Bilaga 5

Apnétest vid diagnostik av total hjärninfarkt - en systematisk litteraturöversikt, rapport 310 (2020)

Bilaga 5 Tabeller, beskrivning av studier

SBU Statens beredning för medicinsk och social utvärdering • www.sbu.se
Telefon 08-412 32 00 • **Fax** 08-411 32 60 • **Organisationsnummer** 202100-4417
Besöksadress S:t Eriksgatan 117, Stockholm • **Postadress** Box 6183, 102 33 Stockholm

Table 1 Safety of confirmatory apnea testing in patients with a clinical diagnosis of brain death.

First author Country Year Reference	Aim, design, population and criteria for BD	Description apnea test	Rate of interrupted or not attempted apnea tests due to risk factors Rate of complications
Ashwal USA 1993 [1]	***Aim*** Determine whether guidelines for Criteria for BD in infants and children were appropriately used ***Study design*** Retrospective chart review of heart transplant donors ***Patients*** n=52 Age: mean 14.3 months (range 1 week to 9 years) ***Criteria for BD*** According to guidelines [2,3] ***Examiners of BD*** Two physicians (mostly a pediatric neurologist or neurosurgeon)	***Methods*** Not described ***Criteria for central apnea*** pCO2 ≥60 mmHg ***Number of apnea tests*** n=27	***Not attempted due to risk factors*** None ***Interrupted*** 10% ***Complications*** None reported
Belsh USA 1986 [4]	***Aim*** Assess the safety of AT in Criteria for BD ***Study design*** Prospective case series ***Patients*** n=20, mean age 47 years (range 1 to 90)	***Methods*** Preoxygenation: at least 30 minutes. The ventilator was adjusted so that prior to disconnection, pCO2 was ≥36 mmHg and pH ≤7.44 Oxygenation: 6 l/min, was delivered to the endotracheal tube via a T-piece Duration: 10 minutes.	***Not attempted due to risk factors*** None ***Interrupted*** None ***Complications*** None reported

	Criteria for BD Deep, unresponsive coma, absence of brain stem reflexes, need for ventilator ***Examiners of BD*** Not reported	***Criteria for central apnea*** PaCO2 ≥60 mmHg ***Number of apnea tests*** n=33	
Benzel USA 1989 [5]	***Aim*** Assess the validity and safety of AT ***Study design*** Prospective case series ***Patients*** n=20 consecutive patients who met neurological criteria for BD. Mean age was 35 years (range 44 months to 86 years) ***Criteria for BD*** Not reported ***Examiners of BD*** Not reported	***Methods*** Preoxygenation: not described Oxygenation: 6 l/min, catheter placed into the endotracheal or tracheostomy tube to the estimated location of the carina. Arterial blood drawn every 2 minutes ***Criteria for central apnea*** PaCO2 ≥60 mmHg ***Number of apnea tests*** n=20	***Not attempted due to risk factors*** None ***Interrupted*** None ***Complications*** Hypoxia 15%
Benzel USA 1992 [6]	***Aim*** Evaluate the effect of an increased baseline PaCO2 on the duration of apnea ***Study design*** Prospective case series ***Patients*** n=11; mean age 39 years (range 17 to 69); n=6 had a baseline PaCO2 between 40 and 45 mmHg; n=5 had a baseline PaCO2 above 45 mmHg.	***Method*** Pre-oxygenation: 15 minutes. The ventilation was adjusted to allow the PaCO2 to rise to ≥40 mmHg. Oxygenation: catheter placed through the endotracheal tube. Duration: 12 minutes ***Criteria for central apnea*** PaCO2 ≥60 mmHg ***Number of apnea tests***	***Not attempted due to risk factors*** None ***Interrupted*** None ***Complications*** No CV instability, otherwise, not described

