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Review

The role of hyperbaric oxygen therapy in the treatment of sternal wound infection

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Summary

Sternal wound dehiscence and infection are major problems for patients and health care providers. A range of risk factors, including diabetes, obesity and internal thoracic artery harvest, has been implicated. Several pathophysiological mechanisms, which may account for the development of infection, have been proposed. There is a growing body of evidence which suggests that sternal ischaemia may play a significant role in the initiation of wound infection, and that this may be exacerbated by harvest of the internal thoracic artery. Current treatments for infection include wound debridement, irrigation and tissue flap reconstruction. In addition, several novel therapies such as negative pressure dressings have been shown to be safe and useful. Hyperbaric oxygen therapy – the administration of 100% oxygen at pressures greater than atmospheric pressure – is widely used in the treatment of various chronic wounds. The mechanism whereby hyperbaric oxygen exerts its effects is being elucidated and there is a growing body of clinical evidence that supports its use. It has been suggested that there may be a role for hyperbaric oxygen therapy in the treatment of sternal infection. The theoretical mechanisms would seem plausible, but at present there is only limited evidence to support its use. This review addresses the theory and evidence supporting the role of hyperbaric oxygen therapy in the treatment of sternal wound infection.

Keywords: Surgical wound infection; Hyperbaric oxygenation; Coronary artery bypass

1. Sternal wound infection

More than 30,000 sternotomies are performed each year in the UK [1], and the majority of patients do not experience wound complications. However, a number of patients (historically between 0.15% and 19% in reported series, depending on inclusion criteria [2,3]) suffer problems with delayed or impaired wound healing, wound dehiscence and infection. Recent work suggests that infection rates are about 1.9% [4].

Sternal wound dehiscence and infection is a serious complication that carries significant consequences for the patient and for service provision. Some cases require further surgery, including repeated debridement and major surgical reconstruction. There is almost invariably considerable increase in the length of hospital stay [5], and the incidence of further complications is high. Patients who develop sternal wound infection have an inpatient mortality of 14% (normally about 2%), a threefold increase in mortality over the first 4 years after surgery and a significantly higher short term and long-term morbidity [6]. Wound infection also carries a 2.8 times increase in the financial cost of the procedure [7].

Median sternotomy wound complications range from sterile wound dehiscence to suppurative mediastinitis and it is difficult to make comparisons between cases and between treatments. This has been recognised and has been attributed, partly, to the lack of a widely accepted and comprehensive definition of what constitutes wound infection [8]. A system of classification and definitions has been proposed by El Oakley and Wright [8] and are summarised in Table 1.

A range of organisms have been isolated from the infected mediastinum. Coagulase negative staphylococci have been particularly associated with sternal dehiscence, whilst *Staphylococcus aureus* is more often isolated in patients with a stable sternum. In patients who develop mediastinitis after re-operation, gram-negative organisms, particularly rods, are commonly identified [9]. Methicillin resistant *S. aureus* is increasing in prevalence and is now found to be the infecting organism 'relatively frequently' [10].

2. Risk factors for sternal infection

A large number of prospective and retrospective studies have been published that identify risk factors predisposing to

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Table 1
Definitions and classification of sternal wound infection [8]

Mediastinal dehiscence	Median sternotomy wound breakdown in the absence of clinical or microbiological evidence of infection
Mediastinal wound infection	Clinical or microbiological evidence of infected presternal tissue and sternal osteomyelitis, with or without mediastinal sepsis and with or without unstable sternum
Infection subtypes	
A: superficial wound infection	Wound infection confined to subcutaneous tissue
B: deep wound infection (mediastinitis)	Wound infection associated with sternal osteomyelitis with or without infected retrosternal space
Mediastinitis subtypes	
Type I	Mediastinitis presenting within 2 weeks after operation in the absence of risk factors[a]
Type II	Mediastinitis presenting 2–6 weeks after operation in the absence of risk factors
Type IIIA	Mediastinitis Type I in the presence of 1 or more risk factors[a]
Type IIIB	Mediastinitis Type II in the presence of 1 or more risk factors[a]
Type IVA	Mediastinitis Type I, II or III after one failed therapeutic intervention
Type IVB	Mediastinitis Type I, II or III after more than one failed therapeutic intervention
Type V	Mediastinitis presenting for the first time more than 6 weeks after operation

[a] Risk factors are diabetes, obesity and immunosupression.

sternal infection. More than 20 independent risk factors have been identified. The most frequently documented risks include obesity [11], prolonged ventilation [2], diabetes mellitus [12,13], previous cardiac surgery [13,14], re-exploration for bleeding [11,12,15], postoperative blood transfusion [7,16] and use of the internal thoracic artery as bypass conduit [11,12,15,17]. However, most risk factors identified by one study are refuted or fail to be identified by others. Even obesity, which has been found to be a significant independent risk factor in a large number of the studies, was not identified by a large retrospective study of more than 12,000 operations [18]. Studies aimed specifically at characterizing the risks associated with obesity have also drawn contradicting conclusions [19,20].

