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REVIEW ARTICLE

Patent foramen ovale and neurosurgery in sitting position: a systematic review

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We have conducted a systematic review of air embolism complications of neurosurgery in the sitting position and patent foramen ovale (PFO) closure. It assesses the risk and benefit of PFO closure before neurosurgery in the sitting position. The databases Medline, Embase, and Cochrane Controlled Trial Register were systematically searched from inception to November 2007 for keywords in both topics separately. In total, 4806 patients were considered for neurosurgery in sitting position and 5416 patients underwent percutaneous PFO closure. The overall rate of venous air embolism during neurosurgery in sitting position was 39% for posterior fossa surgery and 12% for cervical surgery. The rate of clinical and transoesophageal echocardiography detected paradoxical air embolism was reported between 0% and 14%. The overall success rate for PFO closure using new and the most common closure devices was reported 99%, whereas the average risk of major complications is <1%. On the basis of our systematic review, we recommend screening for PFO and considering closure in cases in which the sitting position is the preferred neurosurgical approach. Our proposed management including the time of PFO closure according to available data is presented. However, the conclusions from our systematic review may be limited due to the lack of level A evidence and from using data from observational cohort studies. Thus, definite evidence-based recommendations require prospective evaluation of the issue in well-designed studies.

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Fatal air embolism in a patient operated on in the sitting position was first reported by Barlow[9] in 1830, and the sitting position in brain and cervical spine surgery has been a subject of interest since then.[30 37 85 90] During this time, expert opinion has been revised repeatedly. The sitting position has advantages but also has intrinsic complications.[73 85] The most severe risks are venous air embolism (VAE) and its potentially fatal complication, paradoxical air embolism (PAE).[32 52 79 90] VAE is defined as the entrainment of air (or exogenously delivered gas) into the venous system from the operative site or another communication with the environment. It may produce a broad array of systemic effects and outcomes. PAE occurs when VAE passes into the systemic arterial circulation, for example, through a patent foramen ovale (PFO). A negative pressure in cranial veins in the sitting position leads to air aspiration. However, a lower incidence of VAE during neurosurgery has also been reported in the horizontal position.[2 19 42 92 99]

VAE may have catastrophic cardiovascular, pulmonary, and neurological sequelae regardless of the presence of a PFO. A PFO is the major mechanism for cerebral arterial air embolism during neurosurgery in that situation.[37 38 59 69 85 87 89] Its prevalence in the normal population is about 25%,[56] and >40% in adults with cryptogenic stroke.[72]

The presence of a PFO represents a significant contraindication to neurosurgery in the sitting position, and many surgeons avoid the sitting position in order to minimize the risk of PAE.[19 37 45 49 52 74 76 90 96] Therefore, transoesophageal echocardiography (TOE) or transcranial Doppler ultrasound has become a routine preoperative evaluation in many

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centres to rule out a PFO in such patients.[52 70 74 85 90 95] However, neurosurgery in the sitting position cannot always be avoided in this population, as some neurosurgeons feel uncomfortable with the horizontal position for certain operations and are prepared to accept the increased risk for PAE.[19 94] Meanwhile, percutaneous PFO closure using dedicated devices has become a routine procedure with a low risk and high success rate.[116]

The indications of preoperative PFO closure in order to minimize the risk for neurosurgery in the sitting position remain to be defined.

The aim of this systematic review is to assess the risk and benefit of PFO closure before neurosurgery in the sitting position.

Literature search

Two groups were defined for the literature review: Group 1, studies of air embolism during neurosurgical procedures in sitting position, and Group 2, percutaneous PFO closure studies. The databases Medline, Embase, and Cochrane Controlled Trial Register were systematically searched from inception to November 2007 by various combinations of the keyword groups: (i) neurosurgery, sitting position, air embolism, complications, patent foramen ovale and (ii) patent foramen ovale, persistent foramen ovale, PFO, and closure. All abstracts were screened according to the research question. Bibliographies of identified articles and reviews in this field were also searched. Additionally, hand searching of pertinent journals for issues in the last 6 months was undertaken. Articles in multiple languages were searched.

Inclusion criteria for Group 1 were cohort studies with 10 or more patients undergoing neurosurgical procedures in the sitting position with reporting of episodes of VAE or PAE. Inclusion criteria for Group 2 were cohort studies including 10 or more patients undergoing percutaneous PFO closure for any reason with follow-up of at least 3 months. The reports including both PFO and atrial septal defect (ASD) closures were included when the data were stratified for PFO and ASD closures. Exclusion criteria for both groups were studies of exclusively paediatric patients, experimental studies, animal studies, case reports, expert opinions, repeated reports from individual centres (the last all-inclusive report was used), and studies with unclear methods.

Data extraction and analysis

Database search and data extraction were performed independently by two authors and resulted in 127 abstracts meeting the inclusion and exclusion criteria for Group 1 and 89 for Group 2. After full-text analysis, 28 remained in Group 1 and 33 in Group 2. All were in English, except for two papers in French. Quality was independently assessed by two reviewers (A.-R.F. and P.E.) and differences were reconciled by mutual agreement of the senior author (B.M.). The following data were tabulated from included studies and inserted into a standardized excel sheet (Microsoft Office 2000, Microsoft, Redmond, WA, USA). Groups 1 and 2: author, publication year, journal, language, study design, number of cases, mean age of patients. Group 1: type of neurosurgical procedure, rates of VAE and PAE, method of air embolism detection, screening for PFO, PFO prevalence, author recommendations regarding PFO, and neurosurgery in the sitting position. Group 2: PFO closure reasons, PFO closure devices, procedural success rates, major and minor peri-procedural complication rates, and residual shunt rates. Comparison of clinical outcome of air embolism was not feasible due to clinical heterogeneity between studies with regard to populations, interventions, form of outcome assessment, or study method. The data were pooled using Comprehensive Meta-analysis Version 2, Biostat, Englewood, NJ, USA (2005), when it was feasible, and there was no heterogeneity in definitions or methodologies.

