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Assessment of the relationship between age and continuous intracranial compliance

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Summary

The aim of this open, descriptive and prospective study was to determine if the new monitoring parameter "continuous intracranial compliance (cICC)" decreases with age in patients with traumatic brain injury (TBI).

30 patients with severe and moderate TBI (Glasgow Coma Scale score ≤ 10) contributing to a European multicenter study, organized by the Brain-IT group, underwent computerized monitoring of blood pressure, intracranial pressure (ICP), cerebral perfusion pressure and cICC.

Regression analyses of individual median ICP and median cICC versus patients' age revealed no significant dependency. Median cICC declined significantly with increasing ICP (when median ICP $= 10, 20$ and 30 mmHg, cICC $= 0.64, 0.56$ and 0.42 ml/mmHg respectively, $p < 0.05$). These three ICP groups were then subdivided according to age (0–20, 21–40, 41–60 and 61–80 years). Median cICC declined with age in both high ICP groups (median ICP $= 20, 30$ mmHg). Percentage cICC values below a set pathological threshold of lower than 0.05 ml/mmHg across the four age groups were 28% (0–20 yrs), 59% (21–40 yrs), 60% (41–60 yrs) and 70% (61–80 yrs) respectively.

The observed phenomenon of decreased intracranial volume challenge compensation with advancing age may contribute to the well-known fact of a worse outcome in elderly patients after TBI.

Keywords: Multimodal cerebral monitoring; head injury; intracranial pressure; outcome.

Introduction

The tight functional relationship between increases in intracranial pressure (ICP) and intracranial volume is strongly influenced by the underlying neuropathology and the actual speed of volume expansion within the closed intracranial cavity. Due to the exponential function of the intracranial pressure-volume curve, small increases in intracranial volume can result in massive increases in ICP once compensatory mechanisms have been exhausted as shown experimentally [15] and clinically [10, 11]. The rapid development of hematomas and edema formation in face of a rather late assessment when only measuring ICP predispose to undetected perturbations. Thus, it is thought that continuous assessment of changes in intracranial compliance (ICC) – determined by repeatedly challenging the intracranial compartment with transient injections and withdrawal of a defined volume-reveals ensuing pathological increase in ICP before the ICP is actually increased [9]. This, in turn, could make the ICC technique an early warning system.

The newly developed Aesculap®-Spiegelberg compliance system (ASCS) (Aesculap®, Tuttlingen, Germany) allows for the first time to perform quantitative computerized online measurements of continuous intracranial compliance (cICC), using a fully automated and "closed" external volume load. The ASCS has been shown to be feasible and safe in both experimental [18] as well as clinical settings, in hydrocephalus and TBI research [7, 12, 13, 17, 19].

As observed in a preliminary study in seven patients with severe TBI [6], cICC seemed to be influenced by the age of these patients which may interfere with correct interpretation of the measured cICC data. In the present open, descriptive, and prospective study we focused on the relationship between changes in cICC and age in a multi-center study enrolling thirty TBI patients.

Patients, materials and methods

Demographic characteristics

From 1998 to 2002, a total of thirty patients (3 females/27 males) with closed TBI requiring extended computerized monitoring of ICP and cICC on the intensive care units (ICU) at the Charité, Virchow Medical Center in Berlin, Germany (n = 12), Ospedale San Gerardo in Monza, Italy (n = 9) and the University Hospital in Uppsala, Sweden (n = 9) contributed to a European multi-center study organized by the "Neuro-Intensive Care Monitoring Research Group" ("Brain-IT"; http://www.brainit.org) [12], primarily designed to define the inherent variability of cICC in TBI, subarachnoid hemorrhage, hydrocephalus and brain tumor. Based on the Glasgow coma score (GCS), patients presented with a severe (GCS $\leq$ 8; n = 26) or moderate (GCS 9–10; n = 4) TBI. All patients with initial moderate TBI deteriorated later, i.e. within 48 hrs post trauma to unconsciousness (GCS $\leq$ 7) due to progressing contusions, thus making invasive intracranial monitoring indispensable. The underlying intracranial pathology was graded according to the Marshall CT-classification [8] from the "worst" CT scan by the assigned center investigators (Berlin: K. Kiening, Uppsala: P. Enblad, Monza: G. Citerio). Major concomitant injuries were middle facial or limb fractures resulting in a median injury severity score (ISS) of 27 (range: 18–57) [2]. Any space occupying lesions (solid intacerebral contusions/hematoama, epidural/subdural hematomas) with a midline shift more than 5 mm were evacuated immediately (n = 13). Hereby, the skull flap was re-fixed tightly and the dura was sutured "water tight" following subdural procedures to ensure a closed intracranial compartment and thus guarantee valid cICC measurements.

