Original Papers

Necrotising soft tissue infections: the effect of hyperbaric oxygen on mortality

B. Devaney*, G. Frawley†, L. Frawley‡, D. V. Pilcher§

Summary

In a single-centre, retrospective, case-controlled study of patients attending the Alfred Hospital in Prahran, Victoria, we assessed the effect of hyperbaric oxygen therapy (HBOT) in reducing mortality or morbidity in patients with necrotising fasciitis (NF) over a 13-year period from 2002 to 2014. A total of three hundred and forty-one patients with NF were included in the study, of whom 275 received HBOT and 66 did not. The most commonly involved sites were the perineum (33.7%), lower limb (29.9%) and trunk (18.2%). The commonest predisposing factor was diabetes mellitus (34.8%). Polymicrobial NF (type 1 NF) occurred in 50.7% and Group A streptococcal fasciitis (type 2 NF) occurred in 25.8% of patients. Mortality was 14.4% overall, 12% in those treated with, and 24.3% in those not treated with, HBOT. ICU support was required in 248 (72.7%) patients. Independent factors impacting on mortality included HBOT (odds ratio [OR] 0.42 [0.22 to 0.83], *P*=0.01), increased age (OR 1.06 [1.03 to 1.08], *P*=0.001) and immunosuppression (OR 2.6 [1.23 to 5.51], *P*=0.01). Mortality was linked to illness severity at presentation, however when adjusted for severity score and need for intensive care management, HBOT was associated with significant reduction in mortality.

Key Words: necrotising fasciitis, hyperbaric oxygenation, gas gangrene, *Streptococcus pyogenes*, Fournier's gangrene

Necrotising fasciitis (NF) is an aggressive necrotising soft tissue infection (NSTI) characterised by rapidly progressive necrosis of the fascia and subcutaneous tissue with relative sparing of the underlying muscle[1]. Rapid bacterial proliferation in the fascia is followed by leukocyte infiltration, progressive thrombosis of the fascial vasculature, occlusion of the perforating skin vessels and secondary ischaemia and gangrene. Tissue necrosis is often accompanied by systemic toxicity, which may progress to septic shock, multiple organ failure and death.

At the Alfred hospital, management of NSTIs involves diagnostic cultures; antibiotics (penicillin, imipenem, gentamicin, clindamycin); aggressive, early[3–5], extensive and repeated debridement by experienced surgical teams; intensive care; and hyperbaric oxygen. Hyperbaric oxygen therapy (HBOT) involve treatment at 2.8 ATA (atmospheres absolute) three times in the first 24 hours, twice in the second 24 hours, and then daily as required. Adjuvant intravenous immunoglobulin therapy is used in the event of presumed streptococcal toxic shock syndrome. Even with early aggressive surgical intervention, mortality rates are in the region of 30% to 35% in most published case series[4,6,7].

There is level III evidence for the use of HBOT for patients with NSTI[8–11] and case reports and cohort studies are generally positive[12,13]. However, the benefit of HBOT in NF treatment continues to be debated and current practice varies widely[14]. At the Alfred Hospital, HBOT is an integral part of the standard treatment regimen, while at other centres it is used only in severe cases, in cases with significant comorbidities[15], or not at all[16]. While many smaller studies also suggest improved outcomes in terms of mortality and amputation, a number of hospitals across Australia and many internationally do not offer HBOT for patients with NSTI, despite having hyperbaric facilities. This appears, in part, to be related to surgeon and/or intensivist preference, and in part to several small studies which showed no benefit from HBOT[14,17].

Our aim was to determine if administration of hyperbaric oxygen in our hospital reduced mortality and morbidity in patients with NF who otherwise received similar surgical approaches, antibiotics and intensive care management.

