SECTION 1

Monitoring Techniques

1

Intracranial pressure monitoring in cerebrovascular disease

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Introduction to intracranial pressure monitoring

Intracranial pressure monitoring remains a central tenet of neurocritical care monitoring and has the potential to improve outcome (1–3). While the importance of monitoring and controlling intracranial pressure (ICP) and cerebral perfusion pressure (CPP) in traumatic brain injury is fairly well understood, its significance in acute cerebrovascular disease and the modulatory effect of therapies remain largely unexplored. This review helps to clarify basic principles and evidence for ICP monitoring and ICP-based treatment and applies these principles to the management of acute cerebrovascular disease.

Principles of intracranial dynamics

The intracranial contents (and average volumes in the adult male) contributing to the ICP are the brain (1300 mL), blood (110 mL) and cerebrospinal fluid (CSF) (65 mL) (4). In normal subjects, average ICP has been reported to be approximately 10 mmHg (5). According to the Monro-Kellie doctrine, because the intracranial contents are encased in a rigid skull and the components are relatively inelastic, change in the volume of one component must be compensated for by reduction in the volume of another component of the system or ICP will increase. Without this compensation, increased ICP may result in brain herniation by direct compression or ischemia/infarction by compromising cerebral blood flow (CBF). While arguably a simplification of the complex pathophysiology involved, the Monro-Kellie doctrine remains a helpful principle in understanding derangements in intracranial pressure.

The brain is considered a viscoelastic solid, comprising approximately 80% water, of which the extracellular compartment represents approximately 15% and the intracellular compartment the other 85% (6). Neither of these components has significant compressibility and, as a result, the brain can be displaced minimally, although it can expand under certain circumstances.

The CSF makes up about 10% of the intracranial volume and is produced predominantly by the choroid plexus, with a small amount produced as interstitial fluid from brain capillaries (7). Production is approximately 500 cc/day and is not significantly reduced by rising ICP (8). Resorption of CSF into cerebral venous sinuses occurs over a pressure gradient at the arachnoid villi by a poorly understood mechanism (9). In normal subjects, resorption increases linearly with ICP above about 7 mmHg (10). However, it is hypothesized that in cases of increased venous pressure, such as cerebral venous thrombosis, that resorption is impaired and can lead to elevated ICP (11).

As long as obstructive hydrocephalus is not present, displacement of CSF into the lumbar subarachnoid space through the foramen magnum is the initial compensatory mechanism after addition of excessive

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volume to the system (12). In reality, this compensation may often be insufficient in cases of low distensibility of the spinal compartment and is dependent on a normal spinal subarachnoid space and open foramen magnum. Head-up positioning to maximize this compensation and allow CSF displacement, are essential. Compensation is compromised by supine/Trendellenberg position, tonsillar herniation or pathology causing spinal epidural block (13). Another potential adaptive mechanism may be a decrease in CSF volume caused by increased absorption due to lowering of outflow resistance at the arachnoid villi (5).

Another potential compensatory mechanism for increased ICP is shunting of cerebral and dural venous sinus blood out of the cranial compartment into the central venous pool. While resistance to venous drainage by compression of the neck veins is a well-established cause of increased ICP, shift of venous blood volume in response to ICP elevation has less direct evidence (11). Nevertheless, increasing intrathoracic pressure with positive pressure ventilation and high intra-abdominal pressure have been implicated in causing ICP elevation via reduced cerebral venous drainage (14).

Once the limits of compensatory mechanisms for displacement of CSF and blood are exceeded, the slope of the intracranial pressure–volume curve increases substantially, representing decreased compliance (Fig. 1.1). Intracranial compliance ($\Delta V/\Delta P$), decreases quickly (exponential part of the curve) followed by the vertical portion where increased ICP may be irreversible and herniation occurs. Thus, in states of poor compliance, a seemingly insignificant increase in intracranial volume can result in a dramatic increase in ICP. Finally, when ICP increases beyond mean arterial blood pressure (MAP), blood is unable to enter the skull, leading to global ischemia and eventual infarction.

