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CLINICAL INVESTIGATIVE STUDY

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Accuracy of bedside bidimensional transcranial ultrasound versus tomodensitometric measurement of the third ventricle

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Abstract

Background and Purpose: To evaluate the accuracy of transcranial duplex sonography (TCS) for measuring the diameter of the third ventricle (DTV) and the brain midline shift (MLS), as compared to cerebral CT.

Methods: Single-center retrospective study including 177 patients admitted to the neurological intensive care unit (NICU). We studied the correlation between TCS and CT measurements of DTV and MLS using a Bland-Altman analysis. The best threshold of DTV to diagnose acute hydrocephalus was evaluated with a receiver operating characteristic (ROC) analysis.

Results: We analyzed 177 pairs of CT-TCS measurements for DTV and 165 for MLS. The mean time interval between CT and TCS was 87 ± 73 minutes. Median DTV measurement on CT was 4 ± 3 mm, and 5 ± 3 mm by TCS. Median MLS on CT was 2 ± 3 mm, and 2 ± 4 mm by TCS. The Pearson correlation coefficient (r^2) was .96 between TCS and CT measurements ($p < .001$). The Bland-Altman analysis found a proportional bias of 0.69 mm for the DTV with a limit of agreement ranging between –3.04 and 2.53 mm. For the MLS, the proportional bias was 0.23 mm with limits of agreements between –3.5 and 3.95. The area under the ROC curve was .97 for the detection of hydrocephalus by DTV on TCS, with a best threshold of 5.72 mm (Sensitivity [Se] = 92% Specificity [Sp] = 92.1%).

Conclusions: TCS seems to be a reliable and accurate bedside technique for measuring both DTV and MLS, which might allow detection of acute hydrocephalus among NICU patients.

KEYWORDS
brain midline shift, hydrocephalus, transcranial duplex sonography

INTRODUCTION

Acute hydrocephalus, by inducing an elevation of intracranial pressure (ICP), is a frequent and serious complication of many neurological pathologies as well as postoperative intracranial neurosurgery.[1] The increase in the diameter of the third ventricle (DTV) is classically used to assess hydrocephalus on cerebral CT.[1] False negative CT examination, diagnosis and treatment delay due to unavailability of CT, life-threatening complications during the transportation of potentially unstable critically ill patients, and radio-ionization are commonly identified CT drawbacks.[2–4] Conversely, transcranial duplex sonography (TCS) is immediately available at the bedside without side effect. TCS could reduce the delay of acute hydrocephalus diagnosis and also limit CT complications by precluding unnecessary exams.[3,5,6]

The main objective of this study was to evaluate the correlation between TCS and cerebral CT to measure the DTV in a sample of neurological intensive care unit (NICU) patients. In addition, we aimed at assessing the accuracy of TCS measurement of brain midline shift (MLS) compared to cerebral CT.

METHODS

We carried out a monocentric retrospective observational study in a 30-beds NICU of a French Academic Hospital (Hôpital Pierre Wertheimer of Bron) where TCS is a standard care for adequate neuromonitoring, in agreement with the recommendations for screening the secondary effects of intracranial hypertension on cerebral hemodynamics.[6,7] Patients were included between December 2013 and May 2014. The herein study was approved by the local ethics committee (No. 18-04).

Patients who required a cerebral CT, and for whom a TCS examination had been performed within 4 hours before or after that CT, were included.

The exclusion criteria were as follows: patients under 18 years old, spinal pathology, peripheral surgery, no TCS measurement, inadequate temporal acoustic window, or a delay of over 4 hours between TCS and CT.

Demographic (sex, age, clinical context), TCS, and CT data were retrospectively collected from patients' medical records. With regard to TCS measurements, when the transcranial window was only found on one side (because of surgical staples or anatomical reasons), no MLS measurement was possible. However, we chose to keep the DTV measurement from one side only for those patients.

Ultrasound measures of DTV and MLS

For TCS examination, two color-coded phased-array ultrasound systems (Vivid S6, GE Healthcare, Chicago, IL, USA; and CX50, PHILIPS Healthcare, Amsterdam, The Netherlands) were employed with a low-frequency transducer (1-5 MHz) that allowed both brain structures and intraarterial blood flow velocities analysis. For the transcranial modality, the spatial resolutions of the probe were between 1.5 and 2.5 mm. The mechanical and thermal indexes were set around 1.