	Criteria for BD Not reported ***Examiners of BD*** Not reported	n=11	
Blanot France 2016 [7]	***Aim*** Assess the safety of AT in children, 18 years or younger ***Study design*** Retrospective case series ***Patients*** n=103 children with suspected BD mean age: 6 years +/- 5 years ***Criteria for BD*** According to AAN guidelines ***Examiners of BD*** Not reported	***Method*** Preoxygenation: 15 min PaCO2 was normalized to 40 mmHg Oxygenation: 1–6 l/min via catheter placed in the intubation tube Duration: 10 min ***Criteria for central apnea*** No respiratory movements when PaCO2 60 mmHg was reached, verified by blood gas measurements ***Number of apnea tests*** Probably 83	***Not attempted*** n=60 for unclear reasons ***Interrupted*** n=3 due to hypoxemia or hypotension according to preset criteria. Of these n=1 had severe hypotension with elevated adrenaline levels ***Complications*** No cases of pneumothorax, arrythmia or cardiac arrest Hypotension: 9/41 Desaturation: 4/41
Chantorojanasiri Thailand 1993 [8]	***Aim*** Evaluate guidelines for documentation of apnea in children with suspected BD ***Study design*** Prospective case series ***Patients*** n=11 children, aged 5 months to 13 years ***Criteria for BD***	***Method*** Preoxygenation: 10 minutes. The ventilator adjusted for a PaCO2 of 40 mmHg. Oxygenation: 10 l/min provided via a T-piece. Blood gases were measured every 10 minutes. ***Criteria for central apnea*** PaCO2 ≥60 mmHg	***Not attempted due to risk factors*** None ***Interrupted*** None ***Complications*** Hypoxia in 2/11 children

	Cerebral unresponsiveness and lack of brain stem reflexes ***Examiners of BD*** Not reported	***Number of apnea tests*** n=11	
Daneshmand USA 2019 [9]	***Aim*** Assess the frequency of complications of the apnea test ***Study design*** Retrospective chart review from the organ donation agency ***Patients*** n=129 Age: >16 years ***Criteria for BD*** According to AAN guidelines ***Examiners of BD*** Mostly neurointensivists	***Method*** According to AAN guidelines. Only commenced after a pO2 >200 mmHg and a pCO2 between 35 and 45 mmHg. ***Criteria for central apnea*** According to AAN guidelines ***Number of apnea tests*** n=116	***Not attempted due to risk factors*** 13/129 (10%) ***Interrupted*** 2/116 (2%) due to hypotension or hypoxia ***Complications*** No patient developed cardiac arrythmia, arrest or pneumothorax
Datar USA 2014 [10]	***Aim*** Evaluate the safety of AT ***Study design*** Retrospective, consecutive case series of patients with BD that had undergone AT ***Patients*** n=63 underwent apnea test, mean age 46.4+/–17 years n=7 were excluded due to risk factors	***Method*** Pre-oxygenation: at least 10 minutes. Oxygenation: 6 l/min provided via a catheter inside the endotracheal tube and the tip located near the carina. Duration: 8 minutes ***Criteria for central apnea*** PaCO2 >60 mmHg or >20 mmHg above baseline and no spontaneous respiration	***Not attempted due to risk factors*** n=7 (10%) ***Interrupted*** n=1 (1,6%) due to hypoxia ***Complications*** Mild hypoxia: n=3 (5%) Mild hypotension: n=11 (17.4%)

	Criteria for BD According to AAN guidelines ***Examiners of BD*** The apnea test was performed by an experienced neurointensivist in 59 cases.		
Ebata Japan 1991 [11]	***Aim*** Determine the haemodynamic responses to acute hypercapnia during AT and assess the safety of AT ***Study design*** Prospective case series ***Patients*** n=9 with severe head injury and suspected BD Age: mean 53.4 years (range 38 to 78 years) ***Criteria for BD*** A protocol recommended by the Japanese Ministry of Public Welfare ***Tests performed by*** Not reported	***Method*** Preoxygenation: yes The rate of ventilation was slowed to increase the initial value of pCO2 to appr 45 mmHg. Oxygenation: 6 l/min provided via a catheter (id 2.1 mm) inside the endotracheal tube Duration: 10 min ***Criteria for central apnea*** No respiratory movements during the 10 min off ventilator and a PaCO2 >60 mmHg at the end of the test	***Not attempted due to risk factors*** None ***Interrupted*** None ***Severe complications*** No arrythmias; other complications not mentioned ***Mild complications*** No haemodynamic disturbances if the increase of PaCO2 is limited to 60 mmHg.
Fathi USA 2019 [12]	***Aim*** Examine if venous blood sampling can substitute arterial blood sampling ***Study design*** Prospective case series ***Patients*** n=7, admitted to PICU for suspected BD Age: >37 gestation weeks up to 16 years	***Method*** Preoxygenation: yes Oxygenation: catheter inserted in the oral cavity. Duration: if no spontaneous effort to breathe was seen within 8–10 minutes, blood gas samples were drawn and the ventilator placed back. ***Criteria for central apnea***	***Not attempted due to risk factors*** Such patients were excluded from the study ***Interrupted*** n=1 (14%) due to hypoxia and hypotension ***Complications*** Not described

