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When is Urgent Revascularisation Unnecessary for Acute Lower Limb Ischaemia?

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Objectives: *To predict the risk of gangrene by the use of simple clinical parameters available on admission.*
Design: *Retrospective comparison using logistic regression and χ^2 analyses of prospectively registered data from two patients series.*
Methods: *One group of patients with acute lower limb ischaemia, (n = 61) was managed by selective initial non-operative treatment (NO) in a university hospital. The other group (n = 173) contained patients managed by early revascularisation in a multicentre (MC) study from 10 university, county and district hospitals. Gangrene and death within one month were recorded.*
Results: *57% of patients in the NO group were initially managed by intravenous heparin followed by surgery when necessary. Impaired motor function and skin cyanosis in the ischaemic limb predicted gangrene. Patients without this combination were low risk (LR) patients and constituted 62% (NO) and 67% (MC). Non-operatively managed LR patients did not develop gangrene, whereas 14% of those undergoing early revascularisation in the two series did ($p < 0.05$).*
Conclusions: *The results suggest that patients without motor disturbance and cyanosis are at low risk of gangrene and may benefit from initial non-operative treatment, irrespective of the presumed aetiology.*

Key Words: Ischaemia; Embolism; Gangrene; Risk.

Introduction

Irreversible tissue damage occurs within 4 to 6 h of total limb ischaemia.[1] In the clinical situation, collateral blood flow usually decreases the ischaemic insult following occlusion of a major limb artery. Since many patients with acute lower limb ischaemia have substantial collateral blood flow, urgent revascularisation is often unnecessary.[2] Urgent surgical revascularisation using a balloon tipped catheter is widely accepted as optimal treatment for embolic, but not for thrombotic ischaemia.[3] Differentiation between arterial embolism and thrombosis is often difficult.[4–5] Furthermore, many patients with embolic ischaemia have pre-existing atherosclerotic occlusive disease (AOD), and early surgical thromboembolectomy is associated with less rewarding results in these patients.[6] One way of diminishing the problems associated with uncertain aetiology is to avoid urgent surgery for acute limb ischaemia whenever possible, thereby allowing time for a proper evaluation of the patient[2] and possible percutaneous treatment by thrombolysis or clot aspiration.[7–10] The use of such techniques often requires that the limb can withstand a further period of ischaemia while recanalisation occurs, thus demonstrating the need for simple and reliable identification of limbs that need urgent revascularisation.

The nervous tissue is highly sensitive to ischaemia.[11] Nervous function may therefore be used for assessment of the severity of acute ischaemia.[12] Other clinical parameters may also be of importance.[8] We compared simple clinical parameters with the outcome for 61 patients with acute leg ischaemia included in a study in a centre where selective initial non-operative (NO) treatment was employed, and for 173 patients included in a multi-centre study (MC) where early revascularisation was routine. The aim was to define a simple clinical parameter identifying patients at low and high risks for gangrene respectively, and to compare results of treatment for low risk patients in the two series.

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Methods

Patients

Patients with a sudden onset of non-traumatic lower limb ischaemia of less than 96 h duration and with no previous vascular reconstruction in the affected limb were included. Patients with an obviously non-viable limb on admission (ischaemic muscle rigidity) were not included. One group contained consecutive patients undergoing treatment for acute lower limb ischaemia at the Sahlgrenska University Hospital during the years 1986 to 1989 (NO series, n = 61). Patients with acute lower limb ischaemia at this hospital are subjected to emergency revascularisation procedures only if severe disturbances in sensory-motor functions are observed in the ischaemic limb.[13] Patients without such findings are, irrespective of the presumed aetiology of the ischaemia, initially anti-coagulated with intravenous heparin (20 000–30 000 IU/day) and subjected to arteriography and surgery if the limb deteriorates or fails to improve.[2]

The other patient series contained patients with acute lower limb ischaemia who had been included in a prospective randomised multicentre series performed in ten other hospitals during the same 4 year period.[14] These patients (MC series, n = 173) were managed by routine early surgery, and registration on admission of clinical features of the limb ischaemia was included in the protocol of the original study.[14]

