Bilaga 4

Nukleärmedicinska metoder som stöd för diagnosen total hjärninfarkt - en systematisk litteraturöversikt, rapport nr 311 (2020)

Bilaga 4 Tabeller, beskrivning av studier

Table 1 Diagnostic accuracy of radionuclide cerebral perfusion scintigraphy with four vessel angiography as reference test.

Author Country Year Reference	Study design Patients	Index test	Reference test	Diagnostic accuracy
Berlit et al Germany 1990+1992 [1,2]	***Study design*** Retrospective case series ***Number of patients*** n=9 with a clinical diagnosis of BD ***Age*** Range 17 to 30 years ***Causes of brain injury*** See Table 2 ***Confounders*** Yes	***Criteria for BD*** Not reported ***Radionuclide*** ^{99m}Tc HMPAO ***Imaging technique*** SPECT	***Method*** Not described ***Criteria for BD*** Not described ***Number and competence of radiologists*** Not reported	100% agreement between the two methods
Munari et al Italy 2005 [3]	***Study design*** Prospective cross-sectional ***Number of patients*** n=20 with a clinical diagnosis of BD ***Age*** Mean age: 43.3 years (range 21–78 years) ***Causes of brain injury*** Head injury: n=7 Subarachnoid hemorrhage: n=7 Brain tumour: n=2 Stroke: n=2 Other: n=2	***Criteria for BD*** Empty skull ***Radionuclide*** ^{99m}Tc HMPAO ***Imaging technique*** SPECT	***Method*** Femoral catheterization and selective injection of iodinated contrast medium into the common carotid artery and vertebral artery of each side ***Criteria for BD*** Absent filling of the intracranial arteries at the entry into the skull and minimal arterial opacification with absent parenchymal and venous phases ***Number and competence of radiologists*** A specialist in neuroradiology	100% agreement between the two methods (BD for 19/20; flow for 1/20)

	Confounders Yes, all had been sedated			
Schwartz et al USA 1983+1984 [4,5]	***Study design*** Case series ***Number of patients*** n=15 with clinical signs of BD ***Age*** n=6 children: 1,2 to 12 years (n=2 infants <2 years) n=9 adults: 19 to 60 years ***Causes of coma*** Head trauma: n=4 Anoxia: n=2 Meningitis: n=1 Brain abscess: n=1 Reye's syndrome: n=1 ***Confounders*** Barbiturates	***Criteria for BD*** Absence of both direct arterial flow and by absence of activity within the sagittal sinus ***Radio nuclide*** ^{99m}Tc pertechnate ***Imaging technique*** Portable gamma camera; dynamic and static images	***Criteria for BD*** In cases of extracranial occlusion of the vertebral and carotid arteries, no contrast material (no flow) is identified within the intracranial vault or contrast material enters the cranium but flow stops at the level of the circle of Willis and vascular stasis occurs ***Number and competence of radiologists*** Not reported	100% agreement between the methods
Wieler et al Germany 1993 [6]	***Study design*** Retrospective cross-sectional ***Number of patients*** n=16 with suspected BD ***Age*** Adults, range 19–69 years ***Causes of brain injury*** Head injury: n=6 Near drowning: n=1 Subdural hematoma: n=2	***Criteria for BD*** No uptake of in cerebrum and cerebellum ***Radio nuclide*** ^{99m}Tc HMPAO ***Imaging technique*** SPECT	***Criteria for BD*** Not described ***Number and competence of clinicians*** Not described	100% agreement between the two methods (No flow for 15/16 patients and flow for 1/16 patients)

	Other: n=7 ***Confounders*** Free of analgesics, barbiturates and muscle relaxants for 24 hours			

BD = Brain death; **SPECT** = Single photon emission computed tomography; **^{99m}Tc HMPAO** = Technetium-99m hexamethylpropyleneamine oxime; **^{99m}Tc pertechnate =** Technetium-99m-pertechnate

Table 2 Diagnostic accuracy of radionuclide cerebral perfusion scintigraphy with clinical diagnosis of brain death as reference test.

