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General Review

Intracranial Compliance, Resistance to CSF-Outflow, and Pressure-Volume Index in Hydrocephalus Patients: A Systematic Review and Meta-Analysis

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HIGHLIGHTS

- R_{out} was higher in adult hydrocephalus compared to pediatric, opposite trend for PVI.
- NPH patients had a higher R_{out} compared to communicating hydrocephalus.
- All ICP characteristics correlated with both the ICC and R_{out}.
- ICC correlated with ventricular score and R_{out} correlated with third ventricle index.

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ABSTRACT

Objectives: How changes in intracranial compliance (ICC), resistance to cerebrospinal fluid (CSF)-outflow (R_{out}), and pressure-volume index (PVI) can play a prominent role in clarifying the complexities in the biomechanism and treatment outcomes of hydrocephalus. This study aims to provide a comprehensive review to find the correlation between ICC, R_{out}, and PVI with intracranial pressure (ICP) characteristics, as well as morphometric parameters, in hydrocephalus patients.

Material and methods: Electronic searches were conducted using the PubMed/MEDLINE, Scopus, Google Scholar, Ovid, Cochrane, and EMBASE databases from their dates of inception to December 2022 using filters for English-language articles. The article selection and data collection were conducted in accordance with PRISMA guidelines and recommendations. We assigned a quality score for each study to evaluate the information and selection bias. The certainty of the pooled data for all articles was assessed based on GRADE criteria. The Funnel plot asymmetry study was used to evaluate publication bias.

Results: The overall pre-treatment ICC, R_{out}, and PVI were 0.45 ml/mmHg (95% CI, 0.33-0.57; I^2=99.7%; P<0.001), 14.93 mmHg/(ml/min) (95% CI, 13.65-16.21; I^2= 99.7%; P<0.001) and 19.26 ml (95% CI, 15.63-22.89; I^2=98.7%; P<0.001), respectively. The pooled R_{out} was observed to be higher in adult hydrocephalus compared to pediatric hydrocephalus, whereas the opposite trend was found for PVI. Patients with normal pressure hydrocephalus (NPH) exhibited a higher pooled R_{out} compared to communicating hydrocephalus. Patients with unimproved outcomes demonstrated a decrease in the effect size of the pooled R_{out}. The results also showed significant correlations were observed between all ICP characteristics and both the ICC and R_{out}. The correlation between ICC and the ventricular score was significant. R_{out} had a significant correlation with the third ventricle index. PVI had significant correlations with Evan's ratio, inverse cella media, and ventricular score.

Conclusion: The results indicate the possible reason for publication bias in some subgroups may be related to methodological heterogeneity in the measurement of pressure-volume parameters. This finding motivates researchers to investigate the effects of different invasive and non-invasive methods on the measurement results of ICC, R_{out}, and PVI.

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1. Introduction

Hydrocephalus is the enlargement of the ventricles of the brain due to failed cerebrospinal fluid (CSF) homeostasis. The bulk flow model of CSF circulation proposes inadequate CSF passage from its main site of production to sites of absorption as the most common cause [1]. In addition, genetic studies showed that in some forms of congenital hydrocephalus, changes in the regulation of neuronal stem cell fate can be a critical factor for hydrocephalus [2]. The increasing prevalence of hydrocephalus in pediatrics is 88/100,000, while in adults, it is 11/100,000, and in the elderly is 175/100,000 [3]. There are many complexities and ambiguous aspects in terms of the pathophysiology, diagnosis, prognosis, and treatment of hydrocephalus patients, as well as, the pathology and biomechanics of the hydrocephalic brain [4,5]. Intracranial compliance (ICC), resistance to CSF-outflow (R_{out}), and pressure-volume index (PVI) are three indicators that mirror homeostasis and pathology of the brain [6–8], as well as the interaction of CSF and brain tissue [7,9]. These indicators can play a prominent role in decreasing the complexities in the diagnosis of hydrocephalus and determining the optimal therapeutic strategies [10–13]. ICC is defined as CSF volume change per intracranial pressure (ICP) change [7,9]. ICC reflects the capacity of the intracranial compartment to expand without a considerable ICP rise [7,14]. Absorption capacity is approximated by R_{out} and is generally used for the evaluation of the treatment of hydrocephalus patients [11]. PVI is defined as the slope of the CSF volume-log ICP graph. PVI also represents the CSF volume value that needs to increase ICP tenfold [10,14]. The changes in ICC, PVI, and R_{out} based on the patient's characteristics indicate great importance in the hydrocephalus study. On the other hand, ICP characteristics can be the practical tools needed for a neurosurgeon to evaluate the hydrocephalic condition [15–19]. Morphometric parameters that are obtained using head medical images are also useful in the diagnosis of hydrocephalus. Hence, evaluation of the changes in ICC, PVI, and R_{out} with regard to the ICP characteristics and morphometric parameters has also great potential to help neurosurgeons optimize individualized therapeutic decisions as well as early and exact diagnosis of hydrocephalus patients.

We aimed to aggregate the data of previous studies to evaluate the changes in three indicators of ICC, PVI, and R_{out} based on patient characteristics including gender, age, and the type of hydrocephalus, as well as, patient outcomes. This study also aimed to find the correlation between these three indicators and ICP characteristics, as well as morphometric parameters. This may be helpful to clarify the role of these parameters in the diagnosis, pathogenesis, planning treatment, and management of hydrocephalus patients, and shed light on the brain pathology and biomechanical complexities of hydrocephalus.

2. Methods

2.1. Search strategy

We performed a detailed systematic review and meta-analysis based on PICOS (Patient, Population or Problem, Intervention, Comparison, Outcomes, Study type) questions. The article selection and data collection were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and recommendations [20]. Electronic searches were carried out using the PubMed/MEDLINE, Scopus, Google Scholar, Ovid, Cochrane, and EMBASE databases from their dates of inception to December 2022 using filters for English-language articles. A rather simple strategy was used to perform a broad search based on the following terms: "hydrocephalus" OR intracranial compliance OR brain compliance OR resistance to cerebrospinal fluid-outflow OR pressure-volume index OR volume pressure response OR volume pressure parameter. The searches were also repeated with the abbreviations of these phrases.

2.2. Selection criteria

The included articles were defined as follows: 1) peer-reviewed articles with full text in the English language, 2) human studies, 3) studies included communicating hydrocephalus, non-communicating hydrocephalus, and/or normal pressure hydrocephalus (NPH) patients, 4) studies included ICC, PVI, and/or R_{out} values with at least one of the following parameters: gender, age, type of hydrocephalus, patient outcomes, at least one of the ICP characteristics, or at least one of the head morphometric parameters.

The excluded articles included: 1) conference proceedings, comments, letters to Editors, correspondences, theses, or papers with unavailable full text. It should be noted that case studies/series including fewer than 3 patients were excluded to decrease the risk of selection bias. Moreover, we did not consider the results of review papers during data collection, 2) studies that included repetitive data. Only papers that include the most comprehensive data were considered, 3) patients with low-pressure hydrocephalus, 4) patients with high-pressure hydrocephalus, 5) patients with intracranial hypertension, 6) studies that measured ICC, PVI, and/or R_{out} in non-hydrocephalus patients, 7) studies that included incomplete data such as median of an indicator instead of average, an open interval for an indicator instead of close interval/average, or lack of units of the parameters, 8) qualitative studies of ICC, PVI, and R_{out} without numerical values, 9) Long-term (a couple of months) evaluation of hydrocephalus patients to measure ICC, PVI, and/or R_{out}, 10) studies that included compliance or volume pressure response of hydrocephalus patients in the spinal canal.

2.3. Data extraction

Two independent authors (S.C. and A.N.) systematically searched literature to abstract data from text, tables, and figures, and cross-check data for accuracy. Discrepancies and conflicts were noted by an independent arbiter (S.G.). References of searched papers were validated and related papers were considered in the literature. The identified records were moved to EndNote software (EndNote version 20; Thomson Reuters, Sunnyvale, CA) for detecting and removing duplicated articles. It should be noted that we used a 2-level screening process (Fig. 1). Study characteristics (author, publication year, type of study (prospective, retrospective, case report, clinical trial), patient characteristics (sample size, age, gender, type of hydrocephalus, treatment method (shunt, endoscopic third ventriculostomy (ETV), LP, and non-surgical treatments)), patient outcomes (improved/unimproved) for each study were extracted and reported. The main results were changes in ICC, PVI, and R_{out} of hydrocephalus patients based on the patient's characteristics and also their correlations with changes in ICP characteristics and morphometric parameters. It should be noted that ICP characteristics included baseline and monitoring ICP, and pulse wave amplitude (PWA) of baseline and monitoring ICP. The morphometric parameters included Evan's index, inverse cella media index, third ventricle index, and ventricular score. We reported the ICC/PVI/R_{out} measurement methods for each article: pressure and volume measurement methods, method description (invasive or noninvasive), probe location and diameter, production company of catheter, and ICP measurement information. The relevant data were extracted from each paper and imported into Excel worksheets for data aggregation and analysis. The general information of evaluated articles and the indicators (ICC, R_{out}, and/or PVI) assessed in each study are listed in Supplementary Table S1 with a brief finding for each study.

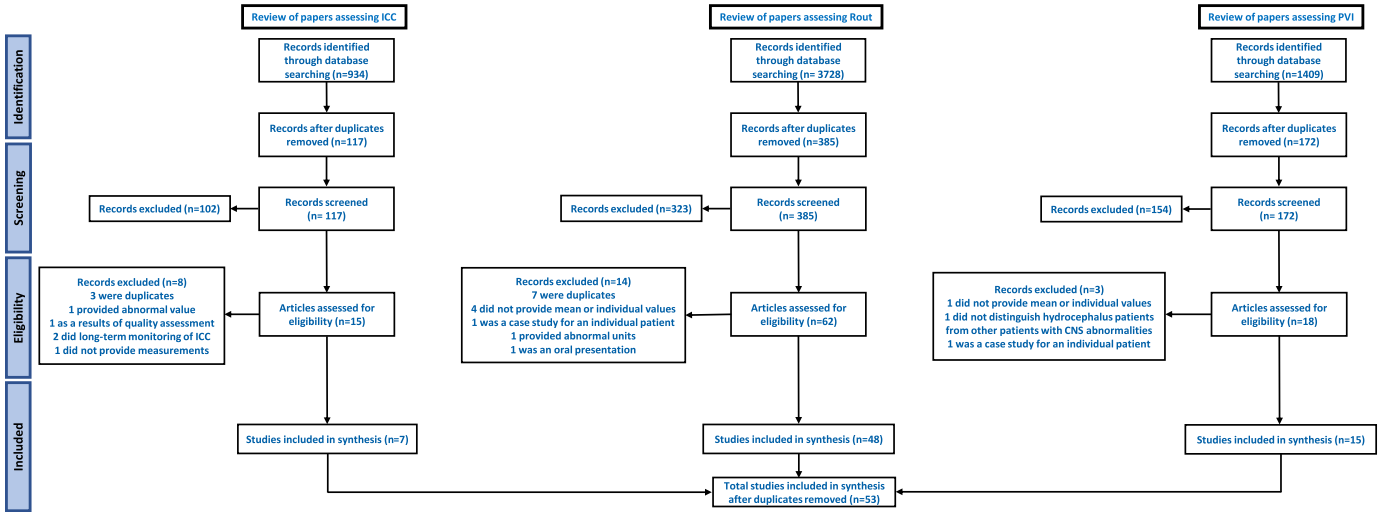

Fig. 1. PRISMA flow chart detailing the study selection process.