Several studies have highlighted combinations of risk factors that pose a particularly high risk. Diabetes mellitus combined with obesity carries a relative risk of 5.0 for the development of sternal infection and bilateral internal thoracic artery harvest in diabetics has also been singled out as particularly venturesome [7,17]. Scoring systems to estimate the risk of sternal infection have been developed and validated but are not regularly used in clinical practice [21].

3. Theoretical mechanisms for the development of sternal wound infection

Several mechanisms have been proposed to explain the development of sternal wound dehiscence and infection.

It has been suggested that localised ischaemic osteomyelitis is a primary event. Sternal wires become loose in the affected region and sternal instability follows, with subsequent dehiscence of the overlying skin incision. The osteomyelitic bone and open wound are an ideal focus for the development of infection.

Other theories suggest that inadequate sternal fixation and the resulting instability lead to skin dehiscence as a primary event. The open wound becomes secondarily infected and infected material drains backwards into the pericardium and mediastinum. Alternatively, inadequate surgical drainage has been offered as a primary event. Insufficient drainage of the mediastinum in the postoperative period results in collection of blood and serous fluid in the mediastinum that forms an excellent culture medium for bacteria. Once a focus of infection is formed, infected material can then track forwards and discharge through the skin wound.

Although inadequate sternal fixation or mediastinal drainage probably does increase risk, there are many instances of wound dehiscence where neither of these factors can be shown to be present.

4. Ischaemic sternal osteomyelitis

Studies and experiments investigating the anatomy of the internal thoracic artery in human cadavers have demonstrated its role in the blood supply of the sternum, and support the suggestion that impaired sternal healing may be due to ischaemia [22–25]. Animal models of the postoperative sternum, where flow has been studied using radiolabelled micro-spheres, also support this hypothesis [26–28].

In man, however, observations are less consistent. Intraoperative laser Doppler fluximetry has failed to demonstrate a reduction in flow in the sternal tissues when the internal thoracic artery is harvested [29,30]. Conversely, nuclear medicine techniques demonstrated a significant hypo-perfusion in some regions of the sternum after internal thoracic artery harvest [31]. This may reflect differences in the methodology and sensitivity of the various techniques used to measure perfusion, but, as outlined earlier, internal thoracic artery harvest has been both identified and refuted by the various risk factor analyses.

5. Current treatment of deep sternal wound infection

The optimum treatment of sternal infection has been the subject of considerable debate. The high mortality and low success rate of conventional wound management techniques led to the development of the sophisticated techniques used today. The first of these was the introduction of closed irrigation [32]. Both antiseptic and antibiotic solutions have been successfully employed. The next major development was the use of muscle flaps for wound closure [33]. Early

concerns over the functional and cosmetic sequelae resulting from the use of pectoralis major muscle flaps have proved to be unfounded and it is now frequently used.

Novel therapies have also been tested in the management of sternal infection. Granulated sugar has been employed as a dressing, whereby it is poured directly into the open wound. The resulting high osmotic load destroys bacterial cells and authors have reported excellent rates of wound resolution associated with its use [34]. More recently, negative pressure dressings have been introduced and shown to be safe and effective in the management of sternal wounds [35–37]. However, although widely used, there are no randomised trials comparing the efficacy or costs of either of these therapies with the use of more conventional wound dressings.

Currently, effective sternal wound management involves a multidisciplinary approach that depends on the early recognition of the problem, the timely introduction of investigations and appropriate non-surgical management, combined with appropriate surgical intervention when required. Early debridement has been recommended by several authors [38,39]. As soon as the diagnosis is made specimens should be collected for microbiological analysis and broad-spectrum antibiotics instituted, based on local patterns of resistance and gram stain results. A combination of a cephalosporin and vancomycin has been recommended as empirical therapy until sensitivities are known [10]. The heterogeneity of wounds dictates that the extent of debridement and reconstruction is tailored to the operative findings. A range of overall surgical strategies have been used, from reconstruction in every case, to a more selective approach depending on findings [40]. Reconstruction techniques include sternal rewiring [10], pectoralis or rectus muscle and omental flap rotation [39,41,42].

