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TOPICAL REVIEW

Continuous monitoring methods of cerebral compliance and compensatory reserve: a scoping review of human literature

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Abstract

Objective. Continuous monitoring of cerebrospinal compliance (CC)/ cerebrospinal compensatory reserve (CCR) is crucial for timely interventions and preventing more substantial deterioration in the context of acute neural injury, as it enables the early detection of abnormalities in intracranial pressure (ICP). However, to date, the literature on continuous CC/CCR monitoring is scattered and occasionally challenging to consolidate. *Approach.* We subsequently conducted a systematic scoping review of the human literature to highlight the available continuous CC/CCR monitoring methods. *Main results.* This systematic review incorporated a total number of 76 studies, covering diverse patient types and focusing on three primary continuous CC or CCR monitoring metrics and methods—Moving Pearson's correlation between ICP pulse amplitude waveform and ICP, referred to as RAP, the Spiegelberg Compliance Monitor, changes in cerebral blood flow velocity with respect to the alternation of ICP measured through transcranial doppler (TCD), changes in centroid metric, high frequency centroid (HFC) or higher harmonics centroid (HHC), and the P2/P1 ratio which are the distinct peaks of ICP pulse wave. The majority of the studies in this review encompassed RAP metric analysis ($n = 43$), followed by Spiegelberg Compliance Monitor ($n = 11$), TCD studies ($n = 9$), studies on the HFC/HHC ($n = 5$), and studies on the P2/P1 ratio studies ($n = 6$). These studies predominantly involved acute traumatic neural injury (i.e. Traumatic Brain Injury) patients and those with hydrocephalus. RAP is the most extensively studied of the five focused methods and exhibits diverse applications. However, most papers lack clarification on its clinical applicability, a circumstance that is similarly observed for the other methods. *Significance.* Future directions involve exploring RAP patterns and identifying characteristics and artifacts, investigating neuroimaging correlations with continuous CC/CCR and integrating machine learning, holding promise for simplifying CC/CCR determination. These approaches should aim to enhance the precision and accuracy of the metric, making it applicable in clinical practice.

1. Introduction

Cerebrospinal compliance (CC)/cerebrospinal compensatory reserve (CCR) is a key factor in preserving healthy intracranial pressure (ICP). It reflects the ability of the cerebrospinal system to accommodate or buffer the changes in intracranial volume without a significant shift in ICP (Portella *et al* 2005). In cases of acute traumatic neural injury (i.e. traumatic brain injury (TBI)), hydrocephalus or hemorrhages, ICP can increase in a potentially fatal manner (Donnelly *et al* 2020). Continuous monitoring of CC/CCR potentially allows for the identification of abnormalities in ICP at an early stage, which is critical for timely interventions and preventing more significant deterioration (Kiening *et al* 2003, Ng *et al* 2005).

In recent years, research has been conducted on the different approaches of continuous monitoring of CC/CCR aimed at objective quantification of patient state to get a more robust understanding, potentially leading to personalized routes of care. Initially, compliance measurements relied on assessing ICP responses to changes in volume induced invasively (such as through bolus injection or infusion of fluid), a method impractical for continuous monitoring. Consequently, alternative approaches were necessary. As time has advanced, the importance of monitoring compliance in a continuous manner for critically head-injured patients has become evident. Recent advancements making continuous monitoring of CC/CCR possible are the analysis of ICP pulse waveform, sophisticated tools like transcranial doppler (TCD), Spiegelberg Compliance Monitor, and data acquisition software platforms for live time signal analytics at the bedside (Abdullah *et al* 2005, Ziółkowski *et al* 2021).

RAP is the most popular metric for measuring continuous CC/CCR, defined as the moving Pearson's correlation between ICP pulse amplitude waveform (AMP) and ICP (Zeiler *et al* 2018a). RAP value ranges from -1 to $+1$. The lack of correlation in AMP and ICP (i.e., RAP is close to 0) suggests a favourable state of CC/CCR. On the contrary, the RAP value close to $+1$ indicates the increase of ICP with the rise of AMP, in other words, decreased CC/CCR (Zhu *et al* 2023). However, when ICP continues to rise beyond the critical ICP level, the cerebral autoregulation will collapse, and AMP and ICP show a negative correlation. That means a negative RAP value signifies an exhausted CC/CCR (Jin *et al* 2019). It is noteworthy to mention that the RAP index does not estimate compliance directly but assesses the compensatory reserve based on its position on the pressure–volume (PV) curve. Conversely, by placing an intraventricular or intraparenchymal catheter within the patient's brain, the Spiegelberg Compliance Monitor provides real-time data on compliance (Piper *et al* 1999). CC/CCR ($\Delta V/\Delta P$) is calculated from the small ICP perturbations (ΔP) caused by a sequence of up to 200 pulses of added volume (ΔV). After achieving a stable average, a minute-by-minute measurement of CC/CCR can be obtained from the Spiegelberg Compliance Monitor (Yau *et al* 2002). Furthermore, examining the relation between cerebral blood flow velocity (CBFV) and compliance (more specifically, cerebral arterial compliance (Ca) and cerebrospinal space compliance (Ci)), continuous compliance can also be assessed using TCD (Carrera *et al* 2011, Kim *et al* 2012). From CBFV, Cerebral arterial Blood Volume (CaBV) can be calculated. Ca is the ratio of the pulsatile amplitude of CaBV (AMP_CaBV) and the pulsatile amplitude of ABP (AMP_ABP), whereas Ci is calculated as the ratio between the pulsatile amplitude of CaBV (AMP_CaBV) and the pulsatile amplitude of ICP (AMP_ICP) (Kim *et al* 2012). Another approach for estimating CC/CCR continuously is the high frequency centroid (HFC), determined as the average power-weighted frequency within the 4–15 Hz frequency range of the ICP power density spectrum (Robertson *et al* 1989, Contant *et al* 1995). Additionally, the utilization of another centroid metric, higher harmonics centroid (HHC), defined as the centre of mass of the ICP pulse waveform harmonics from the 2nd to the 10th, was also notable (Zakrzewska *et al* 2021, Uryga *et al* 2022). Finally, distinct peaks from the ICP pulse wave (ICPW), namely P1 (percussion wave) and P2 (tidal wave), were observed to be utilized for assessing continuous CC/CCR, as alterations in the P2/P1 ratio can indirectly indicate changes in CC/CCR (Lee *et al* 2016, Brasil *et al* 2021). Aside from these more commonly described continuous CC/CCR measures, researchers use a few additional techniques and metrics in this aspect, which are parabolic regression models derived from the PV curve and the ICP-PCO2 compliance index (PCI) (Lai *et al* 2016, Wolf *et al* 2021).

In summary, while the RAP index is extensively researched, the Spiegelberg Compliance Monitor comes closest to directly measuring compliance. This method resembles fully invasive intermittent approaches but operates continuously (Kiening *et al* 2005, Carrera *et al* 2011). Conversely, RAP and TCD-based measurements do not directly estimate compliance but operate under the assumption that the ICP pulse waveform is the response to changes in CaBV within a single cardiac cycle (Steiner *et al* 2005, Carrera *et al* 2011a, Pineda *et al* 2015, Kazimierska *et al* 2021). However, TCD-based measurements uniquely distinguish between cerebrospinal and arterial components of total cerebral compliance (Ci and Ca), a differentiation absent in RAP (Carrera *et al* 2011a, Kazimierska *et al* 2021). Additionally, the P2/P1 ratio and centroid metrics (HFC and HHC) also indirectly estimate compliance by analysing characteristics of the ICP pulse shape (i.e. the height of the peaks and frequency of the ICP pulse, respectively) (Robertson *et al* 1989, Brasil *et al* 2021, 2023, Zakrzewska *et al* 2021, Galdino *et al* 2022, Uryga *et al* 2022). Combining these five principal approaches will present a persuasive depiction of the continuous measurement of CC/CCR.

Despite these previously described methods, the literature on continuous CC/CCR methods in humans remains difficult to navigate and often scattered. This systematic review aims to provide an insightful and comprehensive overview of existing literature for continuous CC/CCR measurement by highlighting the methodologies employed, significant findings, areas requiring further investigation, and notable trends or developments in the field. Our objective is to illuminate the developing field of continuous CC/CCR monitoring, sub-categorizing by type of techniques and patients, aiming to enhance comprehension of compliance and improve patient care within the neurocritical care domain.

