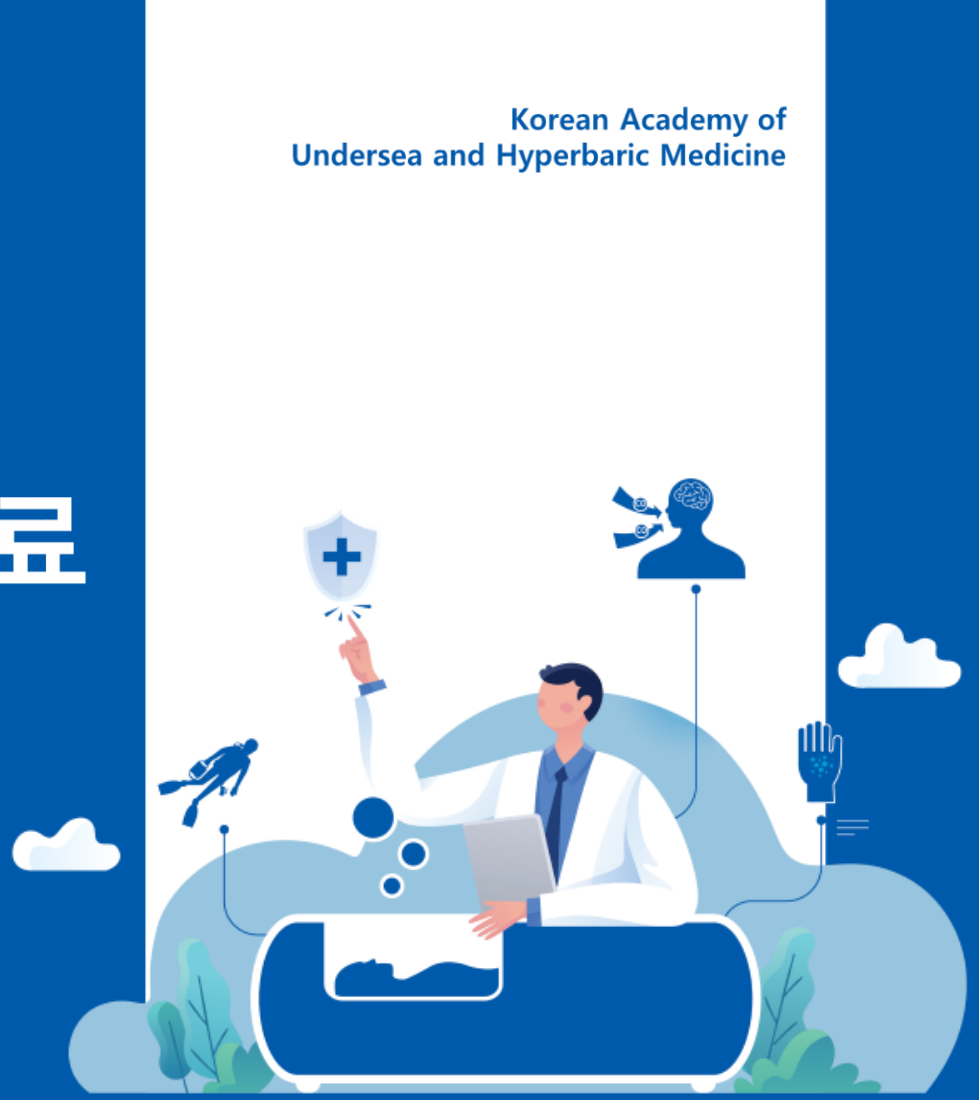
연조직 괴사 감염 및 당뇨발에서의 고압산소치료



2021.09.09~10

소 속 : 전남대학교병원 응급의학과
이 름 : 이 성 민 교수

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고압산소치료 Mechanisms

Primary

- Direct effect of increased oxygen partial pressure
- Direct effects of pressure

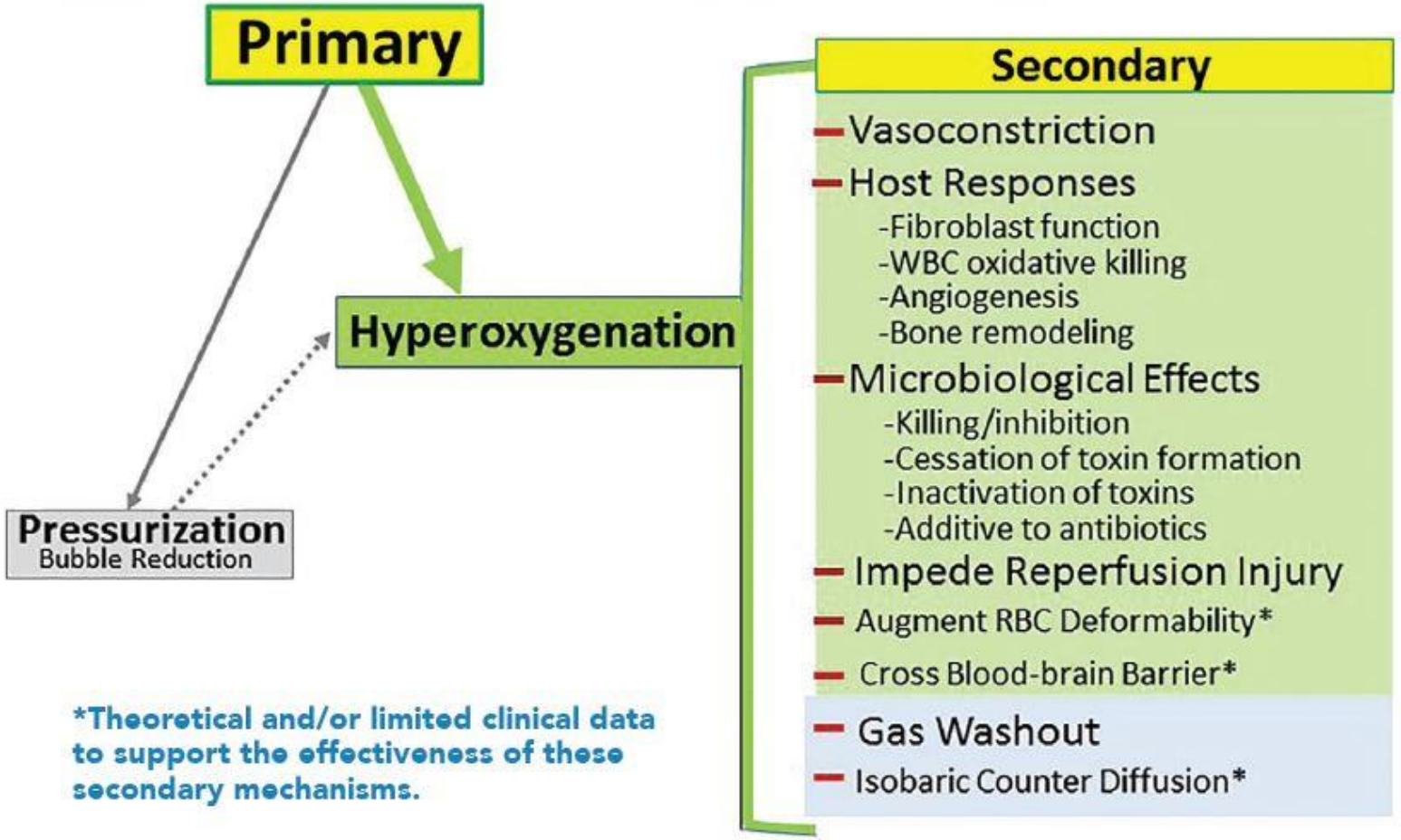
Dose, frequency, duration, effects

Secondary

- Effects of enriched oxygen environment have on cellular functions.
- The effects increased ambient pressures have in producing gradients between gases in body tissues.

Accumulative effects

TABLE 7. MECHANISMS OF HYPERBARIC OXYGEN



*Theoretical and/or limited clinical data to support the effectiveness of these secondary mechanisms.

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I 연조직 괴사 감염(Necrotizing soft tissue infection) 에 대한 임상적 특징

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Terminology

Confusing and illogical

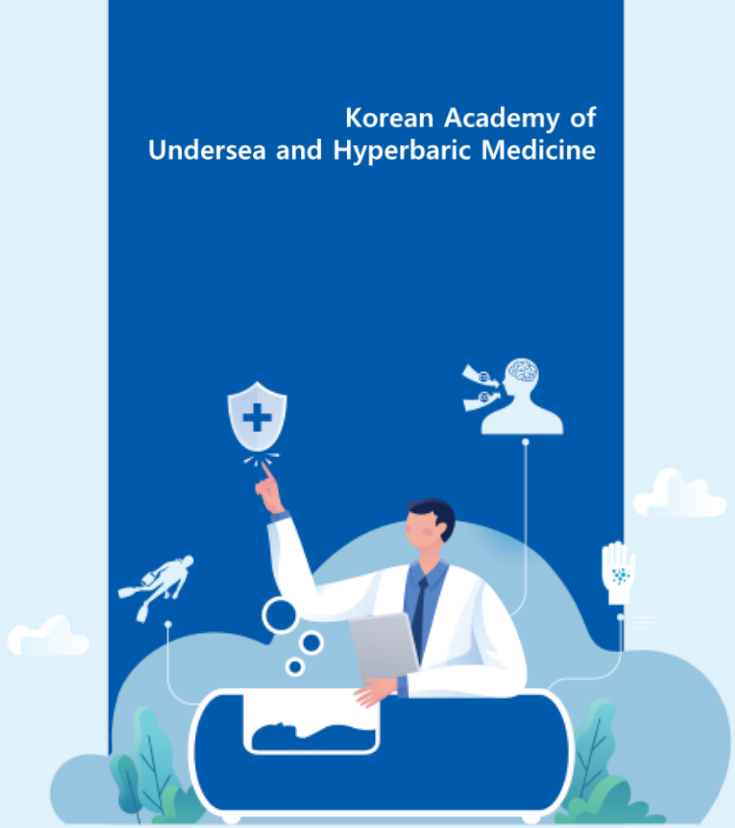
- Necrotizing soft tissue infection
- Gas gangrene/Clostridial myonecrosis
- Necrotizing fasciitis
- Fourniere's gangrene
- Mixed aerobic and anaerobic infection
- Ischemic gangrene with tissue infection

개 요

- Aerobic / Anaerobic / Mixed bacterial floras

- Immune-compromised
  - Underlying systemic disease
    - DM, malignancy, vascular insufficiency, alcoholism
  - Transplantation : immunosuppressive drug
  - Neutropenia

- After trauma
- Surgical wound : around foreign body
- Spontaneously : *i.e.* Fournier's gangrene
- Post op. : C-sec (without risk factors), even after "sterile" op.



suspicion

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Epidemiology

- 미국의 경우 한해 약 500-1,500건의 괴사성 연조직염이 발생(10만명 당 4건) , 8-65%(평균 21.9%)의 높은 사망률

- 국내의 경우 2000-2010년 입원한 환자들을 대상으로 한 다기관 연구에서 21.2%(21/99)의 환자가 입원 치료 중 사망, 최근(2012-2015년) 시행된 연구에서도23.2%(39/168)의 환자가 사망

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Pathophysiology

- Deep fascial layer에 infective process (anaerobe)
  - Phlegmon(abscess) with edema and necrosis
- Blood supply to skin is affected
  - Skin: Perfusion pressure ↓, ischemia ↑

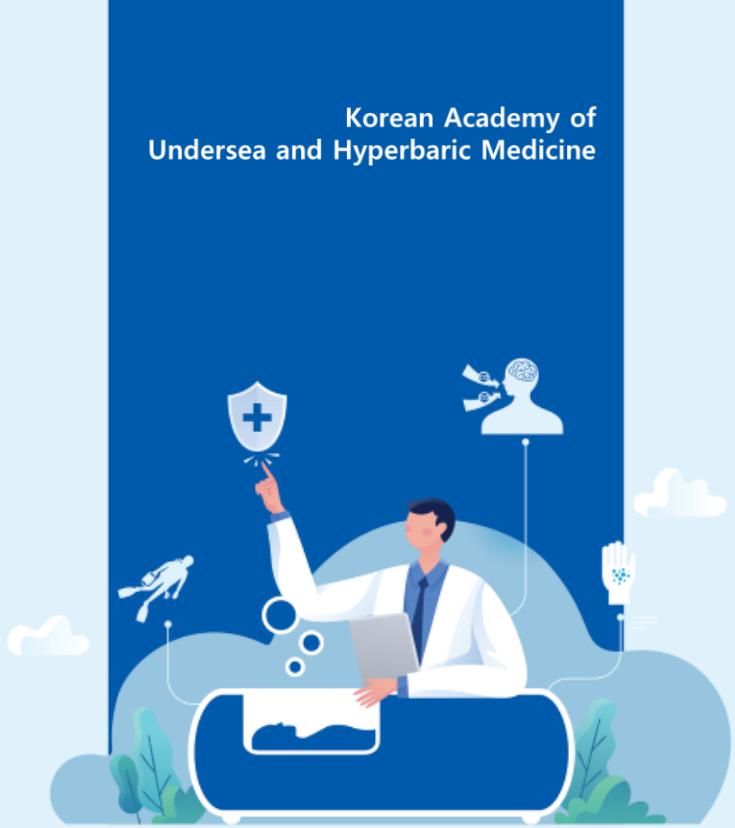
    → Rapid progression of Infection

    (hypoxia induced PML dysfunction)
- Local hypoxia with Up-regulation of endothelial adherence molecule

  : leukocyte adhesion, endothelial cytotoxicity
- Tissue necrosis, purulent discharge, gas production

- Early recognition
- Etiology
- Bacteriology
- Clinical course

- Morbidity
- Mortality
  - From 20%
  - Up to 70-80%
    - older, debilitated, diabetic



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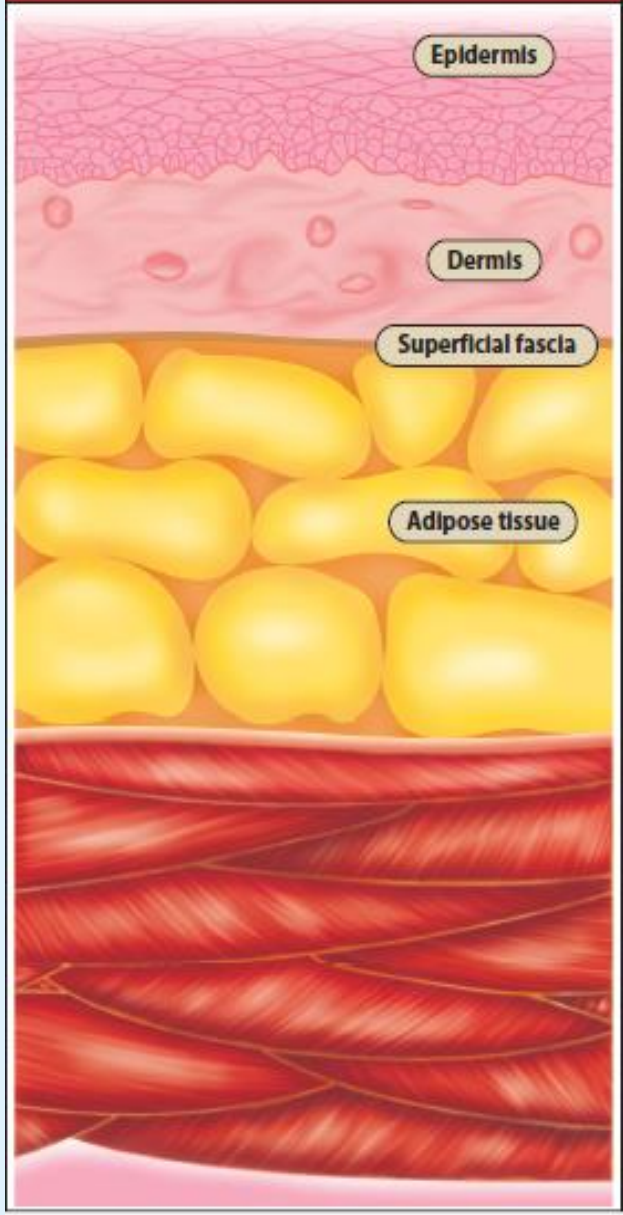

Anatomy	Syndrome	Etiology
Skin	Erysipelas	Group A *Streptococcus*
	Impetigo	Group A *Streptococcus* *Staphylococcus aureus*
	Ecthyma	Group A *Streptococcus* *Pseudomonas aeruginosa*
	Folliculitis	*S aureus; P aeruginosa* (whirlpools); rarely *Candida*
	Furunculosis	*S aureus*; group A *Streptococcus* *P aeruginosa*
Subcutaneous tissue	Cellulitis	Group A *Streptococcus* *S aureus* (MSSA or MRSA) Occasionally gram-negative enteric bacilli *Aeromonas hydrophila; Vibrio vulnificus*
	Anaerobic cellulitis	*Clostridium perfringens* *Bacteroides, Peptostreptococcus, Peptococcus, Prevotella* + gram-negative enteric bacilli *(E coli, Klebsiella, Proteus)*
Deep fascia	Meleney gangrene	*S aureus* or *Proteus* and microaerophilic streptococci
Muscle	Necrotizing fasciitis	Mixed gram-positive and negative organisms (*S aureus, E coli, Klebsiella, Proteus*) and anaerobes (*Bacteroides, Peptostreptococcus, Peptococcus, Prevotella*) Group A *Streptococcus* *S aureus* (MRSA)
	Clostridial myonecrosis	*C perfringens* (sometimes non-*perfringens* species)
	Nonclostridial synergistic myonecrosis	As for necrotizing fasciitis
	Pyomyositis	*S aureus*; rarely group A *Streptococcus*; *P aeruginosa*

Source: Jesse B. Hall, Gregory A. Schmidt, John P. Kress: *Principles of Critical Care*, 4th Edition: www.accessmedicine.com
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CLASSIFICATION

It is difficult to classify...

