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Assessment of functional limitations caused by *Mycobacterium ulcerans* infection: towards a Buruli Ulcer Functional Limitation Score

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Summary

The purpose of this study of treated Buruli ulcer patients in Ghana was to identify and assess late sequelae of treated Buruli ulcer using a goniometer, and to develop a scoring system for functional limitations. Of 78 patients, 58% ($n = 45$) had a reduction in the range of motion of one or more joints: 30% ($n = 23$) had one or more functional limitations of the leg and 21% ($n = 16$) of the arm; 49% ($n = 38$) had a functional limitation. Of all patients with affected knees, the predicted average extent of limitation was 63%. In patients with affected ankles, limitation was 78% on average; in those with elbow involvement, this was 76% on average, and in wrists involved, 65%. All of the hands involved were markedly restricted. We propose a simplified and functional scoring system that should be tested for validation in a second patient sample, and, if properly validated and adjusted, can be used in future intervention trials.

keywords rehabilitation, functional limitations, Buruli ulcer, *Mycobacterium ulcerans*

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Introduction

Buruli ulcer, caused by *Mycobacterium ulcerans*, is an ulcerating skin disease mainly affecting the limbs. It has an indolent, chronic course; most patients do not present with febrile or acute illness. Buruli ulcer is endemic in scattered foci in swampy tropical areas and its prevalence has dramatically increased in recent years in West African countries.

A skin prick during farming or playing, or an insect bite could transmit the microorganism to the subcutaneous fat (Meyers *et al.* 1974; Portaels *et al.* 1999). *Mycobacterium ulcerans* is probably present in the natural environment. Although the disease occurs in any age group, children are affected most frequently (van der Werf *et al.* 1999).

The disease starts as a painless nodule. Other possible pre-ulcerative lesions in the first stage are plaques or oedema. In the second stage, ulceration of the skin with an undermined edge can be seen. In stage three, a granulomatous healing response occurs and in stage four, scarring occurs, often resulting in contractures and ankylosis. Other sequelae such as severe muscular atrophy, reduced growth

of the limbs and lymph oedema may occur. Occasionally, the infection has been reported to spread to other tissues like bone. All these sequelae may lead to severe and permanent functional limitations (van der Werf *et al.* 1999).

A retrospective study on socio-economic implications of Buruli ulcer in Ghana showed that treatment costs are high and that sequelae of the disease are frequently severe (Asiedu & Etuaful 1998). The disease indeed imposes a substantial financial burden on patients and their families. Moreover, it has great impact on the social, mental and spiritual well-being of the afflicted patients and their families (Stienstra *et al.* in press). No formal follow-up studies of treated Buruli ulcer patients have been conducted to identify and assess functional limitations as yet. We expect that future intervention studies may benefit from a scoring system, in which functional limitations can be described quantitatively.

The purpose of this follow-up study was to identify and assess the late sequelae of treated Buruli ulcer in Ghana and to develop and propose a scoring system for functional limitations caused by *M. ulcerans*.

Methods

In 2001, we followed-up treated Buruli ulcer patients in Ghana, in two hospitals in areas highly endemic for Buruli ulcer: Agogo Hospital, a missionary hospital in the Ashanti region in the vicinity of the planes of the Afram river (van der Werf *et al.* 1989), and Dunkwa Hospital, a governmental hospital in the Central region located in the area near the rivers Offin and Subin (Amofah *et al.* 1993).