2.4. Quality assessment

We assigned a quality score for each study to evaluate the information and selection bias. In the quality assessment form ($0 \leq score \leq 20$, Supplementary Table S2), the articles with a score higher than 13 were considered good-quality studies. The final score of each study is listed in Supplementary Table S3. The certainty of the pooled data for all articles was assessed based on the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) criteria [21]. The potential for selection of studies and their information bias were blindly assessed by two independent authors (S.C. and A.N.) and an arbiter (S.G.). We used the Funnel plots and Egger's regression test for publication bias assessment.

2.5. Statistical analysis

We conducted a single-arm meta-analysis using Stata software (STATA 16.0, Stata Corp, College Station, TX, USA). The random effects model was used for meta-analysis. Effect sizes for ICC, R_{out}, and PVI were reported. We also reported the weight of each study and the confidence interval (CI) of 95% for pooled data. We used the Chi-squared test to evaluate the presence of heterogeneity. Tau-squared was used to assess the variance between the groups of studies, and the I-squared statistic was used to describe the level of heterogeneity. The forest plots provide an overview of the combined effects of the parameters in all studies. A meta-regression was performed with random effects to study the changes in ICC, R_{out}, and PVI based on the ICP characteristics and morphometric parameters. The concept of all ICC, R_{out}, and PVI indicators is based on pressure and volume changes, and conceptually there is a dependency between these indicators. Hence, Bonferroni corrected P-value (0.05/3=0.017) was used as the statistical threshold of significance.

3. Results

3.1. Study characteristics

Preliminarily reviewed abstracts for ICC, R_{out}, and PVI included 934, 3,728, and 1,409 studies, respectively. After performing screening and eligibility processes for these 6,071 studies, the total studies included in the synthesis (after duplicates were removed) contained 53 studies [22–74]. The selection process of the eligible studies is shown by the flow chart in Fig. 1. The included studies based on subgroups and the reasons for exclusion studies are listed in Table 1. The distribution based on the publication year and geographical distribution per one million population of included studies are shown in Supplementary Figs. S1 and S2, respectively.

To evaluate pre-treatment ICC, R_{out}, and PVI, we used 7 (445 patients) [22–28], 48 (2178 patients) [22–25,28–71], and 15 (453 patients) studies [24,27,29–32,34,36–38,55,58,72–74], respectively. There were 33 studies that included ICP characteristics data with ICC, R_{out}, and/or PVI values [22,24,26,27,30,32,35,37–44,47–50,53–57,59,64–66,68,69,71–73], and the corresponding studies for morphometric parameters were 13 papers [22–24,29,32–34,40,48,63,65,68,71].

In the final step of the eligibility process, we found 8, 14, and 3 excluded studies to evaluate ICC, R_{out}, and PVI, respectively. After removing the duplicate excluded studies, there were 21 excluded studies [9,12,75–93]. The reasons for the exclusion of these studies are listed in Table 1. We listed the changes in ICC, PVI, and R_{out} values based on study and patient characteristics, treatment methods, and patient outcomes regarding the extracted data from included studies in Table 2. For correlation analysis, we reported the changes of ICC, R_{out}, and PVI regarding ICP characteristics, as well as morphometric parameters, in Table 3.

3.2. Effectiveness of ICC

Pooled results from 7 studies revealed that the overall pre-treatment ICC was 0.45 ml/mmHg (95% CI, 0.33-0.57; I^2=99.7%; P<0.001) (Fig. 2a). The pooled ICC value in adult patients was 0.49 (95% CI, 0.35-0.62; I^2=99.8%; P<0.001) (Table 4). The pooled ICC in patients with NPH was 0.44 (95% CI, 0.25-0.64; I^2=99.9%; P<0.001) (Table 4). It should be noted that there was considerable heterogeneity in the pooled ICC values. A meta-regression was conducted to study the correlation between ICC and ICP characteristics, as well as morphometric parameters. There were significant correlations between ICC and all ICP characteristics including baseline ICP (P<0.001), monitoring ICP (P=0.013), PWA of baseline ICP (P<0.001), and PWA of monitoring ICP (P<0.001). Among morphometric parameters, the correlation between ICC and the ventricular score was significant (P<0.001) and there was no correlation between ICC and Evan's ratio (P=0.68).

Table 1
The included studies based on subgroups and the reasons for exclusion studies. ICC: intracranial compliance; R_{out}: resistance to cerebrospinal outflow; PVI: pressure-volume index; ICP: intracranial pressure; PWA: pulse wave amplitude.

Indicator	Variable		Included studies	Excluded studies	
			Sources	Sources	Reasons
ICC	Pre-treatment		[1–7]	[8–15]	Studies [12–14] are duplicate datasets. Studies [8,15] performed long-term monitoring of ICC. Studies [11] provided abnormal ICC units. Study [10] was excluded because of the low-quality score during the quality assessment of the papers. [9] only provided a difference between ICC values in various measurement methods, not exact ICC values.
	Type of hydrocephalus	Non-communicating, communicating, and NPH	[1–4,7]		
	Patient outcomes	Improved and unimproved	[1,2]	[12]	[12] was excluded because of the same dataset as [2].
	ICP characteristics	Baseline and monitoring of ICP	[1,3,5,6]		
		PWA of baseline and monitoring ICP	[1,5]		
	Morphometrics	Evan's ratio, inverse cella media index, third ventricle index, and ventricular score	[1–3]	[12]	[12] was excluded because of the same dataset as [2].
R_{out}	Pre-treatment		[1–4,7,16–58]	[12,13,59–70]	[70] was a case study that focused on 1 patient. Study [59] did have the same dataset as [19], hence, [59] was excluded. Studies [60,61] only provided median values. Studies [12,13,62–65] are excluded because of duplicate datasets. [69] provided abnormal unit. Study [68] was the abstract of the conference paper with unavailable full text. [66] provided open ranges as values. [67] did not provide exact values for R_{out}.
	Type of hydrocephalus	Non-communicating, communicating, and NPH	[1–4,7,16,18,19,21,22,24,26–31,33,35–39,41–43,45–47,49,50,52–57]		
	Patient outcomes	Improved and unimproved	[1,2,16,19,20,22,24,28,30,34,38,40–42,54,56,57]	[12,59,62–65]	Study [59] is excluded because of the same dataset as [19]. Studies [12,62–65] are excluded because of the same dataset as [2]. For the other studies, the value for R_{out} was not provided.
	ICP characteristics	Baseline and monitoring ICP	[1,3,17,19,22,24–31,34–37,40–44,46,51–53,55,58]	[59]	Study [59] is excluded because of the same dataset as [19]. For the other studies, the value for R_{out} was not provided.
		PWA of baseline and monitoring of ICP	[1,19,25,41,46,51,53,55,56]	[59]	
	Morphometric parameters	Evan's ratio, inverse cella media index, third ventricle index, and ventricular score	[1–3,16,19–21,27,35,50,52,55,58]	[12,59,62–65]	Study [59] is excluded because of the same dataset as [19]. Studies [12,62–65] are excluded because of the same dataset as [2].
PVI	Pre-treatment		[3,6,16–19,21,23–25,42,45,71–73]	[67,70,74]	[70] was a case study that focused on 1 patient. Study [67] only provided open ranges for the values. Study [74] did not distinguish hydrocephalus patients from patients with other CNS anomalies.
	Type of hydrocephalus	Non-communicating, communicating, and NPH	[3,19,21,24,42,45,73]		
	Patient outcomes	Improved and unimproved	[16,19,24,42]		
	ICP characteristics	Baseline and monitoring of ICP	[3,6,17,19,24,25,42,71,73]		
		PWA of baseline and monitoring of ICP	[19,25]		
	Morphometric parameters	Evan's ratio, inverse cella media index, third ventricle index, and ventricular score	[3,16,19,21]		

Table 2
Changes in ICC, PVI, and R_{out} of hydrocephalus patients based on the study and patient's characteristics in the included studies. It should be noted in some papers they measure elastance instead of compliance or conductive instead of resistance of outflow. We used the inverse of these values in our database [15,75]. For more information about the ICP measurement methods, please refer to the Supplementary Table S1. AHT: anti-hypertension, CP: cystoperitoneal, ETV: endoscopic third ventriculostomy, EVD: external ventricular drain, ICC: intracranial compliance, MRI: magnetic resonance imaging, MoD: mean of differences, NPH: normal pressure hydrocephalus, PVI: pressure-volume index, R_{out}: resistance to cerebrospinal outflow, SAH: subarachnoid hemorrhage, SAS: subarachnoid space, VA: ventriculoatrial, VD: ventricular drainage, VP: ventriculoperitoneal.

