal vasculature, including the aortic arch, brachiocephalic artery (BCA), subclavian arteries (SCA), axillary and brachial arteries. The most extreme example of this process is aortic arch syndrome, where all branches of the aortic arch are occluded. Usually, only isolated branches occlude or become stenosed, also referred to as partial aortic arch syndrome. Anecdotal evidence suggests that UEAOD frequently involve a single segment of the arterial tree, compared to the predominantly multi-segmental disease encountered in symptomatic lower extremity atherosclerotic occlusive disease.

Less frequently, other more distal segments are affected. These include arteries of the forearm and hand. Obliterative disease of these segments are usually caused by distal embolization from a proximal atheromatous source. The symptomatology may become more severe with coexisting downstream lesions or pre-existing anastomoses.

4.1.2) Thromboangiitis obliterans (TAO)

Thromboangiitis obliterans (also known as Buerger's disease) is a segmental, occlusive, inflammatory condition of small and medium sized arteries and veins, characterized by

thrombosis and recanalization of the affected vessels.[34,35] It is a non-atherosclerotic inflammatory disease of unknown aetiology, usually affecting young men who are heavy smokers.[36] It differs from other vasculitides in that the serological markers of inflammation and autoantibody formation, are either absent or normal. Pathologically, it differs from other forms of vasculitis in that the vessel wall architecture is relatively well spared and fibrinoid necrosis is absent. Progressive organization of a highly inflammatory thrombus in the vessel lumen, is a consistent finding.[37]

The association between tobacco use and the development of TAO, is incontestable. Use or exposure to tobacco plays a central role in the initiation and progression of the disease. It remains debatable whether cannabis exposure is really implicated in the pathophysiology of distal arteritis in young adults. A recent comprehensive review of the literature[38] collected 70 published cases of the so-called cannabis arteritis. In this review, 97% of cannabis users also smoked tobacco, as cannabis is always consumed mixed with tobacco in Europe. Confounding factors like these add to the difficulty in assessing the effect of cannabis on the initiation and progression of TAO. In a recent retrospective review of 38 consecutive patients with TAO,[39] investigators found that cannabis users were significantly younger at onset of arterial disease despite a similar tobacco exposure. This greater precocity might suggest an accelerating effect of cannabis on TAO pathophysiology. However, a more addictive personality or earlier initiation of tobacco use in cannabis consumers, may have affected this observation. Also, in the absence of toxicological tests, quantification of cannabis exposure cannot be objectively assessed, due to the variability of cannabis concentrations and methods of consumption.

Upper extremity involvement is classic, especially if it presents with Raynaud's phenomenon of recent onset in a young man. Although TAO most commonly affect the extremities, case reports implicating this disease process in other vascular beds (including cerebral, coronary, intestinal arteries, aorta as well as multi-organ involvement), have been published. [40-43]

A marked decrease in the frequency of the HLA-B12 antigen in patients with TAO (2.2% *vs*. 28% in controls), was previously reported.[44] Similar to other autoimmune diseases, TAO may have a genetic predisposition without the presence of a direct causative gene mutation. Most investigators agree that TAO is an immune-mediated endarteritis. Recent immunocytochemical studies have demonstrated a linear deposition of immunoglobulins and complement factors along the elastic lamina.[45] The inciting antigen has not been discovered. The role of hyperhomocysteinaemia in the pathogenesis of TAO is controversial.[46] An association between thrombophilic conditions such as antiphospholipid syndrome and TAO, has also been suggested.[47]

4.1.3) Small vessel vasculitides and secondary vasospastic disorders

A host of inflammatory and vasospastic disorders can result in digital ischaemia. Current nomenclature, when describing the clinical manifestation of these disorders, includes the terms phenomenon, syndrome and disease. The inconsistency with which terms are used to describe these conditions, have led to considerable confusion.

In Europe, Raynaud's phenomenon (RP) is used as a blanket term describing all forms of cold-related vasospasm, with the term Raynaud's syndrome (RS) being reserved for RP

associated with another (secondary) disease process. Raynaud's disease (RD) describes the clinical scenario where RP occurs in isolation. American and Australasian researchers use the terms syndrome and phenomenon interchangeably, but differentiate primary from secondary RP. The American nomenclature, as described above, has been adopted and applied to the current text.

In the Framingham Offspring Study, the prevalence of RP was 9.6% in women and 5.8% in men.[48] A familial predisposition have been described, especially if the onset of RP was under the age of 30 years.[49] Primary RP has been described in monozygotic twins, but the concordance rate is not currently known.[50]

Vasospasm is the key feature of RP. Maurice Raynaud originally described this phenomenon as "episodic digital ischaemia induced by cold and emotion."[51] The classical manifestation of pallor, preceding cyanosis and rubor, reflects the initial vasospasm followed by deoxygenation of static blood and reactive hyperaemia. However, the full triphasic colour change is not essential for diagnosis.

The precise mechanism causing RP is poorly understood, but believed to be due to multiple, interdependent factors that interact closely to produce symptoms. These include neurogenic, inflammatory, immunological and genetic factors as well as interactions of blood constituents with the vessel wall.

In approximately half of patients with RP, a significant underlying systemic cause can be identified. Half of these cases are caused by a connective tissue disorders, most

commonly systemic sclerosis or mixed connective tissue disease. Other conditions associated with secondary RP, are listed in *Table 3*.

Secondary, compared to primary RP, often present with a more severe degree of ischaemia due to the presence of established occlusive disease. Residual symptoms on long term follow-up as well as mortality, is higher in the patient group with systemic disease, compared to local disease associations.

Table 3: Conditions associated with secondary Raynaud's phenomenon.

Category and condition	Incidence of RP
Connective tissue disorders	
Systemic sclerosis (Scleroderma)	**95%**
Mixed connective tissue disease	**85%**
Systemic Lupus Erythematosus	**40%**
Polymyositis / Dermatomyositis	**40%**
Sjögren's syndrome	**33%**
Rheumatoid arthritis	**10%**
Obstructive	
Distal UEAOD	
Thromboangiitis obliterans	
Micro-emboli (Cardiogenic / Arterio-arterial)	
ATOS (especially when associated with cervical ribs)	
Occupational	
Hypothenar Hammer Syndrome (HHS)	
Vinyl chloride disease	
Ammunition workers	
Frozen food packers	
Pharmacological	
β-blockers	
Miscellaneous	
Hypothyroidism	
Cryoglobinaemia	
Reflex sympathetic dystrophy	

Interesting occupation-related causes of secondary RP include Hypothenar hammer syndrome (will be discussed in the section on thrombo-embolic disease), cold exposure, vinyl chloride disease (affecting approximately 3% of exposed workers) and ammunition workers (only manifests once the vasodilatory effects of nitrates are removed, i.e. at home or when on leave).

4.2) Thrombo-embolic disease (TED) of the upper extremity

At this point, the reader is invited to review *Table 2* once more (below), as this will be used as a framework to guide discussion on the aetio-pathological aspects of TED.

Table 2: A proposed aetio-pathological classification of upper limb ischaemia

UEOD	TED
Atherosclerosis (UEAOD) **Thromboangiitis obliterans** **Vasculitides** Small vessels: Connective tissue disorders Systemic sclerosis (Scleroderma) Mixed connective tissue disease Systemic Lupus Erythematosus Polymyositis / Dermatomyositis Sjögren's syndrome Rheumatoid arthritis Large vessels: Giant cell arteritis Takayasu's disease Radiation arteritis **Secondary vasospastic disorders** Drug-induced Iatrogenic Recreational Occupational Ammunition workers Cold exposure **Fibromuscular dysplasia**	**Cardiac source** Non-valvular: Atrial fibrillation Ischaemic cardiomyopathy Myocardial infarction Ventricular aneurysm Atrial myxoma Paradoxical emboli via PFO Valvular: Rheumatic heart disease Bacterial endocarditis Sequelae of cardiac valve replacement **Extra-cardiac source** Aortic: Ascending aortic aneurysm Non-specific / atypical Complicated atheromatous plaque Pseudo-aneurysm Post-traumatic / iatrogenic Aortic dissection Congenital anomaly Aberrant right subclavian artery Kommerrell's diverticulum Peripheral: Subclavian aneurysm Atherosclerotic / atypical Pseudo-aneurysm Post-traumatic / iatrogenic Entrapment syndromes Arterial thoracic outlet syndrome Quadrilateral space syndrome Brachial artery entrapment Arterio-venous fistula / graft Occupational Hypothenar Hammer Syndrome

The most common causes of ALI include arterial embolism, thrombosis and trauma. Embolic and thrombotic disease processes will be discussed separately.

4.2.1) Embolic disease: General remarks

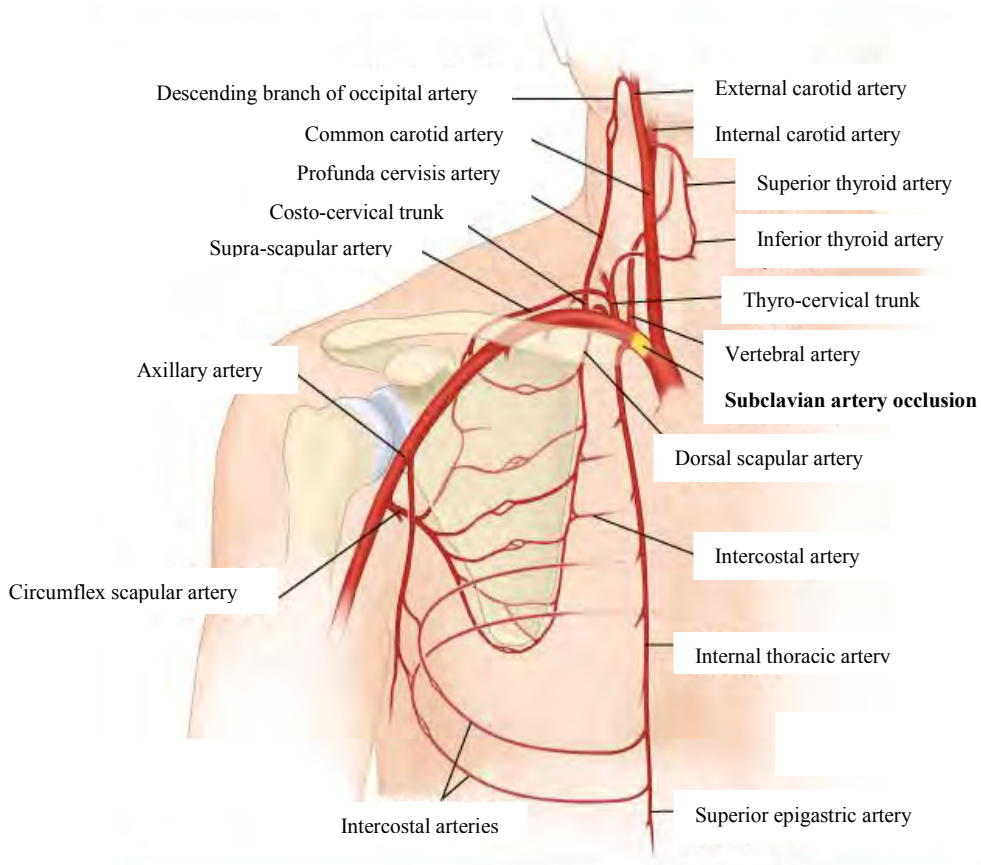
Emboli may arise from several possible origins. Traditionally, embolic sources have been classified as either cardiac or extra-cardiac in origin. Consistently, it has been reported that the heart is the most frequent source of emboli followed by the proximal aorta and supra-aortic trunk.[12,52-53] *Approximately two-thirds of emboli involving the upper extremities, originate from the heart,* with 9–12% classified as cryptogenic.

The origin of the embolus affect the size and consequently the level at which it occludes the affected vessel. Emboli originating from the heart are usually larger in size and tend to lodge more proximally, often at the bifurcation of the brachial artery. Arterial emboli travel more distally, however exceptions to the rule do exist. Haimovici,[13] reported the subclavian artery to be the site of occlusion in 11.7%, the axillary artery in 23%, the brachial artery in 61%, the radial artery in 23% and the ulnar artery in 1.6% of patients with AULI. Comparison between studies is difficult due to different methods used to establish the site of occlusion (clinical, operative and angiographic findings). Despite this confounding factor, *multiple reports have confirmed the brachial artery to be the most commonly occluded artery in the upper limb*.[1,2,54,55]

Most authors describe a higher incidence of embolism affecting the right arm compared to the left. This phenomenon can probably be explained by the larger diameter of the brachiocephalic artery compared to the left subclavian artery as well as the favourable angle that exists between the aorta and the brachiocephalic artery.[4]

The natural clinical course of a peripheral arterial embolus depends upon the location of the occlusion, the completeness of luminal obliteration, the extent of secondary thrombosis and the degree of spontaneous restoration of the collateral circulation. Occlusion of the subclavian artery is usually well tolerated and compensated for by collateral blood supply. The axillary artery, too, has a rich collateral blood supply from the more proximal subclavian branches (*Figure 3*). Combined subclavian and axillary occlusion usually cause ischemia of the entire arm.

Figure 3: Schematic representation of collateral circulation pathways around the right shoulder joint in the setting of SCA occlusion



Occlusion of the brachial artery has different effects, depending on the site of occlusion, presence of collateral branches as well as the metabolic requirements of tissue distal to the occlusion. The brachial artery is often occluded at the origin of the deep brachial or at the bifurcation into ulnar and radial arteries.[52] If the occlusion occurs proximal to the deep brachial artery origin, the arm usually presents with ischaemic signs and symptoms due to a lack of collateral blood supply. Conversely, the collateral blood supply for an occlusion distal to the deep brachial artery is profuse (including the deep brachial, superior and inferior ulnar collateral arteries as well as the cubital vessels), hence the clinical picture is commonly less severe. Occlusion of either the radial or ulnar arteries is not markedly injurious. However, occlusion of the more distal deep palmar arch can result in tissue necrosis.

4.2.2) Embolic disease: Non-valvular origins of cardio-emboli

Cardio-embolic sources can be of valvular or non-valvular origin. *By far the most common non-valvular cause, is atrial fibrillation.* Due to the erratic, uncoordinated contraction of the atria, a variable amount of static blood occupies the atrial appendage, predisposing to thrombus formation. Part of this thrombus may gain entry to the systemic circulation, resulting in systemic embolization.

Ischaemic conditions of the myocardium can manifest with cardio-embolic events. This may present in the acute setting due to an acute myocardial infarction complicated by a dramatic increase in afterload (also referred to as “pump failure”) or in a delayed fashion by presenting with ischaemic cardiomyopathy. In both conditions, pooling of near-static blood within the chambers lead to thrombus formation. A small percentage follows acute

myocardial infarction, be it clinically apparent or occult (also referred to as a silent myocardial infarction or SMI). SMI is not an infrequent event, with an incidence of 1-4% in the non-diabetic population and 10-20% in diabetic patients. The pathogenesis is incompletely understood, but thought to be sequelae of diabetic autonomic neuropathy.[56-57] This condition should always be borne in mind, especially when confronted with diabetic patients.

Atrial myxoma is the most common benign tumour of the heart, representing approximately 50% of all cardiac tumours. Clinical manifestations are determined by the location, size and mobility of the tumour. Possible presentations include cardiac obstruction, arrhythmias and peripheral embolization. The embolization of tumour fragments or thrombotic material covered with tumour cells, occur in approximately 30% of myxoma patients.[58,60] Most of these tumours embolize to the central nervous system, resulting in ischaemic cerebrovascular incidents. Secondary embolization to the coronary arteries, kidneys, intestines and peripheral arteries have been described.[61] Among 4396 reports of myxoma in the literature,[59] only 10 cases of atrial myxoma, complicated with AULI, have been reported. Even though rare, an embolizing myxoma should be included in the differential diagnosis of a young, otherwise healthy patient presenting with acute arterial ischaemia.[62]

Various forms of *interatrial communications*, such as patent foramen ovale (PFO) and atrial septal defect (ASD), occur in a significant proportion of the general population. In an autopsy study of 965 hearts from normal people spanning an age range of 10 decades, the overall incidence of PFO was 27%.[63] The earliest documentation of paradoxical

embolism through a PFO, was in the 1877 text of Julius Cohnheim. In more modern times, a group of investigators based in Paris, France first postulated an important role for PFO's in young patients (younger than 55 years of age) with cryptogenic stroke based on a case-control study.[64]

The mechanistic model of systemic embolization caused or facilitated by a PFO, is paradoxical embolism. Venous clots and rarely other particles (such as air, fat, amniotic fluid, tumor emboli or emboli from right heart endocarditis), pass from the systemic venous circulation to the arterial circulation by means of a variable right-to-left shunt. The clinical diagnosis of paradoxical embolism relies on the concurrence of arterial embolism, venous thrombosis, interatrial communication and a gradient favouring right-to-left shunting.[65] This gradient occurs transiently in normal individuals during early ventricular systole as well as the strain and release phase of the Valsalva maneuver. During the straining phase the right atrial pressure rises disproportionately, followed by a sudden increase in systemic venous return to the right atrium in the release phase.[66]

4.2.3) Embolic disease: Valvular origins of cardio-emobli

Few complications of valvular heart disease can be more devastating than systemic embolism. Causes include rheumatic heart disease, bacterial endocarditis and sequelae of valve replacement surgery.

The incidence of systemic embolism in *rheumatic mitral valve disease* (mitral stenosis and/or mitral regurgitation), is greater than in any other form of valvular heart disease and increases dramatically with the development of atrial fibrillation (AF).[67] The risk of

systemic emboli in rheumatic mitral valve disease is also greater in older patients[68-71] and those with lower cardiac indices,[68] but appears to correlate poorly with mitral calcification[67] and mitral valve area.[68]

Clinically detectable systemic emboli in isolated *aortic valve disease*, are uncommon. The small, but consistent frequency of systemic emboli reported in earlier studies of aortic valve disease, may best be explained by unrecognized mitral valve disease, ischemic heart disease or coexisting AF. However, one centre emphasized the thrombo-embolic potential of severe calcific aortic valve disease by histologically demonstrating micro-thrombi in 10 of 19 calcified and stenotic aortic valves.[72] It appears, therefore, that calcific micro-emboli from heavily calcified aortic valves are not as rare as previously thought, but rather difficult to detect due to their small size (unless visualized in the retinal artery).

With the advent of effective antimicrobial therapy, the incidence of systemic emboli in *Infective Endocarditis* (IE), has decreased. In the pre-antibiotic era, clinically detectable emboli occurred in 70 to 97% of patients with IE.[74] Recent reports suggest figures in the region of 12 to 40%.[75-80] The use of echocardiography was met with great enthusiasm, in order to identify the patient at risk of embolization. Initial reports proposed a high correlation between echocardiographically demonstrable vegetations and embolism.[81-84] However, in a more recent review of this subject, one centre reported that 80% of patients with IE had echocardiographic evidence of vegetations, while only one third had features of systemic emboli.[85]

The patient with *prosthetic valve endocarditis* deserves special mention. With the exception of patients with bio-prostheses in normal sinus rhythm, patients with prosthetic valves are at a constant risk of thrombo-embolism, emphasizing the importance of uninterrupted anticoagulation therapy. The risk of thrombo-embolic events in prosthetic valve endocarditis are higher than in native valve endocarditis, approaching 50-88%.[86,87]

4.2.4) Embolic disease: Extra-cardiac origins

An extra-cardiac source of emboli is nowadays identified in 5–12% of patients presenting with peripheral embolic disease. *Aneurysms are the most common extra-cardiac source of peripheral emboli*, followed by ulcerated atherosclerotic plaque rupture and disruption, leading to macro-embolization of plaque components (athero-embolism) or micro-embolization of platelet aggregates. Systemic athero-embolism may present in any of three clinical forms:

- The asymptomatic form, not diagnosed during the subject's lifetime, but recognized at autopsy.
- A benign form, such as blue toe / digit syndrome or cutaneous livedo, with a relatively good prognosis if managed correctly.
- A diffuse multi-systemic form with a poor prognosis.

Although less commonly encountered, a few interesting disease processes may manifest with peripheral arterial embolism. These include entrapment syndromes of the peripheral arteries, congenital anomalies of the aortic arch as well as occupational / recreational diseases.