Definitions

The definitions of PAE and VAE were given above. The most frequently used methods were TOE, precordial Doppler study, and end-tidal CO_2 (E'_{CO_2}). PFO closure success rates were defined as successful device implantation. Minor procedural complications were haematoma or bleeding not requiring transfusion, transient atrial arrhythmia or atrioventricular node block, device embolization, air embolization, transient ST-segment elevation, or femoral arteriovenous fistula. Major complications were death, stroke, cardiac tamponade, emergency surgery, haematoma, or bleeding requiring blood transfusion or surgery, transient ischaemic attack, significant (persistent) arrhythmia, cardiac perforation, device malposition, septicaemia, myocardial infarction, and massive pulmonary embolism.

Results

No randomized controlled trial or studies with level A evidence were found. Therefore, we included both retrospective and prospective clinical cohort studies (evidence level B of American Academy of Family Physicians).[104]

VAE and PAE in sitting position

Twenty-eight studies published between 1972 and 2007 were included for data analysis.[2 3 15 18 19 25 33 38 42 47 52 53 70 71 75 77 79 81 84 87 92 97 99 103 107 109 115 120] In total, 4806 patients were included (Supplementary Table S1 in online version). Fifty-four per cent of the studies were prospective, six reported on VAE rates during posterior fossa surgery alone, two during cervical procedures alone, and 21 reported on both procedures. No study evaluated the occurrence of PAE for either procedure separately. The overall occurrence of VAE ranged from 0%

Table 1 Comparison of the rate of VAE between sitting position and horizontal position

Authors	Year of publication	VAE in SP	VAE in HP	Method of detection
Albin and colleagues	1976	25%	11%	PD
Black and colleagues	1988	45%	12%	PD
Duke and colleagues	1998	28%	5%	E'_{CO_2} and PD
Rath and colleagues	2007	15%	1%	E'_{CO_2}
Schwarz and colleagues	1994	27%	0%	E'_{CO_2} and PD
Overall		28.4% (95% CI, 20.3–38.0)	5.5% (95% CI, 2.6–11.3)	

Table 2 Comparison of the rate of VAE between posterior fossa surgery and cervical surgery in sitting position

Authors	Year of publication	VAE in posterior fossa surgery	VAE in cervical surgery	
Michenfelder and colleagues	1972	42%	24%	
Albin and colleagues	1976	25%		
Buckland and Manners	1976	33%		
Cucchiara and colleagues	1984	60%		TOE
Standefer and colleagues	1984	7%		
Matjasko and colleagues	1985	41%	9%	
Young and colleagues	1986	43%	13%	
Black and colleagues	1988	45%		
Losasso and colleagues	1992	43%	7%	
Papadopoulos and colleagues	1994	76%	25%	TOE
Simo Moyo and colleagues	1995	31%		
Duke and colleagues	1998	28%		
Stendel and colleagues	2000	75%	35%	TOE
Schmitt and Hemmerling	2002	72%		TOE
Girard and colleagues	2003		2%	
Bithal and colleagues	2004	28%		
Leslie and colleagues	2006	15%	6%	
Overall		38.6% (95% CI, 30.5–47.4)	11.8% (95% CI, 6.7–19.9)	
Overall of studies with TOE		73.7% (95% CI, 66.9–79.5)	30.6% (95% CI, 21.7–41.2)	

to 76% irrespective of the method of detection and position. The incidence of VAE derived from pooled data was 1–76% in the sitting position and 0–12% in the horizontal position. The incidence of VAE from the studies comparing two positions was 28.4% (15–45%) (95% CI, 20.3–38.0) sitting and 5.5% (0–12%) (95% CI, 2.6–11.3) horizontal (Table 1). The rate of VAE was 38.6% (7–76%) (95% CI, 30.5–47.4) in posterior fossa surgery and 11.8% (2–35%) (95% CI, 6.7–19.9) in cervical procedures (Table 2). In the studies included, patients were screened before operation for the presence of PFO in 10 (36%) studies, and seven of them published their prevalence. A PFO was detected in 5–33% of the neurosurgical patients. Overall, 10 studies considered the presence of PFO as an absolute contraindication for the sitting position and patients were operated in the horizontal position. Two of the 28 studies did not consider the presence of PFO, if known, as a contraindication for neurosurgery in the sitting position. Of note, none of the studies mentioned the possibility of preoperative PFO closure. The rate of clinical and TOE detected PAE was reported in 20 of 28 studies (0−14%, 0% in 14 studies). Of the 28 studies included, TOE was used as a detection method in nine. In three studies, the presence of a PFO was not regarded as a contraindication to neurosurgery in the sitting position (or at least not mentioned as a contraindication). In these three studies, VAE was found in 38%, 43%, and 60% and PAE in 14%, 0%, and 6.6% of the study population, respectively (the one with 0% PAE had partly excluded patients with PFO).

Patent foramen ovale

Thirty-three non-randomized studies published between 1992 and 2007, 19 prospective and 14 retrospective, were included for data analysis (Supplementary Table S2 in online version).[1 6–8 11–13 21–24 27 28 31 40 41 44 46 60 61 63–66 80 86 91 93 101 105 106 111 116] In total, 5416 patients were included. The cohorts ranged from 10 to 1006 patients and the mean age of the patients from 30 to 57 yr. More than 80% of PFO closures were performed as a secondary prevention for paradoxical embolism in patients with at least one documented thromboembolic event. The remaining indications were mostly migraine and diving. PFO closure devices were ASDOS, Rashkind, Sideris, Buttoned Device, Double-Umbrella, Angel Wing, PFO-Star, Amplatzer ASD occluder, Amplatzer PFO occluder, CardioSEAL family (including Clamshell and STAR-Flex), Cardia PFO occluder (including IntraSept), Premere, Cierra, and Helex. Amplatzer PFO occluder, CardioSEAL family, and PFO-Star family were the most common devices. The principle of percutaneous PFO closure is shown in Figure 1.

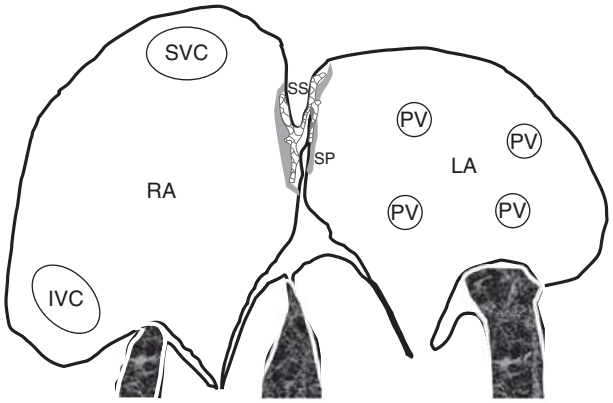

Fig 1 Schematic diagram of an Amplatzer PFO occluder placed in a PFO. The grey area represents endocardium embedding the device within a few months after the implantation. IVC, inferior vena cava; LA, left atrium; PV, pulmonary vein; RA, right atrium; SVC, superior vena cava.