TCS was carried out bilaterally by two expert physicians (either a senior intensivist [SG] or a trained resident [PL]), according to a predefined protocol: By adjusting the orientation and the angulation of the probe, three anatomic planes could be obtained through the transtemporal window. TCS examination began with a baseline slice, called "mesencephalic view" (Figure 1), to visualize the cerebral peduncles at the upper part of the midbrain (butterfly-shaped brainstem). By the same way, a cerebral blood flow evaluation insonating the mean cerebral artery was provided. Then with a 10-15° cephalic tilting of the ultrasound probe, the "diencephalic view" (Figure 2) was obtained to visualize the pineal gland as the main posterior hyperechoic structure (for adults) and the hypoechoic thalami and the lateral walls of the third cerebral ventricle (TV) as a linear double hyperechoic reflex. This incidence was used to perform DTV and MLS measurements. The DTV was measured on the maximum diameter of the TV (edge-to-edge external measure). Each DTV value was then averaged with the contralateral measure, when available.

For MLS calculation, we measured the largest distance so-called A, from the internal temporal bone table to the midline of the TV. On the other side, the lowest (contralesional) B distance was determined by the same method, and the mean value of the MLS was then calculated according to the formula (A – B)/2.[8]

CT scan measurements

DTV and MLS were retrospectively and blindly measured by PL or SG under the supervision of senior radiologists during retrospective data collection. DTV was calculated from the width between the hyperdense margins of the TV. The distance between the theorical midline and the septum pellucidum was used to measure the MLS.[9]

In order to evaluate TCS diagnostic performance to diagnose hydrocephalus or midline shift, CT measurements were chosen as the reference standard: a measurement of an MLS or a DTV > 5 mm was considered pathological. Indeed, a TV < 5 mm was considered normal by Seidel et al. in a series of healthy volunteers under 60 years old.[10] Moreover, A MLS > 5 mm is associated with an impairment of the neurological outcome in traumatology,[11] but also in cases of ischemic or hemorrhagic vascular disease.[12,13]

Statistical analysis

Measurements made on the CT and TCS images were compared using nonparametric Wilcoxon test, and the extent of correlation between the data was analyzed. The correlation between CT and TCS measurements of DTV and MLS was analyzed by the Pearson correlation test. We then compared the TCS and CT measures using the Bland-Altman statistical method to determine the proportional bias and the limits of agreement.[14,15] The accuracy of TCS measurements was illustrated by

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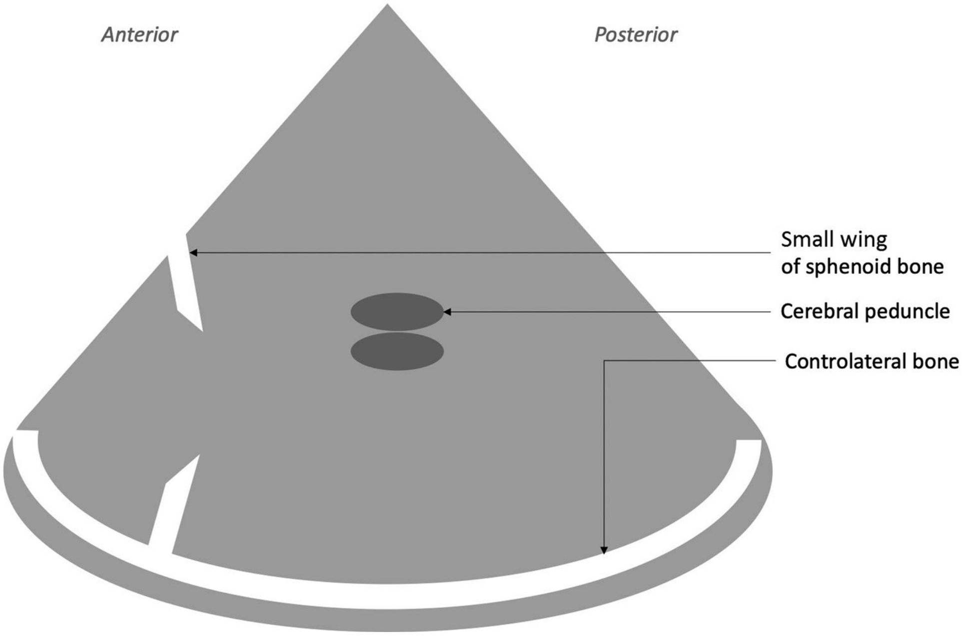