Study protocol

On admission, basal patient characteristics such as age, sex, and previous diseases (diabetes mellitus, angina pectoris, myocardial infarction, intermittent claudication, previous acute or chronic limb ischaemia episodes) were registered in formal protocols in both series. Signs of cardiac decompensation on admission were recorded. Furthermore, clinical characteristics of the limb (ischaemic pain, motor and sensory loss, and the appearance of the skin) were specifically evaluated as risk predictors for gangrene. The degree of ischaemic pain, and loss of sensation and motor function were assessed on a scale from zero to two, with two denoting the most severe dysfunction (Table 1). The skin appearance in the ischaemic area of the limb was registered (no cyanosis or cyanosis) by the admitting surgeon and scored as dummy variables one and two respectively (Table 1). Measurement of ankle pressure (AP) in the ischaemic limb on admission was included in the protocol in the MC, but not in the NO series.

Table 1. Evaluation of the acute ischaemia

	Range	Mean ± S.D.	
		NO series	MC series
Ischaemic pain	0–2*	1.3 ± 0.7 (n = 61)	1.3 ± 0.6 (n = 166)
Motor/sensibility	0–4**	1.9 ± 1.4 (n = 61)	1.8 ± 1.3 (n = 172)
Temperature zone	1–6†	3.0 ± 1.4 (n = 60)	3.6 ± 1.7 (n = 168)
Skin appearance	1–2‡	1.4 ± 0.6 (n = 61)	1.5 ± 0.5 (n = 173)

* 0 = no, 1 = moderate and 2 = severe pain;
** for motor and sensibility disturbance respectively: 0 = no, 1 = moderate and 2 = severe, or total loss; † 1 = distal to ankle, 2 = distal part of calf, 3 = proximal calf, 4 = level of the knee, 5 = distal thigh and 6 = proximal thigh; ‡ 1 = normal or pale and 2 = cyanosis or mottled cyanosis.

Whenever possible, the duration of symptoms on admission and by the time surgery was completed was recorded.

A potential cardiac source of emboli (atrial fibrillation and/or recent myocardial infarction) was registered as present or absent based on previous and present history, physical status and electrocardiograms. The aetiological diagnosis, based on data available on admission, was defined as probable embolism or not depending on whether the patient had a source of emboli (atrial fibrillation and/or a recent myocardial infarction). During the operation, AOD in the femoral artery was classified as present or absent.

All patients were followed for one month from admission, and all deaths were registered. Amputations within one month of more than the forefoot were defined as gangrene, irrespective of whether the patient survived for one month or not. A good result was defined as a patient surviving 1 month without gangrene.

Data analysis and statistics

The studied admission variables were compared with gangrene within 30 days using dummy variables and stepwise logistic regression analysis in the NO and MC series individually, and in combination. Admission variables that were significant in either, or the combined series, were then studied further. Combinations between these variables and gangrene within 30 days were studied by χ^2 analysis in the two series, and an optimal parameter defining patients at low risk for gangrene was defined. The results of treatment in the two series were compared. Two-tailed parametric tests and non-parametric tests were used for significance testing and a p value of less than 0.05 was considered

significant. Unless otherwise stated, results are given as mean ± S.D.

Results

Basal characteristics of the patients in the two series were similar (Tables 1–2). An admission diagnosis of arterial embolism was equally common in the two series (Table 2). In the NO series, 26 patients were operated upon as emergency cases, and 35 (57%) were initially treated with heparin and subsequent arteriography. Early preoperative arteriography was performed in only seven of the 26 emergency operation cases. Eighteen of the initially non-operated patients were operated upon within one month (average time from admission to operation was 94 ± 80 h). The 17 patients who were not operated upon within one month either improved significantly (n = 14), or were considered inoperable and died with (n = 1), or without (n = 2), gangrene. The gangrene rate in patients who were not operated upon within one month was 11% (n = 2) as compared to 9% (n = 4) in those who were. Thirty-seven percent of all operations included more than a simple arterial thromboembolectomy. Overall, the mortality rate was 25%, and good results were obtained in 70% of the NO series: 46% following emergency surgery and 89% in patients selected for initial non-operative treatment.

