

The effect of adjuvant oxygen therapy on transcutaneous pO₂ and healing in the below-knee amputee

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Abstract

The effects on tissue oxygenation of post-operative adjuvant oxygen have been studied in a group of 20 patients undergoing below-knee (BK) amputation for vascular disease. Ten patients received no therapy, the remainder receiving 28% oxygen for 48 hours following surgery. The results showed that the transcutaneous pO₂ in the amputation flaps fell significantly by some 20 mmHg ($p < 0.01$) following surgery and that this fall was prevented by the use of adjuvant oxygen. The fall was not observed in the non-amputated limbs. TcpO₂ took almost two weeks to reach its pre-operative levels in the amputated limbs.

The effect on stump healing of adjuvant oxygen therapy was investigated in a randomized controlled trial in a series of 39 patients undergoing BK amputation. There were 22 patients in the control (untreated) group and 17 in the treated group (adjuvant oxygen for 48 hours). In the treated group 14 patients healed primarily and three amputations failed. In the untreated group 14 limbs healed primarily, one secondarily and there were 7 failures. The pre-operative transcutaneous values in the stumps which failed (26 mmHg \pm 14) was significantly lower ($p < 0.005$) than in those which healed (40 mmHg \pm 9). The mean pre-operative TcpO₂ in the patients in whom healing occurred in the treated group (35 mmHg \pm 10) was significantly lower ($p < 0.001$) than the mean pressure observed in the untreated group (44 mmHg \pm 9).

Introduction

Despite the many advances which have been made in the early diagnosis of arterial disease

and in vascular reconstructive procedures, amputation of the limb remains the final outcome for many patients. As the anticipated life span of these amputees is relatively short (Finch et al, 1980), rapid and effective rehabilitation is essential. It is now widely agreed that a below-knee (BK) amputation gives the vascular amputee the best chance of independent mobility on a prosthesis (Jamieson and Hill, 1976). However, a failure rate of 15-20% leads some surgeons to opt for the more likely healing of an above-knee (AK) amputation in patients with ischaemia despite the higher mortality and less satisfactory rehabilitation (Finch et al, 1980; Jamieson and Hill, 1976). The latest available figures for England and Wales show an overall ratio of 55% above to 45% below-knee amputation if other levels are excluded (McColl, 1986) and although these figures show a trend towards more BK amputations there is still some way to go to achieve the much higher BK rates reported by some centres (Lim et al, 1967; Ham et al, 1987).

In recent years there have been many reports of methods designed to help the surgeon pre-operatively to predict the likely healing of amputation stumps. Doppler ultrasonic assessment of segmental pressure (Pollock and Ernst, 1980; Lepentalo et al, 1982; Cederberg et al, 1983), thermography (Spence et al, 1981), measurement of skin blood flow (Moore et al, 1981) and pressure (Holstein et al, 1979; Spence and Walker, 1984) have all been found to be of some value. More recently, with the advent of the skin oxygen electrode, transcutaneous pO₂ (TcpO₂) has been suggested as a more reliable indicator of the potential for healing (Franzeck et al, 1982; Burgess et al, 1982; Mustapha et al, 1983; Ratcliff et al, 1984; Katsamouris et al, 1984; Harward et al, 1985; McCollum et al, 1986).

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In fields unrelated to vascular amputation, a number of animal and human studies have shown that increasing inspired oxygen concentration results in increased available tissue oxygen and that this may be of benefit in reducing wound infection and improving tissue healing (Hunt and Pai, 1972; Knighton et al, 1984; Chang et al, 1983). Mustapha and colleagues have reported that increasing inspired oxygen concentration results in an increase in below-knee $TcpO_2$ in patients with ischaemic limbs (Mustapha et al, 1984), though they have not reported on its effect on healing.

This present study was designed firstly to investigate the effects of amputation surgery on stump $TcpO_2$ and to test the hypothesis that increasing inspired oxygen concentration could beneficially increase stump transcutaneous oxygen levels and secondly, to assess prospectively the value of post-operative adjuvant oxygen therapy in relation to stump survival.