Authors, Year [Source]	Type of hydrocephalus	Age (years)	Gender (male/female)	Sample size	Patient outcome (improved/ unimproved)	ICC (ml/mmHg) by cohort	R_{out} (mmHg/(ml/min)) by cohort	PVI (ml) by cohort
Trevisi et al., 2021 [57]	Idiopathic normal pressure hydrocephalus	Adult (73.2±6.6)	41/23	64	40/23	Unspecified	15.2	Unspecified
Kazmierska et al., 2021 [7]	Normal pressure hydrocephalus (36)	Adult (54.0)	Unspecified	36	Unspecified	0.27	12.1	Unspecified
Lalou et al., 2020 [58]	Post-traumatic hydrocephalus	Adult (53±17)	24/12	36	VP shunt (5/11)	Unspecified	Post-traumatic hydrocephalus (13.5); VP shunt (16.7), Untreated (10.6) — Improved (18.9) Follow-up (19.0)	Unspecified
	Idiopathic normal pressure hydrocephalus	Adult (66.2±12.8)	26/19	45	VP shunt (45/0)			
Jacobsson et al., 2018 [55]	Idiopathic normal pressure hydrocephalus	Adult (74.0±6.0)	43/19	62	Unspecified	Unspecified	All (17.1): Probable NPH (17.9), Possible NPH (16.2)	Unspecified
Lalou et al., 2018 [56]	Normal pressure hydrocephalus	Adult (63.2±5.6)	77/54	131	64/19	Unspecified	Treated (14.9); Shunt (16.3), ETV (12.0) — Improved (12.6), Unimproved (11.7)	Unspecified
Tuniz et al., 2017 [54]	Idiopathic normal pressure hydrocephalus	Adult (71.7±6.8)	10/13	23	13/10	Unspecified	All (12.3); Male (12.2), Female (11.6) — VP shunt (13.5), Untreated (9.8) — Improved (13.5), Unimproved (9.8)	Unspecified
Eide, 2017 [1]	Communicating hydrocephalus Noncommunicating hydrocephalus	Adult (55.2±13.0)	68/54	122	82/28	All (0.55); Communicating hydrocephalus (0.55), Noncommunicating hydrocephalus (0.56) — VP Shunt (0.53), ETV or ETV and VP shunt (0.55), Non-surgical (0.63) — Improved (0.49), Unimproved (0.71)	All (9.8); Communicating hydrocephalus (10.1), Noncommunicating hydrocephalus (9.5) — VP Shunt (10.4), ETV or ETV and VP shunt (9.9), Non-surgical (6.4) — Improved (10.8), Unimproved (8.3)	Unspecified
Mahr et al., 2016 [53]	Idiopathic normal pressure hydrocephalus	Adult (70.5)	47/21	68	26/7	Unspecified	All (15.0); VP Shunt and/or ETV (16.0), Untreated (14.0) — Improved (15.8), Unimproved (18.0)	Unspecified
Eide, 2016 [5]	Communicating hydrocephalus Noncommunicating hydrocephalus	Adult (53.0*)	40/42	82	57/15	All (0.52); Shunt or ETV (0.51), Non-surgical (0.60) — Improved (0.47), Unimproved (0.66)	Unspecified	Unspecified
Czepko and Cieslicki, 2016 [52]	Normal pressure hydrocephalus *Secondary communicating hydrocephalus Idiopathic normal pressure hydrocephalus*	Adult (51.3)	13/14	27	6/21	Unspecified	Pre-treatment (7.5): Secondary communicating hydrocephalus (7.8), Idiopathic normal pressure hydrocephalus (7.3) — Follow-up (7.5): Secondary communicating hydrocephalus (7.7), Idiopathic normal pressure hydrocephalus (7.4)	Unspecified

(*continued on next page*)

Table 2 (*continued*)

Authors, Year [Source]	Type of hydrocephalus	Age (years)	Gender (male/female)	Sample size	Patient outcome (improved/ unimproved)	ICC (ml/mmHg) by cohort	R_{out} (mmHg/(ml/min)) by cohort	PVI (ml) by cohort
Swallow et al., 2014 [51]	Hydrocephalus	Mixed (41.0)	9/9	18	Unspecified	Unspecified	12.2	Unspecified
Wikkelsø et al., 2013 [50]	Normal pressure hydrocephalus	Adult (70.0)	58/57	115	97/18	Unspecified	16.0	Unspecified
Andersson et al., 2013 [73]	Idiopathic normal pressure hydrocephalus	Adult (71.2±8.9)	33/14	47	Unspecified	Unspecified	Unspecified	16.7
Poca et al., 2012 [49]	Idiopathic normal pressure hydrocephalus	Adult (75.0*)	145/91	236	212/24	Unspecified	16.4	Unspecified
Piechnik et al., 2012 [48]	Hydrocephalus	Adult (65.0±10.0)	13/17	30	Unspecified	Unspecified	12.0	Unspecified
Paidakakos et al., 2012 [47]	Normal pressure hydrocephalus	Adult (72.2)	21/23	44	30/14	Unspecified	VP shunt (15.2); Lumbar (19.6), Ventricular (10.8) —Improved: Lumbar (20.2), Unimproved: Lumbar (18.7) — ETV (14.1); Lumbar (9.1), Ventricular (19.1) — Improved: Ventricular (19.1), Unimproved: Ventricular (19.0)	Unspecified
Czosnyka et al., 2011 [46]	Idiopathic normal pressure hydrocephalus	Adult (74.0)	60/32	92	46/18	Unspecified	16.5	Unspecified
Sundström et al., 2010 [45]	Communicating hydrocephalus with probable or possible idiopathic normal pressure hydrocephalus	Adult (72.6±9.0)	14/6	20	Unspecified	Unspecified	Untreated (12.9); Constant-pressure infusion (16.0) — Constant-flow infusion (13.0) — Bolus injection (9.8)	Untreated (22.4); Constant-flow Infusion (22.3) — Bolus injection (22.5)
Cieslicki and Czepko, 2010 [44]	Acute hydrocephalus	Adult (49.0)	5/4	9	4/4	Unspecified	12.3	Unspecified
Andersson et al., 2008 [43]	Idiopathic normal pressure hydrocephalus	Adult (71.0±10.0)	23/7	30	11/5	Unspecified	22.3	Unspecified
Marmarou et al., 2007 [42]	Idiopathic normal pressure hydrocephalus	Adult (79.5±7.0)	7/10	17	7/10	Unspecified	All (11.2); Male (6.0), Female (12.9) — Shunt (13.9), Untreated (7.4) — Improved (19.0), Unimproved (7.3)	All (20.1); Male (17.7), Female (21.2) — Shunt (18.7), Untreated (22.6) — Improved (18.3), Unimproved (21.4)
Kahlon et al., 2005 [41]	Normal pressure hydrocephalus	Adult (73.5±7.1)	22/33	55	43/12	Unspecified	All (20.5); Improved (20.8), Unimproved (19.9)	Unspecified
Juniewicz et al., 2005 [40]	Hydrocephalus	Adult (61.1±19.2) Pediatric (6.0±0.0)	19/8	27	9/5	Unspecified	All (12.9); Adult (13.5), Pediatric (7.3) — Male (12.9), Female (12.7) — Shunt (15.6), Untreated (9.9) — Improved (15.4), Unimproved (16.1)	Unspecified
Eide and Sorteberg, 2005 [39]	Idiopathic normal pressure hydrocephalus	Adult (68.0*)	11/8	19	14/5	Unspecified	All (15.7); Improved (16.9), Unimproved (20.1)	Unspecified

Table 2 (*continued*)

Authors, Year [Source]	Type of hydrocephalus	Age (years)	Gender (male/female)	Sample size	Patient outcome (improved/ unimproved)	ICC (ml/mmHg) by cohort	R_{out} (mmHg/(ml/min)) by cohort	PVI (ml) by cohort
Delwel et al., 2005 [38]	Normal pressure hydrocephalus	Adult (69.5)	43/23	83	39/27	Unspecified	VP shunt (16.1): Improved (16.9), Unimproved (15.1)	Unspecified
Sorteberg et al., 2004 [37]	Normal pressure hydrocephalus	Adult (65.0*)	7/10	17	15/2	Unspecified	16.6	Unspecified
Kasprowicz, et al., 2004 [36]	Normal pressure hydrocephalus	Adult (68.0±12.6)	30/20	50	Unspecified	Unspecified	All (16.5); Elevation of ICP (15.9), No elevation of ICP (17.6)	Unspecified
Eide et al., 2003 [35]	Normal pressure hydrocephalus	Adult (57.9±12.6)	5/11	16	Unspecified	Unspecified	All (13.4); Lumbar (12.1), Cranial (14.8) — Male (11.9): Lumbar (12.7), Cranial (11.0) — Female (14.2): Lumbar (15.7), Cranial (12.6)	Unspecified
Tisell et al., 2002 [34]	Hydrocephalus with aqueductal stenosis	Adult (57.6±15.8) Pediatric (16.0)	11/4	14 1	ETV (10/5) VP shunt (3/3)	Unspecified	Pre-Treatment (16.5); Ventricular (17.1), SAS (15.9) — Adult (17.2): Ventricular (17.9), SAS (16.6) — Pediatric (7.3): Ventricular (7.5), SAS (7.1) — Male (18.7): Ventricular (19.5), SAS (18.0); Female (11.0): Ventricular (11.3), SAS (10.8) — Improved (18.0): Ventricular (19.3), SAS (16.7); Unimproved (13.9): Ventricular (13.3), SAS (14.5) —Post-ETV follow-up (9.7); Adult (10.1), Pediatric (4.2) — Male (10.8), Female (6.5) — Improved (8.7), Unimproved (11.7) — Post-VP-shunt follow-up (3.0)	Unspecified
Savolainen et al., 2002 [33]	Normal pressure hydrocephalus	Adult (66.5)	27/24	51	25/26	Unspecified	All (11.7); Shunt (12.9), Untreated (10.7)	Unspecified
Kahlon et al., 2002 [32]	Normal pressure hydrocephalus	Adult (72.0±9.0)	29/39	68	43/25	Unspecified	14.0	Unspecified
Meier and Bartels, 2001 [4]	Normal pressure hydrocephalus	Adult (52.0)	122/78	107	60/42	All (0.29); Early NPH (0.16), Advanced NPH (0.39)	All (28.2); Early NPH (29.5), Advanced NPH (27.3)	Unspecified
Lundkvist et al., 2001 [31]	Communicating hydrocephalus	Adult (73.0±6.0)	4/8	12	Unspecified	Unspecified	Pre-treatment (17.8), 3-month follow-up (2.2), 12-month follow-up (2.4)	Unspecified
Takeuchi et al., 2000 [30]	Idiopathic normal pressure hydrocephalus	Adult (60.4)	15/10	25	12/13	Unspecified	All (24.8); Improved (35.3), Unimproved (9.1)	Unspecified
Schmidt et al., 2000 [29]	Normal pressure hydrocephalus	Adult (68.0±7.0)	8/2	10	Unspecified	Unspecified	9.6	Unspecified
Bech et al., 1999 [28]	Hydrocephalus Noncommunicating hydrocephalus	Pediatric (1.6±0.4)	2/1	3	3/0	Unspecified	All (14.8); Lumbar (17.0), Ventricular (12.5) — Hydrocephalus (13.3): Lumbar (14.0), Ventricular (12.5); Noncommunicating hydrocephalus (23.0) — Male (13.3): Lumbar (14.0), Ventricular (12.5); Female (23.0) — VP shunt (21.3): Lumbar (22.5), Ventricular (17.0) — Untreated (7.0): Lumbar (6.0), Ventricular (8.0)	Unspecified