Regardless of the exact treatment, the potential chronicity of sternal wounds must always be appreciated. Appropriate nitrogen balance and blood glucose control, enteral and parenteral nutrition, and vitamin and trace element supplementation should be maintained until the wound has healed.

6. Wound healing and oxygen

Wound healing is a complex and dynamic process that aims to restore cellular structures and tissue layers. It is broadly divided into the inflammatory, proliferative and remodelling phases. Within these phases a complex and co-ordinated series of events takes place that includes chemotaxis, phagocytosis, collagen formation, collagen degredation and remodelling. In addition, angiogenesis and epithelialisation are critical to the process of wound healing [43].

Most surgical incisions undergo primary wound healing. The wound is created in aseptic conditions with minimal contamination and a minimum of damage to the surrounding tissues. The wound edges are well vascularised and supplied with nutrients, and are accurately opposed and stabilised with sutures. A steep O_2 gradient exists from the surrounding tissue to the wound space, and these wounds heal rapidly with minimal inflammation. There is a rapid increase in wound strength up to 80% of normal after only 4 weeks [44].

Where primary healing is not achieved, or is not possible, then secondary healing takes place. A much more vigorous inflammatory response is generated and a much larger quantity of granulation tissue is formed to bridge the tissue defect [44]. Both primary and secondary healing are dependent on the delivery of sufficient nutrients to the healing tissues for the process to complete successfully.

Oxygen plays a critical role in several of the processes involved in both primary and secondary wound healing. A common feature of chronic wounds is a marked reduction in O_2 partial pressure in the tissues around the wound. The steep O_2 gradient described earlier is an important chemotactic stimulus for the migration of leukocytes into the wound space. When the tissues around the wound have a low O_2 partial pressure, the gradient is less steep [45]. As a result, leukocyte migration, and wound healing, are impaired.

Energy in the form of ATP is essential for the biosynthetic processes taking place in the wound, and in addition, molecular oxygen is a key cofactor in the hydroxylation of proline, a necessary step for the formation of stable collagen [46]. In large wound spaces, capillary growth is required to maintain continued delivery of nutrients to the wound space. The stimulation and co-ordination of this process is very sensitive to the local O_2 concentration. Its success depends on the production of stable collagen by fibroblasts, whose function is oxygen dependent [47].

Polymorph neutrophils have an important role in the wound space, preventing infection and clearing microorganisms. Oxygen plays a key role in their function [48]. Neutrophils in the wound space are responsible for the phagocytosis and killing of microorganisms [43]. Killing is achieved by way of the 'respiratory burst', utilising O_2 in the generation of superoxide, peroxide and singlet oxygen free radicals. In hypoxic tissue the respiratory burst and thus host defences are markedly impaired.

A combination of the mechanisms described results in either delayed or impaired wound healing, or a complete failure of healing with the development of a chronic wound. This is particularly the case where the surrounding tissues are ischaemic and hypoxic because O_2 plays such a central role in several of the repair and host defence mechanisms.

In patients with chronic wounds, the underlying pathology is a deficiency of nutrient delivery, often due to hypoperfusion with ischaemia and cellular hypoxia. Infection may also be superimposed. Tissue oxygen concentrations around non-healing wounds are usually low [49,50], and as described earlier, fibroblast proliferation, collagen production and capillary angiogenesis all suffer, delaying healing [51]. Tissue hypoxia impairs bacterial killing, forming the ideal environment for bacteria to flourish and further reduce local oxygen tension [51,52].

7. Hyperbaric oxygen therapy (HBO)

HBO is the use of raised partial pressures of oxygen for the treatment of disease. It is delivered by means of a hyperbaric chamber and there are two general chamber designs, mono-place and multi-place. Mono-place chambers are most numerous worldwide. Multi-place chambers are less readily available but allow direct access to the patient during

Table 2
Indications for use of hyperbaric oxygen

Air or gas embolism
Carbon monoxide poisoning
Crush injury, compartment syndrome and other acute traumatic peripheral ischaemia
Decompression sickness
Enhancement of healing of problem wounds
Exceptional blood loss anaemia
Gas gangrene
Intracranial abscess
Necrotizing soft tissue infection
Radiation tissue damage
Refractory osteomyelitis
Skin grafts and flaps
Thermal burns

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treatment; however, they require a much more significant infrastructure and a large number of trained staff. In the UK, there are at present, approximately 20 hyperbaric units within the British Hyperbaric Association, divided into classes depending on chamber type and level of medical and hospital support available. The standard indications for HBO are shown in Table 2.

