学 位 論 文

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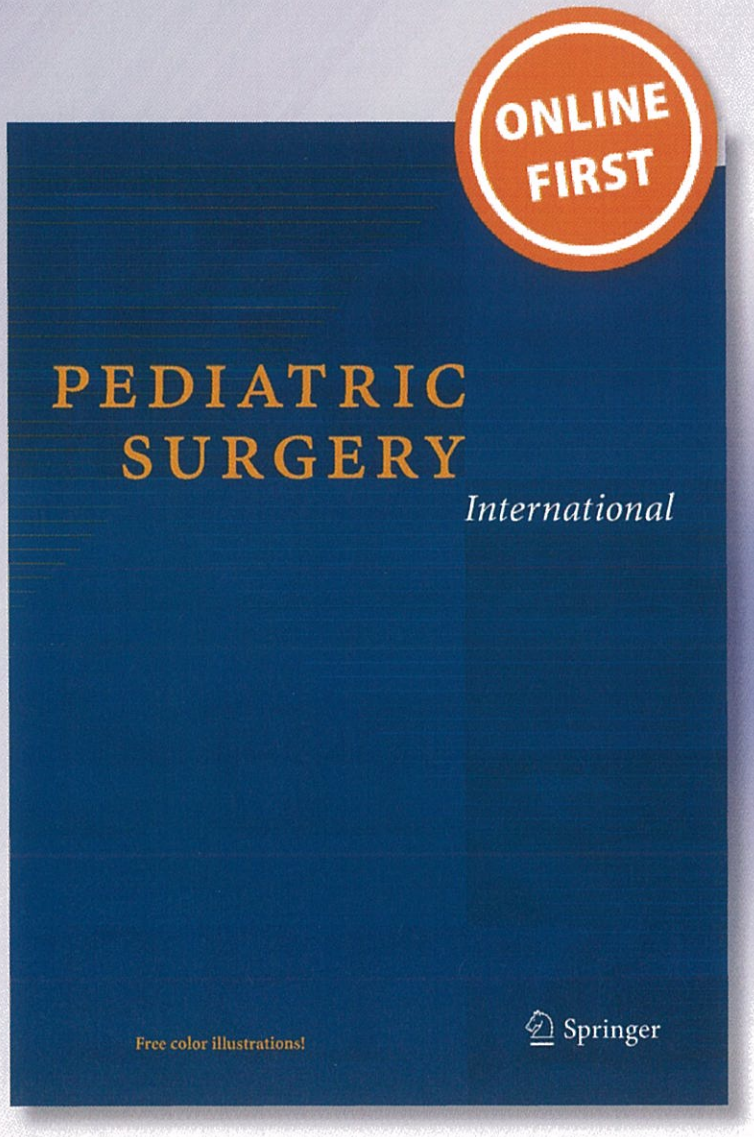

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ORIGINAL ARTICLE

Evaluation of antireflux surgery using multichannel intraluminal impedance-pH measurement in neurologically impaired patients

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Abstract
Purpose This study aimed to evaluate esophageal function before and after antireflux surgery (ARS) in neurologically impaired (NI) patients using 24 h multichannel intraluminal impedance (MII)-pH measurement.
Methods Seven NI patients (age, 0–33 years; median, 13 years) were assessed before and after ARS using 24 h MII-pH. We described reflux parameters such as pH reflux index, bolus exposure index, number of acidic and nonacidic reflux episodes, mean acid clearance time and median bolus clearance time, and esophageal motility parameters in dry swallows such as bolus presence time (BPT), total bolus transit time (TBTT), and total propagation velocity (TPV).
Results The postoperative reflux parameters such as pH reflux index, acid clearance time, bolus exposure index, and the number of acidic reflux episodes significantly decreased ($P < 0.05$) compared with the preoperative ones. The esophageal motility parameters including all sites of BPTs, TBTT, and TPV did not change in the MII-pH measurement after ARS (P = non-significant).
Conclusion ARS effectively reduced gastro-esophageal reflux (GER) in NI patients without the impairment of esophageal motility by MII-pH measurement. MII-pH was useful to detect the subtype of GER before and after ARS and appeared to be appropriate for evaluating esophageal motility.