2. Methods

The Cochrane Handbook for Systematic Reviews (Cochrane Handbook) was used as a guide for this systematic review. We followed the guidelines outlined in the preferred reporting items for systematic reviews and meta-analysis (PRISMA) (Page *et al* 2020) and the PRISMA Extension for Scoping Review in our reporting (Tricco *et al* 2018). The methodology and search resembled those utilized in previous systematic reviews conducted by the research team (Gomez *et al* 2022, Sainbhi *et al* 2023). The collaborative efforts of the primary authors (AI and LF) and senior author (FAZ) formulated the review objectives and developed the search strategy. The PRISMA checklist can be found in supporting information A.

2.1. Search questions, population, and inclusion/ exclusion criteria

The question addressed in this systematic review is as follows: What techniques and metrics have been used for the continuous measurement of CC/CCR in humans?

This systematic review encompasses all human studies that involve continuous quantified measurement of CC/CCR regardless of whether they were prospective or retrospective in nature. There are no limitations on sample size, patient characteristics, age, or data sampling method. There were studies where CC/CCR measurement was not the primary focus but rather a factor contributing to the main objective, which were also considered and incorporated in this review (Calviello *et al* 2018, Zeiler *et al* 2018a, Froese *et al* 2020).

The exclusion criteria posed in this study were as follows: non-English language studies, animal studies, theoretical studies, non-continuous measurement of compliance, qualitative measurement of compliance, non-original studies, and abstract-only studies. Non-original and abstract-only studies were excluded to prioritize significant and original research contributions in our analysis. Recognizing the critical significance of continuous measurement of CC/CCR, the primary emphasis of this particular scoping review was real-time data, and therefore excluded any non-continuous and qualitative studies. The animal studies were excluded because we aimed to comprehensively review the continuous CC/CCR measurement techniques directly applied to human subjects.

2.2. Search strategy

Searches were conducted in major databases, including PubMed, Embase, Scopus, BIOSIS, and Cochrane Library, which covered records dating from the inception of each database up to mid-June 2023. Individualized search strategies were developed for each of these databases and can be seen in supporting information B. Additionally, a meticulous search in the reference lists of the finally selected studies was conducted to ensure that no studies were overlooked.

2.3. Study selection

Two reviewers, AI and LF, performed a thorough two-step review of all the articles retrieved through the individual search strategies for each database. In the first step, reviewers independently screened all the retrieved articles without access to each other’s review progress. In this phase, the inclusion or exclusion decision was made based on the title and abstract content. Following the initial screening, the second phase of study selection involved a thorough assessment of full texts. Studies that deviated from our primary focus, which is identifying continuous measurement techniques quantifying CC/CCR, were excluded. Similar to the first one, this phase was also conducted independently, and any disagreements between the two reviewers were resolved by a third party (FAZ). To enhance the comprehensiveness of our review, we meticulously examined the reference lists of the reviewed articles, focusing on the continuous measurement of CC/CCR.

2.4. Data collection

The data field encompasses patient characteristics such as age, population, male/female quantity or percentage, and Glasgow Coma Scale (GCS) score. In addition, it includes measurement and processing methods of CC/CCR, CC/CCR quantified values and relation with other factors, primary and secondary outcomes, and lastly, limitations and conclusions, particularly regarding continuous CC/CCR metrics/methods.

2.5. Bias assessment

As the aim of this review was to offer a comprehensive and wide-ranging overview of the existing literature, a formal bias assessment was not carried out.

2.6. Statistical analysis

Since the objective of this review was to provide a scoping overview of the existing literature, a meta-analysis was not conducted. This decision was also influenced by the existence of extensive heterogeneity in the study designs and data.

3. Results

Using a PRISMA flow diagram, the search and filtration method of this systematic review has been summarized in figure 1. A total of 15 682 papers were identified from the search strategies applied from the five databases. Among them, 8725 studies were identified as duplicates and removed, resulting in 6957 studies. These 6957 studies were screened through their title and abstracts. 6497 studies were excluded for being irrelevant studies (n = 5891), non-continuous studies (n = 344), abstract-only studies (n = 80), review studies (n = 16), animal studies (n = 133) or non-English studies (n = 33). Then the 460 retrieved studies were studied through full-text examination, and 387 studies were excluded based on these criteria—non-continuous studies (n = 363), review studies (n = 8), animal studies (n = 13), and non-English studies (n = 3). Later, three studies were identified from the reference lists of the included papers, and finally, 76 papers were incorporated into this systematic review.

This review includes 43 studies (Czosnyka *et al* 1988, 1994, 1996, Balestreri *et al* 2004, Steiner *et al* 2005, Petrella *et al* 2008, Schuhmann *et al* 2008, Shahsavari *et al* 2008, 2011, Smielewski *et al* 2008, Timofeev *et al* 2008a, 2008b, Kim *et al* 2009a, 2015, Weerakkody *et al* 2011, Budohoski *et al* 2012, Howells *et al* 2012, Speil *et al* 2012, Eide and Sorteberg 2013, Haubrich *et al* 2013, 2015, 2016a, 2016b, Pineda *et al* 2015, 2018, Varsos *et al* 2015, Moyse *et al* 2016, Calviello *et al* 2018, Zeiler *et al* 2018a, 2018b, 2019, Jin *et al* 2019, Sekhon *et al* 2019, Donnelly *et al* 2020, Froese *et al* 2020, 2021, Lalou *et al* 2020, Green *et al* 2021, Levrini *et al* 2021, Ziółkowski *et al* 2021, Liu *et al* 2022, Uryga *et al* 2022, Zhu *et al* 2023) that measured and assessed CC/ CCR continuously using the RAP metric, 11 studies (Piper *et al* 1999, Raabe *et al* 1999, Kiening *et al* 2002, 2003, 2005, Yau *et al* 2002, 2005, Abdullah *et al* 2005, Ng *et al* 2005, Portella *et al* 2005, Salci *et al* 2006) that used the Spiegelberg Compliance Monitor, nine studies (Kim *et al* 2009b, 2010, 2012, Carrera *et al* 2011, 2011a, 2011b, Capel *et al* 2014, Kazimierska *et al* 2021, Moir *et al* 2021) that utilized the TCD. Furthermore, five studies (Robertson *et al* 1989, Contant *et al* 1995, Lang *et al* 2003, Zakrzewska *et al* 2021, Uryga *et al* 2022) employed HFC/HHC for CC/CCR assessment, and six studies (Kuramoto *et al* 1986, Lee *et al* 2016, Nucci *et al* 2016, Brasil *et al* 2021, 2023, Galdino *et al* 2022) utilized the P2/P1 ratio from ICPW. Lastly, two studies (Lai *et al* 2016, Wolf *et al* 2021) employed techniques distinct from the aforementioned methodologies. The summaries of RAP, Spiegelberg Compliance Monitor, TCD, HFC/HHC, P2/P1 ratio and other techniques are provided in supporting information C.

3.1. RAP-based continuous measurement

Among the 43 studies investigating continuous CC/CCR measurement using RAP, 26 of them (Czosnyka *et al* 1988, Steiner *et al* 2005, Shahsavari *et al* 2008, 2011, Smielewski *et al* 2008, Timofeev *et al* 2008a, 2008b, Budohoski *et al* 2012, Howells *et al* 2012, Haubrich *et al* 2013, 2015, 2016b, Pineda *et al* 2015, 2018, Calviello *et al* 2018, Zeiler *et al* 2018a, 2018b, 2019, Donnelly *et al* 2020, Froese *et al* 2020, 2021, Lalou *et al* 2020, Levrini *et al* 2021, Liu *et al* 2022, Uryga *et al* 2022, Zhu *et al* 2023) included patients with TBI, 11 studies (Czosnyka *et al* 1988, Petrella *et al* 2008, Schuhmann *et al* 2008, Kim *et al* 2009a, 2015, Weerakkody *et al* 2011, Speil *et al* 2012, Varsos *et al* 2015, Haubrich *et al* 2016a, Green *et al* 2021, Ziółkowski *et al* 2021) examined hydrocephalus patients, two studies (Czosnyka *et al* 1994, Balestreri *et al* 2004) involved patients with intracranial hypertension (ICH), 2 studied (Eide and Sorteberg 2013, Jin *et al* 2019) subarachnoid hemorrhage and intracerebral hemorrhage patients, ones incorporated (Moyse *et al* 2016) patients with cerebellar infarction and infratentorial mass effect and the remaining one study (Sekhon *et al* 2019) analyzed subjects with hypoxic ischemic brain injury (HIBI).