FIGURE 1 Mesencephalic view

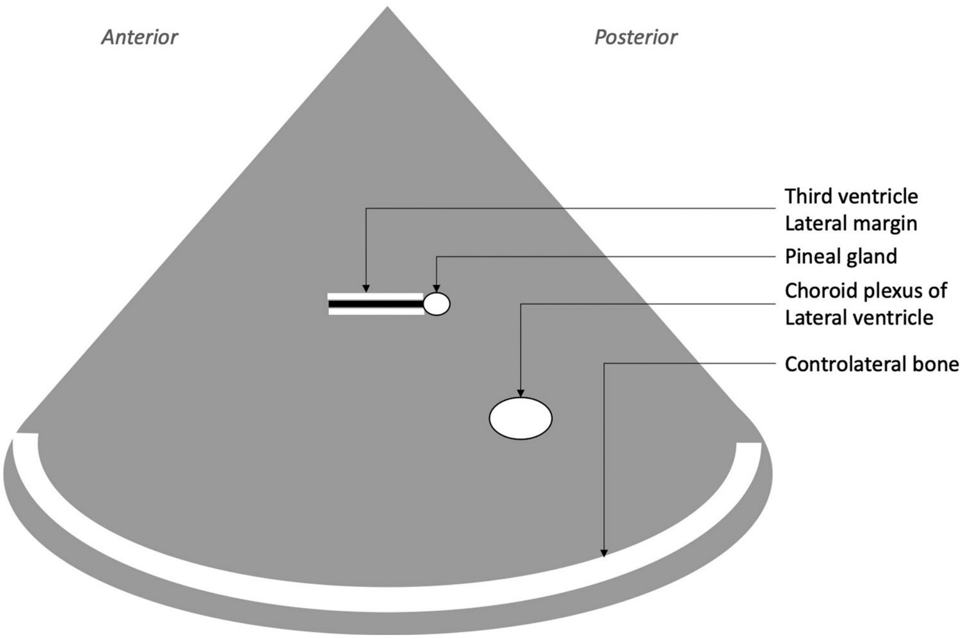

FIGURE 2 Diencephalic view

means of a Bland-Altman diagram. The diagnostic performance of the TCS for the detection of hydrocephalus (defined as TV > 5 mm dilation on CT or an MDS > 5 mm) was tested by constructing a receiver operating characteristics (ROC) curve and calculating the area under the curve (AUC). The best threshold was chosen according to the upper top left point on the ROC curve.

Fisher's exact test was used for univariable comparisons of categorical variables.

The results were expressed in mean ± standard deviation or median ± interquartile range of the median. The median absolute deviation is a variation of the average absolute deviation that is even less affected by outlying values because these values have less influence on the calculation of the median than they do on the mean. In general, for data with extreme values, the median absolute deviation or interquartile range can provide a more stable estimate or variability than the standard deviation.

A probability values <.05 was taken as statistically significant. All statistical analyzes were performed using the StatView® software for Windows (Abacus® Concepts Inc., Berkeley, CA, USA, 1996, version 4.57).

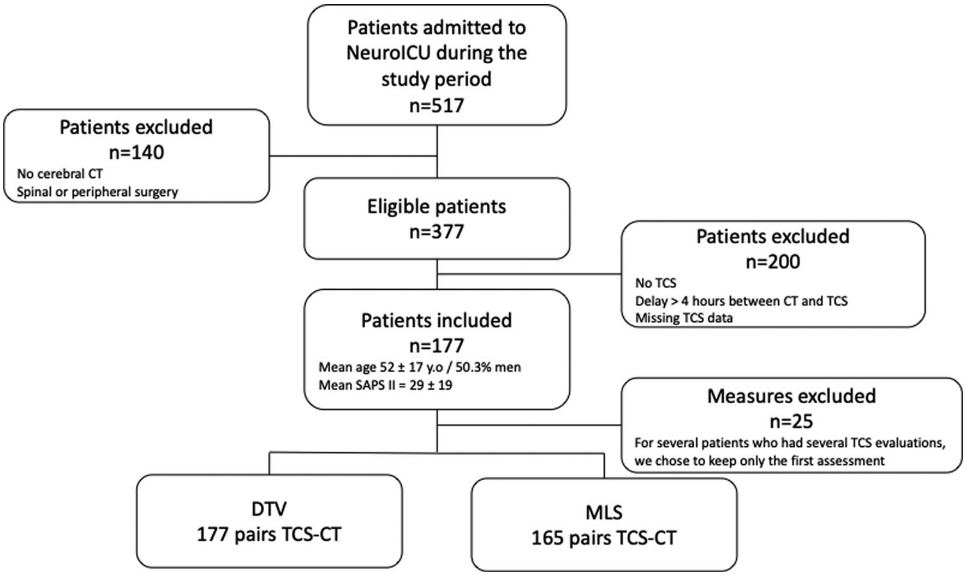

FIGURE 3 Flow chart of the study. n = number; SAPS III = New simplified acute physiology score; y.o = years old

The herein manuscript was written in accordance with the guidelines Strengthening the Reporting of Observational Studies in Epidemiology.[16]

RESULTS

Among the 517 patients admitted to our NICU between December 2013 and May 2014, 377 patients were eligible for the study. Most of these patients were admitted in emergency for acute traumatic, hemorrhagic, or ischemic conditions (52% in total), but also some of them were admitted postoperatively after intracranial neurosurgery (41.3%).