In the MC series all patients underwent early surgery, and in 7% more than an arterial thromboembolectomy was performed. Only 4% of the patients in the MC series underwent preoperative arteriography compared to 63% in the NO series. Overall, 62% good results were obtained in the MC series, while the gangrene and mortality rates were 21% and 26% respectively. The AP in the ischaemic limb was studied in 124 patients (72%) in the MC series. No AP was measurable in 114 (92%) patients whereas 10 patients had an AP ranging from 20 to 75 mmHg. The gangrene rate was 20% in patients with an AP of more than zero *vs.* 22% in those with a non-measurable AP.

Stepwise logistic regression analysis in the NO series revealed motor function as a significant risk factor for gangrene (p = 0.008, Table 3). In the MC series, only the appearance of the skin (cyanosis) was of significance (p = 0.05). In the combined NO and MC series cyanosis was a significant risk parameter for gangrene (p = 0.0088). Using χ^2 analysis, the most discriminating combination of the two identified risk factors (motor function and cyanosis) for gangrene was then identified. Patients with disturbed motor function in combination with cyanosis of the limb were high risk cases for gangrene (Figs. 1 and 2).

According to the above definition, there were 38 (62%) and 116 (67%) low risk (LR) cases in the NO and MC series respectively. In the MC series patients, in whom the AP had been studied, there were 69% LR patients in those with a non-measurable AP versus 70% in those with a measurable AP. Overall, there were 3% gangrenes in LR patients in the NO series as compared to 14% in the MC series (p = 0.057, χ^2 test). Thirty-one (82%) of the LR patients in the NO series were initially managed with heparin. There were no gangrenes in these patients as compared to 14% (p = 0.028, χ^2 test) in the 123 LR patients managed by early surgery in the two series. The mortality rates in LR patients were 18% and 22% in the NO and MC series, while good results were obtained in 82% and 72% respectively (NS). In the initially non-operatively

Table 2. Basal characteristics

	NO (n = 61*)	MC (n = 173*)
Age (years)	78,3 ± 9	79,9 ± 9
Females	61%	62%
Duration of symptoms on admission		
average (h)	16 ± 20 (n = 59)	15 ± 27 (n = 139)
median (h)	6	7
≤ 12 h	69%	69%
Previous TE	8%	6%
Diabetes	13%	16%
History of AOD	26%	22%
Source of emboli	66%	70% (n = 170)
Angina pectoris	25% (n = 56)	34%
Myocardial infarction		
previous	20%	19%
recent	15%	12%
Cardiac decompensation on admission		
	35% (n = 56)	27% (n = 166)

* n for all parameters if not otherwise indicated in the table; TE = thromboembolectomy; AOD = atherosclerotic occlusive disease in the limb.

Table 3. Significance in stepwise logisitic regression analyses of admission variables vs gangrene in NO and MC series respectively, and in NO + MC series

	MC	NO	MC + NO
Pain	NS	NS	NS
Temperature zone	NS	NS	NS
Skin appearance	*	NS	***
Motor function	NS	***	**
Sensibility function	NS	NS	NS
HR/LR classification	***	***	***

HR = patients with disturbed motor function in combination with cyanosis of the ischaemic limb; LR = patients without this combination; * p = 0.05; ** $p < 0.05$ and *** $p < 0.01$.

managed LR patients, 90% good results were obtained as compared to 70% in patients undergoing early surgery in the two series ($p = 0.021$, χ^2 test). In high risk (HR) patients, results were similar in the NO and MC series (mortality rates were 35% and 34%, good results were obtained in 53% and 43%, gangrene rates: see Table 4).

The influence of ischaemia duration on outcome was studied in the MC series. There was a significant relationship between the duration of symptoms and the gangrene rate in HR, but not in LR, patients (Fig 3).