The pooled procedural success rate (reported in all included studies) was 99.2% (95% CI, 98.5–99.6). Minor peri-procedural complication rates were reported in 29 studies with a mean of 3.5% (95% CI, 2.7–4.5). Moreover, pooled data of 30 studies showed the rate of 1.4% (95% CI, 1.1–1.9) for major peri-procedural complications mostly seen using the first generation devices and in early experiences. Residual shunt rates evaluated by TOE were reported at different follow-up time points and are summarized in Supplementary Table S2 (online version).

As this initial review included a number of PFO closure devices which are not used any more, and also some studies of early experiences with some devices, we performed a subanalysis of PFO closure studies which used only the most common and current PFO closure devices (Amplatzer PFO occluder, CardioSEAL family, PFO-Star family, and Helex), and not early clinical experience. There were 15 studies (Supplementary Table S2 in online version)[10–15 18–22 24 26 28 29] meeting these criteria. The success rate was reported in all of them and was 99% (95% CI, 99.0–99.7). Minor and major peri-procedural complication rates were reported in 13 studies with the mean of 4% (95% CI, 2.4–5.6) and 1% (95% CI, 0.7–1.8), respectively, with seven studies reporting no major complication.

Discussion

Since the sitting position for neurosurgery was advocated by De Martel[35] in 1931, the debate about its value and risk has not abated (Table 3). Recently, there has been a worldwide decline in its use.[19 45 74 76 95] A few studies have shown better neurological outcome and less blood loss in the sitting position compared with the horizontal position.[2 19 42 92 99] The main reason for not performing neurosurgery in the sitting position is the risk of PAE through a PFO. Many authors consider the presence of a PFO as absolute contraindication for neurosurgical procedures in the sitting position (Supplementary Table S1 in online version). However, some neurosurgeons prefer the sitting position according to their personal results and positive experience and still perform neurosurgery in the sitting position even in the presence of a PFO.[30 42 47 76 94 107]

Table 3 Advantages of neurosurgery in sitting position[5 9 42 92]

Improved surgical exposure
Improved anatomical orientation
Improved venous drainage from the surgical field
Better haemostasis
Gravitational drainage of the cerebrospinal fluid and blood from the operative field
Improved access to the tracheal tube, chest wall, and arms by the anaesthesiologist
Free diaphragmatic movements
The ability to observe the face for neuromonitoring
Better surgical teaching due to the non-rotated anatomical situation
Shorter surgical time[14]
Decreased intracranial pressure

Our pooled data analysis revealed an overall incidence of VAE in the sitting position of about 39% in posterior fossa surgery and 11% in cervical procedures. The reported incidence of PAE during neurosurgical procedures is quite low in most studies (between 0% and 14%, Table 2).[25 33 79 87] Possible reasons for this are avoidance of surgery in the sitting position in patients with PFO, non-standard and inaccurate methods of detection (most of the studies did not search for and detect PAE using intraoperative TOE, and the report of PAE was only limited to clinically symptomatic PAEs), and incomplete data registration. However rare, PAE can result in severe brain ischaemia and potentially other organ damage.[34 48 50 55 78 88 112 118]

Relationship between VAE and PAE

In general, the morbidity and mortality of VAE are directly related to the volume of air entrainment and rate of accumulation.[85] In several animal models, a close relationship between VAE and PAE has been described.[29 114 119] However, not every VAE results in PAE, and the clinical consequences depend on the quantity of air that crosses over into the arterial circulation.[33] Accordingly, great attention should be paid to minimizing the frequency and volume of air in any position during surgery, as VAE also occurs in the horizontal position and in other types of surgery regardless of the presence of PFO.[85] One explanation of the pathophysiology of PAE could be that the distribution of blood volume between the intra- and extrathoracic compartment occurs after a change from the supine to the sitting position.[26] With the number of monitoring modalities available, most episodes of VAE are preventable.[39 47 58]

As demonstrated in the study of Duke and colleagues,[42] the percentage of patients who were monitored intraoperatively with TOE or Doppler in the horizontal position was

much lower than that in the sitting patients. This underestimates the effective rate of VAE in the horizontal position. Other factors raising the hazard of VAE are the early stage of surgery, including muscle preparation and craniotomy, the use of nitrous oxide (N_2O), and the use of PEEP over 5 cm H_2O.[2 3 15] Both N_2O and PEEP should be used cautiously to minimize further harm by entrained air.[17 43 77] Furthermore, a large prospective study found that PEEP (10 cm H_2O) is associated with adverse cardiopulmonary effects without altering the incidence of VAE.[51] This confirms an earlier study conducted in paediatric neurosurgical procedures.[83]

Methods of detection

Early detection of left-sided cardiac air is vital to prevent poor neurological outcome and the use of TOE or precordial Doppler is essential in this way.[38 77 79] Depending on the method of detection, the frequency of VAE detection is up to 70% (Table 1). The most commonly used methods are TOE, precordial Doppler, E'_{CO_2}, right heart catheterization, and oesophageal stethoscope in decreasing order of sensitivity for air detection.[16]

The potential hazard of PFO

PFO has been increasingly recognized as a source of paradoxical embolism. The mechanism for this phenomenon is thought to involve the passage of air, thrombus, or fat from the right atrium to the left atrium through the PFO and then on to the systemic circulation.[20 36 72 117] As the prevalence of PFO decreases with age from 35% during the first decade to 20% during the ninth decade of life, a selective mortality (increased risk of early death in patients with PFO) has to be considered in addition to spontaneous closure.[56] An additional proof of the prognostic importance is the doubled mortality risk and the tripled stroke risk of patients with pulmonary embolism in the presence of a PFO.[67]

Percutaneous PFO closure with modern closure devices is the most simple of all catheter-based cardiac interventions. The procedure can be performed as an outpatient procedure in <30 min with a fluoroscopy time of <5 min and good long-term safety.[116] The currently accepted indications are limited to patients with (recurrent) cryptogenic stroke, but are likely to expand soon to those with migraine and divers.

