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ARTICLE

The use of classification and regression tree analysis to identify the optimal surgical timing for improving neurological outcomes following motor-complete thoracolumbar traumatic spinal cord injury

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Abstract

Study design Observational cohort study.

Objectives To identify the optimal surgical timing for improving neurological outcomes in patients that sustained a motor-complete traumatic spinal cord injury (TSCI) secondary to a thoracolumbar injury.

Setting Level 1 trauma center specialized in TSCI care.

Methods We prospectively analyzed clinical data of 35 patients admitted for motor-complete TSCI secondary to a thoracolumbar injury. We quantified neurological recovery with three different outcomes: the improvement of at least one grade on the American Spinal Injury Association Impairment Scale (AIS), of at least one neurological level of injury (NLI), and of at least 10-points on the motor score (MS). Classification and regression tree analysis was used to identify outcome predictors and to provide cutoff values of surgical timing associated with recovery.

Results The proportion of the patients improving by at least one AIS grade was higher in the group undergoing early surgery within 25.7 h of the TSCI (46% vs 0%). The proportion of patients that improved by at least one NLI was also higher in the group undergoing early surgery within 21.5 h of the TSCI (71% vs 18%). Lastly, 25% of the AIS grade A patients undergoing early surgery within 25.6 h of the TSCI improved 10 MS points or more as compared with 0% in the other group.

Conclusions Earlier surgery was effective in improving neurological outcome in motor-complete TSCI at the thoracolumbar levels. Performing surgery within 21.5 h from the traumatic event in these patients increases the likelihood of improving the neurological recovery.

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Introduction

Traumatic spinal cord injury (TSCI) is a debilitating condition. In the past decades, efforts to improve medical and surgical management of TSCI patients have resulted in better neurologic and functional outcomes after trauma. Whereas many predictors of such outcomes are non-modifiable for the clinicians, controversy regarding best management of modifiable elements remains. Debate is still ongoing when looking at optimal timing of surgical intervention in this patient population.

The literature strongly suggests that earlier surgery leads to better outcomes but there is a lack of evidence supporting an objective optimal timing of surgery in TSCI

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patients. Discrepancy between studies that investigate the association of early surgery with neurological outcome mainly comes from the wide range of time thresholds used in the definition of "early surgery" and the inclusion of a vast array of neurological levels and severity of neurological injury at presentation [1].

Paucity in the literature in this regard is particularly striking when looking at thoracolumbar TSCI. This population of patients is important to study because it is one of the most prevalent group of patients with TSCI living in the community [2]. In addition, it is a subset of TSCI patients in which prediction of neurological outcome is very difficult because of the variability of mechanisms of injury, specific relevant anatomical characteristics such as the transition from the spinal cord to the conus medullaris to the cauda equina, and associated injuries to surrounding organs. Review of the subject by El Tecle in 2016 showed only six retrospective studies with variable results and conflicting conclusions, with time thresholds extending from 8 to 72 h from the traumatic event [3]. Cenzig et al. suggested that operating before 8 h is favorable [4]. However, this study included a small number of paraplegic patients and compared outcomes in patients operated either before 8 h or after 3 days. Such strategy is not applicable in the current Canadian hospital service system [5, 6]. McLain and Benson claimed better proportion of neurological recovery in patients operated under 24 h (8/9, 88% vs 6/12, 50%), without providing thorough statistical analysis [7]. More recently, Burke et al. [8] added the definition of "ultra-early" surgical strategy as an operation taking place 12 h from the traumatic event. In a series of 78 patients, they found that "ultra-early" strategy provided better neurological outcome that "early" (>12 h, <24 h) or "late" (>24 h) strategy. They found no difference in neurological outcome between early (>12 h, <24 h) and late strategies (>24 h) [8]. Clohisy et al. compared a small number of paraplegic patients and supported a cut-off of 48 h, demonstrating better Frankel and motor score in early decompression surgery [9]. Likewise, Landi et al. provided multivariable analysis to support surgery within 48 h of the traumatic event but compared patients injured at the thoracic, thoracolumbar and lumbar levels, with only 9 patients fitting our inclusion criteria [10].

However, many larger retrospective studies that included paraplegic patients did not find significant differences when looking at neurological recovery according to timing subgroups [11–14].

