Short Report

A 10-year experience of managing acute limb ischaemia in India

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ABSTRACT

Background. Acute limb ischaemia is threatening to both limb and life. There is little information about this disease entity from India.

Methods. We did a retrospective analysis of the clinical profile of patients presenting with non-traumatic acute limb ischaemia to our department (a tertiary care centre in India) from January 1998 to December 2007. The demography, risk factors, time taken to present to the emergency from the onset of symptoms, time taken to administer the first dose of heparin upon arrival to the emergency, primary interventions and outcomes in terms of amputation rates and in-hospital mortality were studied.

Results. The mean (SD) age of the 84 patients was 48.9 (14.3) years. Only one patient died (1.2%) and 24 patients had an amputation (28.6%). Among the predisposing risk factors a significant association was found between smoking and the rate of amputation. Early presentation to emergency and early administration of heparin was associated with lower amputation rates though this did not achieve statistical significance.

Conclusion. Acute limb ischaemia is a catastrophic event. Smoking is a risk factor associated with poorer outcomes. Early arrival to the emergency and early administration of heparin was associated with lower amputation rates.

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INTRODUCTION

The natural history of acute limb ischaemia (ALI) has remained largely unchanged despite the advent of the Fogarty catheter and thrombolysis. In western studies, the incidence of ALI in the general population is estimated to be 14 per 100 000 and constitutes 10%–16% of the vascular workload.[1] Patients presenting with ALI continue to have a particularly grim short term outlook both in terms of loss of limb and mortality, with 30-day amputation rates between 10% and 30% and mortality rates of 5%–15%.[2,3]

The factors that lead to improved outcomes include: (i) precise categorization of the degree of ischaemia; (ii) ascertaining the aetiology by history and physical examination; and (iii) appropriate therapeutic intervention.[4] For patients with acute arterial emboli or thrombosis, guidelines recommend treatment with immediate systemic anticoagulation to prevent propagation of the thrombosis.[5]

There are no data on the demography of ALI and its outcomes from India. We studied the demography of ALI in our patients and compared their risk profile with outcome to determine if factors such as early presentation to the emergency, the grade of ischaemia and early administration of heparin improved outcome.

METHODS

In a retrospective analysis, clinical profiles of patients were reviewed for those presenting with non-traumatic ALI to the Department of Surgery, Christian Medical College, Vellore, Tamil Nadu from January 1998 to December 2007. Patients of all age groups who had ALI defined as symptoms of arterial occlusion for <14 days were included. Both inpatient and outpatient charts were reviewed retrospectively using the ICD code I 74.2 and I 74.3. The demography, risk factors, time taken to present to the accident and emergency department from the onset of symptoms, time taken to administer the first dose of heparin upon arrival to the emergency, primary interventions and outcomes in terms of amputation and hospital mortality rates were extracted from the records. The categories of ALI were classified according to the protocol of Rutherford *et al.* (Table I).[6]

Smoking, hypertension, hypercholesterolaemia, diabetes, renal disease and ischaemic heart disease were ascertained based on the documented history. The first dose of heparin was considered as given when a patient received 5000 i.u. of intravenous unfractionated heparin within 24 hours of the diagnosis of ALI. Anticoagulation was characterized by a starting dose of heparin at 1000 i.u./hour titrated to maintain an activated partial thromboplastin time between 50 and 70 seconds. No patient received low molecular weight heparin due to financial limitations. Those who were administered urokinase were considered to have received thrombolysis.

The primary outcome was the need for a major amputation (below/above knee) during the hospital stay.

Statistical analysis

Categorical data were presented using frequency and percentage, and continuous variables using mean and standard deviation. Median and range were used to describe skewed variables. Associations between categorical variables were performed using the chi-square test with Yates correction. A p value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS 11.0 for Windows.

RESULTS

A total of 84 patients with ALI were seen during the study period. The mean (SD) age of the patients was 48.9 (14.3) years and 48 were men. Upper extremity involvement occurred in 35 patients and lower extremity in 49. Only 4 patients had bilateral involvement. One patient died (1.2%) while 24 had an amputation (28.6%).

Among the risk factors, male sex and smoking were the most common, followed by hypertension (Table II). The amputation rates in relation to the risk factors showed smoking to be the most important association (p<0.05; Table II).