Standard HBO treatments are a balance between using the highest possible oxygen partial pressure and the development of oxygen toxicity. The most commonly used treatment schedule involves breathing 100% oxygen at 2.2–2.4 atmospheres absolute (ATA) (222.9–243.2 kPa) for a total of 90 min. Brief air breaks are incorporated during the treatment to reduce the incidence of oxygen toxicity. A typical treatment profile is shown in Fig. 1. This profile has been developed empirically to maximise delivery of hyperbaric oxygen whilst keeping the risk of oxygen toxicity low. Although the exact timings and depths may differ slightly between facilities, the majority of research into clinical hyperbaric medicine involves a treatment profile similar to this. Treatments are generally administered either once or twice each day based mainly on logistical considerations. The initial management plan generally involves 20–30 treatments before a review and consideration of further treatments. In wounds that respond well, HBO can be continued until the wound has closed completely, or until the wound is suitable for reconstructive surgical intervention.

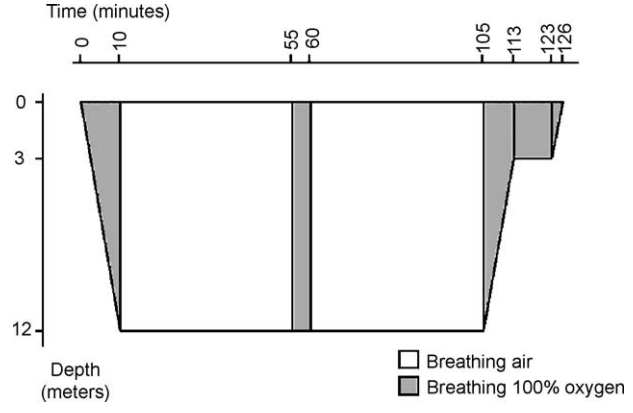

Fig. 1. Typical treatment dive profile.

This scheme has been used in those studies which consider the use of HBO in sternal infections.

Hyperbaric oxygen therapy can improve the environment in which wound healing and host antibacterial mechanisms take place. Phagocyte bacterial killing only functions optimally at oxygen tensions above 30 mmHg (4.0 kPa) [48,53]. When tissue hypoxia is present, increasing the tissue oxygen tension may be as effective as antibiotics in clearing infecting organisms [54]. In these circumstances, optimal treatment for infected wounds is felt to be a combination of systemic antibiotics and adjunctive HBO. Bacterial clearance is improved and increased oxygenation in the hypo-perfused tissue provides direct benefits to the wound repair process [45,51,53].

A large amount of clinical experience in the use of adjunctive HBO for the treatment of chronic wounds has been gained from the treatment of diabetic foot ulcers. In common with the proposed pathology of sternal wounds, these ulcers frequently have an ischaemic component and the surrounding tissues can often be shown to be hypoxic. Many heal with appropriate wound care and revascularisation when indicated, but some go on to become a chronic wound.

Many published series and randomised controlled trials report favourable rates of ulcer healing with HBO used as an adjunct. A systematic review in 2002 concluded that, in the studies reviewed, there was evidence to suggest that HBO may be beneficial in some cases but they were unable to determine the best time to start therapy, or which particular patients would benefit. They suggested that properly controlled, high-quality randomised trials would be required to assess the short- and long-term risk benefit ratios [55]. Since this review further studies have been published on the use of HBO to treat diabetic foot ulcers showing beneficial results [56,57], and also in the use of transcutaneous oxygen monitoring to select patients with a high likelihood of successful HBO treatment [58].

A 2004 Cochrane Review cautiously supported the use of adjunctive HBO in the treatment of diabetic foot ulcers but recommended further studies and economic evaluation [59]. At present, UK Primary Care Trusts, many European health funding bodies and insurance companies in the US fund the use of HBO as a cost effective treatment for diabetic foot ulcers.

8. Beneficial effects of HBO in sternal infection

The theoretical mechanisms described for the development of sternal infection support the suggestion that ischaemic hypoxia is a feature of the pathogenic process. There is a convincing theoretical basis and experimental and clinical trial evidence to support the use of adjunctive HBO in the treatment of wounds of this kind. Evidence from randomised controlled trials and systematic reviews suggest that HBO can enhance healing in some cases, particularly chronic diabetic wounds [55–57,59,60]. However, there is only a small body of evidence that describes the successful use of adjunctive HBO in sternal infection.

In constructing this review we searched the Pubmed online electronic database using the search terms 'hyperbaric oxygenation', 'sternal infection' and 'mediastinitis' as

search criteria. We manually screened the reference lists of any articles identified in an attempt to identify material not listed in Pubmed. In addition, we reviewed the relevant chapters and reference lists in standard hyperbaric medicine textbooks. Any manuscripts describing the use of HBO in the management of sternal infection were included. The literature we identified is described in the following text.