One hundred and seventy-seven patients were included, with a mean age of 52 ± 17 years; 50.3% were men, and average new simplified acute physiology score (SAPS II) was 29 ± 19 (Figure 3).

The reasons for admission are summarized in Table 1. Sixty-three patients only received medical therapy, 18 were assessed before surgery or external ventricular drainage, and 122 after surgery or external ventricular drainage.

The mean time interval between CT and TCS was 88 ± 74 minutes. Twenty-two patients had more than one (maximum 3) TCS assessment, but we chose to keep only one TCS assessment per patient (the first one) and to exclude additional measurements in order to limit statistical bias.

DTV results

One hundred and seventy-seven pairs of DTV measurements by TCS and cerebral CT were analyzed.

DTV measured by CT ranged from 0 to 20 mm (median 4 ± 3 mm). DTV measured by TCS ranged from 0 to 21 mm (median 5 ± 3 mm).

Regarding the comparison of DTV measurements, the main criterion of our study, the Pearson correlation coefficient (r^2) was .96 ($p < .001$; Figure 4). The Bland-Altman method revealed a proportional bias of 0.69 mm (95% confidence interval [CI]: 0.56-0.81, $p < .001$), with limits of agreement ranging from −3.04 to 2.53 (10 measures [4.9%] out of range; Figure 5).

For the diagnosis of hydrocephalus (ie, an enlargement of DTV > 5 mm) by TCS, the AUC was .97 (95% CI: .94-1); and for a threshold of 5.47 mm, the sensitivity was 92% (95% CI: 83.2%-96.5%) and the specificity was 92.1% (95% CI: 85.9%-95.8%), with a positive likelihood ratio of 11.68 (Figure 6).

MLS results

One hundred and sixty-five pairs of MLS measurements by TCS and cerebral CT were analyzed.

MLS measured by CT ranged from 0 to 22 mm (median 2 ± 4 mm). MLS measured by TCS ranged from 0 to 18 mm (median 2 ± 3 mm).

For MLS, the Pearson correlation coefficient (r^2) was .74 ($p < .001$; Figure 7). The statistical comparison by the Bland-Altman method showed a bias of 0.23 mm (95% CI: −0.04 to 0.49, $p = .003$). The limits of agreement were between −3.5 and 3.95 (12 measures [or 6.3%] out of range; Figure 8).

The sensitivity of the TCS to detect an MLS > 5 mm was studied by performing an ROC curve. AUC was .94 (95% CI: .88-1). Thus, for an optimal threshold of MLS of 5.10 mm, the sensitivity of the TCS was 89.2% (95% CI: 74.5%-96.2%) and the specificity was 92.8% (95% CI: 87.3%-96%), with a positive likelihood ratio of 12.32 (Figure 9).

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TABLE 1 Baseline demographic and clinical data

Characteristics	Total	Hydrocephalus $n = 62$	Nonhydrocephalus $n = 115$	Midline shift $n = 37$	No midline shift $n = 140$
Age, years	52 ± 17	58 ± 11	51 ± 12	56 ± 15	51 ± 17
Gender, female	49.7%	56.5%	43.5%	48.6%	50%
SAPS II score on admission	29 ± 19	32 ± 18	27 ± 19	31.9 ± 19	28.2 ± 19
Reasons for admission					
Intracranial tumor	74 (41.8%)	22 (35.5%)	52 (45.2%)	19 (51.4%)	55 (39.3%)
Subarachnoid hemorrhage	40 (22.6%)	25 (40.3%)	15 (13.0%)	4 (10.8%)	36 (25.7%)
Severe traumatic brain injury	30 (16.9%)	2 (3.2%)	28 (24.3%)	7 (18.9%)	23 (16.4%)
Acute hemorrhagic stroke	13 (7.3%)	4 (6.5%)	9 (7.8%)	5 (13.5%)	8 (5.7%)
Acute ischemic stroke	8 (4.5%)	5 (8.1%)	3 (2.6%)	1 (2.7%)	7 (5%)
Intracranial infection	3 (1.7%)	1 (1.6%)	2 (1.7%)	0 (0%)	3 (2.1%)
Others[a]	9 (5.1%)	3 (4.8%)	6 (5.2%)	1 (2.7%)	8 (5.7%)

Note: Data are presented as number (*n*) (%) or mean ± standard deviation.
Abbreviation: SAPS II, New simplified acute physiology score.
[a]Status epilepticus, epilepsy surgery, surgery for chronic hydrocephalus, microvascular decompression for trigeminal neuralgia.

