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## **Maggot debridement therapy in surgery**

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Chapter

3

**MDT and factors influencing  
outcome**



Based on the following article:

**Annals of the Royal College of Surgeons of England**

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*Maggot Debridement Therapy of infected ulcers: patient- and woundfactors influencing outcome. A study on 101 patients with 117 wounds. Ann of the Royal Coll of Surg England 2007; 89(6): 596-602.*

## Introduction

Despite antibiotic treatment and other measures many chronic ulcers do not heal. Infection and bacterial colonization is one of the factors delaying wound healing. Based on literature, there seem to be no clear indications or contra-indications for MDT, but patients with open wounds and ulcers that contain gangrenous or necrotic tissue with infection seem suited for MDT.<sup>88</sup> Success-rates of MDT, reported in literature, vary, but seem to be around 80 to 90%.<sup>55;89-90</sup> The present study discusses the observations of MDT in patients with complex and chronic wounds in whom major limb amputation or sepsis was the only alternative, if no MDT would be performed. In total, 101 patients with 117 wounds, seen in our surgical department, were treated. Patient characteristics, wound characteristics and treatment characteristics are described. Moreover, factors are identified that significantly influence MDT-outcome. On the basis of these factors, patient selection for MDT could be improved.

## Methods

### *Study characteristics*

**PATIENTS:** In the period August 2002 and December 2005, all patients who presented at the surgical department of the Rijnland Hospital, Leiderdorp, The Netherlands, with infected wounds with signs of gangrenous or necrotic tissue who seemed suitable for maggot debridement therapy (MDT), were asked whether they would enrol in a prospective case series study regarding MDT. All types of patients were included: patients from the dermatology department sent directly for this therapy, patients with infected diabetic feet, with arterial leg ulcers, with traumatic infected ulcers and with chronic wounds that would not heal despite treatment by the primary physician. Patients were excluded from the study if the treating surgeon believed an urgent amputation could not be postponed (for example in case of severe sepsis) or if life expectancy was shorter than a few weeks. Most patients had wounds of worst-case scenarios, for which the only alternative seemed to be amputation or surgical debridement (in theatre).

**PROTOCOL:** Standard protocol prescribed patients to be treated in the outpatient department. If patients were too sick or already admitted, treatment was preformed while admitted. All black dry necrotic tissue was removed prior to the therapy. All patients gave informed consent to be treated by MDT. Antibiotic treatment was not a contraindication for MDT. Indications for antibiotic therapy were based on those formulated by the international consensus on diagnosing and treating the infected diabetic foot. These indications are bone or joint infection, extensive cellulites (>2.0 cm) or systemic signs.<sup>91</sup> Antimicrobial therapy was always broad covering staphylococci, streptococci, gram-negative bacilli and anaerobic bacteria. When culture and sensitivity results were

available, more specific therapy was considered. According to literature antibiotic therapy does not influence the effects of maggots.<sup>92</sup>

**TECHNIQUE OF MAGGOT APPLICATION:** Patients would come to the clinic twice a week for maggot placement or maggot changes. Maggots arrive early in the morning and can be ordered until 24 hours before the clinic begins (BiologiQ™, Apeldoorn, the Netherlands). Every three to four days, new maggots were placed on the wound until thorough debridement was reached.

**OUTCOME:** We defined 8 different outcomes of MDT, based on outcome definition in the literature.<sup>55;88-90;93</sup> and experience with the technique:

Effect of MDT observed (beneficial outcome)

- Wound fully closed by second intervention (for example split skin graft);
- Wound spontaneous fully closed;
- Wound free from infection and  $<1/3$  of original wound size;
- Clean wound (free from infection/necrosis/slough), but same as initial size;

No effect of MDT observed (unsuccessful outcome)

- No difference observed between the pre- and post-MDT-treated wound;
- The wound is worse;
- Minor amputation (for example partial toe amputation);
- Major amputation (for example below knee amputation).