Author Country Year Reference	Study design Patients	Index test	Reference test	Diagnostic accuracy
Al-Shammri et al Kuwait 2004 [7]	***Study design*** Prospective case series ***Number of patients*** n=28 with suspected BD ***Age*** Mean 30 years (range 17 to 63 years) ***Cause of coma*** Head trauma: n=10 ICH: n=10 Anoxic encephalopathy: n=3 Ischemic stroke: n=3 Others: n=2 ***Confounders*** Not reported	***Criteria for BD*** Absent flow on the dynamic study, non-visualization of sagittal sinus, no uptake of the radiotracer within the brain regions on planar and SPECT ***Radionuclide*** ^{99m}Tc HMPAO ***Imaging technique*** Dynamic, planar static and SPECT	***Criteria for BD*** Standard clinical criteria performed twice at an interval of 24 hours ***Number and competence of examiners*** Not reported	Confirmed BD in all patients. One patient had infratentorial perfusion in the first test that disappeared in a second test 24 hours later.
Berlit et al Germany 1990+1992 [1,2]	***Study design*** Retrospective case series ***Number of patients*** n=27 with a clinical diagnosis of BD ***Age*** Mean 31 years (range 1,5 to 67 years) ***Causes of brain injury*** Head trauma: n=18 ICH: n=5	***Criteria for BD*** Not reported ***Radionuclide*** ^{99m}Tc HMPAO ***Imaging technique*** SPECT	***Criteria for BD*** German Guidelines 1986. Brain-stem areflexia, apnea test, EEG and evoked potentials. Examination repeated after 12 hours – 3 days depending on age ***Number and competence of examiners*** Not reported	No flow: 25/27 patients Discrete cortical rest perfusion: n=2. Died in cardiac arrest before repeat test

	Others: n=4 ***Confounders*** Yes			
Erbengi et al Turkey 1991 [8]	***Study design*** Prospective ***Number of patients*** n=19 underwent RN ***Age*** 12–61 years ***Causes of brain injury*** Brain tumour: n=11 Head trauma: n=2 SAH: n=5 ICH: n=1 ***Confounders*** No	***Criteria for BD*** Absence of uptake ***Radionuclide*** ^{99m}Tc HMPAO ***Imaging technique*** SPECT ***Number and competence of examiners*** Not reported	***Criteria for BD*** Complete unresponsiveness, fixed and dilated pupils, absence of brain stem reflexes, apnea Observation time at least 12 hours ***Number and competence of examiners*** Not reported but the study was conducted at the department of Neurosurgery	17/19 had no uptake; 1 patient had irregular uptake and one had cerebellar uptake
Facco et al Italy 1998 [9]	***Study design*** Prospective ***Number of patients*** n=50 BD: n=38 Deeply comatose: n=12 ***Age*** Range 10 days to 75 years ***Causes of brain injury*** Head injury: n=28 ICH: n=10 Anoxia: n=5	***Criteria for BD*** Empty skull ***Radionuclide*** ^{99m}Tc HMPAO ***Imaging technique*** SPECT with four-headed gamma camera	***Criteria for BD*** According to Italian law: Absence of brainstem reflexes and oculovestibular responses; absence of motor responses to painful stimuli; absence of oropharyngeal and respiratory reflexes, apnea, flat EEG. Observation lasting 6 hours for adults, 12 hours for children <5 years, 24 hours for infants <1 year; confirmatory test for confounders and infants <1 year	BD with confounders: 15/21 at first measurement BD without confounders: 11/17 at first measurement 12/12 deeply comatose patients had brain perfusion; 9 progressed to BD which was also shown by SPECT. 3 survived and had perfusion