The most commonly used devices so far for PFO closure are Amplatzer PFO occluder, CardioSEAL family, and PFO-Star family. Partially bioabsorbable devices (BioSTAR device), self-expanding stent (Coherex FlatStent PFO Closure System), and suturing devices (HeartStich Suturing device) are under clinical investigation. Finally, a radiofrequency energy source for closure of PFO (PFx Closure System) has been clinically tested but has not yet reached the market.

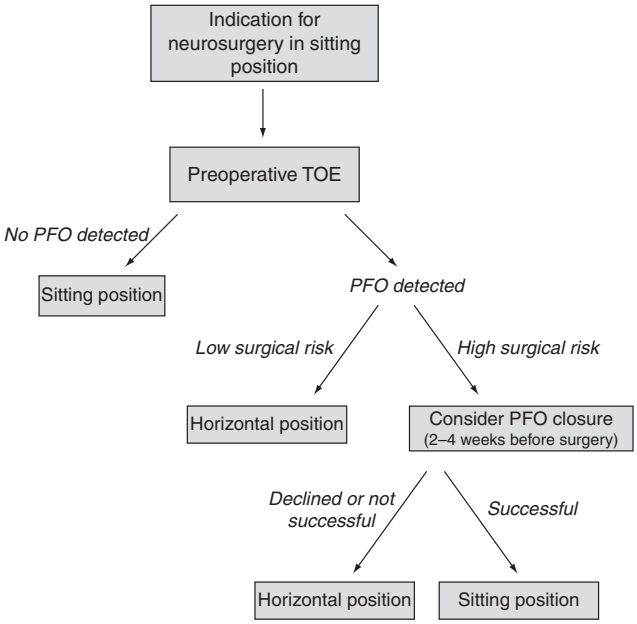

Fig 2 Flow chart for PFO closure as a preoperative management in candidates of neurosurgery in the sitting position.

The review of percutaneous PFO closure in 5416 patients showed the safety and efficacy of this procedure in the short and long term with a high procedural success rate and low morbidity. Consequently, based on the best available scientific evidence, it is appropriate to consider percutaneous PFO closure in the preoperative management of patients requiring neurosurgery in the sitting position. This is particularly important when PFO is the only concern, and the sitting position confers a significantly lower surgical risk (Fig. 2).

Complications

Cerebrovascular ischaemia as a complication during or after PFO closure is a rare event. Peri-interventional complications were mostly minor, reversible, and decrease further with experience and device improvement. Some studies reported no complications with new devices.[100 116] Our subanalysis in 15 studies using newer and more common closure devices showed an overall 3.7% minor complication rate, and 1.2% major complication rate with no major complications in half of the studies. Mid- and long-term complications are also rare and mostly without clinical significance.[82]

Residual shunt

Many studies indicate that small PFOs are a very rare source of paradoxical embolism in patients with cryptogenic stroke and not clinically relevant.[5 62 98 108 110 113] Moreover, Braun and colleagues[22] showed that the presence of a minimal residual shunt after percutaneous PFO closure cannot be considered as a risk factor for recurrent

thromboembolic events. Hence, the small residual shunt rate at 1 month in our systematic review of the literature may not be a matter of concern as these shunts were mostly trivial, and considered as clinically effective occlusion. Neurosurgery in the sitting position could be safely performed at that time.

Antithrombotic therapy

Initial antithrombotic therapy after the percutaneous PFO closure is recommended to prevent device thrombus formation. Although there is no established antithrombotic therapy regimen and duration after percutaneous PFO closure, a common regimen is acetylsalicylic acid for 6 months, occasionally accompanied by clopidogrel for 1–3 months. No study has verified the efficacy and necessity of such antiplatelet therapy. One study[10] has shown no increase in the platelet activation markers after percutaneous PFO closure and questioned the necessity of antiplatelet therapy. Moreover, acetylsalicylic acid has been prescribed in different dosages in different studies. In a report of 63 cases with percutaneous PFO closure,[64] only 46% of patients were on acetylsalicylic acid and 17% on anticoagulation therapy after implantation. No device thrombosis during the mean follow-up period of 2.6 yr was found. Krumsdorf and colleagues[68] did not find any influence of anticoagulation regimens on device thrombus formation. Overall, the reported incidence of thrombus formation is low, and in most cases without clinical sequela. However, there are some differences which favour Amplatzer and Helex occluders.[4 68 116]

Endothelialization of different devices for closure of patent ductus arteriosus in animal models was reported to start as early as 13 days and to be completed at 5 weeks.[54 102] An animal study[57] showed partial and complete endothelialization at 1 and 3 months, respectively, after the implantation of Amplatzer occluders. Early endothelialization was observed 2 weeks after implantation of a PFO Star in a patient who underwent surgical explantation of the device due to dislocation.[22]

For most intra-dural surgical procedures, antithrombotic therapy should be stopped 7–10 days before surgery and not recommenced until 1 week after surgery, provided no perioperative major bleeding occurs. A significant proportion of patients who undergo neurosurgical procedures are already on treatment with aspirin or anticoagulants, and their perioperative management is well established. In view of this, it seems safe to stop acetylsalicylic acid and clopidogrel for neurosurgery for 2 weeks even early after PFO device implantation. Ideally, PFO closure should take place at least 2–4 weeks before surgery. In an emergency operation or when it cannot be delayed, we suggest closure of the PFO immediately before surgery or to use the horizontal position. Even the PFO has been closed before operation, techniques for prevention of air embolism should still be used.[85]

Conclusions

On the basis of our systematic review, we recommend screening for PFO and considering PFO closure in cases where using the sitting position for neurosurgery has major advantages for the outcome. However, the result of our systematic review may be limited due to the lack of data of level A evidence and from using data from cohort studies with observational nature. Therefore, our proposal is based on available evidence, and we have proposed a policy to reduce the risk of PAE and consequently the risk of neurosurgery in the sitting position in patients with PFO. The evidence-based recommendations require prospective evaluation in well-designed studies.