Methods

The study received low-risk ethics committee approval (Approval No.: AH 431-13). We searched International Classification of Diseases, Clinical Modification (ICD-9-CM

* MBChB, Registrar, Department of Intensive Care and Hyperbaric Medicine, Alfred Hospital, Prahran, Victoria
† MBBS FANZCA, Anaesthetist, Department of Intensive Care and Hyperbaric Medicine, Alfred Hospital, Prahran, Victoria
‡ MBBS, Intern, Department of General Medicine, John Hunter Hospital, Newcastle, New South Wales
§ MBBS MRCP FRACP FCICM, Intensivist, Department of Intensive Care, Alfred Hospital, Prahran, Victoria
Address for correspondence: Assoc Prof Geoff Frawley. Email: g.frawley@alfred.org.au
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9 or 10) codes from the hospital administrative dataset to identify patients admitted to the Alfred Hospital with NSTIs. The search covered the 13-year period from 1 January 2002 to 31 December 2014. The ICD codes appropriate to our study were: Necrotising Fasciitis (M 72.6), necrotising soft tissue infection (M72.61-68), invasive Group A Streptococcal infection (A40.0) and Gas Gangrene (A 48.0). A separate search of the Alfred hyperbaric database was performed for the search term 'necrotising soft tissue infection'. These patients were then matched to those identified by the ICD code search.

Inclusion criteria were any of the above discharge diagnoses, as well as both surgical (from operation reports) and histological confirmation of NSTI. Patients were excluded if there was histopathological evidence of an alternative diagnosis or if the operation reports did not

Table 1

Demographics of survivors of necrotising soft tissue infection

	Survivors n=292	Non-survivors n=49	*P*-value
Patients			
Age, yrs	50.8 (17.8)	64.6 (14.1)	<0.001
Gender, male	181 (62%)	27 (55%)	0.36
Referral base			
Inpatient	50 (17.1%)	10 (20.4%)	0.57
Other hospital	242(82.9%)	39 (79.6%)	
Predisposing factors			
Antecedent trauma	78 (26.4%)	8 (16.3%)	0.49
Antecedent surgery	44 (15%)	11 (22.5%)	
Infection	108 (37%)	14 (28.6%)	
Spontaneous	61 (21%)	16 (32.7%)	
Wound location			
Head and neck	9 (3.1%)	0	0.31
Perineal/abdominal	98 (33.6%)	17 (34.7%)	
Truncal	49 (16.8%)	13 (26.5%)	
Extremity	136 (46.6%)	19 (38.8%)	
Illness severity score			
APACHE II score	15.8 (6.3)	20.9 (6.3)	0.001
APACHE II ROD, % (SD)	25.9 (17.5)	40.6 (20.3)	0.001
APACHE III score	49.8 (29.9)	73.6 (35.7)	0.001
APACHE III ROD, % (SD)	16 (2.0)	33.2 (31.5)	0.001
LRINEC	5.94 (2.9)	6.7 (2.6)	0.08
Comorbidities			
Obesity, BMI >30	100 (34.3%)	19 (46.3%)	0.08
Diabetes	98 (34.8%)	15 (34.9%)	0.08
Smoker	156 (53.4%)	22 (44.9%)	0.01
Intravenous drug use	16 (5.5%)	2 (4.1%)	0.17
Immunosuppression	35 (21%)	17 (43.6%)	0.01
Organism			
Group A *Streptococcus*	70 (24%)	18 (36.7%)	0.06
Clostridia spp.	24 (8.2%)	4 (8.2%)	0.99
Enteric organism	80 (27.4%)	21 (42.9%)	0.05
Mixed anaerobes	57 (19.5%)	15 (30.6%)	0.24

ROD=risk of death, APACHE=Acute Physiology and Chronic Health Evaluation, LRINEC=Laboratory Risk Indicator for Necrotizing Fasciitis, BMI=body mass index.

document a necrotising process. A search of the local ICU database was performed to obtain details of ICU admission, duration of stay in ICU, mechanical ventilation time, Acute Physiology and Chronic Health Evaluation (APACHE) II or III scores and associated predicted risk of death. For patients who received hyperbaric treatment, details were obtained including time to first hyperbaric treatment, the number of treatments in first 24 hours, total number of treatments and initial treatment table.