Patients and methods

The study was in two parts. The first, involving 20 patients undergoing BK amputation, was aimed at gaining an understanding of the effects of adjuvant oxygen and amputation surgery on the transcutaneous oxygen levels in below-knee stumps. The second, involving 39 patients undergoing BK amputation, was aimed at evaluating the effects on healing of post-operative adjuvant oxygen therapy. All patients admitted consecutively to the vascular unit of Dulwich Hospital and requiring major amputation for ischaemia were considered for entry. The only criteria for exclusion were visible ischaemic demarcation above a suitable level for below-knee amputation or severe disease of the ipsilateral knee joint precluding satisfactory prosthetic fitting. All remaining patients were entered sequentially into the study. These patients underwent skew-flap myoplastic below-knee amputation after identical pre-operative ward preparation and antibiotic prophylaxis using the regime and operative techniques described by Robinson et al (1982).

Skin oxygen study

The first 20 patients entering the study were allocated using a restricted randomization into either treated or untreated groups. The

operations were performed alternately by one of two surgeons only (CB or KL). The treated group ($n=10$) received 28% adjuvant oxygen by Ventimask (Vickers Medical) for 48 hours post-operatively at a rate of 4 litres per minute. The untreated group ($n=10$) received nothing. Only light gauze dressings were used and conventional stump bandaging or plaster were not used.

Transcutaneous pO_2 ($TcpO_2$) measurements were made independently (RH) and the results not examined until the end of the study. A Roche cutaneous pO_2 monitor (Kontron Medical) containing two 632 modules, enabling simultaneous recording at two sites, was used throughout. Electrode positions were at a central site 5cm below the clavicle and at anterior and posterior sites 10cm below the knee at the centre of the amputation flaps on the stump and 5cm medial to the tibial shaft and at the same level on the contralateral limb. The measurements were made in each case on the day prior to operation and at 1, 2, 7 and 14 days post-operatively. The measurement on the second post-operative day was made at least two hours after stopping oxygen therapy.

All readings were made with the patient semi-supine having been resting in bed for at least 20 minutes. Sensor temperature was $44^\circ C$ and the calibration of the modules and derivation of $TcpO_2$ was described by Ratliff et al (1984). All patients had regular physiotherapy, early ambulation using the P.P.A.M.-Aid (Vessa Ltd.) and were measured for their artificial limb in the early post-operative period on the ward by a team from the Department of Health and Social Security (DHSS) limb fitting centre at Roehampton.

Healing study

In this study 39 patients selected as above for BK amputation were entered consecutively into a randomized controlled trial of the effects on healing of post-operative adjuvant oxygen therapy. Using this randomization 17 patients fell in the treated group and 22 in the untreated group. Patient treatment was as for the previous study, the treated group receiving the adjuvant oxygen and the untreated group no additional therapy. Healing was independently assessed as 'primary', 'secondary' when partial or complete breakdown of the stump occurred with subsequent satisfactory healing, or 'failed' when

a proximal reamputation was necessary to achieve healing. Patients were followed up for at least one year following amputation. The composition of the two groups is shown in Table 1.

Results

The results from the study of transcutaneous oxygen have been assessed using the Student-t test and those for the healing study using the Chi² test with Yates' correction.

There was no morbidity associated with the use of adjuvant oxygen and the patients and ward staff were able to manage the Ventimasks without problems.

The heated TcpO₂ electrode usually produced a spot of erythema, but no significant skin damage.

Table 1. Composition of groups

	Treated Group	Untreated Group
Men (mean age)	11 (71)	13 (65)
Women (mean age)	6 (72)	9 (68)
Insulin dependent diabetic	4	6
Previous vascular surgery	7	7
Paravertebral block	6	7
Previous amputation (contralateral)	2	5
Mean pre-op TcpO ₂	33 (±10)	39 (±14)

Skin oxygen

The results of the transcutaneous oxygen study are illustrated in Figure 1. The top figure shows the TcpO₂ levels for the treated group and the bottom one the untreated group. The hatched bar indicates the duration of therapy. Each point indicates the mean value of each set of ten readings, and the vertical bars indicate one SD. For clarity, levels for the posterior flap have not been shown. They followed the anterior flap figures, usually at a slightly higher level.