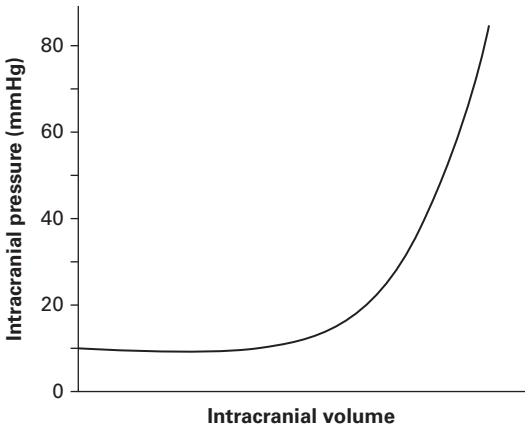

Fig. 1.1 The effect of increasing intracranial volume on intracranial pressure.

The intracranial blood volume, about 10% of the volume within the skull, is approximately 2/3 venous, 1/3 arterial. Arterial blood flow is regulated primarily by change in caliber of arterioles, which adjusts in response to systemic arterial pressure, partial pressure of oxygen (pO2), and partial pressure of carbon dioxide (pCO2). Carbon dioxide tension in arteriolar blood appears to be the most significant determinant of vessel diameter. Over the range of PCO2 usually encountered clinically, CBV decreases as PCO2 level decreases. Even though CBF (and therefore CBV) remain fairly static at physiologic levels of PO2, CBF increases rapidly if PO2 dips below 50 mmHg. Thus, hypoxia and hypercarbia may significantly increase ICP through increases in CBV. Hypocarbia, on the other hand, significantly decreases CBV and hence ICP. Overall, changes in vessel caliber at the arteriolar level allow significant alteration in total intravascular blood volume (from 15 to 70 mL) and can thus compensate for relatively large increases in intracranial volume (5). These are the principles that inform the practice of hyperventilation to lower ICP.

Cerebral autoregulation refers to the ability of the system to maintain constant CBV throughout a range of mean arterial blood pressure (MAP) from approximately 50–150 mmHg (Fig. 1.2). In normal subjects who experience a decrease in CPP, CBV remains normal due to compensatory arteriolar vasodilation. However, when the normal compensatory system is breeched such as with global ischemia (MAP below range) or malignant hypertension (MAP above range), the CBF becomes dependent on MAP. In both cases, CBF varies linearly with MAP. The main mechanism of cerebral autoregulation is vasodilatation and constriction guided by CPP induced changes in cerebral blood flow (CBF = CPP/cerebrovascular resistance). The cerebral blood vessels respond little to changes in arterial PO2 above

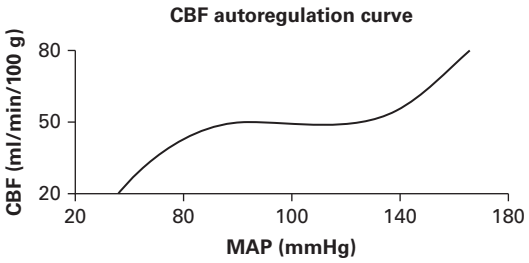

Fig. 1.2 Cerebral blood flow autoregulation curve. From: Gardner CJ, Lee K. *CNS Spectr*. **12**(1): 2007.