Once the cohort of patients was established, demographic and clinical data was sourced from hospital medical records, ICU and HBOT databases. Information regarding the relevant predisposing factors, supported in the published literature[1,18–20], was collected including diabetes mellitus, chronic kidney disease, peripheral vascular disease, antecedent trauma, recent surgery, immunosuppression (human immunodeficiency virus or use of immunosuppressive medications), malignancy (both solid organ and haematological) and alcoholism. Wound location was recorded together with the number of HBOT treatments.

A Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score was generated from laboratory data on presentation[21]. The total number of debridements and amputations performed were recorded, as well as any prior interventions or surgery performed at referring hospitals. Histopathological evidence of NSTI was sought when it was performed on surgically debrided tissue. Microbiological results, including the initial Gram stain and culture, were recorded. The most frequent missing variables were C-reactive protein (2.6%), history of smoking (3%), and diabetes (4.7%). We conducted a multiple imputation by chained equations approach in Stata (StataCorp, College Station, TX, USA) to address missing data and to estimate and combine the primary outcome of interest across ten imputed datasets. We then performed multivariable regression analyses to determine whether differences in LRINEC values (of which C-reactive protein is a major component) were statistically significant after controlling for other confounding factors. The use of the multiple-imputation method to account for missing data did not alter conclusions based on a complete case analysis.

Statistics

Parametric data are presented as mean (SD), non-parametric as median (IQR), and categorical as proportions. A two-sample t-test was used to compare the ages and weights of the HBOT and non-HBOT groups. The Pearson chi-square test was used to test the association between the confounders (gender, admission source, site of NSTI, aetiology of NSTI), the outcomes (mortality, amputations and complications) and predictors (HBOT or non-HBOT). Multivariate logistic regression was used for all independent variables found to be associated with mortality on univariate logistic regression with a two-tailed significance set at a *P*-value of less than 0.05. Results were expressed as odds ratio (OR) with 95% confidence intervals (CI). Data from patients with missing values were not analysed.

Results

Over the 13-year period, 341 patients were identified with an initial diagnosis of a NSTI. A total of 275 patients were treated by the Alfred Hyperbaric Service and 66 were not. Table 1 details the characteristics of the cohort. There was a male predominance (61%) and more than three-quarters of patients (281 patients, 82.4%) were transferred from another hospital. The most common predisposing factor was diabetes mellitus (113 patients, 34.8%). Seventy-seven patients (22.7%) had no history of a predisposing factor. Approximately half of the patients had perineal or abdominal wounds and half had wounds involving extremities.

Mortality increased with increasing age, particularly for patients over 70 years of age (Figure 1). There was no consistent trend in yearly admissions for NF (median 25.1, 95% CI 20.8 to 30.2) whereas the mortality was relatively consistent (median 14.8%, 95% CI 10.8 to 19.1). This contrasts with a rising incidence and ICU admission rate, but declining hospital mortality rate for severe sepsis with multifunction organ dysfunction at the same hospital. Between 2000 and 2012 the number of patients entering ICUs with sepsis increased from 7.2% in 2000 to 11.1% over the 12 years. However, over the same time span, deaths from sepsis in the ICU dropped from 35% to 18.4%.