3.1.1. Studies with TBI patients

This systematic review identified 26 studies that used the RAP metric to assess CC/CCR and included TBI patients as subjects (Czosnyka *et al* 1988, Steiner *et al* 2005, Shahsavari *et al* 2008, 2011, Smielewski *et al* 2008, Timofeev *et al* 2008a, 2008b, Budohoski *et al* 2012, Howells *et al* 2012, Haubrich *et al* 2013, 2015, 2016b, Pineda *et al* 2015, 2018, Calviello *et al* 2018, Zeiler *et al* 2018a, 2018b, 2019, Donnelly *et al* 2020, Froese *et al* 2020, 2021, Lalou *et al* 2020, Levrini *et al* 2021, Liu *et al* 2022, Uryga *et al* 2022, Zhu *et al* 2023).

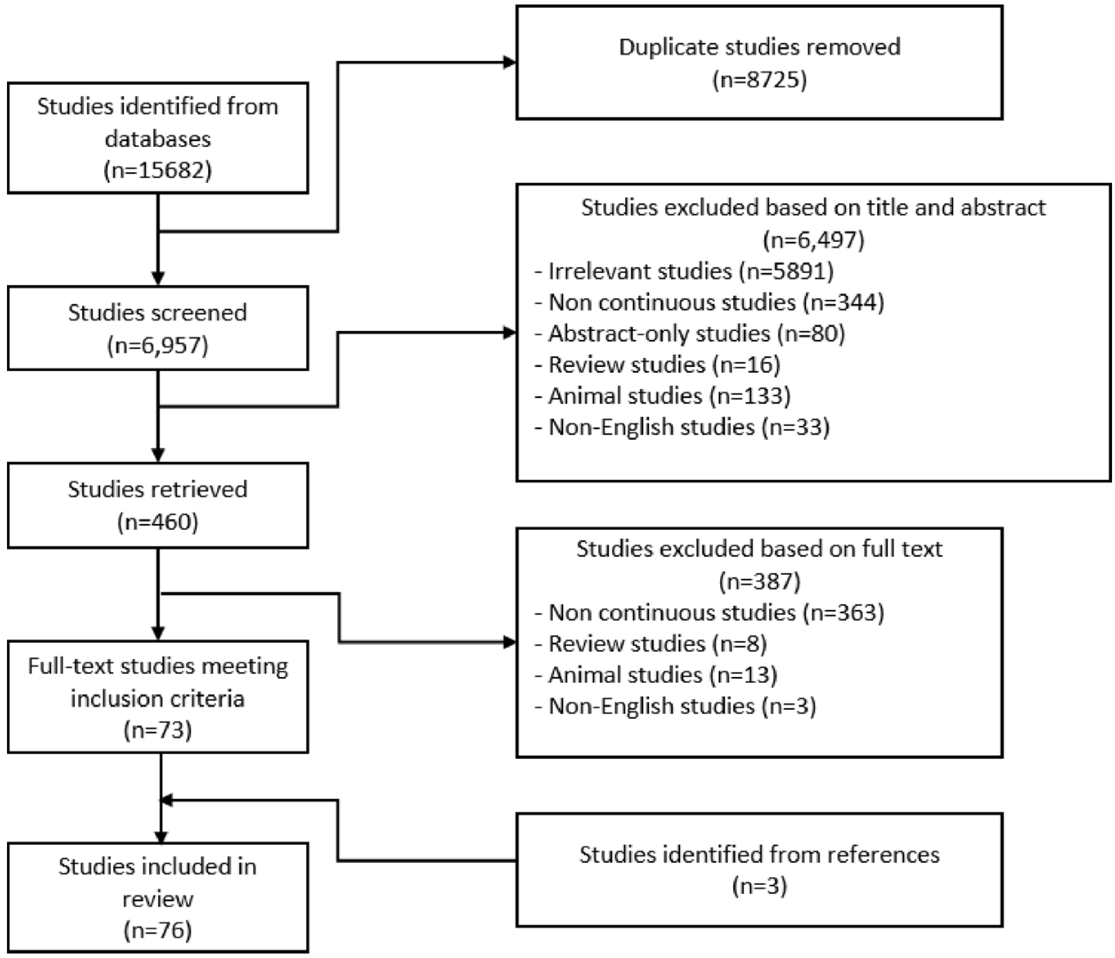

Figure 1. PRISMA flow diagram.

In studies that reported the age of the patients, in most cases, the mean age was between 30–50 years range, except for three studies (Lalou *et al* 2020, Levrini *et al* 2021, Zhu *et al* 2023), where the mean age was 59.6, 55.7, and 53.2 years, respectively. The majority of these studies experimented and reported the association of RAP with patient outcome, other physiology, and brain imaging.

3.1.1.1. Association with other physiologic parameters

Three studies (Calviello *et al* 2018, Pineda *et al* 2018, Zeiler *et al* 2018a) demonstrated the relationship between ICP and RAP. Evident sign changes and significant variance were shown with the change of ICP. Moreover, when ICP was unchanged, RAP was found to be constant. This proves the future potential of RAP for predicting ICP events and patient outcome. The effect of surgery, medical treatment and agents on RAP was investigated in five studies (Timofeev *et al* 2008a, 2008b, Howells *et al* 2012, Froese *et al* 2020, 2021). The association of RAP with decompressive craniectomy was observed in two studies (Timofeev *et al* 2008a, Howells *et al* 2012). Both of the studies were aligned with the findings of decreasing RAP after decompressive craniectomy. In addition, Howells and collaborators studied RAP's association with the Glasgow Motor Score (GCS-M), motor component of GCS, age and thiopental treatment. One of the major findings was that RAP had a less significant correlation with GCS-M and age compared to that of AMP, whereas in the case of thiopental treatment, a significant or marginally significant downward shift of RAP was noticed, which indicates improved intracranial compliance. Another medical procedure, ventriculostomy, demonstrated improving compensatory reserve, i.e. reducing RAP (Timofeev *et al* 2008b). Two studies examined the impact of vasopressor and sedative agents on RAP (Froese *et al* 2020, 2021). In both cases, their findings revealed that, overall, there was no significant change in RAP due to these medications. This was experimented with mean hourly dose and incremental dose change protocols. Moreover, sedation depth was examined, and a negative linear relation was revealed between the bispectral index (BIS) and RAP (Froese *et al* 2021).

The relation between respiratory oscillations (R waves) and RAP was researched by Haubrich and colleagues, and they found that an increase in RAP is associated with a decrease in GainFv (the transfer function gains of R waves between arterial blood pressure (ABP) and Doppler flow velocity (FV)), i.e. reduction in R waves. This suggests an exhausted cerebral compensatory reserve (Haubrich *et al* 2015). One study conducted research on the association of RAP with the transfer function of ABP to ICP at the fundamental cardiac frequency. This transfer function was denoted as MTF, and the result showed that RAP is positively correlated with MTF and negatively correlated in their variances. This indicates an increased value of MTF during poor compensatory reserve (Shahsavari *et al* 2008). Shahsavari and colleagues also explored the status of RAP in various conditions of cerebral autoregulation and corresponding regimes within the cerebrovascular system in TBI patients. In this experiment, the population was divided into three groups based on pressure reactivity as follows—a. the intact pressure reactivity group, b. impaired pressure reactivity case I group, and c. impaired pressure reactivity case II group. In the case of the intact pressure reactivity group and the impaired pressure reactivity case I group, the result showed that the average RAP is close to +1. However, in the impaired pressure reactivity case II group, RAP was close to +1 before the plateau wave. During the plateau wave, RAP decreased significantly (Shahsavari *et al* 2011). In another experiment, after exploring the association of RAP with hyperventilation in TBI patients, the result showed that RAP was reduced due to hyperventilation and showed a significant correlation with hyperventilation-induced reduced ICP (Steiner *et al* 2005). Baseline ICP and RAP were both significant predictors of ICP reduction, with RAP being the more powerful parameter (Steiner *et al* 2005). A different study showed that RAP decreased due to spindle waves, a distinctive pattern observed in EEG during the non-rapid eye movement (NREM) sleep stage. This was evident in both scenarios—scenario 1, a comparison between the control and spindle wave group, and scenario 2, a comparison (within the spindle wave group) between during spindle wave occurrence and before and after the period of that occurrence (Zhu *et al* 2023).