Patients who had received surgical treatment for Buruli ulcer in the period 1994 to July 2000 were included in the study. Patients who had been admitted during this period but who had also undergone surgery before or after this period, were excluded. Patients were identified through hospital records, from which relevant medical information was extracted. In co-operation with members of the public health team, field trips were undertaken in search of the patients identified. The members of the public health team acted as interpreters and assistants. To retrieve information concerning course of disease, treatment, sequelae and its impact on social life and career, a semistructured interview was used. In addition, the site of the ulcer was inspected. When a reduced range of motion (ROM) of an affected joint was observed, this reduction was measured using a transparent goniometer (OIM, Orthopaedic Products, The Netherlands) with 20 cm arms and a 2° calibration. The joints involved were the knee, ankle, shoulder, elbow, wrist, and the joints of the hand. A photograph was taken of the Buruli ulcer scar and its sequelae. As it proved to be difficult to measure the ROM of the hand using a 20-cm goniometer, we assessed functional limitations (yes/no) on the basis of the interview. The ranges of motion measured were transformed into a score using a provisional scoring system for functional limitations. For the performance of functional activities (e.g. sitting, walking, eating) a certain degree of ROM is required. Ranges of motion were recorded according to the Sagittal, Frontal, Transverses, Rotation (SFTR) method (Gerhardt & Rondinelli 2001). If the ROM measured was not sufficient to perform the functional activity, the patient received one point. A total score can thus be acquired for all joints together per patient. In Appendix 1 the ranges of motion required for the different functional activities needed in daily life are summarized. Severity of functional limitation per joint was assessed by dividing the number of total limited functional activities, by the total number of functional activities listed in Appendix 1 for that joint.

The study protocol was approved by the Investigations Review Board of the Groningen University Hospital and the Ministry of Health, Ghana. Patients or their guardians gave informed consent prior to examination and interview parts of the study.

Results

Between 1994 and July 2000, 417 patients had been admitted for Buruli ulcer in both hospitals. Of these 417 patients, 136 patients lived in areas covered by the researchers in the research period of 6 months. Of these 136 patients, 78 (57%) patients were included in the study. The other 58 patients either had incomplete addresses ($n = 26$), moved ($n = 14$), were not at home ($n = 12$), died ($n = 5$) or refused to participate ($n = 1$). Of the five patients that died, two deaths were related to Buruli ulcer. To assess whether the patients seen were a representative sample of the patient population from which they were derived, analysis of distribution of gender, age and year of admission to hospital was performed. There was no difference in the distribution of gender between the patient populations retrieved and not retrieved (chi-square test; $P = 0.820$). The retrieved population was significantly younger (median age 11 years) than the patient population at large (median age 18 years) (Mann–Whitney U -test; $P = 0.001$). However, there was no significant relationship between age and presence of contractures (Mann–Whitney U -test; $P = 0.197$). The median age of patients with contractures ($n = 45$) was 12 years; the median age of patients without contractures ($n = 33$) was 11 years. The time elapsed between the first admission and the study period did not differ between the two groups; 2.6 years in the retrieved patients and 2.9 years in the patients not retrieved (Mann–Whitney U -test; $P = 0.253$).

Of our study population ($n = 78$), 58% ($n = 45$) had a reduced ROM of one or more joints. Of these 45 patients, the number of joints affected was 1.7 on average per patient. The elbow, wrist, hand, knee and ankle joints were mostly involved. Except for the shoulder, the joints were more or less involved equally (Table 1). The ranges of motion measured were transformed into a score using a provisional scoring system for functional limitations. In 30% ($n = 23$) of our sample population ($n = 78$), we predicted one or more functional limitation(s) of the leg and in 21% ($n = 16$) we predicted one or more functional limitation(s) of the arm because of a reduced ROM. Functional limitation of the leg implies involvement of the ankle, knee or both joints. Involvement of the arm indicates that one or more of the following joints were affected: wrist, elbow or shoulder. If one or more finger joints of one hand were involved, these were scored as an affected hand (Table 1). Overall, we predicted one or more functional limitation in 49% ($n = 38$) of the retrieved population, based on a reduced ROM.

Of all patients with affected knees, the average score of functional limitations was 63%. In patients with affected ankles, the average score of functional limitations was

Table 1 Distribution of affected joints as seen in the retrieved population and their functional limitation*

Joint	Knee	Ankle	Shoulder	Elbow	Wrist	Hand†
Number affected ($n = 75$)‡	13	20	4	14	13	11
Number with functional limitation ($n = 65$)	13	16	0	13	12	11

* Functional limitation based on reduced range of motion.