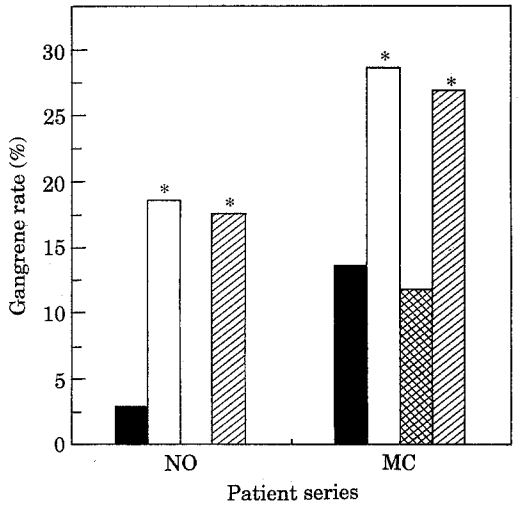

Fig. 1. Gangrene rates as a function of cyanosis and disturbed motor function, respectively. ■ = no cyanosis; □ = cyanosis; ▩ = no motor disturbance; ▨ = motor disturbance. * $p < 0.05$ vs corresponding patients without the dysfunction (Mann-Whitney U test).

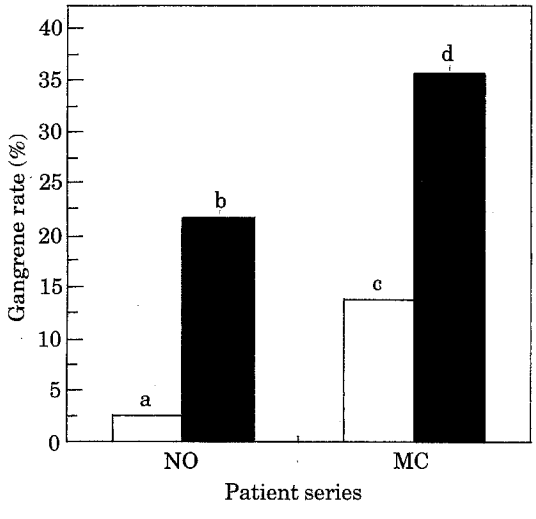

Fig. 2. Gangrene rates in high risk (cyanosis in combination with disturbed motor function) and low risk (neither or only one of the above factors) patients. □ = low risk; ■ = high risk. Significances: a *vs.* b, $p = 0.003$ and c *vs.* d, $p = 0.001$ (Mann-Whitney U test); a *vs.* c, $p = 0.05$ and b *vs.* d, NS (Chi-square test).

Table 4. Gangrene rates in LR and HR patients as a function of the presence† of a cardiac source of emboli (Emb), or not (Non-emb)

	Emb		Non-emb		Emb + non-emb	
	NO	MC	NO	MC	NO	MC
LR	0%* (26)	13% (76)	8%(12)	15% (40)	3%	14%
HR	21% (14)	31% (42)	22% (9)	55% (11)	22%	36%
LR + HR	8%	20%	14%	25%	10%	21%

* $p < 0.05$ *vs* corresponding MC patients; † data on embolic source missing in three MC patients. The number of patients in each group is denoted within parentheses.

In HR patients having surgery completed within, as compared to after more than, 10 h from the onset of symptoms, respectively, the gangrene rates were 9% and 59% ($p < 0.001$, Fisher's test). The corresponding gangrene rates in LR patients were 6% *vs.* 16% (NS). Gangrene in patients with an admission diagnosis of embolism in the MC series was related to femoral AOD (Table 5). In LR patients with embolism as admission diagnosis, and who were found to have femoral AOD, there was no significant relationship between the duration of the ischaemia and the gangrene rate (Spearman correlation coefficient).

Discussion

This study is based on prospectively registered data from two studies. Retrospective analysis of the data suggest that the risk for early gangrene in patients

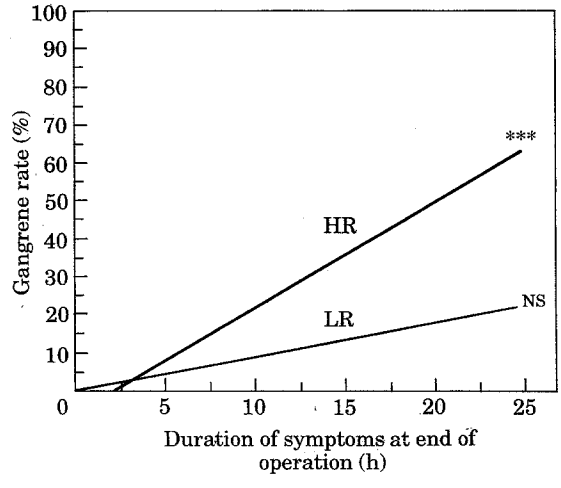

Fig. 3. Gangrene rate as a function (linear regression) of the duration of symptoms on admission in HR and LR cases in MC series patients admitted with a duration of symptoms of ≤24h. *** $p = 0.0001$ (Spearman rank correlation). Equation for regression line (linear regression) in HR patients: $Y = -5 + 2.8x$.