## Patient and wound characteristics

**PATIENT CHARACTERISTICS:** At presentation, the following patient characteristics were recorded: age, sex, weight, height, presence of diabetes mellitus, smoking behaviour, the presence of chronic limb ischemia and other relevant medical history.

Weight and height of the patient were used to calculate the patient's Body Mass Index (BMI), dividing weight (kg) by squared height (m). A BMI between 25 and 30 indicates that the person is overweight, while a BMI of 30 or more is classified as obesity.<sup>94</sup> A patient was recorded overweight accordingly. If a patient's height and weight at the time of MDT were lacking, the patient was scored as overweight if the treating surgeon and the nurse doing the actual maggot changes, thought so. Smoking behaviour was recorded as yes or no. A patient was recorded a non-smoker if non-smoking for more than three months. The diagnosis of lower chronic limb ischemia (CLI) was made if both pedal pulses of the involved foot were absent and/or the ankle-brachial pressure index was less than 0.6 and/or the absolute ankle pressure was below 50 mm Hg. Conservative wound healing usually takes place above the threshold of chronic critical limb ischemia. If the absolute systolic ankle pressure and/or the ankle-brachial index are below this threshold, foot pulses tend to be absent, the extremities are cold and wound pain is common. Wound healing in this group is difficult. The Second European Consensus<sup>74</sup> has outlined the following criteria for a diagnosis of chronic limb ischemia: recalcitrant rest pain or distal necrosis of more than 2 weeks' duration in the presence of (1) a systolic ankle pressure of 50 mm Hg or less, or (2) systolic toe pressure of 30 mm Hg or less, or (3) a transcutaneous oxygen pressure of 10 mm Hg or less. For patients with wounds above the ankle, these data were not recorded.

**WOUND CHARACTERISTICS:** The following characteristics related to the wounds were recorded: ulcer site, presence of chronic venous insufficiency, whether trauma was cause of the wound, whether a fracture accompanied the trauma, depth of the wound, presence

of septic arthritis and the presence of wound infection.

Chronic venous insufficiency was recorded on clinical grounds and standard treatment consisted of three or four layer compression treatment. Depth of the wound was recorded as following: superficial (containing only epidermal and dermal layers) or deep containing bone, joint or tendon. In case of infection near a joint, it was recorded whether there was a septic arthritis. A diagnosis of wound infection was made if there was purulent discharge and/or two local signs present (warmth, erythema, lymphangitis, lymphadenopathy, edema or pain).

**THERAPY CHARACTERISTICS:** Regarding the therapy, the following characteristics were recorded: the total number of maggots needed to reach the outcome, the number of maggot applications and whether or not the patient was admitted during the maggot therapy. Also the application-type was recorded.

## Statistical analysis

To find characteristics of patients or wounds that might predict beneficial outcome of MDT, univariate analyses using Chi-square and T-test statistics were performed. If characteristics were showing a statistical trend ( $p < 0.100$ ) in the univariate analyses, they were included in the multivariate statistics. Multivariate logistic stepwise regression was performed with the dichotomous outcome (good result vs. bad result) as the dependent variable and the selected patient-, wound-, and treatment characteristics as the independent variables. Results were considered statistically significant if p-values were below 0.05. For inclusion in the multivariate analysis, the worst wound of a patient (if a patient presented with more than one wound) was included. If patients had similar wounds at both sides, one was chosen. If then no choice of wounds had been made, wounds at the heel or infected below knee amputation wounds were selected.