A case report describes the use of HBO, as an adjunct to conventional therapy, to treat an established sternal infection in an immuno-suppressed post-cardiac transplant patient. The reported case developed presternal fat necrosis and subsequent sternal osteomyelitis 2 months after orthotopic heart transplantation. Two areas of wound dehiscence developed. Initial management included local debridement, sternal wire removal and antiseptic irrigation. This achieved closure of one wound but the second only demonstrated limited granulation tissue formation. With the institution of HBO, rapid healing was observed and the wound epithilialised completely. In total, 40 HBO treatments were required [61].

A retrospective review of 27 cases of sternal infection, treated over a 2-year period, is described by Riddick [62]. Patients are divided according to acute or delayed infection and whether they received HBO. No strategies for randomisation, blinding or case matching appear to have been used. Data regarding the times and dates of surgery, recognition of infection, debridement, wound closure and discharge from hospital were collected by analysis of patient notes. In addition, the number of surgical procedures and duration of antibiotic treatment was recorded. From these data the author was able to demonstrate a reduction in length of hospital stay and readmission rate in the HBO group; however, no statistical analysis is presented to support the conclusions.

A retrospective review has compared conservative antibiotic therapy with aggressive surgical management [63]. Stage I surgical management involved early debridement, removal of wires and closed irrigation, followed, if this failed, by Stage II, open dressing with granulated sugar and HBO therapy. Of the 61 survivors in the surgery group, 76% were healed after Stage I with a further 18% responding to Stage II. The authors made no conclusions about the specific benefits of HBO.

Recently, Siondalski et al. [64] present a case series of 55 patients with sternal infection collected over a 5-year period. The management plan consisted of aggressive surgery in combination with 20–40 HBO treatments. Surgical procedures included wound debridement, sternal rewiring, omental pedicle flap insertion and sternectomy. In-hospital mortality in this series was 0%, all wounds healed and patients were discharged on average after 8 weeks. The authors conclude that the combination of aggressive surgical treatment and HBO may improve clinical outcome but they provide no statistical analysis of their data to support this conclusion.

Beyond these few studies we could find no other published work and no randomised controlled trials to support or refute the use of HBO in the management of sternal infection. All the articles described here constitute level V evidence and, although encouraging, only provide a weak evidence base on which to support the use of HBO in the treatment of sternal infection.

9. Conclusion

Sternal infection and mediastinitis are uncommon but devastating complications that continue to pose a clinical management problem, despite advances in treatment techniques. Established wounds are associated with increased morbidity, mortality and cost.

Surgery is widely established as the primary treatment although several adjunctive techniques have been used to increase the success rate. However, none of these techniques are supported by randomised controlled trials. Despite this they are widely used. They do have the advantage that they are widely and easily available.

In many cases, HBO treatment is only practical when the hyperbaric unit is located close to the cardiac surgical unit, or where a mono-place chamber can be placed on the ward/intensive care unit and appropriately staffed. The postulated mechanism for the development of sternal infection, as a result of sternal ischaemia and hypoxia, provides a theoretical basis for the use of hyperbaric oxygen in the management and treatment of this condition. There is a small body of evidence to support the use of HBO as an adjunct in the management of sternal infection. The level of this evidence is low and only provides weak support for its use.

Although the usefulness of HBO in the management of diabetic wounds cannot be extrapolated to apply to other conditions, there may be some similarities between ischaemic sternal wounds (particularly in diabetics) and indolent diabetic ulcers.

As with many such issues, the case for or against HBO will be best demonstrated by a well-conducted, appropriately blinded randomised controlled trial. If HBO is shown to be of benefit, then a thorough economic evaluation, comparing HBO with other already established treatments will be needed to establish the cost effectiveness of the available options. Such a randomised trial, however, is not straightforward. The incidence of sternal infection is relatively low and there is considerable heterogeneity between patients. Co-morbidity, primary surgery and the extent and nature of the wound are very variable. Appropriate treatment options differ from case to case. No widely agreed standard management has been established. Due to these factors, such trials would be very large, costly and time consuming. In the UK, there are only a handful of hyperbaric units in close proximity to cardiac surgical units.

Currently the treatment of sternal infection is not a recognised indication for HBO treatment although it may be considered a 'selected problem wound'. At present, there is no level I or II evidence to support the use of any of these adjunctive treatments in the management of sternal infection. Until more evidence is available, HBO can only really be considered on a case-by-case basis, when other, more easily available treatment options have been unsuccessful.

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