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Table 2 (*continued*)

Authors, Year [Source]	Type of hydrocephalus	Age (years)	Gender (male/female)	Sample size	Patient outcome (improved/ unimproved)	ICC (ml/mmHg) by cohort	R_{out} (mmHg/(ml/min)) by cohort	PVI (ml) by cohort
Boon et al., 1997 [27]	Normal pressure hydrocephalus	Adult (73.7±6.3)	60/41	101	72/29	Unspecified	17.3	Unspecified
Gideon et al., 1994 [26]	Normal pressure hydrocephalus	Adult (68.4±6.7)	5/4	9	Unspecified	Unspecified	All (17.9); Male (16.0), Female (20.3) — VP shunt (17.0), Untreated (18.0)	Unspecified
Shapiro et al., 1993 [25]	Hydrocephalus	Pediatric (1.6±2.3)	Unspecified	16	12/2	Unspecified	7.8	29.5
Sahuquillo et al., 1991 [3]	Normal pressure hydrocephalus	Adult (65.0±11.0)	30/24	54	54/0	All (0.68); Active (0.33), Compensated (0.71) — Stable (0.78), Unstable (0.67)	All (22.1); Active (38.8), Compensated (23.5) — Stable (14.3), Unstable (28.5)	All (14.8); Active (24.1), Compensated (12.7) —Stable (12.9), Unstable (13.7)
Kosteljanetz et al., 1990 [24]	Normal pressure hydrocephalus	Adult (60.3±11.5)	7/7	18	8/6	Unspecified	VP shunt (11.3); Improved (10.0), Unimproved (14.4) — Male (18.6), Female (6.5)	VP shunt (16.2); Improved (18.4), Unimproved (12.7) — Male (9.6), Female (21.8)
Czosnyka et al., 1990 [23]	Hydrocephalus	Adult (unspecified) Pediatric (unspecified)	Unspecified	43 28	Unspecified	Unspecified	All (12.9); Adult (13.8): Static (11.4), Dynamic (16.1) — Pediatric (11.4): Static (10.1), Dynamic (12.7)	All (15.2); Adult (12.4): Static (12.1), Dynamic (12.6) — Pediatric (19.6): Static (16.2), Dynamic (22.9)
Tans and Poortvliet, 1989 [72]	Normal pressure hydrocephalus	Adult (unspecified)	Unspecified	35	Unspecified	Unspecified	Unspecified	15.4
Maksymowicz et al., 1989 [22]	Communicating hydrocephalus and Normal pressure hydrocephalus	Adult (47.7±13.3)	5/7	12	9/3	Unspecified	Pre-treatment (12.2): Communicating hydrocephalus (14.1), Normal Pressure hydrocephalus (11.6) — Male (8.1), Female (15.2) — Improved (12.9), Unimproved (10.2); Follow-up (7.2): Communicating hydrocephalus (8.9), Normal Pressure hydrocephalus (6.6) — Male (6.3), Female (7.8) — Improved (7.4), Unimproved (6.4)	Unspecified
Tans and Poortvliet, 1988 [21]	Normal pressure hydrocephalus	Adult (unspecified)	Unspecified	30	Unspecified	Unspecified	21.3	15.2
Thomsen et al., 1986 [20]	Normal pressure hydrocephalus	Adult (56.3±9.2)	29/11	40	16/24	Unspecified	All (24.2); Male (23.1), Female (27.0) — Improved (31.0), Unimproved (19.7)	Unspecified
Shapiro and Fried, 1986 [6]	Hydrocephalus	Pediatric (unspecified)	Unspecified	20	Unspecified	0.32	Unspecified	18.4
Kosteljanetz, 1986 [19]	Communicating hydrocephalus	Adult (64.6±11.6) Pediatric (14.0±5.3)	12/17	29	9/2	Unspecified	All (11.6); Adult (11.6), Pediatric (10.3) — Male (13.2), Female (10.6) — Shunt (17.5), Untreated (7.8) — Improved (21.1), Unimproved (11.9)	All (9.5); Adult (8.8), Pediatric (15.0) — Male (10.9), Female (8.4) — Shunt (9.5), Untreated (11.4) — Improved (10.9), Unimproved (6.3)

Table 2 (*continued*)

Authors, Year [Source]	Type of hydrocephalus	Age (years)	Gender (male/female)	Sample size	Patient outcome (improved/ unimproved)	ICC (ml/mmHg) by cohort	R_{out} (mmHg/(ml/min)) by cohort	PVI (ml) by cohort
Fried and Shapiro, 1986 [71]	Hydrocephalus	Pediatric (unspecified)	Unspecified	18	10/8	Unspecified	Unspecified	35.5
Tans and Poortvliet, 1985 [18]	Hydrocephalus	Adult (unspecified)	Unspecified	58	Unspecified	Unspecified	All (9.7); Bolus (6.0), Infusion (13.3)	All (19.5); Bolus (17.5), Infusion (21.4)
Shapiro et al., 1985 [17]	Hydrocephalus	Pediatric (0.3±0.3)	Unspecified	16	Unspecified	Unspecified	7.2	28.1
Tans and Poortvliet, 1984 [16]	Communicating hydrocephalus and Noncommunicating hydrocephalus	Adult (42.3)	Unspecified	26	15/3	Unspecified	All (11.1); Bolus (5.1), Infusion (17.2) — Communicating (10.6): Bolus (4.9), Infusion (16.3) — Noncommunicating (11.6): Bolus (5.4), Infusion (17.8) — Shunt (13.9): Bolus (6.3), Infusion (21.4) — Untreated (5.0): Bolus (2.5), Infusion (7.5) — Improved (14.8): Bolus (7.0), Infusion (22.7) — Unimproved (9.0): Bolus (3.0), Infusion (15.0)	All (13.6); Communicating (15.0), Noncommunicating (12.6) — Shunt (11.1), Untreated (19.5) — Improved (10.6), Unimproved (13.3)
Børgesen, 1984 [2]	Normal pressure hydrocephalus	Adult (57.0±10.4)	51/29	80	41/23	0.53	All (19.6); Male (20.5), Female (17.9) — VA shunt (23.0), Untreated (6.1) — Improved (27.4), Unimproved (15.2)	Unspecified

*Represents a median value for age rather than a mean.

Table 3
Correlations of ICC, R_{out}, and PVI with ICP characteristics and morphometric parameters in the included studies. It should be noted in some papers they measure elastance instead of compliance or conductive instead of resistance of outflow. We used the inverse of these values in our database [15,75]. EDP: epidural pressure, ETV: endoscopic third ventriculostomy, ICC: Intracranial compliance, ICP: intracranial pressure, AHT: anti-hypertension, IPP: intraparenchymal pressure, IVP: intraventricular pressure, PTH: post-traumatic hydrocephalus, PVI: pressure-volume index, R_{out}: resistance to cerebrospinal outflow, VP: ventriculoperitoneal.

Authors, Year [Source]	Cohort	Sample size	Stage	ICP measurement information				Morphometric parameters				ICC (ml/mmHg)/R_{out} (mmHg/(ml/min)) /PVI (ml)
				Method	Time and/or duration when measured[1]	Pulse wave amplitude (mmHg)	ICP (mmHg)	Evan's index	Inverse cella media index	Third ventricle index	Ventricular score	
Kazmierska et al., 2021 [7]	All	36	Pre-treatment	Infusion test	Baseline	Unspecified	13.4	Unspecified	Unspecified	Unspecified	Unspecified	0.27/12.1/unspecified
Lalou et al., 2020 [58]	Post-traumatic hydrocephalus	36	Pre-treatment	Infusion test	Baseline	Unspecified	9.3	0.38	Unspecified	Unspecified	Unspecified	Unspecified/13.5/unspecified
	Post-Traumatic hydrocephalus and VP shunt	16					8.7	0.39	Unspecified	Unspecified	Unspecified	Unspecified/16.7/unspecified
	Post-Traumatic hydrocephalus and untreated	13					9.9	0.36				Unspecified/10.6/unspecified
	Idiopathic normal pressure hydrocephalus	45	Follow-up				9.5	Unspecified				Unspecified/19/unspecified
Jacobsson et al., 2019 [55]	All	62	Pre-treatment	Infusion test	Baseline	2.4	11.5	0.39	Unspecified	Unspecified	Unspecified	Unspecified/17.1/unspecified
Lalou et al., 2018 [56]	Treated	83	Pre-treatment	Infusion test	Baseline	2.1	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/14.9/unspecified
	Shunt	56				2.4						Unspecified/16.3/unspecified
	ETV	27				1.5						Unspecified/12.0/unspecified
Eide, 2017 [1]	All	122	Pre-treatment	Monitoring	Overnight	4.7	8.0	0.43	Unspecified	Unspecified	109.9	0.55/9.8/unspecified
				Infusion test	Baseline	3.0	7.7					
	Communicating hydrocephalus	61		Monitoring	Overnight	4.7	8.3	0.44			113.9	0.55/10.1/unspecified
				Infusion test	Baseline	2.9	7.9					
	Noncommunicating hydrocephalus	61		Monitoring	Overnight	4.6	7.7	0.41			106.0	0.56/9.5/unspecified
				Infusion test	Baseline	3.1	7.5					
	VP Shunt	6		Monitoring	Overnight	4.9	8.4	Unspecified			Unspecified	0.53/10.4/unspecified
				Infusion test	Baseline	4.0	8.1					
	ETV or ETV and VP shunt	6		Monitoring	Overnight	4.8	7.7					0.55/9.9/unspecified
				Infusion test	Baseline	3.1	7.4					
	Non-surgical	14		Monitoring	Overnight	3.3	7.2					0.63/6.4/unspecified
				Infusion test	Baseline	2.8	7.2					
	Improved	14		Monitoring	Overnight	5.5	8.7					0.49/10.8/unspecified
				Infusion test	Baseline	3.9	8.1					
	Unimproved	41		Monitoring	Overnight	3.1	6.2					0.71/8.3/unspecified
				Infusion test	Baseline	2.6	6.7					

Table 3 (*continued*)