	Brain tumours: n=4 Others: n=3 ***Confounders*** For n=21 patients with BD		***Number and competence of examiners*** Not reported	For two children (10 days, 12 months) residual perfusion persisted, and the children died from cardiac arrest a few days later
Kahveci et al Turkey 2002 [10]	***Study design*** Prospective ***Number of patients*** n=15 with spinal automation after BD ***Age*** Mean 24 years (range 1,5 to 48 years) ***Causes of brain injury*** Head trauma: n=5 SAH: n=3 ICH: n=4 SH: n=2 CO-poisoning: n=1 ***Confounders*** No	***Criteria for BD*** Empty skull, i.e. no uptake in cerebrum, cerebellum and brainstem ***Radionuclide*** ^{99m}Tc HMPAO ***Imaging technique*** SPECT ***Number and competence of examiners*** Visual analysis with consensus of two examiners	***Criteria for BD*** Coma with cerebral unresponsiveness, absence of corneal reflexes, light-fixed mydriatic pupils, absence of oculovestibular reflexes, apnea, electro-cerebral silence on an EEG or no filling of cerebral vessel on a four-vessel angiogram ***Number and competence of examiners*** Not reported	Empty skull for all patients
Kraft et al Czech Republic 2006 [11]	***Study design*** Unclear, case series ***Number of patients*** n=34 with suspected BD ***Age*** Mean: 37.6 years (range 3–65 years) ***Causes of brain injury*** CH: n=8 Cranial injury: n=14 SAH: n=2	***Criteria for BD*** Empty skull ***Radionuclide*** ^{99m}Tc HMPAO ***Imaging technique*** Gamma camera, dynamic and static images ***Number and competence of examiners***	***Criteria for BD*** Not clearly described ***Number and competence of examiners*** Not reported	Empty skull for all patients

	Others: n=10 ***Confounders*** Unclear	Physicians with nuclear medicine attestation		
Laurin et al Canada 1989 [12]	***Study design*** Retrospective case series ***Number of patients*** n=33, with suspected brain death or severe CNS injury ***Age*** 1–73 years ***Causes of brain injury*** Not reported ***Confounders*** Not excluded	***Criteria for BD*** No uptake in cerebrum and cerebellum; activity in the sagittal or transverse sinus was not used ***Radionuclide*** ^{99m}Tc HMPAO ***Imaging technique*** Gamma camera; planar images ***Number and competence of examiners*** Not reported	***Criteria for BD*** According to American and Canadian guidelines ***Number and competence of examiners*** Not reported	Not clinically brain-dead: perfusion for 9/9 Brain-dead without confounders: perfusion for 1/17 Suspected brain-dead with confounders: perfusion for 2/10 patients; one disappeared after 18 hours.
Moya Sanchez et al Spain 2018 [13]	***Study design*** Prospective case series ***Number of patients*** n=56 with clinical BD ***Age*** Median 60 years (IQR 51–72) ***Causes of brain injury*** Hemorrhagic stroke: n=27 Ischemic stroke: n=6 TBI: n=17 Post-cardiac arrest anoxic encephalopathy: n=4 ***Confounders*** No	***Criteria for BD*** Empty skull ***Radionuclide*** ^{99m}Tc HMPAO ***Imaging technique*** Portable gamma camera ***Number and competence of examiners*** Not reported	***Criteria for BD*** According to Spanish law ***Number and competence of examiners*** Not reported	BD was confirmed in all cases

Okuyaz et al Turkey 2004 [14]	***Study design*** Retrospective case series ***Number of patients*** n=8 that fulfilled the basic criteria of BD ***Age*** 7 days: n=2 2–8 years: n=6 ***Causes of brain injury*** Traffic accident: n=2 After cardiac surgery: n=2 Head trauma: n=1 CNS infection: n=1 ICH: n=1 Hypoxic ischemic encephalopathy: n=1 ***Confounders*** None	***Criteria for BD*** "Empty skull" ***Radionuclide*** ^{99m}Tc HMPAO ***Imaging technique*** SPECT ***Number and competence of examiners*** Not reported	***Criteria for BD*** According to American pediatric guidelines (included EEG) ***Declaration of BD*** Patients were observed for at least 24 hours after SPECT and two consecutive clinical examinations were made before declaration of BD, 24 hours in between for neonates and 12–24 hours for older children ***Number and competence of examiners*** Not reported	Neonates: flow in first SPECT, empty skull in second SPECT Older children: empty skull in first SPECT
Schlake et al Germany 1992 [15]	***Study design*** Prospective case series ***Number of patients*** n=17 with suspected brain death ***Age*** Range 17 to 78 years ***Causes of brain injury*** CH: n=6 CI: n=4 Others: n=7 ***Confounders*** No	***Criteria for BD*** Not described ***Radio nuclide*** ^{99m}Tc HMPAO ***Imaging technique*** Gamma camera; planar images ***Number and competence of interpreter*** One neurosurgeon	***Criteria for BD*** German Guidelines ***Number and competence of examiners*** Not described	BD was confirmed in n=6/17 patients; perfusion in one patient with brain stem death (who still had normal EEG)