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Keywords Multichannel intraluminal impedance-pH measurement · Gastro-esophageal reflux · Neurologically impaired patients · Antireflux surgery · Esophageal motility

Introduction

A high incidence of gastro-esophageal reflux disease (GERD) in neurologically impaired (NI) patients has been reported, affecting 15–77 % of this patient group [1, 2]. The mechanism of reflux is primarily attributed to the disturbed function of the lower esophageal sphincter with transient relaxation leading to regurgitation and/or vomiting of gastric contents [3]. Complications associated with GERD including reflux esophagitis and recurrent pulmonary aspiration cause significant morbidity and mortality. Acid suppression therapy is one of the effective treatments for esophagitis; however, it is often difficult to control other GERD symptoms, such as malnutrition or pulmonary aspiration, in NI patients suffering from abnormal body posture, scoliosis, and convulsion. When medical treatments fail and reflux symptoms persist, antireflux surgery (ARS) is often required to prevent reflux-associated morbidity such as recurrent aspiration [4, 5]. Several ARS procedures can be used for gastro-esophageal reflux (GER) treatment, with surgical fundoplication, where the gastric fundus is wrapped around the distal esophagus, being the most common. This procedure is performed to prevent reflux by increasing the baseline pressure of the lower esophageal sphincter, decreasing the number of transient lower esophageal sphincter relaxations and increasing the length of the intra-abdominal esophagus to accentuate the angle of His and reduce hiatal hernia [6].

NI patients typically cannot sufficiently describe their symptoms, and therefore, careful observation and exact

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assessment procedures are required before and after ARS. In recent years, combined multichannel intraluminal impedance (MII)-pH measurement has become increasingly important for evaluating GER [7, 8]. MII detects GER episodes based on changes in electrical resistance to the flow of an electrical current between a pair of electrodes placed on the MII probe, when a liquid, semisolid or gas bolus moves between them. Being able to detect reflux regardless of its pH value and to distinguish swallowing (antegrade flow) from authentic GER (retrograde flow), combined esophageal pH monitoring and impedance offer several advantages over standard pH monitoring. It can also accurately detect the height of the refluxate. Moreover, it is able to determine whether the refluxate is a liquid, gas or mixture (both liquid and gas) [9, 10].

Esophageal manometry is the gold standard method, and several reports have described its utility in assessing esophageal motility [11]. Fluoroscopy and scintigraphy are used as alternative tools, although the applicability of these tools is limited in children because of the exposure to radiation. Recent studies have revealed that MII-pH is useful for the evaluation of esophageal function because it can detect the direct bolus transport in the esophagus [9, 12].

Although there are some reports on the role of MII-pH measurement in mainly adult patients who have undergone ARS [13, 14], there are only limited data available from studies of NI patients [15]. There is no study comparing the efficacy of ARS and change in esophageal motility before and after ARS in the same NI patients using MII-pH measurement. Evaluation of the ARS effect and the esophageal function affected by ARS could be useful for understanding the pathophysiological mechanisms of GERD in NI patients. In this study, we evaluated the impact of ARS using MII-pH and compared esophageal motility before and after ARS.

Patients and methods

The study included seven NI patients (six males and one female) aged 0–33 years (median, 13 years). In this study, the patients were measured using 24 h MII-pH before and after ARS (five patients underwent laparoscopic Nissen fundoplication, one patient received open Nissen fundoplication and the remaining patient received laparoscopic Toupet fundoplication) with gastrostomy. Before the operation, one patient was being fed orally, three were fed via a nasogastric tube, one via a gastrostomy and two were fed via a nasojejunal tube.

An MII-pH catheter (outer diameter, 2 mm) with two pH antimony electrodes and six pairs of impedance electrodes (Sandhill Scientific Inc., Highlands Ranch, CO, USA) was used. We chose the length of catheter (ZPN-BG-07 or CZPN-BG-57) depending on patient height. The catheter was inserted transnasally through the esophagus, and pH sensor placement was confirmed by radiography. Impedance data were automatically evaluated using the BioVIEW analysis software program, and each tracing was manually reviewed by the same author. All medications for GERD were discontinued at least 7 days before the subjects entered the study. The median duration from ARS to postoperative MII-pH measurement was 24 days (range, 13–34 days).