ICU therapy was required in the majority (247 patients,

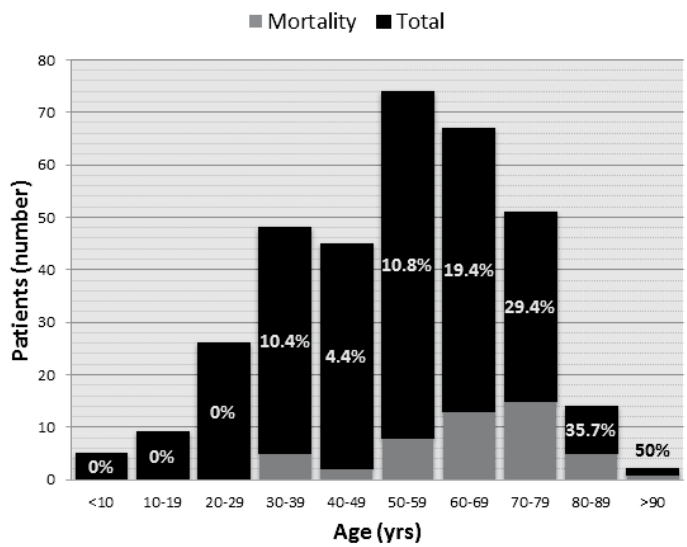

Figure 1: Mortality (% of total) and age distribution of patients with necrotising soft tissue infection (NSTI) presenting to the Alfred Hospital between 2002 and 2014. The poor survival in older patients with NSTI and multisystem involvement should be considered prior to inter-hospital transfer and major surgery.

74.2%), with a median ICU length of stay of 7.4 days (IQR 3.0 to 13.5 days). The in-hospital mortality for the whole cohort was 14.4%. No deaths occurred in patients who were managed outside of the ICU. Thus, for patients admitted to the ICU, in-hospital mortality was similar (19.8%) to the predicted risk of death from the APACHE III-j scoring system (20.3%). Those patients who died were more likely to have higher APACHE III scores (73.6 [35.7] versus 49.8 [29.9], *P*=0.0001) and higher predicted risk of death (33.2% versus 16%, *P*=0.001). Early mortality was reflected by shorter hospital length of stay (2.9 [IQR 1 to 16.3] versus 24.8 [IQR 12 to 38.9] days, *P*=0.001), fewer HBOT treatments (3.5 versus 6.9 treatments, *P*=0.001) and fewer surgical debridements (2.9 versus 4.7 operations, *P*=0.001) in this group.

The patients who received HBOT had lower APACHE III scores (51.2 [31.9] versus 68.8 [30.6]) and were more likely to have perineal disease (36% versus 24.2%). The number of debridements was higher in the HBOT group. There were 30 amputations in the cohort (four hindquarter, ten above-knee, five below-knee, one upper limb and ten other amputations). This was likely to be a function of survivor bias. Patients were acutely managed in hospital for a prolonged inpatient stay (29.8 days, IQR: 12.6 to 50.0 days), and only around one-third (39.0%) of patients were discharged directly home (Table 2).

Compared to the HBOT group, patients who did not receive HBOT were older (55.7 versus 52.2 years), male (75.7% versus 57.5%) and obese (42.2% versus 34.8%). There was no difference between treatment groups in the incidence of diabetes (33.8% versus 35%), smoking (50.8% versus 54.6%), immunosuppression or infection with Group A *Streptococcus* (27.3% versus 25.5%). The ICU length of stay of the non-HBOT group was shorter compared to the HBOT group (4.9 versus 6.9 days) but hospital length of stay was longer (33.7 versus 28.9 days). The non-HBOT group had fewer debridements (3.0 versus 4.8) and fewer amputations (10.0 versus 21.0), possibly as a result of the higher mortality rate in the non-HBOT group.

In this study, LRINEC scores of 6 or greater had a sensitivity of 67.1% and specificity of 51.4% for NSTI confirmed at operation. The positive predictive value of an accurate NSTI diagnosis was 92.3% and the negative predictive value was 15.2%. A LRINEC score of 6 or greater did not predict amputation (sensitivity 61.3%, specificity 34.1%, positive predictive value 8.7).

On univariate analysis, independent factors associated with mortality included HBOT (OR 0.42 [0.22 to 0.83],

Table 2

Medical and surgical interventions of patients presenting with necrotising fasciitis