Ethical permission

Permission to enroll patients in the European multi-center study organized by the BrainIT group [12] was granted by the local institutional ethics committees at the Charité (Berlin), Ospedale San Gerardo (Monza) and University Hospital (Uppsala).

General management of patients

General intensive care and specifically the management of pathologically elevated ICP adhered to the "Guidelines for the Management of Severe Traumatic Brain Injury" brought forward by the Brain Trauma Foundation of The American Association of Neurological Surgeons on behalf of the Joint Section on Neurotrauma and Critical Care [4].

Multimodal cerebral monitoring

Invasive mean arterial blood pressure (MAP), ICP, cerebral perfusion pressure (CPP), and cICC were recorded simultaneously using local multimodal computerized cerebral monitoring systems digitizing parameter signals with a frequency of 1/min. Data communication via the Internet between BrainIT data base located in Glasgow, UK and the analyzing center (Berlin) was performed using "WS_ftp Pro-software" (Ipswich, Inc., Lexington, MA). The ASCS catheter was positioned via a conventional frontal burr hole into the frontal horn of lateral ventricles (either left or right). Correct catheter location was assured by CT scan.

Data analyses

After electronical re-transmission of the entire data set of the investigated 30 patients to Berlin, artifacts were removed off-line according to specific remarks documented by nurses and physicians. Thus, a total of 150, 407 minutes artifact-free monitoring time was achieved. From this dataset, individual median ICP and cICC were calculated. 9,133 minutes were taken to determine age-related changes in cICC at distinct ICP levels (ICP = 10, 20, 30 mmHg).

(1) In a first step, regression analyses of individual median ICP and median cICC vs. patient ages were performed followed by **(2)** median cICC determination for each patient at different ICP levels (ICP = 10, 20, 30 mmHg). **(3)** Finally, each ICP group was further subdivided into age blocks (0–20, 21–40, 41–60, 61–80 years) in which median cICC was determined.

Statistics

Results are either given as medians or expressed in box plots showing mean, median, 5th, 25th, 75th, and 95th-percentiles. Sigmaplot 2001 7.0® for Windows (SPSS Science™, Chicago, IL) was used for regression analyses (regression line, 95-confidence interval, Spearman rank correlation coefficient $\{r_s\}$, p value) and the generation of box plots. Differences assessed by ANOVA on ranks (Sigmastat 3.0. Jandel Scientific, Corte Madera, CA) were rated significant at $p < 0.05$.

Results

Median ICP and median cICC did not correlate with age of individual patients (Figs. 1a and b). Median cICC was significantly reduced with increasing ICP in a stepwise fashion (Fig. 2). At ICP 10 mmHg, median cICC was reduced stepwise from 0.64 to 0.42 ml/mmHg at ICP 30 mmHg, which was below the presumed critical cICC of 0.5 ml/mmHg in TBI [7]. In the low ICP group 10 mmHg, the lowest median cICC (0.35 ml/mmHg) was found in the youngest patients (0–20 yrs), which was significantly elevated with increasing age (Fig. 3).

In both high ICP groups at 20 and 30 mmHg, the highest median cICC values were observed in the youngest age group (0–20 years), median $cICC_{ICP=20\,mmHg} = 0.76$ ml/mmHg and median $cICC_{ICP=30\,mmHg} = 0.58$ ml/mmHg, being significantly elevated compared to all other age groups (Fig. 3). By taking the presumed critical cICC threshold of 0.5 ml/mmHg, percentage reduction in this threshold continued through ascending ICP groups of 20, and 30 mmHg with age (0–20 yrs: 28%; 21–40 yrs: 59%; 41–60 yrs: 60%; 61–80 yrs: 70%) (Fig. 1).