Liquid reflux was defined by MII-pH as a fall in impedance $\geq$50 % from baseline occurring in at least two consecutive channels in one reflux direction. Each type of reflux was defined as follows: acidic reflux was diagnosed in case of associated pH dropping to $\leq$4 with liquid reflux, and non-acidic reflux was diagnosed in cases associated with a pH >4 with liquid reflux. The pH reflux index was defined as the proportion of time with a pH $\leq$4. We defined 4.2 % as the upper cut-off value. The bolus exposure index was defined as the proportion of time with retrograde movement of intraluminal esophageal material, with 1.4 % set as the upper cut-off value. Mean acid clearance time was defined as the time in seconds required for the pH to go back to 4.5 after an episode of acidic reflux. Median bolus clearance time was defined as the median time in seconds required for the impedance to go back to the initial threshold value after an episode of bolus reflux. Mean acid clearance and median bolus clearance times were calculated in each patient using the Bioview Analysis software program.

Esophageal motility was manually assessed using the following specific parameters: (1) bolus presence time (BPT), which is the time elapsed between bolus entry and exit at each impedance-measuring site, (2) total bolus transit time (TBTT), which is the time elapsed between bolus entry at the most proximal recording segment and bolus exit at the most distal recording segment, and (3) total propagation velocity (TPV), which is the speed with which the bolus crosses all of the impedance channels. Dry swallows, leading to a decrease in impedance to 50 % of the baseline value in all recording channels with downward direction, were performed to evaluate the intraluminal liquid transfer indicating esophageal motility. A complete dry swallow was defined as one for which BPT at all sites (BPT Z1-Z6) and 1 value of TBTT and TPV. Ten dry swallows randomly selected in the whole record of MII-pH in each patient were measured, and average BPTs, TBTT, and TPV were calculated before and after ARS.

The study protocol was approved by the Kagawa University Graduate School of Medicine Ethics Review Board (No. H26-137). All the patients were examined after informed consent was obtained from their parent or guardian to participate in the study.

All statistical analyses were performed with the Wilcoxon test. Probability (P) values <0.05 were considered statistically significant.

Results

Pre- and postoperative MII-pH reflux parameters are shown in Table 1. All the patients showed a significant decrease in pH reflux index. Acid clearance times also decreased significantly after ARS (Fig. 1). In the analyses of MII, the bolus exposure index had significantly decreased after ARS, whereas bolus clearance time did not change significantly (Fig. 2). In the analyses of both MII and pH, the number of acidic reflux episodes exceeded that of nonacidic reflux episodes before ARS. After ARS, the number of acidic reflux episodes significantly decreased and nonacidic episodes tended to decrease (Fig. 3).

The details of the changes in motility parameters are shown in Table 2. BPT at all sites, TBTT, and TPV did not change after ARS (Fig. 4).

Table 1 MII-pH reflux parameters pre- and post-surgery

Parameters	Pre	Post	P value
pH reflux index (%)	17.84	0.09	0.0156
Acid clearance time (s)	681.71	12.00	0.0156
Bolus exposure index (%)	10.90	0.19	0.0156
Bolus clearance time (s)	20.14	14.00	0.1563
Number of acidic reflux episodes	83.14	0	0.0156
Number of nonacidic reflux episodes	30.86	5.14	0.0625

MII multichannel intraluminal impedance

Discussion

NI patients account for the great majority of patients with GERD requiring ARS in the pediatric surgical field, but no studies are available evaluating GER in NI patients both before and after ARS using MII-pH monitoring. In this study, we set out to evaluate the effectiveness of ARS and esophageal motility before and after ARS. In our study, reflux parameters significantly improved and esophageal motility parameters did not changed after ARS. The goal of ARS is to control reflux with least impairment of the function of the esophagus and stomach. Our study showed that ARS is effective for GERD and does not impair esophageal motility in NI patients, based on MII-pH results.