Three studies reported their subject as head injured patients (Smielewski *et al* 2008, Haubrich *et al* 2013, 2016b). One of the studies analysed the impact of increasing ICP on R-waves based on RAP value. RAP exceeding 0.85 reflects a substantial impact on R-waves gain with increasing ICP. Conversely, while RAP was below 0.85, it resulted in a lower impact on R-waves gain with rising ICP. Haubrich and colleagues also studied the effect of RAP in response to mild hypocapnia. Their findings indicated a significant level of decrease below baseline in RAP, and hypocapnic ICP showed a positive correlation with baseline RAP. Additionally, the hypocapnic vasomotor response (VMR) was linearly and positively correlated with RAP (Haubrich *et al* 2013). The remaining study centred on the ICM+ software and illustrated its usefulness in measuring the RAP metrics (Smielewski *et al* 2008).

The relations of RAP with two newly derived indices were observed in three studies (Calviello *et al* 2018, Zeiler *et al* 2018a, 2019). A new physiological index RAC, defined as the moving correlation coefficient between AMP and cerebral perfusion pressure (CPP), exhibited a significant negative correlation with RAP. The study also delved into the association between RAP and CPP. With the increase of CPP, RAP was reduced to zero. However, a steep increase was evident in RAP when CPP decreased towards the lower limit of autoregulation (Zeiler *et al* 2018a). The compensatory reserve weighted variable, weighted ICP (wICP), is another derived variable obtained from ICP and RAP. In the cases of good compensatory reserve (i.e. low RAP) and exhausted compensatory reserve (i.e. RAP close to +1), if the ICP remained low, then wICP stayed low as well. On the other hand, when ICP crossed its critical threshold, RAP led toward negative, resulting in an abrupt increase in wICP (Calviello *et al* 2018, Zeiler *et al* 2019).

Two studies conducted a comparative analysis of the RAP metric between TBI and idiopathic normal pressure hydrocephalus (iNPH) patients (Lalou *et al* 2020, Levrini *et al* 2021). RAP baseline was insignificantly different between the two groups, with the TBI group exhibiting a slightly higher RAP (Lalou *et al* 2020). Additionally, when comparing shunted post-traumatic hydrocephalus (PTH) vs non-shunted PTH, the group of shunted PTH showed a slightly higher RAP, but this difference was not significant (Lalou *et al* 2020). However, following continuous infusion tests, a notable increase in RAP of the PTH group was noticed, which is higher than the atrophy group (Levrini *et al* 2021).

3.1.1.2. Association with neuroimaging features

The association of RAP with imaging was observed in one study (Zeiler *et al* 2018b). The relation of RAP with admission computer tomography (CT) injury characteristics was examined, and the integrated area under the curve was found to be statistically associated with CT markers of diffuse TBI across different RAP thresholds (Zeiler *et al* 2018b).

3.1.1.3. Association with patient outcomes

Research was conducted to find out the association of RAP with patient outcome in four studies (Budohoski *et al* 2012, Calviello *et al* 2018, Pineda *et al* 2018, Donnelly *et al* 2020). Significant distinction in RAP was found between the survivor and dead group, though non-invasive AMP (nAmp) showed the most significant difference (Budohoski *et al* 2012). Whereas Calviello and colleagues found RAP to be significantly distinctive between individuals with severe disability and those with a favourable outcome. RAP performed better in distinguishing between severe disability and favourable outcome than differentiating between survival and fatal outcome (Calviello *et al* 2018). In a different study, RAP illustrated a significantly lower value in dead patients or patients in the vegetative state and RAP declined and oscillated towards 0 and negative value (Czosnyka *et al* 1996). Similarly, low RAP was identified in patients with severe ICH as well (Donnelly *et al* 2020). Another study investigated the potential of RAP in predicting cerebral hemodynamic instability and found RAP can identify unstable periods if it exceeded 0.6, providing a better distinguishing factor than ICP or AMP (Pineda *et al* 2018). However, the study conducted by Kazimierska and colleagues did not find a significant correlation between RAP and patient outcome (Uryga *et al* 2022). Nevertheless, they observed a significant positive association of RAP with the dominant ICP pulse type. This refers to the pulse type occurring most frequently throughout the entire recording, excluding pulses classified as artifacts from the analysis (Uryga *et al* 2022).

3.1.2. Studies with hydrocephalus patients

The evaluation of the RAP metric of patients affected with hydrocephalus was discussed in 11 studies (Czosnyka *et al* 1988, Petrella *et al* 2008, Schuhmann *et al* 2008, Kim *et al* 2009a, 2015, Weerakkody *et al* 2011, Speil *et al* 2012, Varsos *et al* 2015, Haubrich *et al* 2016a, Green *et al* 2021, Ziółkowski *et al* 2021). The majority of these subjects were elderly patients, more than 50 years old. However, two studies included children as their subjects (Czosnyka *et al* 1988, Schuhmann *et al* 2008).

3.1.2.1. Association between RAP, infusion testing and shunting

The effect of cerebrospinal fluid (CSF) infusion on RAP was explored in 6 studies (Czosnyka *et al* 1988, Kim *et al* 2009a, Weerakkody *et al* 2011, Varsos *et al* 2015, Haubrich *et al* 2016a, Ziółkowski *et al* 2021). Czosnyka and colleagues divided subjects into two groups considering RAP trends; group 1: RAP was low before and after infusion, whereas during infusion, RAP increased to a high value; group 2: before infusion, RAP was high, close to 1, whereas during infusion RAP typically decreased. Before and during recovery after an infusion test, RAP can be used as an indicator of the equilibrium state (Czosnyka *et al* 1988). Increased RAP during infusion of CSF was observed in four studies (Kim *et al* 2009a, Weerakkody *et al* 2011, Haubrich *et al* 2016a, Ziółkowski *et al* 2021). In the case of non-shunted patients with ventriculomegaly, during infusion, RAP stayed high, usually exceeding 0.6 (Weerakkody *et al* 2011). However, the majority of the atrophic profile exhibited low RAP during infusion. These atrophic profiles were caused by cerebrovascular or neurodegenerative disease and typically demonstrated low baseline pressure, resistance to CSF outflow (RCSF) and AMP (Weerakkody *et al* 2011).

Experiments were conducted on NPH patients to assess the impact of shunting on RAP (Petrella *et al* 2008, Schuhmann *et al* 2008, Kim *et al* 2009a, Weerakkody *et al* 2011). Among patients with ventriculomegaly, RAP significantly improved (i.e. RAP decreased) in both RAP baseline and RAP plateau (Petrella *et al* 2008, Kim *et al* 2009a). A functioning shunt had an important impact on CSF circulation and pressure–volume compensation, and RAP. On the other hand, Schuhmann and collaborators evaluated the effect of a shunt malfunction on RAP, which led to the classification of 3 groups: normal, questionable and pathological group, with the latter indicating shunt malfunction. RAP was significantly different between these groups and notably elevated in the pathological group compared to the normal group (Schuhmann *et al* 2008). In a comparison between properly functioning shunt, overdrainage and underdrainage states, RAP was noted to be low for the first two cases, while exceeding 0.6 for the latter (Weerakkody *et al* 2011).

3.1.2.2. Association with other physiologic measures

Furthermore, several studies investigated the association of RAP with other parameters and cases (Kim *et al* 2009a, 2015, Speil *et al* 2012, Varsos *et al* 2015, Green *et al* 2021, Ziółkowski *et al* 2021). For instance, exploring the relationship between RAP and phase shift angle between fundamental harmonics of CBFV and ICP illustrated a negative correlation (Kim *et al* 2015). In a study comparing mean RAP values, both iNPH and late-onset idiopathic aqueductal stenosis (LIAS) patients exhibited impaired values, with no significant difference noted (Green *et al* 2021). In another study, a strong positive correlation was observed between RAP and the RCSF, while a weaker correlation was observed with ventriculomegaly (Kim *et al* 2009a). Speil and collaborators conducted a study comparing RAP with both elastance (E) and pressure–volume index (PVI). In this study, E and PVI were measured through a lumbar infusion test. However, no significant correlation existed between them (Speil *et al* 2012).