† ≥ 1 finger joint(s) affected per hand.

‡ Number of affected joints in 45 patients.

78%; in those with elbow involvement, this was 76% on average, and in wrists involved, 65%. The shoulder joint appeared to be affected in four patients. However, this did not lead to functional limitations. The hand was scored 0 (no functional limitations present) to 1 (functional limitation present). All of the hands involved ($n = 11$) showed important functional limitation (Figure 1).

In a *post hoc* analysis, functional limitation scores of the patient were compared with disability in social life or discontinued education or professional activities (as a result of Buruli ulcer) as indicated by the patients themselves in the interview. The patients were divided into two groups: group A consisted of patients who admitted to have any of such problems ($n = 32$) and group B consisted of patients who denied such problems ($n = 42$). The total score of all functional limitations listed differed among the two groups, with group A scoring almost five times higher than group B [Mann-Whitney *U*-test; $P < 0.001$; score group A (mean): 7.3; score group B (mean): 1.5].

Of the 45 patients that were going to school at the time of acquiring Buruli ulcer, 10 indicated to have discontinued school as a result of Buruli ulcer. Another 10 indicated to have problems in school as a result of Buruli ulcer. Of 48 questioned patients with an occupation prior to infection,

14 had to discontinue their occupation as a result of Buruli ulcer. Another 20 said to have Buruli ulcer related problems in performing their work.

Discussion

This study identified and assessed functional limitations as a result of Buruli ulcer in Ghana. We developed a score to predict functional limitations caused by *M. ulcerans*.

Almost half of our study population (49%) had one or more functional limitation(s) based on our measurements of restrictions in the ROM; 30% ($n = 23$) in the leg and 21% ($n = 16$) in the arm. It was difficult to measure the ROM of the fingers accurately with the 20-cm goniometer. The required ROM of the ankle for squatting activities was not included in our scoring system, because of differences in methods of assessment in the literature. It was therefore not possible to score this activity.

The ranges of motion required for functional activities as reported in the literature were the basis of our scoring system (Appendix 1). The functional activities were selected because they were supposed to reflect relevant functional activities in daily life. Various scoring systems designed for assessing impairments, disabilities and handicaps have been proposed in literature but did not apply to Buruli ulcer. In 1980, the WHO published an International Classification of Impairments, Disabilities and Handicaps scoring-system, which was later adjusted and improved by the WHO and other organizations (Halbertsma *et al.* 2000). This scoring system consists of an extensive questionnaire of the ability to perform certain tasks and activities. We did not collect such extensive data.

The Eye/Hand/Feet-score (EHF-score), used as a scale to grade disability of leprosy (Thappa 1994) and to assess activities of daily living (ADL) in persons affected by leprosy (van Brakel *et al.* 1999), was not suitable for Buruli ulcer patients. The EHF-score system reflects anaesthesia and disfigurements (Thappa 1994). These impairments are not applicable to Buruli ulcer patients. The Escola Paulista de Medicina (EPM)-ROM scale evaluates 10 distinct movements and is based on movements and degrees of motion that are important in the performance of basic

Figure 1 Severe limitation in hand function of a 12-year-old boy with previously treated Buruli ulcer. Hand function limitation was scored as either present (1) or absent (0).

ADL. For patients affected by rheumatoid arthritis it has been proved to be a useful instrument in the evaluation of treatment (Vliet Vlieland *et al.* 1993). However, the EPM-ROM scale is not a suitable scale to score functional limitation as a result of Buruli ulcer because it reflects involvement of the whole body. But Buruli ulcer mostly affects one or more joints of only one extremity.