The present study showed that the reflux parameters improved following ARS. All the patients clinically experienced relief from GERD symptoms, although one patient developed a wrap herniation 6 months after ARS. Recent reports suggest that the effect of ARS is doubtful because of significant complications and the high GER recurrence rate [12, 16, 17]. However, O'Loughlin et al. [5] reported that fundoplication in NI patients indicated high levels of caregiver satisfaction with the results of the surgical intervention. Moreover, Mauritz et al. [4] showed in their systematic review that the success rate of ARS in NI patients may not be inferior to that of normally developed children. Additionally, advances in minimum surgical procedures include the use of ARS, which is characterized by reduced complication rates, less postoperative pain, shortening of the recovery period and easier home management [18, 19]. Consequently, ARS is a reasonable procedure for NI patients for controlling reflux-associated morbidity and mortality.

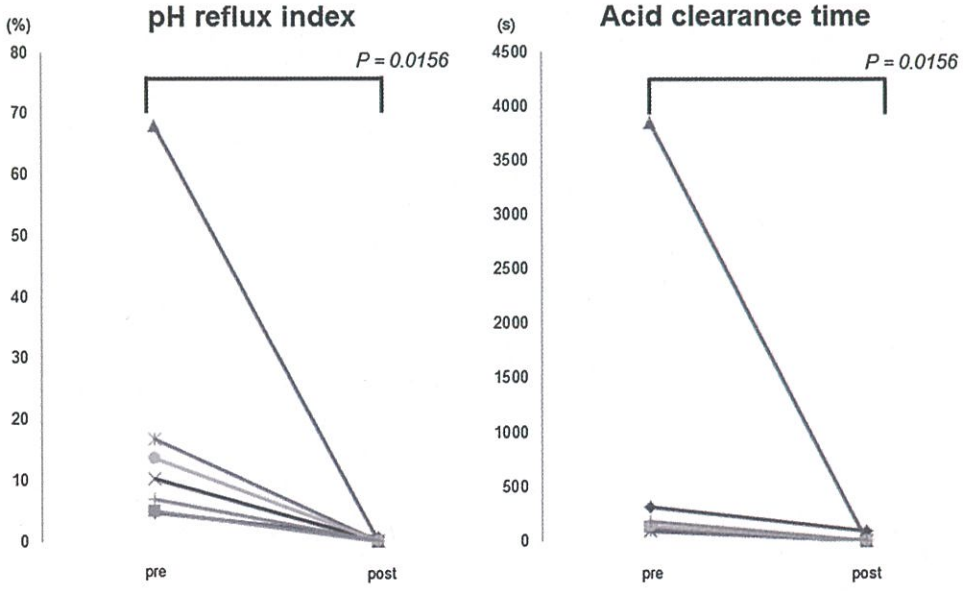

Fig. 1 Pre- and postoperative pH analyses. Reflux index (%) and mean acid clearance time (s) are shown

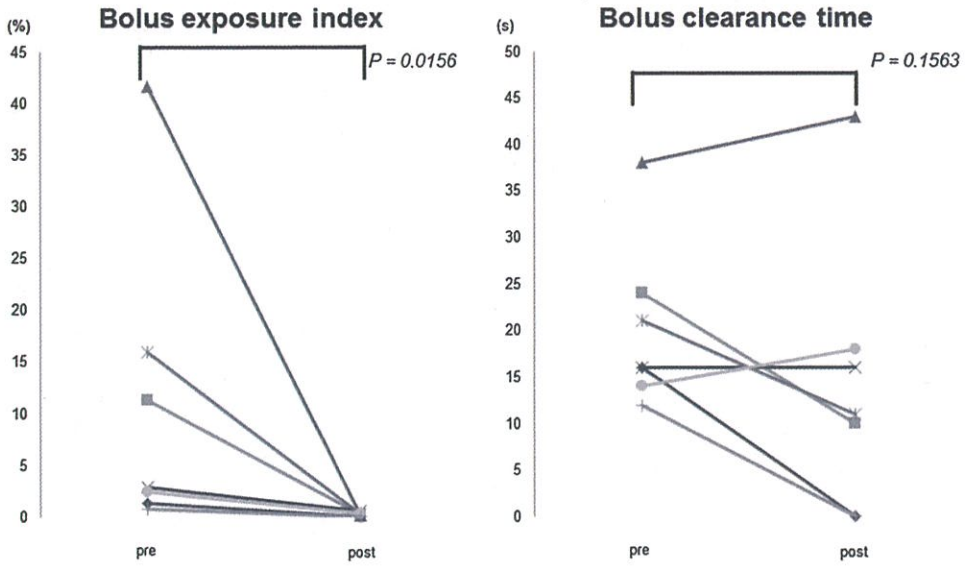

Fig. 2 Pre- and postoperative impedance analyses. Bolus exposure index (%) and median bolus clearing time (s) are shown