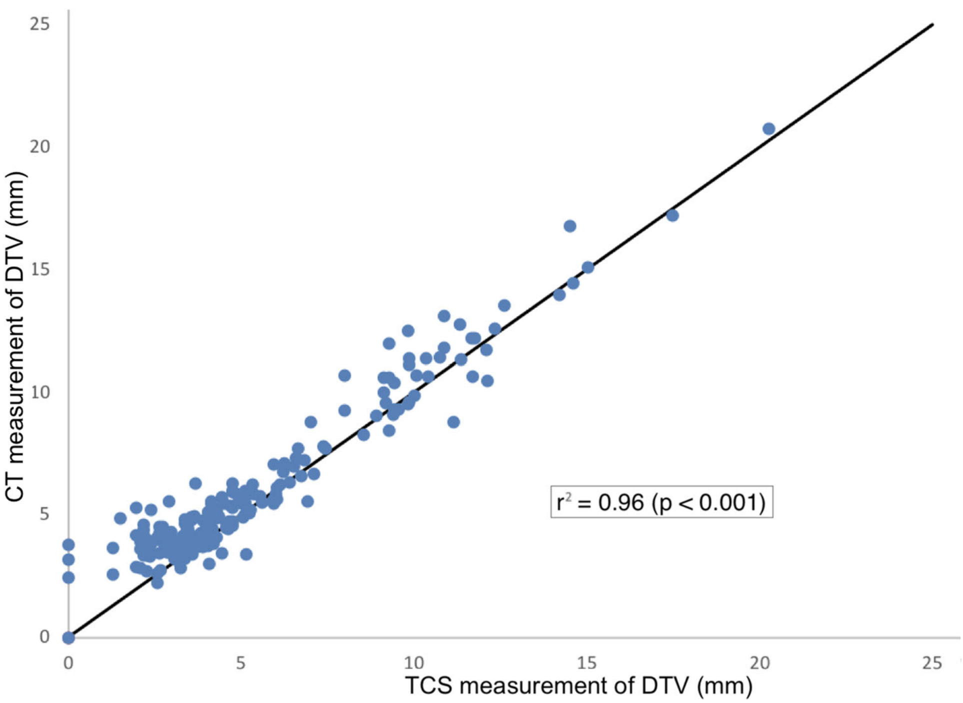

FIGURE 4 Pearson correlation for diameter of the third ventricle (DTV)

DISCUSSION

The pioneer works in the early 1990s suggested that TCS was useful for a rapid examination of deep brain structures and for detecting acute complications, with limited risks compared with transportation to CT scan.[8,20,25]

However, despite some introduction of TCS in the 1990s, its use for sonoanatomic exploration remains limited in NICU. Beyond morphological considerations, further standard of care protocols should define the place of TCS management of NICU patients in particular situations, such as indication of brain CT examination or timing for invasive procedures.

In this retrospective study of 177 neurocritical care patients, TCS has a good correlation with CT for measuring DTV and is potentially useful for estimating MLS. Our study suggests that TCS could allow for a rapid detection of patients at risk of neurological deteriorations (with