	Mortality			Hyperbaric		
	Survivors, n=292	Non-survivors, n=49	*P*-value	HBOT, n=275	Non-HBOT, n=66	*P*-value
Mortality				33 (12%)	16 (24.3%)	0.01
Medical						
Triple antibiotics*	286 (96.9%)	49 (100%)	0.11	275 (100%)	46 (69.7%)	0.001
IVIG	75 (25.7%)	12 (26.7%)	0.02	75 (27.6%)	12 (18.8%)	0.03
Intensive care						
Pts req ICU	199 (68.1%)	49 (100%)	0.01	210 (76.4%)	37 (63.8%)	0.05
ICU LOS Median (IQR)	4 (0.1–10.1)	2 (1–6.1)	0.07	4.2 (0.4–10.5)	1.34 (0–5)	0.005
Ventilation days (95% CI)	4.4 (3.7–5.2)	4.9 (2.3–7.4)	0.66	4.9 (4.1–5.8)	2.6 (1.3–3.9)	0.01
Hyperbaric oxygen						
HBOT	242 (82.9%)	33 (71.7%)	0.01	275 (100%)	0	n/a
Treatments	6.9 (6.2)	3.5 (6.3)	0.001	8 (6.1)	0	n/a
Hrs to first HBOT, median (IQR)	38.8 (20.8–86.2)	28.0 (18.5–47)	0.12	38.8 (21.5–86.3)	0	n/a
Treatments first 24 hrs	2 (1–3)	2 (2–3)		2 (2–3)	0	
Surgical						
Debridements	4.7 (3.3)	2.9 (2.2)	<0.001	4.8 (3.4)	3 (2.1)	<0.001
Amputations	28 (9.6%)	3 (6.1%)	0.05	21 (7.6%)	10 (15.2%)	
Hospital						
Hospital LOS, median (IQR)	24.8(12–38.9)	2.9 (1–16.3)	<0.001	21.8 (9–36.7)	24 (10–39)	0.52

*Triple antibiotics involved use of meropenem, lincomycin and gentamicin on admission prior to identification of causative organism.
HBOT=hyperbaric oxygen therapy, IVIG=intravenous immunoglobulin, LOS=length of stay.

Table 3

Univariate logistic regression analysis of patient, hyperbaric and operative factors on mortality

Variable	OR	Robust std error	*P*-value	95% CI
Patient factors				
Age	1.06	0.01	<0.001	1.03–1.08
Obesity	1.42	0.46	0.27	0.76–2.67
Smoking	0.75	0.24	0.37	0.40–1.40
Diabetes	1	0.34	0.99	0.51–1.97
Comorbidities				
IVDU	0.73	0.56	0.68	0.16–3.28
Immunosuppression	2.6	0.99	0.01	1.23–5.51
Illness severity				
LRINEC >6	1.1	0.06	0.08	1.0–1.23
APACHE III	1.02	0.005	<0.001	1.01–1.03
Hyperbaric oxygen organism				
HBOT:non-HBOT	0.42	0.14	0.01	0.22–0.83
GAS	1.84	0.6	0.06	0.92–3.5
Enterics	1.86	0.59	0.05	0.99–3.47
Anaerobes	1.65	0.56	0.14	0.85–3.21
Clostridia	1	0.56	0.99	0.33–2.99

Data is expressed as odds ratio for mortality with 95% confidence intervals (95% CI). For factors with a binary outcome (obesity, smoking, hyperbaric oxygen), the odds ratio (OR) represents the presence or absence of the factor. For continuous data, the estimate is the OR for a unit increase for the factor (per year). IVDU=intravenous drug use, LRINEC=Laboratory Risk Indicator for Necrotizing Fasciitis, APACHE=Acute Physiology and Chronic Health Evaluation, GAS=Group A *Streptococcus*.

Table 4

Multivariate logistic regression analysis of patient, hyperbaric and operative factors on mortality adjusted for illness severity by requirement for intensive care admission

	Variable	OR	*P*-value	95% CI
Hyperbaric oxygen	HBOT:no HBOT	0.26	0.01	0.11–0.62
Immunosuppression		2.6	0.01	1.23–5.51
Age		1.06	0.01	1.03–1.09
Illness severity	LRINEC >6	1.1	0.08	1.0–1.23
	APACHE III	1.02	<0.001	1.01–1.03
Organism	GAS	1.84	0.06	0.92–3.5
	Enterics	1.86	0.05	0.99–3.47

Variables with *P*-values <0.06 from univariate logistic regression analysis were used to identify the variables for multivariate regression. Data is expressed as odds ratio (OR) for mortality with 95% confidence intervals (95% CI). OR for age expressed per one year of patient age. HBOT=hyperbaric oxygen therapy, LRINEC=Laboratory Risk Indicator for Necrotizing Fasciitis, APACHE=Acute Physiology and Chronic Health Evaluation, GAS=Group A *Streptococcus*.