4.2.4.1) Arterial thoracic outlet syndrome (ATOS)

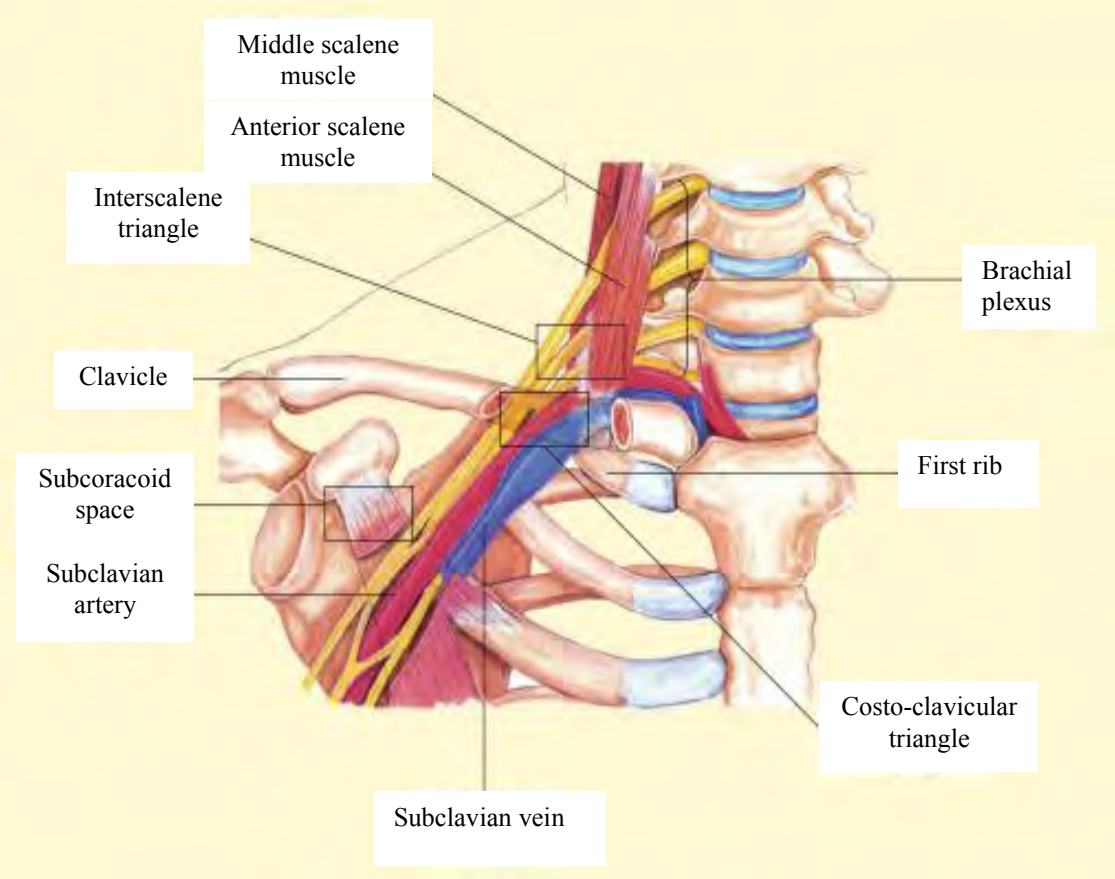
Historically, when Adson first described his manoeuvre in 1927,[89] thoracic outlet syndrome was called scalenus anticus syndrome. The underlying abnormality was thought to be compression of the subclavian artery (SCA) by the anterior scalene muscle (ASM). Approximately 30 years later, it was recognized that in addition to the SCA, the subclavian vein or brachial plexus can also be compressed and that structures other than the ASM, were also implicated in compression. In 1956, Peet et al renamed the condition by coining the all-inclusive label, thoracic outlet syndrome (TOS).[90]

Throughout the course of medical history, TOS has developed a reputation as a condition based on convoluted neurological and vascular symptoms. Physicians have continually disagreed about the relevance and pathogenesis of TOS, leading to a wide spectrum of opinions and research directions. This disagreement is augmented by the presence of anatomic anomalies and abnormal diagnostic tests observed in an asymptomatic population, resulting in further dispute about the specificity and sensitivity of commonly used diagnostic tests.[91]

Thoracic outlet syndrome describes a variety of symptoms caused by compression of the brachial plexus or subclavian vessels, at the thoracic outlet. In the majority of cases, symptoms are neurological in nature, with pain and weakness resulting from C8 or T1 nerve root compression. Arterial or venous symptoms resulting from compression are uncommon, accounting for 5% of cases in a large published series by Roos et al.[88] Anatomically, the thoracic outlet and corresponding area of neurovascular compression, is considered to incorporate 3 areas, namely the interscalene triangle, costoclavicular triangle

and subcoracoid space (*Figure 4*).[92-93] Typically, the left and right SCA ascend into the neck before arching laterally towards the medial border of the ASM. They descend laterally from the lateral margin of the ASM towards the outer border of the first rib, at which point they become the axillary arteries.[94] There are many variations described in the literature concerning the course of the SCA relative to the ASM. These include the right subclavian artery passing anterior, within, or posterior to the ASM.[94-98] These variations may occur because of a hypertrophied muscle, muscle strain or accompanying soft tissue abnormalities such as fibrosis or congenital bands.[99] Cervical ribs occur in 1–6% of the general population and in approximately 10% of patients with TOS.[93,100-102]

Figure 4: Schematic representation illustrating the anatomical relations of structures to the 3 areas of entrapment (interscalene and costoclavicular triangle, subcoracoid space)



The list of *causative mechanisms* in TOS is extensive (*Table 4*), yet one of the earliest and most consistently described, is the presence of a cervical rib. Galen first documented the presence of cervical ribs in 2 AD and further elaboration by the anatomist Vesalius during the first dissections of human bodies in 1543, provided additional insight.[103-104]

Table 4: Causative mechanisms described in TOS

Soft tissue lesions	Bony lesions
Scalene muscles + fibro-muscular bands Subclavian muscle + costo-clavicular ligament Pectoralis minor muscle + fibro-muscular band	Cervical rib (Complete / Partial) First rib anomalies (Synostosis / Bifid) Long C7 transverse process Clavicular abnormalities

In a review of their experience with ATOS, the University of Natal reported the largest South African series to date.[105] The most common bony lesion identified, was that of a compressed SCA between a cervical rib and the insertion of the anterior scalene muscle (See *Table 5* for summary of findings).

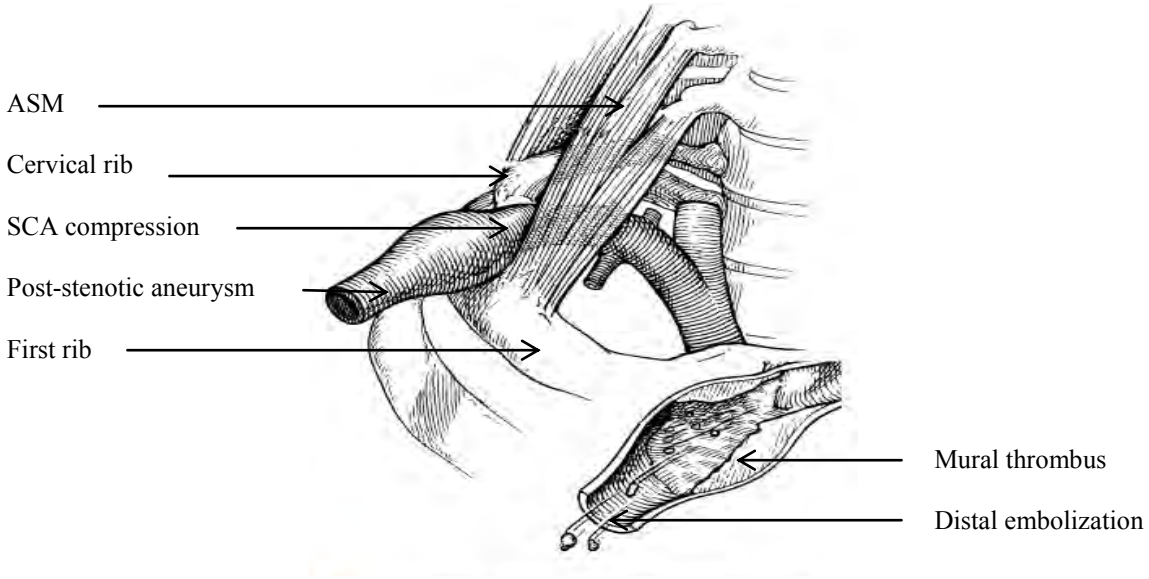
Table 5: Summary of underlying bony pathology encountered in ATOS.[105]

Bony lesion	n
Bony lesion	
Complete cervical rib, articulated on scalene tubercle of 1st rib	15
Partial cervical rib with fibrous band to scalene tubercle	7 (+2 declined surgery)
Osseous anomaly of 1st rib, articulated on 2nd rib	2
	26

The *sequelae* of a chronically compressed SCA represent the end stage of an undiagnosed condition. Compressive stenosis (postural or fixed) at the thoracic outlet develops with fibrous cuffing of the affected vessel, followed by post-stenotic dilatation (PSD) and

aneurysm formation. Aneurysmal degeneration leads to mural thrombus formation and with it, risk of serial distal embolization (*Figure 5*). Most emboli are small and localized to the palmar and digital vessels, commonly presenting with Raynaud's phenomenon. If unrecognized, severe digital ischaemia with digital ulceration or gangrene may occur. Although the genesis of PSD by wall vibration secondary to turbulent flow dynamics has been well studied, the natural history and clinical outcome of this chronic process is poorly understood, but certainly not benign. Experimental evidence suggests that PSD is a reversible phenomenon after release of the stenotic or compressive lesion. [106-107]

Figure 5: Schematic representation illustrating the anatomical relations and sequelae of a chronically compressed SCA (As depicted by Clagett)[108]



The axillary artery is vulnerable to compression as it passes beneath the tendon of the pectoralis minor muscle, where it is fixed at the origin of the circumflex humoral arteries. Repetitive vessel injury can lead to intimal hyperplasia and stenosis, aneurysmal degeneration of the arterial wall with distal thrombo-embolism, pseudoaneurysm formation or propagating dissection.[109]

By means of a retrospective analysis of 41 patients with objective findings of ATOS, Criado et al identified a spectrum of underlying arterial pathologies associated with this condition.[110]

Table 6: Spectrum of arterial pathologies associated with ATOS (adapted from Criado et al) [110]

Finding	Number of cases
Subclavian artery aneurysm	12
Postural stenosis with post-stenotic dilatation	10
Postural stenosis with post-stenotic dilatation	
Subclavian artery	5
Axillary artery	2
Fixed subclavian stenosis	5
Fixed stenosis with post-stenotic dilatation	4
Luminal filling defect	2
Subclavian artery occlusion	1
Total	**41**

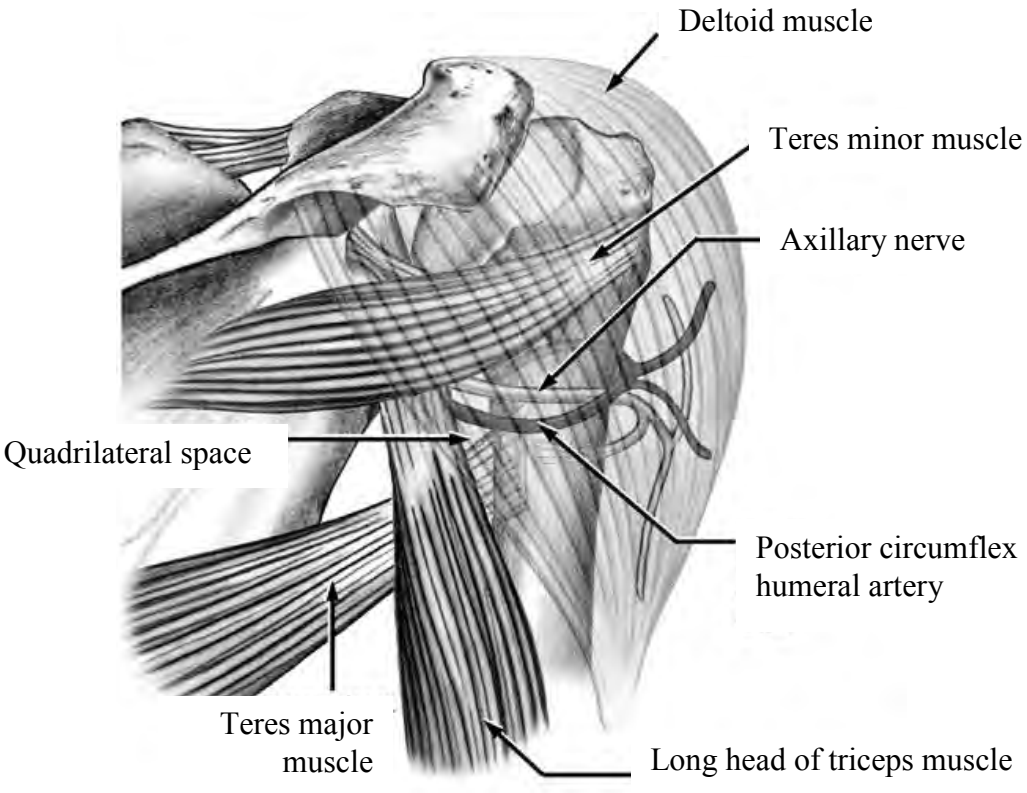
Muscular hypertrophy (particularly of the scalene muscles) in athletes performing repetitive overhead activities (including weight lifters, swimmers and baseball players),[108] may put these athletes at risk of ATOS. Baseball pitchers and volleyball players are at particular risk of axillary artery injury due to repetitive and forceful arm elevation and extension. Male athletes appear to be at greater risk of axillary artery injury, with no gender-specific difference related to subclavian artery injury.[111]

4.2.4.2) Quadrilateral space syndrome

This syndrome usually affects athletes performing repetitive, strenuous shoulder activity, such as baseball pitchers and volleyball players.

The quadrilateral space is formed by the teres minor (superiorly) and major (inferiorly), the long head of the triceps (medially) and the humerus (laterally) (*Figure 6*). After arising from the third part of the axillary artery, the posterior circumflex humeral artery (which can reach up to 8mm in size among major league baseball players)[112] joins the axillary nerve as it traverses the quadrilateral space. At this point, structures are vulnerable to compression, particularly in the setting of hypertrophied surrounding muscles.

Figure 6: Schematic representation illustrating the anatomical relations of the quadrilateral space, with particular reference to the posterior circumflex humeral artery and axillary nerve.



Clinical presentation may include poorly localized discomfort within the shoulder girdle, paresthesia or numbness within the axillary nerve distribution or fatigue and weakness on

extreme abduction and external rotation. Distal ischaemic symptoms may occur as a result of serial arterial embolization in association with aneurysm formation.

Definitive diagnosis is made at arteriography by establishing position-dependant (abduction and external rotation of the shoulder joint) occlusion of the posterior circumflex humeral artery.

4.2.4.3) Brachial artery entrapment

Rarely, position-dependant ischaemia may occur during hyperextension of the elbow joint. Associated anatomical anomalies include the presence of a supracondylar spur with anomalous insertion of the pronator teres muscle, responsible for compression of the brachial artery.[113] A case study of brachial artery entrapment exclusively due to muscular hypertrophy, have been reported.[114] Although exceedingly rare, these conditions should be considered in patients presenting with atypical symptoms of ATOS.

4.2.4.4) Hypothenar Hammer Syndrome (HHS)

HHS is often overlooked in the absence of a thorough occupational and recreational history. Importantly, this condition is usually reversible through cessation of the offending activity, but can lead to morbidity and even amputation if not timeously recognized.

Other terminology used to refer to an occupational disease triggered by continuous use of vibrating hand-held machinery, include *hand-arm vibration syndrome* (HAVS) and *vibration white finger* (now largely superseded by the broader concept of HAVS). HAVS refers to a disorder that affects the blood vessels, nerves, muscles and joints of the hand,

wrist and arm. Injury can occur at frequencies between 5 and 2000 Hz, but the greatest risk exists between 50 and 150 Hz. HHS refers to the vascular component of HAVS.

The concept of HHS was first described in 1934,[115-116] but the term 'Hypothenar Hammer Syndrome' was coined by Conn, after recognizing the mechanism of injury.[117] The incidence of HHS is remarkably low when one considers the relatively large segment of population exposed to the relevant occupational hazards. Possible explanations include anatomical variability of the vasculature in this region as well as the presence of subclinical disease. These factors may also explain the variable presentation of patients, ranging from asymptomatic disease to tissue necrosis.

Although most commonly encountered within the work place (including carpentry,[117] motor mechanics and metal workers), HHS is not restricted to this environment. Recent case reports and case series have confirmed the presence of *HHS in recreational and professional sport activities*, including volley ball,[115] hockey,[115] mountain biking,[118] tennis,[119] badminton,[120] weight lifting and baseball.

The underlying pathogenesis of HHS is based on repetitive blunt trauma to a relatively unprotected terminal ulnar artery. After emerging from Guyon's canal (between the pisiform and hook of the hamate), the distal ulnar artery becomes somewhat fixed as it runs superficially across the hypothenar musculature.[117] Between its deep palmar branch and the origin of the superficial palmar arch, it is particularly vulnerable as it is only protected by skin, subcutaneous tissue, palmaris brevis muscle and superficial aponeurosis.[117,121] Repetitive blunt trauma to the hypothenar eminence (*Figure 8*)

compresses the ulnar artery against the hook of the hamate (the so called “hammer and anvil effect”), triggering vasospasm.[117,122,123] Trauma to the adventitial layer may cause thickening and fibrosis, ultimately leading to extrinsic scarring with post-stenotic dilatation / aneurysm formation or arterial occlusion.[117,121] Distal embolization of the digital arteries may exacerbate ischaemia.