	Criteria for BD According to guidelines ***Tests performed by*** Attending physician at the PICU	No respiratory effort, arterial PaCO2 at least 60 mmHg with a minimal increase of 20 mmHg from the pre apnea level ***Number of apnea tests*** n=9 (once for seven children and twice for two children)	
Giani Italy 2016 [13]	***Aim*** Evaluation of an AT-technique (PEEP combined with pulmonary recruitment) ***Study design*** Retrospective analysis of data for a cohort of brain-dead patients admitted to the ICU ***Patients*** n=25 patients on ECMO n=144 patients not on ECMO Adults >18 years ***Criteria for BD*** Full neurological examination, 30 min EEG-recording and an AT twice with 6 hours interval ***Tests performed by*** One intensivist in presence of a neurologist and a legal medicine specialist	***Method*** Preoxygenation: 5 minutes. Oxygenation: the endotracheal tube was connected to a resuscitator bag, providing 8 l/min O2. An adjustable PEEP valve is connected to the bag and set to provide the same PEEP level used during mechanical ventilation. ***Criteria for central apnea*** Increase at least 20 mmHg pCO2. ***Number of apnea tests*** n=339 (two ATs required for BD and one patient died of cardiac arrest after first AT)	***Not attempted due to risk factors*** None ***Interrupted*** None ***Complications*** Short-lasting severe hypoxia: n=7 (2.4%) not ECMO n=4 (8%) on ECMO p=0.063 Severe hypoxia was more frequent in patients having a baseline PaO2 <200 mmHg
Goudreau USA 2000 [14]	***Aim*** Investigated how many tests were performed according to AAN guidelines and whether inappropriately performed tests had increased risk of complications ***Study design***	***Method*** According to AAN guidelines ***Criteria for central apnea*** pCO2 ≥60 mmHg or increase 20 mmHg from a normal pre-test level	***Not attempted due to risk factors*** NA ***Interrupted*** None ***Complications***

	Retrospective chart review of patients with data on apnea tests for 9 years ***Patients*** n=121 Age: average 39 years (+/– 20 years) ***Criteria for BD*** Unresponsiveness to noxious stimuli, absence of brainstem reflexes, and apnea ***Examiners of BD*** Not reported	***Number of apnea tests*** n=145	n=38/145 (26%) Hypotension: 35/145 (24%) Cardiac arrythmia: 4/145 (<1%) The complications nearly doubled in tests without adequate precautions. The majority (85%) of AT were performed without complications when precautions were taken. Complications occurred most frequently in patients with inadequate preoxygenation and acid-base or electrolytic abnormalities
Harrar USA 2019 [15]	***Aim*** Describe experiences of Criteria for BD in pediatric patients on ECMO ***Study design*** Retrospective, consecutive case-series ***Patients*** n=8 children aged between 1,9 and 16 years ***Criteria for BD*** According to American pediatric guidelines [16]. Interval between examinations at least 12 hours Performed a median of 2.5 days after initiation of ECMO (IQR 2–3.75 days). Interval between examinations median 18 hours (IQR 15–18.75 hours) ***Examiners of BD*** Not reported	***Method*** According to American pediatric guidelines [16] Preoxygenation: more than 10 min. Oxygenation: provided via a self-inflating bag with the patient valve open and PEEP set to 5–10 cmH2O or via a flow-inflating bag with 100% oxygen and PEEP set to 5–10 cmH2O. Adjustments were made to the ECMO circuit during 13/14 AT to mitigate complications. Sweep gases were e.g. decreased at the start to permit a rise in PaCO2 (n=10) ***Criteria for central apnea*** Rise in PaCO2 to ≥60 mmHg and ≥20 mmHg above baseline ***Number of apnea tests***	***Not attempted due to risk factors*** None ***Interrupted*** None ***Complications*** Hypotension: n=2/14 (14%) Hypoxia: n=1/14 (7%)