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TABLE I. Rutherford classification of clinical categories of acute limb ischaemia[6]

Category	Description/prognosis	Findings		Doppler signals	
		Sensory loss	Muscle weakness	Arterial	Venous
I. Viable	Not immediately threatened	None	None	Audible	Audible
II. Threatened					
a. Marginally	Salvageable if promptly treated	Minimal (toes) or none	None	Inaudible	Audible
b. Immediately	Salvageable with immediate revascularization	More than toes, associated with rest pain	Mild, moderate	Inaudible	Audible
III. Irreversible	Major tissue loss or permanent nerve damage inevitable	Profound, anaesthetic	Profound, paralysis (rigor)	Inaudible	Inaudible

TABLE II. Frequency of risk factors for acute limb ischaemia and the corresponding amputation rates

Risk factor	*n* (%)	Amputation rate (%)	p value
Male sex	48 (57.1)	33.3	0.27
Age >60 years	14 (16.7)	42.9	0.20
Diabetes	16 (19)	31.3	0.79
Ischaemic heart disease	10 (11.9)	30.0	0.92
Renal disease	5 (5.9)	0	0.15
Smoking	30 (35.7)	43.3	0.03
Hyperlipidaemia	11 (13.1)	9.1	0.13
Hypertension	24 (28.6)	20.8	0.32
Previous episode of ischaemia	24 (28.6)	25.0	0.65

The main cause of ALI was thrombosis in 75% of patients; 68 patients had atherosclerosis and in 5 patients the thrombus was iatrogenic. None of our patients had thromboangiitis obliterans; 21.4% had an embolism, the source of which in all the patients was the heart and the aetiology was rheumatic heart disease. Graft occlusion (3.6%) was the other important cause of ALI (Table III). The amputation rate in those with embolism was lower than that in those who had thrombosis or graft occlusion.

Most cases of lower limb ischaemia were due to an iliofemoral block and were associated with higher amputation rates than distal levels of occlusion. However, since the number of patients in each group was few, the difference was not statistically significant (Table IV).

A quarter of the patients presented within 24 hours of the onset of symptoms and 4 (19%) required an amputation. The remaining patients (*n*=63) presented after 24 hours and had a higher amputation rate (20; 32%) independent of the grade of ischaemia. As expected, patients with a higher grade of ischaemia at presentation had higher rates of amputation (Table V).

We evaluated the policy of administration of unfractionated heparin (low molecular weight heparin was not used because it was expensive) and its effect on the amputation rate in our patients. Sixty patients (71.4%) received the first dose of heparin after the clinical diagnosis of ALI was made and 16 (26.7%) had an amputation. Of the 24 patients who did not receive heparin only 4 patients had a contraindication to its use (1 had an associated upper gastrointestinal bleed, 1 a recent cerebrovascular accident and 2 were already on heparin due to a recent surgery). In the remaining 20 patients, heparin was given only after a primary intervention. Eight of these 24 patients (33.3%) had an amputation. The median duration of administration of heparin after arrival to the emergency room was 235 minutes (range 1–1314 minutes). Among the 12 patients who received heparin within an hour of arrival to the emergency only 1 had amputation compared with 15 of 48 (31.3%) who received heparin after an hour of arrival to the emergency.

TABLE III. Cause of acute limb ischaemia and the corresponding amputation rate

Aetiology	*n* (%)	Amputation rate (%)
Thrombosis	63 (75)	31.7
Artherosclerosis	58 (69)	31.7
Iatrogenic	5 (6)	0
Embolism (all rheumatic heart disease)	18 (21.4)	16.7
Graft occlusion	3 (3.6)	33.3

TABLE IV. Relation between level of occlusion and amputation rate

Level	*n* (%)	Amputation rate (%)
Lower limb		
Iliofemoral	33 (39.3)	45
Popliteal	13 (15.5)	30
Distal	3 (3.6)	33.3
Upper limb		
Subclavian	5 (6)	20
Axillary	13 (15.5)	0
Brachial	17 (20.1)	17.6

TABLE V. Grade of ischaemia at presentation and amputation rate

Grade	*n* (%)	Amputation rate (%)
I (viable)	11 (13.1)	9.1
IIA (marginally threatened)	32 (38.1)	6.3
IIB (immediately threatened)	28 (33.3)	35.7
III (irreversible)	13 (15.5)	84.6

TABLE VI. Primary intervention and the corresponding amputation rate

Primary intervention	*n* (%)	Amputation rate (%)
Anticoagulation	34 (40.5)	17.6
Thrombolysis	8 (9.5)	25
Embolectomy/thrombectomy	30 (35.7)	16
Amputation	11 (13.1)	na

na not applicable

The amputation rates in relation to the primary intervention are shown in Table VI.