Authors, Year [Source]	Cohort	Sample size	Stage	ICP measurement information				Morphometric parameters				ICC (ml/mmHg)/R_{out} (mmHg/(ml/min)) /PVI (ml)
				Method	Time and/or duration when measured[1]	Pulse wave amplitude (mmHg)	ICP (mmHg)	Evan's index	Inverse cella media index	Third ventricle index	Ventricular score	
Mahr et al., 2016 [53]	All	68	Pre-treatment	Monitoring	24 to 48 hours	1.9	8.5	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/15.0/unspecified
	VP shunt and/or ETV	33				2.1	9.8					Unspecified/16.0/unspecified
	Untreated	35				1.8	7.2					Unspecified/14.0/unspecified
	Improved	26				2.0	9.7					Unspecified/15.8/unspecified
	Unimproved	7				2.2	10.2					Unspecified/18.0/unspecified
Eide, 2016 [5]	All	82	Pre-treatment	Infusion test	Baseline	5.5	7.6	Unspecified	Unspecified	Unspecified	Unspecified	0.52/unspecified/unspecified
	Shunt or ETV	72				5.7	8.0	0.4*			108*	0.51/unspecified/unspecified
	Non-surgical	10				4.4	5.3	0.4*			99*	0.60/unspecified/unspecified
	Improved	57				6.3	8.1	Unspecified			Unspecified	0.47/unspecified/unspecified
	Unimproved	15				3.5	7.4					0.66/unspecified/unspecified
Czepko and Cieslicki, 2016 [52]	All	27	Pre-treatment	Infusion test	Baseline	Unspecified	6.5	0.38	Unspecified	1.12	Unspecified	Unspecified/7.5/unspecified
			Follow-up				7.3	0.38		1.11		Unspecified/7.5/unspecified
	Idiopathic normal pressure hydrocephalus	15	Pre-treatment				6.7	0.36		1.08		Unspecified/7.3/unspecified
			Follow-up				7.8	0.36		1.08		Unspecified/7.4/unspecified
	Secondary communicating hydrocephalus	12	Pre-treatment				6.1	0.40		1.17		Unspecified/7.8/unspecified
			Follow-up				6.6	0.40		1.14		Unspecified/7.7unspecified
Swallow et al., 2014 [51]	All	18	Pre-treatment	Infusion test	Baseline	1.6	10.6	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/12.2/unspecified
Wikkelsø et al., 2013 [50]	All	115	Pre-treatment	Unspecified	Unspecified	Unspecified	Unspecified	0.42	Unspecified	Unspecified	Unspecified	Unspecified/16.0/unspecified
Andersson et al., 2013 [73]	All	47	Pre-treatment	Infusion test	Baseline	Unspecified	8.3	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/unspecified/16.7
Czosnyka et al., 2011 [46]	All	92	Pre-treatment	Infusion test	Baseline	2.2	9.1	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/16.5/unspecified
Cieslicki and Czepko, 2010 [44]	All	9	Pre-treatment	Bolus injection	Baseline	Unspecified	11.6	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/12.3/unspecified
Andersson et al., 2008 [43]	All	30	Pre-treatment	Infusion test	Baseline	Unspecified	11.7	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/22.3/unspecified
Marmarou et al., 2007 [42]	All	12	Pre-treatment	Infusion test	Baseline	Unspecified	10.8	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/11.2/20.1
	Male	3					6.0					Unspecified/6.0/17.7
	Female	9					12.3					Unspecified/12.9/21.2
	Shunt	7					11.0					Unspecified/13.9/18.7
	Untreated	5					10.4					Unspecified/7.4/22.6
	Improved	4					11.8					Unspecified/19.0/18.3
	Unimproved	8					10.3					Unspecified/7.3/21.4
Kahlon et al., 2005 [41]	All	55	Pre-treatment	Infusion test	Baseline	4.7	11.9	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/20.5/unspecified
	Improved	43				4.9	12.0					Unspecified/20.8/unspecified
	Unimproved	12				4.0	11.6					Unspecified/19.9/unspecified

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Table 3 (*continued*)

Authors, Year [Source]	Cohort	Sample size	Stage	ICP measurement information				Morphometric parameters				ICC (ml/mmHg)/R_{out} (mmHg/(ml/min)) /PVI (ml)
				Method	Time and/or duration when measured[1]	Pulse wave amplitude (mmHg)	ICP (mmHg)	Evan's index	Inverse cella media index	Third ventricle index	Ventricular score	
Juniewicz et al., 2005 [40]	All	27	Pre-treatment	Infusion test	Baseline	Unspecified	11.1	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/12.9/unspecified
	Adult	23					10.9					Unspecified/13.5/unspecified
	Pediatric	2					8.6					Unspecified/7.3/unspecified
	Male	19					11.4					Unspecified/12.9/unspecified
	Female	8					10.2					Unspecified/12.7/unspecified
	Shunt	14					12.6					Unspecified/15.6/unspecified
	Untreated	15					9.4					Unspecified/9.9/unspecified
	Improved	9					13.0					Unspecified/15.4/unspecified
	Unimproved	5					11.9					Unspecified/16.1/unspecified
Sorteberg et al., 2004 [37]	All	17	Pre-treatment	Monitoring Infusion test	24 hours Baseline	Unspecified	8.8 12.3	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/16.6/unspecified
Kasprowicz et al., 2004 [36]	All	50	Pre-treatment	Infusion test	Baseline	Unspecified	10.1	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/16.5/unspecified
	Elevation of ICP	31					9.7					Unspecified/15.9/unspecified
	No elevation of ICP	19					10.7					Unspecified/17.6/unspecified
Eide et al., 2003 [35]	All	16	Pre-treatment	Monitoring	1.8 to 9.7 hours overnight	Unspecified	6.2	0.39	Unspecified	Unspecified	110.8	Unspecified/13.4/Unspecified
	Male	5					5.7	0.39			115.4	Unspecified/11.9/unspecified
	Female	11					6.4	0.39			108.5	Unspecified/14.2/unspecified
Tisell et al., 2002 [34]	All	14	Pre-treatment	Monitoring	20 hours	Unspecified	8.8	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/16.5/unspecified
	Adult	13					9.4					Unspecified/17.2/unspecified
	Pediatric	1					4.2					Unspecified/7.3/unspecified
	Male	10					9.9					Unspecified/18.7/unspecified
	Female	4					6.2					Unspecified/11.0/unspecified
	Improved	9					10.2					Unspecified/18.0/unspecified
	Unimproved	5					6.4					Unspecified/13.9/unspecified
Kahlon et al., 2002 [32]	All	68	Pre-treatment	Infusion test	Baseline	Unspecified	11.0	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/14.0/unspecified
Lundkvist et al., 2001 [31]	All	12	Pre-treatment 3-month follow-up 12-month follow-up	Infusion test	Baseline	Unspecified	16.3 14.3 9.8	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/17.8/unspecified Unspecified/2.2/unspecified Unspecified/2.4/unspecified
Takeuchi et al., 2000 [30]	All	25	Pre-treatment	Monitoring	5-9 hours	Unspecified	8.8	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/21.7/unspecified
Schmidt et al., 2000 [29]	Normal pressure hydrocephalus	9	Pre-treatment	Infusion test	Baseline	Unspecified	11.6	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/9.6/unspecified
Bech et al., 1999 [28]	All	3	Pre-treatment	Infusion test	Baseline	Unspecified	12.2	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/14.8/unspecified
	Hydrocephalus	2					11.8					Unspecified/13.3/unspecified
	Noncommunicating hydrocephalus	1					13.0					Unspecified/23.0/unspecified
	Male	2					11.8					Unspecified/13.3/unspecified
	Female	1					13.0					Unspecified/23.0/unspecified
	VP shunt	2					10.8					Unspecified/21.3/unspecified
	Untreated	1					15.0					Unspecified/7.0/unspecified

Table 3 (*continued*)

Authors, Year [Source]	Cohort	Sample size	Stage	ICP measurement information				Morphometric parameters				ICC (ml/mmHg)/R_{out} (mmHg/(ml/min)) /PVI (ml)
				Method	Time and/or duration when measured[1]	Pulse wave amplitude (mmHg)	ICP (mmHg)	Evan's index	Inverse cella media index	Third ventricle index	Ventricular score	
Boon et al., 1997 [27]	All	101	Pre-treatment	Infusion test	Baseline	Unspecified	11.2	0.39	Unspecified	1.19	Unspecified	Unspecified/17.3/unspecified
Gideon et al., 1994 [26]	All	9	Pre-treatment	Monitoring	24 hours	Unspecified	10.3	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/17.9/unspecified
	Male	5					10.2					Unspecified/16.0/unspecified
	Female	4					10.5					Unspecified/20.3/unspecified
	VP shunt	1					12.0					Unspecified/17.0/unspecified
	Untreated	8					10.1					Unspecified/18.0/unspecified
Shapiro et al. 1993 [25]	All	16	Pre-treatment	Bolus injection	Baseline	5.2	14.3	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/7.8/29.5
Sahuquillo et al., 1991 [3]	All	54	Pre-treatment	Monitoring	24 hours	Unspecified	11.8	0.35	0.29	0.10	98.1	0.68/22.1/14.8
Kosteljanetz et al., 1990 [24]	VP Shunt	13	Pre-treatment	Bolus injection	Baseline	Unspecified	6.6	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/11.3/16.2
	Male	6					6.4					Unspecified/18.6/9.6
	Female	7					6.7					Unspecified/6.5/21.8
	Improved	8					5.1					Unspecified/10.0/18.4
	Unimproved	5					8.9					Unspecified/14.4/12.7
Maksymowicz et al., 1989 [22]	All	12	Pre-treatment	Infusion test	Baseline	Unspecified	8.8	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/12.2/unspecified
			5-20-month follow-up				5.3					Unspecified/7.2/unspecified
	Communicating hydrocephalus	3	Pre-treatment				15.0					Unspecified/14.1/unspecified
			5-20-month follow-up				4.0					Unspecified/8.9/unspecified
	Normal pressure hydrocephalus	9	Pre-treatment				6.7					Unspecified/11.6/unspecified
			5-20-month follow-up				5.9					Unspecified/6.6/unspecified
	Improved	9	Pre-treatment				9.8					Unspecified/12.9/unspecified
			5-20-month follow-up				5.3					Unspecified/7.4/unspecified
	Unimproved	3	Pre-treatment				5.8					Unspecified/10.2/unspecified
			5-20-month follow-up				5.7					Unspecified/6.4/unspecified
	Male	5	Pre-treatment				6.9					Unspecified/8.1/unspecified
			5-20-month follow-up				7.14					Unspecified/6.3/unspecified
	Female	7	Pre-treatment				10.1					Unspecified/15.2/unspecified
			5-20-month follow-up				4.04					Unspecified/7.8/unspecified
Tans and Poortvliet, 1988 [21]	Normal pressure hydrocephalus	30	Pre-treatment	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified	122.9	Unspecified/21.3/15.2
		30	1st follow-up								94.5	Unspecified/unspecified/
		30	2nd follow-up								73.7	unspecified
		21	3rd follow-up								76.3	
		6	4th follow up								60.3	
		2	5th follow-up								45.5	