## Results

### Patient characteristics

From august 2002 until 31 December 2005, 101 patients with 117 wounds were treated with MDT in our hospital. During this period, 1 patient presented with 4 wounds in total (1.0%), 1 patient with 3 wounds (1.0%), 11 patients with 2 wounds (10.9%) and 88 patients with 1 wound each (87.1%). The patient group consisted of 56 men (55.4%) and 45 women (**Table 1**). Their average age was 71.0 years (range: 25-93 years, standard deviation (SD): 14.6 years). Forty-one patients (40.6%) were treated while admitted. Within the study period, 24 patients (23.8%) died. None of the patients died because of postponed amputation or from sepsis occurring at the wound site. One of these patients died during the actual MDT, although this death was not related to the therapy or wound. The patients who died were significantly more often classified in ASA class III or IV at study entry (91.7% vs. 64.9%,  $P = 0.023$ ), and suffered more often from diabetes mellitus (70.8% vs. 37.7%,  $P = 0.009$ ) than the other patients (81.8% versus 43.4%;  $p = 0.047$ ). Moreover, the patients who died seemed somewhat older than the other patients (75.4 years, SD: 12.0; vs. 69.6 years, SD: 15.1;  $P = 0.086$ ). There were two male diabetic patients treated with chronic wounds of the lower extremity who were on dialysis. Both diabetic patients unfortunately required a major amputation. Lower limb amputation in diabetics on dialysis is 14%. The proportion of patients requiring amputation on dialysis is approximately 4% per year.<sup>95</sup>

## Wound characteristics

Most wounds (N=110; 94.0%) were lower extremity wounds, of which most were located on the lower leg (N=35; 29.9%) and heel (N=30; 25.6%) (**Table 2**). The wounds existed on average for 7.2 months before starting with MDT (range 1 week-11 years; SD: 16.1 month). In 56.4% of the wounds (N=66), tendon, muscle or bone was visible.

## Therapy characteristics

On average, 2.4 maggot applications (range: 1-11) were used on the wounds, with one (N=43) or two (N=35) applications as the most frequent (**Table 2**). As one application remains 3 or 4 days on the wound, the treatment ended for most patients within or after one week. In total, 21,740 maggots were used to treat the 117 wounds, indicating an average of 186 maggots per wound (range 20-780).

## Therapy results

In this study we defined 8 different outcomes. Of the 117 wounds treated with MDT, for 116 an outcome could be determined: 78 wounds (67.2%) had beneficial outcomes and 38 wounds (32.8%) had unsuccessful outcomes (**Table 3**). MDT resulted in complete debridement and epithelialization in 37 of the 116 wounds (31.6%), it resulted in complete debridement and closure by secondary intervention in 23 wounds (19.7%), in 12 wounds (10.3%) the wound was free from infection and the wound size was less than one third of the initial wound size, and in 6 wounds (5.1%) the wound was free from infection, necrosis and slough, but remained its initial size.

## Factors influencing outcome

All wounds caused by trauma had beneficial outcomes (N=24). All wounds in which there was a septic arthritis, had unsuccessful outcomes (N=13), as the entire joint including a part of the proximal adjacent bone had to be amputated (N=8/9; **Table 2**). These two characteristics are therefore very important as predictors of MDT outcome. The univariate analyses revealed the following characteristics that had a negative impact on successful outcomes of MDT treatment (**Tables 1 and 2**): older age ( $P$ -value=0.033), chronic limb ischemia ( $P<0.001$ ), non-traumatic origin of the wound ( $P<0.001$ ), a duration of the wound of 3 months or more prior to MDT ( $P<0.001$ ), a deep wound ( $P<0.001$ ), and septic arthritis ( $P<0.001$ ). Furthermore, the presence of diabetes mellitus ( $P=0.066$ ) and clinical instead of outpatient treatment ( $P=0.096$ ) showed a trend significance. The use of a biobag had a significant negative impact on successful outcome in the univariate analysis. ( $p=0.01$ )

The multivariate analysis showed that three characteristics additional to non-traumatic origin of the wound and the presence of septic arthritis, had predictive value for MDT outcome. An age of 60 years and older (Odds Ratio (OR): 7.3; 95% Confidence Interval (95% CI): 1.3-40.0), chronic limb ischemia (OR: 7.5; 95% CI: 1.8-31.1), and a wound with visible tendon, muscle or bone (OR: 14.0; 95% CI: 2.8-70.4) negatively influenced good outcome of MDT. These characteristics were adjusted for the other characteristics in the model.