Most assessed activities as reported in the literature are based on studies performed in Western societies and therefore the activities may not be relevant in the African – cultures. In future studies it is therefore important to extend research of ROM to non-western cultures. In Asia and the Middle East, for instance, many activities are performed while squatting, kneeling, or sitting cross-legged. These positions demand a greater ROM than typically required in Western populations (Mulholland & Wyss 2001). As we have observed that squatting and kneeling activities are important in everyday life in Ghana, these activities were scored for the knee joint.

Although reviews and text books frequently mention that treated Buruli ulcer patients are left with important restrictions in ROM of affected joints, we are not aware of previous formal follow-up studies such as the present study, and a scoring system to quantify functional limitations has not been developed. In this study we showed that despite treatment the disease indeed leads to permanent functional limitations in almost half of the patients.

The impact of these functional limitations on well-being of patients would best be studied using a Quality of Life (QoL) scoring system using a questionnaire that is appropriate for African (Ghanaian) cultures. Yet no such questionnaire is available. We checked whether our scoring system, at least partly, corresponds with perceived functional limitations by the patient. Our scores were compared between patients who did and who did not perceive limitations as indicated in the interview. The total scores of functional limitations were about five times higher in the group of patients who did perceive limitations compared with the group who did not perceive functional limitations.

The decision to discontinue school or work could however, be confounded by fear, social stigma and financial problems (Stienstra *et al.* in press). Some patients were afraid to contract the disease again if they would resume work. Others indicated to be ashamed to attend school. One patient was told by his teacher to stay away from school. Other patients could simply not afford school fees after paying the high costs of treatment. However, difference in coping with functional limitations and expressing opinions and emotions could influence acknowledgement of problems in daily life. We observed patients who were apparently severely restricted in their

Figure 2 Although upper limb function appears clearly limited in this 18-year-old man, he denied having any limitations in every day activities resulting from previously treated Buruli ulcer.

ROM, but denied having any problems in daily life (Figure 2).

A limitation in our study is the limited proportion of the total number of patients identified in the hospital records included in the follow up. We are not able to correct a potential selection bias based on the sample size. Another limitation in our study is that we did not directly measure functional limitations, but predicted these from goniometric measurements. We realize that using a 20-cm long goniometer does not enable a very precise measurement of ROM. In future research adequate measuring instruments should be used to increase precision in the estimate of ROM. On the other hand, future studies could also have a simplified design by directly assessing functional activities such as squatting, walking, writing, eating, hoeing, using cutlasses, and possibly other relevant functional activities in daily life, adjusted for this predominantly rural and farming population studied. No such scoring system has been designed for Buruli ulcer before. We therefore propose a new scoring system, simplified in comparison with the scoring system we used. This proposed scoring system enables direct assessment of functional activities (Appendix

2), scoring the upper and lower limb both separately and together. Before applying the Buruli ulcer Functional Limitation Score (BUFLS) in follow-up studies, the functional activities as listed should be tested for relevance and actual performance in daily life. For instance, when young children are affected, the scoring needs to incorporate the predicted skills adjusted for age. Further, illiterates should not be scored for the use of a pen. Finally, the BUFLS needs to be tested for its psychometric properties.

The BUFLS is a simplified scoring system compared with the predicted score we used in the current study, which was based on measurements of limitations in ROM, and is therefore a more suitable and useful tool for direct assessment of functional limitations as a result of Buruli ulcer. It may be an appropriate tool to investigate and evaluate the impact of various interventions (such as physiotherapy, adjuvant antimicrobial therapy, and type, extent and timing of surgery) that potentially modify scarring and other sequelae that eventually impact on functional limitations. Timing of help seeking behaviour, immobilization of affected limbs and compliance with therapy may also impact on the final BUFLS. The proposed scoring system should be relevant to rural African populations, and imply activities of basic daily life, but also the capability to function as an active member in society: walking to school, caring for children, farming, and other vital activities.