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

References

1 Alameddine F, Block PC. Transcatheter patent foramen ovale closure for secondary prevention of paradoxical embolic events: acute results from the FORECAST registry. *Catheter Cardiovasc Interv* 2004; **62**: 512–6

2 Albin MS, Babinski M, Maroon JC, Jannetta PJ. Anesthetic management of posterior fossa surgery in the sitting position. *Acta Anaesthesiol Scand* 1976; **20**: 117–28

3 Albin MS, Carroll RG, Maroon JC. Clinical considerations concerning detection of venous air embolism. *Neurosurgery* 1978; **3**: 380–4

4 Anzai H, Child J, Natterson B, *et al*. Incidence of thrombus formation on the CardioSEAL and the Amplatzer interatrial closure devices. *Am J Cardiol* 2004; **93**: 426–31

5 Anzola GP, Zavarize P, Morandi E, Rozzini L, Parrinello G. Transcranial Doppler and risk of recurrence in patients with stroke and patent foramen ovale. *Eur J Neurol* 2003; **10**: 129–35

6 Aslam F, Iliadis AE, Blankenship JC. Percutaneous closure of patent foramen ovale: success and outcomes of a low-volume procedure at a rural medical center. *J Invasive Cardiol* 2007; **19**: 20–4

7 Azarbal B, Tobis J, Suh W, Chan V, Dao C, Gaster R. Association of interatrial shunts and migraine headaches: impact of transcatheter closure. *J Am Coll Cardiol* 2005; **45**: 489–92

8 Bailey CE, Allaqaband S, Bajwa TK. Current management of patients with patent foramen ovale and cryptogenic stroke: our experience and review of the literature. *WMJ* 2004; **103**: 32–6

9 Barlow J. An account of the removal of a tumor situated on the cheek. *RocMedChirSoc* 1830; **16**: 19

10 Bedard E, Rodes-Cabau J, Houde C, *et al*. Enhanced thrombogenesis but not platelet activation is associated with transcatheter closure of patent foramen ovale in patients with cryptogenic stroke. *Stroke* 2007; **38**: 100–4

11 Beitzke A, Schuchlenz H, Gamillscheg A, Stein JI, Wendelin G. Catheter closure of the persistent foramen ovale: mid-term results in 162 patients. *J Interv Cardiol* 2001; **14**: 223–9

12 Berger F, Ewert P, Bjornstad PG, *et al*. Transcatheter closure as standard treatment for most interatrial defects: experience in

200 patients treated with the Amplatzer Septal Occluder. *Cardiol Young* 1999; **9**: 468–73

13 Bijl JM, Ruygrok PN, Hornung TS, Wilson NJ, West T. Percutaneous closure of patent foramen ovale. *Intern Med J* 2005; **35**: 706–10

14 Bithal PK, Pandia MP, Chouhan RS, *et al*. Hemodynamic and bispectral index changes following skull pin attachment with and without local anesthetic infiltration of the scalp. *J Anesth* 2007; **21**: 442–4

15 Bithal PK, Pandia MP, Dash HH, Chouhan RS, Mohanty B, Padhy N. Comparative incidence of venous air embolism and associated hypotension in adults and children operated for neurosurgery in the sitting position. *Eur J Anaesthesiol* 2004; **21**: 517–22

16 Black S, Cucchiara RF. Tumor surgery. In: Cucchiara RF, Black S, Michenfelder JD, eds. *Clinical Neuroanesthesia*. New York: Churchill-Livingstone, 1998; 340–65

17 Black S, Cucchiara RF, Nishimura RA, Michenfelder JD. Parameters affecting occurrence of paradoxical air embolism. *Anesthesiology* 1989; **71**: 235–41

18 Black S, Muzzi DA, Nishimura RA, Cucchiara RF. Preoperative and intraoperative echocardiography to detect right-to-left shunt in patients undergoing neurosurgical procedures in the sitting position. *Anesthesiology* 1990; **72**: 436–8

19 Black S, Ockert DB, Oliver WC, Jr, Cucchiara RF. Outcome following posterior fossa craniectomy in patients in the sitting or horizontal positions. *Anesthesiology* 1988; **69**: 49–56

20 Bogousslavsky J, Garazi S, Jeanrenaud X, Aebischer N, Van Melle G. Stroke recurrence in patients with patent foramen ovale: the Lausanne Study. Lausanne Stroke with Paradoxal Embolism Study Group. *Neurology* 1996; **46**: 1301–5

21 Braun M, Gliech V, Boscheri A, *et al*. Transcatheter closure of patent foramen ovale (PFO) in patients with paradoxical embolism. Periprocedural safety and mid-term follow-up results of three different device occluder systems. *Eur Heart J* 2004; **25**: 424–30

22 Braun MU, Fassbender D, Schoen SP, *et al*. Transcatheter closure of patent foramen ovale in patients with cerebral ischemia. *J Am Coll Cardiol* 2002; **39**: 2019–25

23 Bridges ND, Hellenbrand W, Latson L, Filiano J, Newburger JW, Lock JE. Transcatheter closure of patent foramen ovale after presumed paradoxical embolism. *Circulation* 1992; **86**: 1902–8

24 Bruch L, Parsi A, Grad MO, *et al*. Transcatheter closure of interatrial communications for secondary prevention of paradoxical embolism: single-center experience. *Circulation* 2002; **105**: 2845–8

25 Buckland RW, Manners JM. Venous air embolism during neurosurgery. A comparison of various methods of detection in man. *Anaesthesia* 1976; **31**: 633–43

26 Buhre W, Weyland A, Buhre K, *et al*. Effects of the sitting position on the distribution of blood volume in patients undergoing neurosurgical procedures. *Br J Anaesth* 2000; **84**: 354–7

27 Buscheck F, Sievert H, Kleber F, *et al*. Patent foramen ovale using the Premere device: the results of the CLOSEUP trial. *J Interv Cardiol* 2006; **19**: 328–33

28 Butera G, Bini MR, Chessa M, Bedogni F, Onofri M, Carminati M. Transcatheter closure of patent foramen ovale in patients with cryptogenic stroke. *Ital Heart J* 2001; **2**: 115–8

29 Butler BD, Leiman BC, Katz J. Arterial air embolism of venous origin in dogs: effect of nitrous oxide in combination with halothane and pentobarbitone. *Can J Anaesth* 1987; **34**: 570–5

30 Charbel F, Kehrli P, Pain L. The sitting position in neurosurgery: the viewpoint of the surgeon. *Ann Fr Anesth Reanim* 1998; **17**: 160–3