**Table 1:** Characteristics of patients treated with maggot debridement therapy (N=101).

Characteristics*		Total	Good Result	Bad Result	P-value†
Number of patients		101 (100)	69 (69.0)	31 (31.0)	
Age (yrs)	Mean (SD)	71.0 (14.6)	69.6 (15.9)	74.1 (11.0)	
	< 60	21 (20.8)	19 (27.5)	2 (6.5)	0.033
	≥ 60	80 (79.2)	50 (72.5)	29 (93.5)	
Gender	Male	56 (55.4)	37 (53.6)	19 (61.3)	
	Female	45 (44.6)	32 (46.4)	12 (38.7)	
Quetelet Index	≤ 25	62 (61.4)	46 (66.7)	16 (51.6)	
	> 25	39 (38.6)	23 (33.3)	15 (48.4)	
Diabetes Mellitus	No	55 (54.5)	42 (60.9)	12 (38.7)	0.066 (trend)
	Yes	46 (45.5)	27 (39.1)	19 (61.3)	
Current Smoker	No	66 (65.3)	46 (66.7)	19 (61.3)	
	Yes	35 (34.7)	23 (33.3)	12 (38.7)	
Chronic limb ischemia	No	48 (47.5)	44 (63.8)	3 (9.7)	<0.001
	Yes	53 (52.5)	25 (36.2)	28 (90.3)	
Outpatient treatment	No	41 (40.6)	24 (34.8)	17 (54.8)	0.096 (trend)
	Yes	60 (59.4)	45 (65.2)	14 (45.2)	
ASA-class	I	5 (5.0)	5 (7.2)	0 (0.0)	
	II	24 (23.8)	18 (26.1)	6 (19.4)	
	III	48 (47.5)	33 (47.8)	14 (45.2)	
	IV	24 (23.8)	13 (18.8)	11 (35.5)	
Deceased	No	77 (76.2)	14 (20.3)	9 (29.0)	
	Yes	24 (23.8)	55 (79.7)	22 (71.0)	

\*: characteristics are displayed in N(%), unless otherwise specified.

†: Univariate results



**Table 2:** Wound and treatment characteristics (N=117) of 101 patients treated with maggot debridement therapy.

Wound characteristics*		Total	Good Result <sup>£</sup>	Bad Result <sup>£</sup>	P-value <sup>\$</sup>
Number of wounds		117 (100)	78 (67.2)	38 (32.8)	
Traumatic origin	No	92 (78.6)	54 (69.2)	38 (100.0)	<0.001
	Yes	25 (21.4)	24 (30.8)	0 (0.0)	
Location	Too	9 (7.7)	5 (6.4)	4 (10.5)	0.030
	Foot	27 (23.1)	16 (20.5)	11 (28.9)	
	Heel	30 (25.6)	19 (24.4)	11 (28.9)	
	Lower leg	35 (29.9)	29 (37.2)	5 (13.2)	
	BKA <sup>†</sup>	9 (7.7)	3 (3.8)	6 (15.8)	
	Other	7 (6.0)	6 (7.7)	1 (2.6)	
Duration (months)	Mean (SD)	7.2 (16.1)	8.2 (19.4)	5.4 (5.0)	
	< 3	48 (41.0)	41 (52.6)	6 (15.8)	<0.001
	≥ 3	69 (59.0)	37 (47.4)	32 (84.2)	
Depth	Superficial	51 (43.6)	47 (60.3)	4 (10.5)	<0.001
	Deep <sup>‡</sup>	66 (56.4)	31 (39.7)	34 (89.5)	
Septic arthritis	No	104 (88.9)	78 (100.0)	25 (65.8)	<0.001
	Yes	13 (11.1)	0 (0.0)	13 (34.2)	
Wound diameter >2cm	No	28 (23.9)	60 (76.9)	29 (74.4)	
	Yes	89 (76.1)	18 (23.1)	10 (25.6)	
Biobag application	No	58 (49.6)	46 (59.0)	12 (31.6)	0.010
	Yes	59 (50.4)	32 (41.0)	26 (68.4)	
Outpatient	No	48 (41.0)	28 (35.9)	20 (52.6)	
	Yes	69 (59.0)	50 (64.1)	18 (47.4)	
Number of treatments	Mean (SD)	2.4 (1.8)	2.4 (1.9)	2.4 (1.6)	
	< 3	75 (64.1)	48 (61.5)	26 (68.4)	
	≥ 3	42 (35.9)	30 (38.5)	12 (31.6)	
Total maggots	Mean (SD)	185.8 (135.3)	179.7 (143.9)	200.5 (117.6)	
Maggots per treatment	Mean (SD)	85.1 (48.3)	79.8 (44.6)	95.6 (54.6)	