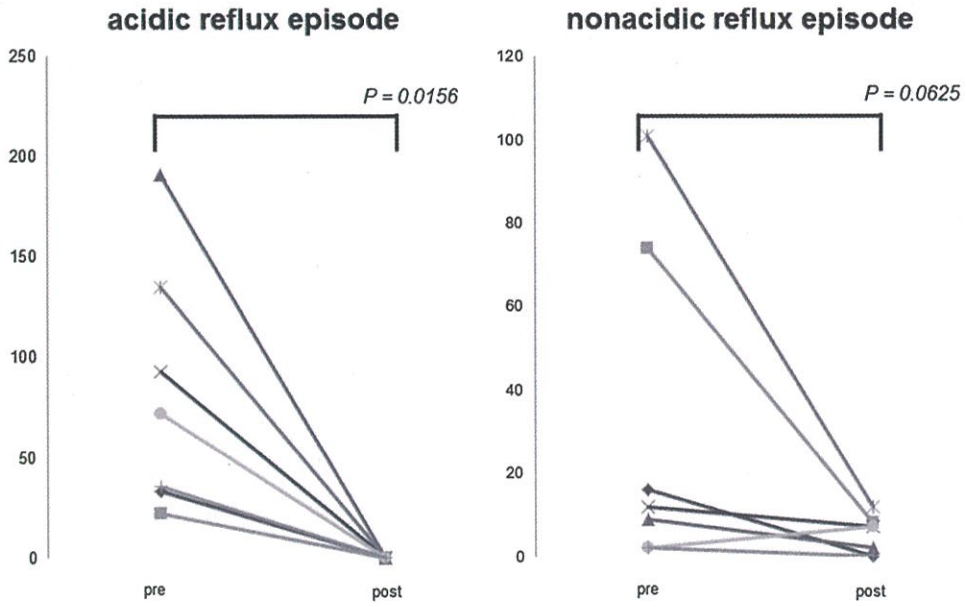

Fig. 3 Pre- and postoperative combined impedance and pH analyses. The number of acidic reflux episodes and nonacidic reflux episodes are indicated

Table 2 Impedance motility parameters for dry swallows pre- and post-surgery

Parameters	Pre	Post	*P* value
Bolus presence time (s)			
Z1	1.17	1.00	0.3750
Z2	1.36	1.14	0.2813
Z3	1.39	1.56	0.8125
Z4	1.84	1.63	0.0625
Z5	1.94	1.71	0.4688
Z6	2.04	1.91	0.6719
Total bolus transit time (s)	4.83	4.56	0.4531
Total propagation velocity (cm/s)	2.13	2.22	0.5781

In this study, the median duration of ARS to postoperative measurement was 24 days, and therefore, only short-term follow-up was assessed; evaluating the results of mid- and long-term follow-up would also have been relevant.

In the assessment of esophageal motility, MII-pH measurement allows bolus transport throughout the entire esophagus by its passing downward between multiple pairs of electrodes. MII-pH has been shown to accurately determine the timing of esophageal lumen filling and emptying compared with fluoroscopy studies [20]. In adults, the combination of MII-pH and intraluminal manometry has become widely used and has been useful to study the pathophysiology of motility disorders. The