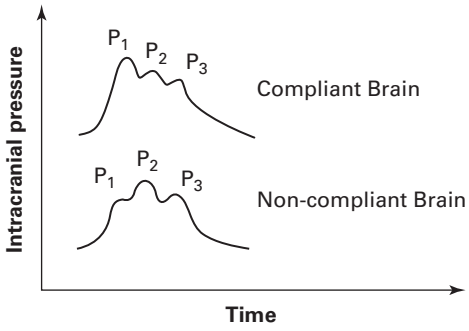

Fig. 1.3 Relationship between ICP and brain compliance

50 mmHg. Below this level, in conditions such as neurogenic pulmonary edema, status epilepticus, or pulmonary embolism, CBF increases significantly, almost doubling at PO2 30 mmHg (5). This point highlights the importance of avoiding hypoxemia and subsequent cerebral arteriolar dilation in patients with elevated ICP. Additionally, vasodilatation in response to elevated PCO2 is maximized at levels above 80 mmHg (doubling of baseline). As expected, vasoconstriction occurs with mild lowering of the PCO2 below normal; however, extremely low PCO2 (<20 mmHg) levels may cause a paradoxical increase in ICP since extreme vasoconstriction can cause tissue ischemia, triggering vasodilation (5). Elevation in ICP does not change autoregulatory responses; rather an autonomic response increases MAP with reflex bradycardia as part of the Cushing response. Acute intracranial hypertension shifts the lower limit of autoregulation towards lower CPP levels, which may be due to dilatation of small resistance vessels (15). Longstanding systemic hypertension shifts the entire curve right by 20–30 mmHg, a change that is protective against hypertensive encephalopathy when large increases in blood pressure occur.

Autoregulation may be impaired regionally in conditions such as stroke or more globally in diffuse anoxic injury or traumatic brain injury (TBI), which can result in an abnormal linear relationship between MAP and CBF. The many possible types of cerebral insults result in highly variable levels and types of impairment of autoregulation from case to case.

Cerebral perfusion pressure (CPP) is a key therapeutic target to prevent potentially fatal cerebral hypoperfusion. Defined as MAP – ICP, the CPP is dependent on both ICP and systemic blood pressure.

The ICP at equilibrium is below 10 mmHg with no pressure gradient between brain regions. The normal ICP waveform has three peaks: the percussion wave (P1), due to choroid plexus pulsation, the tidal wave (P2), a manifestation of compliance, and the dicrotic wave (P3), due to pulsations of the major cerebral arteries. When ICP increases and the slope of the pressure–volume curve rapidly increases, this is a reflection of decreased compliance. In this setting, P2 increases in magnitude and P1 is blunted, merging into P2 as compliance declines (Fig. 1.3) (16). Therefore, by examining the ICP waveform the physician can estimate the amount of compliance remaining in the system and adjust therapy to improve these parameters.

Failure of brain compliance may be accompanied by plateau, Lundberg A waves, or sudden increases in ICP up to 50–80 mmHg lasting 5–20 mins (17). Plateau waves are indicative of cerebral ischemia and may be triggered by usual ICU procedures such as tracheal suctioning, lowering the head of the bed, and routine hygiene (Fig. 1.4).

Neuromonitoring

Several studies have shown that estimation of ICP and herniation risk by clinical grounds alone is inaccurate, arguing for the need for objective ICP monitoring devices (18). Much of the data in support of intensive

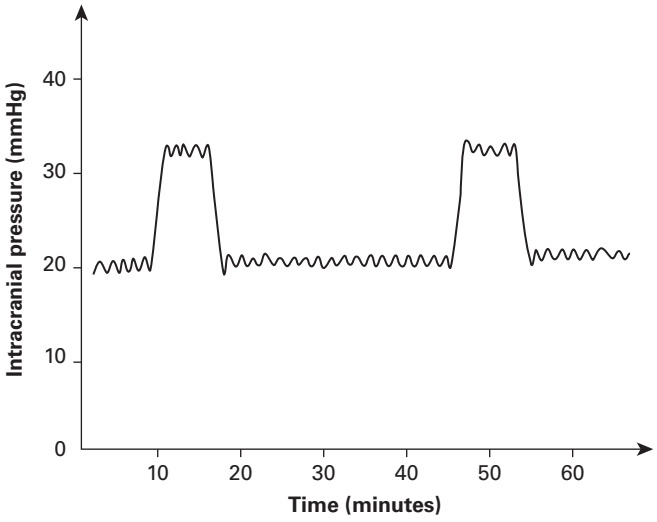

Fig 1.4 Lundberg A waves

ICP monitoring has its origin in the TBI literature. Although a randomized controlled trial of ICP monitoring with and without treatment is unlikely to ever be done, ICP monitoring is now considered standard management for patients with severe TBI and is associated with improved outcomes (18). It is clear that after brain injury of any type that ICP is not static, but instead reflective of a dynamic system with many inputs including CPP, intracranial volume changes, and the effectiveness of adaptive mechanisms. As in TBI, acute cerebrovascular events also follow stages of evolution including mass expansion, vascular changes and edema formation, which occur over several days. Without direct ICP measurement over this time period, there is no way to calculate CPP and thus no way to understand any given patient's cerebral blood flow and adaptive limitations. Finally, since there is considerable risk involved with prophylactic treatment of elevated ICP (hyperosmotic therapy, hyperventilation, hypothermia, surgery), it is imperative that ICP estimations be accurate to avoid unnecessary harm to patients.