Figure 7: DSA of a 49-year-old recreational baseball player’s right hand[124]

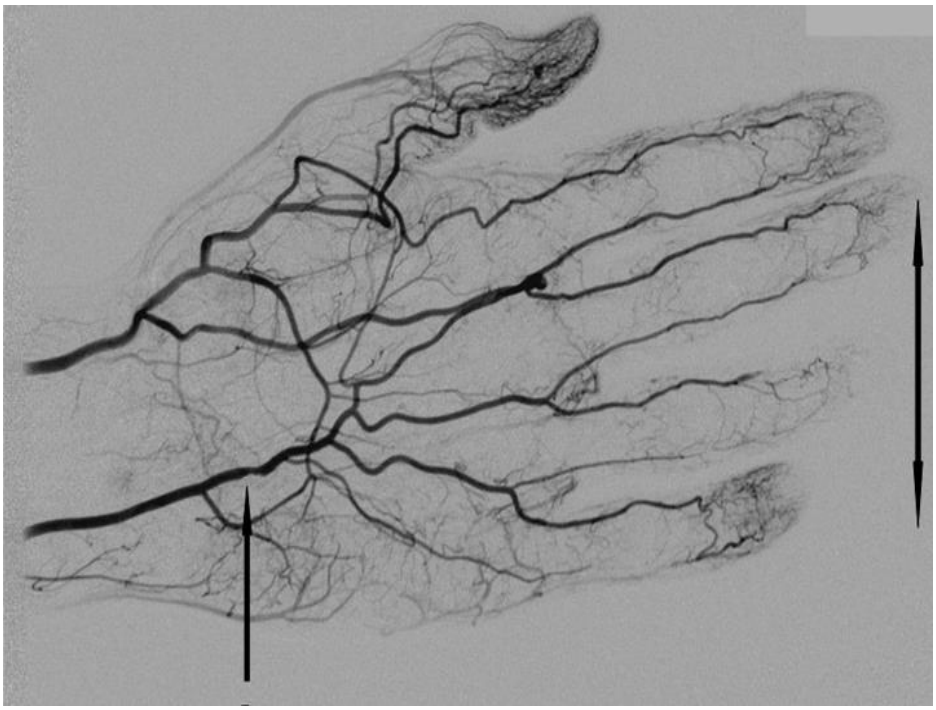
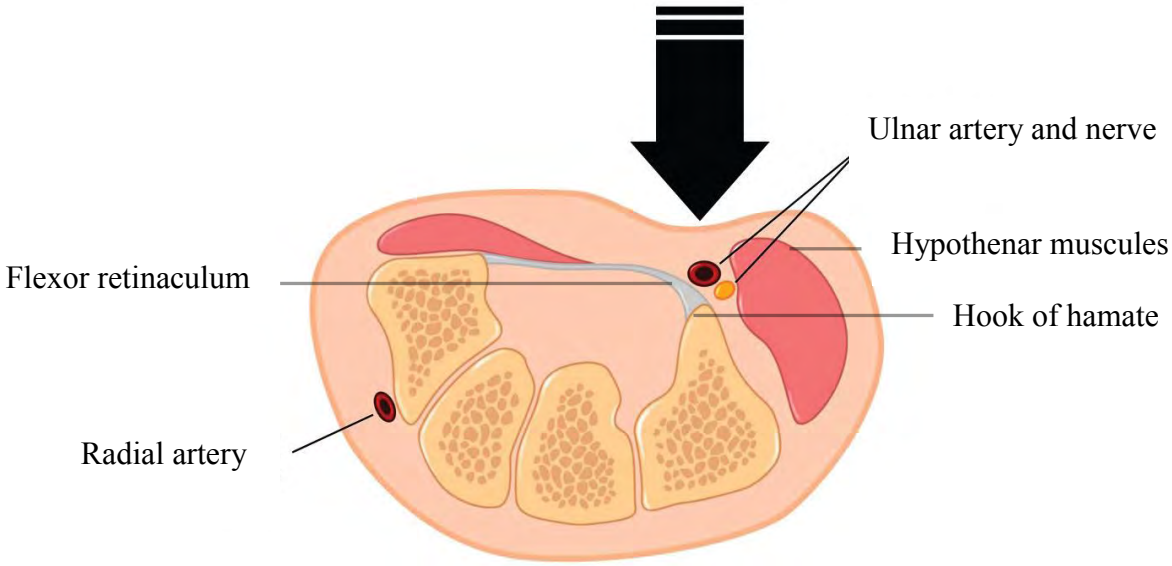


Figure 8: Axial anatomy, demonstrating vulnerability of the terminal ulnar artery and accompanying nerve (sensory portion), to repetitive trauma (black arrow). (As depicted by Swanson et al)[125]



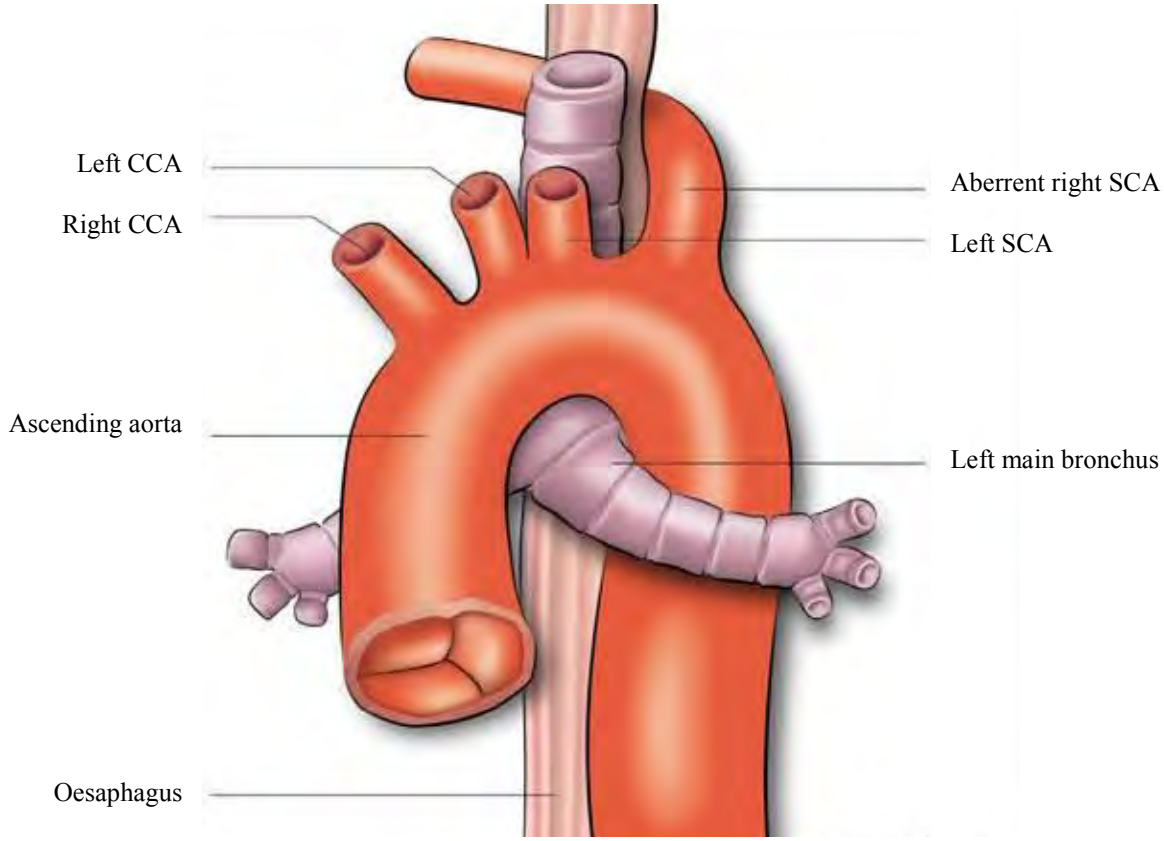
4.2.4.5) Congenital anomalies

Anatomical anomalies of the aortic arch and upper limb vasculature are rare occurrences (estimated frequency of 3%) that have been implicated in the pathogenesis and development of ischaemic conditions. These congenital anomalies may create stenoses, aneurysms (often manifesting as thrombo-embolism) and occlusive disease of the upper extremities, but are usually fortuitous radiological findings as it frequently follows an asymptomatic course.

The most common aortic arch anomaly (as described by Hunauld in 1735) is the occurrence of a *left aortic arch with an aberrant right SCA*, seen in 0.5% of the population.[126] The vessel originates distal to the left subclavian origin (typically posterior and inferior on the arch) and crosses the midline between the oesophagus and vertebral

column (*Figure 9*). In 1794, Bayford described the first case of symptomatic compression of the oesophagus by the posteriorly positioned aberrant right SCA, known as dysphagia lusoria. These patients may also have associated anomalies, such as a common carotid trunk and right vertebral artery originating directly from the right common carotid artery.

Figure 9: Anatomic relations of an aberrant right SCA.



Other, less common anomalies include the occurrence of a *right aortic arch with an aberrant left SCA*. Degenerative aneurysmal changes at its aortic origin may occur in up to 60% of patients, known as Kommerell's diverticulum.

Variations in the arterial anatomy of the upper extremities, are uncommon and *rarely cause ischaemia of the upper extremity in isolation*. Most of these variants occur in either the radial or ulnar artery; brachial artery variations are less common.[127,128] Variability in the path or source of the radial artery is reported in up to 30% of patients. The most common variation is a high radial artery origin, arising from the brachial or axillary artery proximal to the antecubital fossa. This is estimated to occur in between 2% and 14% of extremities. Substantially less common variations include absence of the radial artery, duplication of the radial artery and superficial passage of the radial artery above the tendons of the snuffbox (adductor pollicis longus and extensor pollicis brevis). Variation in the ulnar artery pathway or position is much less commonly seen (3% to 5%).[129]

The blood vessels in the hand communicate via 3 major arches—2 palmar and one dorsal arch. A great number of studies have elucidated the extreme anatomic variance in this network of vessels, particularly on the radial aspect of the hand. Studies demonstrate the superficial palmar arch to be complete in more than 80% of patients, with the deep palmar arch complete in more than 90%.[129] A clinically relevant anatomic variant is the presence of a communication between a persistent median artery (an embryologic remnant that normally undergoes apoptosis during upper limb development) and the superficial palmar arch, which serves to complete the arch. This was seen in 15.5% of specimens in a well-performed cadaveric study.[130]

4.2.5) Thrombotic disease

Atherosclerosis of the upper extremity arteries is a relatively rare occurrence, leading some investigators to label all non-traumatic cases of AULI, as embolic. While this may hold true for a large proportion of cases, it fails to distinguish the rarer causes of arterial occlusion, such as native arterial thrombosis. The true incidence of thrombosis as a cause of AULI is difficult to determine. Reports suggest that 5% of AULI cases in population studies and 9–35% in surgical series are due to native artery thrombosis. Establishing the correct diagnosis is essential in order to offer appropriate management options. Treatment usually requires bypass surgery or thrombolytic therapy, with inappropriate embolectomy or thrombectomy associated with higher morbidity and mortality rates.

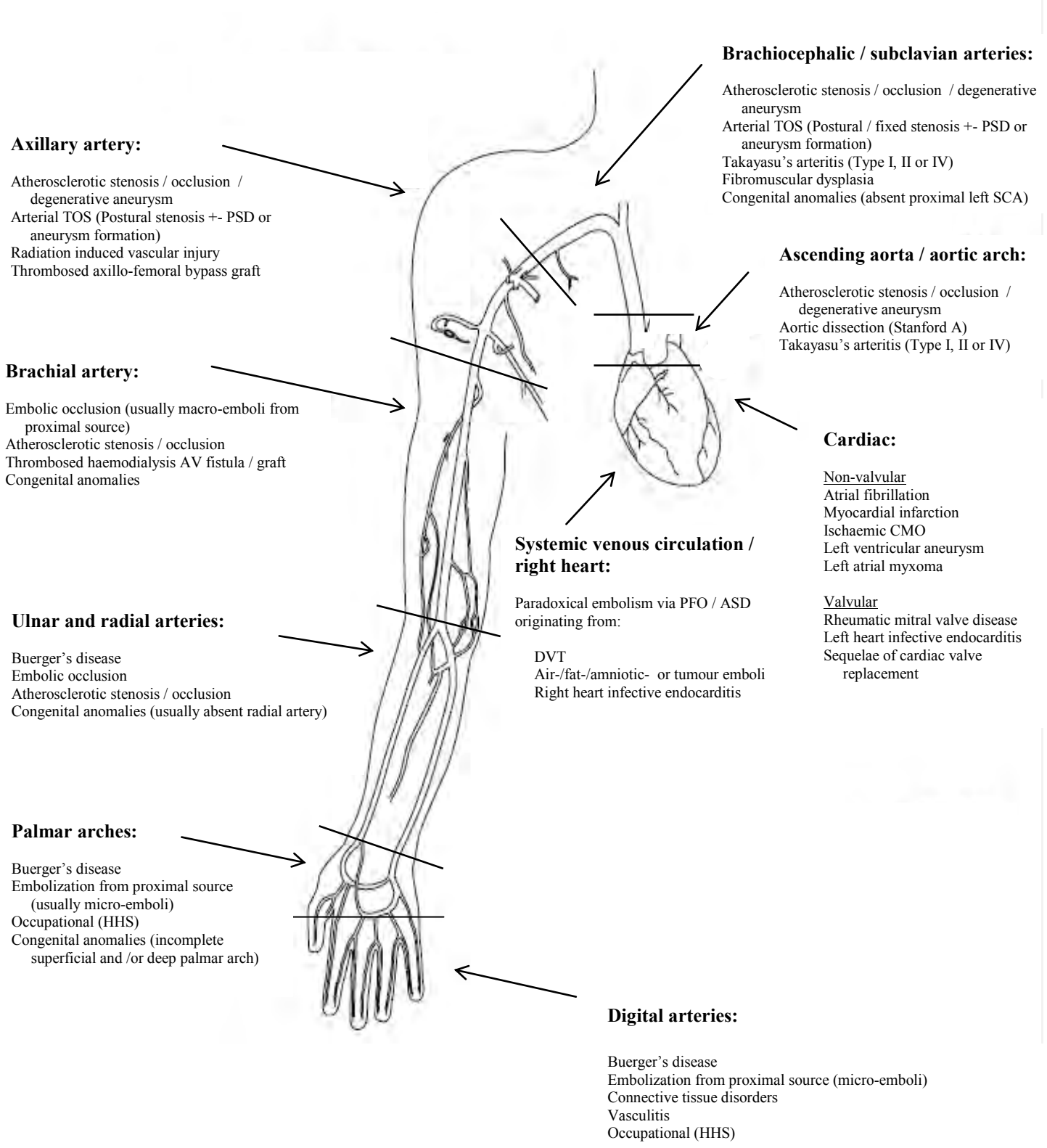
Most of the proximal arterial lesions that cause emboli, can also result in thrombosis (including atherosclerotic plaques, aneurysms and arteritis). As Virchow suggested in 1856, thrombus formation is the result of an interaction between an injured vascular surface, stasis and hypercoagulability of blood. Arterial thrombosis most often develops at the points of severe stenosis. However, a thrombus can form in the absence of significant pre-existing stenosis, particularly when the surface of the plaque is ulcerated or after intra-plaque haemorrhage has occurred (vulnerable / unstable plaque). Low-flow haemodynamic states, such as congestive heart failure, hypovolaemia or hypotension of any cause may predispose to arterial thrombosis. Hypercoagulable states, such as myeloproliferative disorders, hyperviscosity syndromes and coagulation disorders, may also contribute to thrombosis of the diseased artery.

5) THE ANATOMICAL BASIS OF DISEASE

On initial evaluation of this condition, it may be difficult to establish the precise aetio-pathological process involved. Therefore, making use of a structured approach will be of benefit to the clinician. Some authors prefer classifying causes according to local, regional and systemic disease processes. Others categorize patients into two main groups, namely Upper Extremity Occlusive Disease and Thrombo-embolic Disease (refer to section on Aetio-pathology).

As surgeons, an attractive approach to the myriad of underlying aetiologies, is the implementation of an anatomical framework. A differential diagnosis for each arterial segment can be compiled (*Figure 10* below), but should be interpreted in terms of the relevant clinical information.

Figure 10: A proposed anatomical approach to the aetiology of upper limb ischaemia



6) CLINICAL PRESENTATION AND MANAGEMENT PATHWAYS

Clinicians prefer categorizing presenting patients into acute or chronic ischaemia, according to the duration of their symptoms. Acute ischaemia should be immediately assessed and the severity of ischaemia used to guide early management decisions.

6.1) Acute upper limb ischaemia

According to the TASC II consensus document,[11] acute limb ischemia (ALI) is defined as any sudden decrease in limb perfusion posing a potential threat to limb viability. Patients usually present within 2 weeks following the acute event, but time to presentation may be influenced by the severity of ischaemia and access to healthcare.[24] Clinical decision-making hinges upon a focused, but thorough history and clinical examination. Essential questions need to be answered pertaining to limb viability, the severity of ischaemia, suspected underlying aetiology, the presence of serious concurrent systemic diseases and conditions mimicking AULI.

Limb viability

An inappropriate attempt at revascularization of an irreversibly ischaemic limb, may result in preventable mortality. Signs that preclude limb salvage include the presence of compartmental rigidity and fixed skin staining (*Table 6* – Rutherford category III). A small number of patients present in a moribund state with signs of irreversible limb ischaemia. Terminal care may be the kindest and most appropriate management option in these patients. Primary amputation, after adequate resuscitation and stabilization, should be offered to candidates deemed fit for a general or loco-regional anaesthetic.

Severity of ischaemia

The severity of ischaemia can be accurately established by a systematic clinical examination and bedside doppler investigation. The duration, location and intensity (including change in the severity over time) of pain as well as the presence of motor or sensory deficiencies, guide early management decisions regarding the urgency of revascularization. Immediately threatened extremities should undergo an emergent attempt at revascularization, while a period of further investigation, observation and non-operative treatment may be appropriate in managing the marginally threatened limb. Rutherford et al[131] suggested a classification system (*Table 7*) in an attempt to standardize reports dealing with ALI.

Table 7: Suggested classification of acute limb ischaemia[131]

	Category	Description/prognosis	Sensory loss	Muscle weakness	Doppler signal	
					Arterial	Venous
I	**Viable**	Not immediately threatened	None	None	Audible	Audible
II	**Threatened**					
	a)Marginal	Salvageable if promptly treated	Minimal/none	None	Often inaudible	Audible
	b)Immediate	Salvageable if immediately treated	Pain at rest	Mild/moderate	Usually inaudible	Audible
III	**Irreversible**	Major tissue necrosis or permanent nerve damage	Profound, insensate	Profound, paralysis	Inaudible	Inaudible

Suspected underlying aetiology

Importantly, the clinician should attempt to distinguish embolic from thrombotic occlusions, considering that management pathways differ considerably. Typically, the patient that presents with an embolic occlusion will do so early (usually within 24 hours) due to a lack of arterial collateralization and often present with a more severe grade of ischaemia.

Thrombotic occlusions present later, usually within days of the acute event. One particularly important implication, is the relative ineffectiveness of thrombolysis in the management of thrombosis present for more than 2 weeks duration (as per post-hoc analysis of the STILE trial data).[132] It is important to enquire about a history of arm claudication and previous revascularization procedures. Signs of atherosclerotic occlusive disease of the contralateral upper extremity, favour the diagnosis of thrombosis.

Serious concurrent diseases

The identification of serious systemic illnesses in patients with AULI, is important for several reasons. Poorly optimized systemic diseases (including hypertension, diabetes, ischaemic heart disease / recent cardiac events and renal dysfunction), can influence the patient's fitness for a general or loco-regional anaesthetic, contribute to the underlying disease process and drastically affect the patient's prognosis. This can be best appreciated in the subgroup of patients presenting with embolic disease of the upper extremities. Deguara et al[1] reported, in a subgroup of patients that underwent embolectomy, that all early (30 day) mortalities were attributable to cardiopulmonary incidents, none being a consequence of arm ischemia or gangrene. The majority of patients (84%) with embolic disease had associated ischaemic heart disease or a recent myocardial infarction and between 51 - 63% was diagnosed with atrial fibrillation. The higher mortality rate of patients undergoing a seemingly small surgical procedure under general anaesthesia compared with loco-regional anaesthesia, may also reflect an increased risk of cardiovascular events.

Conditions mimicking AULI

Though AULI may often be an easy diagnosis to make, one has to consider certain conditions that may mimic or influence patient presentation. These include systemic shock / low flow states (especially if associated with chronic occlusive disease), subclavian-axillary vein thrombosis presenting with phlegmasia cerulea dolens, acute cervical compressive neuropathy and exertional forearm compartment syndrome.

Non-operative vs operative management

Individual events of AULI, are not usually as limb-threatening as those in the lower extremity and thrombo-embolectomy is not always required for limb salvage. AULI may be managed by implementing various treatment modalities, but no real guidelines exist to clarify when a conservative approach is warranted. Previous publications suggest that conservative management of patients with AULI results in functional limb impairment in 50 – 75% of cases and is therefore not advocated.[52,133] Recent publications have challenged this view by highlighting several case series reporting successful conservative management in a selected subgroup of patients, with excellent functional outcome. Conservative management takes advantage of the superior collateral arterial supply in the arm, compared with the lower extremities.

The best level of evidence on this topic, takes the form of a recently performed systematic review.[134] Conservative therapies included anticoagulation, rehydration and treatment of contributing medical conditions. A total of 34 retrospective studies and 3 review articles were recovered. Operative management was performed most commonly (86%), followed by conservative management (11%) and interventional radiological approaches (3%).

Catheter-directed embolectomy procedures, when performed as the primary treatment modality, revealed an overall success rate of 85%–90%. Significant selection bias and treatment inconsistencies in the subgroup of patients receiving conservative management, hampered the interpretation of results. The perused literature only reported the use of conservative management in patients deemed to be unfit for surgical management or those with symptomatically mild disease, not considered worth treating. On worsening of symptoms, patients initially treated conservatively, were crossed over to the surgical intervention group. Furthermore, some patients were managed supportively without the initiation of anticoagulants. In those studies where anticoagulants were initiated, long-term anticoagulation rates were poor with some authors reporting a 22% effective anticoagulation rate in patients representing with recurrent embolism.[135].

When considering the evidence, it is clear that inherent challenges do exist. Significant numerical and ethical dilemmas may arise when attempting to perform a randomized controlled clinical trial to attain level-one evidence. The tendency to treat ‘‘fit’’ and ‘‘unfit’’ patients differently, is deeply ingrained in clinical practice and it may be viewed unethical to deny a ‘‘fit’’ patient operative therapy in view of the current literature.

