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Abstract

Objective: To investigate the influence of the presence of a tracheostomy tube to assess pain with the Nociception Coma Scale – Revised (NCS-R) in patients with disorders of consciousness (DOC).

Design : A cohort study in which patients were evaluated at a single time point.

Setting : Patients were evaluated in a tertiary care hospital.

Participants: 125 patients (Unresponsive Wakefulness Syndrome (UWS): 46 patients, Minimally Conscious State (MCS): 74 patients, Emerging from MCS: 5 patients; mean age: 46 years +/- 16; time since injury: 817 days +/- 1280) in a convenience sample, were evaluated with the NCS-R after noxious stimulation.

Interventions : Not applicable.

Main Outcome Measures : We compared the NCS-R scores of patients with and without tracheostomy with a U Mann-Whitney test. A secondary outcome was to evaluate the influence of the presence of a tracheostomy on the previously described cut-off score of 2.

Results: The presence of a tracheostomy was associated with lower verbal subscores (p=0.002) as well as total scores (p=0.039). The cut-off score of 2 remained valid for the group of patients with tracheostomy with a high sensitivity (71.43%) and specificity (89.29%), as well as when we excluded the verbal subscore of the NCS-R (Sensitivity=83,2% and Specificity=92,4%.)

Conclusion: Our study confirms the validity of the NCS-R in DOC patients with a tracheostomy. However, the presence of a non-speaking tracheostomy should be clearly mentioned when applying the NCS-R, as it significantly lowers the verbal subscore.

Keywords: nociception, pain, cut-off score, nociception coma scale-revised, tracheostomy, minimally conscious state, unresponsive wakefulness syndrome.

Abbreviations: CRS-R = Coma Recovery Scale Revised, NCS-R = Nociception Coma Scale Revised, DOC = Disorders of Consciousness, UWS = Unresponsive Wakefulness Syndrome, MCS = Minimally Conscious State.

Introduction

Following a severe brain injury leading to coma, some patients will remain in a pathological state of impaired consciousness often referred to as “disorders of consciousness” (DOC), encompassing (1) patients showing only reflexive behaviors (Unresponsive Wakefulness Syndrome [UWS] [1], also known as vegetative state) and (2) patients exhibiting fluctuating purposeful behaviors, but unable to functionally communicate (Minimally Conscious State [MCS]) [2]. Seminal studies showed that DOC patients may present at least a partial cortical process of noxious stimuli. More specifically, patients in MCS, at a group level, showed the same pattern of functional activation as healthy subjects [3,4]. These findings have had a significant clinical and ethical impact and highlight the necessity to develop bedside tools to identify and manage pain in this population. In 2010, a behavioral scale was developed specifically for patients with DOC, the Nociception Coma Scale – Revised (NCS-R; [5,6]). This scale encompasses 3 subscales, evaluating motor, verbal and facial expressions, each one ranging from 0 to 3, with a maximal total score of 9 (Text Box 1). In a recent multicenter study, a cut-off score of 2 was identified [7] to detect responses related to nociceptive stimuli.

<< Insert Text Box 1 here>>

If it has been shown useful to manage pain in intensive care patients [8,9,10], the frequent presence of a tracheostomy tube may prevent patients to emit any sound, secondary to the endotracheal tube by-passing the vocal chords, resulting in a low to null score on the verbal subscale. In this retrospective study, we investigated the influence of the presence of a tracheostomy on the verbal subscale and on the NCS-R total score. We also aimed to replicate the previously defined cut-off of 2 and to investigate if it would be different in a subgroup of patients with a tracheostomy.

Methods

Participants

Participants were recruited from the intensive care unit and neurology ward of the University Hospital of Liège, from neurorehabilitation centers and nursing homes that are part of the Belgian federal network for DOC patients, between 2011 and 2017. Inclusion criteria were: (1) age>16 years; (2) no administration of neuromuscular blockers or sedation within the 24 h of enrollment; (3) the presence of periodic eye opening; (4) a diagnosis of UWS, MCS or emergence from MCS (eMCS) without functional communication, based on behavioral assessment performed using the Coma Recovery Scale Revised (CRS-R – [11]). Exclusion criteria were: (1) history of brain injury (2) developmental, psychiatric or neurologic illness resulting in documented functional disability up to time of the injury; (3) upper limb contusions, fractures or flaccid paralysis. A subset of patients (n=64) were previously included in a study published elsewhere [6]. The study was approved by the Ethics committee of the Faculty of Medicine of the University of Liège and the patient's legal representatives gave their written informed consent.

Two samples of patients assessed with the NCS-R were included for analyses. The first one included patients for which we had information on the presence or absence of a tracheostomy. For the secondary analyses, we included any patient who underwent NCS-R assessments.