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Table 3 (*continued*)

Authors, Year [Source]	Cohort	Sample size	Stage	ICP measurement information				Morphometric parameters				ICC (ml/mmHg)/R_{out} (mmHg/(ml/min)) /PVI (ml)
				Method	Time and/or duration when measured[1]	Pulse wave amplitude (mmHg)	ICP (mmHg)	Evan's index	Inverse cella media index	Third ventricle index	Ventricular score	
Thomsen et al., 1986 [20]	All	40	Pre-treatment	Unspecified	Unspecified	Unspecified	Unspecified	0.37	Unspecified	Unspecified	Unspecified	Unspecified/24.2/unspecified
			12-month follow-up					0.30				Unspecified/unspecified/ unspecified
	Male	29	Pre-treatment					0.37				Unspecified/23.1/unspecified
			12-month follow-up					0.30				Unspecified/unspecified/ unspecified
	Female	11	Pre-treatment					0.36				Unspecified/27.0/unspecified
			12-month follow-up					0.30				Unspecified/unspecified/ unspecified
	Improved	16	Pre-treatment					0.39				Unspecified/31.0/unspecified
			12-month follow-up					0.30				Unspecified/unspecified/ unspecified
	Unimproved	24	Pre-treatment					0.36				Unspecified/19.7/unspecified
			12-month follow-up					0.30				Unspecified/unspecified/ unspecified
Shapiro and Fried, 1986 [6]	Shunt functioning	20	Pre-treatment	Bolus injection	Baseline	Unspecified	10.6	Unspecified	Unspecified	Unspecified	Unspecified	0.32/unspecified/18.4
Kosteljanetz, 1986 [19]	All	29	Pre-treatment	Monitoring	Overnight	Unspecified	10.1	0.38	0.30	Unspecified	95.9	Unspecified/11.6/9.5
				Bolus injection	Baseline	4.0	5.1					
	Adult	26		Monitoring	Overnight	Unspecified	10.1	0.37	0.29		93.3	Unspecified/11.6/8.8
				Bolus injection	Baseline	4.1	4.9					
	Pediatric	3		Monitoring	Overnight	Unspecified	9.8	0.47	0.35		118.0	Unspecified/10.3/15.0
				Bolus injection	Baseline	2.8	6.8					
	Male	12		Monitoring	Overnight	Unspecified	10.9	0.42	0.32		106.0	Unspecified/13.2/10.9
				Bolus injection	Baseline	4.4	6.1					
	Female	17		Monitoring	Overnight	Unspecified	9.6	0.35	0.27		88.7	Unspecified/10.6/8.4
				Bolus injection	Baseline	3.7	4.4					
	Shunt	14		Monitoring	Overnight	Unspecified	12.7	0.39	0.31		100.0	Unspecified/17.5/9.5
				Bolus injection	Baseline	4.1	6.0					
	Untreated	15		Monitoring	Overnight	Unspecified	8.1	0.36	0.28		92.0	Unspecified/7.8/11.4
				Bolus injection	Baseline	3.9	4.3					
	Improved	9		Monitoring	Overnight	Unspecified	14.5	0.41	0.33		105.4	Unspecified/21.1/10.9
				Bolus injection	Baseline	3.7	6.7					
	Unimproved	2		Monitoring	Overnight	Unspecified	6.3	0.34	0.27		83.5	Unspecified/11.9/6.3
				Bolus injection	Baseline	3.3	3.9					

Table 3 (*continued*)

Authors, Year [Source]	Cohort	Sample size	Stage	ICP measurement information				Morphometric parameters				ICC (ml/mmHg)/R_{out} (mmHg/(ml/min)) /PVI (ml)
				Method	Time and/or duration when measured[1]	Pulse wave amplitude (mmHg)	ICP (mmHg)	Evan's index	Inverse cella media index	Third ventricle index	Ventricular score	
Fried and Shapiro, 1986 [71]	All	18	Pre-treatment	Bolus injection	Baseline	Unspecified	17.5	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/unspecified/35.5
Shapiro et al., 1985 [17]	All	16	Pre-treatment	Bolus injection	Baseline	Unspecified	11.7	Unspecified	Unspecified	Unspecified	Unspecified	Unspecified/7.2/28.1
Tans and Poortvliet, 1984 [16]	All	26	Pre-treatment	Unspecified	Unspecified	Unspecified	Unspecified	0.46	Unspecified	Unspecified	Unspecified	Unspecified/11.1/13.6
Børgesen, 1984 [2]	All	80	Pre-treatment	Unspecified	Unspecified	Unspecified	Unspecified	0.37	Unspecified	Unspecified	Unspecified	0.53/19.6/unspecified
	Male	52						0.37				0.61/20.5/unspecified
	Female	28						0.37				0.47/17.9/unspecified
	VA shunt	54						0.37				0.50/23.0/unspecified
	Untreated	16						0.37				0.69/6.1/unspecified
	Improved	37						0.38				0.45/27.4/unspecified
	Unimproved	27						0.35				0.56/15.2/unspecified
	VA shunt	19	3-month follow-up					0.35				Unspecified/unspecified/unspecified
	Improved	9						0.35				
	Unimproved	10						0.36				
	VA shunt	15	12-month follow-up					0.36				
	Improved	8						0.34				
	Unimproved	7						0.37				

*Represents a median value rather than a mean.
[1]Lists the time at which the measurement was taken, for example at baseline during an infusion test, and/or the duration over which it was recorded.

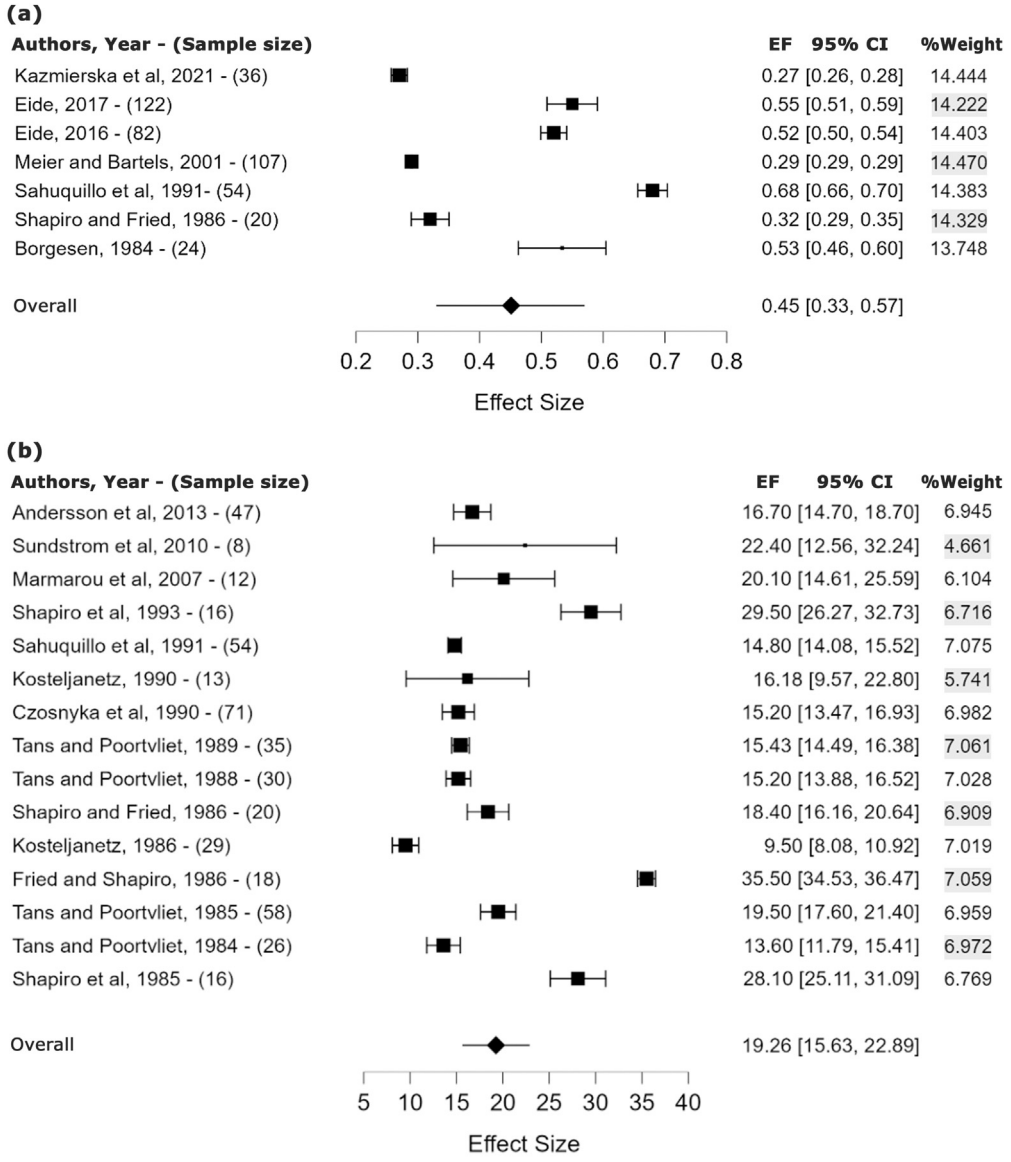

Fig. 2. Forest plots showing the overall pre-treatment ICC (a) and overall pre-treatment PVI (b). The units of ICC and PVI values are ml/mmHg and ml, respectively. ES: effect size; CI: confidence interval; ICC: Intracranial compliance; PVI: Pressure-volume index.

3.3. *Effectiveness of R_{out}*

Data pooled from 48 studies as shown in Fig. 3 displayed that the overall pre-treatment R_{out} was 14.93 mmHg/(ml/min) (95% CI, 13.65-16.21; I^2= 99.7%; P<0.001). We defined subgroups of adults (15.37; 95% CI, 14.07-16.66; I^2= 99.7%; P<0.001) and pediatrics (8.91; 95% CI, 6.38-11.44; I^2= 53.5%; P=0.001), as well as male (11.22; 95% CI, 7.65-14.79; I^2= 85.7%; P<0.001) and female (13.91; 95% CI, 11.11-16.72; I^2= 83.4%; P<0.001) (Table 4). We defined a subgroup based on the type of hydrocephalus. The pooled R_{out} values in communicating and NPH patients were 12.46 (95% CI, 10.25-14.68; I^2= 76.7%; P<0.001) and 16.23 (95% CI, 14.67-17.78; I^2= 99.8%; P<0.001) (Table 4). We also calculated pooled R_{out} results in patients with unimproved (13.18; 95% CI, 10.98-15.39; I^2= 98.9%; P<0.001) and improved (17.63; 95% CI, 14.68-20.58; I^2= 96.6%; P<0.001) outcomes. Except for pediatric hydrocephalus patients (I^2= 53.5%), there was considerable heterogeneity for other pooled R_{out} values. The correlations between R_{out} and ICP characteristics, as well as morphometric parameters, were studied using meta-regression analysis. There were significant correlations between R_{out} and all ICP characteristics (all P<0.001). Among morphometric parameters, the correlation between R_{out} and the third ventricle index (P<0.001) was significant.