Some authors believe that an initial conservative approach in suitable patients, are practiced more commonly than is reported. This underreporting limits the literature’s ability to report progress and when combined with selection bias, leads to poor quality data. Therefore, units regularly practising a non-operative approach to the acutely ischaemic upper limb, has a responsibility to audit and publish their results.

7) OUTCOME

Series that combine both acute and chronic ischaemia are rare.[1,5-7] The largest of these, included 172 patients undergoing revascularization procedures for upper limb ischaemia over a 20 year period.[1] About two-thirds of the procedures were performed for acute ischaemia, with embolic disease being the most common underlying pathology in this subgroup, closely followed by trauma. More than half of the patients presenting with chronic ischaemia had an intrinsic atherosclerotic stenosis or occlusion of the subclavian or axillary artery, with the rest made up by thoracic outlet syndrome and iatrogenic injuries.

7.1) Acute upper limb ischaemia: Embolic disease

Numerous reports have been published with regard to outcome after lower extremity embolectomy. In contrast, few reports have focused on upper extremity embolic disease[53,136-141] with most of these only presenting early (30 day) outcome.[53,136-139] Generally, the functional outcome after upper extremity embolectomy is excellent, provided that there was minimal delay in presentation and severe ischaemia was not present at the time. However, early (30 day) mortality remains high, mostly as a result of severe comorbid disease.

The concept that mortality following embolectomy is a consequence of the patient's comorbidity rather than the embolus itself, is well supported.[1,52] Throughout the literature, it is generally agreed that patients who present with acute embolic episodes, have a high early (30 day) mortality rate ranging between 9 – 19%.[1,138,142,143] Deguara et al[1] reported a 30-day mortality rate of 18.2% in patients undergoing upper extremity

embolectomy (n = 10). All deaths were attributable to cardiopulmonary events. A further 11 patients died within a year of surgery, resulting in a 12-month mortality rate of 38.2% (n = 21). In a retrospective single centre study of 148 patients admitted with acute upper limb ischaemia, Licht et al reported that the cause of death was mostly due to cardiovascular (32%) and cerebrovascular (22%) incidents with 8% of patients dying from malignancy during the 5 year follow-up period.[142]

These high mortality rates are convincing of poor short-term outcome, however, the relative paucity of long-term follow-up data led some authors to question whether this phenomenon persist after discharge from hospital. This was addressed by a National Cohort Study in Denmark, published in 2010, that followed 1 377 patients after thrombo-embolectomy for a period of 5 to 17 years. Age- and sex-specific risk of stroke was 2 to 16 times higher and risk of death 3 to 11 times higher than that of the general population.[143]

Specific populations have been described, where the outcome is even worse than mentioned above. Javid et al[144] reported on the outcome of 20 patients with an underlying malignancy and arterial thrombosis. The outcome was generally poor. Two patients underwent major amputations. The mortality rate from the time of presentation was 50% at 3 months and 83% at 12 months. Therefore, arterial thrombosis should probably be viewed as an agonal event in many of these patients and palliative treatment may be the most appropriate management option.

Authors generally agree that prompt operative intervention is the single most important determinant of a successful functional outcome. Be that as it may, some reports claim that the duration of symptoms before embolectomy does not significantly impact on functional outcome.[136,142] Licht et al[142] disclosed that 26% of patients in their series were treated more than 24 hours after the onset of symptoms and that the time interval between symptom onset and revascularization, did not significantly influence long-term result as measured by arm-function (*Table 8*; Chi-square = 3.9 with p = 0.42 between the three time intervals).

Table 8: Relationship between arm-function and duration of ischaemia (Licht et al)[142]

Time interval	Normal arm-function	Slightly decreased arm-function	Severely decreased arm-function	Total
Less than 12h	33 (87%)	4 (11%)	1 (2%)	38
12-24h	13 (93%)	1 (7%)	-	14
More than 24h	11 (69%)	4 (25%)	1 (6%)	16
Total	57 (84%)	9 (13%)	2 (3%)	**68**

It may be argued that analysis of the length of ischaemia and arm function does not take into account the severity of ischaemia. Thus, patients who presented after 24 hours may have had less severe ischaemia than those who presented earlier because of pain. Even though one should aim to operate promptly in these patients in order to minimise potential functional compromise, the time interval per se should not be seen as a contra-indication to surgery. The extremity should only be regarded as being out of therapeutic reach if the patient presents with a rigid limb, indicating irreversible ischemia.

7.2) Acute upper limb ischaemia: Thrombotic disease

Few studies report the use of thrombolytic therapy in AULI, even though it's role in the lower extremities has been well established.[145] When studies commenting on the use of thrombolytics in AULI are considered, thrombolysis and surgery have equal efficacy, but small numbers mitigate this conclusion.[146-148] Cejna et al[147] also found thrombolysis to have equivalent results to surgery, with the exception of distal occlusions, where results were found to be inferior. Concerns regarding the use of thrombolytics in AULI revolve around the risk of haemorrhagic cerebro-vascular incidents. Some authors suggest that this risk may be higher with upper than lower extremity thrombolytic therapies.

7.3) Chronic upper limb ischaemia – Bypass procedures in general

Upper limb arterial bypass procedures were first described by Garret in 1965. Since then, only a few small surgical series have reported their single centre experience with this procedure (*Table 9*).

Table 9: Summary of major publications on upper limb bypass procedures

Publication	Study group	Tissue loss as indication	Key results
Spinelli F et al[23] Eur J Vasc Endovasc Surg (2010) Retrospective (Italy)	23 patients (1998-2008)	35%	Primary patency 82.6%, Secondary patency 91.3%, Limb salvage 100%
Hughes K et al[9] J Vasc Surg (2007) Retrospective (USA)	20 patients (1990-2003)	15%	Primary patency 85%, Secondary patency 85%, Limb salvage 100%
Chang BB et al[149] J Vasc Surg (2003) Retrospective (USA)	15 patients (1992-2002)	83%	Primary patency 88.8%, Secondary patency 88.8%, Limb salvage 88.8%
Roddy SP et al[10] J Vasc Surg (2001) Retrospective (USA)	56 patients (1986-1998)	13%	Primary patency 87%, Secondary patency 98%, Limb salvage 100%

In general, the results achieved with upper limb arterial bypass procedures are satisfying, with reported graft patency rates of between 85-98% at 2 years. Multiple factors influence surgical outcome. Certainly the most important factor, the indication for surgical intervention, varied significantly between trials. Spinelli et al reported tissue loss as the indication in 83% of patients compared to 13% reported by Roddy et al. Other indications included exertional arm pain (Roddy et al 30%; Hughes et al 55%) and rest pain (Roddy et al 57%; Hughes et al 30%). Units, implementing a more aggressive approach to the management of relatively minor symptoms, may reflect better surgical outcomes, especially superior limb salvage rates.

In stark contrast with the subgroup of patients presenting with embolic upper limb disease, none of the recent surgical bypass series (Spinelli et al 2010, Hughes et al 2007) reported any perioperative deaths, cardiac complications, wound infection, pulmonary complications or renal failure. The mean length of post-operative hospitalisation was 3- 6 days.

7.4) Chronic upper limb ischaemia – Distal bypass procedures

A systematic review of 16 publications reporting on distal (infra-brachial) upper extremity bypass procedures, was recently performed.[150] At an average follow-up of 37 months, the overall autologous vein graft patency rate was 85% and autologous arterial (including deep inferior epigastric artery; lateral femoral circumflex artery and thoraco-dorsal artery) graft patency rate 100%. All studies reported an improvement of ischemic symptoms including a reduction in cold sensitivity, pain and digital ulceration.

7.5) Chronic upper limb ischaemia – Endovascular procedures

The endovascular management of upper extremity atherosclerotic occlusive lesions, are being progressively explored. Current evidence seems to favour the use of percutaneous techniques in the management of occlusive disease of the supra-aortic trunks, while the treatment of infra-brachial lesions are still controversial.

The technical success rate of open surgical BCA/SCA revascularization is high, but major complications may occur (13-19% incidence) with an expected 30 day mortality rate of 2–3%.[151-154] Multiple publications suggest similar success rates with less morbidity and mortality, when implementing percutaneous revascularization techniques to address occlusive lesions of this arterial segment.[151-154]

Table 10: Summary of studies reporting on SCA / BCA stent placement

Study	Patients	Arterial lesions	Technical success	Mean follow-up	Restenosis	1°patency	2°patency
Rodriguez-Lopez et al.1999[156]	69	70 SCA	95.7%	13mo	10%	92% at 18mo	96% at 18mo
Henry et al. 1999[157]	113	113 SCA	91.2%	51.6mo	15.5%	87% at 30mo	94% at 30mo
De Vries et al. 2005[158]	110	110 SCA	93%	34mo	7.8%	89% at 60mo	-
Przewlocki et al. 2006[159]	75	73 SCA, 2 BCA	93.3%	24.4mo	15.6%	77% at 60mo	95% at 36mo
Patel et al. 2007[155]	170	166 SCA, 11 BCA	98.3%	35.2mo	15.9%	83% at 66mo	96% at 54mo

Patel et al[155] recently published their experience with primary percutaneous revascularization of symptomatic BCA/SCA atherosclerotic lesions. This series is the largest to date, with 170 consecutive patients treated over a 13 year period. The technical

success and patency rates were comparable to previously published reports, however, technical success in recanalizing occlusions (90.5%) were significantly higher than reported by prior studies. The author attributes this to the evolution of recanalization techniques, with 62% of patients with occlusions undergoing a retrograde brachial approach or combined femoral/brachial approach. Complications were reported in 5.9% (n=10) of patients with no procedure-related deaths recorded. This compares favourably with surgical series.[151-154]

Literature on the endovascular management of radial and ulnar occlusive disease, are currently limited to case reports and small case series. [156-157] From this limited pool of data, it is clear that further investigation is required before firm recommendations can be made.

CHAPTER THREE:

AIM

The objective of this study was to comprehensively review the Vascular Surgery Unit's experience with upper limb ischaemia over a 12 year period by defining the pattern and distribution of disease and pathological profile, describing key demographic and clinical features and reporting on conventional clinical outcomes (including mortality, morbidity, limb salvage and re-intervention rates). These findings were interpreted in context of the current literature in order to identify potential areas of interest, perhaps paving the way for further (more focused) research on a variety of related topics.

CHAPTER FOUR:

METHODS

1) STUDY DESIGN

Retrospective descriptive study

All patients that underwent a surgical intervention for upper limb ischaemia at Groote Schuur Hospital's Vascular Unit between January 2000 and December 2011, were included in the audit. Approval from the Department of Surgery Research Committee and Faculty of Health Sciences Human Research Ethics Committee was obtained prior to accessing data *(Appendix 1 & 2)*. A research folder was compiled for each patient and numeric codes assigned in order to maintain patient confidentiality. On completion of the data collection process, both qualitative and quantitative data were analyzed and comparisons made to the current literature. Interesting observations were highlighted and discussed in monograph form.

2) STUDY PARTICIPANTS

Sample selection

All patients that underwent a surgical intervention for upper limb ischaemia from 2000 to 2011, were retrospectively selected from the Groote Schuur Hospital Vascular Unit's operative database.

Inclusion criteria

- Patients that underwent revascularization and ablative procedure(s) for upper limb ischaemia at Groote Schuur Hospital's Vascular Unit
- Procedure(s) performed from January 2000 to December 2011
- Primary as well as secondary procedures

Exclusion criteria

- Penetrating and / or blunt traumatic vascular injuries

The Trauma Unit at our facility published extensively on this topic (including brachial, axillary and subclavian artery injuries[160-162] – a total of 242 patients) between 2003 and 2011. In order to guard against the duplication of data, this subgroup of patients were excluded from the current series.

- Primary Raynaud's phenomenon

3) OUTCOME MEASUREMENTS

Patient hospital records, in the form of a hospital folder or microfilms, were obtained from Medical Records Department and data electronically captured by means of a data collection sheet in Microsoft™ Word *(Appendix 3).* Referral letters, clinical notes, treatment charts and special investigations (including laboratory results sheets in the folder) were perused. The NHLS Disa electronic results system was accessed for each patient to confirm that no laboratory investigations of significance, were overlooked. This process was performed by the researcher, under the following headings:

- **Demographic details**
    - Age, gender and ethnic group
- **Contact details**
    - Address and telephone number of patient or relative
- **Clinical presentation**
    - Acute limb ischaemia
        - Rutherford grade I, IIa, IIb or III, with or without the presence of compartment syndrome

    - Chronic limb ischaemia
        - Digital ulceration (active or healed), Raynauds phenomenon, claudication symptoms or neuro-vascular symptoms
- **Risk factor(s) for atherosclerosis**
    - Hypertension, hypercholesterolaemia, Diabetes mellitus (Type I/II) and cigarette smoking (including estimated pack years)
    - Other substances (including cannabis and TIK)
- **Other systemic diseases**
- **Appropriate medical therapy**
    - Pre-event as well as post-event
- **Underlying aetio-pathology**
    - Embolic source
        - Cardiac or extra-cardiac (including site of occlusion)
    - Thrombotic source
        - Associated with atherosclerosis or thrombophilia (including site of occlusion)
- **Special investigations performed**
    - Upper limb dopplers, upper limb duplex arteriogram, digital doppler pressure with caloric stimulation
    - Angiogram (Arch or select run)
    - MD-CTA, MRA
    - CXR / C-spine X ray
    - Echo / ERNA

- Laboratory investigations
    - S-fibrinogen, CRP and ESR, fasting homocysteine level, S-creatinine, HIV status

- **Procedure(s) performed**
    - Date and length of procedure, time started (within day time or after hours)
- **Open surgical procedure**
    - Embolectomy, bypass graft (including type), fasciotomy performed, ablation performed (including before or after attempt at revascularization and level of amputation)
- **Endovascular procedure**
    - PTA, stentgraft placement (including type and site), thrombolysis (alone or as combination therapy)
- **Peri-operative (30 day) and follow-up (6 months, long term) data**
    - Died / Alive (including reason for death)
    - Systemic complications
    - Procedure related complications
        - Wound complications, bypass graft complications, neuropraxia / nerve injuries and ablation
    - Pulse status / Doppler pressures / Duplex arteriogram
        - Improved, same or deteriorated
    - Function
        - Normal, weakness, contracture, claudication

A clinical research folder was compiled for each patient and numeric codes assigned in order to maintain patient confidentiality. The research folder included the afore mentioned Microsoft™ Word data collection sheet, copies of referral letters, results from special investigations performed as well as operation sheets.

4) DATA ANALYSIS

On completion of the data collection process, data was transferred from the patient research folders and consolidated in a Microsoft™ Excel data collection sheet. The data was appropriately coded to assist data analysis. Data analysis was performed using STATA® statistics / data analysis program by StataCorp, Texas, USA. Frequencies and percentages were calculated for categorical data. Means and standard deviations or medians and percentiles were calculated for continuous data.

CHAPTER FIVE:

RESULTS

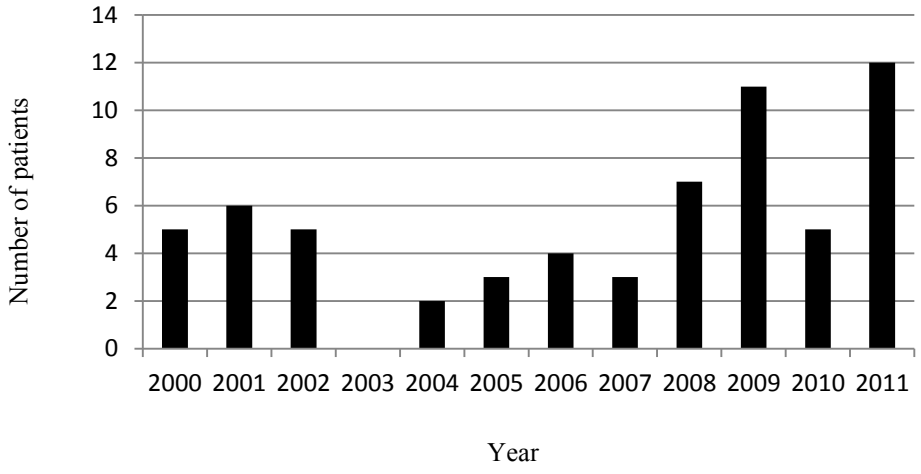
1) INTRODUCTION

When dealing with a broad topic and, in the absence of a specific question being asked, presenting findings in an isolated fashion may be less informative to the reader. Therefore, although slightly unconventional, the results of this study will include concise, relevant discussion of the literature in the interest of capturing the true context of these findings. The "discussion" section (chapter 6) will focus on future research perspectives.

2) INCIDENCE AND DEMOGRAPHICS

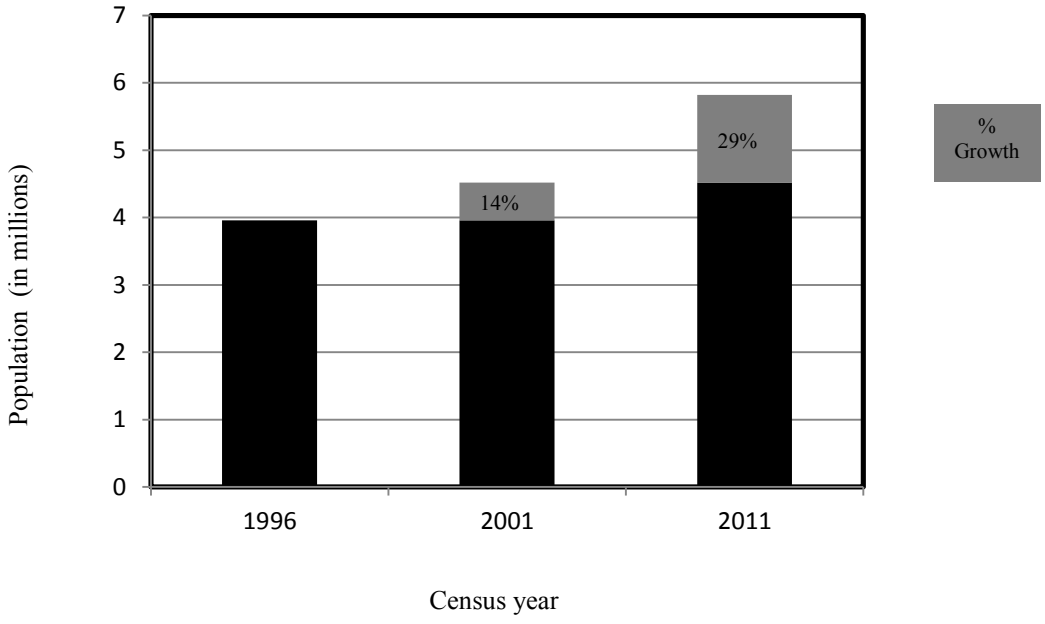
Sixty-four patients presenting with upper limb ischaemia, were evaluated and managed surgically during the 12 year study period (from 01 January 2000 to 31 December 2011). As previously mentioned, referrals managed non-surgically, were excluded from this series. Therefore, *Figure 11* should *not* be interpreted as the total number of referrals received, but as the number of referrals warranting surgical intervention.

Figure 11: Patients receiving surgical intervention



A clear escalating trend was observed, with 56% of surgically managed patients, referred within the last 4 years of the study period (2008-2011). Seeing that subjects were retrospectively selected from an *operative* database, no data pertaining to the total number of referrals were captured. Therefore, no correlation can be made between the number of referrals received and the number of patients managed surgically. Regardless, an increase in the absolute number of referrals is still the most conceivable explanation to rationalize the observed trend. This finding, however, needs to be interpreted in context of the population growth within the Western Cape during the study period and does not necessarily represent a true increase in disease incidence (*Figure 12*).

Figure 12: Western Cape population growth according to recent Census statistics



Another, less likely explanation may be that a more aggressive surgical approach (or more guarded approach to non-operative management) was followed during the last 4 years of the study period. Anecdotally though, the indications for surgical intervention has remained unchanged during this period.

Age and gender

Forty females (62.5%) with a mean age of 51 years (range 15 – 84 years) and 24 males (37.5%) with a mean age of 46 years (range 15 – 76 years), were included in the study, reflecting a male to female ratio of 0.60. Comparatively, the 2011 Western Cape Census figures reported a male to female ratio of 0.96, drastically higher than that of the study group. However, one has to be mindful of the fact that demographic variables may be strongly influenced by the underlying cause of ischaemia (*Table 11*).