Schwartz et al USA 1983 [4]	***Study design*** Prospective case series ***Number of patients*** n=15 with clinical signs of BD ***Age*** 1,2 to 60 years (two children below 2 years) ***Causes of coma*** Head trauma: n=8 Gunshot in the head: n=2 CNS hemorrhage: n=2 Meningitis: n=1 ***Confounders*** Barbiturates	***Criteria for BD*** Absence of both direct arterial flow and by absence of activity with the sagittal sinus. ***Radionuclide*** ^{99m}Tc pertechnate ***Imaging technique*** Portable gamma camera; dynamic and static images	***Criteria for BD*** Unresponsitivity and unreceptivity, absent cephalic reflexes, apnea ***Number and competence of examiners*** Not reported	Confirmed BD in all patients
Singh et al Canada 1994 [16]	***Study design*** Retrospective case series, all children that underwent an HMPAO scan ***Number of patients*** n=39; n=17 were clinically brain dead ***Age*** <1 month: n=9 1 month – 17 years: 30 ***Causes of brain injury*** Trauma: n=11 Anoxia/asphyxia: n=19 Meningitis: n=3 Encephalopathy: n=2 Others: n=4 ***Confounders***	***Criteria for BD*** Not described ***Radionuclide*** ^{99m}Tc HMPAO ***Imaging technique*** Gamma camera. Anterior flow, planar images, and tomographic images if the patient's condition permitted it.	***Criteria for BD*** Irreversible of all function of the entire brain, including the brain stem. Repeated examinations between 6 and 48 hours ***Number and competence of examiners*** One pediatric intensivist and one pediatric neurologist	Clinical BD with flow: 4/17 Clinical BD with flow at repeat scan after 72 hours: 2/9 Clinical BD due to anoxia/asphyxia with flow: 6/11 No survivor had a clinical diagnosis of BD or absence of flow on HMPAO-scan

	Excluded			
Sürücü et al Turkey 2014 [17]	***Study design*** Retrospective case series (all patients 2006–2011) ***Number of patients*** n=24 with suspected BD ***Age*** Mean age: 49.5 years (range 8–76) ***Causes of brain injury*** Not reported ***Confounders*** No	***Criteria for BD*** Empty skull ***Radionuclide*** ^{99m}Tc HMPAO or ^{99m}Tc DTPA ***Imaging technique*** Double headed gamma camera, static and dynamic images ***Number and competence of interpreters*** Two nuclear medicine experts	***Criteria for BD*** Coma, absence of brain stem reflexes and apnea ***Number and competence of examiners*** Not reported	BD was confirmed in 23/24 patients; patient 24 with suspicious findings died 24 hours after the scintigraphy

BD = Brain death; **CH** = Cerebral hemorrhage; **CNS =** central nervous system; **CI** = Cerebral ischemia; **CNS** = Central nervous system; **EEG** = Electro encephalogram; **ICH** = Intracerebral hemorrhage; **IQR** = Interquartile range; **RN SAH** = Subarachnoid hemorrhage; **SH** = Subdural hematoma; **SPECT** = Single photon emission computed tomography; **TBI** = Traumatic brain injury; **^{99m}Tc DTPA** = Technetium-99m-diethylene-triamine-pentaacetate; **^{99m}Tc HMPAO** = Technetium-99m hexamethylpropyleneamine oxime

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