This study intends to provide objective and unbiased cutoffs for surgical timing following TSCI to assist in optimizing the surgical planning of TSCI patients. We limited the heterogeneity of the patient population studied by specifically examining cases of thoracolumbar motor-complete TSCI. The main objective of this study is to assess the influence of surgical timing on the neurological recovery and to identify objective surgical timing cutoffs associated with better neurological recovery using classification and regression tree (CART) analysis.

Methods

Patients

Patients in this study were prospectively enrolled on a voluntary basis at a single Level 1 trauma center. All 35 consecutive adult (>18 years old) patients were admitted between 2010 and 2017 for TSCI secondary to a traumatic thoracolumbar injury, either burst fracture, flexion-distraction or rotation-translational injury between T10 and L2 levels. Included patients had severe TSCI, defined as motor-complete American Spinal Injury Association Impairment Scale (AIS) grade A or B. All benefited from a decompression and stabilization surgical procedure. A minimum of 12 months of clinical follow-up after the traumatic event was set as an inclusion criteria. This study was approved by the Institutional Review Board. All applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

Variables

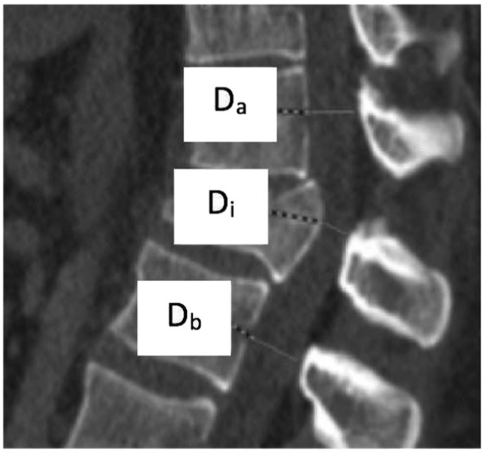
Outcome variables

The International Standards for Neurological Classification of Spinal Cord Injury were utilized in the clinical evaluation of patients to collect AIS grades preoperatively within 3 days of presentation and at a minimum of 12 months of follow-up. The neurological level of injury (NLI) and the total motor score (MS) of each evaluation were also collected at presentation and follow-up. One patient had missing MS data at the yearly follow-up due to contractures preventing full assessment of motor function.

The primary outcome to assess neurological recovery was an improvement of at least 1 grade on the AIS scale. The improvement of at least one NLI and at least 10 points on the MS were considered as secondary outcomes.

Predictor variables

Predictors of neurological recovery following TSCI were chosen according to their potential to influence neurological outcome. Five independent variables were selected based on the literature [15]. The main independent variable consisted of the surgical delay considered as a continuous variable and defined as the time between the traumatic event and the



$$\text{MCC (\%)} = 1 - \left(\frac{D_i}{(D_a + D_b)/2}\right) \times 100\%$$

Fig. 1 Mean Canal Compromise (MCC) calculation formula, where D_a is the anteroposterior canal diameter one level above the injury site, D_i is the anteroposterior osseous canal diameter at the injury site, and D_b is the anteroposterior canal diameter one level below the injury site.

time of surgical incision. Age was considered as a continuous variable. The initial severity of the neurological injury was assessed with the AIS. The Mean Canal Compromise was calculated according to the formula as depicted on Fig. 1 [16]. The energy of the trauma was dichotomized in low (fall from standing or walking, trivial trauma) or high (pedestrian hit by vehicle, motor-vehicle or motorcycle accident, fall from more than 3 m, etc.).

Statistical analysis

The CART analysis engine (Salford Predictive Modeler software, Version 8, Salford Systems, San Diego, CA, USA) was used for statistical analyses. It is a useful tool in the field of predictive analytics and was applied to solve a binary classification from recursive partitioning: the general outcome of interest here being whether patients show neurological recovery or not following TSCI. This statistical method creates prediction models in the form of decision trees by repeatedly partitioning a data set into two subgroups based on an objective splitting criterion (predictor most related to the outcome) until further partitioning no longer adds value to the prediction [17]. The classification trees were elaborated using the Gini splitting rule. Trees were pruned to prevent splitting rules based on a similar predictor variable from appearing more than once. A stopping rule was used to prevent the algorithm from creating subgroups of five patients or less. Overfitting was monitored by choosing the tree exhibiting the minimum relative cost value computed by the software. The CART engine also identifies surrogate splitter, as close approximations of the primary splitters appearing in the trees.