In the treated group there was significant ($p < 0.01$) fall in TcpO₂ of the anterior flap at day 2, following cessation of adjuvant O₂ compared with pre-operatively (Fig. 1, top). This fall occurred immediately in the untreated group (Fig. 1, bottom) and a significant ($p < 0.01$) difference existed between anterior flap TcpO₂ at day 1 between the groups. The oxygen levels in both untreated amputated limbs returned to their pre-operative levels by day 14.

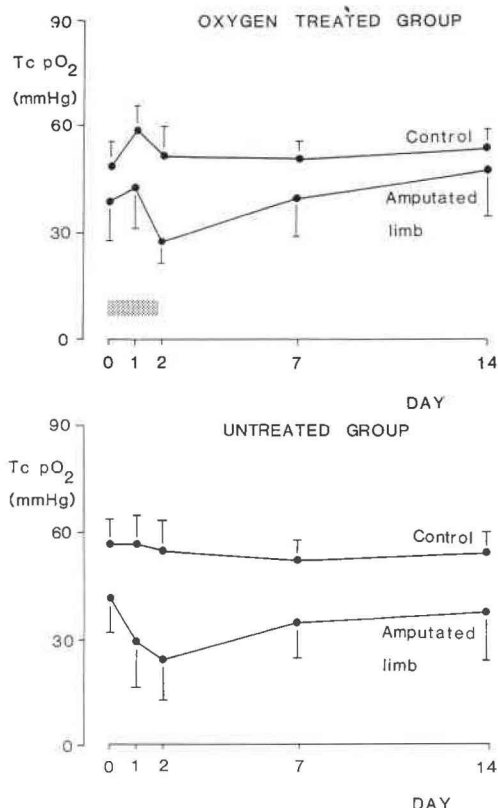


Fig. 1. Top, mean TcpO₂ levels for the oxygen treated group in patients whose stumps healed (n=9). The hatched bar indicates the duration of therapy. Bottom, mean TcpO₂ levels for the untreated group in patients whose stumps healed (n=7). Vertical bars show one standard deviation in both illustrations.

Stump healing

The results of the study into stump healing are indicated in Table 2. In the treated group (n=17) one of the patients who failed appeared to be healing secondarily after a small area of flap necrosis developed. However, considerable deterioration in the stump at two months post operation necessitated conversion to the above-knee level. Two deaths occurred in this group, one of which occurred three days after amputation and the other seven months post amputation of myocardial infarction.

In the untreated group (n=22) one patient had a partial stump breakdown which

Table 2. Effects of treatment on healing

	1° Heal	2° Heal	Failed	Early Death	Late Death
Treated	14	0	2	1	1
Untreated	14	1	4	5	1

subsequently healed and four required proximal reamputation, two at one week, one at two weeks and one at four weeks. Five of the six deaths in the group occurred within a month of surgery. The late death occurred at eight months due to myocardial infarction. Although the mortality in the untreated group was higher than in the treated group, the difference was not significant.

Although overall healing rates appeared better in the treated (oxygen) group (Table 2), the numbers are too small to achieve statistical significance. However, when the pre-operative $TcpO_2$ levels are examined, the results are more revealing. If the two groups are taken as a whole, regardless of post-operative therapy, the mean pre-operative value of $TcpO_2$ in the successful cases ($40 \text{ mmHg} \pm 11$) was significantly higher ($p < 0.005$) than that observed in the failure cases ($26 \text{ mmHg} \pm 14$). Similarly, in both the treated and untreated groups, the $TcpO_2$ values in the failure cases were significantly ($p < 0.005$) lower than the mean values for the successful cases. That is to say low tissue oxygen is more likely to lead to failure.