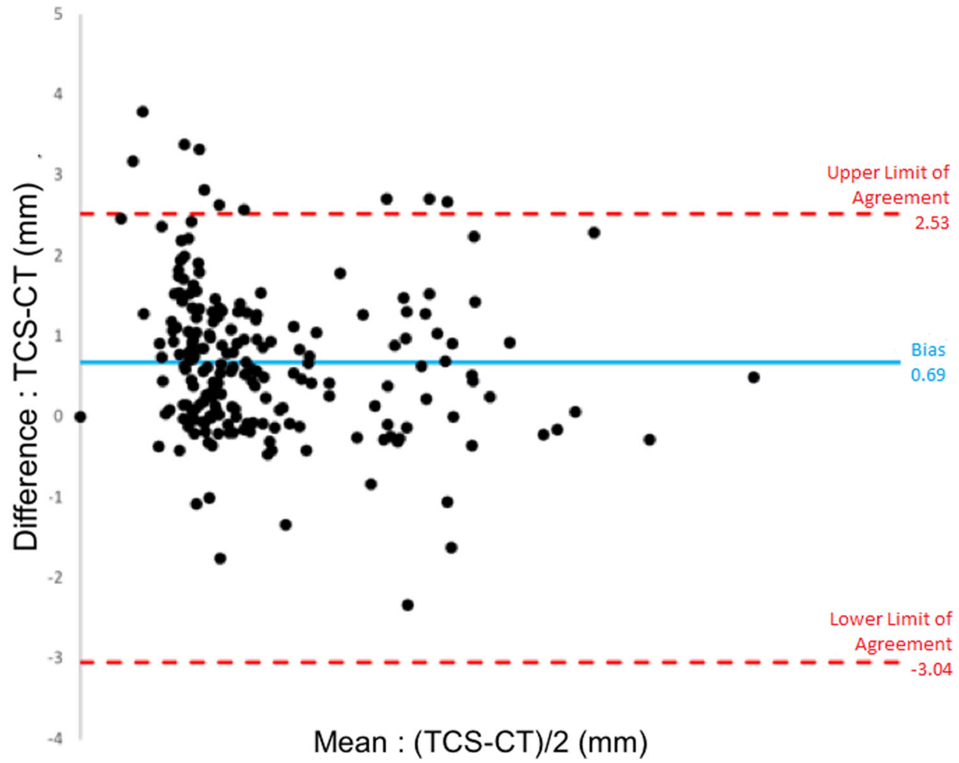

FIGURE 5 Bland-Altman analysis for diameter of the third ventricle (DTV)

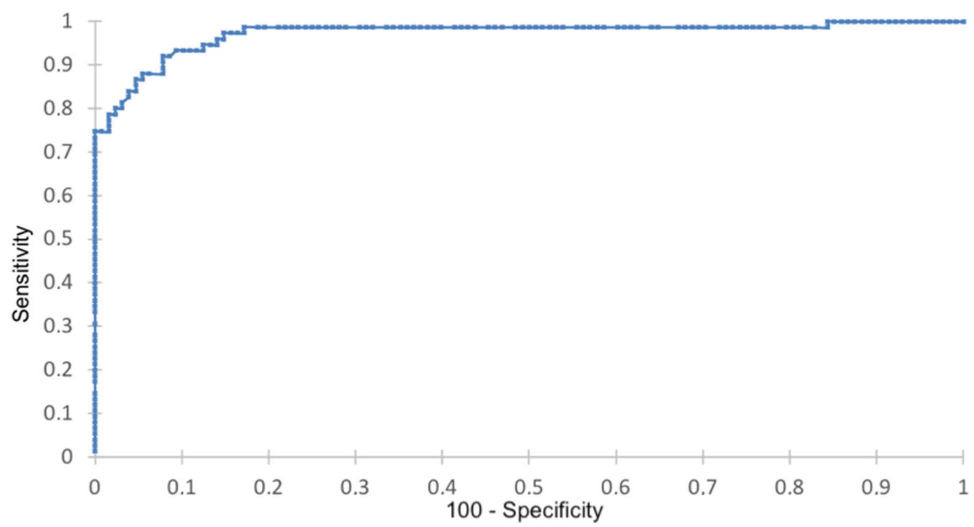

FIGURE 6 Receiver operating characteristic curve for diameter of the third ventricle (DTV), area under the curve 0.97 (95% confidence Interval [CI]: 0.94-1). TCS could detect an enlargement of DTV of 5.47 mm with a sensitivity of 92% (95% CI: 83.2%-96.5%) and a specificity 92.1% (95% CI: 85.9%-95.8%), and with a positive likelihood ratio of 11.68

subsequently earlier diagnosis and treatment), and thus could also limit risky transportation to a redundant CT scanner.

To our knowledge, this neurosonographic study represents the largest cohort of NICU patients explored with a high rate of hydrocephalus (37%). Our results were consistent with previous studies.[10,17–20] However, few of them have focused on the measurement of DTV by TCS and they only investigated chronic hydrocephalus, but not NICU patients.[10,17–20] In fact, chronic hydrocephalus is characterized by a progressive adaptation of the cerebral parenchyma, which may differ from acute processes in NICU patients.

We found a very close correlation between DTV measurements performed by TCS and by CT. However, it would be necessary to confirm the threshold of 5.47 mm for the diagnosis of hydrocephalus by TCS on a validation cohort.