		n=14	
Hubbard USA 2016 [17]	***Aim*** Evaluate use of CPAP to improve lung quality compared to use of a T-piece/O2 cannula ***Study design*** Retrospective analysis. The clinician decided which method to use. ***Patients*** CPAP: n=67; mean age 41+/–15 years T-piece: n=78; mean age 41+/–18 years Only significant difference was rate of pulmonary contusions in the CPAP group ***Criteria for BD*** Not reported ***Examiners of BD*** Not reported	***Method*** Preoxygenation: not described Oxygenation with CPAP: Flow inflating bag. CPAP was accomplished by an adjustable flow control valve and the opening sealed to sustain CPAP. ***Criteria for central apnea*** Not described ***Number of apnea tests*** n=145	***Comparison between methods*** Significantly higher P:F-ratio in CPAP group ***Complications*** No complications reported in the CPAP-group. No mentioning of the T-piece group
Jeret USA 1994 [18]	***Aim*** Study the cardiovascular effects of AT ***Study design*** Prospective, consecutive case series for two years ***Patients*** n=61 adults ***Criteria for BD*** Unresponsive coma, brainstem areflexia, absence of hypothermia, drugs and sedatives, and apnea	***Method*** Pre-oxygenation: 10 min. Oxygenation: 6 l/min provided via a catheter inserted down the endotracheal tube to the carina Duration: 10 minutes. ***Criteria for central apnea*** No spontaneous respiration during the apnea test was the only requirement according to hospital policy. During the study there was a protocol amendment, requiring a pCO2 >60 mmHg (n=23 patients)	***Not attempted due to risk factors*** None ***Interrupted*** n=14/70 (20%) ***Complications*** Hypotension: n=27/70 (39%) Hypoxia: n=3 in 23 patients where ABG was used (13%)

	Examiners of BD Apnea test performed by neurologists	***Number of apnea tests*** n=70 (two tests for nine patients)	
Kramer Canada 2017 [19]	***Aim*** Comparison of insufflation catheter (CAT) and CPAP (MAT) ***Study design*** Prospective multi-center cohort study ***Patients*** CAT: n=33; mean age 38 years (25–56) MAT: n=44; mean age 52 years (27–60) Differences between groups: baseline arterial pH lower in CAT. ***Criteria for BD*** According to Canadian guidelines [20] ***Examiners of BD*** Not reported	***Methods*** Pre-oxygenation: at least 10 min and with PEEP maintained at 5–15 mmHg; arterial PaCO2 adjusted to 35–45 mmHg. Oxygenation: CAT: 5–8 l/min provided via a catheter with a diameter small enough to avoid occlusion of the endotracheal tube MAT: resuscitation bag with a CPAP valve, set at either 10 cm H2O or to match the pre-existing PEEP level, whichever is higher. Duration: ABGA performed after 5–10 min ***Criteria for central apnea*** No spontaneous breathing despite reaching each of the following criteria: pH ≤7.28; paCO2 ≥60 mmHg and PaCO2 increment ≥20 mm relative to baseline ***Number of apnea tests*** n=86	***Comparison between methods*** No significant differences ***Not attempted due to risk factors*** None ***Interrupted*** CAT: 1/36 AT (3%) due to hypoxia and hypotension CPAP: 1/50 AT (2%) due to hypoxia 2/50 (4%) for unclear reasons
Levesque Canada 2006 [21]	***Aim*** Comparison of three methods of apneic oxygenation in AT (catheter, T-piece, CPAP) ***Study design***	***Method*** Preoxygenation: PEEP 5 cm H2O and FiO2 1.0 for 30 min Oxygenation:	***Comparison between methods*** No significant differences except for decrease in PaO2 where CPAP had better performance ***Not attempted due to risk factors***