- Assumed causative microorganism
- Involved tissue
- Required therapy
- Rate of progression
- Initial clinical findings

Amsterdam classification

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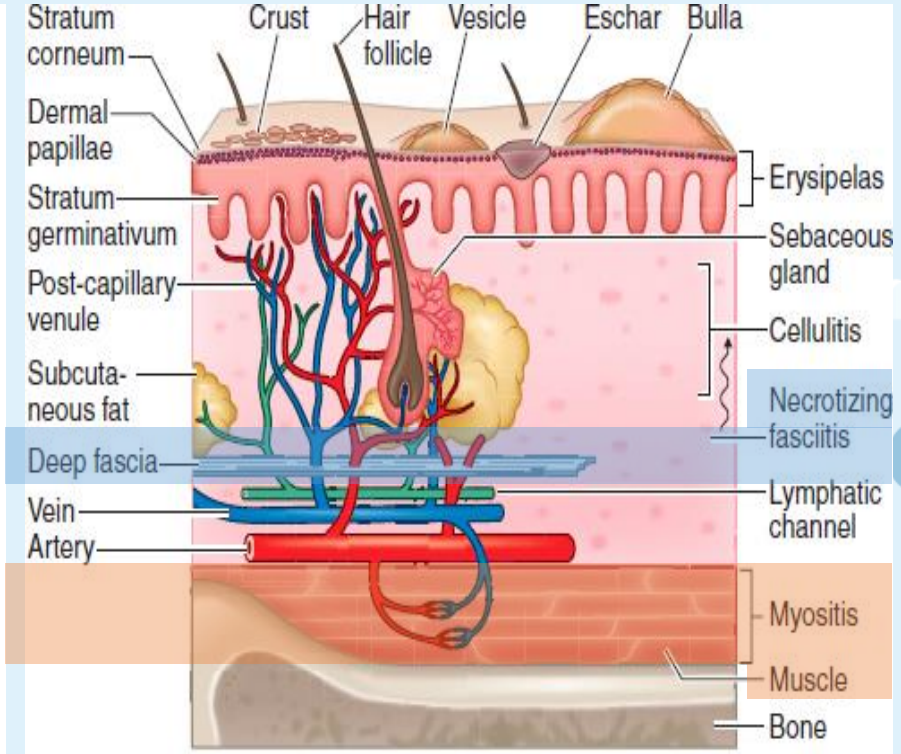
Amsterdam classification

- Progressive bacterial gangrene
  - Anaerobic
    - Clostridial
    - Nonclostridial
  - Aerobic
  - Mixed
- Necrotizing fasciitis
  - Anaerobic
  - Aerobic
  - Mixed
- Myositis and myonecrosis
  - Anaerobic
    - Clostridial
    - Nonclostridial (streptococcal)
  - Others
    - Aerobes
    - Viruses
    - Parasites



Source: J.L. Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Principles of Internal Medicine, 20th Edition
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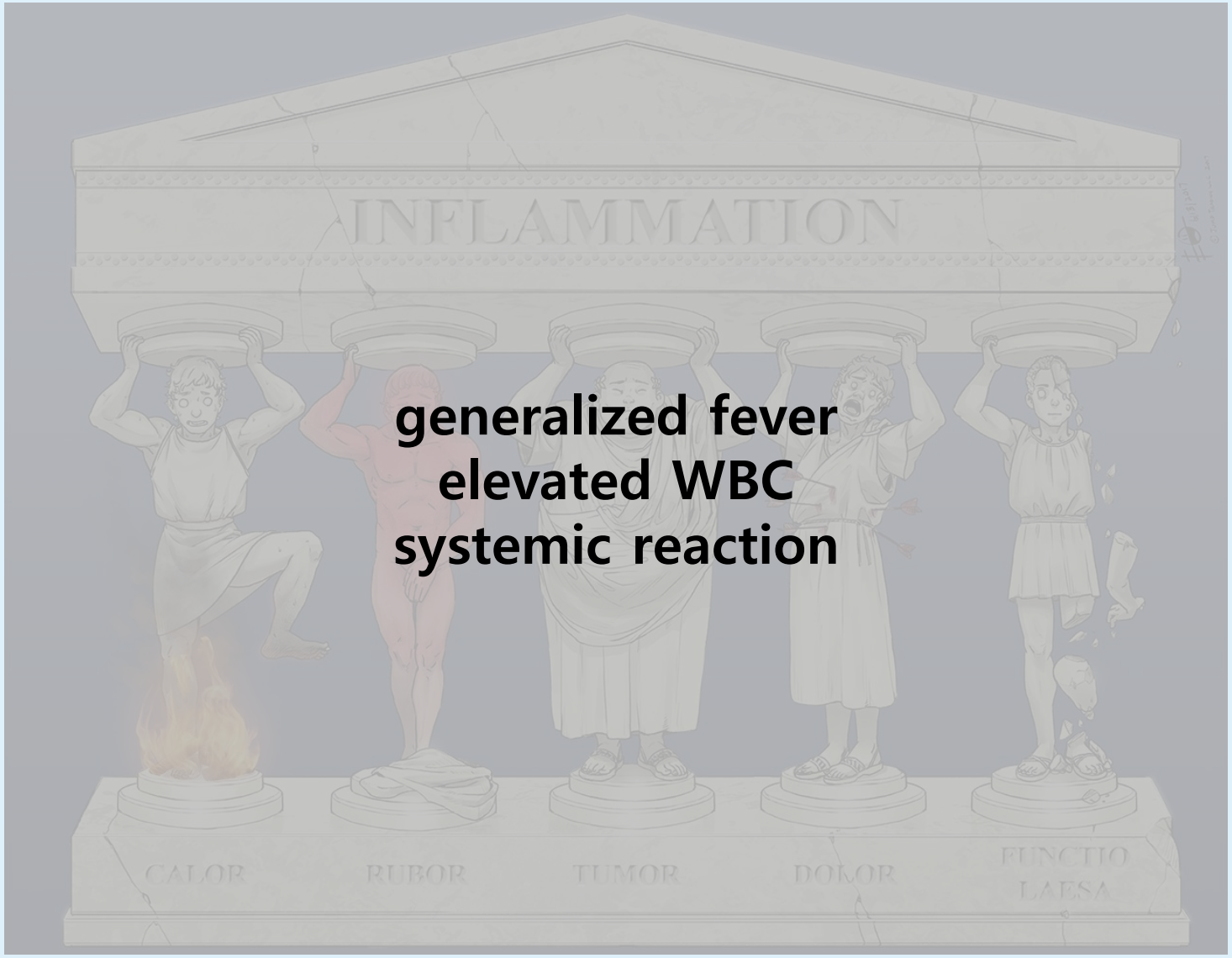
DIAGNOSIS



generalized fever
elevated WBC
systemic reaction

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- Simple model – necrotizing fasciitis vs. nonnecrotizing ST infection At admission
  - ✓ WBC > 15,400
  - ✓ Na^+ < 135 mmol/L

Table 1. LRINEC Score

Variable	Result	Score
C-reactive protein (mg/L)	<150 ≥150	0 4
White blood cell count ($\times 10^9$/L)	<15 15-25	0 1
Hemoglobin (g/dL)	>13.5 11-13.5 <11	1 2 0
Sodium (mmol/L)	≥135 <135	0 2
Creatinine (mcg/L)	≤141 >141	0 2
Glucose (mmol/L)	≤10 >10	0 1

LRINEC: Laboratory Risk Indicator for Necrotizing Fasciitis. Source: References 1, 2.

- A total score of 8 or more is strongly predictive of an NSTI.

- Gram s

Surgical therapy

- Sonography / CT / MRI : to clarify involved anatomic site

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Progressive Bacterial Gangrene

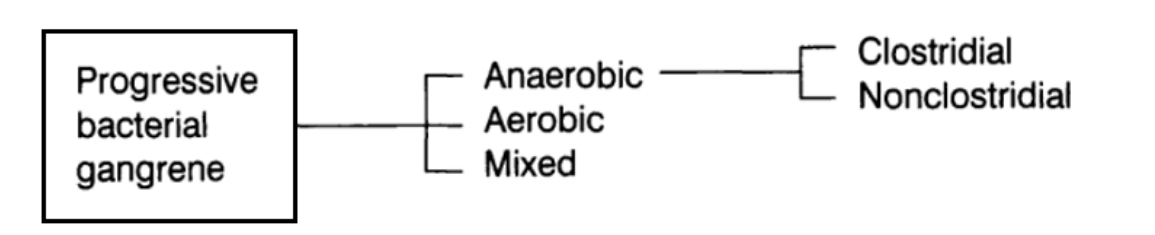
Postoperative progressive bacterial synergistic gangrene
Cullen's ulcer
chronic infectious skin gangrene

- anaerobic crepitant / clostridial cellulitis
- pyoderma gangrenosum
- erysipelas
- gangrenous / necrotizing erysipelas
- symbiotic gangrene
- phagedena geometrica

- directly related to skin infection
- epidermis, dermis, SQ tissue, lymphatics, hair follicle, ~~deep fascia~~

~~muscle compartment~~

- group A streptococci, *S. aureus*
- anaerobic microorganism : *Bacteroides* spp., *Clostridium* spp., Enterobacteriaceae, *Proteus*, *Pseudomonas*...



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Progressive Bacterial Gangrene

- **Always, Very painful!**

- Infection → marginal cellulitis → centrifugal necrosis skin SQ
  patchy, purplish discoloration

- Extensive ST damage, vascular insufficiency
  → true <u>clostridial</u> <u>myositis / myonecrosis</u>

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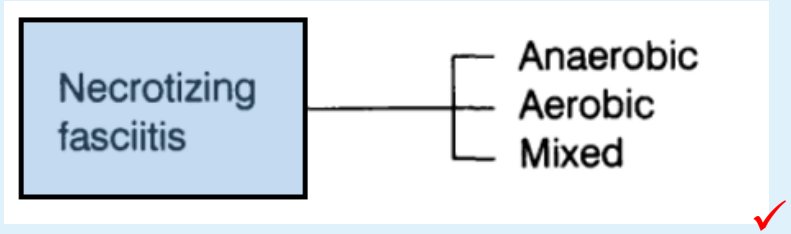
Necrotizing Fasciitis

hemolytic streptococcal gangrene
Meleney's ulcer
acute dermal gangrene

- Hospital gangrene
- Suppurative fasciitis
- Fournier's gangrene
- Synergistic necrotizing cellulitis
- Hemolytic streptococcal gangrene

- **Deep fascia → SQ tissue, skin**
- **rapidly spreading along deep fascial plane**
  mo' extended than visible change

- **Fade-out margin : pathognomonic feature**
- **Surgical wound, injured site, spontaneously**



✓ *Streptococcus pyogenes*

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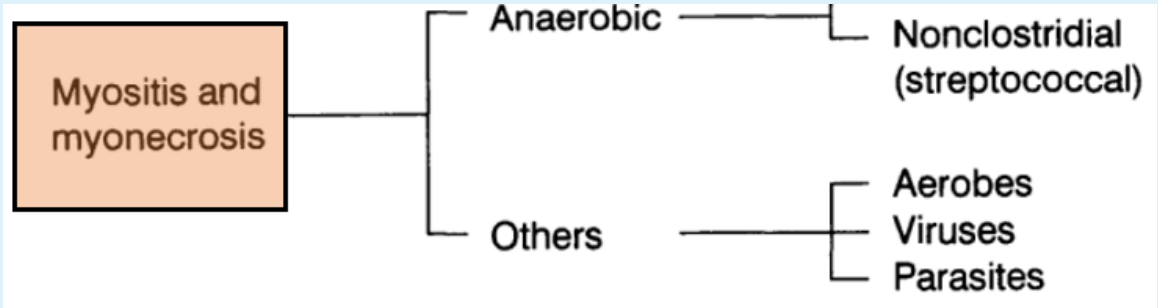
Nonclostridial Myonecrosis

- vs. Gas gangrene?
  - Greenish necrotic muscle
    cf. gas gangrene: black necrotic muscle
  - More inflamed appearance than gas gangrene
  - Less gas amount



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THERAPY

- Surgical debridement
- Appropriate antibiotics
- Nutritional support
- Optimal oxygenation – HBO_2

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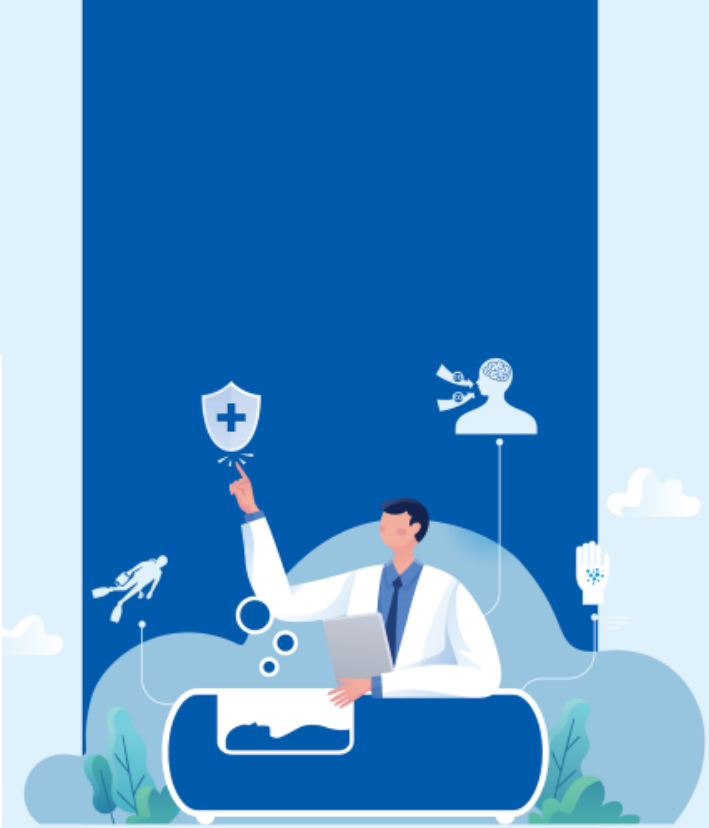
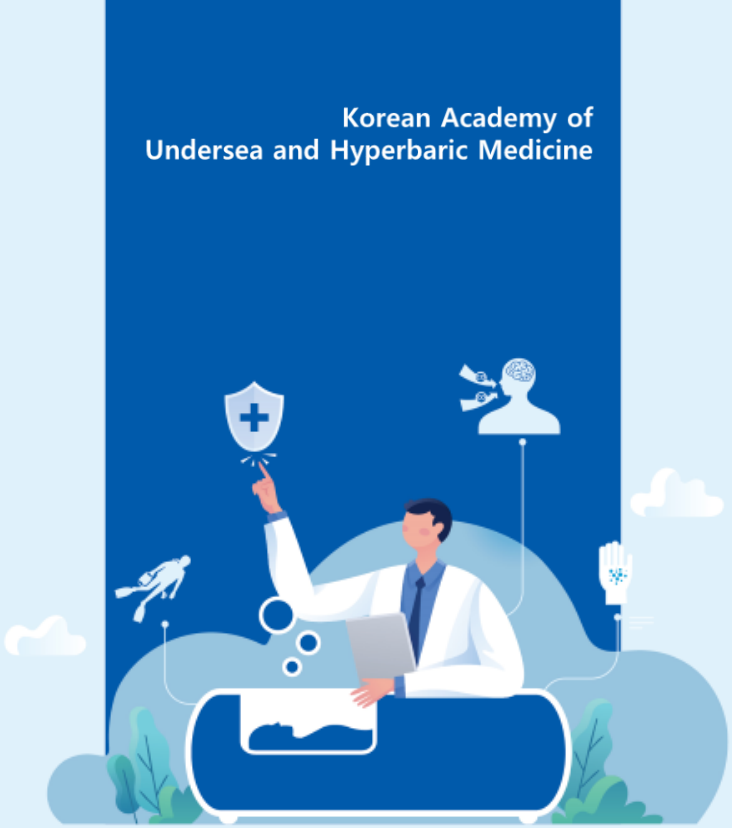
SURGICAL THERAPY

Progressive bacterial gangrene	necrotomy & skin grafting I&D
Necrotizing fasciitis	“fillet” procedure (excision of necrotized fascia)
Myositis and myonecrosis	muscle removal



Ⅱ

연조직 괴사 감염(Necrotizing soft tissue infection)에서 고압산소치료의 작용 기전과 임상적 적용에 대한 이해



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Rationale & Mechanism of adjunctiveHBO$_2$

- **MAIN GOALS ➔ host defense & repair mechanisms**

  ↑ tissue PO$_2$
  ↑ phagocytic function
  ↓ edema
  ↑ circulation
  ↑ fibroblast growth
  ↑ collagen formation

- Hypoxic leukocyte dysfunction을 개선
- Enhance oxygen diffusion
  - -Provide oxygen to ischemic area
  - -Limiting spread of infection
- Enhance antibiotic penetration into target bacteria (eg, Aminoglycoside)
- Bacteriostatic/Bactericidal effect
- Hyperoxygenation – preservation of flaps

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Necrotizing fasciitis HBO_2 positive report

- Necrotizing fasciitis
  - Wilkinson and Doolette *(2004 Arch surg)*
    - Retrospective cohort study, 44 patients
    - HBO_2 increased survival (odd ratio 8.9)
  - Devaney *(2015 Anaesth Intensive Care)*
    - 341 pts, retrospective case controlled study, 275명 HBO_2시행
    - Mortality: HBOT group 12 % Vs. non-HBOT group 24.3%
- Fourniere's gangrene
  - Hollabaugh, retrospective 26 cases *(1998 Plast Reconstr Surg)*
  - Mortality: HBOT group 7% Vs. non-HBOT group 42 %(p=0.04)

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Necrotizing fasciitis HBO_2 positive report

Surg Infect (Larchmt). 2014 Jun 1; 15(3): 328–335. PMCID: PMC4696431
doi: 10.1089/sur.2012.135

Not Just Full of Hot Air: Hyperbaric Oxygen Therapy Increases Survival in Cases of Necrotizing Soft Tissue Infections

Joshua J. Shaw,[1,2] Charles Psoinos,[1] Timothy A. Emhoff,[1] Shimul A. Shah,[3] and Heena P. Santry[1,2]

Author information ▶ Copyright and License information ▶

This article has been cited by other articles in PMC.

Abstract

Go to:

Background: The utility of hyperbaric oxygen therapy (HBOT) in the treatment of necrotizing soft tissue infections (NSTIs) has not been proved. Previous studies have been subject to substantial selection bias because HBOT is not available universally at all medical centers, and there is often considerable delay associated with its initiation. We examined the utility of HBOT for the treatment of NSTI in the modern era by isolating centers that have their own HBOT facilities.

Methods: We queried all centers in the University Health Consortium (UHC) database from 2008 to 2010 that have their own HBOT facilities (n=14). Cases of NSTI were identified by *International Classification of Diseases, Ninth Revision* (ICD-9) diagnosis codes, which included Fournier gangrene (608.83), necrotizing fasciitis (728.86), and gas gangrene (040.0). Status of HBOT was identified by the presence (HBOT) or absence (control) of ICD-9 procedure code 93.95. Our cohort was risk-stratified and matched by UHC's validated severity of illness (SOI) score. Comparisons were then made using univariate tests of association and multivariable logistic regression.

Results: There were 1,583 NSTI cases at the 14 HBOT-capable centers. 117 (7%) cases were treated with HBOT. Univariate analysis showed that there was no difference between HBOT and control groups in hospital length of stay, direct cost, complications, and mortality across the three less severe SOI classes (minor, moderate, and major). However, for extreme SOI the HBOT group had fewer complications (45% vs. 66%; $p<0.01$) and fewer deaths (4% vs. 23%; $p<0.01$). Multivariable analysis showed that patients who did not receive HBOT were less likely to survive their index hospitalization (odds ratio, 10.6; 95% CI 5.2–25.1).

Conclusion: At HBOT-capable centers, receiving HBOT was associated with a significant survival benefit. Use of HBOT in conjunction with current practices for the treatment of NSTI can be both a cost-effective and life-saving therapy, in particular for the sickest patients.

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Necrotizing fasciitis HBO_2 negative report

- George ME *(Surg Infect; 2009)*
  - Retrospecitve 78 case
  - HBO does not improve outcome in NSTI
- Massey PR *(J surg Res; 2012)*
  - Retrospective, 80 case
  - HBO does not appear to decrease in-hospital mortality
- Hassan Z *(Undersea Hyperb Med; 2010)*
  - Retrospective, 67 case
  - No difference in mortality

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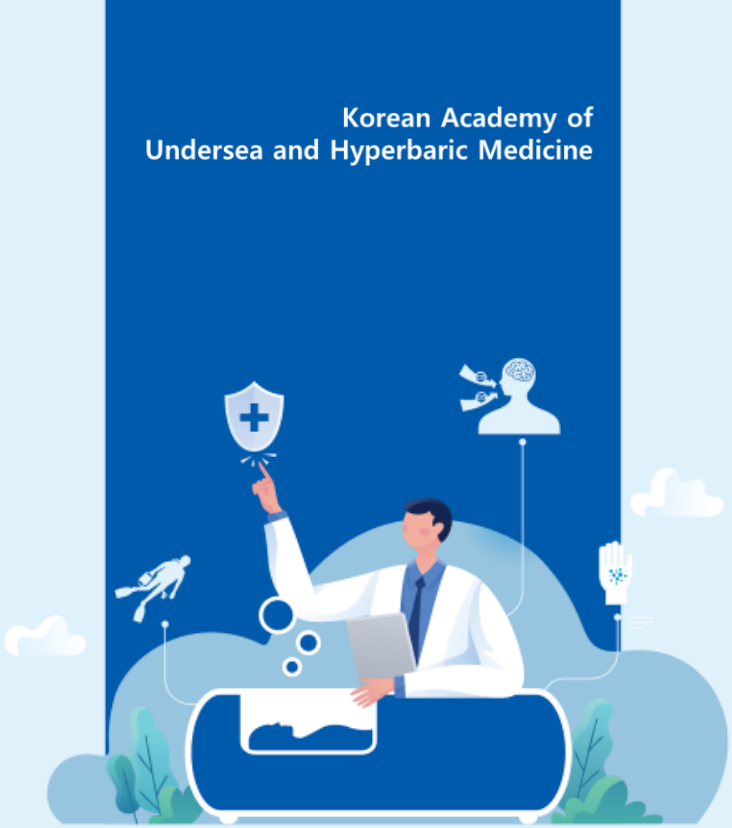
Ⅲ 연조직 괴사 감염(Necrotizing soft tissue infection)에서 기존 치료와 고압산소치료 통합 알고리즘 소개



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치료 과정 알고리즘-1

괴사성 연조직염
의심 소견
피부병변(홍반, 부종, 열감)+전신 증상(발열, 저혈압)

전형적 소견
-피부병변(수포, 점상 출혈, 피부 괴사)
-촉진 시 염발음
-감각저하
-임상 소견에 비해 심한 통증

예

혈액 배양 검사
경험적 광범위 항생제

응급 시험적 수술
조직 표본 확보(그람 염색 및 배양 검사, 병리검사)
적극적 죽은조직제거술
고압산소치료 병행 요법*

재평가(수술 후 24시간 내)에 따라
추가적 죽은조직제거술

아니오

혈액 배양 검사
경험적 광범위 항생제

영상 검사(CT, MRI, US) 양성
LRINEC score ≥ 6
임상 진찰 소견 악화
-촉진 시 염발음
-임상 증상의 급성 악화
-피부 병변에 비해 심한 통증
-지속적인 염증, 발열, 백혈구 증가

예

아니오

배양 검사 결과에 따른 항생제 치료 유지
보존적 치료

고압산소치료 병행요법*
1-3일차: 2.0-2.5기압으로 90분간 2회/24시간
4일차부터: 2.0-2.5기압으로 90분간 1회/24시간
(단, 곰팡이 감염 2.4-3.0기압/클로스트리듐 감염 2.8-3.0 기압)

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치료 과정 알고리즘-2

가스 괴저
배양 결과 양성 또는
임상 양상에 따라 진단

↓

고용량 항생제
죽은조직제거술

↓

고압산소 치료의
이득과 위험 고려

이득 요인
- 포함된 조직의 범위가 넓을 때
- 항생제나 수술의 효과가 미흡할 때
- 수술 하기 어려운 환자 상황
- 면역 저하 환자

위험 요인
- 고농도의 승압제/강심제/인공호흡기 적용 시
- 다 장기 부전시
- 고압 챔버의 사용의 환경적 문제

위험에 비해
이득이 크다면

고압산소 치료 시행
1일차- 2.8-3.0기압으로 90분간 2-4회
2-3일차: 2.8-3.0기압으로 90분간 2회
4-7일차: 2.8-3.0기압으로 90분간 1회

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요 약

- Although RCT's do not exist, the mechanism of HBO make sense in mitigating(완화) the pathophysiology of these conditions

□ HBO_2 is always an adjunct to antibiotics and surgery

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Ⅳ 당뇨발 (Diabetic foot ulcer)의 임상적 특징

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당뇨 임상 양상

- Diabetes has a constellation of pathologies

  - Autonomic neuropathy = Mechanical Deformities (*e.g.,* clawfoot)

  - Sensory neuropathy = Loss of protective sensation

  - Hyperglycemia
    = Osmotic diuresis
    = Limits neutrophil functioning
    = Increased catabolism

  - Microvascular disease
    = Lack of hyperemic response to injury
    = Decrease oxygen diffusion across basement membrane

  - Macrovascular disease
    = Increased atherosclerosis of lower extremity vessels

DFUs (Diabetic foot ulcer) Epidemiology

- DM ⇒ Approximately 25.8 million people, or roughly 8.3% of the U.S. population

National diabetes fact sheet. national estimates and general information on diabetes and prediabetes in the United States. 2011, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention: Atlanta, GA.

- More than 60% of non-traumatic amputations in the US occur in people with DM
  - DM foot ulcer (DFU) precedes 85% of lower-limb amputations in patients with DM.

Cowie Catherine C. Diabetes: 1996 vital statistics. 1996, University of Michigan: American Diabetes Association.

- Contralateral leg amputation ⇒ 56% of patients within three to five years

NIH Cancer Fact Sheet. 2010, National Institutes of Health.

- The five-year mortality rate for DM who have had a single-leg amputation ⇒ 60% ↑ the overall five-year mortality rate of all cancers combined (32%)

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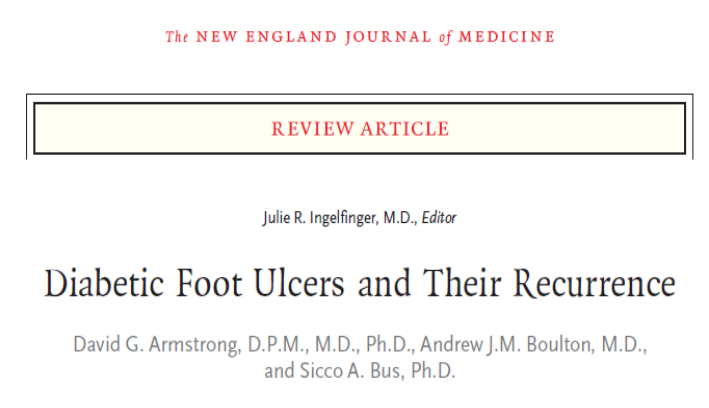
DFUs 발생 및 재발 과정


The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Julie R. Ingelfinger, M.D., *Editor*

Diabetic Foot Ulcers and Their Recurrence

David G. Armstrong, D.P.M., M.D., Ph.D., Andrew J.M. Boulton, M.D., and Sicco A. Bus, Ph.D.

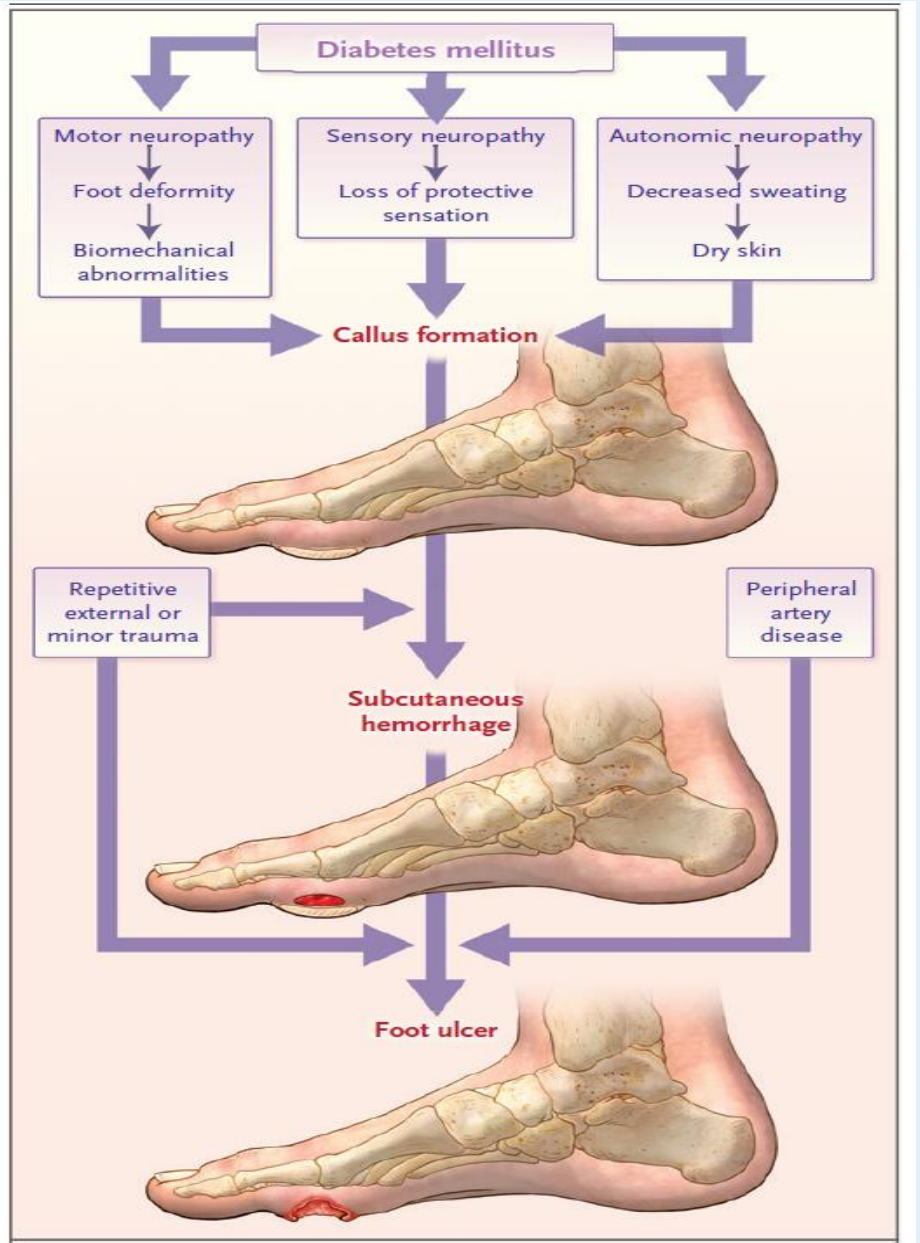


Figure 1. Common Pathway of Diabetic Foot Ulcer Occurrence and Recurrence. Diabetic foot ulcers and their recurrences are caused by a number of factors that ultimately lead to skin breakdown. These factors include sequelae related to sensory, autonomic, and motor neuropathies.

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Courtesy of Dr Huang

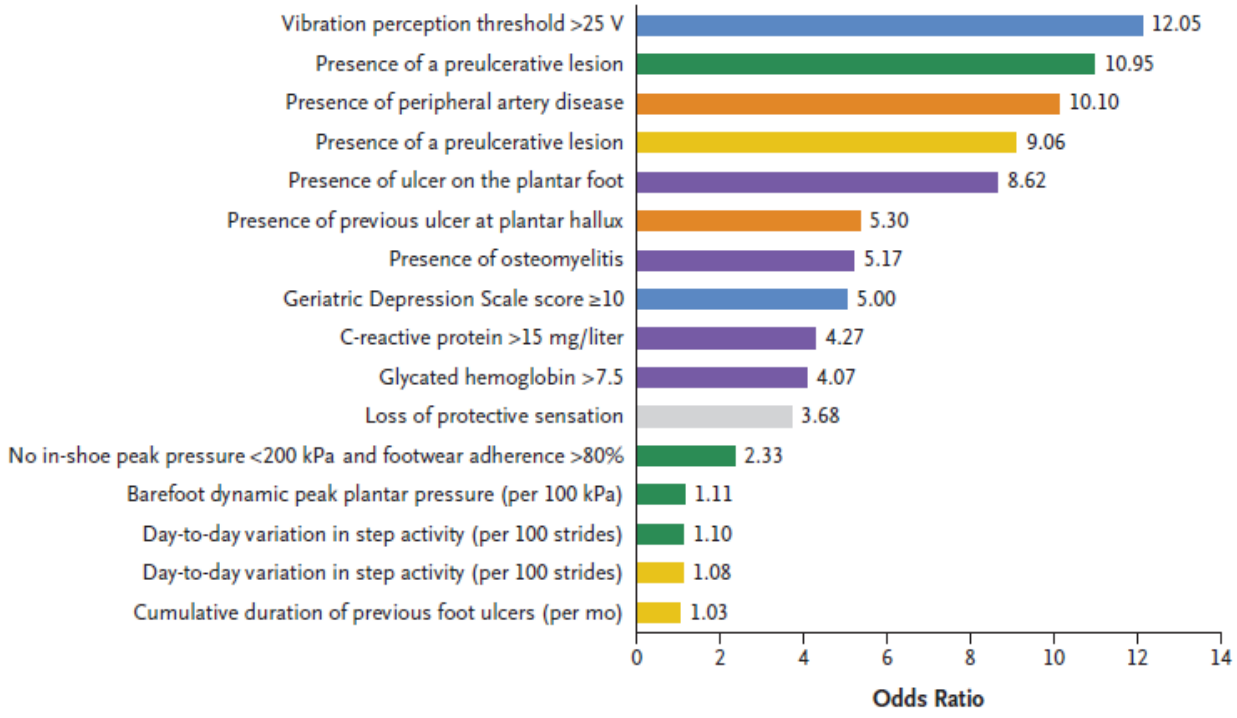
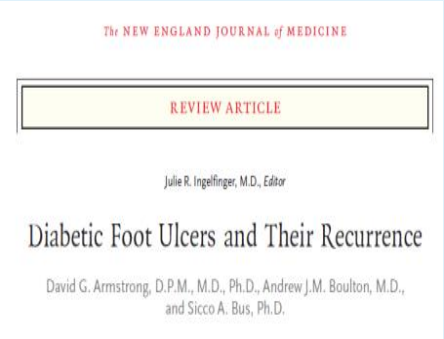


Figure 3. Risk Factors Independently Associated with Ulcer Recurrence.

Data are from five studies that reported an odds or risk ratio.[28,33,42,52,56] According to Monami et al.[42] (blue), risk factors for ulcer recurrence are a vibration perception threshold greater than 25 V and a Geriatric Depression Scale score of 10 or higher (scores range from 0 to 15, with higher scores indicating more severe depression). According to Peters et al.[56] (orange), risk factors for ulcer recurrence are the presence of peripheral artery disease and location of the previous ulcer at the plantar hallux. According to Dubský et al.[28] (purple), a plantar location of the ulcer, the presence of osteomyelitis, and elevated blood levels of C-reactive protein and glycated hemoglobin (all of which were determined at the time of study enrollment for patients with an active foot ulcer) are independent predictors of recurrence of foot ulcers. According to Reiber et al.[33] (gray), loss of protective sensation is a risk factor for recurrence of an ulcer on the plantar surface of the foot. According to Waaijman et al.,[52] risk factors for recurrence of an ulcer on the plantar surface of the foot (yellow) include the presence of a preulcerative lesion, low day-to-day variation in step activity, and a long cumulative duration of previous foot ulcers; risk factors for recurrence of a pressure-related plantar ulcer (green) include the presence of a preulcerative lesion, lack of both in-shoe peak pressure below 200 kPa and therapeutic-footwear adherence higher than 80%, high barefoot dynamic peak plantar pressure, and low day-to-day variation in step activity.


The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Julie R. Ingelfinger, M.D., Editor

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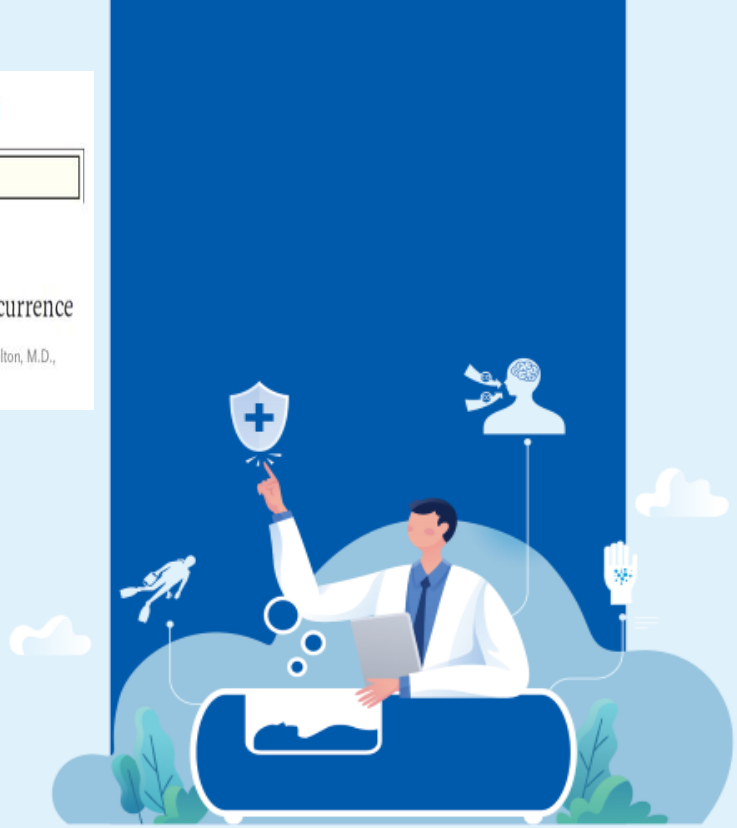

DFUs 재발 위험인자

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DFUs 예방 및 치료 과정

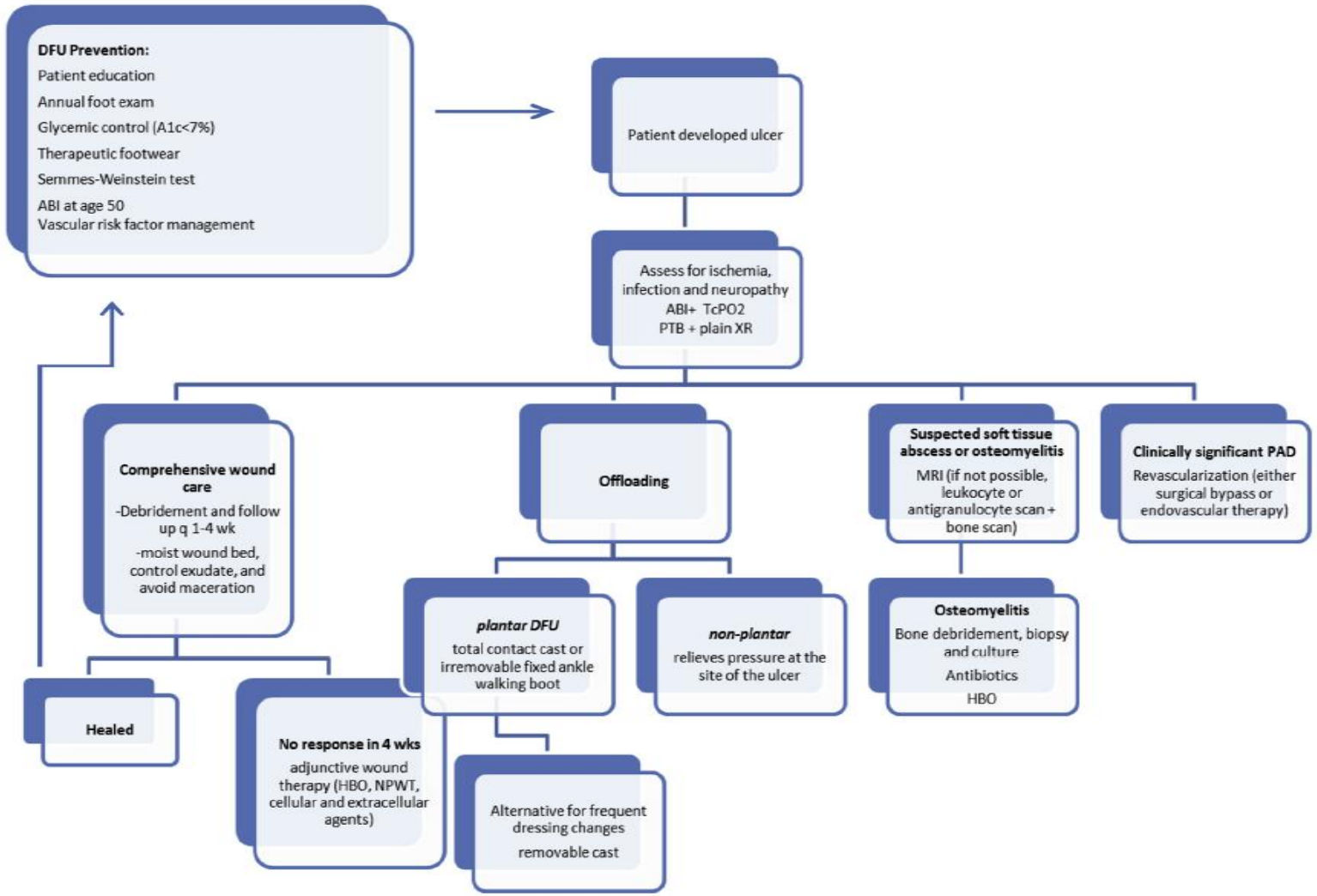

Fig. Algorithm for prevention and care of diabetic foot. *ABI*, Ankle-brachial index; *DFU*, diabetic foot ulcer; *HBO*, hyperbaric oxygen; *MRI*, magnetic resonance imaging; *NPWT*, negative pressure wound therapy; *PAD*, peripheral arterial disease; *PTB*, probe to bone; $TcPo_2$, transcutaneous oxygen pressure; *XR*, radiography.

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- The International Working Group on the Diabetic Foot (IWGDF) guidelines for the best practice treatment of DFUs

- Revascularization if appropriate and feasible (V)
- Off-loading to minimize trauma to the ulcer site (O)
- Treatment of underlying infection (I)
- Management of the wound bed to promote healing (D)

V - Vascular O - Offloading I - Infection D - Diabetes Control

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Risk evaluation

Figure 3 Risk categories

Risk category 0	Risk category 1	Risk category 2	Risk category 3
Normal Plantar Sensation	Loss of Protective Sensation (LOPS)	LOPS with either High Pressure or Poor Circulation or Structural Foot Deformities or Onychomycosis	History of Ulceration, Amputation or Neuropathic Fracture
LOW RISK	MODERATE RISK	HIGH RISK	VERY HIGH RISK

IDF Clinical Practice Recommendations on the Diabetic Foot – 2017

A guide for healthcare professionals

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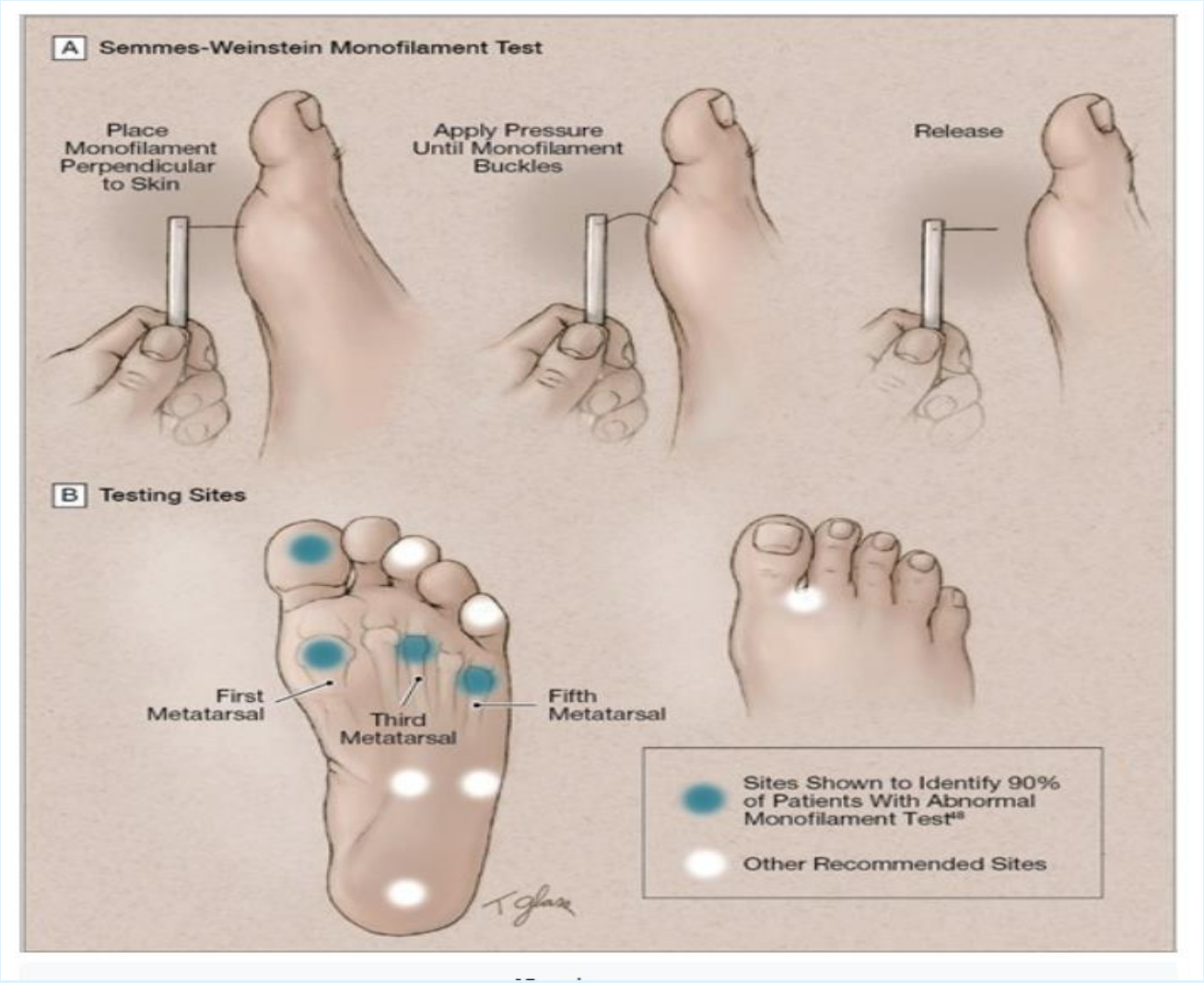
Prevention

- 

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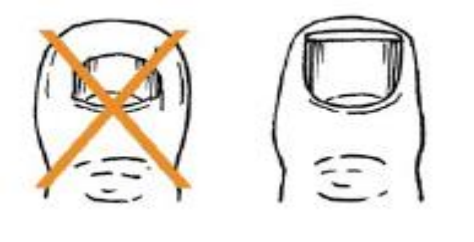
Prevention

- Educating the patients and their family (1C)
  - Check shoes before putting on
  - Change shoes daily if possible
  - Not check bathwater with their feet
  - Wash feet daily
  - Not use perfumed soaps
  - Keep feet moisturized with creams but not between the toes
  - Never walk barefoot
  - Wear shower shoes

  - Self-inspection criteria
    - Redness
    - Blister
    - Callus
    - Open sore (ulcer)
    - Swelling
    - Dryness
    - Nail thickness, length or tenderness

- Use specialized therapeutic footwear in average risk (2C)
- Use custom therapeutic footwear in high-risk (1B)



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Prevention

- HbA1C < 7% (2B)
- Against prophylactic arterial revascularization (1C)
  - Indication
    - = Severe claudication
    - = Rest pain
    - = Tissue loss (1B)

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Off loading DFUs

- Plantar DFU with TCC (1B)
- DFU with frequent dressing remov able cast walker (2C)
  - Against post-op shoes
- With nonplantar wounds anything to relieve pressure (1C)
- For high-risk with healed DFU, we ar therapeutic footwear (1C)

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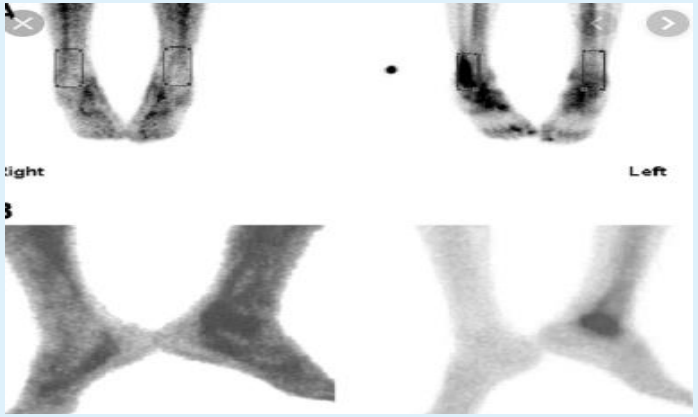
Diagnosis of diabetic foot osteomyelitis

- Diabetic foot infection (DFI) with an open wound
  - Probe to bone test (2C)
    - Diagnosis of OM
      - 60% sensitivity
      - 91% specificity
  - Plain X-ray (2C)
      - 54% sensitivity
      - 68% specificity
  - MRI (1B)
      - 90% sensitivity
      - 79% specificity
  - Leukocyte or antigranulocyte scan (2B)
    - For MRI contraindicated
      - 81% sensitivity
      - 28% specificity
  - Bone biopsy (1C)
    - When debridement done
      - Limited studies
  - Diagnostic bone biopsy (2C)
    - Bone culture
    - Only when empirical treatment fails



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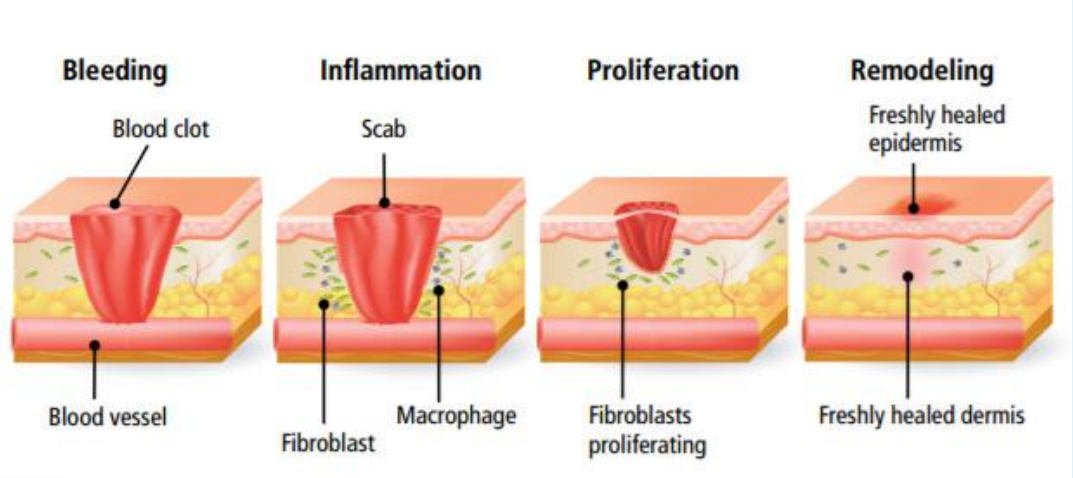
Wound care

- Requires frequent inspection with irrigation and debride ment, protective dressings, inspection and inflammation control, and plantar off-loading.

- Preserve a moist, non-infected wound environment.



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Wound care

- Frequent evaluation at 1 to 4 weeks (1C)
  - Wound size reduction
    - Early predictor of treatment outcome
      - 10%-15% per week or more than 50 in 4 weeks
        - » Decreased complication and amputation
  - Initial surgical intervention for abscess, gas or necrotizing fasciitis (1B)
- Use dressing products that maintain a moist wound bed, contr ol exudate, and avoid maceration. (1B)
  - Non-adherent dressings
  - Silmazine, honey, etc

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Wound care

- Debridement (1B)
  - Drainage of exudate
  - Removal of nonviable tissue
  - Assess the wound
  - Removal of surrounding callus material
- Method of debridement
  - Surgical, Larva, hydrotherapy, ultrasound, hydrogel, enzy matic
  - NO more saline-soaking gauze
- Adjunctive therapy
  - For DFU with no improvement after 4 weeks
    - Negative pressure (2B)
    - PDGF (2B), living cellular (2B), amniotic membrane
    - HBOT (2B) – reduced amputation rate, increased healing rate

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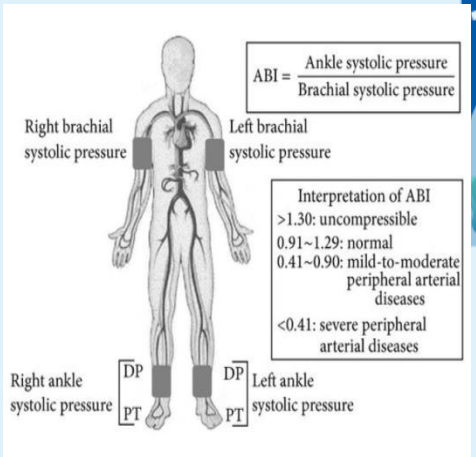
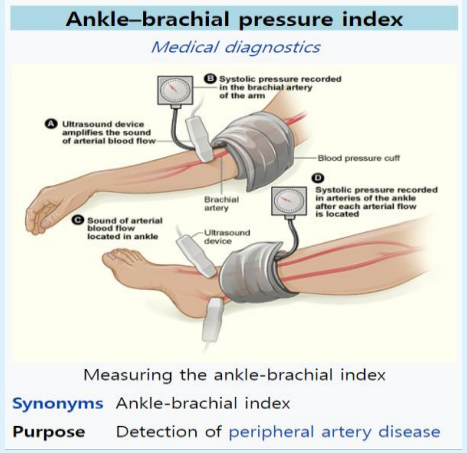
PAD

- ABI measurement from 50 years of age (2C)
  - <0.8 : increased risk of limb loss
- Pedal perfusion assessed by ABI, pedal doppler arte rial waveforms, toe systolic pressure or TcPO2 (1B)
  - Toe Systolic pressure <30 mmHg : increased risk
- DFU with PAD
  - Surgical or endovascular therapy (1B)





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V 당뇨발에서의 고압산소치료 기전과 임상적 적용에 대한 이행

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Hyperbaric oxygen ?

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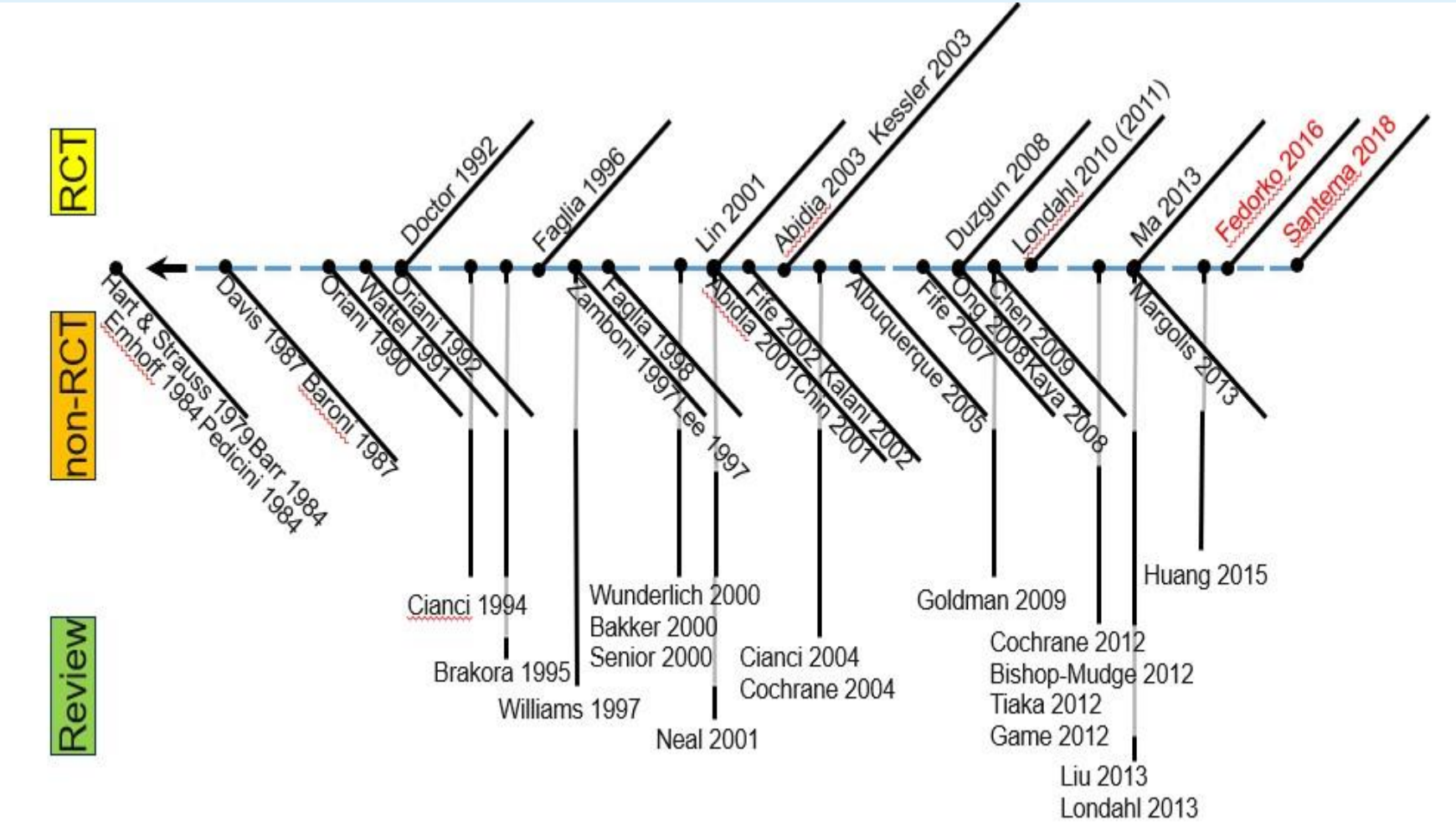
Timeline of Studies



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Overview of Studies

Study	Study Design	N	Study Population (Wagner grade)	Co-Morbidities Addressed				HBO_2 Protocol	Strength of Evidence	Generalizable Results
				V	O	I	D			
Hart 1979	RCaS	11	NS	☆	☆	☆	☆	NS	Low	Low
Davis 1987	RCaS	168	NS	★	☆	★	★	NS	Low	Moderate
Baroni 1987	PCoT	18 vs 10	1 2 3 4 5	★	★	★	★	2.5-2.8 Daily	Low	Moderate
Oriani 1990	RCoT	62 vs 18	1 2 3 4 5	★	★	★	★	2.5-2.8 Daily	Low	Moderate
Wattel 1991	PCaS	59	1 2 3 4 5	☆	★	☆	☆	2.5 BID	Moderate	High
Doctor 1992	RCT	15 vs 15	1 2 3 4 5	★	★	☆	☆	Atypical	Moderate	Low
Faglia 1996	RCT	35 vs 33	1 2 3 4 5	★	★	★	★	2.2-2.5 Daily	High	Moderate
Zamboni 1997	PCoS	5 vs 5	1 2 3 4 5	☆	☆	☆	★	2.0 Daily	Moderate	Moderate
Faglia 1998	RCoT	51 vs 64	1 2 3 4 5	☆	☆	☆	☆	2.2-2.5 Daily	Moderate	Moderate
Lin 2001	RCT	17 vs 12	1 2 3 4 5	☆	☆	☆	☆	2.5 Daily	High	Moderate
Kalani 2002	PCoT	17 vs 21	1 2 3 4 5	☆	☆	☆	☆	2.5 Daily	Moderate	Moderate
Fife 2002	RCaS	774	1 2 3 4 5	★	☆	☆	☆	2-2.5 Daily	Moderate	Moderate
Abidia 2003	RCT	9 vs 9	1 2 3 4 5	☆	☆	☆	☆	2.4 Daily	High	Moderate
Kessler 2003	RCT	14 vs 13	1 2 3 4 5	☆	☆	☆	☆	2.5 BID	Moderate	Low
Fife 2007	RCaS	971	1 2 3 4 5	★	☆	☆	☆	2-2.5 Daily	Moderate	Moderate
Duzgun 2008	RCT	100	1 2 3 4 5	☆	☆	☆	★	Atypical	Moderate	Moderate
Löndahl 2010	RCT	38 vs 37	1 2 3 4 5	★	☆	☆	★	2.5 Daily	High	High
Ma 2013	RCT	18 vs 18	1 2 3 4 5	★	★	★	★	2.5 BID	High	Moderate
Margolis 2013	RCoT	793 vs 5466	1 2 3 4 5	☆	☆	☆	☆	2-2.5 Daily	Low	Low

RCT - Randomized Controlled Trial PCoT - Prospective Cohort Trial PCaS - Prospective Case Series RCoT - Retrospective Cohort Trial RCoS - Retrospective Case Series

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Baroni 1987

The Question	Does HBO_2 improve healing in DFU?					
Study Design	Prospective Cohort Trial (N=28)				Study Population (Wagner grade)	1 2 3 4 5
					Comparison	18 HBO_2 vs. 10 ØHBO_2
Co-Morbidities Addressed	V	O	I	D	HBO_2 Protocol	2.5-2.8 ATA x90 min 6/7 days (34±21 Tx)
	★	★	★	★		
Strength of Evidence	Low				Generalizability	Moderate - all patients hospitalized
The Answer	HBO_2 significantly improved healing rate (89% vs. 10%,p=.001) and decreased amputation rate (11% vs. 40%, p=.001). It suggests faster healing as decreased hospital LOS (62 days vs 82 days, NS).					

★ Well Addressed ★ Moderately Addressed ★ Poorly Addressed ☆ Not Addressed

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Oriani 1990

The Question	Does HBO_2 improve healing in DFU?				
Study Design	Retrospective Cohort Trial (N=80)			Study Population	1 2 3 4 5
				Comparison	62 HBO_2 vs 18 ØHBO_2
Co-Morbidities Addressed	V	O	I	D	
	★	★	☆	★	
				HBO_2 Protocol	2.5-2.8 ATA x 90 min 5-6 days/wk (72±29 Tx)
Strength of Evidence	Low			Generalizability	Moderate - all patients hospitalized
The Answer	HBO_2 significantly improved healing rate (96% vs. 67%,p<.001) and decreased amputation rate (5% vs. 33%, p<.001).				

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Faglia 1996

ORIGINAL ARTICLE

Adjunctive Systemic Hyperbaric Oxygen Therapy in Treatment of Severe Prevalently Ischemic Diabetic Foot Ulcer

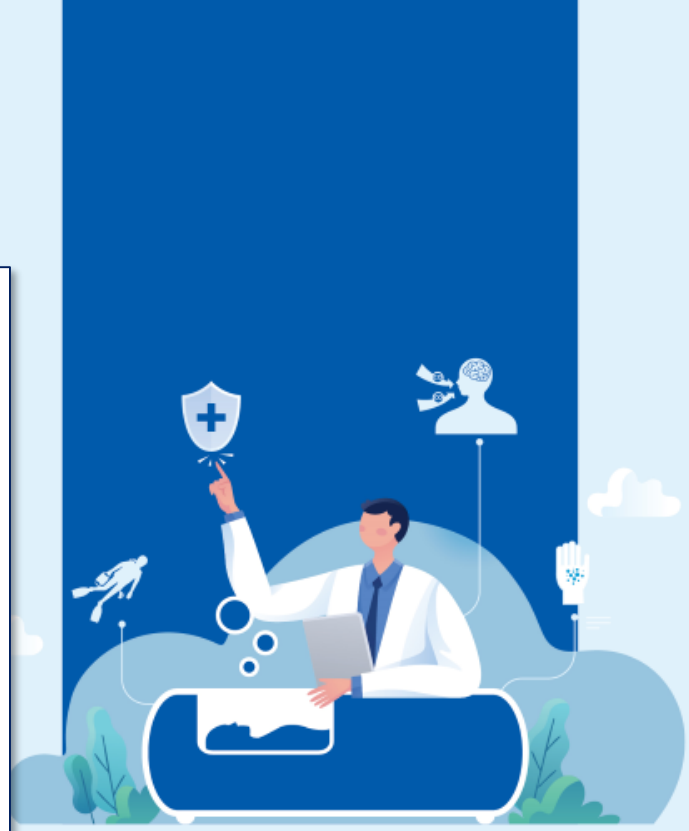
A randomized study

Ezio Faglia, MD
Fabrizio Favales, MD
Antonio Aldeghi, MD
Patrizia Calia, MD
Antonella Quarantiello, MD
Giorgio Oriani, MD
Michael Michael, MD
Pietro Campagnoli, MD
Alberto Morabito, PhD

RESEARCH DESIGN AND METHODS

Study Design

From August 1993 to August 1995, 70 diabetic subjects, consecutively hospitalized in



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Faglia 1996

The Question	Does HBO_2 improve healing and decrease amputation rate in DFU?					
Study Design	Randomized Controlled Unblinded Trial (N=68)				Study Population (Wagner grade)	1 2 3 4 5
					Comparison	35 HBO_2 vs 35 ØHBO_2
Co-Morbidities Addressed	V	O	I	D	HBO_2 Protocol	2.2-2.5 ATA x 90 min 5-7 days/wk (38±8 Tx)
	★	☆	★	★		
Strength of Evidence	High				Generalizability	Moderate - all patients hospitalized
The Answer	HBO_2 group had less major amputations (9% vs 33%, p=.002) and greater increase in $P_{tc}O_2$ (14 mm Hg vs. 5 mm Hg, p=.00002) than the control group					

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- All patients in the study were admitted to the hospital at the start of the study period

  -Wagner IV (Full-thickness gangrene)

  -Wagner III (Abscess)

  -Wagner II (if ulcer was large and infected and showed a defective healing in 30 days of outpatient therapy)

- Aggressive and radical debridement
- Dressing changes with debridement carried out not less than twice a day when necrosis or exudate were present, daily when ulcer was clean, and every 2 days during granulation period

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- Offloading in hospital was addressed with an orthotic insert in an extra deep shoe
- Empirical broad-spectrum antibiotics were started and then adjusted based on culture results
- Diabetes was controlled with oral hypoglycemic agents or SQ insulin based on blood glucose checks (7 times/day)

  -Blood glucose of >22 mmol (396 mg/dL) started on IV insulin until blood glucose < 9.9 mmol (178 mg/dL)

  -$Hb_{a1}c$ checked at time of admission and at discharge

- If ABI (ankle-brachial index) <0.9 and/or $P_{tc}O_2$ <50 mmHg, therapy with prostacyclin was established and angiography performed
- If arteriography showed >50% focal stenosis, then PTA or BPG
- If arteriography showed occlusion of >10cm then BPG if a patent vessel in continuity with the foot was present
- 26 subjects had revascularization during the study (13 in each arm)

- Limb considered salvaged when plantar support was preserved and the ulcer healed despite minor amputation
  - Reduction in major amputations in Wagner IV DFU (9.1% vs. 55%, p=0.002)
  - No difference in major amputations in Wagner III DFU (25% vs. 0%, p=0.33) or Wagner II DFU (0% vs. 0%)
- Pivotal Study for CMS (Centers for Medicare & Medicaid Services) approval of HBO_2 for DFU in the US

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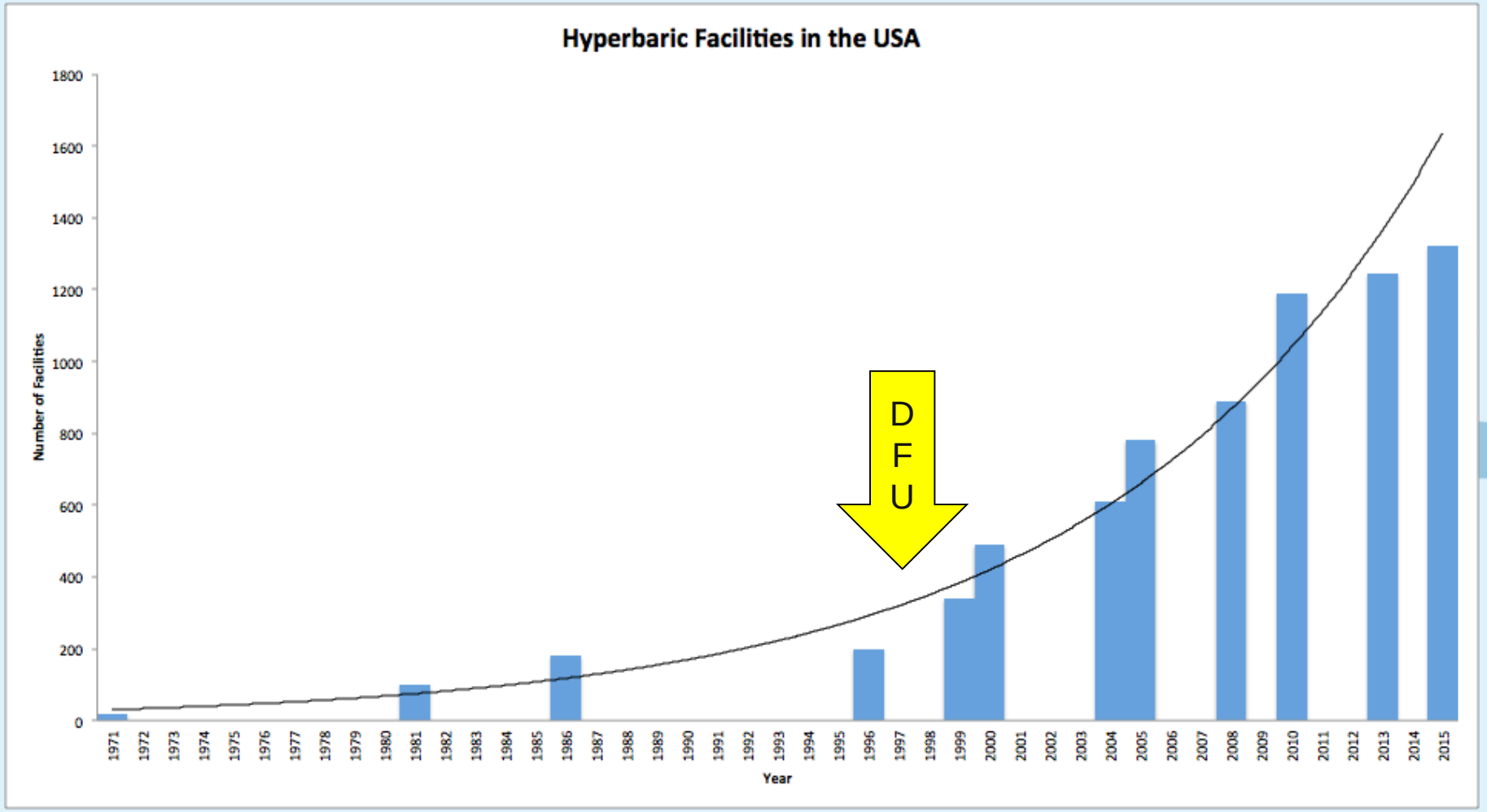

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Löndahl 2010/2011

Clinical Care/Education/Nutrition/Psychosocial Research

ORIGINAL ARTICLE

Hyperbaric Oxygen Therapy Facilitates Healing of Chronic Foot Ulcers in Patients With Diabetes

MAGNUS LÖNDAHL, MD[1]
PER KATZMAN, MD, PHD[1]
ANDERS NILSSON, MD[2]
CHRISTER HAMMARLUND, MD, PHD[3]

grade 1 and 2 ulcers. Therefore, the clinical utility of HBOT in treating diabetic foot ulcers was not established. The final

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Löndahl 2010/2011

The Question	What is the effect of HBO_2 on healing of DFU?				
Study Design	Randomized, Double-Blinded, Placebo-Controlled Trial (N=75)			Study Population	1 2 3 4 5
				Comparison	38 HBO_2 vs 37 HBAir
Co-Morbidities Addressed	V	O	I	D	HBO_2 Protocol: 2.5 ATA x 90 min, 5 days/week, up to 40 Tx
	★	☆	☆	★	
Strength of Evidence	High			Generalizability	High
The Answer	HBO_2 group had significantly better healing at 1 year than the control group (52% vs. 29%, p=0.03) using intention-to-treat (ITT) analysis. Per protocol analysis showed even stronger results (61% vs 27%, p=.009).				

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Fedorko 2016, Diabetes Care

CrossMark

Hyperbaric Oxygen Therapy Does Not Reduce Indications for Amputation in Patients With Diabetes With Nonhealing Ulcers of the Lower Limb: A Prospective, Double-Blind, Randomized Controlled Clinical Trial

Ludwik Fedorko,[1] James M. Bowen,[2,3] Wilhelmine Jones,[1] George Oreopoulos,[1] Ron Goeree,[2,3] Robert B. Hopkins,[2,3] and Daria J. O'Reilly[2,3]

DOI: 10.2337/dc15-2001

EPIDEMIOLOGY

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Fedorko 2016 (negative)

The Question	Does HBO_2 reduce indication for amputation of DFU?				
Study Design	Randomized, Double-Blinded, Placebo-Controlled Trial (N=103)			Study Population	1 2 3 4 5
				Comparison	49 HBO_2 vs 54 Sham
Co-Morbidities Addressed	V	O	I	D	HBO_2 Protocol: 2.5 ATA x 90 min, 5 days/week, up to 40 Tx
	★	☆	☆	★	
Strength of Evidence	Moderate			Generalizability	Low
The Answer	Criteria for major amputation were met in 13 of 54 patients in the sham group and 11 of 49 in the HBOT group (odds ratio 0.91 [95% CI 0.37, 2.28], P = 0.846). Twelve (22%) patients in the sham group and 10 (20%) in the HBOT group were healed.				

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Primary Outcome

- Meeting criteria of need for amputation or undergoing amputation
  - Lack of significant progress in wound healing
  - Persistent deep infection involving bone/tendon
  - Inability to bear weight on affected limb
  - Pain causing significant disability

대한고압의학회
Korean Academy of Undersea and Hyperbaric Medicine

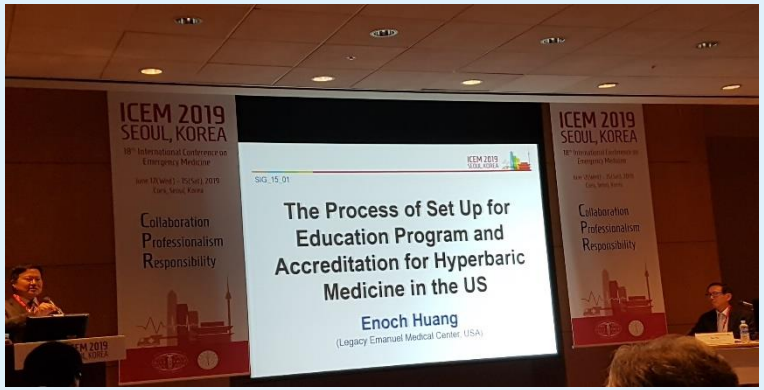
Letters to the editor

COMMENT ON FEDORKO ET AL.