Table 11: Comparative demographic details according to prevailing aetiologies

Aetiology	N of patients	Mean age (range)	M:F ratio
Thrombo-embolic disease	30	55 (37 – 80)	0.43
Atherosclerotic occlusive disease	12	57 (39 – 84)	0.71
Thoracic outlet obstruction	8	28 (15 – 59)	1.67
Takayasu's disease	4	27 (20 – 36)	0.33
Thromboangiitis obliterans	4	46 (36 – 53)	3.00

Considering that we are dealing with an aetiologically heterogeneous group of patients, significant demographic findings should rather be discussed in context of the underlying cause of ischaemia.

Embolic versus UEAOD

Multiple publications support the view that patients with thrombo-embolic ULI, when compared to UEAOD, present at a more advanced age.[1,163] One of these series included 172 patients undergoing revascularization procedures for ULI over a 20 year period.[1] The mean age of presentation in the thrombo-embolic subgroup (n=61) was appreciably older (72.4 years) than those presenting with UEAOD (n=29, mean age 62.5 years). Interestingly, this finding was not observed in our series, with the thrombo-embolic

subgroup (n=30) notably younger than expected (mean age of 55 years) compared to the subgroup presenting with UEAOD (n=12, mean age of 57 years). A larger proportion of females were affected by thrombo-embolic disease in our series, than reported by Deguara et al[1]. The reasons for these findings are still unclear and further investigation is warranted.

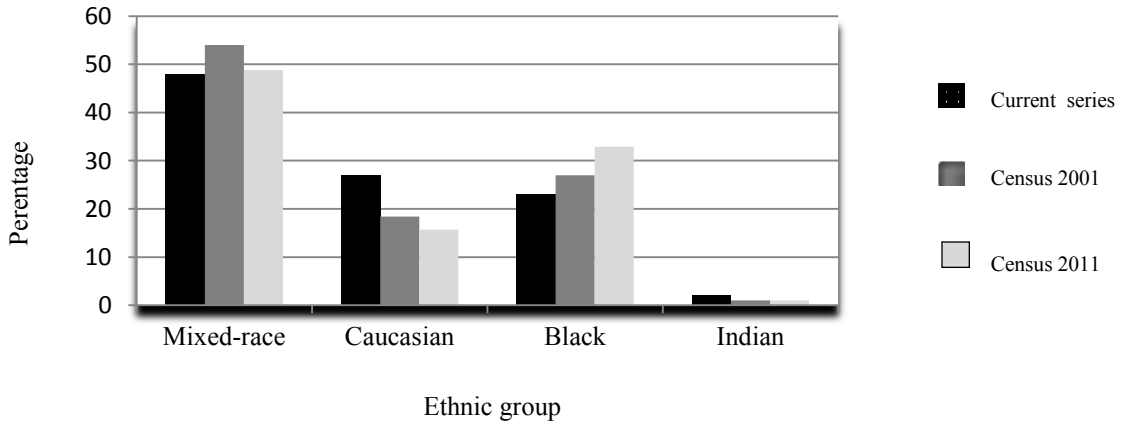
Table 12: Demographic comparison of TED versus UEAOD subgroups

Current series			Subgroup	Deguara et al		
n	Mean age	M:F ratio		n	Mean age	M:F ratio
30	55 years	1:2.3	**Thrombo-embolic**	61	72.4 years	1:1.1
12	57 years	1:1.4	**UEAOD**	29	62.5 years	1:1.9

Race

Patients of mixed-race heritage contributed 48% to the study group, followed by Caucasians (27%), Blacks (23%) and Indians (2%). Once again, it is important to interpret these findings in terms of the 2001/11 Western Cape Census figures (*Figure 13*). Unfortunately, due to multiple confounding factors being present, no firm conclusions can be drawn regarding the race-specific incidence of ULI. One such factor is the unknown number a patients seeking medical attention from private health care facilities.

Figure 13: Race prevalence



Referral patterns

As expected, the majority of cases (84%) were referred from health care facilities located within the Cape Metropole. Approximately 8% of patients were referred from centres outside of the Cape Metropole, but within the borders of the Western Cape with 2 patients referred from the Eastern Cape.

Table 13: Source of referral according to province

Province	n	Percentage	Cumulative
Western Cape			
Cape Metropole	54	84.4	
Outside Cape Metropole	5	7.8	92.2
Eastern Cape	2	3.1	
Unknown	3	4.7	100.0

Most referrals were received from Secondary Hospitals (52%), with Community Health Centres (16%), Tertiary Hospitals (13%), Private facilities (13%) and Primary Hospitals (3%) contributing to the rest of the referrals.

Table 14: Level of referring facility

Level of facility	n	Percentage
Community Health Centre	10	15.6
Primary Hospital	2	3.1
Secondary Hopsital	33	51.6
Tertiary Hospital	8	12.5
Private sector	8	12.5
Unknown	3	4.7

Table 15: Specific referring facility

Facility	n	Percentage	Cumulative
Community Health Centres			
Khayalitsha CHC	2	3.1	
Mitchell's Plane CHC	2	3.1	
Retreat CHC	3	4.7	
Hanover Park CHC	3	4.7	15.7
Primary Hospitals			
False Bay Hospital	2	3.1	18.8
Secondary Hospitals			
Conradie Hospital	2	3.1	
Victoria Hospital	9	14.1	
New Somerset Hospital	9	14.1	
GF Jooste Hospital	6	9.4	
George Hospital	5	7.8	
Frere Hospital	1	1.6	
Livingstone Hospital	1	1.6	70.3
Tertiary Hospitals			
Groote Schuur Hospital	8	12.5	82.9
Private Sector			
Private GP	4	6.3	
Private Casualty	1	1.6	
Private Surgeon	2	3.1	
Private Physician	1	1.6	95.3
Unknown	3	4.7	100.0

3) RISK FACTORS

Risk factors for atherosclerosis and the development of UEAOD

Compared to previous publications reporting on the incidence of atherosclerotic risk factors in UEAOD, [9,23] our series reflected small numbers (n=12).

The most striking feature recognized was the disproportionately high prevalence of cigarette smoking (83%), almost double that reported by Spinelli et al[23] (*Table 16*).

Smoking history could be quantified from the clinical records in 8 out of 10 patients, with an average of 31 pack years.

As previously mentioned, tobacco use is particularly prevalent in patients with upper extremity atherosclerotic occlusive disease (UEAOD) and seems to have a stronger causative association than diabetes, hypertension and dyslipidaemia. The above figures reaffirm the undeniable role played by cigarette smoking in the different manifestations of peripheral arterial disease as well as the importance of addressing this modifiable risk factor.

Recently, substance abuse has been implicated in the process of accelerated and precocious atherosclerosis as well as Thromboangiitis obliterans (TAO). A history of substance abuse were present in 9% of subjects with 5 patients reporting regular cannabis use and 1 patient presenting with a complication of intra-arterial heroin injection.

Hypertension was present in 50% of patients in the UEAOD subgroup, which compared well with the 2007 report by Hughes et al[9] (*Table 16*). Numerous authors (including Roddy[10] and Hughes et al[9]) have reported on the significantly lower incidence of diabetes mellitus in upper extremity bypass patients, compared to the lower extremity bypass population from the same centres. Nonetheless, our series estimated the incidence of diabetes mellitus to be 17%, much lower than suggested by preceding reports. In addition, 33% of patients were previously diagnosed with dyslipidaemia.

The most recently published surgical series reporting on procedures performed for UEAOD, quote the following risk factor incidences:

Table 16: Studies evaluating incidence of risk factors in atherosclerotic occlusive disease

Study	n	Smoking(%)	HPT(%)	DM (%)
Hughes et al, 2013 [9]	55	35	Not reported	29
Spinelli et al, 2009 [23]	23	43	26	48
Hughes et al, 2007 [9]	20	Not reported	45	40
Current series	12	83	50	17

Pharmacological modification of atherosclerotic risk factors

After an in depth evaluation of clinical records (including referral letters, prescription charts and clinical admission notes), it was estimated that as many as 16 out of 60 patients (27%) were not receiving adequate pharmacological therapies aimed at addressing pre-existing risk factors. The TASC II document (section B1.2)[24] was used as a guideline to assess the appropriateness of pre-referral therapy. In 4 patients, clinical information regarding pre-referral treatment was insufficient in order to assess the appropriateness of medical therapy.

Systemic comorbidities in the Thrombo-embolic subgroup

The presence of serious concurrent illness in this specific patient group, impact greatly on clinical outcomes. Deguara et al[1] attributed all early (30 day) mortalities to cardiopulmonary incidents, none being a consequence of arm ischemia or gangrene. The majority of patients (84%) with embolic disease, had associated ischemic heart disease or

a recent myocardial infarction and between 51 - 63% was diagnosed with atrial fibrillation.

In the current series, 8 of the 30 patients (27%) had recent clinical, electrocardiographic, echocardiographic and / or angiographic signs of ischaemic heart disease. Four patients (13%) were in atrial fibrillation at the time of initial presentation. Intra-cardiac thrombus could be identified in one patient. These figures suggest that concurrent cardiac conditions might be underdiagnosed in our setting, however this needs to be interpreted in context of the demographic profile. One such demographic consideration is the difference in mean age of 17 years (current series 55 years; Deguara[1] 72 years) in the TED subgroup of patients, perhaps indicating a younger population with a lower risk of developing CAD.

Other associated systemic diseases were pulmonary tuberculosis (5 patients), previous cerebro-vascular incidents (3 patients) and underlying carcinoma (3 patients – lung, breast and cervix cancer respectively).

4) AETIO-PATHOLOGY

The largest surgical series investigating patients undergoing revascularization procedures for ULI, was published by Deguara et al[1] in 2005. A total of 172 patients were included over a 20 year period, with 53 cases related to upper extremity trauma (excluded in the current series). Comparison of data between the two series (*Table 17* and *18*), makes for interesting discussion. Some similarities and differences have been highlighted and will be discussed subsequently.

Table 17: Summary of **current series** *according to underlying aetio-pathology*

Aetio-pathology	N of patients (%)	N of procedures	Mean age	M:F ratio	30-Day mortality (%)
Acute	**35 (55%)**	**57**	**55**	**1:2.2**	**14.3**
Thrombo-embolic	30 (47%)	47	55	1:2.3	16.7
Arterial thoracic outlet syndrome	2 (3%)	5			-
Iatrogenic	2 (3%)	4			-
Polymyositis compartment syndrome	1 (2%)	1			-
Chronic	**29 (45%)**	**33**	**44**	**1:1.1**	**3.4**
Atherosclerotic disease	12 (19%)	16	57	1:1.4	8.3
Arterial thoracic outlet syndrome	6 (9%)	6	28	5:1	-
Takayasu's disease	4 (6%)	4	27	1:3	-
Thromboangiitis obliterans	4 (6%)	4	46	3:1	-
Occupational small vessel disease	3 (5%)	3	32	1:2	-

Table 18: Summary of cases according to underlying aetio-pathology, by **Deguara** *et al*[1]

Aetio-pathology	N of patients (%)	N of procedures	Mean age	M:F ratio	30-Day mortality (%)
Acute	**116 (67%)**	**124**			
Thrombo-embolic	61 (35%)	68	72	1:1.1	18.2
Trauma	53 (31%)	54	33	5.6:1	3.8
Iatrogenic	2 (1%)	2	46	0:2	-
Chronic	**56 (33%)**	**59**			
Atherosclerotic disease	29 (17%)	32	63	1:1.9	6.9
Subclavian steal syndrome	15 (9%)	15	63	2:3	-
Arterial thoracic outlet syndrome	8 (5%)	8	47	1:1.7	-
Iatrogenic	4 (3%)	4	51	1:1	-

Ratio of acute to chronic presentations

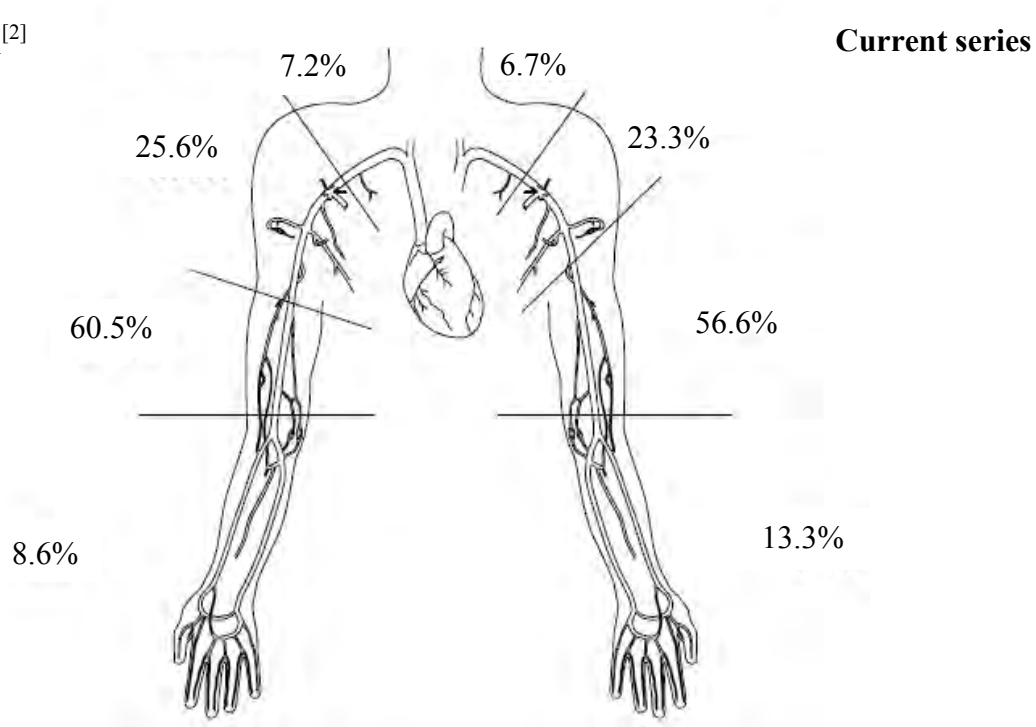
Despite the apparent disproportion of acute to chronic presentations in the Deguara group, the ratios are similar to the current series after exclusion of the trauma subgroup. The

percentage of patients presenting with TED (current series 45%; Deguara et al 51%) and UEAOD (current series 18%; Deguara et al 24%) were similar in both series.

Thrombo-embolic disease

As expected, the majority of thrombo-embolic events resulted in occlusion at the level of the brachial artery (17 patients in total). Nine patients presented with higher occlusions (2 subclavian artery, 7 axillary artery). Three patients had thrombo-embolic occlusions distal to the elbow (2 radial artery, 1 ulnar artery) and one patient presented with blue finger syndrome. Eyers et al[2], in an excellent review of this subject, collected data from multiple series in order to establish the most common level of arterial occlusion. Our series compare well with these figures (*Figure 14*).

Figure 14: Comparative diagram (Eyers et al[2] vs Current series) translating the incidence of arterial occlusion within relevant arterial segments.



In the current series, a left-sided predominance was noted across all levels of obstruction with a right to left sided ratio of 1:2. This is exceedingly unusual, as most authors describe a higher incidence of embolism affecting the right arm, probably due to the larger diameter of the BCA compared to the left SCA as well as the favourable angle that exists between the aorta and BCA.[4]

Atherosclerotic lesions

The subclavian artery was predominantly involved (8 patients), the axillary artery in 1 patient and the brachial artery affected in 3 patients. Therefore, a clear proximal pattern was observed in this subgroup of patients. Once again, as observed in the thrombo-embolic subgroup, clear left sided predominance was noted with a right to left ratio of 1:5. All subclavian lesions were left sided. Morphologically, 6 lesions were described as stenotic, 5 as occlusions and 1 patient presented with thrombosis of a degenerative aneurysm. Unfortunately, it was not possible to accurately ascertain from clinical notes whether predominantly ostial, mono- or multi-segmental disease was present.

Table 19: Summary of underlying arterial lesions in UEAOD subgroup

Morphological lesion	n
Stenosis	6
Occlusion	5
Degenerative aneurysm	1
	12

Arterial thoracic outlet syndrome (ATOS)

Eight patients developed upper limb ischaemia as a consequence of ATOS, of which 7 (88%) presented with underlying bony pathology. This subgroup of patients was generally younger than patients presenting with thrombo-embolic or UEAOD, with a mean age of 28 years (*Table 11*). Interestingly, two of these patients presented with AULI (Rutherford I and IIa), with 6 patients presenting with chronic symptomatology.

Table 20: Summary of ATOS presentations

Underlying lesion	Acute presentation	Chronic presentation	Total
Cervical rib	1	4	5
Muscular band	1	–	1
Anomalous 1st rib	–	1	1
Clavicle fracture (old)	–	1	1
			8

Takayasu's disease

Four patients with Takayasu's disease presented with chronic upper limb ischaemic symptoms. The mean age of the patients was 27 years with a male to female ratio of 1:3 (*Table 11*). Three patients complained of upper limb claudication symptoms with one suffering two ischaemic cerebro-vascular incidents prior to presentation. Level of disease ranged from stenosis of the BCA with occlusion of its outflow (one patient) to proximal left CCA stenosis with associated left SCA occlusion (two patients). One patient presented with prosthetic graft sepsis complicated by an acute bleed from the right CCA anastomosis after previous aortic arch reconstruction for aneurysmal disease.

Thromboangiitis obliterans

Four patients with active digital ulceration due to Buerger's disease, were evaluated and surgically managed during the study period. The mean age at presentation was 46 years and a male to female ratio of 3:1 was noted. The average smoking history was 36 pack years in this subgroup of patients. One patient acknowledged the regular use of cannabis in conjunction with cigarettes.

Small vessel disease

Two patients presented with active digital ulceration in combination with cold-related vasospasm and one with cold-related vasospasm alone. The mean age at presentation was 32 years and the male to female ratio 1:2. The secondary associations were connective tissue disease (SLE), occupational (HHS) and atherosclerotic small vessel disease.

Iatrogenic

The unfortunate occurrence of iatrogenic compartment syndrome was diagnosed in two patients. One patient presented with ALI after tissue infiltration of a peripheral venous catheter (Rutherford IIa) and the other due to acute brachial artery thrombosis after arterial catheterization (Rutherford I).

5) INITIAL CLINICAL PRESENTATION

When considering the timing of symptom onset, 55% of cases were classified as acute ischaemia and 45% as chronic. On comparison of the current series (*Table 17*) with the Deguara group (*Table 18*), an apparent disproportion of acute to chronic presentations is noted. However, in order to compare the above data sets reliably, the trauma subgroup of

patients had to be excluded as specified by the current series' exclusion criteria. After exclusion, the ratio of acute to chronic cases was remarkably similar. (Current series 1.22; Deguara et al[1] 1.13).

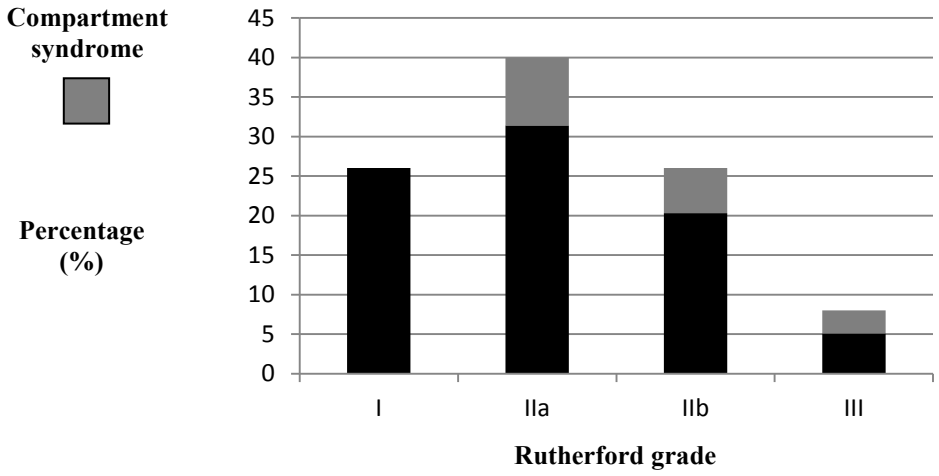
Thirty-five patients presented with AULI necessitating surgical intervention during the study period. *Table 21* and *Figure 15* further reflect relevant detail regarding the clinical presentation of these patients.