3.4. *Effectiveness of PVI*

The pooled data from 15 studies showed that the overall pre-treatment PVI value was 19.26 ml (95% CI, 15.63-22.89; I^2=98.7%; P<0.001) (Fig. 2b). The pooled PVI value for adults and pediatrics hydrocephalus were 14.68 (95% CI, 12.61-16.75; I^2=93.4%; P<0.001) and 24.45 (95% CI, 18.04-30.86; I^2=97.7%; P<0.001) (Table 4). We defined another subgroup for males 11.85 (95% CI, 8.07-15.63; I^2=70.6%; P<0.001) and females (16.30; 95% CI, 7.06-25.55; I^2= 88.0%; P<0.001) (Table 4). The pooled PVI value in patients with NPH was 15.06 (95% CI, 14.53-15.60; I^2= 17.2%; P<0.001). The pooled PVI values for patients with unimproved and improved outcomes were 13.74 (95% CI, 6.71-20.77; I^2=97.4%; P<0.001) and 10.64 (95% CI, 9.80-11.48; I^2= 0.0; P<0.001) (Table 4). A meta-regression was performed to evaluate the correlation between PVI and ICP characteristics, as well as morphometric parameters. The correlations between PVI and the baseline ICP (P<0.001), as well as the monitoring ICP (P<0.001), were significant. However, there was

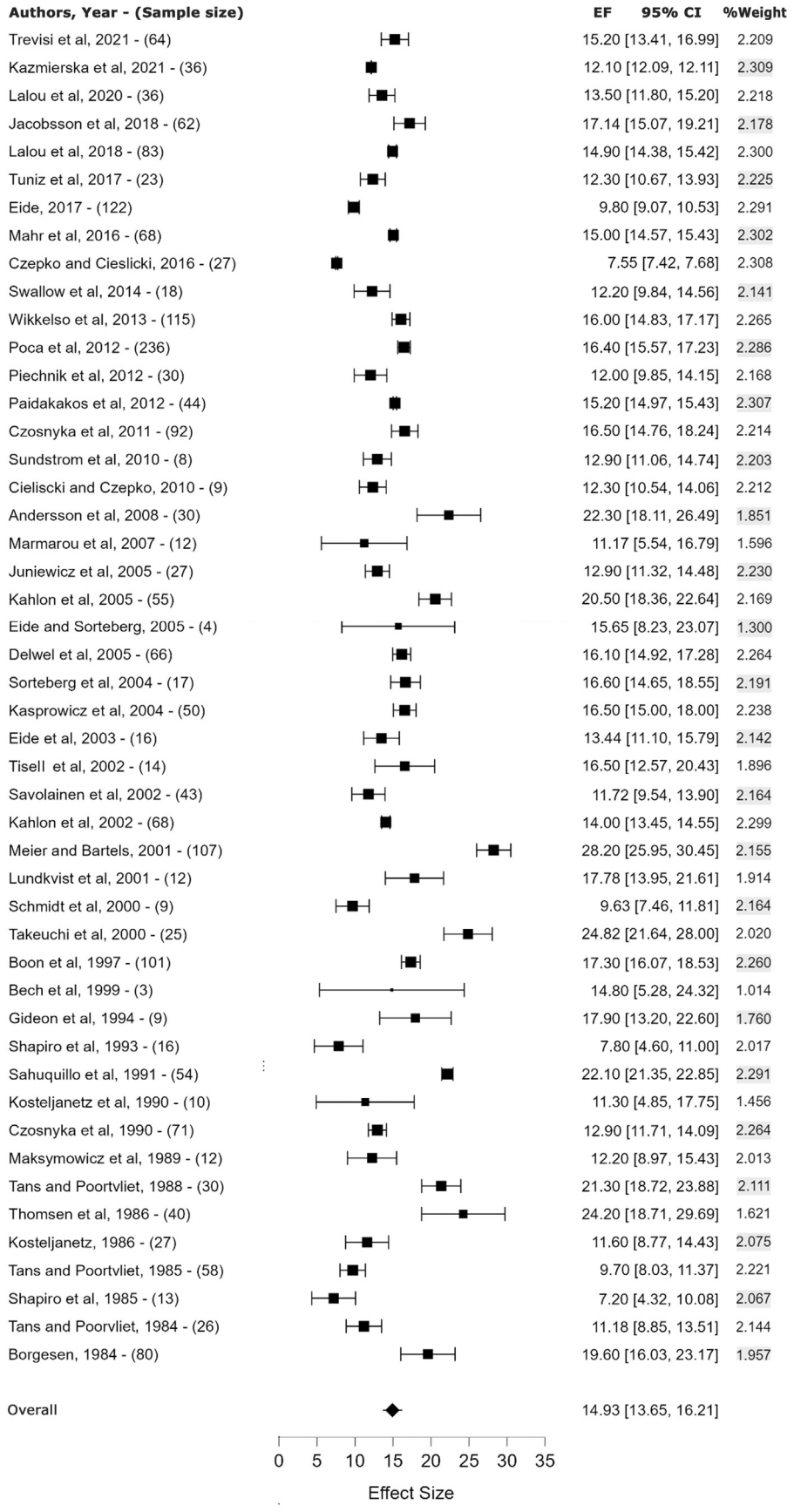

Fig. 3. Forest plot showing the overall pre-treatment R_{out}. The unit of R_{out} value is mmHg/(ml/min). ES: effect size; CI: confidence interval; R_{out}: resistance to CSF-outflow.

Table 4
Subgroup analysis of the effect sizes of ICC, R_{out}, and PVI. The empty cells correspond to subgroups where the number of available studies for calculating ICC or R_{out} or PVI was not more than two. ICC: Intracranial compliance, PVI: pressure-volume index, R_{out}: resistance to cerebrospinal outflow, NPH: Normal pressure hydrocephalus.

Subgroup		ICC (ml/mmHg)	R_{out} (mmHg/(ml/min))	PVI (ml)
Age	Adult	0.49 (95% CI, 0.35-0.62; I^2=99.8%; P<0.001)	15.37 (95% CI, 14.07-16.66; I^2= 99.7%; P<0.001)	14.68 (95% CI, 12.61-16.75; I^2=93.4%; P<0.001)
	Pediatric	–	8.91 (95% CI, 6.38-11.44; I^2= 53.5%; P=0.001)	24.45 (95% CI, 18.04-30.86; I^2=97.7%; P<0.001)
Gender	Male	–	11.22 (95% CI, 7.65-14.79; I^2= 85.7%; P<0.001)	11.85 (95% CI, 8.07-15.63; I^2=70.6%; P<0.001)
	Female	–	13.91 (95% CI, 11.11-16.72; I^2= 83.4%; P<0.001)*	16.30 (95% CI, 7.06-25.55; I^2= 88.0%; P<0.001)*
Type of hydrocephalus	Non-communicating	–	–	–
	Communicating	–	12.46 (95% CI, 10.25-14.68; I^2= 76.7%; P<0.001)	–
	NPH	0.44 (95% CI, 0.25-0.64; I^2=99.9%; P<0.001)	16.23 (95% CI, 14.67-17.78; I^2= 99.8%; P<0.001)	15.06 (95% CI, 14.53-15.60; I^2= 17.2%; P<0.001)*
Outcomes	Improved	–	17.63 (95% CI, 14.68-20.58; I^2= 96.6%; P<0.001)*	10.64 (95% CI, 9.80-11.48; I^2= 0.0; P<0.001)*
	Unimproved	–	13.18 (95% CI, 10.98-15.39; I^2= 98.9%; P<0.001)	13.74 (95% CI, 6.71-20.77; I^2=97.4%; P<0.001)*
Pre-treatment		0.45 (95% CI, 0.33-0.57; I^2=99.7%; P<0.001)	14.93 (95% CI, 13.65-16.21; I^2= 99.7%; P<0.001)	19.26 (95% CI, 15.63-22.89; I^2=98.7%; P<0.001)

*It is important to consider the potential impact of publication bias on this finding.

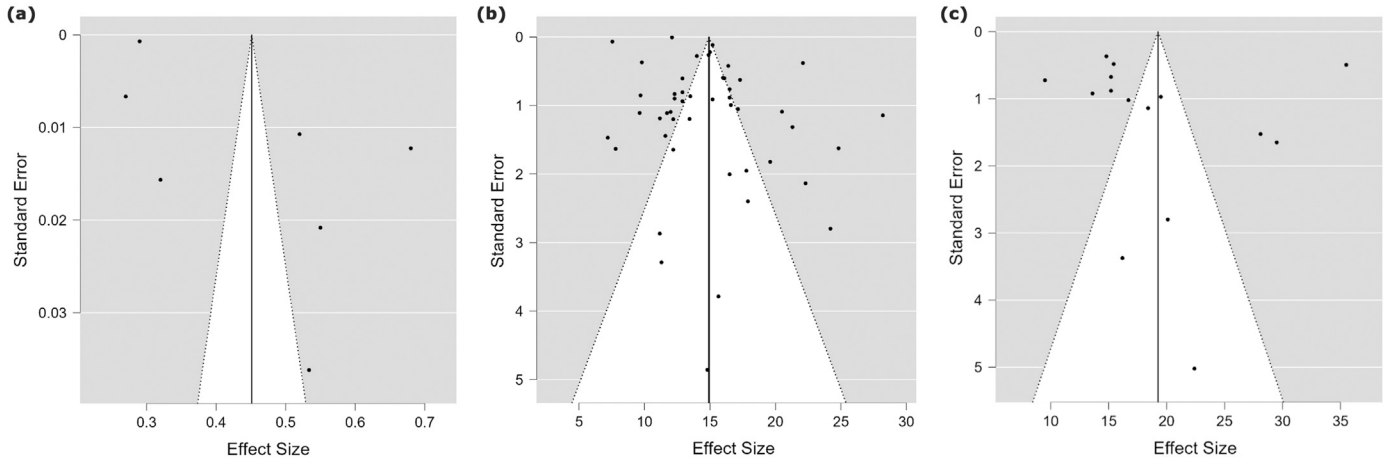

Fig. 4. (a), (b), and (c) show the Funnel plots of the meta-analysis of included papers for ICC, R_{out}, and PVI, respectively. The white triangles reflect the area where 95% of included studies were expected to lie in the absence of a publication bias. The vertical line reflects the overall effect size. ICC: Intracranial compliance; PVI: Pressure-volume index; R_{out}: resistance to CSF-outflow.

no significant correlation between PVI and the PWA of baseline ICP (P=0.073). The correlations of PVI with three morphometric parameters were significant: Evan's ratio (P=0.014), inverse cella media index (P=0.006), and the ventricular score (P<0.001).