There is evidence to support the notion that lowering ICP early is superior to an approach that relies on imaging or clinical deterioration before initiation of treatment (19). Often elevations in ICP can be an early indicator of worsening pathology, which could warrant urgent imaging and lead to timely medical or surgical treatment (18). Moreover, even though imaging assessment is essential, a significant percentage of TBI patients in coma with normal initial CT scans will later develop elevated ICP (20).

While elevated ICP can often be detected on clinical exam in conjunction with imaging and fundoscopic exam, none of these techniques provides an objective measure that can be followed frequently. Studies suggest that optic disc edema often takes at least one day to develop on fundoscopic exam, which is an unacceptable delay (21). Studies to evaluate CT scanning as a screening tool suggest that compression of the third ventricle and basal cisterns are correlated with abnormally high ICPs (22), but this method provides only a 'snap shot' in time and thus does not allow continuous monitoring. Results of studies on transcranial Doppler ultrasonography (TCD), which evaluates the basal cerebral arterial blood flow, has also been shown to correlate with high ICP in the context of changes in CPP but is not considered a sensitive screening or monitoring tool with regards to ICP (23). Some investigators have shown that the TCD pulsatility index correlates with ICP (24) while other more recent studies question the

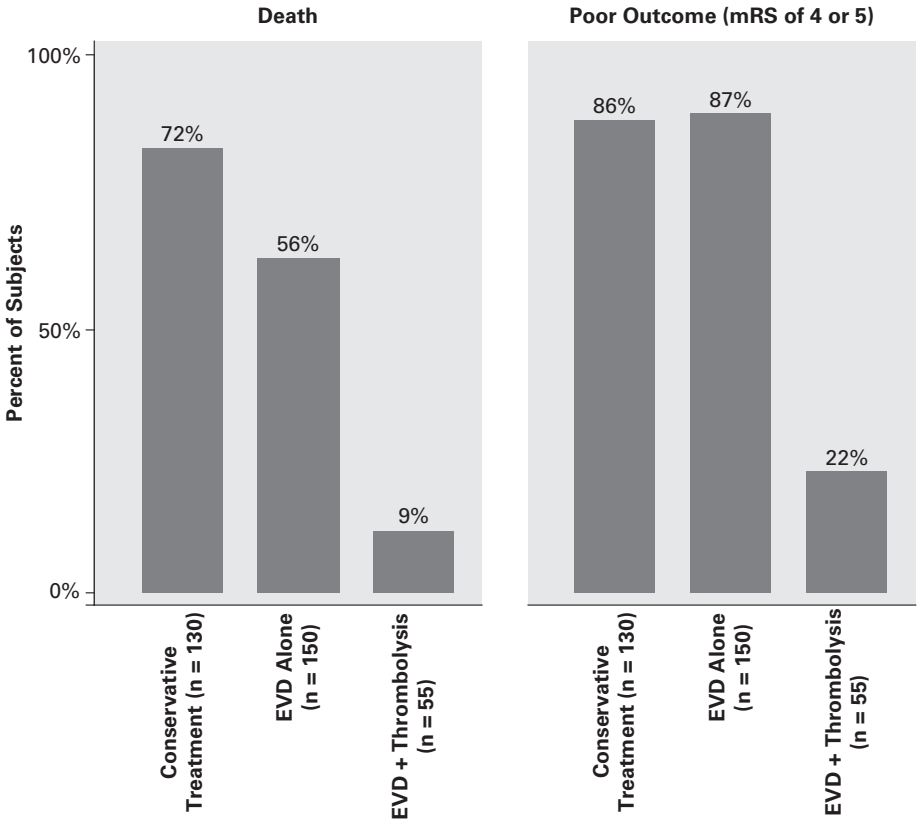

Fig 1.5 The effect of EVD on mortality as compared to traditional treatments.