Table 1 Summary of outcomes and predictor variables considered.

Outcome measures		
1 or more AIS grade improvement	%	37.14
1 or more NLI improvement	%	54.29
10 or more total MS improvement	%	29.41
Input parameters		
Age, years	Median (IQR)	43 (33–55)
Initial AIS grade	AIS A, n	28
	AIS B, n	7
Surgical delay, hours	Median (IQR)	20.00 (13.73–22.52)
Energy	% High	60.0
	% Low	40.0
MCC, %	Median (IQR)	55.2 (44.8–70.0)

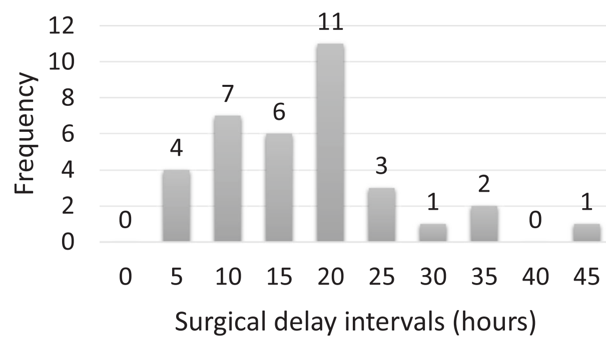


Fig. 2 Number of patients operated in surgical delay intervals.

Surrogates splitters are used by the algorithm to handle eventual missing data and are taken into account when computing the variable importance [18]. Continuous data were reported as median and interquartile range (IQR), whereas categorical data were reported as percentages. χ^2-square tests were used to assess whether the proportion of patients who improved neurologically was statistically different from the proportion of patients who did not improve as determined following the split based on the surgical timing. The significance level was set at $p < 0.05$.

Results

Table 1 summarizes the outcome measures and the algorithm input parameters that were considered for analyses. Among the 35 patients, 13 (37.14%) demonstrated recovery of at least 1 AIS grade, 19 (54.29%) demonstrated recovery of at least 1 NLI and 10 (29.41%) demonstrated recovery of at least 10 points on the total MS. The median age (IQR) admission was 43 years (33–55) and median surgical delay was 20.00 h (13.73–22.52). Figure 2 shows the distribution of surgical delay across the population. Most of the traumatic events (60%) were classified as high energy, and the median MCC (IQR) was 55.2% (44.8–70.0). The majority of patients (80%) were classified with motor and sensory complete lesion (AIS A) at admission. Table 2 depicts the AIS grade change over the follow-up period.

Figure 3 portrays the classification tree obtained when considering a neurological improvement of at least one AIS grade as the dependent variable. Surgical delay was the single most important predictor of improvement in AIS grade. The 35 patients were split in two subgroups according to a surgical delay threshold of 25.66 h. Of the 28 patients operated before this cut-off, 13 (46%) showed neurological recovery, compared with 0 (0%) of the 7 patients operated after. Chi-square test showed significant difference in the proportions of patients showing neurological recovery ($p = 0.023$).

Figure 4 portrays the classification tree obtained when considering a neurological improvement of at least one NLI as the dependent variable. Surgical delay was the single most important predictor of improvement in NLI. The 35 patients were split in two subgroups according to a surgical delay threshold of 21.47 h. Of the 24 patients operated before this cut-off, 17 (71%) showed neurological recovery, compared with 2 (18%) of the 11 patients operated after. Chi-square test showed significant difference in the proportion of patients showing neurological recovery ($p = 0.004$).

Table 2 Neurological status at admission and follow-up.