\*: all characteristics are displayed in N(%), unless otherwise specified.

£: One patient died before the wound could be checked; therefore a result could only be given for 116 wounds.

\$: Univariate results

†: BKA= below knee amputation

‡: Deep: visible tendon, bone or muscle

**Table 3:** Results of MDT in 101 patients with 117 wounds<sup>†</sup>.

	First wounds* (N=100 <sup>†</sup> )	All wounds (N=116 <sup>†</sup> )
	N (%)	N (%)
<b>Good outcome</b>		
1. Wound fully closed by second intervention (for example split skin graft)	23 (22.8)	23 (19.7)
2. Wound spontaneous fully closed	30 (29.7)	37 (31.6)
3. Wound free from infection and <1/3 of original wound size	11 (10.9)	12 (10.3)
4. Clean wound (free from infection/necrosis/slough), but same as initial size	5 (5.0)	6 (5.1)
<b>Bad outcome</b>		
5. There is no difference between before and after MDT	3 (3.0)	5 (4.3)
6. The wound is worse	1 (1.0)	1 (0.9)
7. Minor amputation (for example toe)	5 (5.0)	5 (4.3)
8. Major amputation (below knee amputation or above knee amputation)	22 (21.8)	27 (23.1)

†: One patient died before the wound could be checked; therefore no result could be given.

\*: First wounds are the wounds for which the patients were included in the study.

## Discussion

In this study we described the results of Maggot Debridement Therapy (MDT) in 101 patients with 117 wounds in total. Of the 117 wounds treated, 78 (67.2%) had beneficial outcomes and 38 (32.8%) had unsuccessful outcomes. It is very difficult to determine meaningful outcomes of MDT. It is even more difficult to compare MDT-results with results of other studies. In this study outcomes were not defined as wound scores<sup>96</sup>, but outcomes were based on an intention to salvage limbs. Church and Courtenay suggested the following outcomes for MDT: complete, temporarily complete, relatively complete, significantly beneficial, partially beneficial, economical and failed.<sup>88</sup> These categories are somewhat misleading. A patient for example, that unfortunately, dies before complete wound healing falls in their category failed, but could in our study be placed in outcome category 3.

Wolff et al. reported successful debridement (66-100% of necrosis and slough removed) in 59/74 patients (79%). Their wounds were of mixed aetiology, with 51% arterial leg ulcers, 39% diabetes and 14% venous leg ulcers.<sup>89</sup> According to their definition our categories 1-4 would be defined as successful debridement. Courtenay et al.<sup>90</sup> reported their results of 70 MDT treated patients. Most wounds were leg ulcers.