Procedure

The NCS-R was administered in two different conditions: (1) baseline and (2) noxious condition. During baseline, we observed the patient's spontaneous behaviors for 60 seconds [11]. During the noxious condition, we applied pressure on the nailbed of the middle finger of the right and left hand [11,12] for a minimum of 5 seconds and stopped as soon as a behavioral response was observed. Behavioral responses were recorded 10 seconds after each stimulation [11]. The highest score obtained across right and left side stimulation was

considered. To ensure a sufficient level of arousal, each condition was administered while patients showed spontaneous eye opening. The entire procedure lasted less than 5 min.

Patients' level of consciousness was assessed before or after this procedure with the CRS-R [13].

Statistics

Statistical analyses were performed using GraphPad Prism 7 (GraphPad Prism version 7.04, GraphPad Software, La Jolla California, USA).

In the first step, U Mann-Whitney tests were used to investigate the difference in NCS-R subscores and total scores in response to noxious stimulation between patients with and without a tracheostomy tube. We set significance at $p<0.05$ (one-tailed).

In a second step, receiver operating characteristic (ROC) analyses were used to determine the best cut-off score allowing to differentiate the noxious condition versus baseline using the NCS-R total scores and the sum of both the motor and facial expression subscales excluding the verbal one. We ran those analyses on a larger sample of patients assessed with the NCS-R as well as on a subset of patients with tracheostomy.

Results

For the first step, 65 patients (UWS (n=25), MCS (n=35) and eMCS (n=5)) were included, of which 28 had a tracheostomy (43%; UWS (61%), MCS (32%), eMCS (7%)). Mean age of the population was 42 +/- 13yo (time since injury 1198+/- 1495 days). Lower scores were observed on the NCS-R verbal subscores ($p = 0.002$) and total scores ($p = 0.039$) in the tracheostomy group as compared with patients without a tracheostomy in response to noxious

stimulation (Figure 1). Moreover, there was no difference in facial (p=0.241) and motor subscores (p=0.967) between both groups.

<< Insert Figure 1 here >>

For the second step, we included 125 DOC patients (UWS= 46, MCS= 74, eMCS= 5 patients; mean age: 46 +/- 16yo; time since injury: 817 +/- 1280 days) assessed with the NCS-R. The ROC analyses reported a score of 2 or higher as the best threshold for nociception with a sensitivity of 87.2% and a specificity of 79.2% for differentiating noxious condition from baseline (Figure 2). Removing the verbal subscale (MF score) did not modify the cut-off, with a score of 2 associated with a sensitivity of 83,2% and a specificity of 92,4% (Figure 2).

The same analyses performed on a sample of 28 patients with tracheostomy led to the same cut-off score of 2 at the NCS-R total score, with a lower sensitivity (71.43%) and specificity (89.29%), while removing the verbal subscale led to the same results (Figure 2; also see Supplementary material for more details).

<< Insert Figure 2 here >>

Discussion

We here showed that the presence of a tracheostomy is associated with a lower score on the verbal subscale, resulting also in a lower total score. Patients with tracheostomy also tended to display similar pattern of responses at the motor and facial subscales of the NCS-R when compared to non-tracheostomized patients. These findings are in line with our hypothesis that the NCS-R scores are mainly influenced by the presence of a tracheostomy itself and the difference is not due to a difference in the type of DOC or disease severity.

We also replicated the previously reported cut-off score of 2 [7] to identify nociception, which remained the same after removal of the verbal subscore or when focusing on a subgroup of patients with tracheostomy.

Study limitations

Future studies should use a Newton-meter to control stimulus intensity and limit interrater variability on the amount of pressure administered during noxious condition. Investigating NCS-R responses in patients with a speaking tracheostomy vs. non-speaking tracheostomy would also enable to confirm the hypothesis that a difference is solely due to the medical device itself. Finally, the clinical implication of the cut-off score of 2 should also be further investigated, as the score of 2 can easily be reached with only reflexive behaviors (ie, flexion withdrawal), limiting its interest in a clinical setting to identify a (potentially) painful condition.

Conclusion

Our study confirms the validity of the NCS-R in DOC patients with a tracheostomy. However, the presence of a non-speaking tracheostomy should be clearly mentioned when applying the NCS-R as it significantly lowers the verbal subscore.

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Figure legends

Text Box 1 : Description of the 3 subscales and items included in the NCS-R.

Figure 1 : Median (and IQR) of NCS-R total scores (upper rows) and verbal subscores (lower rows) in response to noxious stimuli, in subgroups of patients without (n=37) (on the graph "w/o trach") or with a tracheostomy (n=28) (on the graph "w/ trach"). Asterisks mark significant difference between the scores of the two groups (*one-tailed $p<0.05$ for total scores and **one-tailed $p= 0.01$ for verbal subscores).

Figure 2 : ROC curves representing the relation between sensitivity and specificity for the different potential threshold scores allowing to discriminate a NCS-R score at baseline (i.e., resting scores) and a NCS-R score after noxious stimulations using different scores (i.e., NCS-R total scores or total score without the verbal subscore (MF)) or population (i.e., for the whole group) (n=125) and for the subgroup of patients with tracheostomy (n=28)). Area Under Curve (AUC) values as well as values of each point of the curves are collected in supplementary table 1.