In a different experiment, the association between cerebral hemodynamic indices (critical closing pressure (CrCP), wall tension (WT), closing margin (CM)) and CSF compensatory parameter (i.e. RAP) was observed. No association between RAP and CrCP, WT or CM was found. However, it was suggested that CM at baseline pressure could be utilized as an indicator of RAP since it was negatively correlated with cerebrospinal elasticity (Varsos *et al* 2015). Additionally, analysis was conducted to determine the relation between ICP pulse shape changes, CBFV, and intracranial compliance (Ziółkowski *et al* 2021). A new index called the ratio of pulse slopes (RPS) was introduced for this purpose, based on the inclinations of the ascending parts of the ICP and CBFV pulse waveforms. The findings included a strong positive correlation of baseline RAP with intracranial elasticity and negative correlations with the height ratio of the first and second peaks of the ICP pulse (P1/P2) and RPS (Ziółkowski *et al* 2021).

3.1.3. Studies with other patient populations

Aside from TBI and NPH patients, there are an additional six studies that include diverse patient population investigating RAP metric (Czosnyka *et al* 1994, Balestreri *et al* 2004, Eide and Sorteberg 2013, Moyse *et al* 2016, Jin *et al* 2019, Sekhon *et al* 2019). The mean age across these studies varies from each other, since they explored different aspects within various types of patients.

Analysis of RAP in patients with ICH was conducted in two studies (Czosnyka *et al* 1994, Balestreri *et al* 2004). In the study of the comparison between patients with favourable and fatal outcomes, a progressive increase of RAP was observed over time, along with a sudden decrease when ICP started to increase in cases of the patients who died. In contrast, patients with a favourable outcome persistently showed a higher RAP (Balestreri *et al* 2004). Czosnyka and colleagues, while studying cerebrospinal dynamics, classified patients into group 1 with low RAP (good compensatory reserve), group 2: RAP is high and increasing with decreasing CPP, and group 3: RAP is close to $+1$ (nearly exhausted RAP). Furthermore, RAP became negative when CPP dropped below 30 mmHg, indicating a critical disturbance in cerebral circulation (Czosnyka *et al* 1994).

Two studies concentrated on patients with subarachnoid hemorrhage and intracerebral hemorrhage (Eide and Sorteberg 2013, Jin *et al* 2019). Combining RAP with ICP monitoring proved to be an effective marker in an experiment of subarachnoid hemorrhage patients (Jin *et al* 2019). The total population was split into two groups: group 1: receiving ICP monitoring only ($n = 5$), and group 2: receiving ICP monitoring with RAP index ($n = 2$). Out of the 5 patients 3 died from group 1, whereas none from the group 2 faced fatal outcome. The monitoring of RAP index allowed an opportunity for implementing additional interventions to reduce ICP before clinical worsening, thus minimizing irreversible damage to brain tissue (Jin *et al* 2019). In another study, variations in RAP value were noted within the same patient when measured using two different sensors. The second sensor was categorized into four types—category A: a solid sensor; category B: a fluid sensor; category C: an air-pouch sensor; and category D: a fibreoptic sensor. A difference in RAP $\geqslant 0.4$ was found while comparing the measurements from the two sensors, among which 4%, 44%, 20%, and 28% belonged to category A, category B, category C, category D respectively. Additionally, when applying a threshold RAP of 0.6, the two sensors showed a difference in measurements in more than 20% of scores (Eide and Sorteberg 2013).

Moyse and collaborators examined states of RAP in the supratentorial and infratentorial compartment of a 70 year old patient with acute cerebellar infarction and infratentorial mass effect. The correlation of RAP in the two compartment was strong and their values did not align precisely but were close (Moyse *et al* 2016). Observation of RAP in HIBI patients showed impaired RAP along with normal ICP in most of the cases (Sekhon *et al* 2019).

3.2. Spiegelberg Compliance Monitor-based continuous measurement

Recently, Spiegelberg Compliance Monitor has become a prevalent tool for assessing continuous CC/CCR and in this systematic review 11 studies utilized this for their analysis (Piper *et al* 1999, Raabe *et al* 1999, Kiening *et al* 2002, 2003, 2005, Yau *et al* 2002, 2005, Abdullah *et al* 2005, Ng *et al* 2005, Portella *et al* 2005, Salci *et al* 2006). Among them six studies experimented on TBI patients (Kiening *et al* 2002, 2003, 2005, Abdullah *et al* 2005, Portella *et al* 2005, Salci *et al* 2006), four studies concentrated on hydrocephalus patients (Piper *et al* 1999, Raabe *et al* 1999, Yau *et al* 2002, 2005) one study explored patients with abnormal hematoma volume (Ng *et al* 2005). The median age of the population of these studies lies between 45–60 years, with the exception of one study (Abdullah *et al* 2005) that included younger subjects, aged between 18–27 years.

3.2.1. Studies with TBI patients

Out of the six studies (Kiening *et al* 2002, 2003, 2005, Abdullah *et al* 2005, Portella *et al* 2005, Salci *et al* 2006) focusing on TBI patients, Abdullah and colleagues explored the relationship between continuous CC/CCR and decompressive craniectomy. Their findings revealed that, after receiving decompressive craniectomy, compliance improved substantially in all alive patients (Abdullah *et al* 2005). Analysis was conducted on the potential of continuous CC/CCR to predict increased ICP (Kiening *et al* 2003, 2005). CC/CCR correctly predicted 37 increased ICP episodes from 225 episodes. Furthermore, continuous CC/CCR and ICP had a scattered correlation (Kiening *et al* 2003), which reduced significantly with a rise in ICP (Kiening *et al* 2005). Kiening and team also researched the association of age with continuous CC/CCR and observed that it declined with the increase of age in patients with high ICP (Kiening *et al* 2005). The association of continuous CC/CCR with CPP was explored with a designated threshold of CPP = 60 mmHg. CC/CCR was significantly lower when CPP was below 60 mmHg. Though CPP exceeding 60 mmHg resulted in a higher CC/CCR, it dropped dramatically when CPP reached 100 mmHg (Portella *et al* 2005). The relationship between continuous CC/CCR and the lactate/pyruvate (L/P) ratio was observed by Salci and team. As compliance decreased, the L/P ratio increased with or without high temperature. This relationship was differed by coma treatment. Furthermore, when the temperature is elevated, there is a greater increase in the L/P ratio. Furthermore, the analysis revealed that individuals with lower CC/CCR were more susceptible to secondary hyperthermia (Salci *et al* 2006). In a different research study, a relation between CC/CCR and age was observed; as age increased, CC/CCR increased as well (Kiening *et al* 2002).

3.2.2. Studies with hydrocephalus patients

The application of the Spiegelberg Compliance Monitor to measure continuous CC/CCR in hydrocephalus patients was researched for different aspects. The performance and result of this continuous measurement method were compared with a manual volume injection /withdrawal method, and a strong positive correlation was found between them. Their average measurements were quite similar, with the continuous method showing a slightly higher value (Piper *et al* 1999). In another study, continuous CC/CCR remained unchanged across different body positions (Raabe *et al* 1999). Analyzing the contrast between continuous CC/CCR and cerebral elastance, the latter exhibited fewer outliers and a better correlation with ICP. Moreover, the exponentially-weighted moving average (ewma) method was introduced in this analysis, and the result showed it was more strongly correlated with ICP than the conventional Spiegel 'rolling' method in terms of calculating continuous CC/CCR (Yau *et al* 2005). The functional and compliance improvement following CSF shunting was also investigated with the Spiegelberg Compliance Monitor measurement. Except for one, all the other patients had noteworthy improvement (Yau *et al* 2002).

3.2.3. Studies with other patient populations

Other than research on TBI and hydrocephalus patients, Spiegelberg Compliance Monitor was also used for other aspects to determine continuous CC/CCR. One of the studies researched continuous CC/CCR as a bedside monitoring technique. Ng and collaborators observed the impact of applying ultrasound-guided aspiration to patients with abnormal hematoma volume. It was found that this procedure led to a sustained improvement in compliance accompanied by a gradual reduction in ICP (Ng *et al* 2005).