accuracy of this measure (25). Interestingly, there is some promising preliminary evidence supporting the use of ultrasound of the optic nerve sheath as a screening and monitoring tool for elevated ICP, but this is not routinely available in most centers at this time (26). With this technique, ultrasound measurement of the optic nerve sheath is done rapidly at the bedside and is currently being validated as a diagnostic tool. Several studies have found the threshold optic nerve sheath diameter (ONSD) which provides the best accuracy for the prediction of intracranial hypertension (ICP >20 mmHg) is 5.7–6.0 mm, and that ONSD values above this threshold should alert the clinician to the presence of raised ICP (Fig. 1.5) (26). Unfortunately, even in the hands of a skilled physician, these noninvasive screening techniques currently determine only whether high ICP is present but most likely are not sensitive enough to gauge subtle changes in response to therapy.

In deciding whom to monitor ICP with invasive techniques, many centers use GCS <9 as a cutoff, with the assumption being that patients who are able to follow commands are likely to not have devastatingly high ICP, and the neurologic exam itself substitutes for the monitor. Still, there may be circumstances where an invasive ICP monitor is indicated in a patient with a preserved level of consciousness when the imaging suggests high likelihood of pending deterioration, when a change in the patient's care is expected to increase ICP further (such as high positive end-expiratory pressure (PEEP) or when

sedation is needed and therefore the ability to follow the patient's neurologic exam will be impaired.

Duration of ICP monitoring is variable depending on the patient and the institution, but decision to remove the monitor is usually based on neurologic stabilization or normalization of ICP. Extended monitoring is unadvisable except in rare cases due to increased infectious risk over time. On the contrary, when deciding to remove the monitor, caution must be taken to avoid missing delayed increases in ICP, which can occur after a period of pseudo-normalization. For example, a secondary rise in ICP after 3–10 days has been observed in a significant percentage of TBI patients (3).

Types of monitors

All currently commercially available ICP monitors are invasive and necessitate the creation of a dural breach. While sometimes used to estimate ICP, measurements from lumbar cistern catheters (either opening pressure or drain catheter) are more dependent on patient positioning and do not reflect pressure gradients in obstructive hydrocephalus. A recent study suggests that lumbar drain pressure measurements correlate well with EVD measurements in acute post-hemorrhagic communicating hydrocephalus (27). There are several other options available for measuring ICP through the skull, allowing a more direct evaluation. The gold standard remains the intraventricular catheter, commonly referred to as an external ventricular drain (EVD) (28). An EVD is a catheter placed in the ventricle to allow transduced pressure readings as well as serving as a conduit for therapeutic drainage of CSF. Since it can be recalibrated it is felt to be more accurate and less prone to drift over time (21). However, intraventricular monitoring may not reflect compartmental increases in pressure that do not immediately result in transmission of pressure to the lateral or third ventricles, such as with the case of infratentorial masses or focal herniations. Intraventricular catheters may also be difficult to place in the context of traumatic brain injury or diffuse edema, which often causes the ventricles to shrink down to slit-like proportions. Other problems encountered with the use of EVDs include system damping from positioning of the catheter against the ventricular wall and catheter occlusion with blood or tissue clot.

Intraparenchymal monitors are extremely useful in certain cases, although they may be more prone to drift over time (21). These monitors are usually placed via a burr hole in the brain parenchyma and use a fiberoptic transducer at the catheter tip. CSF cannot be drained using this type of monitor. Some studies have shown that the Camino catheters correlate very well with IVCs, making this type of monitor preferred in some centers due to its ease of insertion, especially in the head-injured patient with small ventricles.

Subdural and subarachnoid screws are fluid-filled bolts which are screwed into a burr hole until flush with the incised dura, allowing CSF pressure to be transduced. Although they have advantages of ease of insertion and low complication rates, they are felt by many experts to be less accurate and can provide falsely low (dampened) readings with high ICP if tissue obstructs the lumen (29).