DISCUSSION

People with ALI are among the seriously sick subgroup of patients that a vascular practitioner treats. Though there has been

improvement in limb salvage rates since 1950, only 70% of patients leave with an intact limb. Of the remaining 30%, half will die and the other half require a major amputation.[7] Early and appropriate intervention can save both life and limb.

There are no data on the demography of ALI and its outcomes in the Indian literature. We analysed our experience to understand the demography and outcome of ALI in the Indian population and compared the results with available western data.

In our study there was a male preponderance, as reported in several other studies,[8] and lower limb ischaemia was more common than upper limb ischaemia. The overall amputation rate was 28.6%, which was similar to data in the literature.[2,3] Despite improvement in operative techniques and postoperative care the morbidity and mortality rates of ALI remain high.[9]

In our case series only 1 patient died—a surprisingly low mortality rate. Most western studies report mortality rates of 5%–15%,[1,4] with rates as high as 40% in the elderly population.[10] A younger patient population and early amputation in category IIB and III may be the reasons for a low mortality in our study. Other factors such as lower incidence of cardiac ischaemia and referral bias may also have a role to play. Another factor that may play a role is that financial constraints compel some patients to leave the hospital in a critical stage, who are then lost to follow up.

An analysis of risk factors for ALI showed that 40% of our patients had no predisposing condition. We suppose that non-atherosclerotic, non-cardiac risk factors could also play a role in the development of ALI and further research into their identification and prevention may be useful.

Cigarette smoking is a major risk factor for developing peripheral arterial disease[11,12] and its complications. There was a statistically significant association between smoking and the outcome of ALI. In our study the amputation rates were twice as high in smokers compared with those in non-smokers. The link between smoking and occlusive peripheral arterial disease is dose-dependent and can be broken by cessation of smoking. Cessation of smoking is the cornerstone for the management of occlusive peripheral arterial disease at any stage as shown by Lepäntalo and Lassila.[12]

Thrombosis was more frequent than embolism as a cause of non-traumatic ALI. A higher proportion of embolism,[13] thrombosis[14] and a similar frequency of both conditions[15] have been described. Thrombosis was associated with better outcomes than embolism in our study. Illuminati *et al*. observed a higher mortality rate in ALI due to embolism rather than thrombosis (31% *v*. 19.6%) and more major amputations in thrombosis than in embolism (37.7% *v*. 17.2%).[16] Thrombosis has a better effect on outcome since it is most often an incomplete and slow process allowing for collaterals to develop as opposed to an embolus which is most often sudden and complete.[17]

The duration of symptoms (occlusion) before presentation to the emergency was an important modifiable cause of amputation in our analysis. Fagundes *et al*. showed that the duration of occlusion was associated with poor prognosis with significantly higher amputation rates in patients with symptoms for >24 hours.[8] We could not analyse specific causes for the long interval between the beginning of symptoms and the arrival at the emergency department. We speculate that reasons for the delayed presentation could be the lower level of health awareness of most patients, their financial constraints and their ability to tolerate till disabling symptoms manifest and become non-remedial to local or household therapies.

Early heparinization appears useful. If there are no absolute contraindications (acute aortic dissection, serious head injury), guidelines recommend an intravenous bolus of heparin to limit propagation of the thrombus and protect the collateral circulation.[17] However, no literature is available regarding the beneficial effect of this. We studied the role of unfractionated heparin in early management of ALI and found that early administration of heparin was associated with lower amputation rates. However, in our hospital only 71.4% received heparin and of these only 20% got it within the first hour after presentation.

The use of thrombolysis or surgery in the treatment of ALI has long been debated and there are studies describing the indications, advantages and disadvantages of these interventions.[18,19] Treatment protocols for ALI have improved over the years and in the era of evidence-based medicine, an individualized treatment algorithm depending upon the age, co-morbid conditions, duration of occlusion, grade of ischaemia and aetiology may be the best option. In our study doing an embolectomy/thrombectomy rather than thrombolysis improved patient outcomes, results akin to those of Eliason *et al*.[4]

We advocate the need for greater awareness and education among general physicians and surgeons who are the primary responders to this potentially limb- and life-saving emergency since they are an important source of referral to the vascular surgeon.

Limitations

Due to the lack of a standardized ICD coding for ALI, codes which included thrombosis and embolism of the upper and lower limbs were used resulting in elimination of a small percentage of the population treated at our centre. Due to this, our series has small numbers.

Definitive conclusions are difficult to draw from any retrospective study including this one. However, some important information regarding the risk factors and management of patients with ALI does emerge. Also, we included only those patients in whom all the information was available and acknowledge that a referral bias exists in our patient data.