	Follow-up AIS grade	A	B	C	D	E	Total
Initial AIS	A	20	5	0	3	0	28
	B		2	2	3	0	7

Figure 5 portrays the classification tree obtained when considering a neurological improvement of at least 10 points on the total MS as the dependent variable. The data for 34 patients were available. They were first split according to the AIS grade. Of the 27 AIS A patients, only 5 (19%) showed neurological recovery, compared with 5 (71%) of the 7 AIS B patients. Chi-square test showed significant difference in the proportion of patients showing neurological recovery ($p = 0.006$). The 27 AIS A patients were then split according to a surgical delay threshold of 25.66 h. Of the 20 patients operated before this cut-off, 5 (25%) showed neurological recovery, compared with 0 (0%) of the 7 patients operated after. Chi-square test did not show significant difference in the proportion of patients showing neurological recovery at this level of the classification tree ($p = 0.143$).

Discussion

This article is the first to determine objectively which optimal surgical delay cutoff should be adopted when managing thoracolumbar spinal injuries with neurological deficit. Even if most surgeons believe that thoracolumbar SCI patients should be operated in a timely manner [6, 19], there is no clear literature supporting a specific timing threshold for this population [1, 3]. No studies thoroughly evaluated optimal timing for decompression and stabilization surgery in paraplegic patients. Considering the wide variability in the definition of early surgery throughout the literature, this study is not only important for surgical planning but also for research purposes to better account for

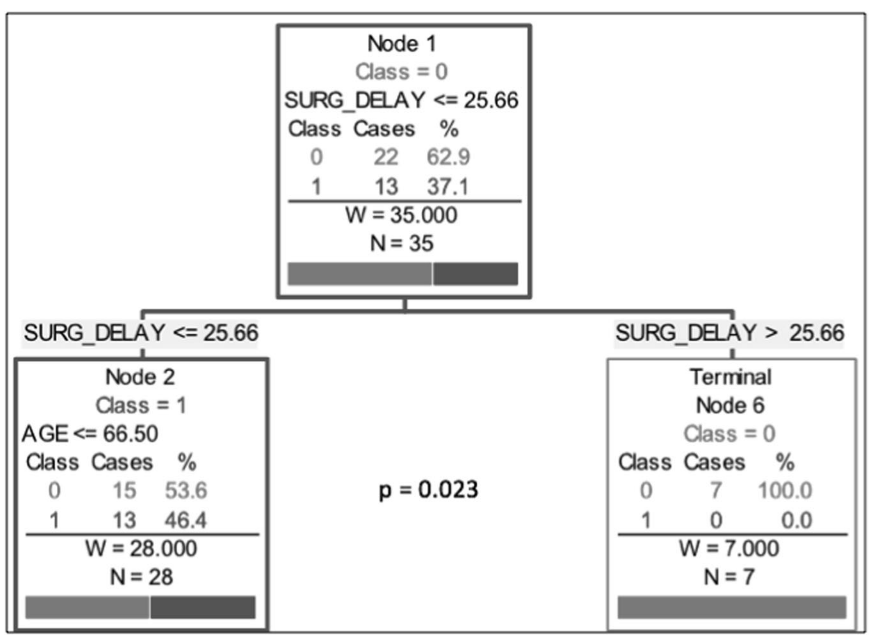


Fig. 3 Classification tree obtained when considering a neurological improvement of at least one AIS grade as the dependent variable, with corresponding *p* value. Class = 0: refers to class corresponding to no neurological improvement. Class = 1: refers to the class corresponding to neurological improvement. Node X: refers to the number attributed to the node. W: Terminal: refers to no split possible from the node. Further nodes were excluded from display because of the stopping rule, preventing display of nodes with five patients or less.