Complications of invasive ICP monitoring

Complications of ICP monitoring include hemorrhage, infection, and parenchymal brain injury. Catheter-related hemorrhages (intraparenchymal, intraventricular, subdural or along the catheter tract) occur in 1–33% of patients, many of which are small and asymptomatic (30). Risk for hemorrhage seems to be the highest with EVDs (31). Hemorrhage most often occurs at the time of catheter placement but may also be a delayed phenomenon. Malpositioning of EVDs is also not infrequent, but is clearly dependent on definition (32).

While infection is a bona fide concern due to associated morbidity, clinically insignificant catheter colonization is far more common. Neither fever, CSF pleocytosis, nor peripheral leukocytosis carry a high predictive value for infections (33). The high occurrence of these laboratory abnormalities in patients with acute brain injuries and effects of catheter placement probably explain these observations. Several series evaluating infection risk with IVCs have shown that risk is highest after five days and this complication is rare if used for three days or less (21). Level III evidence exists against

routine antibiotic prophylaxis or IVC exchange, especially with newer antibiotic-coated catheters (34).

Other risk factors for IVC-related infection include ICH, SAH or IVH, ICP>20, system irrigation, leakage, open skull fractures, and systemic infection. Sterile insertion of the IVC in the ICU (rather than the operating room) has not been associated with an increased risk of infection and neither has previous IVC, drainage of CSF, or steroids)(35–37).

Intracranial pressure vs. cerebral perfusion pressure

The TBI literature is engaged with a controversy over the importance of CPP or ICP as targets for ICU management. The occurrence of brain ischemia, reduced CPP and jugular venous desaturation in the context of elevated ICP have been well described and brain ischemia after TBI is treated almost as a 'dogma' (38) . However, since severe TBI is so often accompanied by diffuse axonal injury, it may be difficult to extrapolate data from the TBI population to patients with primary cerebrovascular pathology. The Rosner protocol emphasizes preservation of cerebral blood flow to prevent cerebral ischemia (39). Although unproven by a randomized controlled study, it is argued that treatment directed at maintaining CPP > 70 mmHg is superior to traditional techniques focused on ICP management.

In Rosner's study, methods used included vascular volume expansion, cerebrospinal fluid drainage via ventriculostomy, systemic vasopressors (phenylephrine or norepinephrine), and mannitol. Barbiturates, hyperventilation, and hypothermia were specifically not used. Comparisons of outcome classification across GCS categories (survival vs. death, favorable vs. nonfavorable) with other reported series were significantly better in Rosner's series. Mechanistically, decreased CPP due to either increased ICP or low blood pressure results in vasodilatation. This vasodilation increases cerebral blood volume (CBV) and exacerbates ICP and thus further reduces CPP, which can only be improved by increasing blood pressure. The Achilles heel of this approach is that permitting a high CPP can worsen cerebral edema especially where the blood brain barrier is not intact.

The relative influence of ICP and CPP on outcome was assessed in patients who had neurological deterioration from the international, multicenter, randomized, double-blind trial of the N-methyl-D-aspartate antagonist Selfotel in patients with TBI (40). The most powerful predictor of neurological worsening was intracranial hypertension (ICP > or = 20 mmHg) either initially or during neurological deterioration. There was no correlation with CPP as long as CPP was greater than 60 mmHg. It has therefore become more common that treatment protocols for the management of severe head injury emphasize immediate reduction of elevated ICP to less than 20 mmHg. A CPP greater than 60 mmHg appears to have little influence on the outcome of patients with severe head injury. These basic tenets highlight the relative importance of ICP and CPP in the TBI population.

Intracranial pressure and ischemic stroke

Stroke has been associated with increased ICP usually in the context of major hemispheric infarction leading to cerebral edema with risk for herniation and death. Most often this phenomenon is observed after a malignant middle cerebral artery infarction, which carries 70–80% mortality if treated conservatively. Furthermore, uncal herniation complicates malignant MCA infarction in 78% of cases (41).