This notwithstanding, we believe that our data represent a realistic and reasonably accurate overview of the risk profile and post-intervention outcomes in patients with ALI and provides background information for a future prospective study.

Conclusions

ALI caused by thrombosis, embolus or graft occlusion was a serious event at our centre and a major cause of in-hospital morbidity. Smoking was the most important risk factor associated with poorer outcomes. Early presentation to the emergency and early heparinization were associated with decreased rates of amputation. Hence, the interval between the onset of symptoms and availability of appropriate care is probably an important modifiable factor to decrease the rates of amputation. With adequate emergency care and appropriate post-interventional management and the decision to amputate at the right time, the mortality rate can possibly be decreased.

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REFERENCES

1 Dormandy J, Heeck L, Vig S. Acute limb ischemia. *Semin Vasc Surg* 1999;**12:** 148–53.

2 Blaisdell FW, Steele M, Allen RE. Management of acute lower extremity arterial ischemia due to embolism and thrombosis. *Surgery* 1978;**84:**822–34.
3 Jivegard L, Holm J, Schersten T. Acute limb ischemia due to arterial embolism or thrombosis: Influence of limb ischemia versus pre-existing cardiac disease on postoperative mortality rate. *J Cardiovasc Surg (Torino)* 1988;**29:**32–6.
4 Eliason JL, Wainess RM, Proctor MC, Dimick JB, Cowan JA Jr, Upchurch GR Jr, *et al*. A national and single institutional experience in the contemporary treatment of acute lower extremity ischemia. *Ann Surg* 2003;**238:**382–9.
5 Clagett GP, Sobel M, Jackson MR, Lip GY, Tangelder M, Verhaeghe R. Antithrombotic therapy in peripheral arterial occlusive disease: The Seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest* 2004;**126** (Suppl):S609–S626.
6 Rutherford RB, Baker JD, Ernst C, Johnston KW, Porter JM, Ahn S, *et al.* Recommended standards for reports dealing with lower extremity ischemia: Revised version. *J Vasc Surg* 1997;**26:**517–38.
7 Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG, *et al*. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *Eur J Vasc Endovasc Surg* 2007; **33** (Suppl 1):S1–S75.
8 Fagundes C, Fuchs FD, Fagundes A, Poerschke RA, Vacaro MZ. Prognostic factors for amputation or death in patients submitted to vascular surgery for acute limb ischemia. *Vasc Health Risk Manag* 2005;**1:**345–9.
9 Results of a prospective randomized trial evaluating surgery versus thrombolysis for ischemia of the lower extremity. The STILE trial. *Ann Surg* 1994;**220:**251–66.
10 Braithwaite BD, Davies B, Birch PA, Heather BP, Earnshaw JJ. Management of acute leg ischaemia in the elderly. *Br J Surg* 1998;**85:**217–20.
11 Kannel WB, Shurtleff D. The Framingham Study. Cigarettes and the development of intermittent claudication. *Geriatrics* 1973;**28:**61–8.
12 Lepäntalo M, Lassila R. Smoking and occlusive peripheral arterial disease. Clinical review. *Eur J Surg* 1991;**157:**83–7.
13 Aune S, Trippestad A. Operative mortality and long-term survival of patients operated on for acute lower limb ischaemia. *Eur J Vasc Endovasc Surg* 1998;**15:** 143–6.
14 Ouriel K, Veith FJ. Acute lower limb ischemia: Determinants of outcome. *Surgery* 1998;**124:**336–41.
15 Gutowski P, Soltys J, Rac M, Szmania A, Cnotliwy M. [The treatment of acute lower limb ischemia]. *Wiad Lek* 1999;**52:**252–6.
16 Illuminati G, Bertagni A, Calio FG, Ciulli A, Guglielmi R, Vietri F, *et al.* [Acute ischemia of the lower limbs]. *Riv Eur Sci Med Farmacol* 1996;**18:**19–27.
17 Callum K, Bradbury A. ABC of arterial and venous disease: Acute limb ischaemia. *BMJ* 2000;**320:**764–7.
18 Ouriel K. Thrombolytic therapy for acute arterial occlusion. *Curr Opin Gen Surg* 1994:257–64.
19 Weaver FA, Comerota AJ, Youngblood M, Froehlich J, Hosking JD, Papanicolaou G. Surgical revascularization versus thrombolysis for nonembolic lower extremity native artery occlusions: Results of a prospective randomized trial. The STILE Investigators. Surgery versus Thrombolysis for Ischemia of the Lower Extremity. *J Vasc Surg* 1996;**24:**513–21.