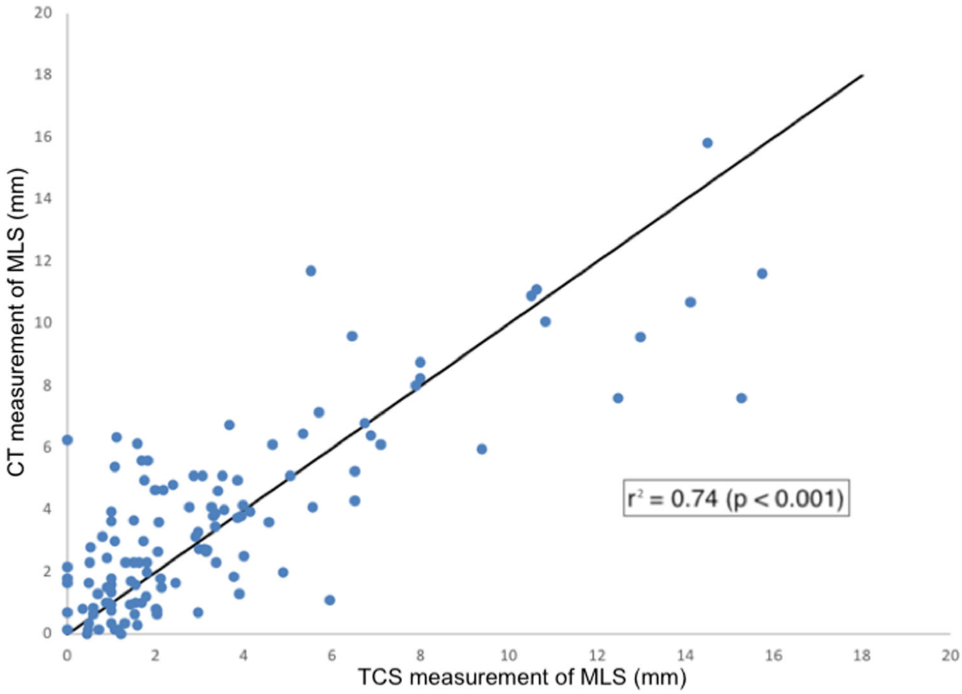

FIGURE 7 Pearson correlation for brain midline shift (MLS)

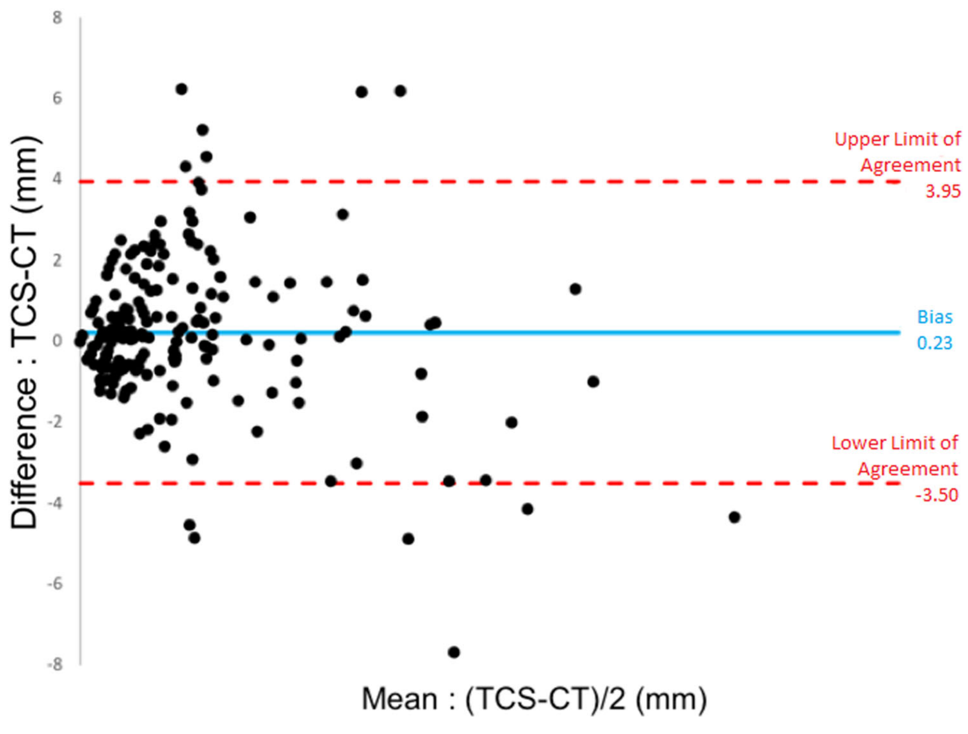

FIGURE 8 Bland-Altman analysis for brain midline shift (MLS)

These preliminary results suggested that TCS could be helpful for decision-making in the management of neurocritical patients. This is concordant with the study of Kiphuth et al. who investigated the ability of TCS to predict the need for reopening an external ventricular drainage in patients with posthemorrhage hydrocephalus. The authors defined an optimal threshold of 5.5 mm increase in DTV.[21] Another study showed a good accuracy of the TCS measurement of DTV compared to cerebral CT, in a small series of 15 consecutive severe traumatic brain injury patients.[22]

Regarding the MLS, our results confirmed a good accuracy of TCS in detecting clinically significant MLS according to the previous published cohort of 52 neurosurgical patients.[23] However, we found a