31 Chatterjee T, Petzsch M, Ince H, *et al*. Interventional closure with Amplatzer PFO occluder of patent foramen ovale in patients with paradoxical cerebral embolism. *J Interv Cardiol* 2005; **18**: 173–9

32 Clayton DG, Evans P, Williams C, Thurlow AC. Paradoxical air embolism during neurosurgery. *Anaesthesia* 1985; **40**: 981–9

33 Cucchiara RF, Nugent M, Seward JB, Messick JM. Air embolism in upright neurosurgical patients: detection and localization by two-dimensional transesophageal echocardiography. *Anesthesiology* 1984; **60**: 353–5

34 Cucchiara RF, Seward JB, Nishimura RA, Nugent M, Faust RJ. Identification of patent foramen ovale during sitting position craniotomy by transesophageal echocardiography with positive airway pressure. *Anesthesiology* 1985; **63**: 107–9

35 De Martel T. Surgical treatment of cerebral tumors: technical considerations. *Surg Gynecol Obstet* 1931; **52**: 381–5

36 Di Tullio M, Sacco RL, Venketasubramanian N, Sherman D, Mohr JP, Homma S. Comparison of diagnostic techniques for the detection of a patent foramen ovale in stroke patients. *Stroke* 1993; **24**: 1020–4

37 Domaingue CM. Anaesthesia for neurosurgery in the sitting position: a practical approach. *Anaesth Intensive Care* 2005; **33**: 323–31

38 Domaingue CM. Neurosurgery in the sitting position: a case series. *Anaesth Intensive Care* 2005; **33**: 332–5

39 Draganov J, Scheeren TW. Incidental detection of paradoxical air embolism with a transoesophageal Doppler probe inserted for measuring descending aortic blood flow. *Br J Anaesth* 2003; **90**: 520–2

40 Du ZD, Hijazi ZM, Kleinman CS, Silverman NH, Larntz K. Comparison between transcatheter and surgical closure of secundum atrial septal defect in children and adults: results of a multicenter nonrandomized trial. *J Am Coll Cardiol* 2002; **39**: 1836–44

41 Dubiel M, Bruch L, Liebner M, *et al*. Exclusion of patients with arteriosclerosis reduces long-term recurrence rate of presumed arterial embolism after PFO closure. *J Interv Cardiol* 2007; **20**: 275–81

42 Duke DA, Lynch JJ, Harner SG, Faust RJ, Ebersold MJ. Venous air embolism in sitting and supine patients undergoing vestibular schwannoma resection. *Neurosurgery* 1998; **42**: 1282–6, discussion 6–7

43 Eger EI, 2nd, Saidman LJ. Hazards of nitrous oxide anesthesia in bowel obstruction and pneumothorax. *Anesthesiology* 1965; **26**: 61–6

44 Egred M, Andron M, Albouaini K, Alahmar A, Grainger R, Morrison WL. Percutaneous closure of patent foramen ovale and atrial septal defect: procedure outcome and medium-term follow-up. *J Interv Cardiol* 2007; **20**: 395–401

45 Elton RJ, Howell RS. The sitting position in neurosurgical anaesthesia: a survey of British practice in 1991. *Br J Anaesth* 1994; **73**: 247–8

46 Ende DJ, Chopra PS, Rao PS. Transcatheter closure of atrial septal defect or patent foramen ovale with the buttoned device for prevention of recurrence of paradoxic embolism. *Am J Cardiol* 1996; **78**: 233–6

47 Engelhardt M, Folkers W, Brenke C, *et al*. Neurosurgical operations with the patient in sitting position: analysis of risk factors using transcranial Doppler sonography. *Br J Anaesth* 2006; **96**: 467–72

48 Furuya H, Suzuki T, Okumura F, Kishi Y, Uefuji T. Detection of air embolism by transesophageal echocardiography. *Anesthesiology* 1983; **58**: 124–9

49 Gale T, Leslie K. Anaesthesia for neurosurgery in the sitting position. *J Clin Neurosci* 2004; **11**: 693–6

50 Garachemani A, Eshtehardi P, Meier B. Paradoxical emboli through the patent foramen ovale as the suspected cause of myocardial and renal infarction in a 48-year-old woman. *Catheter Cardiovasc Interv* 2007; **70**: 1010–2

51 Giebler R, Kollenberg B, Pohlen G, Peters J. Effect of positive end-expiratory pressure on the incidence of venous air embolism and on the cardiovascular response to the sitting position during neurosurgery. *Br J Anaesth* 1998; **80**: 30–5

52 Girard F, Ruel M, McKenty S, *et al*. Incidences of venous air embolism and patent foramen ovale among patients undergoing selective peripheral denervation in the sitting position. *Neurosurgery* 2003; **53**: 316–9, discussion 9–20

53 Glenski JA, Cucchiara RF. Transcutaneous O_2 and CO_2 monitoring of neurosurgical patients: detection of air embolism. *Anesthesiology* 1986; **64**: 546–50

54 Grabitz RG, Schrader R, Sigler M, *et al*. Retrievable patent ductus arteriosus plug for interventional, transvenous occlusion of the patent ductus arteriosus. Evaluation in lambs and preliminary clinical results. *Invest Radiol* 1997; **32**: 523–8

55 Gronert GA, Messick JM, Jr, Cucchiara RF, Michenfelder JD. Paradoxical air embolism from a patent foramen ovale. *Anesthesiology* 1979; **50**: 548–9

56 Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. *Mayo Clin Proc* 1984; **59**: 17–20

57 Han YM, Gu X, Titus JL, *et al*. New self-expanding patent foramen ovale occlusion device. *Catheter Cardiovasc Interv* 1999; **47**: 370–6

58 Harrison EA, Mackersie A, McEwan A, Facer E. The sitting position for neurosurgery in children: a review of 16 years' experience. *Br J Anaesth* 2002; **88**: 12–7

59 Heckmann JG, Lang CJ, Kindler K, Huk W, Erbguth FJ, Neundorfer B. Neurologic manifestations of cerebral air embolism as a complication of central venous catheterization. *Crit Care Med* 2000; **28**: 1621–5

60 Hein R, Buscheck F, Fischer E, *et al*. Atrial and ventricular septal defects can safely be closed by percutaneous intervention. *J Interv Cardiol* 2005; **18**: 515–22

61 Herrmann HC, Silvestry FE, Glaser R, *et al*. Percutaneous patent foramen ovale and atrial septal defect closure in adults: results and device comparison in 100 consecutive implants at a single center. *Catheter Cardiovasc Interv* 2005; **64**: 197–203