	RCT with cross-over (all patients measured with all three tests in a randomized order) and blinded evaluator of PCO2-values ***Patients*** n=20 with suspected BD and no sedatives or neuromuscular blocking agents or hypothermia Age: mean 46 years (range 26 to 72 years) ***Criteria for BD*** Criteria of the Canadian Neurocritical Care Group ***Examiners of BD*** Not reported	Catheter: 6 l/min, 3.2 mm tubing inserted through the endotracheal tube to its distal end. T-piece: standard corrugated tubing (22 mm id) connected to a 12 l/min continuous flow of O2 with a 15 cm T-piece extension CPAP: as the T-piece system with the addition of a 10 cm H2O CPAP valve attached to the distal extremity of the T-piece. Duration: 8–10 min ***Criteria for central apnea*** No respiratory movement; pCO2 at least 60 mmHg; increased pCO2 by at least 20 mmHg compared with baseline ***Number of apnea tests*** n=57 (one patient was withdrawn due to severe hypoxemia)	n=1/20 due to severe hypoxemia ***Interrupted*** n=3 (16%); for two of them CPAP was feasible although the test was interrupted with the T-piece ***Complications*** Not described
Melano Argentina 2002 [22]	***Aim*** Safety of two types of apnea test, with apneic oxygenation and artificial CO2 augmentation (not included in the table) ***Study design*** Retrospective case series ***Patients*** n=68 ***Criteria for BD*** According to national guideline	***Method*** Preoxygenation: yes Oxygenation: 6 l/min, via a catheter to the endotracheal tube to the level of the carina. Duration 5–10 min ***Criteria for central apnea*** No respiratory movements at PaCO2 60 mmHg. ***Number of apnea tests*** n=68	***Not attempted*** Not reported ***Interrupted*** None ***Complications*** n=23 patients had at least one complication Irreversible cardiac arrest: n=1 Arrythmia: n=1 Hypoxemia: n=17 Hypotension: n=8

	Examiners of BD One neurologist and one critical care specialist		
Paret Israel 1995 [23]	***Aim*** To assess the validity, safety and feasibility of apnea testing in children in whom BD is suspected ***Study design*** Prospective case series ***Patients*** n=38 with suspected BD Age: mean age 4.7 years (range 2 months to 17 years) None were hypotensive, hypothermic, sedated of paralyzed. ***Criteria for BD*** Not described ***Examiners of BD*** Not described	***Methods*** Preoxygenation: 10 minutes. Oxygenation: 3–6 l/min provided via a catheter in the endotracheal tube. Duration: ABGA at 0, 5, 10 and 15 min of apnea ***Criteria for central apnea*** pCO2 ≥60 mmHg ***Number of apnea tests*** n=61 (once in 19 patients, twice in 15 and three times in 4 patients)	***Not attempted due to risk factors*** Probably none (not clearly described) ***Interrupted*** n=8 patients (hemodynamic instability); for n=2 patients a repeat AT could be performed and for n=5 patients PaCO2 was already above 60 mm; one child had cardiac arrest for unknown reasons ***Complications*** Not described
Park South Korea 2019 [24]	***Aim*** Evaluate a modified AT (MAT) compared to conventional AT (CAT) ***Study design*** Prospective, where CAT was replaced by MAT during the study time ***Patients*** MAT: n=39 CAT: n=26	***Method*** Pre-oxygenation: yes. Oxygenation: CAT: 15 l/min was supplied through a cannula (2.9 mm id). MAT: an AMBU-bag with PEEP valve was connected to the endotracheal tube and 15 l/min O2 was supplied for maintenance of PEEP. Duration: Serial ABGA was performed after 2–3 minutes. If requirements for BD	***Comparison between methods*** There was no significant difference between CAT and MAT in terms of hypoxemia, acidosis or hemodynamic stabilities. ***Not attempted due to risk factors*** None ***Interrupted***

	Age >18 years Lower APACHE score and dosage NE in MAT-group ***Criteria for BD*** According to the Korean medical law, with 6 hours interval ***Examiners of BD*** Not reported	was not met, ABGA was repeated every minute. Mean duration: 3 minutes ***Criteria for central apnea*** No self-respiration after increase of PaCO2 to >50 mmHg ***Number of apnea tests*** CAT: n=49 in 25 patients MAT: n=77 in 39 patients	n=1 due to unstable vital signs, after treatment a second AT could be performed 24 hours later ***Complications*** Not described
Roth Germany 2015 [25]	***Aim*** To evaluate the cerebral hemodynamic effects of AT ***Study design*** Prospective case series on patients monitored with ICP/CPP during BD determination ***Patients*** n=13; mean age 51 years (range 27 to 71) ***Criteria for BD*** According to German guidelines. ***Examiners of BD*** Jointly by two intensivists at a neuro- intensive care unit	***Method*** According to German guidelines. Pre-oxygenation: several minutes. Oxygenation: The respirator was switched from a controlled mode to an assisted (CPAP-ASB) and the backup volume was turned off, allowing maintenance of positive end-expiratory pressure. Duration: ABGA were performed until PaCO2 of ≥60 mmHg was reached. ***Criteria for central apnea*** paCO2 ≥60 mmHg and observation of respiratory efforts for another 30 to 60 sec ***Number of apnea tests*** n=16	***Not attempted due to risk factors*** Not described ***Interrupted*** None ***Complications*** No hypoxemia, severe hypotension or cardiac arrythmias
Rudolf Germany 1998 [26]	***Aim*** Evaluate the influence of baseline CO2 on the results of AT	***Method*** Year 1: The ventilator was disconnected at PaCO2 40 mmHg.	***Not attempted*** - ***Interrupted***