The value of ICP monitoring in large middle cerebral artery infarction is debated in the literature, but infrequently put into practice. Space-occupying cerebral edema can result in elevated ICP and cerebral herniation. In fact, this was the primary cause of mortality within the first week in ECASS, the European Cooperative Acute Stroke Study (42). In a study of 48 patients with clinical signs of increased ICP due to large hemispheric infarction, epidural ICP sensors were inserted ipsilateral to the primary brain injury and also contralaterally in seven patients (43). ICP was normal at the time of insertion in 74%, 20–25 mmHg in 37 patients, 25–35 mmHg in eight patients, and > 35 mmHg in three patients who all died. ICP increased in all patients

during the first two days after monitor insertion and was significantly higher in patients who died compared with survivors (mean 42 vs. 28 mmHg). ICP was higher ipsilateral to the stroke in patients with bilateral monitors with a difference up to 15 mmHg. All patients with any ICP > 35 mmHg during monitoring died. However, although high ICP correlated with clinical outcome, the initial ICP did not predict outcome and clinical herniation signs preceded critical ICP elevation, casting some doubt on the ability to utilize ICP values to affect clinical outcomes in this context. Moreover, CT findings such as severe midline shift did not correlate with ICP values. Medical management of elevated ICP was initially effective, but failed beyond the first few doses of osmotic therapy. The authors concluded that ICP monitoring did not positively influence outcomes, but may serve as a predictor during therapy. These results are supported by an earlier study by Frank of 19 patients with large hemispheric infarction who underwent ICP monitoring prior to neurologic deterioration (44). In this study, ICP > 18 mmHg within the first 12 hours of clinical progression to stupor predicted 83% mortality despite maximal medical therapy. However, elevated ICP was not commonly associated with initial neurologic deterioration secondary to mass effect. Contrary to the prior study, patients with initial ICP elevation were significantly younger than those without.

Since intra-arterial recombinant tissue plasminogen activator is not an appropriate treatment for malignant MCA infarction due to high rates of brain hemorrhage, many experts have recommended decompressive craniectomy (DC). The rationale for decompressive surgery is to reduce ICP and optimize CBF in addition to minimizing further infarction from cerebral edema. In a study of 42 patients undergoing DC for malignant MCA infarction, ICP was monitored with an intraparenchymal fiberoptic sensor during and post-operatively. An anterior temporal lobectomy was performed if ICP increased > 30 mmHg, which occurred in 13/42 (31%) of patients, including three patients who underwent anterior lobectomy two to three days after initial decompression and regained consciousness promptly after operation (45). Two-thirds of such patients survived compared with no survival in patients who developed ICP > 30 mmHg, but did not undergo further anterior temporal lobectomy.

Numerous reports suggest that DC is an effective means of ICP control at least in the TBI population (46–51). This operation includes a wide range of surgical procedures, all of which involve removal of large parts of the skull with or without dural augmentation, resection of brain tissue and occasional sectioning of the tentorium or falx. A pooled analysis of decompressive craniectomy performed less than 48 hours after ictus for malignant MCA infarction has also been shown to enhance survival in three European trials, although high rates of disability and depression were still observed (52). Physiologic findings after DC include cerebral blood flow (CBF) augmentation that is likely a result of decrease in CPP, but no significant improvement in CMRO2 levels (53). In a comparison of 36 TBI patients who received DC and 86 patients who did not, CMRO2 levels were significantly lower in the operated group, even after adjustment for injury severity, and were strongly associated with poor functional outcome. CBF levels remained above the ischemic threshold suggesting that cellular energy crisis was not of ischemic origin. These data indicate that ICP reduction with CBF elevation may not improve cerebral metabolism in patients with severe mitochondrial damage and that DC should be limited to patients with refractory intracranial hypertension and GCS > 6 on admission (53). Perhaps a logical correlate of these data is the idea that the timing of DC is important, with some experts recommending 'ultra-early' surgery less than six hours after ictus, before neurologic deterioration becomes evident (45).

Overall, ICP monitoring in severe stroke syndromes may be indicated on a case-by-case basis, with the knowledge that herniation events can occur despite normal ICP values (poca), highlighting the need for careful clinical and radiologic observation.

One medical complication that not infrequently arises in the ischemic stroke patient is renal insufficiency requiring dialysis. In patients with acute brain injury (ABI) of any etiology, continuous renal replacement therapy (CRRT) is the preferred mode of renal replacement therapy (RRT) in patients with acute renal insufficiency (ARI) requiring dialysis. Intermittent