3.3. TCD-based continuous measurement

Nine studies of this comprehensive systematic review included research that encompassed TCD-based continuous measurement of CC/CCR (Kim *et al* 2009b, 2010, 2012, Carrera *et al* 2011, 2011a, 2011b, Capel *et al* 2014, Kazimierska *et al* 2021, Moir *et al* 2021). Out of them, three focused on TBI patients (Kim *et al* 2009b, 2012, Carrera *et al* 2011), three researched patients with hydrocephalus (Kim *et al* 2010, Capel *et al* 2014, Kazimierska *et al* 2021), and two studied normal subjects (Carrera *et al* 2011a, 2011b) and the remaining one involved patients with internal carotid artery disease (Moir *et al* 2021).

3.3.1. Studies with TBI patients

Among the TBI studies, Carrera and team investigated the changes of Ci and Ca induced by initial hyperventilation and observed an increase in Ci and a decrease in Ca. ICP was also reduced in this phase and correlated with Ca reduction. The period of sustained hyperventilation was also observed, and though ICP was elevated and Ci was reduced, no noteworthy change in Ca was observed (Carrera *et al* 2011). The state of Ca and Ci was observed in a study regarding continuous monitoring of the Monro–Kellie doctrine (Kim *et al* 2012). An index of CC/CCR (ICC), defined as a moving correlation coefficient between Ca and Ci, was also introduced. Three phases were monitored—a. during arterial hypertension, b. during plateau waves, and c. during ICH. Ca and Ci showed a negative correlation during arterial hypertension, leading to a negative ICC. During plateau waves, both Ca and Ci increased. Meanwhile, Ca and Ci were reduced, and a consistent and positive ICC was exhibited at the ICH phase. Regarding outcome, the study also depicted that higher ICC was associated with a higher mortality rate (Kim *et al* 2012). In addition, this defined ICC demonstrated a significant and positive correlation with pressure reactivity index (PRx) but none with ICP, mean ABP, or CPP (Kim *et al* 2012). Alongside these findings, in another study, Kim and collaborators observed the compartmental compliance changes, i.e. the changes of Ca and Ci, focusing on plateau waves. In the case of Ci, it reduced significantly during the plateau wave, followed by an increase. The opposite case was seen in terms of Ca since it increased during plateau waves and decreased afterwards (Kim *et al* 2009b).

3.3.2. Studies with hydrocephalus patients

CSF infusion tests were performed in all investigations involving hydrocephalus patients (Kim *et al* 2010, Capel *et al* 2014, Kazimierska *et al* 2021). All of the tests demonstrated poorer compliance during the plateau phase of infusion, characterized by an elevated value of Ca. whereas a reduction in Ci and other discussed CC indices (Kim *et al* 2010, Capel *et al* 2014, Kazimierska *et al* 2021). In one of the studies, after a total of 50 infusion tests, a strong negative correlation was found between Ca and cerebrovascular response (CVR) as well as between Ca and CPP. However, no correlation was noted between Ca and any CSF compensatory parameters—Rcsf, elasticity or ICP baseline (Capel *et al* 2014). In a comparative study evaluating three compliance measurement methods, all of them correlated strongly with each other. These three methods—CCSF, CCaBV, and CP1/P2 represented the CC and derived from Marmarou's model of CSF dynamics (CCSF), changes in CaBV (CCaBV), and the amplitudes of peaks P1 and P2 of ICP pulse waveform (CP1/P2) respectively. Comparing their values between the baseline and plateau phase of the infusion test revealed that all of them reduced, with CCaBV exhibiting the largest change, whereas CP1/P2 had the smallest (Kazimierska *et al* 2021). In another infusion test study, brain elasticity was positively correlated with Ci, which was evident when comparing values from the baseline to the plateau phase and during the plateau phase itself (Kim *et al* 2010).

3.3.3. Studies with other patient patients

Regarding predicting ischemic events, Carrera and collaborators researched patients with internal carotid artery disease (Carrera *et al* 2011b). Their findings encompassed a lower value of Ca for the diseased group during baseline, hyperventilation and 5% CO2 inhalation, as well as Ca and the degree of stenosis illustrated a reciprocal characteristic at baseline (Carrera *et al* 2011b). In addition, a comparative analysis was conducted on normal subjects, examining the differences between normo-, hypo- and hypercapnia. While comparing with normocapnia, Ca was eminently lower in hypocapnia; however, in terms of hypercapnia, there was no difference between them. Furthermore, Ca was associated with CVR in an inversely changing manner, evident in both hypo- and hypercapnia (Carrera *et al* 2011a). Another study was conducted on healthy subjects, experimenting with the effect of sublingual sodium nitroglycerin (SNG) protocol and hypercapnia protocol. In both cases, cerebrovascular compliance decreased, with hypercapnia protocol associated with a comparatively higher reduction (Moir *et al* 2021).

3.4. HFC/HHC-based continuous measurement

Five studies demonstrated the measurement method of continuous CC/CCR using HFC or HHC (Robertson *et al* 1989, Contant *et al* 1995, Lang *et al* 2003, Zakrzewska *et al* 2021, Uryga *et al* 2022). All of the studies concentrated on TBI patients. In the study conducted by Contant and colleagues, though a direct association of HFC with CC was not mentioned, it was found that HFC decreased during the refractory ICH changes (Contant *et al* 1995). In contrast, it increased during the transient changes. Since pulse amplitude of ICP (referred to as PAICP in the study) showed an inverse relation with CC/CCR and demonstrated an increased value in refractory ICH (not significant), it can be said that, probably, HFC and CC/CCR had a positive association, i.e. with the increase of HFC, CC/CCR increased (Contant *et al* 1995). However, the association of HFC with compliance is not straightforward since two other studies found that HFC was significantly greater in the group that met the fatal outcome, which was associated with poor CC/CCR (Robertson *et al* 1989, Uryga *et al* 2022). Regarding HHC, a negative correlation was reported with PRx, indicating a negative correlation between cerebral autoregulation and CC (Zakrzewska *et al* 2021). Additionally, Lang and the team found out from their experiment that a noninvasive measured HFC result was similar to the invasively measured HFC, concluding the possibility of measuring CC/CCR by HFC noninvasively (Lang *et al* 2003).

3.5. P2/P1 ratio-based continuous measurement

The measurement of continuous CC using the P2/P1 ratio was examined in six studies (Kuramoto *et al* 1986, Lee *et al* 2016, Nucci *et al* 2016, Brasil *et al* 2021, 2023, Galdino *et al* 2022, Uryga *et al* 2022). Among the studies, three specifically targeted TBI patients (Lee *et al* 2016, Brasil *et al* 2021, 2023), two focused on patients with hydrocephalus (Kuramoto *et al* 1986, Nucci *et al* 2016), and one examined patients with type 2 diabetes (Galdino *et al* 2022). In an approach to assess CC/CCR utilizing ICPW, an increase in P2/P1 ratio was observed, which was associated with impaired CC/CCR in the patients with craniectomy (Brasil *et al* 2021). Another parameter derived from the P2/P1 ratio, known as the brain compliance index, demonstrated a higher value (i.e. impaired compliance) in the early death (ED) group (Brasil *et al* 2023). Furthermore, P2/P1 was higher in patients with ICH (Brasil *et al* 2023). Conversely, in the group with type 2 diabetes mellitus (T2DM), no significant change in the P2/P1 ratio (i.e. no substantial change in CC/CCR) was observed compared to the control group (Galdino *et al* 2022). However, a significant decrease in the P2/P1 ratio was noticed due to active postural change only in the T2DM group (Galdino *et al* 2022). A different study by Kuramoto and colleagues illustrated the influence of P2 in bulk compliance (Kuramoto *et al* 1986). They observed that after the infusion test, P1 was smaller than P2 in the case of subdural hematoma cases, whereas P1 and P2 were either constant or hard to identify in hydrocephalus cases. Additionally, they noted an increment of P2 compared to P1 during the REM period (Kuramoto *et al* 1986).