62 Homma S, Di Tullio MR, Sacco RL, Mihalatos D, Li Mandri G, Mohr JP. Characteristics of patent foramen ovale associated with cryptogenic stroke. A biplane transesophageal echocardiographic study. *Stroke* 1994; **25**: 582–6

63 Hong TE, Thaler D, Brorson J, Heitschmidt M, Hijazi ZM. Transcatheter closure of patent foramen ovale associated with paradoxical embolism using the amplatzer PFO occluder: initial and intermediate-term results of the US multicenter clinical trial. *Catheter Cardiovasc Interv* 2003; **60**: 524–8

64 Hung J, Landzberg MJ, Jenkins KJ, *et al*. Closure of patent foramen ovale for paradoxical emboli: intermediate-term risk of recurrent neurological events following transcatheter device placement. *J Am Coll Cardiol* 2000; **35**: 1311–6

65 Khositseth A, Cabalka AK, Sweeney JP, *et al*. Transcatheter Amplatzer device closure of atrial septal defect and patent foramen ovale in patients with presumed paradoxical embolism. *Mayo Clin Proc* 2004; **79**: 35–41

66 Kiblawi FM, Sommer RJ, Levchuck SG. Transcatheter closure of patent foramen ovale in older adults. *Catheter Cardiovasc Interv* 2006; **68**: 136–42, discussion 43–4

67 Konstantinides S, Geibel A, Kasper W, Olschewski M, Blumel L, Just H. Patent foramen ovale is an important predictor of adverse outcome in patients with major pulmonary embolism. *Circulation* 1998; **97**: 1946–51

68 Krumsdorf U, Ostermayer S, Billinger K, *et al*. Incidence and clinical course of thrombus formation on atrial septal defect and patient foramen ovale closure devices in 1,000 consecutive patients. *J Am Coll Cardiol* 2004; **43**: 302–9

69 Kubo S, Nakata H. Air embolism due to a patent foramen ovale visualised by harmonic contrast echocardiography. *J Neurol Neurosurg Psychiatry* 2001; **71**: 555

70 Kwapisz MM, Deinsberger W, Muller M, *et al*. Transesophageal echocardiography as a guide for patient positioning before neurosurgical procedures in semi-sitting position. *J Neurosurg Anesthesiol* 2004; **16**: 277–81

71 Lechat P, Guggiari M, Lascault G, *et al*. Detection by contrast ultrasonography of patent foramen ovale before neurosurgery. *Presse Med* 1986; **15**: 1409–10

72 Lechat P, Mas JL, Lascault G, *et al*. Prevalence of patent foramen ovale in patients with stroke. *N Engl J Med* 1988; **318**: 1148–52

73 Leivers D, Spilsbury RA, Young JV. Air embolism during neurosurgery in the sitting position. Two case reports. *Br J Anaesth* 1971; **43**: 84–90

74 Leonard IE, Cunningham AJ. The sitting position in neurosurgery—not yet obsolete! *Br J Anaesth* 2002; **88**: 1–3

75 Leslie K, Hui R, Kaye AH. Venous air embolism and the sitting position: a case series. *J Clin Neurosci* 2006; **13**: 419–22

76 Liutkus D, Gouraud JP, Blanloeil Y. The sitting position in neurosurgical anaesthesia: a survey of French practice. *Ann Fr Anesth Reanim* 2003; **22**: 296–300

77 Losasso TJ, Muzzi DA, Dietz NM, Cucchiara RF. Fifty percent nitrous oxide does not increase the risk of venous air embolism in neurosurgical patients operated upon in the sitting position. *Anesthesiology* 1992; **77**: 21–30

78 Loscalzo J. Paradoxical embolism: clinical presentation, diagnostic strategies, and therapeutic options. *Am Heart J* 1986; **112**: 141–5

79 Mammoto T, Hayashi Y, Ohnishi Y, Kuro M. Incidence of venous and paradoxical air embolism in neurosurgical patients in the sitting position: detection by transesophageal echocardiography. *Acta Anaesthesiol Scand* 1998; **42**: 643–7

80 Martin F, Sanchez PL, Doherty E, *et al*. Percutaneous transcatheter closure of patent foramen ovale in patients with paradoxical embolism. *Circulation* 2002; **106**: 1121–6

81 Matjasko J, Petrozza P, Cohen M, Steinberg P. Anesthesia and surgery in the seated position: analysis of 554 cases. *Neurosurgery* 1985; **17**: 695–702

82 Meier B. Closure of patent foramen ovale: technique, pitfalls, complications, and follow up. *Heart* 2005; **91**: 444–8

83 Meyer PG, Cuttaree H, Charron B, Jarreau MM, Perie AC, Sainte-Rose C. Prevention of venous air embolism in paediatric neurosurgical procedures performed in the sitting position by combined use of MAST suit and PEEP. *Br J Anaesth* 1994; **73**: 795–800

84 Michenfelder JD, Miller RH, Gronert GA. Evaluation of an ultrasonic device (Doppler) for the diagnosis of venous air embolism. *Anesthesiology* 1972; **36**: 164–7

85 Mirski MA, Lele AV, Fitzsimmons L, Toung TJ. Diagnosis and treatment of vascular air embolism. *Anesthesiology* 2007; **106**: 164–77

86 Onorato E, Melzi G, Casilli F, *et al*. Patent foramen ovale with paradoxical embolism: mid-term results of transcatheter closure in 256 patients. *J Interv Cardiol* 2003; **16**: 43–50

87 Papadopoulos G, Kuhly P, Brock M, Rudolph KH, Link J, Eyrich K. Venous and paradoxical air embolism in the sitting position. A prospective study with transoesophageal echocardiography. *Acta Neurochir (Wien)* 1994; **126**: 140–3

88 Perkins-Pearson NA, Marshall WK, Bedford RF. Atrial pressures in the seated position: implication for paradoxical air embolism. *Anesthesiology* 1982; **57**: 493–7

89 Pham Dang C, Pereon Y, Champin P, Delecrin J, Passuti N. Paradoxical air embolism from patent foramen ovale in scoliosis surgery. *Spine* 2002; **27**: E291–5