Table 21: Summary of AULI presentations, according to severity of ischaemia

Rutherford grade	n	%	Mean age
I	9	26	51
IIa	14	40	53
IIb	9	26	57
III	3	8	61
	35	**100**	**55**

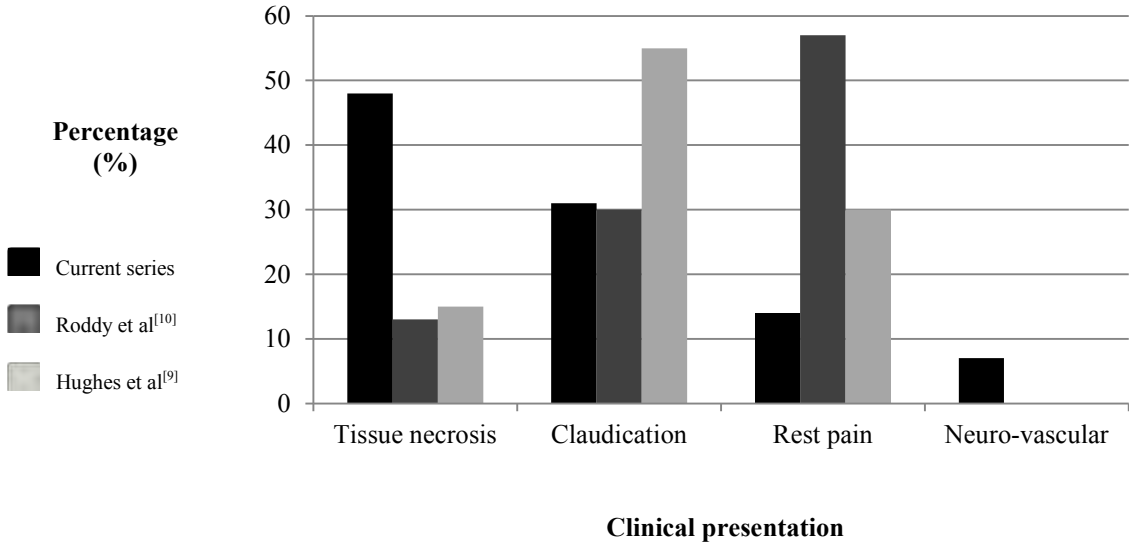
Established compartment syndrome was present in 6 of the 35 AULI cases (17%) and was most prevalent in the Rutherford IIa group (8.6%).

Figure 15: Incidence of compartment syndrome in AULI subgroup



The majority of 29 patients with CULI, presented with signs of tissue necrosis (48%), including digital gangrene, active / healed digital ulceration. Other presentations in this group included upper extremity claudication symptoms (31%), rest pain (14%) as well as neuro-vascular symptoms (7%). *Figure 16* compares the above figures with that of other units.

Figure 16: Summary of CULI presentations



6) SURGICAL INTERVENTIONS

Overview

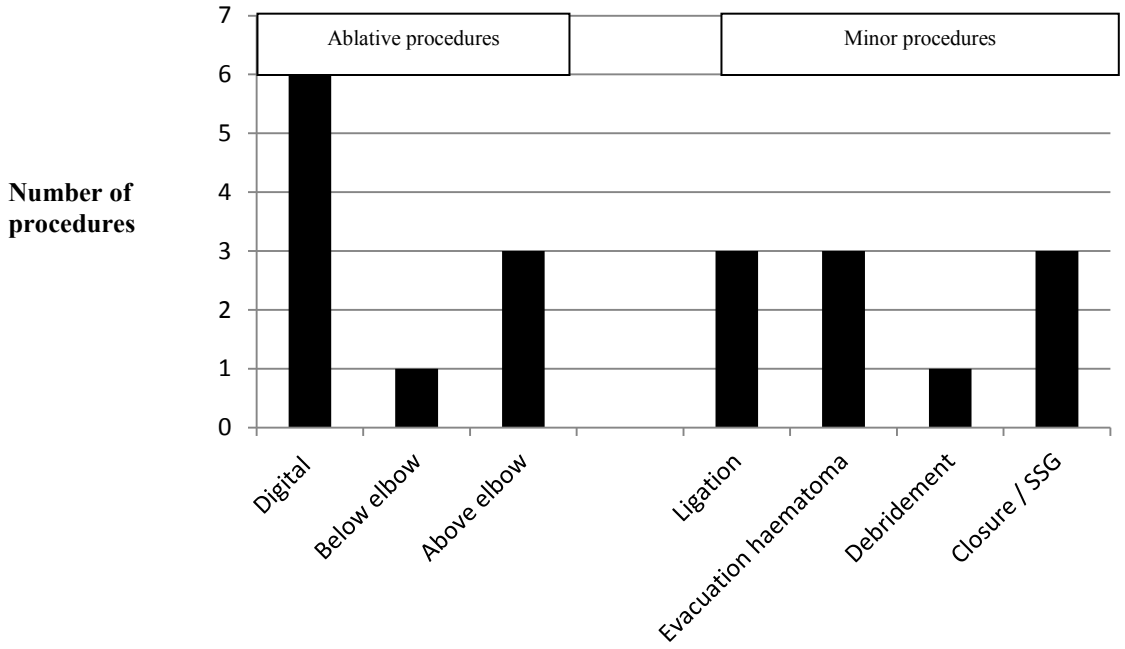
Eighty-nine procedures were performed in 64 patients. Of these, 78 were open procedures, 6 were managed via an exclusively endovascular approach and 5 patients underwent a combination of open and endovascular therapy. A distinction should be made between minor procedures (20 in total, average operating time of 49 minutes) and attempts at revascularization (69 in total, average operating time of 136 minutes). In 75 of the 89

cases performed, it was possible to establish whether the procedure was performed in daytime hours (56%) or afterhours (44%).

Minor and ablative procedures

Most minor procedures were performed as secondary or tertiary procedures. These included wound debridements, evacuation of haematomas, closure of fasciotomy wounds and excision / ligation of bypass grafts.

Figure 17: Summary of ablative and minor procedures performed



Procedures performed for TED

Forty-two procedures for upper limb thrombo-embolism were performed in 26 patients (*Table 22*).

Table 22: Breakdown of procedures performed for thrombo-embolic disease

Procedure	n
Primary procedures	**32**
Thrombo-embolectomy	17
Thrombo-embolectomy and fasciotomy	7
Intra-operative thrombolysis (Streptokinase x1, tPA x1)	2
Brachial-brachial / -distal bypass (Autologous vein graft)	2
Catheter-directed thrombolysis (Streptokinase x1)	1
Stentgraft placement (Fluency® 8x40mm)	1
Aortic arch reconstruction (Gelsoft™ Dacron 8mm graft)	1
Above-elbow amputation	1
Secondary procedures	**10**
Brachial-distal bypass graft	2
Re-embolectomy	1
Fasciotomy	1
Haematoma evacuation	1
Veinpatch angioplasty of veingraft	1
Below-elbow amputation	1
Digital amputation	3

Procedures performed for UEAOD

Twenty-seven procedures were performed in 16 patients. Twenty-one of these were open surgical interventions and 6 were exclusively endovascular.

Open surgical procedures:

Eleven bypass procedures were performed. These included 4 brachial-distal / -brachial bypass grafts (all performed using autologous reverse vein graft), 2 axillary-brachial bypass grafts (autologous reverse vein graft / autologous SFA graft in patient with previous lower limb ablation), 3 subclavian-axillary / -brachial bypass grafts (2 ePTFE 6mm, 1 Dacron® 6mm) and 2 common carotid-axillary (PTFE 8mm) / -brachial bypass grafts (autologous reverse vein graft).

Endovascular procedures:

Lesions managed by endovascular means, were all located within the subclavian artery. Four lesions were primarily managed with bare metal stent placement (1 x Protégé® 8 x 27mm self-expandable stent, 2 x Omnilink Elite® 8x39mm balloon expandable stent, 1 x Sinus-Flex® 8x40mm self-expandable stent) and one managed with self-expandable bare metal stent placement (Complete® SE 8x60mm) after failed PTA previously. A retrograde brachial approach at cutdown was used to address three of the lesions, with a trans-femoral approach implemented in the remaining two cases.

Table 23: Breakdown of procedures performed for UEAOD

Procedure	**n**
Open procedures	**21**
Bypass procedures	11
Brachial-distal / brachial-brachial	4
Axillary-brachial	2
Subclavian-axillary / subclavian-brachial	3
Common carotid-axillary / common carotid-brachial	2
Primary amputations	4
Digital amputations	4
Secondary amputations	3
Above elbow amputations	3
Graft thrombectomies	2
Wound haematoma evacuation	1
Endovascular procedures	**6**
Primary procedures	
Subclavian artery balloon angioplasty	1
Subclavian artery stent placement (Protégé® 8 x 27mm, Sinus-Flex® 8x40mm, 2 x Omnilink Elite® 8x39mm)	4
Secondary procedure	
Subclavian artery stent placement (Complete® SE 8x60mm)	1

Procedures performed for arterial thoracic outlet syndrome (ATOS)

Eight patients developed upper limb ischaemia as a result of thoracic outlet syndrome.

Table 24: Breakdown of procedures in patients presenting with ATOS

Patient	1° procedure	2° procedure	3° procedure	Nr of procedures
1	Thrombo-embolectomy, thrombolysis + fasciotomy	TO decompression	Contra-lateral TO decompression	3
2	Thrombo-embolectomy + fasciotomy	TO decompression	-	2
3	CCA-brachial RSBG bypass + primary digital amputation	Above elbow amputation	-	2
4	SCA-Axillary PTFE bypass + brachial-ulnar RSVG bypass	-	-	1
5	SCA-Axillary PTFE bypass	-	-	1
6	TO decompression	-	-	1
7	TE followed by SCA-Axillary PTFE bypass	-	-	1
8	CCA-brachial Dacron® bypass + brachial-ulnar RSVG bypass + fasciotomy + primary digital amputation	-	-	1
				12

Two of these patients presented with acute upper limb ischaemia (Rutherford I and IIa), necessitating emergency surgical treatment in the form of thrombo-embolectomy combined with intra-operative thrombolysis (in one patient), followed by fasciotomy. The underlying lesions (muscular band and cervical ribs) were addressed during secondary and tertiary procedures.

Six patients presented with chronic complaints. One patient was managed with primary thoracic outlet decompression and 5 patients underwent arterial bypass procedures combined with primary digital amputation where appropriate. The bypass procedures performed included two CCA-brachial artery bypass grafts (reverse basillic vein graft, 8mm Dacron® prosthetic graft) and three SCA-axillary artery bypass grafts (6mm PTFE

prosthetic graft). In two of these patients, a further brachial-ulnar artery bypass was performed at the same sitting (reverse saphenous vein graft). One above elbow amputation was performed after failure of a CCA-brachial artery bypass procedure.

Procedures performed for Takayasu's disease

Two patients underwent aortic arch reconstruction (14 x 7mm bifurcated Albograft®) for Takayasu's disease and one received an axillary-axillary artery bypass graft (6mm PTFE ring-reinforced graft). One patient presented with a stenosis of the brachiocephalic artery at the origin, while two patients had symptomatic (L) SCA occlusion as well as 50% (L) CCA stenosis. One patient presented with graft sepsis that manifested with an acute bleed after previous aortic arch reconstruction (16 x 8mm bifurcated Silvergraft® used for redo-arch reconstruction).

Thoracoscopic sympathectomies

Five thoracoscopic sympathectomies were performed for upper limb ischaemia. A standard T2 ganglionectomy was performed with a video-assisted two port technique in all cases. The indications varied and included non-reconstructable small vessel disease (histologically confirmed to be Thromboangiitis obliterans), HHS, SLE vasculitis and atherosclerotic small vessel disease. The average operating time was 55 minutes and included primary digital amputation in two cases.

7) OUTCOME

Surgical outcome measures were reported by quantifying the mortality, morbidity (including systemic and procedural complications) and amputation rates at different time intervals after the initial surgical procedure was performed. These intervals included 30-day outcome, outcome on 6 month follow-up as well as long term follow-up (more than 6 months after initial procedure). Unfortunately, follow-up appointments were poorly attended, especially affecting long term outcome results.

30-Day outcomes

Follow-up data could be accumulated in 53 of the 64 patients (83%). Eighteen amputations were performed in 64 patients, of which 6 were major amputations (above- or below-elbow level). Most amputations (n=10) were performed primarily, in patients presenting with irreversible tissue necrosis not justifying an attempt at revascularization. Eight secondary amputations (4 digital, 3 above-elbow and 1 below-elbow) were performed within 30 days of an initial attempt at revascularization. Two of these were performed following bypass graft occlusion. Therefore, the 30-day amputation rate after initial revascularization, was 12.5%.

At 30-day review, 35 patients were evaluated by clinical palpation, hand-held doppler pressures and/or duplex arteriogram. These findings were compared to corresponding pre-operative assessment, with patients being categorized into 3 groups. Deterioration of pulse status was observed in only one patient.

Table 25: Summary of 30-day outcome

Outcome	n	%
Adherence to follow-up	**53**	**83**
Mortalities		
Acute coronary syndrome	2	
Acute renal failure	2	
Acute respiratory failure	1	
	5	**7.8%**
Morbidities		
Systemic complications		
Acute kidney injury	3	
Acute respiratory insufficiency	3	
Acute coronary syndrome	1	
Cerebro-vascular incident	1	
	8	**12.5%**
Procedural complications		
Surgical site haematoma	6	
Superficial surgical site infection	4	
Bypass graft occlusion	3	
Pseudo-aneurysm post-angiogram	2	
Delayed fasciotomy	1	
Neuropraxia	1	
Re-thrombosis of native vessels	1	
	18	**23.4%**
Amputation rate		
Primary amputation		
Minor	8	
Major	2	
	10	**15.6%**
Secondary amputation		
Minor	4	
Major	4	
	8	**12.5%**
Pulse status		
Improvement	24	**68.6%**
Unchanged	10	**28.6%**
Deteriorated	1	**2.8%**
	35	

6-Month outcomes

Thirty patients attended their 6 month follow-up appointments. No further mortalities or systemic complications were noted in this group. Seven patients (11.9%) presented with procedural complications in the form of bypass graft occlusion (leading to dense hemiplegia in one patient and above-elbow amputation in another), re-occlusion of native vessels post-embolectomy and improving peripheral nerve neuropraxia (thought to have been fasciotomy-related).

Surveillance by clinical examination, hand-held doppler pressures and/or duplex arteriogram, revealed deterioration of pulse status in 5 patients, all of which presented with bypass graft occlusion.

Twenty-three patients were assessed as having a fully functional ipsilateral upper limb (76.7%). Four patients presented with contractures, 1 with motor weakness (affecting activities of daily living) and two with claudication symptoms.

Table 26: Summary of 6-month outcome

Outcome	n	%
Adherence to follow-up	**30**	**50.8%**
Mortalities	**0**	
Morbidities		
Systemic complications	**0**	
Procedural complications		
Bypass graft occlusion	5	
Neuropraxia (improving)	1	
Re-thrombosis of native vessels	1	
	7	**11.9%**

Amputation rate		
Secondary amputation		
Major	**1**	**1.9%**
Pulse status (since 30-day follow-up)		
Unchanged	25	**83.3%**
Deteriorated	5	**16.7%**
	30	
Functional outcome		
Normal	23	**76.7%**
Contracture	4	
Claudication symptoms	2	
Motor weakness	1	
	30	

Long term outcome

Only 17 patients attended follow-up appointments after the 6 months post-operative period. One patient developed bypass graft occlusion before demising from lung carcinoma 2 months later. No other systemic or procedural complications were noted in this patient group.

Three patients showed signs of pulse status deterioration from the previous 6-month follow-up visit. Thirteen patients reported normal function, 2 patients presented with contractures, 1 patient with motor weakness and 1 patient presenting with claudication symptoms. Due to poor follow-up attendance, these findings have limited interpretational value.

Table 27: Summary of long term (>6 months) outcome

Outcome	n	%
Adherence to follow-up	**17**	**28.8%**
Mortalities	**1**	
Morbidities		
Systemic complications	**0**	
Procedural complications		
Bypass graft occlusion	1	
Amputation rate	**0**	
Pulse status (since 6-month follow-up)		
Unchanged	14	**82.4%**
Deteriorated	3	**17.7%**
	17	
Functional outcome		
Normal	13	**76.5%**
Contracture	2	
Claudication symptoms	1	
Weakness	1	
	17	

Special subgroups

When presenting surgical outcome of patients with upper limb ischaemia as a whole, a valuable overall picture of a distinctly heterogeneous disease process, can be obtained. However, comparing different subgroups in an attempt to identify significant discrepancies in outcome, may facilitate correlation with the international literature on these topics. Therefore, relevant subgroup analyses will be discussed next, with specific reference to surgical outcome.

TED vs UEAOD

It is indeed striking that all 5 of the 30-day mortalities, were observed in the subgroup of patients presenting with embolic AULI (see *Table 25*). The concept that mortality following embolectomy is a consequence of the patient's comorbidity rather than the embolus itself, is well supported.[1,52] In our series, the mortalities were attributable to acute coronary syndrome (n=2), acute renal failure (n=2) and acute respiratory failure (n=1). The only death observed in the CULI group, was documented 2 years after initial surgery for UEAOD, when the patient demised from end-stage lung carcinoma.

Table 28: Comparison of TED- and UEAOD- subgroups

Subgroup	n	Number of procedures	Mean age	30-Day mortality	Amputation rate
TED	30	47	55	16.7%	13.3%
UEAOD	12	16	57	0%	8.3%

These findings are in keeping with recent international literature on the subject, where the 30-day all-cause mortality rate for patients undergoing upper extremity embolectomy, is estimated to be between 9 – 19%.[1,138,142,143] Deguara et al[1] reported a 30-day mortality rate of 18.2% in this subgroup of patients and attributed all deaths to cardiopulmonary incidents.

Four patients in the TED group underwent amputations (2 above-elbow and 2 digital amputations) after revascularization was attempted, compared to one above-elbow amputation in the UEAOD group.

Units implementing a more aggressive approach to the management of relatively minor symptoms, may reflect better surgical outcomes, especially superior limb salvage rates. Therefore, when comparing surgical outcome of the UEAOD subgroup to that of international Vascular Units, one has to interpret the results in terms of the indication for surgery. In the current series, 48% of patients with UEAOD, presented with some form of tissue necrosis as opposed to series from Hughes[9] (15%) and Roddy[10] (13%).

HIV

Of the 64 patients included in this review, 7 were confirmed to be HIV positive by HIV Ag/Ab Combo (ELISA) testing. However, only 30 patients had documented proof (folder laboratory results sheet or NHLS Disa electronic results system) of a recent HIV test being performed. Only 3 of the 7 patients had documentation of a recent CD4 count or viral load. One patient developed superficial surgical site infection and another demised after prosthetic bypass graft sepsis was complicated by an acute bleed. Due to a low rate of HIV testing and the small number of patients involved, it is not possible to reach firm conclusions regarding clinical outcome in this subgroup of patients.

Patients managed exclusively by endovascular means

Six patients, of which one presented with AULI from a proximal embolizing source, were managed by endovascular means alone. All lesions that were addressed, were located in the subclavian artery. Five lesions were managed by primary stent placement, with one lesion stented after failed percutaneous balloon angioplasty. One patient sustained a procedure related complication in the form of an ipsilateral cerebro-vascular incident. No other procedural or systemic complications were noted in this group of patients. All

patients attended follow-up appointments up to 6 months, but only 2 were seen after this period. An improvement in pulse status / perfusion (as evaluated by clinical palpation, hand-held doppler pressures and/or duplex arteriogram) were noted in all patients and normal function of the affected upper limb, were reported.

CHAPTER SIX:

DISCUSSION AND FUTURE RESEARCH PERSPECTIVES

Vascular surgeons are infrequently confronted with the condition of upper limb ischaemia. Compared to other more common vascular pathologies, clinicians are less familiar with the pattern and distribution of disease, variable aetiologies, diagnostic appraisal and treatment modalities related to this condition. This has generated an innate curiosity regarding several facets of ULI, with particular emphases on identifying key areas fit for further, more focused research.