3.5.1. Special cases

The importance of the P2/P1 ratio in assessing the CC in different circumstances was evident in four studies (Kuramoto *et al* 1986, Brasil *et al* 2021, 2023, Galdino *et al* 2022). In conjunction, two studies focused on identifying real-time P1, P2 and P3 peaks from ICPW (Nucci *et al* 2016, Uryga *et al* 2022). Using a clustering method, 95.3%, 87.8%, and 87.5% accuracy was obtained for P1, P2 and P3, respectively (Nucci *et al* 2016). Meanwhile, Nucci and the team used ANN to classify CSFPPW into different classes and found a match of 88.3% of cases between their result and an expert examiner's observation (Uryga *et al* 2022). These classes ranged from class I to class IV. A progressive increase in average elasticity index (EI) values was noted with the advancement of morphological class (Uryga *et al* 2022).

3.6. Other approaches for continuous measurement

Aside from RAP, Spiegelberg Compliance Monitor, TCD, HFC/HHC, and P2/P1 ratio, few other methods have been utilized to measure CC/CCR continuously. Two such studies (Lai *et al* 2016, Wolf *et al* 2021) are included in this systematic review focusing on patients with TBI.

The potential of representing continuous CC/CCR from a PV curve was experimented with. An indicator 'a' was derived from a parabolic regression model, expressed initially from the PV curve but without a conclusive statement (Lai *et al* 2016). PCI is another index defined as the moment-to-moment correlation between ICP change and end-tidal CO2 (ETCO2) change. Throughout most of the observation period, PCI remained within the range of 0.1–0.2, where PCI ≈ 0 suggests good compliance and PCI ≈ 0.2 suggests poor compliance (Wolf *et al* 2021).

4. Discussion

This scoping review comprehensively addressed the existing methods and metrics for calculating continuous compliance. Following a thorough review, the key insights encompass the performance of the metrics, a comparative analysis with conventional parameters, and the association of compliance with various parameters. The three major metrics and methods for assessing continuous CC/CCR are A. RAP, B. compliance measurement from Spiegel compliance monitor, C. TCD-based compliance—Ci and Ca.

Firstly, if attention is directed to the metric's performance, RAP was the most extensively researched continuous CC/CCR measurement metric (Czosnyka *et al* 1988, 1994, 1996, Balestreri *et al* 2004, Steiner *et al* 2005, Petrella *et al* 2008, Schuhmann *et al* 2008, Shahsavari *et al* 2008, 2011, Smielewski *et al* 2008, Timofeev *et al* 2008a, 2008b, Kim *et al* 2009a, 2015, Weerakkody *et al* 2011, Budohoski *et al* 2012, Howells *et al* 2012, Speil *et al* 2012, Eide and Sorteberg 2013, Haubrich *et al* 2013, 2015, 2016a, 2016b, Pineda *et al* 2015, 2018, Varsos *et al* 2015, Moyse *et al* 2016, Calviello *et al* 2018, Zeiler *et al* 2018a, 2018b, 2019, Jin *et al* 2019, Sekhon *et al* 2019, Donnelly *et al* 2020, Froese *et al* 2020, 2021, Lalou *et al* 2020, Green *et al* 2021, Levrini *et al* 2021, Ziółkowski *et al* 2021, Liu *et al* 2022, Zhu *et al* 2023). Nevertheless, in terms of predicting TBI patient outcome, AMP outperformed RAP (Budohoski *et al* 2012). The superiority of AMP over RAP was also evident in distinguishing between iNPH and PTH patients (Lalou *et al* 2020). In addition, it remained unclear if RAP could serve as a predictor for ICH, which led to the suggestion of further investigation (Pineda *et al* 2018). Nevertheless, RAP excelled as a compliance metric and proved to be a potential marker in various aspects. Its association with brain CT injury patterns further confirms its potential use as a measure of continuous CC/CCR in TBI (Zeiler *et al* 2018b). While RAP might not have shown superior performance in predicting mortality rate, it proved to be more effective in distinguishing between severe disability and favourable outcomes (Howells *et al* 2012). It was also proved to be beneficial for TBI patients in terms of controlling elevated ICP (Steiner *et al* 2005). Additionally, regarding indicating an equilibrium state after an infusion test, it also contributed significantly to patients affected with hydrocephalus (Czosnyka *et al* 1988). In the context of shunting applications, several studies utilized RAP as an indicator of improved compliance (Schuhmann *et al* 2008, Kim *et al* 2009a, Weerakkody *et al* 2011), and RAP provided the expected result, even in the case of the malfunctioning shunt (Schuhmann *et al* 2008, Weerakkody *et al* 2011). RAP emerged as a more effective indicator for HIBI patients compared to ICP, showing significant differences from normal cases (Sekhon *et al* 2019). Other than HIBI, for critical intracranial physiological parameters in poor-grade World Federation of Neurosurgical Societies patients, a combination of RAP and ICP was fruitful as a marker (Jin *et al* 2019).

While RAP is the most centric topic regarding the continuous measurement of CC/CCR, the Spiegelberg Compliance Monitor also contributed extensively to the field of research as a tool for assessing continuous compliance (Piper *et al* 1999, Raabe *et al* 1999, Kiening *et al* 2002, 2003, 2005, Yau *et al* 2002, 2005, Abdullah *et al* 2005, Ng *et al* 2005, Portella *et al* 2005, Salci *et al* 2006). Similar to RAP, it also has its limitations. Research conducted in 2003 concluded that the current hardware and software version of the Spiegelberg Compliance Monitor lacked satisfactory data quality, which might hamper predicting increased ICP (Kiening *et al* 2003). In another study, after analysing the effect of shunt application using the Spiegelberg Compliance Monitor, further research was suggested to clarify its clinical implications (Yau *et al* 2002). Nonetheless, comparing the measurement of the Spiegelberg Compliance Monitor with one of the conventional manual methods illustrated a significant correlation, implying its validity as a continuous compliance measurement method (Yau *et al* 2005). As an indicator, compliance measurement from the Spiegelberg Compliance Monitor was competent, indicating when to avoid hyperthermia in TBI patients (Salci *et al* 2006).

As mentioned, Ci and Ca are the two primary compliance metrics derived from TCD measurements. The performance of Ca was evaluated in one of the studies analysing the association of the metric with $ETCO_2$ (Carrera *et al* 2011). In addition, this metric was associated with CPP after infusion, similar to the other defined metrics (Capel *et al* 2014). Lastly, both Ca and Ci showed a strong correlation with the direct method of volumetric manipulation, affirming their validity as valuable parameters for continuous compliance measurement (Kazimierska *et al* 2021).

Additionally, two centroid metrics—HFC and HHC- were observed to assess continuous CC/CCR. While a direct correlation between CC/CCR and HFC/HHC was not evident, these metrics significantly contributed to predicting patient outcomes, which could be associated with either poor or improved CC/CCR (Robertson *et al* 1989, Zakrzewska *et al* 2021, Uryga *et al* 2022). In these scenarios, HFC/HHC were negatively correlated with the state of the CC/CCR (Robertson *et al* 1989, Zakrzewska *et al* 2021, Uryga *et al* 2022). Furthermore, the alternation in the distinct P1 and P2 peaks of ICPW was also used to assess continuous CC/CCR. P2 became greater than P1 (i.e. P2/P1 ratio > 1) in the impaired compliance cases in contrast to the P1 $>$ P2 in normal cases. P2/P1 could also predict the patients' outcomes, with P2/P1 being higher in the ED group and ICH group patients (Brasil *et al* 2023).

Aside from RAP, Spiegelberg Compliance Monitor, TCD, HFC/HHC, and P2/P1 ratio-based compliance assessment, some other approaches were explored with the purpose of measuring compliance continuously. Originating from the PV curve, and modifying through a parabolic regression model, an indicator 'a' was derived. The absolute value of 'a' represented the compliance measurement in the experiment (Lai *et al* 2016). In another study, the newly derived metric PCI looked promising in the field of an indirect assessment of dynamic intracranial compliance measurement (Wolf *et al* 2021).