Table 5. Gangrene rates in HR and LR cases as a function of coexisting femoral atherosclerotic occlusive disease †(FAOD) or not (NFAOD) in patients with a source of emboli in the MC series.

	NFAOD	FAOD
HR	33% (12)	30% (27)
LR	0%* (26)	18% (49)

* $p < 0.02$ *vs* LR FAOD, $p < 0.03$ *vs* HR NFAOD and $p < 0.005$ vs HR FAOD (Chi-square and Fisher's tests). † data were missing in four patients. The number of patients in each group is denoted within parentheses.

managed by selective initial treatment (NO series) can be predicted by the combined parameter motor disturbance and cyanosis of the ischaemic limb. This risk factor was highly predictive for gangrene also in the patients routinely managed with early thromboembolectomy (MC series). There were fewer gangrenes in LR patients, initially treated non-operatively. The one month results of initial non-operative treatment in LR patients were beneficial in embolic as well as non-embolic occlusions. This observation suggests that initial therapy should be based on the severity of the limb ischaemia[2, 13] and not on the aetiology.

Patients with less severe ischaemia benefit from initial non-operative heparin treatment, followed when needed by operation, lysis or other less invasive revascularisation techniques performed by a specialist after proper arteriographical evaluation. The findings in this study further suggest that the poor results of early surgical revascularisation in LR cases are related to the presence of AOD. Hence, in LR patients in the MC series there were no gangrenes in patients without, but 18% in those with, femoral AOD. The presence of iliofemoral atherosclerosis can usually be evaluated by emergency arteriography. The severity of the limb ischaemia can be assessed on admission, and patients undergoing initially non-operative treatment must be continuously followed. The prognostic importance of severe motor disturbance was expected.[2, 3] Cyanosis of the skin in the ischaemic area improved the gangrene predictive value of motor disturbance. The presence of cyanosis is easily evaluated and is likely to reflect stagnant skin circulation, whereas motor disturbance is likely to reflect nerve ischaemia interrupting the neuromuscular transmission. Sensory disturbance did not add any extra prognostic information and neither did the degree of ischaemic pain.

The question of whether the NO and MC series of patients are comparable needs to be addressed. The patients in the two series were included during the same time period. One major difference is that whereas the NO series contains consecutive patients with acute lower limb ischaemia in a university hospital, the MC series contains patients included in a prospective randomised multicentre study performed in university as well as in county and district hospitals and in which emergency operation was a prerequisite for inclusion. Thus patient selection was somewhat different in the two series, and it is possible that patients with more advanced ischaemia were included in the MC series although the techniques employed in this study failed to reveal such a difference.

This is not a randomised study, and the present results therefore need to be confirmed in a prospective randomised study in order to allow definite conclusions. Nevertheless, based on our present and previous[2, 6, 13] results, we suggest that simple evaluation of motor disturbance and appearance of the skin on admission of patients with acute lower limb ischaemia can be used to define a low risk group containing approximately two thirds of the patients. Irrespective of the presumed aetiology on admission, results tend to be better when initial non-operative treatment is used in this group of patients. In high risk patients, initial conservative treatment does not have any place and revascularisation should not be postponed. Improved outcome by initial non-operative management in low risk patients is likely to be partly due to the use of arteriography prior to surgery, and also to the fact that revascularisation can be performed by specialist vascular surgeons and/or radiologists, instead of general surgeons with limited experience in vascular surgery. These factors may be particularly important when there is advanced coexisting AOD: even an embolectomy for embolic disease is a demanding procedure in the presence of severe atherosclerosis.[6] Another advantage of selective initial non-operative management is that any subsequent treatment can be performed during office hours. This may be particularly important for techniques demanding radiological or laboratory surveillance.[7–10]

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