Discussion

It is thought that aging is associated with a loss in brain tissue compressibility [16] and/or reduced

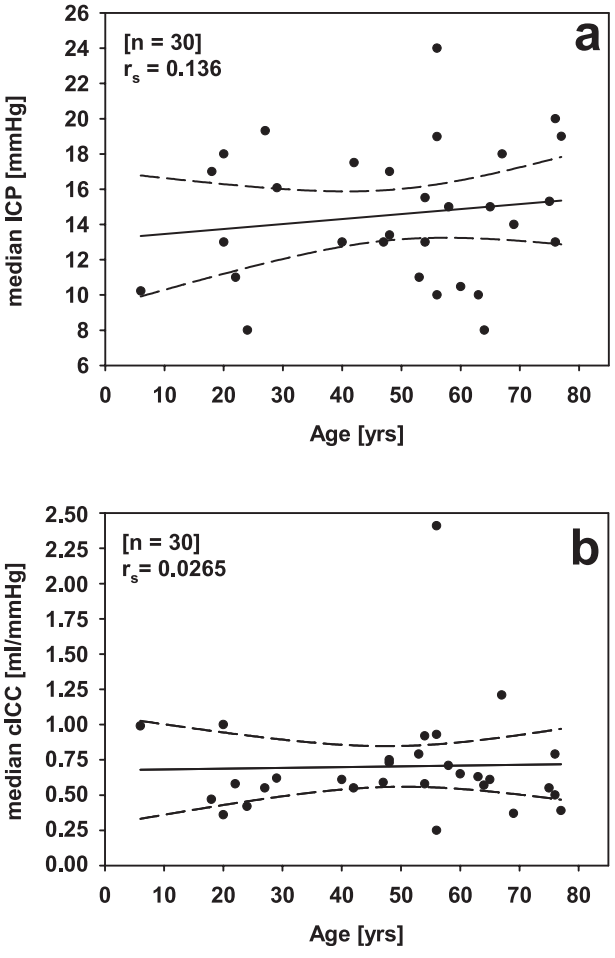

Fig. 1. Linear regression analyses of individual median ICP (a) and median cICC vs. age (b) without significant correlation

cerebro-spinal fluid (CSF) absorption [1, 5], resulting in sustained "stiffness" of the brain and consequently, reduced ICC. Not surprising in line with the hydrocephalus literature [5], ICP does not increase with age in TBI, suggesting that this may be due to an increase pointing to the fact of an increased CSF outflow (R_{csf}) and a simultaneously reduced CSF production (Fig. 1a). Likewise overall cICC does not correlate with age (Fig. 1b). However, by analyzing cICC in more detail (Fig. 3), it became clear that at higher levels of ICP levels 20 and 30 mmHg, the compromised intracranial compliance (Fig. 2), cICC decreases with age, supporting the findings of Czosnyka and colleagues [5] who reported a non-linear increase of elastance coefficient (reciprocal to ICC) with age in hydrocephalic patients. For TBI the observed phenomenon was most pronounced in the 0–20 years age group, where a 28% reduction in cICC below the critical threshold of 0.5 ml/mmHg, which compares favorably to that of the older age group (61–80 years) of 70%. The combination of age and severity of underlying TBI, pushes ICP to higher levels ($\geq$ 20 mmHg), resulting in impaired cICC (Fig. 3). The subsequent increase in resistance of the ageing brain may possibly contribute to a worse outcome in elderly patients [3, 14]. In conclusion ICP monitoring alone may not be sufficient in elderly patients based on the presence cICC threshold data for age.

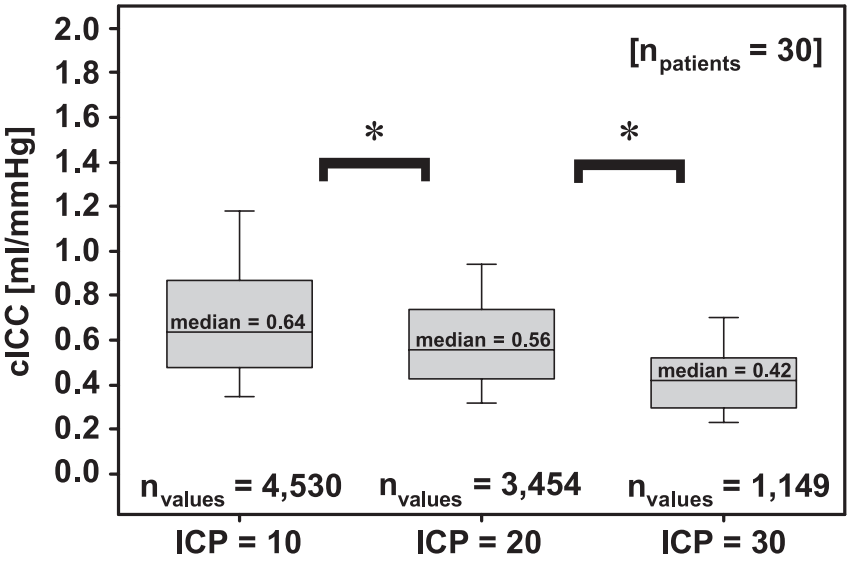

Fig. 2. Changes in continuous intracranial compliance (cICC) determined at three ICP levels (ICP 10, 20, 30 mmHg). With increasing ICP, cICC was significantly decreased (ANOVA on ranks, $p < 0.05$)