On review of the literature, it was clear that even though relatively few patients present with this condition, the potential aetiological factors implicated were variable and extensive. Therefore, in the interest of developing a broad perspective, the decision was made to perform a comprehensive, general overview on the topic, rather than to limit oneself to a specific research question.

On evaluation and analysis of the data, certain inherent limitations of the above research method, became clear. Unfortunately, by attempting to discuss distinctly different aetio-pathological processes in unison, important individual characteristics may be obscured. Also, with no specific research question asked or stated, the researchers could only generate multiple, tentative assumptions to base further research on. With this in mind, a few relevant findings will now be discussed.

The true incidence of ULI in the South African context, still remains speculative. A major limiting factor is the paucity of data on the non-operative management of AULI. Units

where an initial conservative approach is often utilized should be encouraged to collect data regarding the incidence and outcomes. A collaborative effort among units may compensate for low numbers and in the process provide adequate data to estimate the true extent of the problem. With the high prevalence of pulmonary tuberculosis, HIV / AIDS and cigarette smoking (83% in the UEAOD subgroup – *Table 16*) in the study population, it is indeed conceivable that our incidence of ULI may be higher than expected. In the absence of a national registry, a multi-centre trial specifically designed to evaluate these questions, should be performed.

Another interesting phenomenon is the young age at which patients presented with symptomatic disease (*Table 12*), when compared to international literature. This holds especially true for the TED subgroup of patients (mean age 55 years), usually known for their advanced age at presentation (72.4 years reported by Deguara et al). Possible explanations include the assumed impact that a relatively low life expectancy may have on these figures (57.7 years for males and 61.4 years for females) as well as the suspicion of a different risk factor profile (TB, HIV and cigarette smoking) compared to other research populations.

On review of the referral patterns (*Table 14*), it is noteworthy that approximately half of AULI referrals were received from surrounding Secondary Level Hospitals, as opposed to the 19.7% collectively referred from Community Health Centres and Primary Level Hospitals. It has incontrovertibly been shown that outcome in patients suffering from ALI is superior if managed in a Vascular Unit with 24 hour consultant cover.[164] Therefore, it is imperative that patients are directly referred from the healthcare facility of first contact,

to the nearest Vascular Unit without unnecessary delay. Although multiple other factors might have influence this pattern, it will be interesting to evaluate the number of "double referrals" within this subgroup of patients in need of urgent revascularization.

Approximately 27% of patients referred were not receiving appropriate pharmacological therapies aimed at addressing pre-existing, modifiable risk factors for atherosclerosis. This is a worrying statistic bordering on a Public Health catastrophe, as these patients are at an increased risk of sustaining adverse cardiovascular events and would benefit from evidence-based best medical therapy. Further inquiry should be made through focused research, in order to ascertain and further define the system failure at hand.

Poor adherence to follow-up has hampered reliable interpretation of conventional clinical outcome. Although variable factors contribute to this phenomenon, the implementation of a computerized ULI database with pre-set, automated follow-up reminders may assist clinicians and administrative staff in contacting patients due for follow-up visits. Compliance to follow-up appointments, as the primary outcome measure, can be evaluated before and after the implementation of such a system.

CHAPTER SEVEN:

CONCLUSION

Although few firm conclusions could be drawn, this review has expanded our overall perspective of ULI, specific to the population we serve. It is anticipated that the publication of our institutional data will create a clinical awareness and facilitate future research projects in this field. A collaborative research effort between South African vascular units will facilitate a comparison of different institutional experiences and enable pooled data analysis, perhaps further defining the pattern of upper limb vascular disease by identifying distinct geographical confounders.

REFERENCES

1) Deguara J, Ali T, Modarai B, Burnand KG. Upper limb ischemia: 20 year experience from a single center. Vascular. 2005 Mar-Apr;13(2):84-91.

2) Eyers P, Earnshaw JJ. Acute non-traumatic arm ischaemia. Br J Surg. 1998 Oct;85(10):1340-6.

3) McCarthy WJ, Flinn WR, Yao JST, et al. Results of bypass grafting for upper limb ischaemia. J Vasc Surg 1986;3:741-6.

4) Pentti J, Salenius JP, Kuukasjärvi P, Tarkka M. Outcome of surgical treatment in acute upper limb ischaemia. Ann Chir Gynaecol. 1995;84(1):25-8.

5) Quraishy MS, Cawthorn SJ, Giddings AE. Critical ischaemia of the upper limb. J R Soc Med 1992;85:269-73

6) Hammond DC, Gould JS, Hanel DP. Management of acute and chronic vascular injuries to the arm and forearm. Indications and technique. Hand Clin 1992;8:453-63

7) Fujitani RM, Mills JL. Acute and chronic upper extremity ischaemia: Large vessel arterial occlusive disease. Ann Vasc Surg 1993;7:106-12

8) Ueberrueck T, Marusch F, Schmidt H, Gastinger I. Risk factors and management of arterial emboli of the upper and lower extremities. J Cardiovasc Surg (Torino). 2007 Apr;48(2):181-6.

9) Hughes K, Hamdan A, Schermerhorn M, Giordano A, Scovell S, Pomposelli F Jr. Bypass for chronic ischemia of the upper extremity: results in 20 patients. J Vasc Surg. 2007 Aug;46(2):303-7.

10) Roddy SP, DarlingRC, Chang BB, Kreienberg PB, Paty PS, Lloyd WE, et al. Brachial artery reconstruction for occlusive disease: a 12-year experience. J Vasc Surg. 2001;33:802-805

11) Norgeren L, Hiatt WR, Dormandy JA. Inter-society consensus for the management of peripheral arterial disease. Eur J Vasc Endovasc Surg 2007; 33:S1-75

12) Schmidt FE, Hewitt RL. Severe upper limb ischaemia. Arch Surg 1980;115:1188-91.

13) Haimovici H. Cardiogenic embolism of the upper extremity. J Cardiovasc Surg 1982;23:233.

14) Tawes RL Jr, Harris EJ, Brown WH, et al: Arterial thromboembolism. A 20-year perspective. Arch Surg 120:595-599, 1985.

15) Yeager RA, Moneta GL, Taylor LM Jr, et al: Surgical management of severe acute lower extremity ischemia. J Vasc Surg 15:385-391, 1992.

16) Campbell WB, Ridler BM, Szymanska TH: Vascular surgical society of Great Britain and Ireland: Twoyear follow-up after acute thromboembolic lower limb ischaemia: The importance of continuing warfarin treatment. Br J Surg 86:707, 1999.

17) Ouriel K: Current status of thrombolysis for peripheral arterial occlusive disease. Ann Vasc Surg 16:797- 804, 2002.

18) Adanja B, Vlajinac H, Jerebinski M: [Epidemiologic characteristics of rheumatic fever throughout the world.] Reumatizam 38:13-16, 1991.

19) The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. The ARIC investigators. Am J Epidemiol. 1989; 129: 687–702

20) Kagan A, Gordon T, Rhoads GG, et al. Some factors related to coronary heart disease incidence in Honolulu Japanese men: the Honolulu Heart Study. Int J Epidemiol. 1975; 4: 271–279 1)

21) Lee ET, Welty TK, Fabsitz R, et al. The Strong Heart Study: a study of cardiovascular disease in American Indians: design and methods. Am J Epidemiol. 1990; 132: 1141–1155 1)

22) Roberta Oka, Anne B. Newman, William H. Pearce and for Writing Group 1: William R. Hiatt, Jerry Goldstone, Sidney C. Smith, Jr, Mary McDermott, Gregory Moneta. Atherosclerotic Peripheral Vascular Disease Symposium II: Nomenclature for Vascular Disease. Circulation. 2008;118:2826-2829 1)

23) Spinelli F, Benedetto F, Passari G, La Spada M, Carella G, Stilo F, De Caridi G, Lentini S. Bypass surgery for the treatment of upper limb chronic ischaemia. Eur J Vasc Endovasc Surg. 2010 Feb;39(2):165-70.

24) Management of Peripheral Arterial Disease (PAD) TransAtlantic Intersociety Consensus (TASC). J Vasc Surg 2000;31(1 part 2):S1-287.

25) Jorenby DE, Leischow SJ, Nides MA, Rennard SI, Johnston JA, Hughes AR, et al. A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. N Engl J Med 1999; 340(9):685-91.

26) Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati FL, Powe NR, et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med 2004;141(6):421-31.

27) Collins R, Armitage J, Parish S, Sleigh P, Peto R, Heart Protection Study Collaborative Group MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. Lancet [2003, 361(9374):2005-2016]

28) Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet 2005;366(9493):1267-78.

29) Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003;42(6):1206-52.

30) European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens 2003;21(6):1011-53.

31) Bonaa K, Njolstad I, Ueland P, Schirmer H, Tverdal A, Steigen T, et al. Homocysteine lowering and cardiovascular events after acute myocardial infarction. N Engl J Med 2006;354:1578-88.

32) Lonn E, Yusuf S, Arnold MJ, Sheridan P, Pogue J, Micks M, et al. Homocysteine lowering with folic acid and B vitamins in vascular disease. N Engl J Med 2006;354(15):1567-77.

33) O'Hare AM, Vittinghoff E, Hsia J, Shlipak MG. Renal insufficiency and the risk of lower extremity peripheral arterial disease: results from the Heart and Estrogen/Progestin Replacement Study (HERS). J Am Soc Nephrol 2004;15(4):1046-51.

34) Buerger L: Thromboangiitis obliterans: a study of the vascular lesions leading to presenile gangrene. Am J Med Sci 1908, 136:567-580.

35) Buerger L: The circulatory disturbance of the extremities: including gangrene, vasomotor and trophic disorders Philadelphia, Saunders; 1924.

36) Joyce JW (1990) Buerger's disease. Thromboangiitis obliterans. Rheum Dis Clin North Am 16:463–470

37) Hirai M, Shionoya S (1979) Arterial obstruction of the upper limb in Buerger's disease: its incidence and primary lesion. Br J Surg 66:124–128

38) Cottencin O, Karila L, Lambert M, et al. Cannabis arteritis: review of the literature. J Addict Med (In press)

39) Guillaume Martin-Blondel, Fabien Koskas, Patrice Cacoub and Damien S_ene, Is Thromboangiitis Obliterans Presentation Influenced by Cannabis Addiction? Ann Vasc Surg 2011; 25: 469-473

40) Harten P, Muller-Huelsbeck S, Regensburger D, Loeffler H: Multiple organ manifestations in thromboangiitis obliterans (Buerger's disease). A case report. Angiology 1996, 47:419-425.

41) Donatelli F, Triggiani M, Nascimbene S, Basso C, Benussi S, Chierchia SL, Thiene G, Grossi A: Thromboangiitis obliterans of coronary and internal thoracic arteries in a young woman. J Thorac Cardiovasc Surg 1997, 113:800-802.

42) Arkkila PE, Kahri A, Farkkila M: Intestinal type of thromboangiitis obliterans (Buerger disease) preceding symptoms of severe peripheral arterial disease. Scand J Gastroenterol 2001, 36:669-672.

43) Kurata A, Nonaka T, Arimura Y, Nunokawa M, Terado Y, Sudo K, Fujioka Y: Multiple ulcers with perforation of the small intestine in Buerger's disease: a case report. Gastroenterology 2003, 125:911-916.

44) De Moerloose P, Jeannet M, Mirimanoff P, Bouvier CA: Evidence for an HLA-linked resistance gene in Buerger's disease. Tissue Antigens 1979, 14:169-173.

45) Kobayashi M, Ito M, Nakagawa A, Nishikimi N, Nimura Y: Immunohistochemical analysis of arterial wall cellular infiltration in Buerger's disease (endarteritis obliterans). J Vasc Surg 1999, 29:451-458.

46) Diehm C, Stammler F: Thromboangiitis obliterans (Buerger's disease). N Engl J Med 2001, 344:230-231.

47) Adar R, Papa MZ, Schneiderman J: Thromboangiitis obliterans: an old disease in need of a new look. Int J Cardiol 2000, 75:167-170. 1

48) Olsen N, Nielsen SL. Prevalence of primary Raynaud phenomena in young females. Scand J Clin Lab Invest 1978; 38:761-4

49) Porter JM, Bardana EJ Jr, Baur GM et al. The clinical significance of Raynaud's syndrome. Surgery 1976; 80: 756-64

50) Kahaleh MB. Raynaud phenomenon and the vascular disease in Scleroderma. Curr Opin Rheumatol 2004; 16(6):718-22 1)

51) Raynaud MD. Asphyxre et de la gangrene symetriques des extremities. Paris, 1862. (Trans. Thomas Barlow, London, New Sydenham Society, 1988)

52) Savelyev VS, Zatevakhin MD, Stepanov MD. Artery embolism of the upper limbs. Surgery 1977;81:367-75.

53) Davies MG, O'Malley K, Feeley M, et al. Upper limb embolus: a timely diagnosis. Ann Vasc Surg 1991;5:85-7.

54) Karr G, Broe PJ, Bouchier-Hayes DJ. Upper limb emboli. A review of 55 patients managed surgically. J Cardiovasc Surg (Torino) 1989;30:165-8.

55) Galbraith K, Collin J, Morris PJ, et al. Recent experience with arterial embolism of the limbs in a vascular unit. Ann R Coll Surg Engl 1985;67:30-3.

56) Kretz JG, Weiss E, Limuris A, et al. Arterial emboli of the upper extremity. J Cardiovas Surg 1984;25:233-5. Fazzini PF: Epidemiology of silent myocardial ischemia in asymptomatic middle-aged men (the ECCIS project). Am J Cardiol 1993; 72: 1383-1388.

57) Koistinen MJ. Prevalence of asymptomatic myocardial ischemia in diabetic subjects. BMJ 1990; 301: 92-95.

58) Herbst M, Wattjes MP, Urbach H, et al. Cerebral Embolism from Left Atrial Myxoma Leading to Cerebral and Retinal Aneurysms: A Case Report. Am J Neuroradiol 2005; 26: 666-9.

59) Coley C, Lee KR, Steiner M, et al. Complete embolization of a left atrial myxoma resulting in acute lower extremity ischemia. Tex Heart Inst J 2005; 32: 238-40.

60) Rahmanian PB, Castillo JG, Sanz J, et al. Cardiac myxoma: preoperative diagnosis using a multimodal imaging approach and surgical outcome in a large contemporary series. Interact CardioVasc Thorac Surg 2007; 6: 479-83.

61) Liesting C, Ramjankhan FZ, van Herwerden LA, et al. Systemic embolisation as presentation and recurrence of cardiac myxoma two years after surgery. Neth Heart J 2010; 18: 499-502.

62) Coley C, Lee KR, Steiner M, et al. Complete embolization of a left atrial myxoma resulting in acute lower extremity ischemia. Tex Heart Inst J 2005; 32: 238-40.

63) Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale in the first 10 decades of life: an autopsy study of 965 normal hearts. Mayo Clin Proc. 1984;59:17–20.

64) Kizer JR, Devereux RB. Clinical practice. Patent foramen ovale in young adults with unexplained stroke. N Engl J Med. 2005 Dec 1;353(22):2361-72.

65) Lechat P, Mas JL, Lascault G, et al. Prevalence of patent foramen ovale in patients with stroke. N Engl J Med 1988; 318:1148–1152.

66) Messe SR, Schwartz RS, Perloff JK. Atrial septal abnormalities (PFO, ASD, and ASA) and risk of cerebral emboli in adults. In: UpToDate 2006.

67) Coulshed N, Epstein EJ, McKendrick CS, et al. Systemic embolism in mitral valve disease. Br Heart J1970;32,26-34.

68) Cassella K, Abelmann WH, Ellis LB. Patients with mitral stenosis and systemic emboli. Arch Intern Med1964;114,773.

69) Dewar HA, Weightman D. Study of embolism in mitral valve disease and atrial fibrillation. Br Heart J1983;49,133-140.

70) Hay WE, Levine SA. Age and atrial fibrillation as independent factors in auricular mural thrombus formation. Am Heart J1942;24,1-4.

71) Daley R, Mattingly TW, Holt C et al. Systemic arterial embolism in rheumatic heart disease. Am Heart J1951;42,566-581.

72) Stein P, Sabbath H, Apitha J. Continuing disease process of calcific aortic stenosis. Am J Cardiol1977;39,159-163.

73) Daley R, Mattingly TW, Holt C et al. Systemic arterial embolism in rheumatic heart disease. Am Heart J1951;42,566-581.

74) Weinstein L. Infective endocarditis. Braunwald, E eds. Heart disease. 1984; WB Saunders. Philadelphia, PA.

75) Cates JE, Christie RV. Subacute bacterial endocarditis: a review of 442 patients treated in 14 centers appointed by the penicillin trials committee of the MRCQ. J Med1951;20,93.

76) Brunson JG. Coronary embolism in bacterial endocarditis. Am J Pathol1953;26,689.

77) Lerner PI, Weinstein L. Infective endocarditis in the antibiotic era. N Engl J Med1966;274,388-393.

78) Pruitt AA, Rubin RH, Karchmer AW et al. Neurologic complications of bacterial endocarditis. Medicine1978;57,329-343.

79) Carpenter JL, McAllister CK. Anticoagulation in prosthetic valve endocarditis. South Med J1983;76,1372-1375.

80) Garvey CJ, Neu HC. Infective endocarditis: an evolving disease. Medicine1979;57,105-126.

81) Ginzton LE, Siegel RJ, Criley JM. Natural history of tricuspid valve endocarditis: a two-dimensional echocardiographic study. Am J Cardiol 1982;49,1853-1859.

82) Wann LS, Dillon JC, Weyman AE, et al. Echocardiography in bacterial endocarditis. N Engl J Med 1976;295,135-139.

83) Roy P, Tajik AJ, Guiliani ER, et al. Spectrum of echocardiographic findings in bacterial endocarditis.Circulation 1976;53,474-482.

84) Stuart JA, Silimperi D, Harris P, et al. Echocardiographic documentation of vegetative lesion in infective endocarditis: clinical implications. Circulation 1980;61,374-380.

85) O'Brien JT, Geiser EA. Infective endocarditis and echocardiography. Am Heart J 1984;108,386-394.

86) Block PC, DeSanctis RW, Weinberg AN. Prosthetic valve endocarditis. J Thorac Cardiovasc Surg1970;60,540-548.

87) Wilson WR, Geraci JE, Danielson GK et al. Anticoagulant therapy and central nervous system complications in patients with prosthetic valve endocarditis. Circulation1978;57,1004-1007.

88) Roos DB (1984) Thoracic outlet and carpal tunnel syndrome. In Rutherford RB (ed) Vascular surgery, 2nd edn. Saunders, Philadelphia, pp 708–724

89) Adson AW, Coffey JR. Cervical rib: a method of anterior approach for relief of symptoms by division of the scalenus anticus. Ann Surg 1927; 85:839-57.

90) Peet RM, Hendriksen JD, Anderson TP, Martin GM. Thoracic outlet syndrome: evaluation of a therapeutic exercise program. Proc Mayo Clin 1956;31:281-7.

91) Jordan SE, Machleder HI. 1998. Diagnosis of thoracic outlet syndrome using electrophysiologically guided anterior scalene blocks. Ann Vasc Surg 12:260–264.

92) Merrel GA, Wolfe SW. 2002. Adult brachial plexus and thoracic outlet surgery. Tech Should Elb Surg 3:271–281.

93) Charon JPM, Milne W, Sheppard DG, Houston JG. 2004. Evaluation of MR angiographic technique in the assessment of thoracic outlet syndrome. Clin Rad 59:588–595.

94) Gabella G. 1995. Cardiovascular. In: Williams P, Warwick R, Dyson M, Bannister L, editors. Gray's Anatomy. Edinburgh: Churchill Livingstone. p 1529–1530.

95) Sealy WC. 1951. A report of two cases of the anomalous origin of the right subclavian artery from the descending aorta. J Thorac Surg 21:319–324.

96) Stauffer HM, Pote HH. 1946. Anomalous right subclavian artery originating on the left side as the last branch of the aortic arch. Am J Roentgenol 56:13–17.

97) Nathan H, Seidel MR. 1983. The association of a retroesophageal right subclavian artery, a right-sided terminating thoracic duct, and a left vertebral artery of aortic origin: Anatomical and clinical considerations. Acta Anat 117:362–373.