3.5. Publication bias

Funnel plot asymmetry tests yielded P-values of 0.23, 0.30, and 0.60 for pre-treatment ICC, R_{out}, and PVI values, respectively (Fig. 4). Hence, there was no evidence for publication bias to study pre-treatment ICC, R_{out}, and PVI values. Trim and fill analysis showed no imputed studies for overall pre-treatment values of all three indicators.

4. Discussion

The present study aggregated the data of previous human hydrocephalus studies related to ICC, R_{out}, and PVI systematically to find the changes in these indicators based on gender, age, type of hydrocephalus, and patient outcomes. We evaluated the correlation between these three indicators and ICP characteristics, as well as morphometric parameters. It should be noted that conceptually, the sources of both ICC and PVI are CSF volume and ICP, and they measure the same physical mechanism of pressure-volume compensation using two different mathematical methods. Previous studies showed that changes in ICC did not necessarily have the same direction as changes in PVI [24,94], hence, we considered the evaluation of both parameters necessary. Among ICC, R_{out}, and PVI indicators, R_{out} was the parameter that was assessed most frequently, however, ICC or its inverse (elastance) is a more common and practical indicator for neurosurgeons for the clinical evaluation of hydrocephalus patients [5,93,95,96]. The results revealed that the pooled R_{out} value was observed to be significantly higher in adult hydrocephalus compared to pediatric hydrocephalus. Patients with NPH exhibited a higher pooled R_{out} value compared to patients with communicating hydrocephalus. The results also showed that patients with unimproved clinical outcomes exhibited a decrease in the effect size of the pooled R_{out}. On the other hand, the effect size of the pooled PVI was much higher in pediatric hydrocephalus compared to adults. Notably, the results demonstrated

a considerable decrease in the effect size of the pooled PVI in male patients.

Previous studies showed some evidence of the correlation between R_{out} and ICP, and their impacts on shunt dysfunction [27,32,38,47,73,97,98]. Other studies showed that in contrast to elastance (1/ICC) [95], there is not a significant correlation between ICC and ICP [22,99]. Gholampour et al. analyzed pressure-volume response over an extended period of time after shunting and reported the long-term ICC in hydrocephalus patients [93,100]. Their results also showed that the correlation between long-term ICC and ICP was not significant. Some studies evaluated the impact of changes in the PWA of ICP on pressure-volume parameters and cerebral blood flow [22,26,99,101–111]. The results of our pooled data showed significant correlations between all ICP characteristics and both ICC and R_{out}. However, there was no significant correlation between PVI and PWA of baseline ICP. In addition, significant correlations were observed between PVI and both the baseline and monitoring ICP.

Despite the importance of morphometric parameters [112,113], limited studies assessed the correlation between morphometric parameters and pressure-volume parameters in hydrocephalus patients. Sahuquillo et al. showed that the correlation between R_{out} and various morphometric parameters was not significant in active hydrocephalus patients [24]. However, this correlation in compensated hydrocephalus was significant [24]. Kosteljanetz et al. also showed that there was a significant correlation between the PVI and Evan's ratio [32]. The results of our pooled data showed that the correlations between ICC and the ventricular score, and between R_{out} and the third ventricle index were found to be significant. Furthermore, PVI showed significant correlations with Evan's ratio, inverse cella media index, and ventricular score.

The subgroup analysis showed that there was publication bias for R_{out} values for female hydrocephalus and patients with improved outcomes (Table 4). This bias was also observed in PVI values for female hydrocephalus, NPH patients, and patients with improved and unimproved outcomes. The quality scores of the included studies were higher than 7 and the consistency between studies was in the acceptable range (Supplementary Table S3). This can advocate the validity of the results. On the other hand, there was not a paucity of published papers, i.e. for R_{out} values in female hydrocephalus (11 studies) and patients with improved outcomes (17 studies). We used a random-effect model with size-based weightings and for example, the R_{out} value in female hydrocephalus was distributed at the top of the Funnel plot. This also confirms that the sample size of included data was enough. It can be deduced that the reason for publication bias in some subgroups may be related to methodological heterogeneity in the measurements. In this case, the techniques of clinical measurements such as CSF infusion and bolus injection and the locations of infusions (lumbar, ventricular, or lumbo-ventricular) in the measurement of ICC, R_{out}, and PVI must be taken into account.

The result of invasive measurement methods proved that an exponential function governed the trend of volume change with respect to pressure [10,114]. Non-invasive calculation of pressure-volume response using computer simulation to calculate ICC, R_{out}, and PVI was suggested by Alperin et al. [7,95], and developed and optimized by Gholampour et al. [9,100]. Their results also confirmed that an exponential function governed the pressure-volume curve. However, Okon et al. showed non-uniformities in the pressure-volume curve and revealed that this trend is not necessarily exponential [105]. They used a method based on passive drainage of CSF to reduce the ICP and measure pressure-volume response. The basis of CSF infusion and bolus injection methods to measure pressure-volume parameters is the injection of an external excess fluid in the intracranial system. Okon et al. believed that methods based on the injection of excess fluid would be inappropriate in the presence of increased ICP [105]. Smielewski et al. also showed that the possible vasomotor response and error in pressure reading was due to constant infusion, constant pressure infusion, bolus manipulation, and lumbar ventricular perfusion [115]. Gholampour et al. also revealed that brain tissue needs at least two months (a long period of time) to show the effects of its viscous component during the measurement of pressure-volume response [93,100]. While pressure-volume parameters in previous methods based on CSF infusion, bolus injection, and previous computer simulation methods were measured over a short period of time: less than one hour for invasive methods and less than one minute for simulation methods. Therefore, the measurement of the pressure-volume response in hydrocephalus patients using these methods can be controversial. This could be a reason why, in contrast to the monitoring of ICP, the monitoring of pressure-volume parameters (specifically ICC) has not yet fully transitioned into standard clinical care [116]. This motivates researchers to study the effects of various boundary conditions in computer simulation methods [17,117], different invasive methods (bolus injection or CSF infusion), and the different locations of infusion (lumbar, ventricular, or lumbo-ventricular) in invasive methods on the values of ICC, R_{out}, and PVI to find the optimal measurement method and condition. However, we did not evaluate these variables in the present study due to the insufficient number of published papers available for each method or each location of infusion.

4.1. Strengths, limitations, and future prospects

Despite the practical importance of pressure-volume parameters in the clinical evaluation of hydrocephalus patients, there was no systematic review of the values of pressure-volume parameters in previous studies. This is the first systematic review for a comprehensive quantitative evaluation of the changes in ICC, R_{out}, and PVI values in hydrocephalus patients under different conditions. Other studies also evaluated the relationship between pressure-volume response with changes in blood pressure and volume changes of vessels [28,114]. However, the present study only focused on pressure and volume changes in CSF. We did not also evaluate the correlation between pressure-volume parameters and changes in clinical signs/symptoms of hydrocephalus patients, which maybe valuable for future studies. Tisell et al. measured the changes in elastance (the inverse of ICC) and R_{out} in hydrocephalus patients using the CSF infusion method immediately after surgery and three months after surgery [47]. They showed oscillations and non-uniformities in changes in elastance (1/ICC) and R_{out} after three months. Our recent study also showed oscillatory changes in pressure-volume curves in hydrocephalus patients over 12 months after shunting [93,100]. It is suggested that future studies clarify the relationship of long-term ICC, R_{out}, and PVI changes with effective parameters in hydrocephalic conditions such as ICP characteristics and morphometric parameters. Previous studies showed that alterations in brain compliance may thus facilitate secondary ventricular enlargement even without a primary defect in CSF circulation such as aqueductal stenosis or ciliary dysmotility [118–120]. Some human hydrocephalus studies also suggested alterations in brain biomechanics influencing ICC, R_{out}, and PVI amongst other physiological parameters [8,30]. Hence, future studies can further elaborate on how alterations in parenchyma biomechanics may affect ICC, PVI, R_{out}.

5. Conclusion

We aggregated the data of all previous human hydrocephalic studies about ICC, R_{out}, and PVI systematically. The study showed that PVI values were lower in adult hydrocephalus and male hydrocephalus. Patients with NPH exhibited higher R_{out} values com-

pared to communicating hydrocephalus and patients with unimproved outcomes demonstrated a decrease in R_{out}. The results of the present study found significant correlations between all ICP characteristics and both ICC and R_{out}. Significant correlations were also observed between ICC and the ventricular score, and between R_{out} and the third ventricle index. Furthermore, PVI showed significant correlations with Evan's ratio, inverse cella media index, and ventricular score. Our study provides valuable insights into the relationship between ICC, R_{out}, and PVI with ICP characteristics and morphometric parameters, which could be useful for future research and clinical evaluation of hydrocephalus patients. These results could help neurosurgeons better understand complexities in the biomechanics of the hydrocephalic brain and the role of ICC, R_{out}, and PVI in the diagnosis, pathogenesis, and treatment of hydrocephalus patients.

Abbreviations

ICC: Intracranial compliance; CSF: Cerebrospinal fluid; ICP: Intracranial pressure; R_{out}: Resistance to CSF-outflow; PVI: Pressure-volume index; PWA: Pulse wave amplitude, PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; GRADE: Grades of Recommendation, Assessment, Development, and Evaluation; NPH: Normal pressure hydrocephalus; LP: Lumbar puncture; ETV: Endoscopic third ventriculostomy; CI: Confidence interval.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s).

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Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

CRediT authorship contribution statement

SG (Seifollah Gholampour) contributed to the Conceptualization, Design of study, Study selection, Data extraction, Formal analysis, Investigation, Supervised data collection and Analyses, Software, Project administration, and Writing the manuscript. AN (Amber Nguyen) contributed to the Study selection, Data extraction, and Software. SC (Saad Chaudry) contributed to the Study selection, Data extraction, and Software. All authors approved the final manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial or personal relationships that could be viewed as influencing the work reported in this paper.

Code availability

All tools used for the analysis are publicly available and fully described in the 'Methods' sections.

Data availability

All data used in this manuscript are publicly available and can be found in original publications or repositories.

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Appendix A. Supplementary material

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.irbm.2023.100785.

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