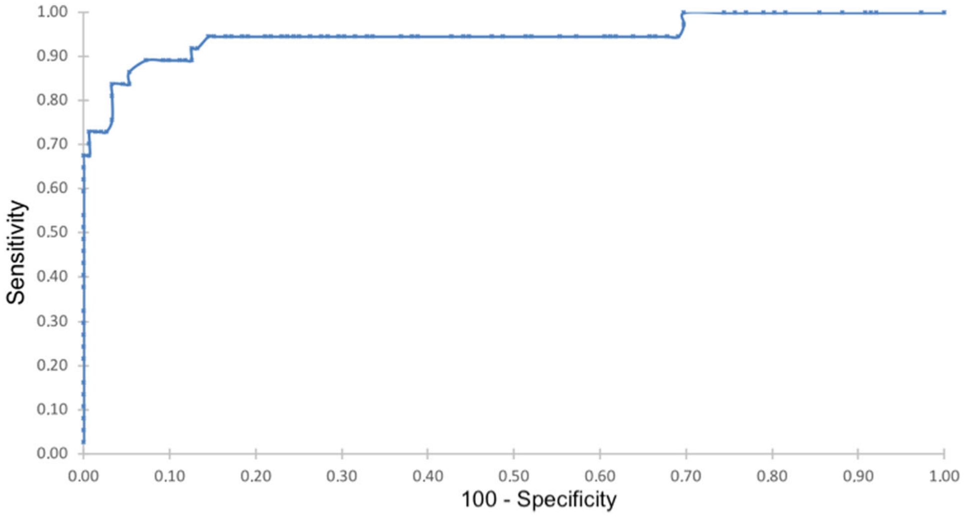

FIGURE 9 Receiver operating characteristic curve for brain midline shift (MLS), area under the curve 0.94 (95% confidence interval [CI] 0.88-1). TCS could detect an MLS of 5.1 mm with a sensitivity of 89.2% (95% CI: 74.5%-96.2%) and a specificity of 92.8% (95% CI: 87.3%-96%), and with a positive likelihood ratio of 12.32

better correlation (.74 vs. .65) than the study of Motuel et al.[23] This could be explained by the larger size of our cohort of measures or by the difference in the sample selected by Motuel et al. who mostly analyzed traumatic brain injury patients.

Also, in the study of Camps-Renom et al., the authors reported an excellent correlation between TCS and CT to measure hematoma volume and MLS in patients with intracerebralbrk hemorrhage.[24]

Our specific TCS screenings allowed diagnoses of other morphological abnormalities in some patients such as detection of intracranial hematoma or malposition of the external ventricular bypass catheter. That was not the main objective in this study, but it highlights other potentialities for TCS than DTV and MLS anomalies description. For example, we reported a case of very early diagnosis of rebleeding following subarachnoid hemorrhage.[26] Similarly, a Korean team recently reported two cases of severe traumatic brain injury for which the intraoperative TCS allowed the diagnosis of hemorrhagic lesions contralateral to the initial surgery.[27]

As stated by others studies, TCS was proposed to be an interesting tool to estimate brain complacency and to detect cerebral edema reflected by perimesencephalic cistern obliteration or Sylvian fissure erasing.[12,24]

Our work has several limitations. First, retrospective design and the recruitment of nonconsecutive patients led to a bias related to the risk of data loss, misrecognition, and random observations. Some selection bias may result from the fact that some individual measurements were impossible because of the patient's insufficient skull acoustic window or postneurosurgical pneumoencephaly. We could not identify those situations that could have helped describing the feasibility of TCS.

Second, as ICP and compliance relationships are dynamic and may vary quickly, the delay between the two assessments that we chose to be shorter than 4 hours is a flaw that cannot be overcome by our study design.

Third, the bed positioning during which each assessment was not described in our work, and it is well know that it may influence ICP and intracranial compliance. Also, we could not know if some clinical intervention (sedation titration, osmotherapy etc.) happened during the time between CT scan and TCS assessment. Fourth, unfortunately, our data did not allow analyses on subgroups (age, pathology) that could have been interesting.

Some would also criticize the operator-dependent nature of the TCS, but the correlation with CT scan data supports the reliability of the procedure. Additionally, all TCS works were carried out by two trained operators, which reduces potential errors but we have not evaluated the interoperator variability. However, Seidel et al. have previously demonstrated a good level of reproducibility of TCS results between operators.[8]

Finally, because this study was focused on techniques, concomitant clinical data such as ICP or therapeutic interventions were not collected. This last point rules out all discussion on clinical relevance of the measurements. In our center, stand of care include a systematic CT examination and TCS for surgical NICU patients at day 1. Most of our patients were assessed in this situation. But for an important part of our cohort, the indication for CT was not available.

Conclusion

We observed a high correlation between TCS to detect third ventricular enlargement and midline shift when compared to contemporaneous cerebral CT.

TCS seems to be a reliable, accurate, and simple noninvasive tool for a detailed bedside diagnosis opening perspectives for a modern personalized therapeutic management in acute neurological situations, from prehospital care to perioperative setting. Larger prospective studies focusing on the TCS-based management of patients with elevated ICP should be carried out to define the place of this technique integrated in the standards of care.

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