98) Stone WM, Brewster DC, Moncure AC, Franklin DP, Cambria RP, Abbott WM. 1990. Aberrant right subclavian artery: Varied presentations and management options. J Vasc Surg 11:812–817.

99) Konuskan B, Bozkurt CM, Murat Tagil S, Ozcakar L. 2005. Cadaveric observation of an aberrant left subclavian artery: A possible cause of thoracic outlet syndrome. Clin Anat 18:215–216.

100) Roos DB. 1976. Congenital anomalies associated with thoracic outlet syndrome. Anatomy, symptoms, diagnosis, and treatment. Am J Surg 132:771–778.

101) Gruss J-D, Geissler C, Hanschke D, Prescher H. 2002. First rib excision is seldom required: Against the motion. In: Greenhalgh RM, editor. The Evidence of Vascular or Endovascular Reconstruction. Edinburgh: WB Saunders. p 85–99.

102) Brewin J, Hill M, Ellis H. 2009. The prevalence of cervical ribs in a London population. Clin Anat 22:331–336.

103) Roos DB. 1996. Historical perspectives and anatomic considerations of thoracic outlet syndrome. Semin Thor Cardiovasc Surg 8:183–189.

104) Nannapaneni R, Marks SM. 2003. Neurogenic thoracic outlet syndrome. Br J Neurosurg 17:144–148.

105) Yusouf Desai and John V. Robbs. Arterial Complications of the Thoracic Outlet Syndrome Eur J Vasc Endovasc Surg 10, 362-365 (1995)

106) Roach MR. Poststenotic dilatation in arteries. In: Bergel DH, editor. Cardiovascular fluid dynamics. Vol 2. London, New York: Academic Press; 1972. p. 111-39.

107) Robicsek F. Pathogenesis and significance of post-stenotic dilatation in great vessels. Ann Surg 1955;147:835-44.

108) Clagett GP (2000), Upper extremity aneurysms. In Rutherford RB (ed) Vascular Surgery, 5th edn, Saunders, Philadelphia, p1359.

109) Thompson RW, Driskill M. Neurovascular problems in the athlete's shoulder. Clin Sports Med 2008; 27: 789–808.

110) Enrique Criado, Ramon Berguer and Lazar Greenfield. The spectrum of arterial compression at the thoracic outlet, J Vasc Surg 2010;52:406-11.

111) Durham JR, Yao JS, Pearce WH, Nuber GM, McCarthy WJ 3rd. Arterial injuries in the thoracic outlet syndrome. J Vasc Surg 1995; 21: 57–70 217) .

112) Mosley JG. Arterial problems in athletes. Br J Surg 2003; 90: 1461–1469.

113) Talha H, Enon B, Chevalier JM, L'Hoste P, Pillet J. Brachial artery entrapment: compression by the supracondylar process. Ann Vasc Surg. 1987 May;1(4):479-82.

114) Biemans RG. Brachial artery entrapment syndrome. Intermittent arterial compression as a result of muscular hypertrophy. J Cardiovasc Surg (Torino). 1977 Jul-Aug;18(4):367-71.

115) Cooke RA. Hypothenar hammer syndrome: a discrete syndrome to be distinguished from hand-arm vibration syndrome. Occup Med (Lond) 2003 Aug;53(5):320e324.

116) Von Rosen S. Ein Fall von Thrombose in der Arteria ulnarix nach
   a. Einwirkung von stumpfer Gewalt. Acta Chir Scand 1934;73:500e506.

117) Van de Walle PM, Moll FL, De Smet AA. The hypothenar hammer syndrome: update and literature review. Acta Chir Belg 1998 Jun;98(3):116e119.

118) Applegate KE, Spiegel PK. Ulnar artery occlusion in mountain bikers. J Sports Med Phys Fitness 1995 Sep;35(3):232e234.

119) Noel B, Hayoz D. A tennis player with hand claudication. Vasa 2000 May;29(2):151e153.

120) Koga Y, Seki T, Caro LD. Hypothenar hammer syndrome in a young female badminton player. A case report. Am J Sports Med 1993 NoveDec;21(6):890e892.

121) Wernick R, Smith DL. Bilateral hypothenar hammer syndrome: an unusual and preventable cause of digital ischemia. Am J Emerg Med 1989 May;7(3):302e306.

122) Tsavellas G, Huang A, Ranaboldo CJ. Soft-tissue case 42. Hypothenar hammer syndrome. Can J Surg 2001 Dec;44(6):409, 466e467.

123) Conn Jr J, Bergan JJ, Bell JL. Hypothenar hammer syndrome: posttraumatic digital ischemia. Surgery 1970 Dec;68(6):1122e1128.

124) Alice A Perlowski and Michael R Jaff. Vascular disorders in athletes. Vasc Med 2010 15:469.

125) Keith E Swanson, John R Bartholomew and Rolf Paulson. Hypothenar hammer syndrome: A case and brief review. Vasc Med 2012 17: 108

126) Berguer R, Kieffer E (1992) Surgery of the arteries to the head. Springer, Berlin Heidelberg New York.

127) Hill RA, Pho RWH, Kumar VP (1993) Resection of vascular malformations. J Hand Surg 18B:17–21.

128) Schwartz CJ, Werthessen NT, Wolf W (1980) Structure and function of the circulation. Plenum, New York.

129) Brzezinski M, Luisetti T, London MJ. Radial artery cannulation: a comprehensive review of recent anatomic and physiologic investigations. Anesth Analg 2009;109:1763–1781.

130) Gellman H, Botte MJ, Shankwiler J, Gelberman RH. Arterial patterns of the deep and superficial palmar arches. Clin Orthop Relat Res 2001;383:41– 46.

131) Rutherford RB, Flanigan DP, Gupta SK et al. Suggested standards for reports dealing with acute limb ischaemia. J Vasc Surg 1986; 4:80-94.

132) The STILE investigators. Results of a prospective randomized trial evaluating surgery versus thrombolysis for ischaemia of the lower extremity. Ann Surg 1994; 220:251-268.

133) Galbraith K, Collin J, Morris PJ, Wood RF(1985) Recent experience with arterial embolism of the limbs in a vascular unit. Ann R Coll Surg Engl 67:30–3.

134) E. Jane H. Turner, Alexander Loh, Adam Howard. Systematic review of the operative and non-operative management of acute upper limb ischemia. Journal of Vascular Nursing Volume 30, Issue 3, September 2012, Pages 71–76.

135) Darling RC, Austen WG, Linton RR. Arterial embolism. Surg Gynecol Obstet 1967;124:106-14.

136) Kretz JG, Weiss E, Limuris A, Eisenmann B, Greff D, Kieny R. Arterial emboli of the upper extremity: a persisting problem. J Cardiovasc Surg (Torino) 1984;25:233–235.

137) Wirsing P, Andriopoulos A, Botticher R. Arterial embolectomies in the upper extremity after acute occlusion. Report on 79 cases. J Cardiovasc Surg (Torino) 1983;24:40–42.

138) Sultan S, Evoy D, Eldin AS, Eldeeb M, Elmehairy N. Atraumatic acute upper limb ischemia: a series of 64 patients in a Middle East tertiary vascular center and literature review. Vasc Surg 2001;35:181–197.

139) Hernandez-Richter T, Angele MK, Helmberger T, Jauch KW, Lauterjung L, Schildberg FW. Acute ischemia of the upper extremity: long-term results following thrombembolectomy with the Fogarty catheter. Langenbecks Arch Surg 2001;386:261–266.

140) Pentti J, Salenius JP, Kuukasjarvi P, Tarkka M. Outcome of surgical treatment in acute upper limb ischaemia. Ann Chir Gynaecol 1995;84:25–28.

141) Vohra R, Lieberman DP. Arterial emboli to the arm. J R Coll Surg Edinb 1991;36:83–85.

142) Licht PB, Balezantis T, Wolff B, Baudier JF, Røder OC. Long-term outcome following thrombembolectomy in the upper extremity. Eur J Vasc Endovasc Surg. 2004 Nov;28(5):508-12.

143) Andersen LV, Mortensen LS, Lindholt JS, Faergeman O, Henneberg EW, Frost L. Upper-limb thrombo-embolectomy: national cohort study in Denmark. Eur J Vasc Endovasc Surg. 2010 Nov;40(5):628-34.

144) M. Javid, T.R. Magee and R.B. Galland. Arterial Thrombosis Associated with Malignant Disease. Eur J Vasc Endovasc Surg 35, 84e87 (2008).

145) Berridge DC, Kessel D, Robertson I. Surgery versus thrombolysis for acute limb ischaemia: initial management. Cochrane Database Syst Rev 2002;(3):CD002784.

146) Baguneid M, Dodd D, Dulford P, et al. Management of acute nontraumatic upper limb ischemia. Angiology 1999;50: 715-20.

147) Cejna M, Salomonowitz E,Wohlschlager H, et al. rt-PAthrombolysis in acute thromboembolic upper-extremity arterial occlusion. Cardiovasc Intervent Radiol 2001;24:218-23.

148) Wildus DM, Venbrux AC, Benenati JF, et al. Fibrinolytic therapy for upper-extremity arterial occlusions. Radiology 1990;175:393-9.

149) Chang BB, Roddy SP, Darling RC 3rd, Maharaj D, Paty PS, Kreienberg PB, et al. Upper extremity bypass grafting for limb salvage in end-stage renal failure. J Vasc Surg 2003;38:1313-5.

150) Derek L. Masden, Mitchel Seruya, James P. Higgins. A Systematic Review of the Outcomes of Distal Upper Extremity Bypass Surgery With Arterial and Venous Conduits J Hand Surg 2012;37A:2362–2367.

151) Brountzos EN, Malagari K, Kelekis DA. Endovascular treatment of occlusive lesions of the subclavian and innominate arteries. Cardiovasc Intervent Radiol 2006;29:503–510.

152) Hadjipetrou P, Cox S, Piemonte T, Eisenhauer A. Percutaneous revascularization of atherosclerotic obstruction of aortic arch vessels. J Am Coll Cardiol 1999;33:1238–1245.

153) Kandarpa K, Becker GJ, Hunink MG, et al. Transcatheter interventions for the treatment of peripheral atherosclerotic lesions: Part I. J Vasc Interv Radiol 2001;12:683–695.

154) Eisenhauer AC. Subclavian and innominate revascularization: Surgical therapy versus catheter-based intervention. Curr Interv Cardiol Rep. 2000;2:101–110.

155) Samir N. Patel, Christopher J. White, Tyrone J. Collins, Gary A. Daniel, J. Stephen Jenkins, J.P. Reilly, Rachael F. Morris and Stephen R. Ramee. Catheter-Based Treatment of the Subclavian and Innominate ArteriesCatheterization and Cardiovascular Interventions 71:963–968 (2008)

156) Rodriguez-Lopez JA, Werner A, Martinez R, Torruella LJ, Ray LI, Diethrich EB. Stenting for atherosclerotic occlusive disease of the subclavian artery. Ann Vasc Surg 1999;13:254–260.

157) Henry M, Amor M, Henry I, Ethevenot G, Tzvetanov K, Chati Z. Percutaneous transluminal angioplasty of the subclavian arteries. J Endovasc Surg 1999;6:33–41.

158) De Vries JP, Jager LC, Van den Berg JC, et al. Durability of percutaneous transluminal angioplasty for obstructive lesions of proximal subclavian artery: Long-term results. J Vasc Surg 2005;41: 19–23.

159) Przewlocki T, Kablak-Ziembicka A, Pieniazek P, et al. Determinants of immediate and long-term results of subclavian and innominate artery angioplasty. Catheter Cardiovasc Interv 2006; 67:519–526.

160) Rene´ Zellweger, Florian Hess, Andrew Nicol, Jones Omoshoro-Jones, Delawir Kahn, Pradeep Navsaria. An analysis of 124 surgically managed brachial artery injuries. American Journal of Surgery 188 (2004) 240–245.

161) Hardeep Gill, William Jenkins, Sorin Edu, Wanda Bekker, Andrew J. Nicol, Pradeep H. Navsaria. Civilian Penetrating Axillary Artery Injuries. World J Surg (2011) 35:962–966.

162) S. Sobnach, A.J. Nicol, H. Nathire, S. Edu, D. Kahn, P.H. Navsaria. An Analysis of 50 Surgically Managed Penetrating Subclavian Artery Injuries. Eur J Vasc Endovasc Surg (2010) 39, 155-159.

163) Sung-Kwan Kim, Hyo-Sung Kwak, Gyoung-Ho Chung, Young-Min Han, et al. Acute Upper Limb Ischemia due to Cardiac Origin Thromboembolism: the Usefulness of Percutaneous Aspiration Thromboembolectomy via a Transbrachial Approach. Korean J Radiol 12(5), Sep/Oct 2011.

164) Clason AE, Stonebridge PA, Duncan AJ et al. Acute ischaemia of the lower limb: the effect of centralizing vascular surgical services on morbidity and mortality. Br J Surg 1989; 76:592-3.

APPENDIX 1: DEPARTMENTAL RESEARCH COMMITTEE APPROVAL

UNIVERSITY OF CAPE TOWN

Department of Surgery

Departmental Research Committee
Professor Anwar Suleman Mall
J-45 Room Old Main Building, Groote Schuur Hospital,
Observatory 7925, South Africa
Tel (021) 406 6168/6232/6227 Fax (021) 448 6461
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26th March 2012

Dr JM du Toit
Department of Surgery
Division of General Surgery
Groote Schuur Hospital
University of Cape Town

Dear Dr du Toit

RE: PROJECT 2012/021

PROJECT TITLE: Upper limb ischaemia- A twelve year experience

The above proposal was reviewed by the Department of Surgery Research Committee and I am pleased to inform you that the committee approved the study.

Please use the above project number in all future correspondence.

Yours sincerely

PROFESSOR ANWAR S MALL
CHAIRMAN: RESEARCH COMMITTEE

APPENDIX 2: HUMAN RESEARCH ETHICS COMMITEE APPROVAL

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences
Human Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
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3 September 2012

HREC REF: 448/2012

Dr J Du Toit
c/o Dr NG Naidoo
General Surgery
OMB

Dear Dr Du Toit

PROJECT TITLE: UPPER LIMB ISCHAEMIA - A TWELVE YEAR EXPERIENCE

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year till the 15th September 2013

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/research/humanethics/forms)

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC. REF in all your correspondence.

Yours sincerely

pp Tuburgess

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN ETHICS
Federal Wide Assurance Number: FWA00001637.

Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

s.thomas

APPENDIX 3: DATA COLLECTION SHEET

Upper limb ischaemia: Data – collection sheet

Groote Schuur Hospital – Vascular Unit

2000 – 2011

Patient sticker

Demographic details

Name: Hospital number:

Age: Gender:

Ethnic group:

Contact details

Address:

Telephone number: (H) (W)

(C)

Clinical data

Presented with:

☐ Acute limb ischaemia

Rutherford grading ☐ I ☐ IIa ☐ IIb ☐ III

Compartment syndrome ☐ Y ☐ N

☐ Chronic limb ischaemia

☐ Digital ulceration

☐ Active ulceration ☐ Healed ulceration / digital infarcts

Digits involved:

☐ Raynauds symptoms

☐ Claudication symptoms

☐ Neuro – vascular symptoms (specify)

☐ Risk factors for atherosclerosis

☐ Hypertension ☐ Hypercholesterolaemia ☐ DM - Type

☐ Cigarette smoking

Specify packyears:

☐ Other substances

☐ Cannabis ☐ TIK

☐ Cardiac disease

☐ IHD ☐ AF ☐ Valvular heart disease

☐ Other systemic disease

Specify:

☐ Relevant medical therapy (indicate class of drug)

Pre-event:
- ☐ Anti-HPT
- ☐ Insulin
- ☐ Anti-platelet agent
- ☐ Anti-TB
- ☐ Oral hypoglycaemics
- ☐ Chol-lowering agent
- ☐ Anti-coagulation
- ☐ ARV's

Post-event:
- ☐ Anti-HPT
- ☐ Insulin
- ☐ Anti-platelet agent
- ☐ Anti-TB
- ☐ Oral hypoglycaemics
- ☐ Chol-lowering agent
- ☐ Anti-coagulation
- ☐ ARV's

Pathology

☐ Embolic

- ☐ Cardiac source

  Specify:

- ☐ Extra – cardiac source

  Specify:

Site of occlusion:

☐ Thrombotic

- ☐ Atherosclerosis associated
- ☐ Thrombophylia

  Specify:

- ☐ Other

  Specify:

Site of occlusion:

Abnormal special investigations

- ☐ Upper limb dopplers
- ☐ Upper limb duplex arteriogram
- ☐ Digital doppler with caloric stimulation
- ☐ Angiogram
  - ☐ Arch
  - ☐ Select
- ☐ MD – CTA
- ☐ MRA
- ☐ CXR / C – spine XR
- ☐ Echo / ERNA
- ☐ Laboratory investigations

Hb	WCC	Platelet count
INR	PTT	Fibrinogen
ESR	CRP	Homocysteine
HIV (CD4=)	RPR	Lupus a/c
AT III	Prot C+S	CardiolipinAb
Vit B6	Vit B12	RCF
ENA	ANF	RF
Complement	Chol	LDL
HDL	Trig	Creatinine

Primary procedure

Date of procedure:

Length of procedure:

☐ Started during day time hours ☐ Started after hours

☐ Open surgical

- ☐ Embolectomy
- ☐ Bypass graft
  - ☐ Aortic arch recon ☐ SCA - Axillary ☐ Axillary - Brachial
  - ☐ Brachial - Brachial ☐ Brachial - Distal
- ☐ Fasciotomy
- ☐ Amputation
  - ☐ Above elbow ☐ Below elbow ☐ Hand - Specify:

☐ Endovascular

- ☐ On – table angiogram
- ☐ PTA ☐ Stent
  - ☐ SCA ☐ Axillary ☐ Brachial
- ☐ Thrombolysis
  - ☐ Alone ☐ In combination with surgery

Secondary Procedure

Date of procedure:

Length of procedure:

☐ Started during day time hours ☐ Started after hours

☐ Open surgical

- ☐ Embolectomy
- ☐ Bypass graft
  - ☐ Aortic arch recon ☐ SCA - Axillary ☐ Axillary - Brachial
  - ☐ Brachial - Brachial ☐ Brachial - Distal
- ☐ Fasciotomy
- ☐ Amputation
  - ☐ Above elbow ☐ Below elbow ☐ Hand - Specify:

☐ Endovascular

- ☐ On – table angiogram
- ☐ PTA ☐ Stent
  - ☐ SCA ☐ Axillary ☐ Brachial
- ☐ Thrombolysis
  - ☐ Alone ☐ In combination with surgery

Describe subsequent procedure(s) if performed:

Follow – up (30 days)

☐ Died ☐ Alive

Specify reason for death:

☐ Systemic complications

Specify:

☐ Procedure related complications

Wound complications

☐ Wound sepsis

☐ Haematoma

Graft complications

☐ Graft occlusion

☐ Graft sepsis

Nerve injuries

☐ Amputation

☐ Upper limb ☐ Arm ☐ Hand ☐ Finger

☐ Pulse status / Doppler pressures

☐ Improved ☐ Same ☐ Deteriorated

☐ Duplex arteriogram

☐ Improved ☐ Same ☐ Deteriorated

Follow – up (30 days to 6 months)

Duration post – procedure:

☐ Died ☐ Alive

Specify reason for death:

☐ Graft complications

- ☐ Graft occlusion
- ☐ Graft sepsis

☐ Pulse status / Doppler pressures

☐ Improved ☐ Same ☐ Deteriorated

☐ Duplex arteriogram

☐ Improved ☐ Same ☐ Deteriorated

☐ Function

☐ Normal ☐ Contracture ☐ Claudication

☐ Other complications

Specify:

Follow – up (6 months to longterm)

Duration post – procedure:

☐ Died ☐ Alive

Specify reason for death:

☐ Graft complications

- ☐ Graft occlusion
- ☐ Graft sepsis

☐ Pulse status / Doppler pressures

☐ Improved ☐ Same ☐ Deteriorated

☐ Duplex arteriogram

☐ Improved ☐ Same ☐ Deteriorated

☐ Function

☐ Normal ☐ Contracture ☐ Claudication

☐ Other complications

Specify: