

KQ 2. 소아두부외상에서 두부 외상 진단을 위한 적절한 영상검사는 무엇인가?

권고 2-1. 글래스고 혼수척도(Glasgow Coma Scale, GCS)가 14 이상이면서 신경학적 증상이나 징후, 혹은 고위험인자(예: 의식손상, 두개저 골절 의심 소견 등)가 없는 두부 외상 소아에서 두부 손상 진단을 위한 영상검사를 시행하지 않는 것을 권고한다.
(권고등급 C, 근거수준 I)

권고 2-2. GCS가 13이하이거나 GCS가 14이상이면서 신경학적 증상이나 징후, 혹은 고위험인자(예: 의식손상, 두개저 골절 의심소견 등)가 있는 두부 외상 소아에서 두부 손상 진단을 위한 영상검사로 조영증강 전 CT(non-contrast brain CT)를 고려할 수 있다.
(권고등급 B, 근거수준 I)

근거요약

소아의 두부 외상에 대해 검색을 통해 7개의 진료지침을 찾았으며 이 중 4개의 진료지침을 최종 선택하였다(1-4). 이 진료지침들에서의 공통적인 관심사는 경한 두부 손상(GCS \geq 14)에서의 적절한 영상검사였다. 여러 연구 및 진료지침을 종합해서 보았을 때 경한 두부 손상의 정의는 14 이상의 GCS를 보이는 것으로 함이 적절하다(5). GCS가 14 이상이면서 신경학적 증상이나 징후, 또는 고위험인자를 보이지 않는 경우에 심각한 두부 손상을 보이는 경우는 매우 드물며 임상적으로 의미있는 외상성 두부 손상을 보이는 전체 비율은 0.9%이며 검사나 병력에서 두개 내 이상의 시사점이 없다면 0.05%로 낮아진다(7). 2세 이상의 환아에 대한 PECARN (Pediatric Emergency Care Applied Research Network)의 연구에서 정상적인 의식, 의식소실, 구토, 심한 손상 기전, 두개저 골절 의심 소견과 심한 두통을 기준으로 삼았을 시 99.9%의 음성예상치(negative predictive value), 96.0%의 민감도를 보였다. 2세 미만의 경우에도 비슷하며 1% 미만의 의미있는 외상성 두부 손상을 보이며 의식변화를 보이면 4%, 골절이 의심되면 3.6%로 증가한다. 또한 2세 미만 소아 만 명 이상을 대상으로 한 PECARN에서 정상적인 의식, 의식소실, 전두부를 제외한 두피 혈종, 심한 손상 기전, 만져지는 두개 골절, 부모가 보기에 평소와 같은 행동 등을 기준으로 보았을 때 100%의 음성 예측치와 100%의 민감도를 보였다(7). 두부 CT 1회 촬영 시 0.02~0.1% 암이 증가한다는 점(12)을 포함하여 방사선에 민감한 소아라는 점과 이러한 연구결과를 고려한다면 GCS 14 이상의 경한 두부 손상을 보이는 소아에서는 영상 검사를 시행하지 않는 것이 적절하다.

표 1. Glasgow Coma Scale (GCS)

Category	Adult	Scale	Infant
Eye Opening	Spontaneous	4	Spontaneous
	To speech	3	To speech
	To pain	2	To pain
	No response	1	No response
Best moter response	obeys verbal command	6	obeys verbal command
	Localizes pain	5	Localizes pain
	Withdraws form pain	4	Withdraws form pain
	Flexion - abnormal*	3	Flexion - abnormal
	Extension**	2	Extension
	No response	1	No response
Best verbal response	Oriented and converses	5	Coos, babbles
	Disoriented and converses	4	Cries but consonable
	Inappropriate words	3	Persistently irritable
	Incomprehensible sounds	2	Grunts to pain/restless
	No response	1	No response

2세 미만에서 두개저 골절이 의심되는 경우 약 7.5%에서 임상적으로 중요한 두부 손상이 있으며(7), GCS가 낮아질수록 두개 내 손상 확률이 증가한다(33). 따라서 신경학적 증상이나 징후, 혹은 고위험인자를 보이는 경한 두부 손상이나 13이하의 GCS를 보이는 두부 손상 소아의 경우에는 영상검사가 필요하다. 급성 출혈 여부 및 두개 골절을 잘 보여주는 CT와 달리 두개골 단순 촬영은 골절 유무만 보여 주며 CT에서 보이는 골절 중 약 21%가 단순 촬영에서는 보이지 않을 수 있으며, 골절이 없는 경우에도 최대 50%까지 두개내 손상이 있을 수 있다(1,21). 또한 Reed의 연구(20)에서는 단순촬영 없이 병력 청취와 CT만 가지고 검사를 하였을 때 두개 내 손상을 놓치는 비율이나 전반적인 방사선량의 증가가 없었다. 이러한 점을 고려했을 때 신경학적 증상이나 징후, 혹은 고위험인자를 보이는 경한 두부 손상이나 13이하의 GCS를 보이는 두부 손상 환자의 경우에는 CT를 시행함이 적절하다 하겠다. 중등도 이상의 두부 손상에서 미만성 축삭 손상이 약 75%에서 보인다는 보고(17)가 있어 MRI가 필요할 수도 있으나 외상환자에게 MRI를 적용하는 것이 시간상으로 혹은 접근성에 있어 부적절하며 소아에 있어서는 추가적인 진정이나 마취와 같이 조치가 필요할 수 있어 응급 상황에서는 CT가 우월하다 할 수 있다.

권고 고려사항

1. 이득과 위해

소아두부외상환자의 일차 진단 검사로 CT 검사를 사용하는 경우 진단정확도가 높은 장점이 있으나 방사선 피폭의 단점이 있다. 따라서 신체 검진과 병력 청취를 통해 검사를 시행할 환자

를 정할 필요가 있다.

2. 국내 수용성과 적용성(Acceptability and Applicability)

진료지침의 국내 수용성과 적용성은 평가결과 Eastern Association for the Surgery of Trauma Practice management guideline에서 발간한 Evaluation and management of mild traumatic brain injury(2012)와 Scandinavian Guidelines for initial management of minimal, mild and moderate head injuries(2000)의 경우 적용성에 무리는 없으나 연구군이 전반적으로 우리 현실과 맞지 않아 수용하기 어렵다. 나머지 진료지침의 국내 수용성과 적용성에 큰 무리가 없는 것으로 판단되었다. 수용성과 적용성 평가표는 부록에 제시한다.

3. 검사별 방사선량

두부 CT 

참고문헌

1. Pinto PS, Poretti A, Meoded A, Tekes A, Huisman TA, The Unique Features of Traumatic Brain Injury in Children. Review of the Characteristics of the Pediatric Skull and Brain, Mechanisms of Trauma, Patterns of Injury, Complications and Their Imaging Findings—Part 1. J Neuroimaging 2012;22(2):1–17.
2. Faul M, Xu L, Wald MM, Coronado VG, Traumatic Brain Injury in the United States: Emergency Department Visits, Hospitalizations and Deaths 2002–2006. Atlanta (GA): Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. 2010; Available from: URL: http://www.cdc.gov/traumaticbraininjury/tbi_ed.html. Accessed September 16, 2013.
3. Schnadower D, Vazquez H, Lee J, Dayan P, Roskind CG, Controversies in the Evaluation and Management of Minor Blunt Head Trauma in Children. Curr Opin Pediatr. 2007;19(3):258–64.
4. Willis AP, Latif SA, Chandratre S, Stanhope B, Johnson K, Not a NICE CT Protocol for the Acutely Head Injured Child. Clin Radiol. 2008;63(2):165–9.
5. Schutzman SA, Greenes DS, Pediatric Minor Head Trauma. Ann Emerg Med. 2001;37(1):65–74.
6. Haydel MJ, Shembekar AD, Prediction of Intracranial Injury in Children Aged Five Years and Older with Loss of Consciousness After Minor Head Injury Due to Nontrivial Mechanisms. Ann Emerg Med. 2003;42(4):507–14. Citation없음(<?)
7. Kuppermann N, Holmes JF, Dayan PS, et al. Identification of Children at Very Low Risk of Clinically Important Brain Injuries After Head Trauma: A Prospective Cohort Study. Lancet 2009;374(9696):1160–70.
8. Tavarez MM, Atabaki SM, Teach SJ, Acute Evaluation of Pediatric Patients with Minor Traumatic Brain Injury. Curr Opin Pediatr. 2012;24(3):307–13.
9. Maguire JL, Boutis K, Uleryk EM, Laupacis A, Parkin PC, Should a Headinjured Child Receive a Head CT Scan? A Systematic Review of Clinical Prediction Rules. Pediatrics 2009;124(1):145–54.
10. Halley MK, Silva PD, Foley J, Rodarte A, Loss of Consciousness: When to Perform Computed Tomography? Pediatr Crit Care Med. 2004;5(3):230–3.
11. Pearce MS, Salotti JA, Little MP, et al. Radiation Exposure from CT Scans in Childhood and Subsequent Risk of Leukaemia and Brain Tumours: A Retrospective Cohort Study. Lancet 2012;380(9840):499–505.
12. Brenner DJ, Hall EJ, Computed Tomography—An Increasing Source of Radiation Exposure. N E

- ngl J Med. 2007;357(22):2277–84.
13. How to Develop CT Protocols for Children. Available from: URL: <http://spr.affiniscape.com/associations/5364/files/Protocols.pdf>. Accessed September 16, 2013.
 14. Datta S, Stoodley N, Jayawant S, Renowden S, Kemp A, Neuroradiological Aspects of Subdural Haemorrhages. *Arch Dis Child*. 2005;90(9):947–51.
 15. Kemp AM, Rajaram S, Mann M, et al. What Neuroimaging Should Be Performed in Children in Whom Inflicted Brain Injury (iBI) Is Suspected? A Systematic Review. *Clin Radiol*. 2009;64(5):473–83.
 16. Hunter JV, Wilde EA, Tong KA, Holshouser BA, Emerging Imaging Tools for Use with Traumatic Brain Injury Research. *J Neurotrauma* 2012;29(4):654–71.
 17. Skandsen T, Kvistad KA, Solheim O, Strand IH, Folvik M, Vik A, Prevalence and Impact of Diffuse Axonal Injury in Patients with Moderate and Severe Head Injury: A Cohort Study of Early Magnetic Resonance Imaging Findings and 1-Year Outcome. *J Neurosurg*. 2010;113(3):556–63.
 18. Tong KA, Ashwal S, Holshouser BA, et al. Hemorrhagic Shearing Lesions in Children and Adolescents with Posttraumatic Diffuse Axonal Injury: Improved Detection and Initial Results. *Radiology* 2003;227(2):332–9.
 19. Holmes JF, Borgianni DA, Nadel FM, et al. Do Children with Blunt Head Trauma and Normal Cranial Computed Tomography Scan Results Require Hospitalization for Neurologic Observation? *Ann Emerg Med*. 2011;58(4):315–22.
 20. Reed MJ, Browning JG, Wilkinson AG, Beattie T, Can We Abolish Skull X Rays for Head Injury? *Arch Dis Child*. 2005;90(8):859–64.
 21. Nakahara K, Shimizu S, Utsuki S, et al. Linear Fractures Occult on Skull Radiographs: A Pitfall at Radiological Screening for Mild Head Injury. *J Trauma* 2011;70(1):180–2.
 22. Crowe L, Anderson V, Babl FE, Application of the CHALICE Clinical Prediction Rule for Intracranial Injury in Children Outside the UK: Impact on Head CT Rate. *Arch Dis Child*. 2010;95(12):1017–22.
 23. Dunning J, Daly JP, Lomas JP, Lecky F, Batchelor J, Mackway-Jones K, Derivation of the Children's Head Injury Algorithm for the Prediction of Important Clinical Events Decision Rule for Head Injury in Children. *Arch Dis Child*. 2006;91(11):885–91.
 24. Oman JA, Cooper RJ, Holmes JF, et al. Performance of a Decision Rule to Predict Need for Computed Tomography Among Children with Blunt Head Trauma. *Pediatrics* 2006;117(2):238–46.
 25. Schachar JL, Zampolin RL, Miller TS, Farinhas JM, Freeman K, Taragin BH, External Validation of the New Orleans Criteria (NOC), the Canadian CT Head Rule (CCHR) and the National Emergency X-Radiography Utilization Study II (NEXUS II) for CT Scanning in Pediatric Patients with Minor Head Injury in a Non-Trauma Center. *Pediatr Radiol*. 2011;41(8):971–9.
 26. Bainbridge J, Khirwadkar H, Hourihan MD, Vomiting—Is This a Good Indication for CT Head Scans in Patients with Minor Head Injury? *Br J Radiol*. 2012;85(1010):183–6.
 27. Nigrovic LE, Lee LK, Hoyle J, et al. Prevalence of Clinically Important Traumatic Brain Injuries in Children with Minor Blunt Head Trauma and Isolated Severe Injury Mechanisms. *Arch Pediatr Adolesc Med*. 2012;166(4):356–61.
 28. Pickering A, Harnan S, Fitzgerald P, Pandor A, Goodacre S, Clinical Decision Rules for Children with Minor Head Injury: A Systematic Review. *Arch Dis Child*. 2011;96(5):414–21.
 29. Mannix R, Meehan WP, Monuteaux MC, Bachur RG, Computed Tomography for Minor Head Injury: Variation and Trends in Major United States Pediatric Emergency Departments. *J Pediatr*. 2012;160(1):136–9 e131.
 30. Gorelick MH, Atabaki SM, Hoyle J, et al. Interobserver Agreement in Assessment of Clinical Variables in Children with Blunt Head Trauma. *Acad Emerg Med*. 2008;15(9):812–8.
 31. Holmes JF, Palchak MJ, MacFarlane T, Kuppermann N, Performance of the Pediatric Glasgow C

- oma Scale in Children with Blunt Head Trauma. *Acad Emerg Med.* 2005;12(9):814–9.
32. Margulies SS, Thibault KL, Infant Skull and Suture Properties: Measurements and Implications for Mechanisms of Pediatric Brain Injury. *J Biomech Eng.* 2000;122(4):364–71.
 33. Claret Teruel G, Palomeque Rico A, Cambra Lasaosa FJ, Catala Temprano A, Noguera Julian A, Costa Clara JM, Severe Head Injury Among Children: Computed Tomography Evaluation as a Prognostic Factor. *J Pediatr Surg.* 2007;42(11):1903–6.
 34. Sigmund GA, Tong KA, Nickerson JP, Wall CJ, Oyoyo U, Ashwal S, Multimodality Comparison of Neuroimaging in Pediatric Traumatic Brain Injury. *Pediatr Neurol.* 2007;36(4):217–26.
 35. Ball WS, Jr, Nonaccidental Craniocerebral Trauma (Child Abuse): MR Imaging. *Radiology* 1989;173(3):609–10.
 36. Ashwal S, Wycliffe ND, Holshouser BA, Advanced Neuroimaging in Children with Nonaccidental Trauma. *Dev Neurosci.* 2010;32(5–6):343–60.
 37. Duhaime AC, Gennarelli TA, Thibault LE, Bruce DA, Margulies SS, Wisner R, The Shaken Baby Syndrome. A Clinical, Pathological, and Biomechanical Study. *J Neurosurg.* 1987;66(3):409–15.
 38. Jenny C, Hymel KP, Ritzen A, Reinert SE, Hay TC, Analysis of Missed Cases of Abusive Head Trauma. *JAMA* 1999;281(7):621–6.
 39. Rubin DM, Christian CW, Bilaniuk LT, Zazyczny KA, Durbin DR, Occult Head Injury in High-Risk Abused Children. *Pediatrics* 2003;111(6 Pt 1):1382–6.
 40. Laskey AL, Holsti M, Runyan DK, Socolar RR, Occult Head Trauma in Young Suspected Victims of Physical Abuse. *J Pediatr.* 2004;144(6):719–22.
 41. Mogbo KI, Slovis TL, Canady AI, Allasio DJ, Arfken CL, Appropriate Imaging in Children with Skull Fractures and Suspicion of Abuse. *Radiology* 1998;208(2):521–4.
 42. Brown RL, Brunn MA, Garcia VF, Cervical Spine Injuries in Children: A Review of 103 Patients Treated Consecutively at a Level 1 Pediatric Trauma Center. *J Pediatr Surg.* 2001;36(8):1107–14.
 43. Ghatan S, Ellenbogen RG, Pediatric Spine and Spinal Cord Injury After Inflicted Trauma. *Neurosurg Clin N Am.* 2002;13(2):227–33.
 44. Davis PC, Wippold FL II, Cornelius RS, et al. American College of Radiology. ACR Appropriateness Criteria® Head Trauma. Available from: URL: <http://www.acr.org/~media/ACR/Documents/AppCriteria/Diagnostic/HeadTrauma.pdf>. 2012. Accessed July 29, 2013.
 45. Keiper MD, Zimmerman RA, Bilaniuk LT, MRI in the Assessment of the Supportive Soft Tissues of the Cervical Spine in Acute Trauma in Children. *Neuroradiology* 1998;40(6):359–63.
 46. Kadom N, Khademian Z, Vezina G, Shalaby–Rana E, Rice A, Hinds T, Usefulness of MRI Detection of Cervical Spine and Brain Injuries in the Evaluation of Abusive Head Trauma. *Pediatr Radiol.* 2014:[E–pub ahead of print].
 47. Hobbs CJ, Skull Fracture and the Diagnosis of Abuse. *Arch Dis Child.* 1984;59(3):246–52.
 48. Prabhu SP, Newton AW, Perez–Rossello JM, Kleinman PK, Three–Dimensional Skull Models as a Problem–Solving Tool in Suspected Child Abuse. *Pediatr Radiol.* 2013;43(5):575–81.
 49. Chen CY, Chou TY, Zimmerman RA, Lee CC, Chen FH, Faro SH, Pericerebral Fluid Collection: Differentiation of Enlarged Subarachnoid Spaces from Subdural Collections with Color Doppler US. *Radiology* 1996;201(2):389–92.
 50. Amodio J, Spektor V, Pramanik B, Rivera R, Pinkney L, Fefferman N, Spontaneous Development of Bilateral Subdural Hematomas in an Infant with Benign Infantile Hydrocephalus: Color Doppler Assessment of Vessels Traversing Extraaxial Spaces. *Pediatr Radiol.* 2005;35(11):1113–7.
 51. Jaspan T, Narborough G, Punt JA, Lowe J, Cerebral Contusional Tears as a Marker of Child Abuse—Detection by Cranial Sonography. *Pediatr Radiol.* 1992;22(4):237–45.
 52. Kemp AM, Jaspan T, Griffiths J, et al. Neuroimaging: What Neuroradiological Features Distinguish Abusive from Nonabusive Head Trauma? A Systematic Review. *Arch Dis Child.* 2011;96(12):

1103–12.

53. Pinto PS, Meoded A, Poretti A, Tekes A, Huisman TA, The Unique Features of Traumatic Brain Injury in Children. Review of the Characteristics of the Pediatric Skull and Brain, Mechanisms of Trauma, Patterns of Injury, Complications, and Their Imaging Findings—Part 2. *J Neuroimaging* 2012;22(2):18–41.
54. Hamilton M, Mrazik M, Johnson DW, Incidence of Delayed Intracranial Hemorrhage in Children After Uncomplicated Minor Head Injuries. *Pediatrics* 2010;126(1):33–9.
55. Hollingworth W, Vavilala MS, Jarvik JG, et al. The Use of Repeated Head Computed Tomography in Pediatric Blunt Head Trauma: Factors Predicting New and Worsening Brain Injury. *Pediatr Crit Care Med*. 2007;8(4):348–56; CEU quiz 357.
56. Stence NV, Fenton LZ, Goldenberg NA, Armstrong–Wells J, Bernard TJ, Craniocervical Arterial Dissection in Children: Diagnosis and Treatment. *Curr Treat Options Neurol*. 2011;13(6):636–48.
57. Sepelyak K, Gailloud P, Jordan LC, Athletics, Minor Trauma, and Pediatric Arterial Ischemic Stroke. *Eur J Pediatr*. 2010;169(5):557–62.
58. Jones TS, Burlew CC, Kornblith LZ, et al. Blunt Cerebrovascular Injuries in the Child. *Am J Surg*. 2012;204(1):7–10.
59. Kopelman TR, Berardoni NE, O'Neill PJ, et al. Risk Factors for Blunt Cerebrovascular Injury in Children: Do They Mimic Those Seen in Adults? *J Trauma* 2011;71(3):559–64; discussion 564.
60. Mortazavi MM, Verma K, Tubbs RS, Harrigan M, Pediatric Traumatic Carotid, Vertebral and Cerebral Artery Dissections: A Review. *Childs Nerv Syst*. 2011;27(12):2045–56.
61. Aoki Y, Inokuchi R, Gunshin M, Yahagi N, Suwa H, Diffusion Tensor Imaging Studies of Mild Traumatic Brain Injury: A Meta–Analysis. *J Neurol Neurosurg Psychiatry* 2012;83(9):870–6.
62. Munson S, Schroth E, Ernst M, The Role of Functional Neuroimaging in Pediatric Brain Injury. *Pediatrics* 2006;117(4):1372–81.
63. Wilde EA, McCauley SR, Hunter JV, et al. Diffusion Tensor Imaging of Acute Mild Traumatic Brain Injury in Adolescents. *Neurology* 2008;70(12):948–55.
64. Worley G, Hoffman JM, Paine SS, et al. 18–Fluorodeoxyglucose Positron Emission Tomography in Children and Adolescents with Traumatic Brain Injury. *Dev Med Child Neurol*. 1995;37(3):213–20.
65. Goshen E, Zwas ST, Shahar E, Tadmor R, The Role of 99Tcm–HMPAO Brain SPET in Paediatric Traumatic Brain Injury. *Nucl Med Commun*. 1996;17(5):418–22.
66. Ewing–Cobbs L, Prasad MR, Swank P, et al. Arrested Development and Disrupted Callosal Microstructure Following Pediatric Traumatic Brain Injury: Relation to Neurobehavioral Outcomes. *Neuroimage* 2008;42(4):1305–15.
67. Ashwal S, Babikian T, Gardner–Nichols J, Freier MC, Tong KA, Holshouser BA, Susceptibility–Weighted Imaging and Proton Magnetic Resonance Spectroscopy in Assessment of Outcome After Pediatric Traumatic Brain Injury. *Arch Phys Med Rehabil*. 2006;87(12 Suppl 2):50–8.
68. Walz NC, Cecil KM, Wade SL, Michaud LJ, Late Proton Magnetic Resonance Spectroscopy Following Traumatic Brain Injury During Early Childhood: Relationship with Neurobehavioral Outcomes. *J Neurotrauma* 2008;25(2):94–103.
69. Quayle K, Jaffe D, Kupperman N, et al. Diagnostic Testing for Acute Head Injury in Children: When Are Head Computed Tomography and Skull Radiographs Indicated? *Pediatrics* 1997;99:1–8.
70. Gruskin K, Schutzman S, Head Trauma in Children Younger than 2 Years: Are There Predictors for Complications? [published erratum appears in *Arch Pediatr Adolesc Med*. 1999 May;153(5):453.
71. Ramundo M, McKnight T, Kempf J, Satkowiak L, Clinical Predictors of Computed Tomographic Abnormalities Following Pediatric Traumatic Brain Injury. *Pediatr Emerg Care* 1995;11:27–30.
72. Greenes D, Schutzman S, Clinical Indicators of Intracranial Injury in Head–Injured Infants. *Pedia*

trics 1999;104:861-7.

73. Schunk J, Rodgerson J, Woodward G, The Utility of Head Computed Tomographic Scanning in Pediatric Patients with Normal Neurologic Examination in the Emergency Department. *Pediatr Emerg Care* 1996;12:160-5.
74. Shane S, Fuchs S, Skull Fracture in Infants and Predictors of Associated Intracranial Injury. *Pediatr Emerg Care* 1997;132:1-6.
75. Kadish H, Schunk J, Pediatric Basilar Skull Fracture: Do Children with Normal Neurological Findings and No Intracranial Injury Require Hospitalization? *Ann Emerg Med.* 1995;26:37-41.
76. Duhaime A, Alario A, Lewander W, et al. Head Injury in Very Young Children: Mechanisms, Injury Types, and Ophthalmologic Findings in 100 Hospitalized Patients Younger than 2 Years of Age. *Pediatrics* 1992;90:179-85.
77. Greenes D, Schutzman S, Clinical Significance of Scalp Abnormalities in Asymptomatic Head-Injured Infants. *Pediatr Emerg Care* 2001;17:88-92.
78. Osmond MH, Klassen TP, Wells GA, et al. CATCH: A Clinical Decision Rule for the Use of Computed Tomography in Children with Minor Head Injury. *Can Med Assoc J.* 2010;182:341-8.
79. Head Injury Triage, Assessment, Investigation and Early Management of Head Injury in Children, Young People and Adults. NICE Clinical Guideline 176.