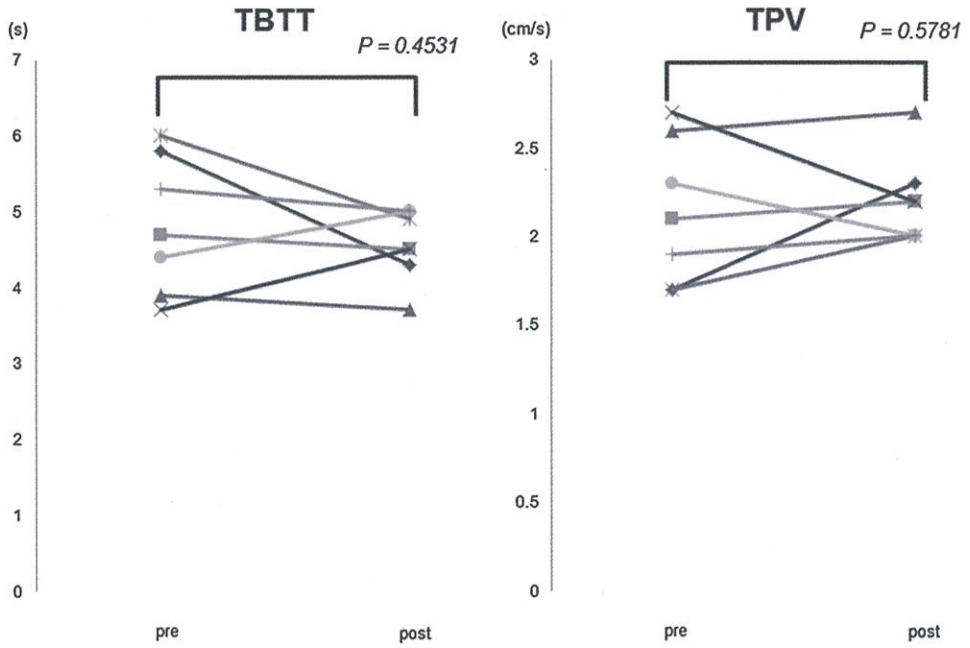

Fig. 4 Pre- and postoperative evaluation of intraluminal liquid transfer. Total bolus transit time (s) and total propagation velocity (cm/s) are shown

evaluation of esophageal motility using only MII is successfully supported by comparative studies with manometry and fluoroscopy [9, 12]. Normal values of MII-pH for children or NI patients have not been established, so larger studies would be required to further elucidate the pathophysiological mechanisms for these populations. We used the randomly selected 10 dry swallows indicating intraluminal liquid transfer as the parameter for esophageal motility. Although dry swallows have been reported to be inferior to liquid or viscous swallows in esophageal manometry studies [11, 21], NI patients usually have difficulty with intentional swallowing and a high risk of aspiration during the test. Hence, alternative methods have been required for such patients. In dry swallows, even if the esophageal contraction is smaller than in wet swallows [21], there would be an impedance-decreasing phenomenon indicating bolus transit throughout the esophagus downward. We speculated that dry swallow indicating intraluminal liquid transfer would reflect esophageal motility. Hence, it is expected that MII-pH could provide information on bolus transport directly throughout the entire esophagus in real time without radiation.

Some authors assume that total fundoplication exposes the patient to delayed transit of the swallowed bolus and thus to an increased risk of dysphagia [22, 23]. Del Genio et al. [13] reported that the postoperative MII-pH showed an increased lower esophageal sphincter pressure, whereas complete esophageal bolus transit and bolus transit time did not change for liquid swallows. Our study showed that BPT, TBTT, and TPV did not change after surgery; that is, esophageal motility was not impaired by ARS. Few comparative studies have performed standardised esophageal function tests before and after ARS, and the number of patients included in these studies was very small [4]. Esophageal function tests evaluating ARS should be standardised because these tests may provide us with the opportunity to identify prognostic factors for the effect of ARS on GER. To prevent postoperative side effects, such as dysphagia and the inability to belch or vomit, we should consider how much wrapping is best. There are several types of ARS: complete versus partial ARS, long wrapping versus short wrapping and tight wrapping versus loose wrapping. Some reports showed a higher rate of postoperative dysphagia in patients with complete fundoplication than that in patients with partial fundoplication [4]. In our study, one patient was treated using the laparoscopic Toupet procedure, whereas the other patients received laparoscopic or open Nissen operation, and it is difficult to identify the better type of ARS because of the small number of subjects included here. The various types of ARS could not be compared in the present study; therefore, we need more investigations to obtain more detailed knowledge. Adequate ARS procedures would lead to a good control of GERD with the least possible impairment of esophageal function.

In conclusion, ARS results in satisfactory control of GER without impairment of esophageal function as evaluated by MII-pH measurements in NI patients. The MII-pH was useful not only to detect the subtype of GER and the effect after ARS but also to evaluate esophageal motility in NI patients.

Compliance with ethical standards

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

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