Supplementary table 1 : AUC = Area Under Curve; MF = Motor + Facial expressions subscores of the NCS-R.

Values of sensitivity and specificity of the different cut-off scores, allowing to discriminate NCS-R scores at baseline (i.e., rest) from NCS-R scores related to a noxious stimulation. The AUC and the best threshold identified are highlighted in light grey.

Figure 1

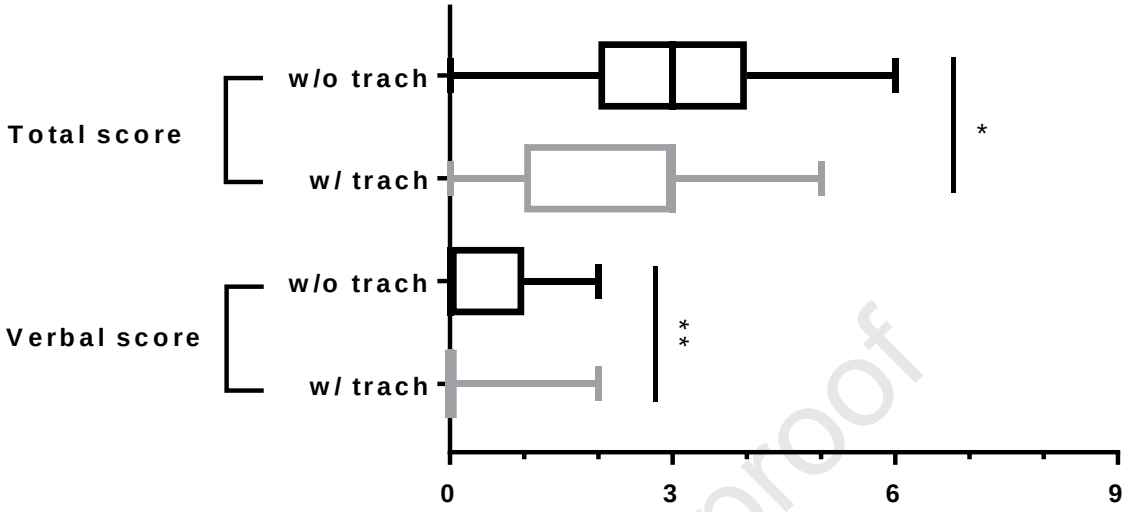
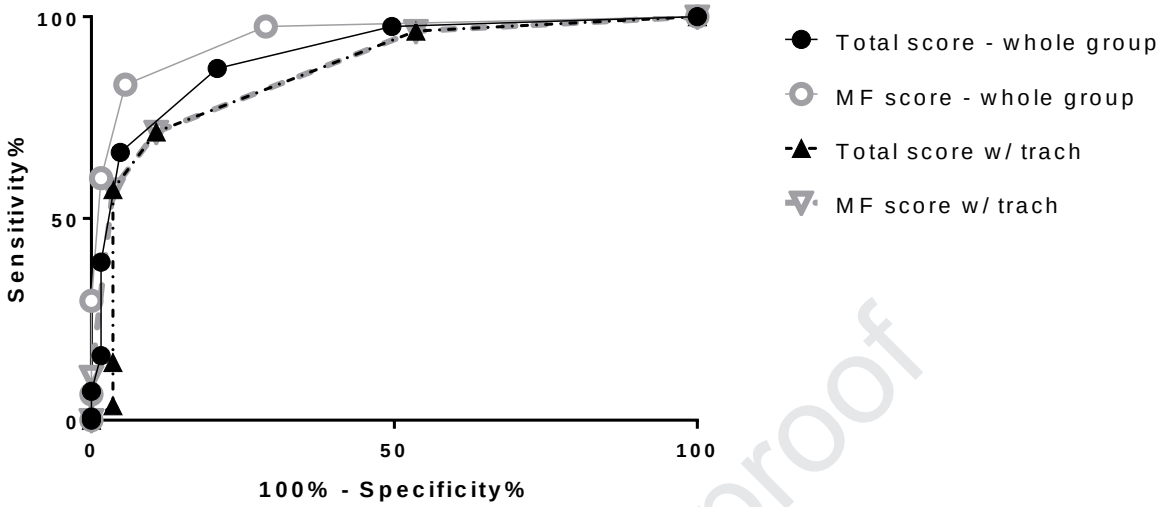


Figure 2



Highlights

- The NCS-R has been developed to assess nociception in patients with a DOC.
- Verbal and total scores of the NCS-R are lower in patients with a tracheostomy.
- Facial and motor subscores do not differ between patients with or without tracheostomy.
- NCS-R scores should be cautiously interpreted in presence of tracheostomy.
- However, our findings support the use of the NCS-R in real clinical practice.