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Appendix I The Buruli Ulcer Functional Limitation Score – range of motion based as used

Joint	Movement	Functional activity	Range of motion (ROM) required (degrees)	References
Knee	Extension/flexion	Walking	0-0-67	(Kettelkamp <i>et al.</i> 1970)
		Climbing stairs	0-0-83	(Laubenthal <i>et al.</i> 1972)
		Descending stairs	0-0-90	
		Sitting down on standard chair	0-0-93	
		Tying a shoe	0-0-106	
		Lifting an object	0-0-117	
		Squatting	0-111-165	(Mulholland <i>et al.</i> 2001)
		Kneeling	0-111-165	
		Ascending slope	0-2-65	(Rowe <i>et al.</i> 2000)
		Descending slope	0-3-72	
		Sitting on/standing up from low chair	0-8-105	
Ankle	Dorsiflexion/plantarflexion	Walking normal	10-0-15	(Murray & Clarkson 1966)
		Walking slow	14-0-15	(Stauffer <i>et al.</i> 1977)
		40 strides/min		
		Walking fast	13-0-6	
		60 strides/min		
Shoulder	Extension/flexion	Drinking from cup	0-16-43	(Safae-Rad <i>et al.</i> 1990)
		Eating with fork	0-11-19	
		Eating with spoon	0-8-36	
	Abduction/adduction	Drinking from cup	31-13-0	
		Eating with fork	19-7-0	
		Eating with spoon	22-7-0	
Elbow	Extension/flexion	Pouring from a pitcher	0-36-58	(Morrey <i>et al.</i> 1981)
		Cutting with a knife	0-89-107	
		Putting fork to mouth	0-85-128	
		Using a telephone	0-43-136	
		Reading a newspaper	0-78-104	
		Rising from a chair	0-20-95	
		Opening a door	0-24-57	
		Putting glass to mouth	0-45-130	
		Eating with a spoon	0-101-123	(Safae-Rad <i>et al.</i> 1990)
Wrist	Dorsiflexion/palmarflexion	Drinking from a cup	6-0-8	(Safae-Rad <i>et al.</i> 1990)
		Eating with a spoon	20-8-0	
		Cut with knife	20-0-4	(Brumfield & Champoux)
		Lift glass to mouth	24-11-0	
		Pour from pitcher	30-9-0	
		Lift fork to mouth	37-9-0	
		Use telephone	43-0-0	
		Read newspaper	35-2-0	
		Rise from chair	63-1-0	
		Hand to occiput (comb hair)	13-0	
		Hand to shoe (tie shoe laces)	0-14	
		Hand to chest (dressing)	0-19	
	Radial deviation/ulnar deviation	Drinking from a cup	0-8-16	(Safae-Rad <i>et al.</i> 1990)
		Eating with a fork	5-0-3	
		Eating with a spoon	4-0-4	

The number that precedes zero always means extension, dorsiflexion, abduction or radial deviation. Positions are recorded in contrast to motions with only two numbers.

Appendix 2 Buruli Ulcer Functional Limitation Score (BUFLS) as proposed for direct assessment of functional limitation

	Functional activity	Score		
		0†	1‡	2§
Upper extremity	Eating with hand			
	Cutting with a knife*			
	Using pen (writing/drawing)			
	Holding a cutlass*			
	Drinking from a cup			
	Dressing (putting on/tying shirt)*			
	Combing hair*			
	Pouring from a pitcher*			
Lower extremity	Walking fast			
	Walking slow			
	Squatting			
	Kneeling			
Both extremities	Lifting an object			
	Sitting down			
	Standing up			
	Using a cutlass*			
	Hoeing*			
Others				
Trunk	Bending			
Breast	Breast feeding a baby*			
Head (eye)	Sight			
Genitals	Fertility and sexual function*			

* Children younger than 6 years of age will not be scored for these activities.

† 0 points indicate no functional limitation when performing the activity.

‡ 1 point indicates functional limitation to a certain degree, but not full limitation.

§ 2 points indicate full functional limitation: no ability to perform the activity.