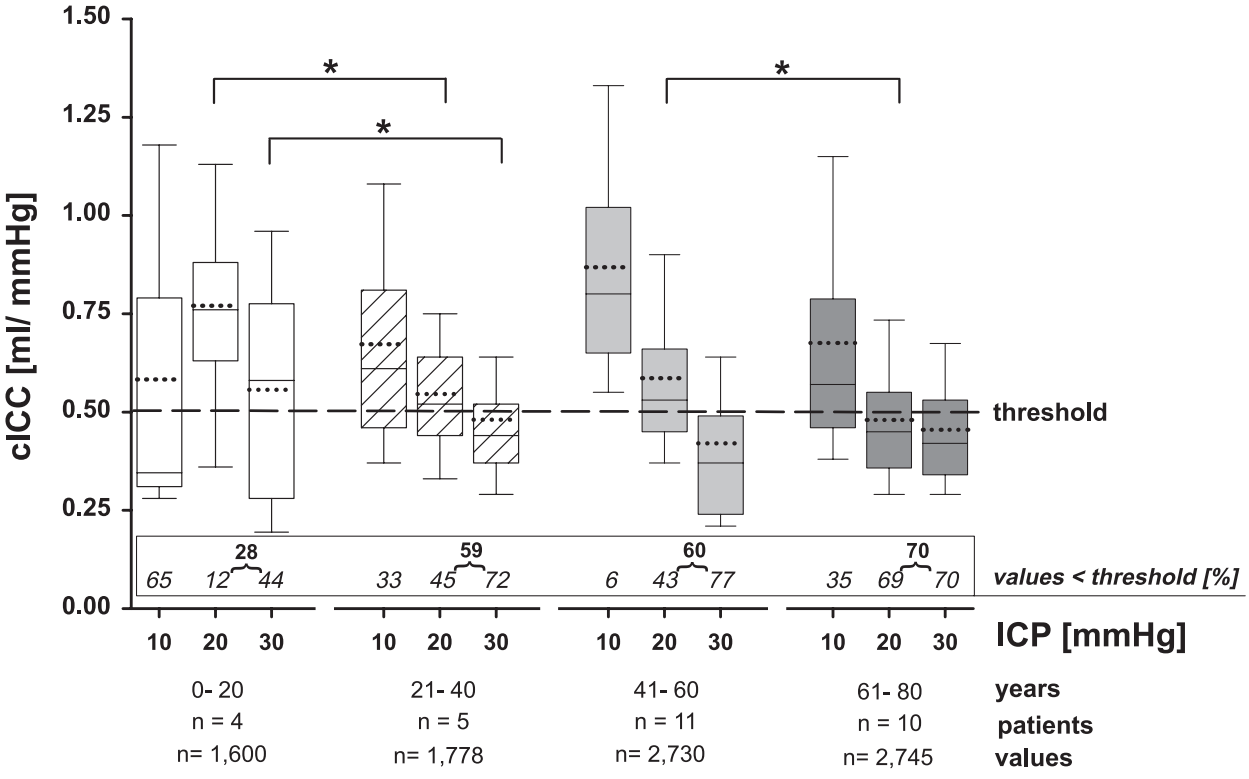

Fig. 3. Distribution of cICC determined at three ICP levels (10, 20, 30 mmHg) for age intervals (0–20, 21–40, 41–60, 61–80 years). At high ICP levels (20 and 30 mmHg), the incidence of pathological cICC levels < 0.5 ml/mmHg expressed in percent to the total number of cICC values determined at each ICP level was significantly increased in patients older than 21 years, being mostly sustained in patients between 61 and 80 years (ANOVA on ranks, $p < 0.05$). The box plots reveal the distribution of the data showing the 5th and 95th percentile (lower and upper error bar), the 25th and 75th percentile (lower and upper rim of the box), the median (solid line), and mean (dotted line). The discongruence of mean and median clearly shows that the data is nonparametric

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