Furthermore, the pre-operative $TcpO_2$ levels of the successful cases in the treated group ($35 \text{ mmHg} \pm 10$) was significantly lower ($p < 0.001$) than the corresponding value in the untreated group ($44 \text{ mmHg} \pm 9$). Also, the mean value of $TcpO_2$ in the untreated failures ($27 \text{ mmHg} \pm 3$) did not differ significantly from the mean value in the treated patients who healed ($35 \text{ mmHg} \pm 10$). In other words, adjuvant oxygen increased the likelihood of healing in patients with a low pre-operative transcutaneous oxygen. There was no significant difference between the pre-operative $TcpO_2$ levels in the treated or untreated groups taken as a whole, nor was the $TcpO_2$ value in the treated (failure) group ($23 \text{ mmHg} \pm 3$) significantly lower than the corresponding value in the untreated group ($27 \text{ mmHg} \pm 17$).

In Table 3 are shown the distribution of successful and unsuccessful amputations as a function of three bands of pre-operative $TcpO_2$. This table shows the pattern of the effect of adjuvant oxygen. However the numbers in each group are insufficient to achieve statistical significance.

All of the surviving patients in this study have been discharged mobile with a prosthesis with the exception of six patients who were

Table 3. Distribution of $TcpO_2$ levels

$TcpO_2$ (mmHg)	Failure		Success	
	Untreated	Treated	Untreated	Treated
0-19	3	0	0	1
20-39	2	3	5	9
40-	2	0	10	4

discharged fully rehabilitated in wheelchairs, four in the untreated group and two in the treated group. The mean time from operation to discharge was 43.5 days with a range of 16-132 days. There was no significant difference in length of hospital stay between the groups, the mean for the treated group being 46 days and the untreated group 42 days.

Discussion

The effects of tissue oxygen on wound healing have been appreciated for many years. For example, it is known that in mountain dwelling peoples wounds heal better in the valleys than in the rarefied mountain air and a similar effect has been observed in divers when wounds healed more quickly during prolonged spells under water (Hunt and Pai, 1972).

It is possible to measure oxygen tensions directly in wounds and the work of Hunt and colleagues using experimental wounds in animals has shown that oxygen supply is usually below the optimum for collagen synthesis and that some of the processes of wound repair benefited from increased inspired oxygen tension (Hunt and Pai, 1972). Kirk and Irvin (1977), however, were unable to demonstrate any benefit of oxygen therapy in experimental skin wounds or colonic anastomoses in rats, and concluded that further studies would be necessary to determine benefit.

More recently Chang and his colleagues (1983) have reported a study in patients in whom tissue oxygen was measured using an implanted silastic catheter. They showed tissue hypoxia to be common and most severe in the immediate post-operative period. They also showed that increasing inspired oxygen resulted in an increase in tissue oxygen levels. Additionally, Knighton et al (1984) have reported that increased inspired oxygen levels significantly inhibit experimentally induced infections in animals.

In the vascular amputee the precarious and variable blood supply to the ischaemic limb complicates the study of wound oxygenation and healing. Strictly $TcpO_2$ values do not

measure skin oxygen, which varies from the PaO_2 of capillary blood to zero at the epidermis. With the probe used here at 44°C , the values of TcpO_2 can reasonably be taken to reflect capillary oxygen levels. The results of the first study have highlighted the profound fall in TcpO_2 which occurs in the amputated limb following surgery. The results also show how this fall can be prevented by the use of adjuvant oxygen therapy. The exact mechanism behind this fall in TcpO_2 is not well understood and needs further investigation. Another study currently being conducted within the authors' department (Fairs et al, 1986) has shown that skin blood flow in an amputation stump, measured with a laser Doppler flowmeter, rises immediately following surgery, thereafter falling to a stable baseline as healing progresses. It is attractive to argue from this evidence that such a simple treatment as adjuvant oxygen would be an aid to healing in such patients (Mustapha et al, 1983) since it would potentiate an already elevated skin perfusion. However, no rationale has been established for an optimum treatment regime. The choice of 48 hours therapy was based on convenience rather than on any scientific basis, but nevertheless, it appears from these present studies that adjuvant oxygen therapy does affect the operative outcome.