Arterial insufficiency 22% and diabetes 16% were the mean etiologic factors. In total 50 wounds were fully or partially debrided (85%), 8 remained unchanged (14%) and 1 (2%) showed progression during the therapy. Mumcuoglu et al. reported their results on twenty-five patients suffering mostly from chronic leg ulcers and pressure sores in the lower sacral area. Underlying diseases were mainly venous ulcers (48%) and paraplegia (20%). Complete debridement was achieved in 38 wounds (88.4%).<sup>55</sup> Given the problems with defining outcome and trying to compare patient-groups with mixed aetiology: MDT seems to benefit the patient in about 70-80% of the cases, which is the case in our study.

Of the 117 wounds treated with MDT, 78 (67%) had beneficial outcomes and 38 (33%) had unsuccessful outcomes (**Table 3**). Some of these wounds, however, were treated with MDT not to prevent a minor amputation, but to prevent a major amputation. Thus for some wounds, the unsuccessful outcome (7= minor amputation) was the only possible outcome (N=4). This unsuccessful outcome may be the best possible outcome, if a patient, for example, presents with a severe osteomyelitis of the toe. MDT is then initiated, and maggots can resolve all necrotic tissue, slough and bacteria, but they are unable to remove infected bone or tendon. This removal needs to be done surgically, thus through amputation of the toe. In such cases, minor amputation may be considered a successful outcome as major amputation has been prevented.

All wounds with a traumatic origin (N=24) healed completely. All wounds with septic arthritis (N=13) failed to heal and led to a unsuccessful outcome. Optimal maggot feeding can only occur when the maggot spiracles are exposed to air, therefore deep joint infections can't be treated with MDT. All septic joint infections described in this study, where small joints (most Metatarsal joints), this factor might therefore be an explanation of these failures. According to a multivariate analysis, wound duration before MDT treatment longer than three months, chronic limb ischemia, and septic arthritis negatively influenced successful outcome of MDT. Previous research showed that ischemia at presentation of diabetic ulcers significantly predicts healing rate.<sup>97</sup>

Outcome was not negatively influenced by sex, diabetes mellitus, smoking, location of the wound, wound size or overweightness. In literature, wound healing seems to be negatively influenced by age<sup>98</sup>, as we also showed in this study. Sex had no effect on the outcome of ulcers, which was comparable to other studies.<sup>97</sup> Ulcer size was a significant predictor in a study on 194 diabetic ulcers for amputation: ulcer size in the healed ulcer group was 1.1 (0.5-2.6) cm<sup>2</sup> and 3.9 (1.4-5.4) cm<sup>2</sup> in the amputation group.<sup>97</sup> In the study of Oyibo et al. the largest ulcers were the deepest and most infected, and were possible confounding factors. In our study, in which 45% of patients were diabetic, ulcer size was defined as smaller or equal to 2 cm in largest diameter or larger than 2 cm. We did not find any association between ulcer size and maggot therapy success. Increasing depth was found to be a major predictor of unsuccessful outcome. In an earlier published study we found that the contained technique significantly reduces its effectivity, which was also the case in this larger series. However in a multi-variate analysis this effect could not be shown.

In conclusion, 78 of 116 wounds (67%) had a successful outcome, of which 53 healed completely and 11 healed almost completely. These results seem to be in line with literature. All wounds with a traumatic origin (N=24) healed completely, whereas all wounds with septic arthritis (N=13) failed to heal. According to a multivariate analysis, chronic limb ischemia (OR: 7.5), the depth of the wound (OR: 14.0), and an age of 60 years or older (OR: 7.3) negatively influenced outcome. Outcome was not influenced by sex, quetelet index, diabetes mellitus, smoking, ASA-classification at presentation,

location of the wound, wound size or wound duration. By carefully selecting patients for MDT could increase MDT-outcomes. This could lead to a reduction in overall-costs, in an improved acceptance of the therapy. Maybe even more importantly, this study seems to be the basis for a randomized study, for patient- treatment and wound-factors influencing outcome are now known.