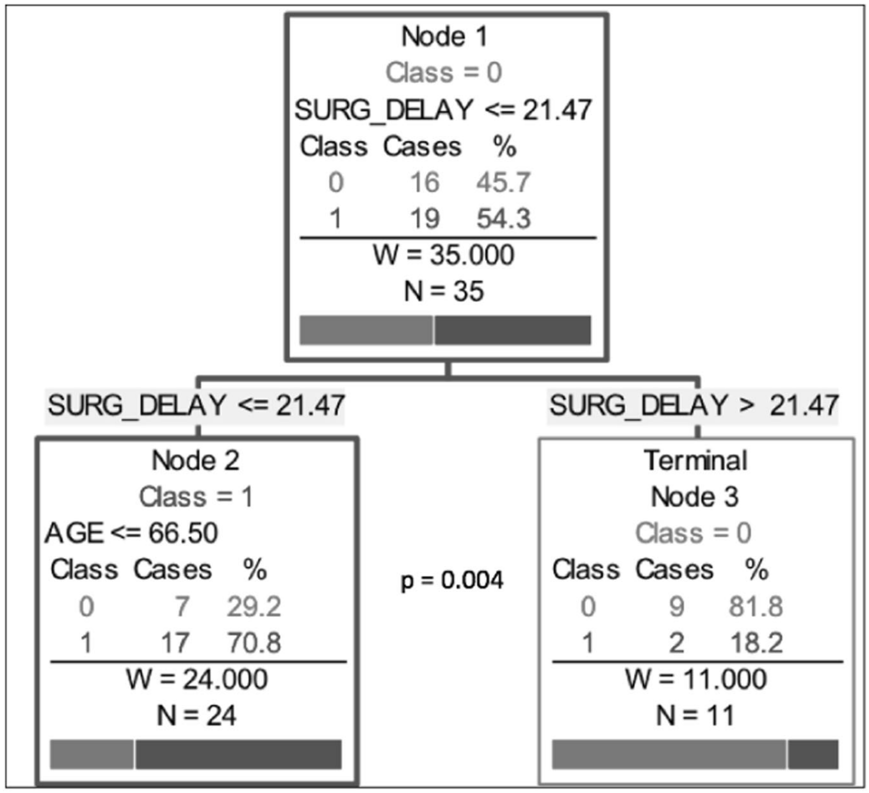


Fig. 4 Classification tree obtained when considering a neurological improvement of at least one NLI as the dependent variable, with corresponding *p* value.

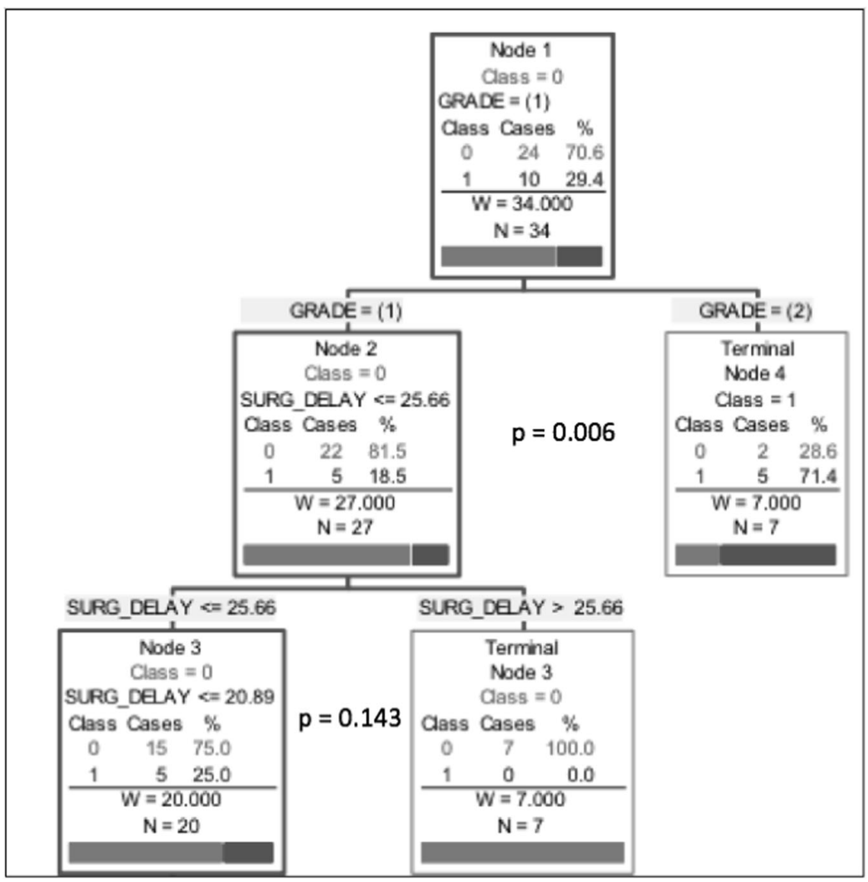


Fig. 5 Classification tree obtained when considering a neurological improvement of at least 10 points on the total MS as the dependent variable, with corresponding *p* values.

the influence of surgical timing in multivariable studies of outcome predictors in TSCI.