Hyperbaric Oxygen Therapy Does Not Reduce Indications for Amputation in Patients With Diabetes With Nonhealing Ulcers of the Lower Limb: A Prospective, Double-Blind, Randomized Controlled Clinical Trial. Diabetes Care 2016;39:392–399

Enoch T. Huang

Diabetes Care 2016;39:e1–e2 | DOI: 10.2337/dc16-0196



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Santema 2018

Diabetes Care 1

Check for updates

Hyperbaric Oxygen Therapy in the Treatment of Ischemic Lower Extremity Ulcers in Patients With Diabetes: Results of the $DAMO_2CLES$ Multicenter Randomized Clinical Trial

Katrien T.B. Santema,[1] Robert M. Stoekenbroek,[1] Mark J.W. Koelemay,[1] Jim A. Reekers,[2] Laura M.C. van Dortmont,[3] Arno Oomen,[4] Luuk Smeets,[5] Jan J. Wever,[6] Dink A. Legemate,[1] and Dirk T. Ubbink,[1] on behalf of the $DAMO_2CLES$ Study Group[*]

https://doi.org/10.2337/dc17-0654

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Santema 2018 (negative)

The Question	Does HBO_2 improve wound healing and limb salvage of DFU at 12 months?					
Study Design	Randomized Controlled Trial (N=120)				Study Population	1 2 3 4 5
					Comparison	60 SC + HBO_2 vs 60 SC
Co-Morbidities Addressed	V	O	I	D	HBO_2 Protocol	2.5 ATA x 90 min 5 days/week up to 40 Tx
	★	☆	☆	★		
Strength of Evidence	High				Generalizability	High
The Answer	No difference between groups after 12 months (28 index wounds were healed in the SC group vs. 30 in the SC+HBOT group). Limb salvage was achieved in 47 patients in the SC group vs. 53 patients in the SC+HBOT. Amputation-free survival (AFS) was achieved in 41 patients in the SC group and 49 patients in the SC+HBOT group Patients who completed HBOT had significantly less major amputations and higher AFS. In the SC+HBOT group, 21 patients (35%) were unable to complete the HBOT protocol as planned.					

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Letters to the editor

Diabetes Care Volume 41, April 2018 e61

COMMENT ON SANTEMA ET AL.

Hyperbaric Oxygen Therapy in the Treatment of Ischemic Lower-Extremity Ulcers in Patients With Diabetes: Results of the DAMO$_2$CLES Multicenter Randomized Clinical Trial. Diabetes Care 2018;41:112–119

Enoch Huang

Diabetes Care 2018;41:e61 | https://doi.org/10.2337/dc17-2440

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A clinical practice guideline for the use of hyperbaric oxygen therapy in the treatment of diabetic foot ulcers

CPG Authors: Enoch T. Huang, Jaleh Mansouri, M. Hassan Murad, Warren S. Joseph, Michael B. Strauss, William Tettelbach, Eugene R. Worth

UHMS CPG Oversight Committee: Enoch T. Huang, John Feldmeier, Ken LeDez, Phi-Nga Jeannie Le, Jaleh Mansouri, Richard Moon, M. Hassan Murad

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Table 2. Steps of the GRADE review methodology

- **Formulate question (PICO format)**
- **Select outcomes of importance**
- **Rate importance of outcomes (1-9)**
- **Literature review**
  - create evidence profile of outcomes across studies
  - summary of findings and estimate of effect for each outcome
- **Rate quality of evidence for each outcome using criteria in Table 3**
  - rate overall quality of evidence across outcomes based on the lowest quality of critical outcomes
- **Formulate recommendations**
  - for or against
  - strong or conditional
    - taking into account quality of evidence, balance of harms vs. benefits, and the values and preferences of patients and clinicians
    - recommendations may also take into account resource use (cost)

- Outcomes of interest
  - Critical outcomes
    - Major amputation
    - Incomplete healing at one year
  - Importance outcomes
    - Resolution of infection
    - Quality of life (SF36)
    - Minor amputation

E.T. Huang, J. Mansouri, M.H. Murad, et al. UHM 2015, Vol. 42, No. 3

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Table 9. Outcomes reported by study

type	study	OUTCOME REPORTED: major amputation	incomplete healing (1 yr)	minor amputation	persistent infection	no change in quality of life	COMMENTS
RANDOMIZED CONTROLLED TRIALS	Doctor 1992						included
	Faglia 1996						included
	Lin 2001						excluded: abstract only without any outcomes of interest
	Abidia 2003						included: data on quality of life were not able to be included
	Kessler 2003						excluded: reported only for short-term outcomes (< 6 weeks)
	Duzgun 2008						included
	Löndahl 2010						included: data on quality of life were able to be included
	Kaur 2012						excluded: did not include populations of interest and did not include outcomes of interest
	Ma 2013						excluded: did not include outcomes of interest
OBSERVATIONAL TRIALS	Hart 1979						excluded: did not include outcomes of interest
	Davis 1987						excluded: did not include outcomes of interest
	Baroni 1987 Oriani 1990						included: these studies may have had overlapping patients, so the last dataset for 1990 was used for analysis
	Oriani 1992						excluded: did not include non-HBO_2 comparison grp
	Wattel 1991						excluded: did not include non-HBO_2 comparison grp
	Cianci 1994						excluded: did not include any outcomes of interest
	Zamboni 1997						included
	Faglia 1998						excluded: did not include non-HBO_2 comparison grp
	Kalani 2001						included
	Grollman 2001						excluded: did not include any outcomes of interest
	Fife 2002						excluded: did not include non-HBO_2 comparison grp
	Strauss 2002						excluded: did not include non-HBO_2 comparison grp
	Niinikoski 2003						excluded: did not include any outcomes of interest
	Fife 2007						excluded: did not include any outcomes of interest
	Oubre 2007						excluded: did not include non-HBO_2 comparison grp
	Ong 2008						excluded: did not include non-HBO_2 comparison grp
	Lyon 2008						excluded: did not include any outcomes of interest
	Kaya 2009						excluded: did not include non-HBO_2 comparison grp
	Chen 2010						excluded: did not include any outcomes of interest
	Margolis 2013						included
	Tongson 2013						excluded: did not include any outcomes of interest
	Bishop 2013						excluded: did not include non-HBO_2 comparison grp

- Initial review
  - -9 RCTs
  - -21 observational studies
- Subsequent formal review
  - -655 references
  - -Not identify any additional RCTs

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Wagner Grades

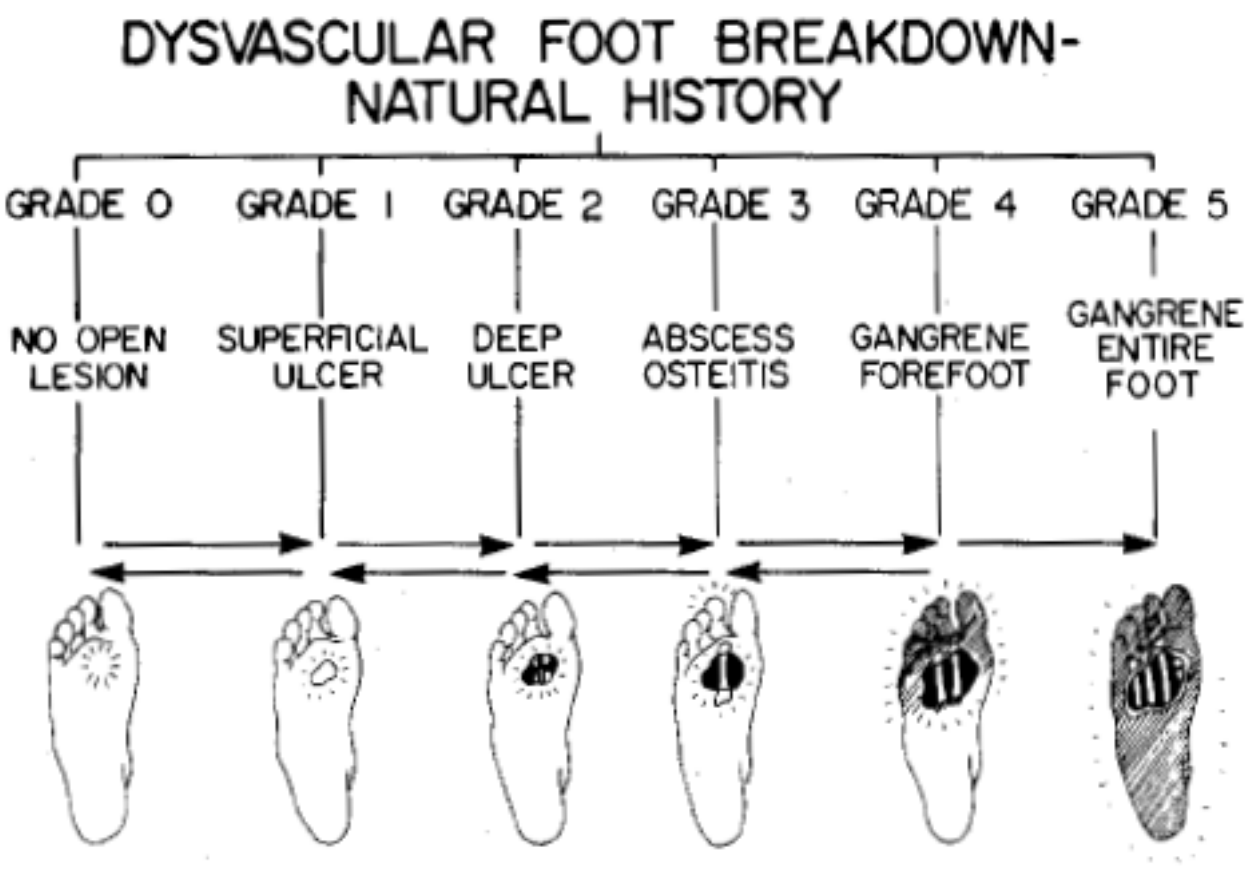

Fig. 1. Grading of foot lesions. The arrow indicates that all grades except Five can be converted to a Grade Zero foot.

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Wagner, FW The Dysvascular Foot, Foot & Ankle 2(2) 1981

- “standard wound care”

  -The optimal management of surgical debridement

  -Mechanical off-loading

  -Infection control

  -Revascularization

  -Metabolic control

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Table 7. Levels of evidence

High	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate of effect.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate of effect.
Very low	Any estimate of effect is very uncertain.

Table 8. Strength of recommendations and implications for the general population, healthcare workers and policy-makers

STRONG

Population
Most people in this situation would want the recommended course of action, and only a small proportion would not.

Healthcare workers
Most people should receive the recommended course of action.

Policy-makers
The recommendation can be adapted as a policy in most situations.

CONDITIONAL

Population
The majority of people in this situation would want the recommended course of action, but many would not.

Healthcare workers
Be prepared to help people to make a decision that is consistent with their own values/decision aids and shared decision-making.

Policy-makers
There is a need for substantial debate and involvement of stakeholders.

- These four questions

  - For a patient with a diabetic foot ulcer, is HBO_2 with standard wound care more effective than standard wound care alone for the outcomes of interest?

  - For a patient with a Wagner Grade 2 or lower DFU that has not shown significant improvement after 30 days of treatment, is HBO_2 with standard wound care more effective than standard wound care alone for the outcomes of interest?

  - For a patient with a Wagner Grade 3 or higher DFU that has not shown significant improvement after 30 days of treatment, is HBO_2 with standard wound care more effective than standard wound care alone for the outcomes of interest?

  - For a patient with a Wagner Grade 3 or higher DFU who has just had a surgical debridement of the foot (e.g., partial toe or ray amputation; debridement of ulcer with underlying bursa, cicatrix or bone; foot amputation; I&D of deep space abscess; or necrotizing soft tissue infection), is acute postoperative HBO_2 with standard wound care more effective than standard wound care alone for the outcomes of interest?

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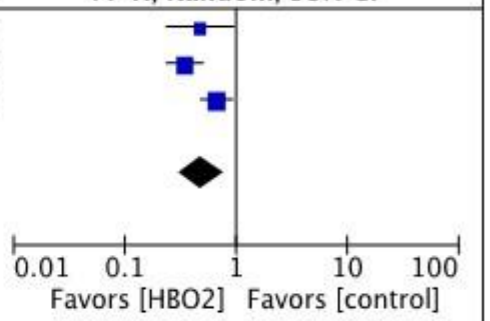
PICO 1

Incomplete Healing

Study or Subgroup	HBO2 Events	HBO2 Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Abidia 2003	4	9	9	9	23.4%	0.47 [0.24, 0.95]	2003
Duzgun 2008	17	50	50	50	37.2%	0.35 [0.24, 0.51]	2008
Londahl 2010	24	49	33	45	39.4%	0.67 [0.48, 0.93]	2010
Total (95% CI)		**108**		**104**	**100.0%**	**0.48 [0.30, 0.77]**	
Total events	45		92				

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 6.58$, df = 2 (P = 0.04); $I^2 = 70\%$

Test for overall effect: Z = 3.07 (P = 0.002)



Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HBO+SC	SC	Relative (95% CI)	Absolute (95% CI)		
Incomplete Healing (follow up: 1 years)												
3	randomised trials	serious [1]	serious [2]	not serious	not serious	none	45/108 (41.7%)	92/104 (88.5%)	**RR 0.48** (0.30 to 0.77)	460 fewer per 1000 (from 203 fewer to 619 fewer)	⊕⊕◯◯ LOW	CRITICAL

MD – mean difference, RR – relative risk

1. Rated down because of unclear methodology for allocation concealment in 2/3 studies, patients lost to follow-up in 1/3 studies, no blinding in 1/3 studies, and unclear intention to treat analysis in 1/3 studies.
2. The data for Incomplete Healing shows some inconsistency as the I2 was >50%, resulting in rating down 1 point

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No Recommendation

- Level of Evidence was Low
- Populations too heterogeneous
- Elected to look at more homogenous populations

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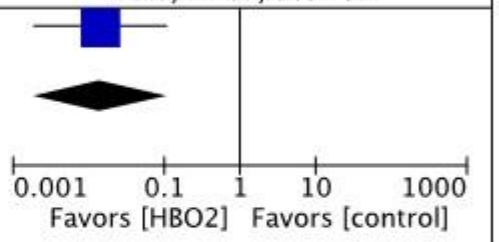
PICO 2

Incomplete Healing

Study or Subgroup	HBO2 Events	HBO2 Total	Control Events	Control Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI	Year
Duzgun 2008	0	6	12	12	100.0%	0.01 [0.00, 0.11]	2008
Total (95% CI)		**6**		**12**	**100.0%**	**0.01 [0.00, 0.11]**	
Total events	0		12				

Heterogeneity: Not applicable

Test for overall effect: Z = 4.12 (P < 0.0001)



Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HBO+SC	SC	Relative (95% CI)	Absolute (95% CI)		
Incomplete Healing (follow up: 1 years)												
1	randomised trials	serious [2]	not serious	not serious	very serious [1]	none	0/6 (0.0%)	0/12 (0.0%)	**RR 0.48** (0.30 to 0.77)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW	CRITICAL

MD – mean difference, RR – relative risk

1. Wide confidence intervals in a single study with small number of events
2. Study was not blinded

2. Wide confidence intervals in a single study with small number of events

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Recommendation 1

- In patients with Wagner Grade 2 or lower diabetic foot ulcers, we suggest against using hyperbaric oxygen therapy
  - -Very low-level evidence in support of HBO2, conditional recommendation

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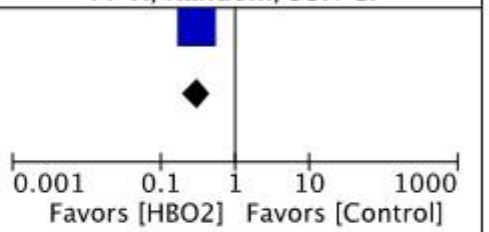
PICO 3