	Study design Prospective, controlled study comparing two baseline levels of CO2. ***Patients*** Year 1: n=24 patients Mean age: 56.4 years Year 2 (6 months): n=12 Mean age: 56.4 years ***Criteria for BD*** According to German guidelines ***Examiners of BD*** Not reported	Oxygenation: 6 l/min provided via a catheter into the endo-tracheal tube, placed at the carina level. Duration: ABGA at baseline and every minute for 5 minutes Year 2: The ventilator was disconnected at PaCO2 60 mmHg. ***Criteria for central apnea*** No respiratory movements, an increase of PaCO2 by at least 20 mmHg, and endpoint PaCO2 above 60 mmHg. ***Number of apnea tests*** Not reported	None ***Complications*** No relevant hypoxia in neither group Respiratory acidosis more severe in group 2
Salih Germany 2019 [27]	***Aim*** Explore the safety of AT in determination of BD, when AT is performed according to current guidelines ***Study design*** Retrospective analysis of all patients diagnosed with BD during 2009 to 2017 ***Patients*** n=34; mean age 57.7 years (range 22 to 80 years) with continuous ICP and CPP data covering the entire time span of AT ***Criteria for BD*** According to German guidelines	***Method*** Preoxygenation: several minutes. Oxygenation: 2–4 l/min was provided via a catheter inserted in the endotracheal tube. ***Criteria for central apnea*** Absence of breathing effort despite an increase of PaCO2 to 60 mmHg or higher. ***Number of apnea tests*** n=34	***Not attempted due to risk factors*** None ***Interrupted*** None ***Complications*** Hypoxia: n=4/34 (12%)

	Examiners of BD Independent determination by two qualified physicians at the neurological and neurosurgical intensive care unit made		
Saposnik Argentina 2004 [28]	***Aim*** Analyse clinical problems related to the apnea test in the diagnosis of brain death ***Study design*** Retrospective analysis of data from a cohort of BD patients considered for organ donation ***Patients*** n=129 with mean age 41+/–18 years ***Criteria for BD*** According to AAN guidelines. Two clinical evaluations, six hours interval ***Examiners of BD*** Not reported	***Method*** According to AAN guidelines. AT was not performed for patients with arterial hypotension, severe acidosis (pH <7.20) or hypoxemia (pO2 <90 mmHg) which could not be corrected ***Criteria for central apnea*** Absent respiratory movements and arterial pCO2 >60 mmHg ***Number of apnea tests*** n=65+2 with incomplete data	***Not attempted due to risk factors*** n=63 (refractory hypotension, hypoxia or not fulfilling guidelines) ***Interrupted*** None ***Complications*** Hypoxemia: n=8 (12%) Hypotension: n=15 (23%) Acidosis: n=41 (63%) ***Severe complications*** Cardiac arrest and pneumothorax: n=1 Cardiac arrest and bradycardia: n=1 Bradycardia: n=1 MI: n=1
Solek-Pastuszka Poland 2019 [29]	***Aim*** Compare insufflation (CAT) and CPAP (MAT) in Criteria for BD ***Study design*** Retrospective analysis of prospectively collected data. MAT was performed app 1.5 hours after CAT and declaration of BD. ***Patients*** n=76 ICU-patients	***Methods*** Pre-oxygenation: 10 min Oxygenation: CAT: 6 l/min through the catheter inserted in the intubation tube. PEEP was 3–15 cm H2O, usually 5 cm. MAT: a CPAP value of 10 cm H2O was delivered with the ventilator. Duration: ABGA was performed after 5 min ***Criteria for central apnea***	***Comparison between methods*** For patients with poor lung function PaO2 decreased significantly during CAT but not during MAT. No other significant differences between the methods ***Not attempted due to risk factors*** None ***Interrupted*** CAT: n=3/76 (4%) due to hypoxia