The investigation for an optimal timing for surgical care in TSCI patients is not easily amenable to randomization for ethical and practical reasons. In addition, the use of statistical tools such as CART allows to identify objectively unbiased cutoffs for surgical timing using a retrospective review of prospective data design.

The results of this study demonstrate that a surgical intervention within 21.5 h after trauma increases the likelihood of improving by at least one NLI, while improvement by at least one AIS grade and by 10 points on the MS are more likely with surgical intervention within 25.6 h of the TSCI. The discrepancies in surgical timing cutoffs for our three outcomes also mirror the variability in previous studies on surgical timing, as the optimal timing may depend on the targeted outcome. While various outcomes can be selected to determine neurological recovery, our study relies on three outcomes typically recognized as important clinically for assessing neurological improvement [20].

Interestingly, our objective cutoffs (21.5–25.6 h) are close to the subjective 24-h threshold for early surgery commonly proposed by surgeons and in the literature [21]. This finding is important because authors generally consider that a time window after the TSCI close to 24 h is realistic in a clinical setting to allow for optimal performance of the surgery (transfer to a specialized SCI center, medical evaluation and stabilization, preoperative imaging, surgical planning, etc) [22, 23]. Accordingly, we believe that performing surgery within 21.5 h will be feasible in the great majority of patients, and that this cutoff could be used as a reference for clinicians and decision-makers dealing with SCI patients, especially since this cutoff was determined regardless of the burden of associated injuries in our patients population.

It is known that factors other than surgical timing can also influence neurological recovery in the setting of a TSCI. We also included the AIS grade, age, energy of the trauma and the MCC in our analyses since they have previously been reported as potential predictors in the literature [24]. Although the initial neurological status is often recognized as the most important predictor of neurological recovery [25], our analyses suggest that specifically for motor-complete thoracolumbar TSCI, surgical delay was the most important predictor for recovery in terms of AIS grade and NLI. This finding also relates to the fact that we have targeted a specific population with a characteristic initial severity of the neurological injury (motor-complete thoracolumbar TSCI). As for the improvement in MS, the initial AIS grade was most important, but surgical delay remained predictive for recovery in AIS grade A patients. These findings strongly support the clinical relevance of early surgery as an important modifiable factor for which defining objective cutoffs is key to facilitate surgical planning.

Limitations

The main limitation of this study relates to the small number of patients. However, our small cohort was sufficient to observe a significant association between surgical timing and neurological recovery. Significance was also reached for the influence of the initial neurological status, as this is a recognized predictor for neurological recovery.

The number of patients with very early surgery within 8 h of the TSCI is particularly small, which limits the conclusion of this study, considering that previous studies suggest that very early surgery would be even more effective. This small subgroup of patients relates to the multiple barriers to early surgery in real clinical setting [22]. Accordingly, the surgical delay from trauma to surgical intervention in our cohort is similar to that typically observed in other observational studies depicting the real case scenario in a clinical environment [6, 19].

We acknowledge the potential concern regarding instability of initial neurologic examination. Examination is performed by treating surgeons and orthopedic spine surgery trained residents and fellows. The timing of preoperative initial AIS grading from the traumatic event remains a potential confounding variable that is merely impossible to control in the clinical context, especially when early surgical care is warranted.

Conclusion

This article bridges the gap in the literature in providing an objective surgical timing cutoff of 21.5 h for optimal neurological recovery in motor-complete TSCI at the thoracolumbar level. This timeframe would serve not only to guide management but also as a reference for defining "early" surgery in other studies pertaining to outcome predictors in this group of TSCI patients.

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Author contributions JG was responsible for designing the protocol, conducting the search, screening potentially eligible patients, extracting and analysing data, interpreting results, creating 'Summary of findings' tables, and writing the article. ARD was responsible for designing the protocol. She contributed to writing the manuscript, extracting and analysing data, interpreting results. JMMT is the senior researcher who was responsible for designing the protocol, he revised the manuscript critically, he also contributed in extracting and analysing data and interpreting results. He also obtained funding for this research project.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

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