Incomplete Healing

Study or Subgroup	HBO2 Events	HBO2 Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Duzgun 2008	13	44	38	38	100.0%	0.30 [0.19, 0.48]	2008
Total (95% CI)		**44**		**38**	**100.0%**	**0.30 [0.19, 0.48]**	
Total events	13		38				

Heterogeneity: Not applicable

Test for overall effect: Z = 5.21 (P < 0.00001)



Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HBO+SC	SC	Relative (95% CI)	Absolute (95% CI)		
Incomplete Healing (follow up: 1 years)												
1	randomised trials	serious [1]	not serious	not serious	not serious	none	13/44 (29.5%)	38/38 (100.0%)	**RR 0.30** (0.19 to 0.48)	700 fewer per 1000 (from 520 fewer to 810 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL

MD – mean difference, RR – relative risk

1. Study was not blinded

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Recommendation 2

- In patients with Wagner Grade 3 or higher diabetic foot ulcers that have not shown significant improvement after 30 days of treatment, we suggest adding hyperbaric oxygen therapy to the standard of care to reduce the risk of major amputation and incomplete healing
  - Moderate-level evidence, conditional recommendation

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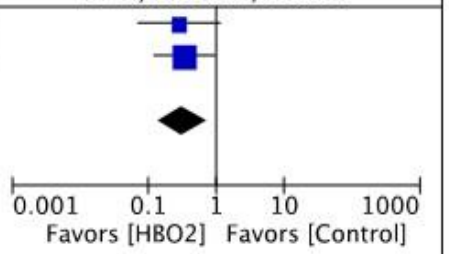
PICO 4

Major Amputation

Study or Subgroup	HBO2 Events	HBO2 Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Doctor 1992	2	15	7	15	35.8%	0.29 [0.07, 1.16]	1992
Faglia 1996	4	36	11	34	64.2%	0.34 [0.12, 0.98]	1996
Total (95% CI)		**51**		**49**	**100.0%**	**0.32 [0.14, 0.74]**	
Total events	6		18				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.04$, df = 1 (P = 0.84); $I^2 = 0\%$

Test for overall effect: Z = 2.66 (P = 0.008)



Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Acute HBO	SC	Relative (95% CI)	Absolute (95% CI)		
Major Amputation												
2	randomised trials	serious 1	not serious	not serious	not serious	none	6/51 (11.8%)	18/49 (36.7%)	**RR 0.32** (0.14 to 0.74)	250 fewer per 1000 (from 96 fewer to 316 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL

MD - mean difference, RR - relative risk

1. 1/2 studies unblinded and 1/2 had single blinding, 2/2 had unclear allocation concealment, 1/2 had unclear patients lost to follow-up, 1/2 had unclear intention-to-treat analysis and 1/2 had no intention-to-treat analysis

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Recommendation 3

- In patients with Wagner Grade 3 or higher diabetic foot ulcers who have just had a surgical debridement of an infected foot (e.g., partial toe or ray amputation; debridement of ulcer with underlying bursa, cicatrix or bone; foot amputation; I&D of deep space abscess; or necrotizing soft tissue infection), we suggest adding acute post-operative hyperbaric oxygen therapy to the standard of care to reduce the risk of major amputation

  -Moderate level evidence, conditional recommendation

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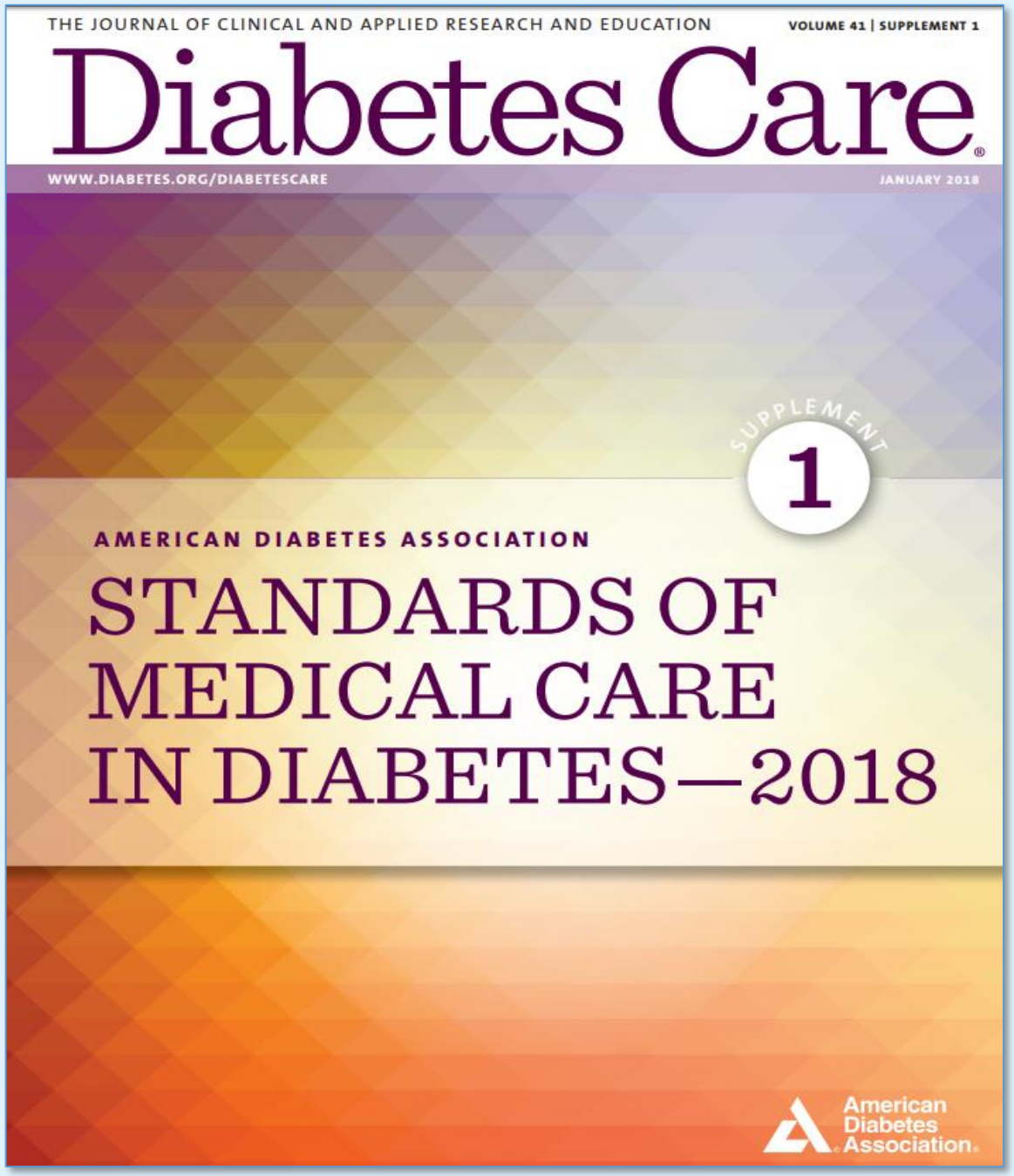

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- Hyperbaric oxygen therapy (HBOT) in patients with diabetic foot ulcers has mixed evidence supporting its use as an adjunctive treatment to enhance wound healing and prevent amputation.

- The Centers for Medicare & Medicaid Services currently covers HBOT for diabetic foot ulcers that have failed a standard course of wound therapy when there are no measurable signs of healing for at least 30 consecutive days.

- HBOT should be a topic of shared decision making before treatment is considered for selected patients with diabetic foot ulcers.

Huang ET, et al. Undersea Hyperb Med 2015;42:205–247

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UHMS Indications Manual (14th edition)

- Available evidence supports HBO_2 for DFU
- 2 – 2.5 ATA for 90 – 120 minutes once or twice daily

  -Serious infection may require IV abx, surgical intervention and glycemic control
- Utilization review after 30 days of treatment

  -At least every 30 days subsequently
- Use of TCOM to risk stratify patients

  -Warrants at least 1 tx to measure $PtcO_2$ in chamber

  -If values low, appropriate to treat 10-15 sessions (2-3 weeks) to see if values increase (neovascularization)

  -If no change in 2-3 weeks, further HBO_2 not warranted

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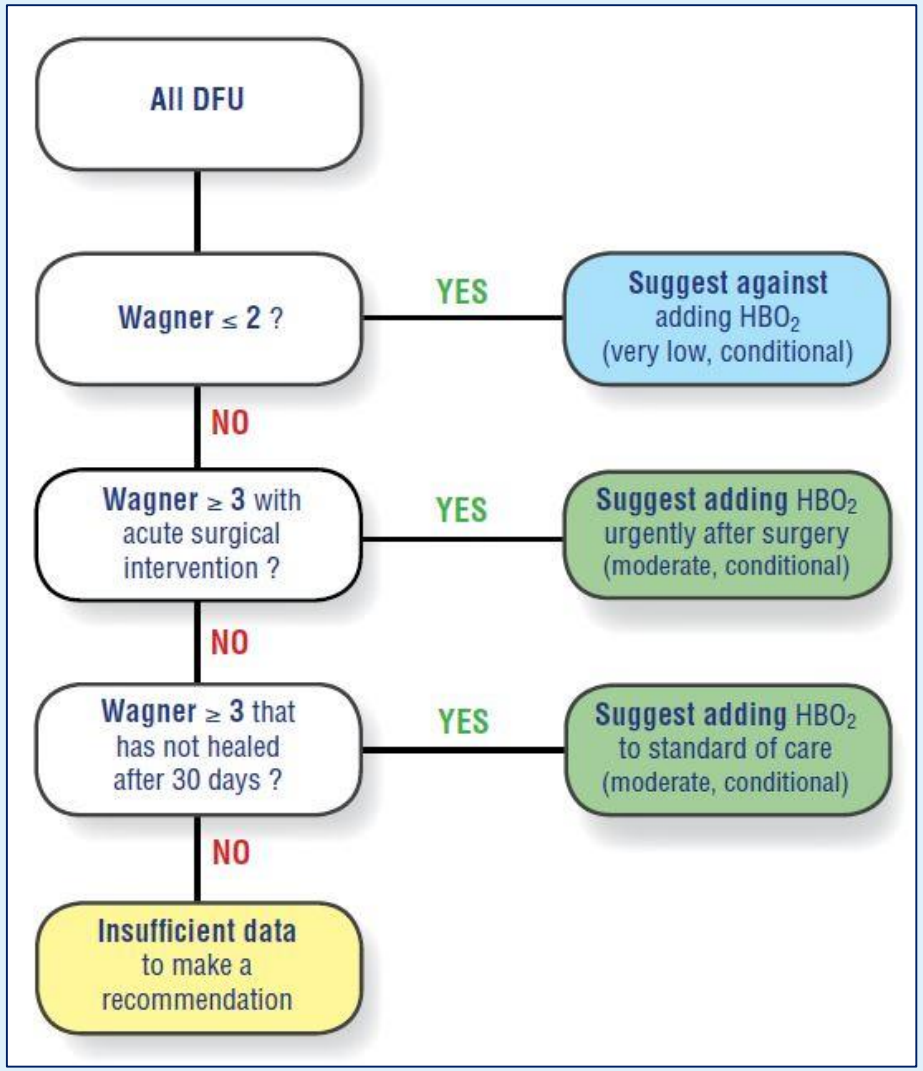
Algorithm for the use of HBO_2



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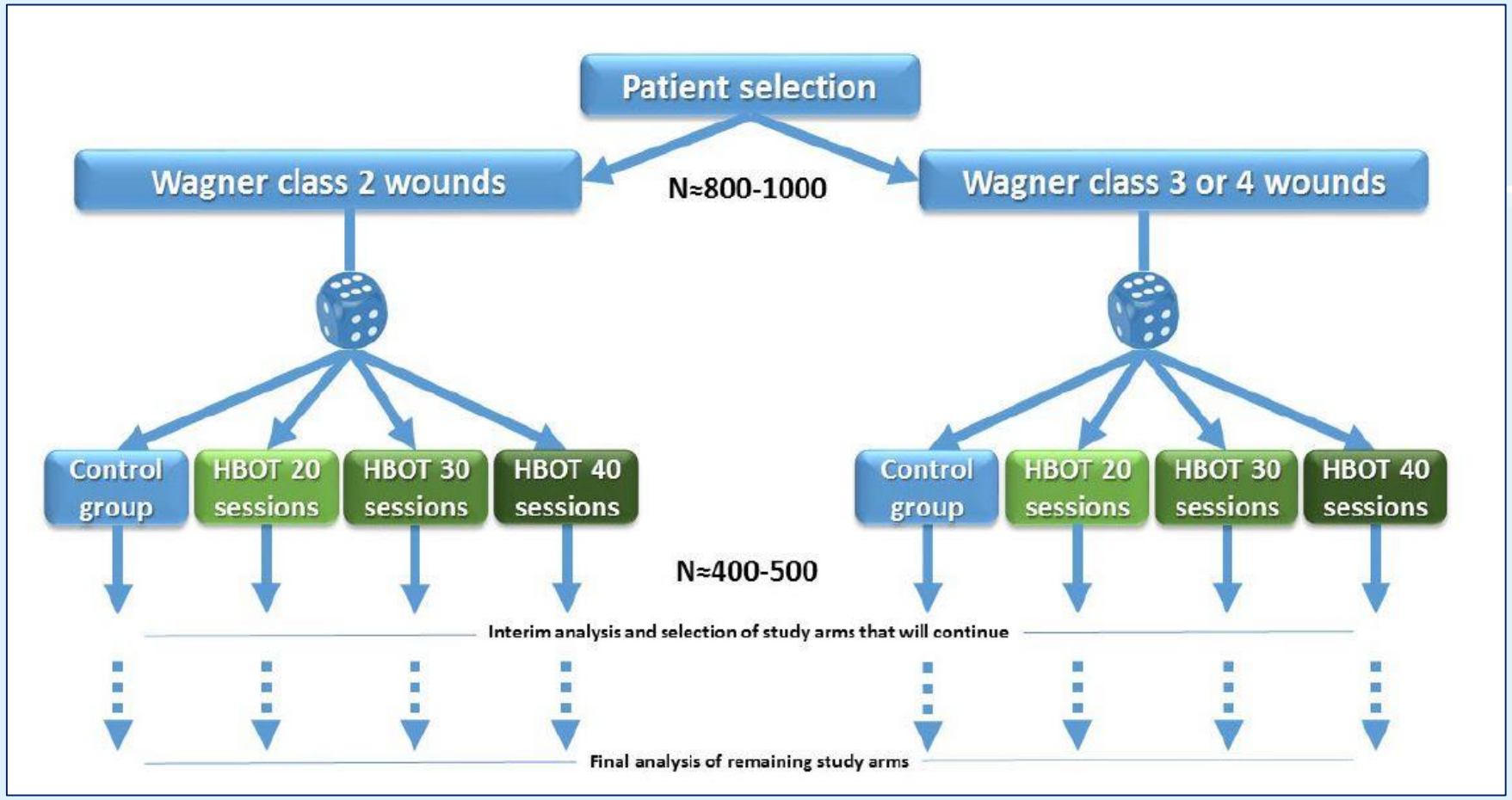
DIONYSIUS trial

(Does Increasing Oxygen Nurture Your Symptomatic Ischemic Ulcer Sufficiently?/ 2020년부터 시작)



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요 약

- Mechanisms of HBO to DFUs
- The major trials on the use of HBO_2 for DFU
- The strengths/weaknesses of the two newest randomized controlled studies on the use of HBO_2 for DFU
- Know the Undersea and Hyperbaric Medical Society Clinical Practice Guideline on the use of HBO_2 for DFU

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Thank you

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