	Criteria for BD According to Polish guidelines. CAT is performed twice. ***Examiners of BD*** According to Polish guidelines: a protocol should be signed by three physicians whereof one specialist in anaesthesiology and one in neurology or neurosurgery	No spontaneous breathing despite the rise of PaCO2 above 60 mmHg and over 20 mmHg above baseline ***Number of apnea tests*** n=60 MAT; for n=8 patients MAT could not be performed for technical reasons; for n=5 data was incomplete or time between tests too long	***Complications*** No severe desaturation, cardiac arrythmia, pneumothorax
Wijdicks USA 2008 [30]	***Aim*** Describe a single center experience of BD determination ***Study design*** Retrospective analysis of data from a database maintained by the organ procurement organization ***Patients*** n=195 adults and 33 children. Median age 46 years (range 2 months to 84 years) ***Criteria for BD*** According to AAN. For children examinations were repeated after 12 to 24 hours as per protocol ***Examiners of BD*** Usually neurointensivists and neurosurgeons	***Methods*** According to AAN guidelines Preoxygenation: 10 minutes Oxygenation: 6–10 l/min provided through a catheter into the endotracheal tube. Duration: ABGA after 8 to 10 minutes ***Criteria for central apnea*** PaCO2 ≥60 mmHg or a 20 mmHg increase ***Number of apnea tests*** Not clearly described	***Not attempted due to risk factors*** n=16 (7%) ***Interrupted*** n=7/212 (3%) due to progressive hypotension or hypoxia ***Complications*** Brief hypotension: n=14 (7%) Hypoxia: n=10 (5%)
Wu China 2008 [31]	***Aim*** To investigate complications during AT ***Study design***	***Method*** Preoxygenation: at least 10 minutes. Oxygenation:	***Not attempted due to risk factors*** None ***Interrupted***

	Retrospective review of charts from 25 cities, collected for four years ***Patients*** n=93 adults with a clinical diagnosis of BD Age: 18 to 82 years ***Criteria for BD*** According to Chinese guidelines (Ministry of Health) ***Examiners of BD*** Not described	6 l/min provided through a cannula placed into the endotracheal tube to the level of the carina. Duration: Until a pCO2 level of 60 mmHg or an increase of >20 mmHg above normocapnia ***Criteria for central apnea*** No respiratory movement ***Number of apnea tests*** n=179 (once for seven patients that died during the observation time and twice for the remaining patients)	n=3/179 (2%) due to hypoxia, but arterial blood was drawn immediately before reconnection to the ventilator ***Complications*** Hypoxia: 10/179 (6%) Hypotension: 30/179 (17%) Both: 3/179 (3%)

AAN = American Academy of Neurology; **ABG** = Arterial blood gas; **ABGA** = Arterial blood gas analysis,; **AMBU-bag** = Air mask bag unit-bag; **APACHE score** = Acute physiology and chronic health evaluation score; **AT** = Apnea test; **BD** = Brain dead; **CAT** = Conventional apnea test; **CPAP** = Continuous positive airway pressure; **CPAP-ASB** = Continuous positive airway pressure - assisted spontaneous breathing; **CV** = Cardiovascular; **ECMO** = Extracorporeal membrane oxygenation; **EEG** = Elektroencefalografi; **FiO2** = Fraction of inspired oxygen; **ICP/CPP** = Intracranial pressure/cerebral perfusion pressure; **ICU** = Intensive care unit; **IQR** = Interquartile range; **MAT** = Modified apnea test; **MI** = Myocardium infarction; **mmHg** = Millimetre of mercury; **NA** = Not applicable; **NE** = Norepinephrine.; **O2** = Oxygen; **PaCO2** = Arterial carbon dioxide partial pressure; **pCO2** = Arterial partial pressure of oxygen; **PEEP** = Positive end-expiratory pressure; **PICU** = Pediatric intensive care; **pO2** = Partial pressure of oxygen; **RCT** = Randomized controlled trial;

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