Secondly, in the realm of exploration and observation, a predominant number of the studies reported the association of continuous CC/CCR with one or multiple different parameters, conditions or factors (Czosnyka *et al* 1994, Abdullah *et al* 2005, Portella *et al* 2005, Steiner *et al* 2005, Yau *et al* 2005, Petrella *et al* 2008, Schuhmann *et al* 2008, Timofeev *et al* 2008b, Kim *et al* 2009a, 2010, 2012, Carrera *et al* 2011, Shahsavari *et al* 2011, Weerakkody *et al* 2011, Budohoski *et al* 2012, Howells *et al* 2012, Capel *et al* 2014, Haubrich *et al* 2015, Varsos *et al* 2015, Zeiler *et al* 2018a, Lalou *et al* 2020, Froese *et al* 2021, Green *et al* 2021, Kazimierska *et al* 2021, Levrini *et al* 2021). Several studies involving TBI patients found a strong correlation between compliance with decompressive craniectomy, that is undertaking this surgical procedure significantly improved compliance (Abdullah *et al* 2005, Timofeev *et al* 2008a, Howells *et al* 2012). Researchers were interested in studying the change of CC/CCR resulting from CSF infusion, which was applied to hydrocephalus patients. Consistent findings across studies indicate a notable decrease in compliance leading to a poorer state during infusion (Czosnyka *et al* 1988, Kim *et al* 2009a, Weerakkody *et al* 2011, Speil *et al* 2012, Varsos *et al* 2015, Haubrich *et al* 2016a, Levrini *et al* 2021, Ziółkowski *et al* 2021) and also during the plateau phase of the infusion, as some studies reported (Kim *et al* 2010, Capel *et al* 2014, Kazimierska *et al* 2021). Another focal area of investigation in the context of hydrocephalus was the effect of shunting (Yau *et al* 2005, Petrella *et al* 2008, Schuhmann *et al* 2008, Kim *et al* 2009a, Weerakkody *et al* 2011, Lalou *et al* 2020). Generally, shunting improved compliance; however, in the case of PTH, no significant difference between shunted and non-shunted was reported (Lalou *et al* 2020). Additionally, malfunctioning shunts demonstrated poorer compliance (Schuhmann *et al* 2008, Weerakkody *et al* 2011).

The association of continuous CC/CCR with different neurological conditions consistently demonstrated a prevalent trend characterized by diminished compliance (Haubrich *et al* 2013, Lalou *et al* 2020, Levrini *et al* 2021). An exception was atrophy, where the patients demonstrated ample compliance during the infusion test (Weerakkody *et al* 2011). However, there was no substantial difference in the quantitative value of compliance between TBI, iNPH and LIAS (Haubrich *et al* 2013, Lalou *et al* 2020, Levrini *et al* 2021). Recording after infusion proved effective in differentiating PTH and atrophy (Levrini *et al* 2021). Various researchers extensively explored the relationship between compliance with CPP (Czosnyka *et al* 1994, Portella *et al* 2005, Kim *et al* 2012, Capel *et al* 2014, Zeiler *et al* 2018a). The majority of the analysis aligns with the findings that compliance showed a negative correlation with CPP becoming more intact with the increase of CPP (Czosnyka *et al* 1994, Portella *et al* 2005, Capel *et al* 2014, Zeiler *et al* 2018a). However, compliance was reduced substantially when CPP exceeded 100 mmHg (Portella *et al* 2005). It is worth noting that one study deviated from this pattern, as it failed to identify a significant correlation between their defined compliance metric and CPP (Kim *et al* 2012).

Other associated parameters are sedation depth-related parameter BIS (Froese *et al* 2021), respiratory oscillations-related parameter GainFV (Haubrich *et al* 2015, Varsos *et al* 2015), thiopental treatment (Howells *et al* 2012), cerebral hemodynamic instability (Pineda *et al* 2018), pressure reactivity (Shahsavari *et al* 2011, Kim *et al* 2012), transfer function between ABP and ICP (Budohoski *et al* 2012), hyperventilation (Steiner *et al* 2005, Carrera *et al* 2011), CT-image (Zeiler *et al* 2018b), ICP spindle waves (Zhu *et al* 2023), phase shift angle between CBFV and ICP (Kim *et al* 2015), the resistance to CSF outflow (Kim *et al* 2009a), VMR (Haubrich *et al* 2013), hypocapnia-hypercapnia (Carrera *et al* 2011a, Haubrich *et al* 2013), supratentorial and infratentorial compartment (Moyse *et al* 2016), age (Kiening *et al* 2005), ultrasound-guided aspiration (Ng *et al* 2005), arterial hypertension (Kim *et al* 2012), plateau waves (Kim *et al* 2009b), CVR (Capel *et al* 2014), L/P ratio (Salci *et al* 2006), brain elasticity (Kim *et al* 2010), internal carotid artery disease (Carrera *et al* 2011b), and SNG and hypercapnia protocol (Moir *et al* 2021).

While compliance demonstrated association with several parameters, some did not show any or significant correlation. These are sedative and vasopressor agents (Froese *et al* 2020, 2021), elastance and PVI measured through lumbar infusion test (Speil *et al* 2012), CrCp, WT or CM (Petrella *et al* 2008) and body position (Raabe *et al* 1999).

4.1. Limitations/future direction

This systematic review was conducted on 76 studies, which varied in patient population, patient type, and different continuous measurement techniques of CC/CCR. In the case of the RAP metric, using two different ICP sensors can result in two different RAP values, which are affected by local differences (Eide and Sorteberg 2013, Calviello *et al* 2018). Additionally, wrong RAP values can be measured using intraparenchymal frontal cortex sensors in patients with infratentorial lesions, which needs to be evaluated. As a consequence of using an anonymized database, that evaluation may be hampered (Calviello *et al* 2018). The data set size is a crucial factor in a compliance study, but due to the effect of surgery like decompressive craniectomy, confounding factors are introduced, which can affect the patient outcome. As a result, the data set becomes small, and the analysis range becomes narrower (Howells *et al* 2012). Furthermore, some of the studies showed a good correlation with the outcome or essential parameters to predict the outcome, but few studies did not conclude if it could be used clinically (Yau *et al* 2002, Ng *et al* 2005, Steiner *et al* 2005, Kim *et al* 2009a, Pineda *et al* 2018). Another limitation of RAP is that researchers may find it unclear how RAP will be affected by an open intraventricular drain, as it depends on a closed intracranial space (Steiner *et al* 2005). During an infusion test, a paradoxical decrease of RAP was noticed for some cases, which could not be interpreted (Czosnyka *et al* 1988). Moreover, in a dataset, a difference in age can affect the RAP result since ICP is a function of age. In addition, studies found an association between continuous CC/CCR with age (Kiening *et al* 2002, 2005). In terms of Ca and Ci, the calibration of these two compliance metrics cannot be completed due to the unknown cross-sectional area of arterial vessels. This makes the comparison between patients impossible, and thereby, only relative changes can be observed (Kim *et al* 2009a, Kazimierska *et al* 2021). While calculating Ca, assuming venous outflow being constant is not correct either (Capel *et al* 2014). Besides, changes in MCA diameter can impact the measure of CBFV and, thereby, Ca (Carrera *et al* 2011b).

This scoping review only includes the methods that involve human subjects. The animal studies were excluded in this review. Consequently, potential methods, crucial associations, findings, or predictive aspects related to continuous CC/CCR might not be encompassed in this review.

The methods for calculating continuous CC/CCR require advancements in precision and accuracy for practical application in clinical settings. RAP is the most researched topic in this field, indicating a potential area for improvement by focusing on its patterns and identifying characteristics and artifacts to improve its precision. Furthermore, there is an evident gap in exploring the neuroimaging sector, with limited studies discussing the correlation between neuroimaging and CC/CCR metrics. A promising avenue for enhancement lies in integrating ML with neuroimaging, potentially simplifying the determination of CC/CCR and their predictability. But in that case, the model needs to provide high accuracy and precision.

5. Conclusion

To conclude, this systematic review provides a thorough overview of continuous compliance measurement methods, emphasizing research related to RAP. At the same time, described the Spiegelberg Compliance

Monitor, TCD feature, centroid metrics, and distinct peaks of ICPW prominently as well. Notably, a majority of studies focus on TBI and hydrocephalus patients, whereas most of the hydrocephalus cases encompass infusion studies and analysis on the effect of shunt. Another crucial aspect highlighted in this review is the numerous associations between these metrics and various physiological parameters, as well as patient outcomes, underscoring the utility of continuous CC/CCR in diverse medical contexts and its potential clinical applications. However, it is noteworthy that many studies recommended further analysis before widespread clinical application.

Data availability statement

All data that support the findings of this study are included within the article (and any supplementary information files).

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