Although significant increases in healing rates with adjuvant therapy have not been demonstrated, the authors have been encouraged by the significantly lower levels of pre-operative TcpO_2 at which healing can be achieved with the help of adjuvant oxygen. Furthermore, it seems likely that with larger numbers the authors would also be able to demonstrate that the TcpO_2 in the oxygen-treated failures was significantly lower than in the untreated failures. This must await further studies. It might be argued that "force healing" by the use of adjuvant oxygen merely delays the breakdown of wounds for a month or so. However the long term follow-up has shown no evidence of this. The fall observed in TcpO_2 after stopping oxygen might suggest a rational basis for continuing therapy for longer than 48 hours, although difficulties will inevitably occur in maintaining continuous therapy as patients become more mobile.

It might reasonably have been expected that if oxygen therapy improved healing the time to

discharge in the treated group would be less than that in the untreated group. That it was not is however more a reflection of the other factors which determine discharge times (such as the delay between measuring and fitting the prosthesis, the completion of home modifications etc). In any event the discharge times achieved during this study were less than the average of 51 days which is typical for the District (Ham et al, 1987). It is anticipated that with more extensive use of oxygen therapy and with a resident prosthetist significantly shorter rehabilitation times might be achieved.

Many reports have appeared on the use of the TcpO_2 monitor (Ratcliff et al, 1984; Mustapha et al, 1983; Dowd et al, 1983; Spence and Walker, 1984; Dowd, 1986). The principle of the technique has been described elsewhere (Simpson and Bryan, 1982) and, although debate continues as to the exact physiological significance and accuracy of TcpO_2 measurement in ischaemic limbs (Spence and Walker, 1984), most authors agree that it is of value as an indicator of skin oxygenation. In the authors' series no additional useful information was obtained by measurement at both anterior and posterior sites. A central measurement is probably useful to exclude significant central hypoxia and the results agree with the findings of Mustapha and his colleagues (1983) that no additional information can be gained by examining the chest to below knee ratio.

Most of the published reports on the prognostic value of pre-operative TcpO_2 monitoring have included patients with amputations at different levels and more importantly performed by many different surgeons using a variety of methods. This makes the results difficult to interpret. The present trial, although of small numbers, was carefully designed to try to keep the treatment of each patient as identical as possible. The authors were satisfied to achieve an overall healing rate of 83% for all the below-knee amputations. This is as good as published series where much more rigorous criteria for exclusion were used. The authors now believe that there can be little expectation of healing of below-knee amputations below a TcpO_2 level of 20 mmHg at the anterior 10cm below knee level. Other authors (Harward et al, 1985) have suggested levels as low as 10 mmHg to indicate potential success. Others specify 30 mmHg or higher (Ito

et al, 1984). These differences appear difficult to reconcile. However, they may be more a reflection of the performance of the instrumentation used than of the tissue oxygen levels (Spence et al, 1985), and each centre must in the end adopt the level which it finds appropriate for its own patients and instrumentation.

It is wrong to assume that a single pre-operative level of $TcpO_2$ will predict success in every case and that adequate tissue oxygenation is the only requirement for a successful amputation. Some would argue that a better identification of potential success or failure can be achieved by measurements following some circulatory provocation such as exercise or oxygen inhalation (Harward et al, 1985; McCollum et al, 1986). This has not yet been the authors' experience. There is no doubt that success in amputation surgery and rehabilitation depends primarily on the interest shown in the individual patient, the use of careful operative technique and enthusiastic post-operative care (Malone et al, 1981). However, the authors believe that this study, where the above criteria have been closely followed, has shown that pre-operative $TcpO_2$ at an anterior below-knee site is a useful prognostic indicator.

A strong move to below-knee amputation has resulted in an overall success ratio of below-knee to above-knee amputations of nearly 70% compared with 30% in previous years in this Unit with similar patients (Ham et al, 1987). It is expected that use of adjuvant oxygen therapy will further increase this success rate.

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