P=0.01), increased age (OR 1.06 [1.03 to 1.08], *P*=0.001) and immunosuppression (OR 2.6 [1.23 to 5.51], *P*=0.01). Infection with Group A streptococcal infection (OR 1.84 [0.92 to 3.5], *P*=0.06), clostridial infection or enteric organisms (OR 1.86 [0.99 to 3.47], *P*=0.05) were not significantly associated with mortality. Diabetes (OR 1.0 [0.51 to 1.97], *P*=0.99), obesity (OR 1.42 [0.76 to 2.67], *P*=0.27) or intravenous drug use (OR 0.73 [0.16 to 3.28], *P*=0.68) were not significantly associated with increased mortality. Other factors such as gender, predisposing factors, or growth of any other pathogens did not significantly impact on mortality, possibly as a result of low absolute mortality rates (Table 3).

Multivariate analysis adjusted for age and illness severity (by need for ICU admission) demonstrated that HBOT (OR 0.45 [0.20 to 0.99], *P*=0.05) was significantly associated with increased survival, whereas immunosuppression (OR 4.56 [1.74 to 11.9], *P*=0.002), was associated with increased mortality. Infection with Group A *Streptococcus* (OR 2.14 [0.92 to 4.93], *P*=0.08) or mixed anaerobes (OR 1.9 [0.83 to 4.3], *P*=0.13) was not significantly associated with increased mortality (Table 4).

Discussion

This is the largest single-centre Australian study specifically describing the impact of HBOT on mortality of NSTIs. This study shows an association between the use of HBOT and reduced mortality in patients with NSTI when HBOT is used as an adjuvant to surgery, antibiotics and intensive care management of sepsis. The patients in this series were largely transferred from other hospitals for intensive care management of sepsis, hyperbaric oxygen, or both. Factors adversely impacting on survival were immunosuppression from either chemotherapy or long-term steroid use, and perineal infection with enteric organisms. Previously stated risk factors for mortality such as diabetes, smoking, and intravenous drug use were prevalent but were not associated with mortality. In this series, there was a reduction in amputations in the treated group which is consistent with previous Australian studies and represents a major advantage to the use of HBOT[23].

Overall mortality in this series (14%) was lower than reported in older series[15,16,24]. APACHE II or III-j scores (only recorded on patients admitted to the ICU) however suggest disparity between the two treatment groups. The non-HBOT group had higher APACHE III scores (68.8 versus 51.1, *P*=0.001) and higher calculated risk of death (30% versus 18%, *P*=0.001).This was comparable to the actual mortality of these groups (15.8% in the hyperbaric group and 36.5% in the non-HBOT group). It is not possible to identify whether lower mortality in this series was related to decreases in Australian sepsis mortality over the study period[25], earlier identification of NSTIs or appropriate

surgical and antibiotic therapy. The survival of patients admitted to ICUs with sepsis has improved dramatically over the past 13 years[25]. Between 2000 and 2012, the number of patients entering ICUs with sepsis increased from 7.2% in 2000 to 11.1% over the 12 years. However, over the same time span, deaths from sepsis in the ICU dropped from 35% to 18.4%[25,26]. One confounder may be the use of APACHE III-j as an indicator of mortality risk[27,28]. Mortality outcomes have progressively dropped below APACHE III-j estimations, but this has not been constant for all diagnoses. Risk-adjusted mortality rates for elective surgery have halved over the past ten years, but medical and emergency surgical deaths have dropped by only 20%. For diagnoses such as cardiac valve surgery, APACHE III-j now predicts three times as many deaths as actually occur[29].