90 Porter JM, Pidgeon C, Cunningham AJ. The sitting position in neurosurgery: a critical appraisal. *Br J Anaesth* 1999; **82**: 117–28

91 Post MC, Van Deyk K, Budts W. Percutaneous closure of a patent foramen ovale: single-centre experience using different types of devices and mid-term outcome. *Acta Cardiol* 2005; **60**: 515–9

92 Rath GP, Bithal PK, Chaturvedi A, Dash HH. Complications related to positioning in posterior fossa craniectomy. *J Clin Neurosci* 2007; **14**: 520–5

93 Reisman M, Christofferson RD, Jesurum J, *et al*. Migraine headache relief after transcatheter closure of patent foramen ovale. *J Am Coll Cardiol* 2005; **45**: 493–5

94 Samii M, Matthies C. Management of 1000 vestibular schwannomas (acoustic neuromas): the facial nerve—preservation and restitution of function. *Neurosurgery* 1997; **40**: 684–94

95 Schaffranietz L, Grothe A, Olthoff D. Use of the sitting position in neurosurgery. Results of a 1998 survey in Germany. *Anaesthesist* 2000; **49**: 269–74

96 Schaffranietz L, Gunther L. The sitting position in neurosurgical operations. Results of a survey. *Anaesthesist* 1997; **46**: 91–5

97 Schmitt HJ, Hemmerling TM. Venous air emboli occur during release of positive end-expiratory pressure and repositioning after sitting position surgery. *Anesth Analg* 2002; **94**: 400–3, table of contents

98 Schuchlenz HW, Weihs W, Horner S, Quehenberger F. The association between the diameter of a patent foramen ovale and the risk of embolic cerebrovascular events. *Am J Med* 2000; **109**: 456–62

99 Schwarz G, Fuchs G, Weihs W, Tritthart H, Schalk HV, Kaltenbock F. Sitting position for neurosurgery: experience with preoperative contrast echocardiography in 301 patients. *J Neurosurg Anesthesiol* 1994; **6**: 83–8

100 Sievert H, Fischer E, Heinisch C, Majunke N, Roemer A, Wunderlich N. Transcatheter closure of patent foramen ovale without an implant: initial clinical experience. *Circulation* 2007; **116**: 1701–6

101 Sievert H, Horvath K, Zadan E, *et al*. Patent foramen ovale closure in patients with transient ischemia attack/stroke. *J Interv Cardiol* 2001; **14**: 261–6

102 Sigler M, Handt S, Seghaye MC, Von Bernuth G, Grabitz RG. Evaluation of in vivo biocompatibility of different devices for interventional closure of the patent ductus arteriosus in an animal model. *Heart* 2000; **83**: 570–3

103 Simo Moyo J, Adnet P, Wambo M. Detection of gas embolism in neurosurgery by capnography. Apropos of 32 patients surgically treated in seated position. *Cah Anesthesiol* 1995; **43**: 77–9

104 Siwek J, Gourlay ML, Slawson DC, Shaughnessy AF. How to write an evidence-based clinical review article. *Am Fam Physician* 2002; **65**: 251–8

105 Slavin L, Tobis JM, Rangarajan K, Dao C, Krivokapich J, Liebeskind DS. Five-year experience with percutaneous closure of patent foramen ovale. *Am J Cardiol* 2007; **99**: 1316–20

106 Spies C, Strasheim R, Timmermanns I, Schraeder R. Patent foramen ovale closure in patients with cryptogenic thrombo-embolic events using the Cardia PFO occluder. *Eur Heart J* 2006; **27**: 365–71

107 Standefer M, Bay JW, Trusso R. The sitting position in neurosurgery: a retrospective analysis of 488 cases. *Neurosurgery* 1984; **14**: 649–58

108 Steiner MM, Di Tullio MR, Rundek T, *et al*. Patent foramen ovale size and embolic brain imaging findings among patients with ischemic stroke. *Stroke* 1998; **29**: 944–8

109 Stendel R, Gramm HJ, Schroder K, Lober C, Brock M. Transcranial Doppler ultrasonography as a screening technique for detection of a patent foramen ovale before surgery in the sitting position. *Anesthesiology* 2000; **93**: 971–5

110 Stone DA, Godard J, Corretti MC, *et al*. Patent foramen ovale: association between the degree of shunt by contrast transesophageal echocardiography and the risk of future ischemic neurologic events. *Am Heart J* 1996; **131**: 158–61

111 Thanopoulos BV, Dardas PD, Karanasios E, Mezilis N. Transcatheter closure versus medical therapy of patent foramen ovale and cryptogenic stroke. *Catheter Cardiovasc Interv* 2006; **68**: 741–6

112 Thompson T, Evans W. Paradoxical embolism. *Q J Med* 1930; **23**: 135–50

113 Van Camp G, Schulze D, Cosyns B, Vandenbossche JL. Relation between patent foramen ovale and unexplained stroke. *Am J Cardiol* 1993; **71**: 596–8

114 Vik A, Brubakk AO, Hennessy TR, Jenssen BM, Ekker M, Slordahl SA. Venous air embolism in swine: transport of gas bubbles through the pulmonary circulation. *J Appl Physiol* 1990; **69**: 237–44

115 Voorhies RM, Fraser RA, Van Poznak A. Prevention of air embolism with positive end expiratory pressure. *Neurosurgery* 1983; **12**: 503–6

116 Wahl A, Kunz M, Moschovitis A, *et al.* Long-term results after fluoroscopy-guided closure of patent foramen ovale for secondary prevention of paradoxical embolism. *Heart* 2008; **94**: 336–41

117 Webster MW, Chancellor AM, Smith HJ, *et al*. Patent foramen ovale in young stroke patients. *Lancet* 1988; **2**: 11–2

118 Windecker S, Wahl A, Chatterjee T, *et al*. Percutaneous closure of patent foramen ovale in patients with paradoxical embolism: long-term risk of recurrent thromboembolic events. *Circulation* 2000; **101**: 893–8

119 Yahagi N, Furuya H. The effects of halothane and pentobarbital on the threshold of transpulmonary passage of venous air emboli in dogs. *Anesthesiology* 1987; **67**: 905–9

120 Young ML, Smith DS, Murtagh F, Vasquez A, Levitt J. Comparison of surgical and anesthetic complications in neurosurgical patients experiencing venous air embolism in the sitting position. *Neurosurgery* 1986; **18**: 157–61