There are no randomised controlled trials comparing the effect of HBOT on outcomes of NSTI and most series are underpowered to determine an effect of HBOT on mortality[17,30]. In these studies, comparison groups are not consistent with some using historical controls and some using other hospitals as controls[14,30,31]. Often, allocation of HBOT in NSTI has been determined by physician preference or by availability of HBOT onsite. Mortality rates, even in case series with early aggressive surgical intervention but without HBOT, vary from 9.5% to 42%[32–34]. In one retrospective study, 38 patients with NSTI managed at one centre were compared to 48 patients at another centre who received HBOT[14]. As noted by Westgard, there is a 80% risk of a type 2 error in a study of this size[35]. A retrospective study of 45,913 patients with NSTI published in 2012 found patients who received HBOT to have lower mortality (4.5% versus 9.4%, *P*=0.001) but unfortunately did not gather several important predictors and confounders for the outcome of patients[30].

In our series, 88.5% of patients were referred from another hospital, with 75.4% having surgery at the parent hospital prior to transfer. Inter-hospital transfer of patients with NF has been noted by other authors as a significant risk factor for mortality[36]. The higher mortality of patients who have been transferred from another hospital may reflect higher illness severity, later stage of the disease and failure of surgical and antibiotic interventions.

The potential benefits of HBOT in NF are attractive from a pathophysiological viewpoint. Hyperbaric oxygen has been demonstrated clinically to increase oxygen transport and diffusion into the areas of injured, oedematous and infected hypoxic tissues[37]. Mechanistically, reducing hypoxia and inducing hyperoxia helps marginally viable tissue to survive, creates a demarcation zone between necrotic and viable tissues and is thus potentially tissue- and limb-sparing[37]. Hyperoxia reduces production of bacterial toxins including *Clostridium* alpha-toxin[38] and inhibits the growth of strict anaerobic bacteria and facultative anaerobes by increasing tissue oxidation reduction potential and direct toxic mechanisms[39]. Hyperoxia also potentiates antibiotic efficacy[40] and improves the efficacy of neutrophil bacterial killing which is highly oxygen dependent[41]. HBOT also exerts important secondary effects on inflammation, modulates reperfusion injury[42] and increases wound healing[43,44], with benefits seen in sepsis models[45].

Limitations

There are several limitations with this study related to the retrospective nature of the data. It was not possible to adequately generate comparator groups of equal size and patients of similar disease severity. Whilst this is the largest Australian study to date, it is still likely to be underpowered to determine a true effect. We believe that it would not be possible to generate a prospective randomised controlled trial as it would be unethical to allocate to the non-hyperbaric arm in many cases.

The retrospective nature of this study introduces selection bias and therefore treatment bias. As 82% of our patients were transferred, it is possible that only those patients stable enough to be transported have been studied. The overall mortality could therefore be higher than we report. Alternatively, following transfer and reassessment by the receiving unit, patients may be too unstable to be effectively treated. If surgery precedes HBOT, and intraoperative findings are consistent with a non-survivable lesion, then mortality in the non-HBOT group is elevated. The lower mortality in the HBOT group could reflect the fact that only patients who survive the initial surgery are able to complete an adequate course of HBOT treatment.

Treatment bias could not be excluded as the reasons for not receiving HBOT are divided between physician preference, patient factors and comorbidities. The most common reasons for not treating were anticipated difficulties with treatment (e.g. with ventilation, arrhythmias), expected futility of treatment or, at the other end of the spectrum, patients referred to the Alfred as possible NSTIs who on reassessment were deemed not to have a necrotising process.

Finally, inclusion in this study was dependent on ICD coding at discharge or death. As NSTIs are a surgical diagnosis, this diagnosis is highly dependent on the experience of the treating surgeon.

Conclusion

Mortality was linked to illness severity at presentation however, when adjusted for severity score and need for intensive care management, HBOT was associated with significant reduction in mortality.

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